PHD DAY
HEALTH

ABSTRACTS

19 JANUARY 2024

AARHUS
UNIVERSITY

PHD DAY 2024 PROGRAMME

19 JANUARY 2024, THE PER KIRKEBY AUDITORIUM, THE LAKESIDE LECTURE THEATRES

8.15 **Welcome by Organizing Committee Chair and by the Chair of the PhD Association (in Per Kirkeby)**
Anders Etzerodt, Associate professor, Department of Biomedicine, Aarhus University
Sofie Abildgaard Jacobsen, PhD student, Chair of the PhD Association at Health, Aarhus University

8.25 **Keynote lecture by Unnur Þorsteinsdóttir, Vice President of Research at deCODE genetics and Dean of the School of Health Sciences at the University of Iceland (in Per Kirkeby)**
Introduced by Anders Etzerodt, Associate professor, Department of Biomedicine, Aarhus University

9.10 **Short break with coffee/tea and fruit**

9.25 **Fogh Nielsen Prize Competition** (60 min)
Per Kirkeby, The Lakeside Lecture Theatres

10.35 **First round of sessions**
The Lakeside Lecture Theatres, Anatomy (build. 1231), Public Medicine Auditorium (build. 1262/101), building 1264 (209 and 310) and Bartholin (build. 1241)

11.55 **Break with lunch and networking**

12.40 **Keynote lecture by Jonas Egebart, Director General of the Danish Health Authority (in Per Kirkeby)**
Introduced by Anders Etzerodt, Associate professor, Department of Biomedicine, Aarhus University

13.35 **Second round of sessions**
The Lakeside Lecture Theatres, Anatomy (build. 1231), Public Medicine Auditorium (build. 1262/101), building 1264 (209 and 310) and Bartholin (build. 1241)

14.55 **Coffee, cake and see you later**
The programme for the day ends on different locations

18.30 **Dinner and award ceremonies**

Turbinehallen, Aarhus C

Festive speech: TB

Practical information

- There will be a name tag for you if you are signed up for a presentation or as chair/co-chair. You can collect this at the reception on the lowest level in the Lakeside Lecture Theatres.
- Lunch is served at two locations: the Lakeside Lecture Theatres and in building 1231 on the ground floor.
- A photographer from Aarhus University will be present at the event. Photos taken at the event will only be used in Aarhus University contexts, for example as publicity for/in the invitation to a similar event. If you do not wish to be photographed, please contact the photographer.

The Organizing Committee, PhD Day 2024

- Anders Etzerodt, Associate professor, Department of Biomedicine, Chair PhD Day 2024
- Akila Aiyar, PhD student, Department of Dentistry and Oral Health, Co-chair PhD Day 2024

- Alisha Silvia Mercedes Hall, PhD Student, Department of Clinical Medicine
- Anika Kofod Petersen, PhD Student, Department of Forensic Medicine
- Fernando Valentim Bitencourt, PhD Student, Department of Dentistry and Oral Health
- Helene Hallas, PhD administrator, Graduate School of Health
- Henning Grønbæk, Clinical professor, Department of Clinical Medicine
- Jasper Carlsen, PhD student, Department of Clinical Medicine
- Jemila Peter Gomes, PhD Student, Department of Forensic Medicine
- Johan Palmfeldt, Associate Professor, Department of Clinical Medicine
- Merete Bjerrum, Associate professor, Department of Public Health
- Mojdeh Mansoori, PhD Student, Department of Dentistry and Oral Health
- Reimar W. Thomsen, Professor, Department of Clinical Medicine
- Rikke Horsted Bundgaard, PhD administrator, Graduate School of Health
- Rubens Spin-Neto, Associate professor, Department of Dentistry and Oral Health
- Salma Karim, PhD student, Department of Clinical Medicine

Social Media: Facebook: PhD Association Health

Session Overview

10.35-11.55 – First round of sessions

PhD Workshop	Lakeside Lecture Theatre, **Eduard Biermann Auditorium**
Session 1:	Lakeside Lecture Theatre, **Per Kirkeby Auditorium**
Session 2:	Lakeside Lecture Theatre, **Merete Barker Auditorium**
Session 3:	Lakeside Lecture Theatre, **Jeppe Vontilius Auditorium**
Session 4:	Lakeside Lecture Theatre, **William Scharf Auditorium**
Session 5:	Anatomy (Building 1231), 2nd floor, **Room 214**
Session 6:	Anatomy (Building 1231), 2nd floor, **Room 216**
Session 7:	Anatomy (Building 1231), 2nd floor, **Room 220**
Session 8:	Anatomy (Building 1231), 2nd floor, **Room 224**
Session 9:	Anatomy (Building 1231), 2nd floor, **Room 228**
Session 10:	Anatomy (Building 1231), 2nd floor, **Room 232**
Session 11:	Anatomy (Building 1231), 4th floor, **Small Anatomy Auditorium**
Session 12:	Building 1262, 1st floor, **Room 101 – Public Medicine Auditorium**
Session 13:	Building 1264, 2nd floor, **Room 209**
Session 14:	Building 1264, 3rd floor, **Room 310**
Session 15:	Bartholin (Building 1241), 1st floor, **Room 114 – Auditorium 4**
Session 16:	Bartholin (Building 1241), 1st floor, **Room 119 – Auditorium 3**
Session 17:	Bartholin (Building 1241), 1st floor, **Room 125 – Auditorium 2**
Session 18:	Bartholin (Building 1241), 1st floor, **Room 135 – Auditorium 1**

13.35-14.55 – Second round of sessions

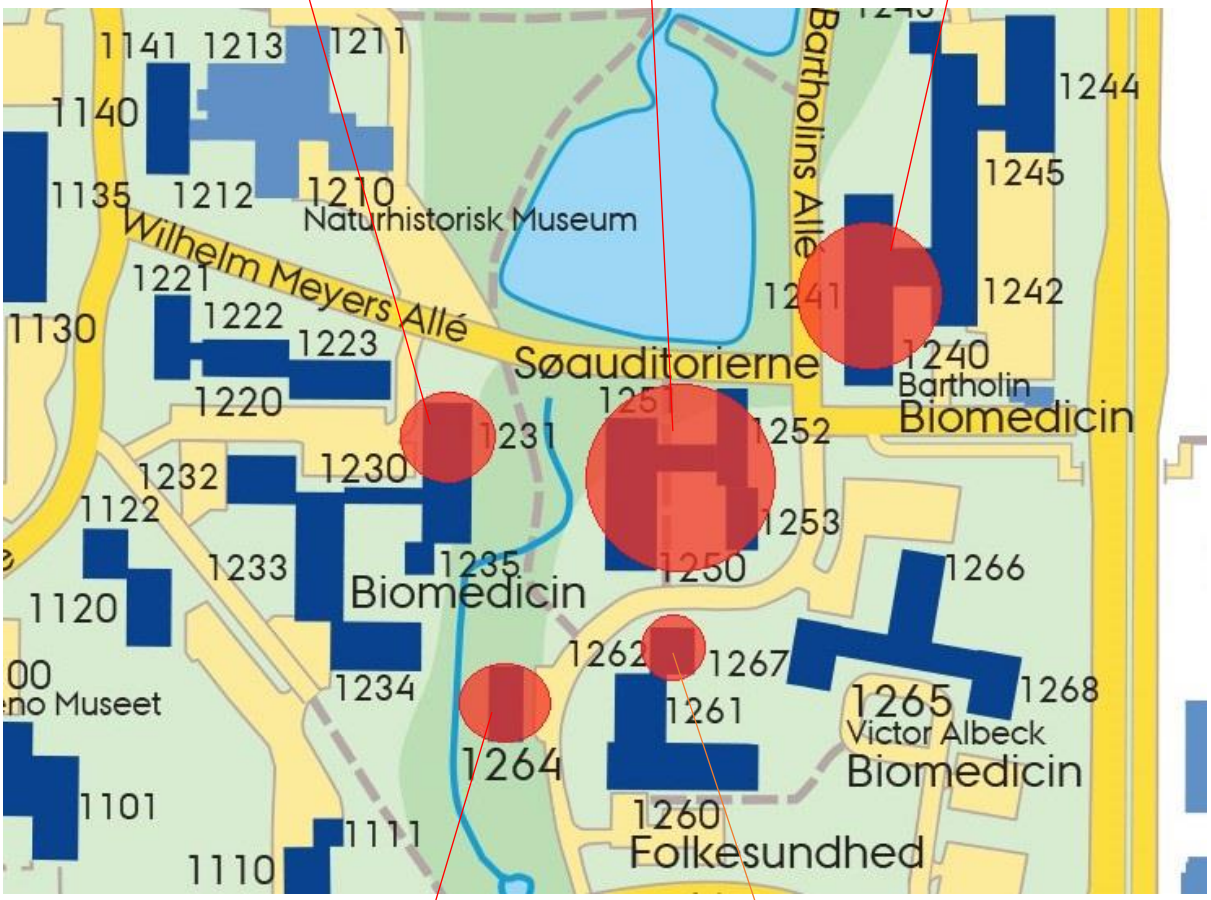
Session 19:	Lakeside Lecture Theatre, **Eduard Biermann Auditorium**
Session 20:	Lakeside Lecture Theatre, **Per Kirkeby Auditorium**
Session 21:	Lakeside Lecture Theatre, **Merete Barker Auditorium**
Session 22:	Lakeside Lecture Theatre, **Jeppe Vontilius Auditorium**
Session 23:	Lakeside Lecture Theatre, **William Scharf Auditorium**
Session 24:	Anatomy (Building 1231), 2nd floor, **Room 214**
Session 25:	Anatomy (Building 1231), 2nd floor, **Room 216**
Session 26:	Anatomy (Building 1231), 2nd floor, **Room 220**
Session 27:	Anatomy (Building 1231), 2nd floor, **Room 224**
Session 28:	Anatomy (Building 1231), 2nd floor, **Room 228**
Session 29:	Anatomy (Building 1231), 2nd floor, **Room 232**
Session 30:	Anatomy (Building 1231), 4th floor, **Small Anatomy Auditorium**
Session 31:	Building 1262, 1st floor, **Room 101 – Public Medicine Auditorium**
Session 32:	Building 1264, 2nd floor, **Room 209**
Session 33:	Building 1264, 3rd floor, **Room 310**
Session 34:	Bartholin (Building 1241), 1st floor, **Room 114 – Auditorium 4**
Session 35:	Bartholin (Building 1241), 1st floor, **Room 119 – Auditorium 3**
Session 36:	Bartholin (Building 1241), 1st floor, **Room 125 – Auditorium 2**
Session 37:	Bartholin (Building 1241), 1st floor, **Room 135 – Auditorium 1**

BUILDING LOCATIONS

Anatomy (1231)
Session 5-11 and 24-30

Lakeside Lecture Theatres
PhD Workshop
Session 1-4 and 19-23

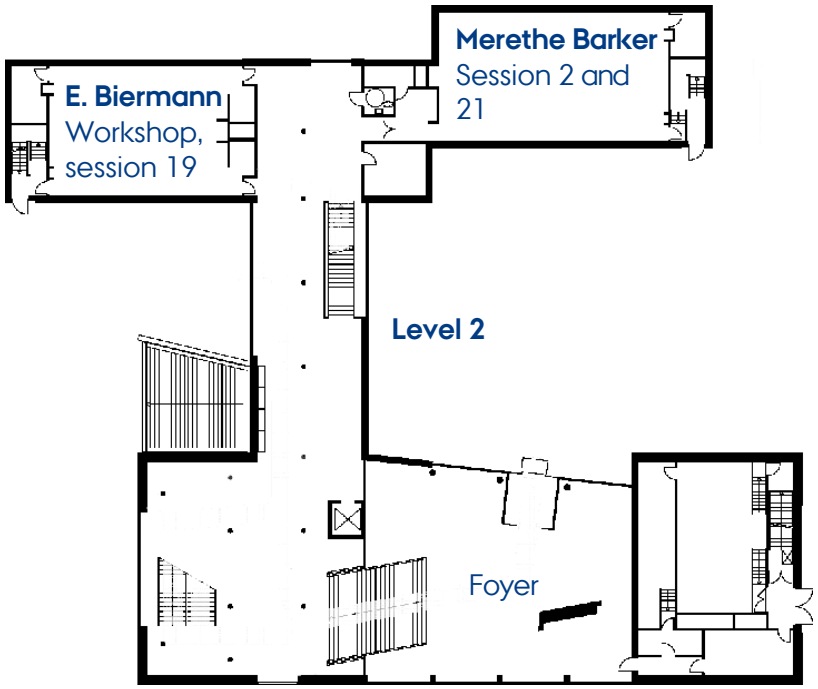
Bartholin (1241)
Sessions 15-18 and 34-37

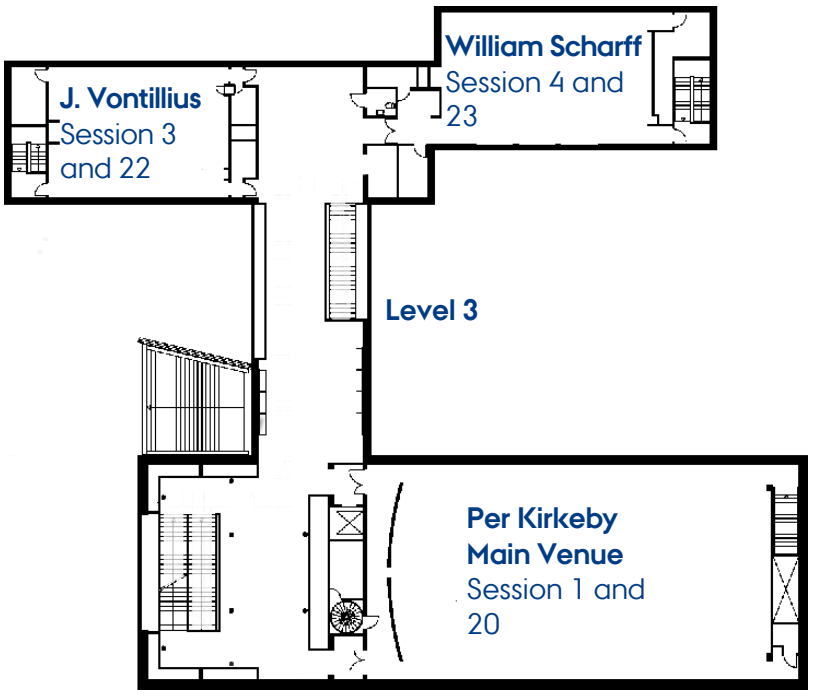


Building 1264
Sessions 13-14 and 32-33

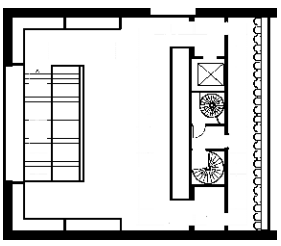
Public Medicine Auditorium (1262)
Session 12 and 31

Lakeside Lecture Theatres





Level 4



Anatomy Building (1231, 2nd and 4th floor)
- Session 5-11 and 24-30

Public Medicine Auditorium (1262, 1st floor)
- Session 12 and 31

Building 1264 (2nd and 3rd floor)
- Session 13-14 and 32-33

Bartholin (1241, 1st floor)
- Session 15-18 and 34-37

Hey, you!

Do you want to help improve the PhD education at AU Health?

Then join the PhD Association!

Follow us on Facebook (PhD Association Health) to be informed about our events!!

All are welcome!

PhD Association
Health, Aarhus University
- Who are we?

The PhD association for all PhD students at the Faculty of Health, Aarhus university

Organisation

GENERAL ASSEMBLY
(open to all PhD students at Health)

19 BOARD MEMBERS
(and an unlimited number of active members)

- GRADUATE PROGRAM FORUM
- PHD COMMITTEE
- THE ACADEMIC COUNCIL
- PHD COURSE EVALUATION
- THE ORGANIZING COMMITTEE OF THE PHD DAY
- AFTER-WORK MEETINGS TOGETHER WITH THE PHD HOUSE
- AARHUS UNIVERSITY PHD ASSOCIATION (AUPA)

We aim to create better education and better conditions for PhD students at the Graduate School of Health

Join us on Facebook at: **PhD Association Health**
or check out our webpage: **phdassociation.dk**

ALL PHD STUDENTS CAN JOIN!

NorDoc
NORDIC DOCTORAL TRAINING IN HEALTH SCIENCES

is going to launch its

7th Nordic PhD Summer School

At Helsinki University, 18-20 August 2024

More information **very soon** at https://www.nordochealth.net/

Attend PhD courses in the NorDoc network for free

PhD courses at the 21 NorDoc partner institutions are **free of charge** for all PhD students at Health. The graduate school offers **financial support to cover your travel and accommodation costs.**

PhD student counselling

You can reach out to the counsellor if you experience:

- A problem related to your PhD study that remains unsolved after discussions with your supervisor and/or the PhD partner at the Graduate School of Health.
- A problem related to your PhD study where you want to reach out for a discussion with a "third party".

If help is needed

Both PhD students and supervisors experiencing problems related to the PhD study can

Seek advice

by the PhD counselor Ebba Nexø

e-mail: enexo@clin.au.dk

The service covers PhD students who experience unsolved problems related to their PhD studies and supervisors who wish to discuss a dilemma or a specific case regarding their supervision.

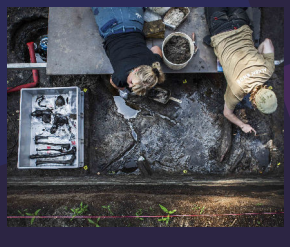
All discussions are confidential, and you are guaranteed anonymity.

For details consult the homepage:
https://phd.health.au.dk/aboutus/phdstudentcounselling

AU Career PhD & JR

Career services for PhDs and Junior Researchers






Would you like to get ahead and engage in career development during you PhD or postdoc?

Do you know which career path to choose when finishing your PhD or postdoc?

Do you know which specific competences companies value when hiring researchers?

Are you aware of your many opportunities?

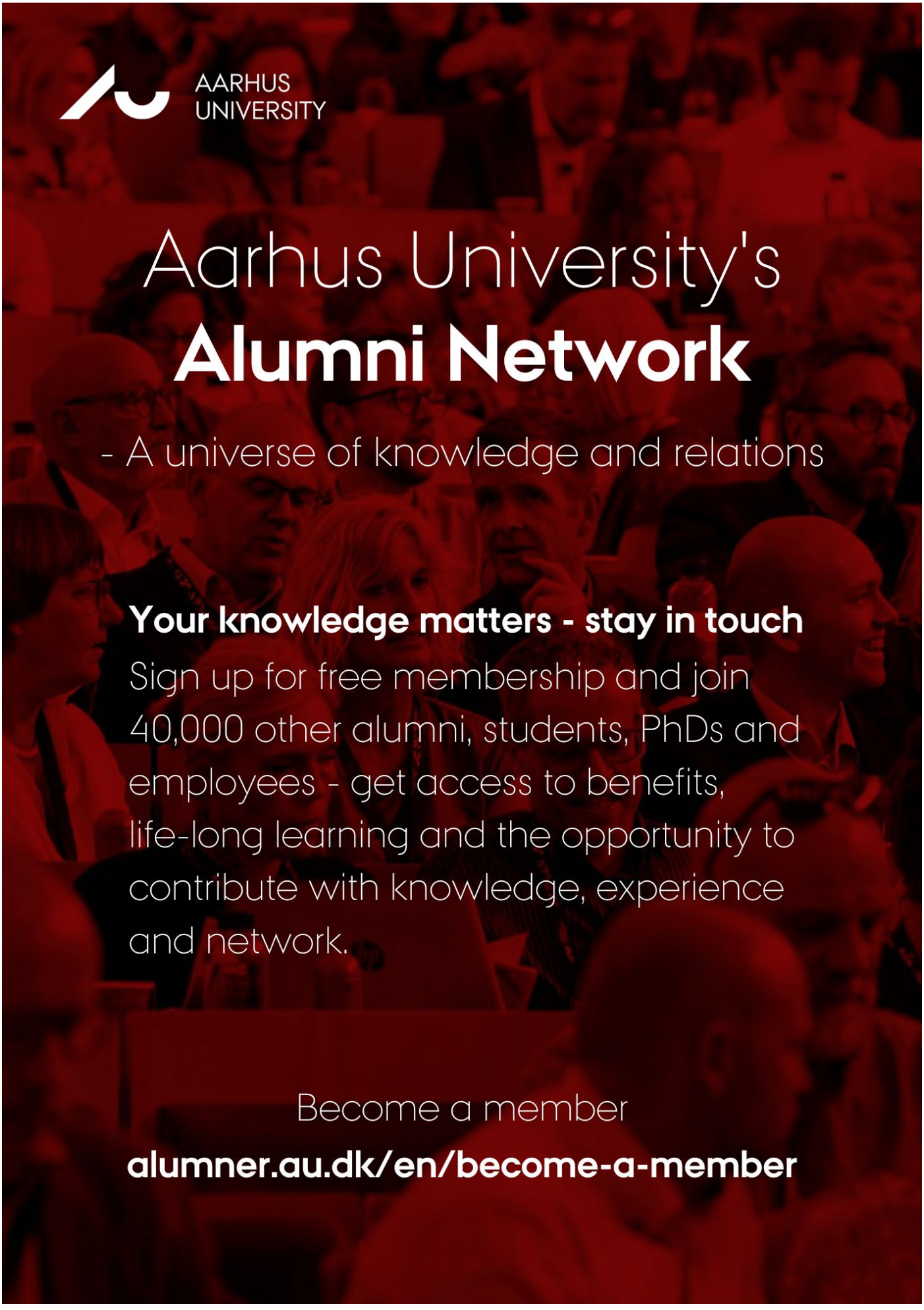
Our services

- Career events
- Interaction with industry
- Individual career counselling
- Support in your career development
- Assessing your competencies and strengths
- Feedback on CVs and cover letters
- Mentor programme

Vibeke Broe
Ph.D. Career Consultant
Phone: +45 2942 6029
Email: vibr@au.dk

Miriam Kobbersmed
Ph.D. Career Consultant
Phone: +45 93522564
Email: mkob@au.dk

AU CAREER PHD & JR


AARHUS
UNIVERSITY
Aarhus University's
Alumni Network
- A universe of knowledge and relations
Your knowledge matters - stay in touch
Sign up for free membership and join 40,000 other alumni, students, PhDs and employees - get access to benefits, life-long learning and the opportunity to contribute with knowledge, experience and network.
Become a member
alumner.au.dk/en/become-a-member

May 2022

AU **LIBRARY**
HEALTH SCIENCES

- Systematic literature search designed for your specific project
- Tips and tricks for PubMed, Embase, UpToDate, Cinahl and other databases
- Citation searches in Scopus and Web of Science
- EndNote – courses and support
- ORCID, Journal impact factor, h-index, and Pure
- Copyright and Open Access
- Courses in PubMed, EndNote etc.

Come by the library, phone or email us and we will help you.

AU Library, Health Sciences
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DK-8000 Aarhus C
Tel. +45 2265 0073
sundhedsvidenskab.aul@kb.dk

Opening Hours
Monday – Thursday 9 a.m. - 5 p.m.
Friday 9 a.m. - 3 p.m.

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Commercialisation and IP

Excellent research can result in inventions which can benefit both you and society and the Commercialisation and IP unit, can help your invention reach society.

How can we assist you?

Support Innovation

Does your invention have what it takes to improve and wow the world? Our unit and external patent lawyers are ready to evaluate your technology as a candidate for innovation funding such as the Innoexplorer Grant.

Connect with the industry

Sometimes university-based research is the missing piece that Ithe market is looking for. Let our Business Developers help you make sense of the Industry and see if your invention have a perfect match with a larger Corporation.

Our unit supports all 5 faculties + Central Denmark Region.

Mail: patent@au.dk

Web: www.au.dk/techtrans

AARHUS UNIVERSITY

CONNECT

REGION MIDTJYLLANDS DATASTØTTECENTER

10 TIMERS GRATIS RÅDGIVNING TIL DIN FORSKNING

HVAD?

RÅDGIVNING OM BRUG AF SUNDHEDSDATA I FORSKNING

HVEM?

FOR FORSKERE OG KLINIKERE PÅ AU OG I REGION MIDTJYLLAND

HVORDAN?

SE MERE PÅ: WWW.CONNECT.AUH.DK

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AUH

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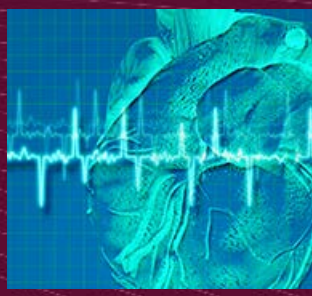
HEALTH

THE CARDIOVASCULAR NETWORK



NETWORK STRATEGY

Cardiovascular research at AU and the hospitals in Region Midt contributes to **patient** welfare and health

Interdisciplinary cardiovascular research to address societal changes

Cardiovascular research and degree programmes of the highest **international** quality

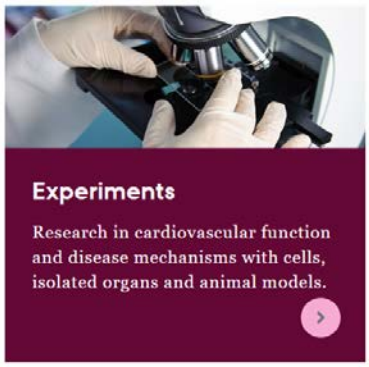
Development of talents within cardiovascular research

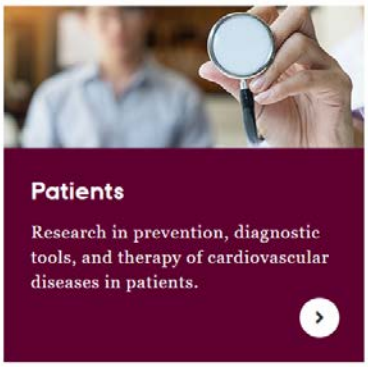
WHAT DO WE OFFER?

- Annual meetings
- Summer schools
- Seminars & workshops
- Networking
- Interdisciplinary collaboration
- Project bank
- PhD courses

Join our network

Visit our website





CONTACT

Anja P. Einholm
Network Coordinator
Phone: +4593508408
E-mail: ape@au.dk

www. health.au.dk/en/the-cardiovascular-network

AARHUS UNIVERSITY HEALTH

THE FOOD AND NUTRITION NETWORK

Join the Food and Nutrition Network at AU Health

Food and Nutrition is relevant for both clinical outcome and research in health and disease. As this field of research often requires a multidisciplinary approach as well as expertise (methodological and/or clinical), the network offers a unique opportunity to collaborate and develop new skills. The network stimulates and connects teaching activities within food and nutrition at a pre- and post-graduate level.

A wide array of technologies and research methodologies are available through the network ranging from experiment clinical-, epidemiological-, biomedical- to qualitative approaches. Method development and increased accessibility to existing research methodologies are important scopes of the network.

Among the pertinent research questions that are addressed by the network are:

- What are health consequences of the green transition?
- What are the potential health benefits from novel food products and food processing technologies?
- How do we prevent obesity and associated negative impact on well-being?
- How do we prevent malnutrition, sarcopenia, and cachexia among vulnerable subjects?
- What is the physiology behind consumption and ingestion of food and nutrition?
- How does disabilities and disease conditions impair normal consumption and ingestion of food?

The network serves as a platform for larger research projects initiated from within the network or through external invitations. This involves communicating with funding institutions, connecting researchers, and stimulating food and nutrition research among peers at AU Health.
The network also serves as a forum for coordination of established network activities in food and nutrition research outside AU Health.

Join the Food and Nutrition Network if you are interested in the activities within the network, wish to broaden your horizon within food and nutrition, or are interested in collaborations! The network is relevant and open for scientists at all levels.

To join the network, please visit https://health.au.dk/en/the-food-and-nutrition-network

AARHUS UNIVERSITY HEALTH

THE INFLAMMATION NETWORK

Join the Inflammation Network

Inflammatory and infectious diseases continue to be significant global health challenges. As a society, our quest for understanding the interplay between inflammation and the development of autoimmunity and cancer, uncovering biomarkers, and deciphering the molecular mechanisms of infectious and inflammatory diseases remains paramount. The Inflammation Network is where multidisciplinary collaboration leads to the formulation of the right questions and the discovery of answers.

Scan this to join via our website

Our network comprises an extensive group of researchers, each with a keen interest in various aspects, including immune-mediated diseases, diagnostic methodologies, epidemiological insights, inflammatory markers, intracellular immune pathways, human genetics, and a deep comprehension of cell populations and tissue structures. Our steering committee also includes **two dedicated PhD student representatives:** Fernando Valentim Bitencourt and Lotte Lindgreen Eriksen.

What´s in it for early career researchers?

The Inflammation Network opens doors for early career researchers, providing an invaluable opportunity to expand your research network. These connections can pave the way for enduring professional relationships that may prove instrumental in shaping the trajectory of your future research endeavors. Researchers at all stages of their careers, including those who are still pursuing education, play an integral role within the Inflammation Network. **PhD student** Morten Kelder Skouboe, a member of the research group at the Department of Biomedicine, shares his perspective:

"I've signed up to get a better idea of what's going on in other areas, and perhaps to get a clearer understanding of how my research skills can be used in other research groups working on things that I find really exciting".

Save the date and sign up!

Mark your calendar for **our 4th Inflammation Network Day**, scheduled for **March 6th**. A day filled with insightful talks that bridge the realms of basic and clinical research in inflammation, infection, and autoimmunity. Our program features excellent keynote speakers who will delve into topics such as infection immunology, the microbiome, tumor immunology, and autoimmunity. You can also expect numerous talks from junior researchers!

Scan this to read more and register for 4th Inflammation Network Day

Our focus the next couple of years

- Continuous promotion and bridging of basal and clinical research within diseases related to inflammation, infection, and immunopathology
- Internationalisation, including Circle U. initiatives
- Engagement of younger researchers in the network, including the steering committee
- Establishment of focus groups related to specific topics, methodologies, and diseases

Network vision

Strengthen Aarhus University's position

Bridge university-based research departments, faculties & clinical medicine

Improve recruitment and visibility

Increase funding opportunities

HOW TO JOIN? https://health.au.dk/en/the-inflammation-network/join-the-inflammation-network

THE PERSONALISED MEDICINE NETWORK

WHO ARE WE?

Members include junior and senior researchers and clinicians across many fields, including genetics, epidemiology, molecular biology, bioinformatics, pharmacology, law and ethics, and more!

READ MORE
& SIGN UP HERE

SCAN ME

WHAT CAN WE OFFER?

- Biennial international conferences with international and national experts
- Annual meetings
- Regular seminars
- Specialised focus group meetings
- Up-to-date news on upcoming events, PhD courses, and grant funding opportunities
- Collaboration with the National Academies: Danish Cardiovascular Academy, Danish Data Science Academy, Danish Diabetes & Endocrine Academy, and Neuroscience Academy Denmark

AARHUS UNIVERSITY
HEALTH

THE TRANSLATIONAL CANCER NETWORK

AARHUS UNIVERSITY HEALTH

AARHUS UNIVERSITY HOSPITAL

VISION & STRATEGY

- **Accelerating translation of scientific discoveries into tangible clinical applications**
- **Bring basic science into clinical practice and vice versa**
- **Involve the public and patients in our translational research through communication and outreach**
- **Encouraging an environment of open dialogue and mutual understanding**

THE NETWORK OFFERS:

- Interdisciplinary collaborations
- Seminars & workshops
- Annual meetings
- Summer schools
- PhD courses

SCAN TO JOIN THE NETWORK

linkedin.com/showcase/the-translational-cancer-network

Circle U. is an alliance of nine strong universities, working together to co-construct a new common European educational offer focusing on international collaboration within **global health**, **democracy**, and **climate**.

With **interdisciplinarity**, **innovation**, **sustainability** as key words, Circle U. offers a wide range of opportunities for students and employees of member universities.

Academics
- Connect with colleagues
- Join networks and forums
- Seed funding
- Mobility options
- Join training programmes

Students
- Study abroad
- Join a summer school
- Participate in Circle U. Challenges
- Join a network
- Get international experience

Administrative staff
- Connect with colleagues
- Join training programmes
- Mobility options
- Circle U. Days
- Seminars and events

Learn more at

www.circle-u.eu

Or contact AU Academic Chair for Global Health,
Professor Christian Wejse

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AARHUS UNIVERSITY · University of Belgrade · Humboldt-Universität zu Berlin · UCLouvain · King's College London

Co-funded by the Erasmus+ Programme of the European Union

Danish Diabetes and Endocrine Academy

Funded by the Novo Nordisk Foundation

Are you an early-career researcher within the research fields of **diabetes**, **metabolism** and/or **classical endocrinology**? Are you seeking funding for your research, excellent education activities or new collaborations? Then take a look at Danish Diabetes and Endocrine Academy's activities in 2024.

7 February	**Deadline for Interdisciplinary PhD Scholarships** *In collaboration with Danish Cardiovascular Academy and Danish Data Science Academy*
27-28 February *Aalborg, DK*	**Course on Scientific Communication: Presentation Skills for Scientists**
14-15 March *TBA, DK*	**Workshop on Navigating as a Researcher in the Era of Artificial Intelligence**
21-22 March *Aarhus, DK*	**PhD course on Nutrition and Dietary Strategies in Prevention and Management of Diabetes**
30 April-3 May *Odense, DK*	**PhD course on Metabolic Bone Disease**
May *Aalborg, DK*	**Intermediate Course on Reproducible Research in R**
May/June	**Call for DDEA PhD Scholarships & Postdoc Fellowships**
26-29 August *Ebberup, DK*	**DDEA PhD Summer School on Diabetes, Metabolism & Endocrinology**
21-24 October *Nyborg, DK*	**PhD course on Basic Cardiometabolic Research**
December *Odense, DK*	**Advanced Course on Reproducible Research in R**

We have many more symposia, networking events and workshops with renowned experts that we encourage PhD students to participate in.

Read more and sign up at www.ddeacademy.dk. We hope to see you!

PHD DAY 2024

Session overview and chairs

Session Chairs

Find yourself, abstract titles, and abstracts belonging to your session by searching the file (Ctrl+F)

Fogh-Nielsen Competition – 9.25 to 10.25

Chair: Ida Vogel

Co-chair: Anika Kofod Petersen

First Round of Sessions – 10.35 to 11.55

Senior chair – name	Session
Julie Schmidt	1
Joanna Kalucka	2
Mai-Britt Worm Ørntoft	3
Karin Birenkamp-Demtröder	4
Jesper Grau Eriksen	5
Christina Dahm	6
Vicki Taasti	7
Mette Nørgaard	8
Bodil Hammer Bech	9
Tina Carstensen	10
Xiaoli Hu	11
Lasse Stensvig Madsen	12
Annette De Thurah	13
Line Kibsgaard	14
Renee van Der Sluis	15
Mette Lise Lousdal	16
Christian Fynbo Christiansen	17
Mats Bue	18

Co-chairs – name	Session
Kasper Kjærgaard	1
Pernille Thordal Larsen	1
Maja Dam Andersen	2
Martin Qvist Rasmussen	2
Ivanka Sojat Tarp	3
Priyanshu Sinha	3
Rikke Kongsgaard Rasmussen	4

Simone Stensgaard	4
Folefac Charlemagne Asonganyi	5
Mikkel Breinholt Kjær	5
Nadia Gadgaard	6
Trine Thøgersen	6
Ludvig Renbo Olsen	7
Christian S. Antoniussen	8
Mette Østergaard Thunbo	8
Christine Cramer	9
Lise Qvirin Krogh	9
Lasse Hansen	10
Tanja Hansen	10
Elnaz Fazeli	11
Malthe Brændholt	12
Nina Lykkegaard Gehr	12
Camilla Tatari	13
Anne Dorte Helgestad	14
Kathrine Carstensen	14
Hakim Ben Abdallah	15
Kristian Antonsen	15
Iben Strøm Darfelt	16
Jane Lauridsen	16
Birgitte Bitsch Gadager	17
Helga Haahr-Lillevang	17
Line Mathilde Brostrup Hansen	18
Rasmus Reinke	18

Second Round of Sessions – 13.35 to 14.55

Senior chairs – name	**Session**
Morten Bøttcher	19
Vladimir Matchkov	20
Maria Louise Gamborg	21
Peter Bross	22
Tue Kragstrup	23
Rikke Nielsen	24
Francesco D'Amore	25
Niels Holm	26
Maja Ludvigsen	27
Marco Eijken	28
Ida Vogel	29

Palle Villesen	30
Cecilia Ramlau-Hansen	31
Poul Henning Jensen	32
Annesofie Jensen	33
Thomas Lindhardt	34
Jan Duedal Rölfing	35
Tábata Bergonci	36
Victor Pando-Naude	37

Co-chairs – name	**Session**
Anders Lehmann Dahl Pedersen	19
Emil Holck	19
Anne Catrine Daugaard Mikkelsen	20
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Fogh-Nielsen Competition – 9.25 to 10.25

1. Caroline Arnbjerg Juhl-Nielsen
2. Mathis Ersted Rasmussen
3. Pernille Gro Thrane

First Round of Sessions – 10.35 to 11.55

Session 1

Pitch

1. Anne Dahl Sørensen
2. Anne Vittrup Jakobsen
3. Jesper Winkler Andersen
4. Malene Andersen

Flash talk

5. Anja Gouliaev Kirkeby
6. Mia Aagaard Doherty
7. Morten Daniel Jensen
8. Sebastian Søby

Oral presentation

9. Ina Marie Dueholm Hjorth

Session 2

Pitch

1. Camilla Yde Hvelplund
2. Emma Frasez Sørensen
3. Karoline Kondrup Torstensson
4. Silke Dahlbom Nielsen

Flash talk

5. Henriette Mathiesen
6. Henriette Winther
7. Johannes Frasez Sørensen
8. Mie Wolff Kristensen

Oral presentation

9. Sofie Andersen

Session 3

Pitch

1. Jeppe Skovbjerg
2. Kristine Høgsbjerg
3. Malene Aastrup
4. Sara Linde

Flash talk

5. Anders W. M. Nielsen
6. Line Kristensen
7. Marjolein Heidotting
8. Uffe Kjærgaard

Oral presentation

9. Casper Dueholm Vestergaard

Session 4

Pitch

1. Aisha Shigna Nadukkandy
2. Christoph Felix Kollmann
3. Henriette Nymark Friis
4. Maria Hønholt Jørgensen
5. Sky Rohrer

Flash talk

6. Eske Glud
7. Jesper Medom Vestergaard
8. Mona Kristiansen
9. Villads Lundsteen Jacobsen

Oral presentation

10. Sofie Tilbæk

Session 5

Pitch

1. Grace McKinney
2. Kristoffer Moos
3. Laura Iisager
4. Sofie Meyer Andersen
5. Stine Vissing
6. Troels Lading

Flash talk

7. Anne Andresen
8. Fardous Reaz
9. Simon Nyberg Thomsen

Oral presentation

10. Mira Mekhael

Session 6

Pitch

1. Anne Hedegaard Arndt
2. Anne Hjorth Thomsen
3. Mathias M. Rønnow
4. Merete Ajstrup

Flash talk

5. Cecilie Schmidt Østergaard
6. Marie Hauge Pedersen
7. Mette Fogh
8. Sarah Cecilie Tscherning

Oral presentation

9. Martin Bernstorff

Session 7

Pitch

1. Jacob Drachmann
2. Maja Kanstrup Jørgensen
3. Sidsel Loft Nagel
4. Siria Pasini

Flash talk

5. Ana Teresa Queiroga
6. Emil Winkel
7. Shirin Haghshenas Bilehsavar
8. Trine Engelbrecht Hybel

Oral presentation

9. Layla Pohl

Session 8

Pitch

1. Anne Nannsen
2. Christina Bisgaard Jensen
3. Ditte Vestergaard Hansen
4. Helene Bei Thomsen
5. Livie Yumeng Li

Flash talk

6. André Sejr Klenø
7. Anne Bech-Drewes
8. Jonas Schaarup
9. Katrine Hoyer

Oral presentation

10. Fernando Valentim Bitencourt

Session 9

Pitch

1. Anne Marie Ladehoff Thomsen
2. Jette Steinbach
3. Josefine Jul Jarbæk Nielsen
4. Martin Mejlby Jensen

Flash talk

5. Fie Langmann
6. Laura Krogh Herlin
7. Lisbeth Moelgaard Laustsen
8. Solvej Videbæk Bueno

Oral presentation

9. Malthe Jessen Pedersen

Session 10

Pitch

1. Anette Faurskov Bundgaard
2. Anneline Rauch
3. Kristian Rasmussen
4. Kirstine Bundsbæk Bøndergaard

Flash talk

5. Charlotte Steen Duholm
6. Christian Jentz
7. Christine Leonhard Birk Sørensen
8. Pernille Bach Steen

Oral presentation

9. Caroline Abild

Session 11

Pitch

1. Anne Mette Gissel Jensen
2. Cecilie Thrue
3. Julius Vadiveal
4. Shubhangi Das Barman
5. Virginia Fochi

Flash talk

6. Kathrine Hyldig Bjerre
7. Mia Heintzelmann
8. Signe Mikkelsen
9. Thomas Stax Jakobsen

Oral presentation

10. Peter Kolind Brask-Thomsen

Session 12

Pitch

1. Anne Marie Gøtke
2. Charlotte Nygaard
3. Johannes Duvander Bülow
4. Saba Molhemi
5. Tarannum Ara

Flash talk

6. Anna Bystrup Jacobsen
7. Camilla Mærsk-Møller
8. Christina Shen-Zhuang Nielsen
9. Kristin Allergodt

Oral presentation

10. Miriam Højholt Terkelsen

Session 13

Pitch

1. Alisha S. M. Hall
2. Andreas Færgemand Laursen
3. Andreas Myhre Baun
4. Frederik Skovbjerg
5. Line Thordahl Jakobsen
6. Silvia Genovese

Flash talk

7. Julie Løye Hejl
8. Maria Louise Jöhnk
9. Thomas Lamm

Oral presentation

10. Chloe Saunders

Session 14

Pitch

1. Ann Hanifa
2. Anne Grøndahl Poulsen
3. Dea Kejlberg Andelius
4. Simon Arvin
5. Sofie Jacobsen

Flash talk

6. Anette Viftrup
7. Rikke Nicoline Stokholm
8. Stinne Eika Rasmussen

Oral presentation

9. Stian Langgård

Session 15

Pitch

1. Anna Memborg Toft
2. Henrik Filskov Aaseby
3. Kia Lærke Madsen
4. Maya Dyveke Schou
5. Savannah Duus Andersen

Flash talk

6. Emma Faddy
7. Ida Monrad Johannsen
8. Vibeke Klastrup
9. Victor Næstholt Dahl

Oral presentation

10. Cecilie Patsche

Session 16

Pitch

1. Caroline Worm
2. Eva Marie Gjørup
3. Helena Hørdum Breum Andersen
4. Matilde Have Kallesøe

Flash talk

5. Maja Raos
6. Ninna Lund Larsen
7. Signe Dalsgaard Justesen
8. Simon Horsholt Thomsen

Oral presentation

9. Emmeli Mikkelsen

Session 17

Pitch

1. Anne Katrine Leonhard
2. Emilia Castro-Pavlik
3. Josephine Gladov
4. Marie Dahl Jørgensen

Flash talk

5. Ida Kaad Faurschou
6. Mette Hindsholm
7. Nicolai Kjældgaard Kristensen
8. Niels Holm

Oral presentation

9. Signe Bergliot Nielsen

Session 18

Pitch

1. Katrine Astrup
2. Kirstine Guld Frederiksen
3. Malene Glud
4. Trine Brøns Nielsen

Flash talk

5. Anne Kraushaar Martensen
6. Helene Rask Dalby
7. Rasmus Kraghede
8. Rupan Paramasivam

Oral presentation

9. Merete Nørgaard Madsen

Second Round of Sessions – 13.35 to 14.55

Session 19

Pitch

1. Doruk Bor
2. Dung Nguyen Riis
3. Maja Thomassen
4. Malene Højgaard Andersen
5. Sie Kronborg Fensman
6. Simon Graff

Flash talk

7. Anne Louise Jensen
8. Christel Gry Aagren Nielsen
9. Malene Kærslund Hansen

Oral presentation

10. Jacob Marthinsen Seefeldt

Session 20

Pitch

1. Laura Bruus Bjerre
2. Oliver Slavensky
3. Pernille Lajer Sørensen
4. Trine Rasmussen

Flash talk

5. Anna Borgognoni
6. Anne Juhl Nielsen
7. Jamal Bousamaki
8. Johannes Jedrzejczyk
9. Simone Juel Dragsbæk

Oral presentation

10. Johannes Bech Steinmüller

Session 21

Pitch

1. Cecilie Langkilde Lauesen
2. Charlotte Hald
3. Louise Krog
4. Manja Bjerring Rothenberg
5. Mette Jertrum Hansen
6. Rikke Daugaard

Flash talk

7. Anders Schram
8. Anne Sofie Frølunde
9. Lene Holst Andersen

Oral presentation

10. Malene Tanderup Sørensen

Session 22

Pitch

1. Anna Bøgh Lindholm
2. Ditte Marie Storm
3. Monja Müller
4. Rasmus Aabling

Flash talk

5. Kristian Savstrup Kastberg
6. Lara Marziani
7. Marie Louise Næstholt Dahl
8. Rachele Rossi
9. Sofie Fonager

Oral presentation

10. Olivia Wagman

Session 23

Pitch

1. Amalie Olsen
2. Camilla Merrild
3. Kerstin De Keukeleere
4. Sofie Jørgensen

Flash talk

5. Cecilie Feidenhansl
6. Cecilie Siem Bach-Nielsen
7. Clàudia Río-Bergé
8. Frederik Søholm Gillesberg
9. Qian Liu

Oral presentation

10. Jacob Storgaard

Session 24

Pitch

1. Amalie Maria Grønning
2. Benjamin Green
3. Cristina Ballester Bergada - **CANCELLED**
4. Sandra Maria Hansen
5. Trine Züricho Lyksholm
6. Victor Ramon Llorente

Flash talk

7. Emma Johannsen
8. Maria Chrysopoulou
9. Nanna Johnsen

Oral presentation

10. Tilde Kristensen

Session 25

Pitch

1. Anne Emilie Morsing
2. Clara Laursen
3. Mathilde Søbye Blaavand
4. Tine Andreasen

Flash talk

5. Anne Sofie Borg Hammer
6. Carmen Oroperv
7. Mikkel Erik Juul Jensen
8. Nanna Kristjánsdóttir

Oral presentation

9. Andrea René Jørgensen

Session 26

Pitch

1. Florentina Krasniqi
2. Frida Hæstrup
3. Marlene Bentestuen
4. Nina Moustgaard Knudsen

Flash talk

5. Jens Kæstel Skov
6. Louise Bjerregaard - **CANCELLED**
7. Mia Skøtt
8. Peter Carøe Lind

Oral presentation

9. Nichlas Vous Christensen

Session 27

Pitch

1. Janni Mølsted
2. Jens Ejrnæs Tønder
3. Nathalie Fryd
4. Peter Engholm Hjort

Flash talk

5. Bayan Sardini
6. Kasper Grooss
7. Katharina Skovhus Prior
8. Malene Blumenau Pedersen

Oral presentation

9. Lene Munk

Session 28

Pitch

1. Ane-Kersti Skaarup Knudsen
2. David Kocemba
3. Kirstine Hermann Jørgensen
4. Mathias Flensted Poulsen
5. Mayuri Charnalia
6. Sebastian Nielsen

Flash talk

7. Akila Aiyar
8. Jesper Fjølner
9. Mads Lamm Larsen

Oral presentation

10. Judit Prat Duran

Session 29

Pitch

1. Anne Katrine Bak Poulsen
2. Ann-Kristine Mandøe Svendsen
3. Emil Krogh
4. Kristian Juul Sandahl

Flash talk

5. Camilla Lomholt Kjersgaard
6. Josefine Tang Rørbech
7. Michella Bjerregaard
8. Sonja Meyer

Oral presentation

9. Marie Bach Sønderskov

Session 30

Pitch

1. Chris Jeppesen
2. Helene Viborg Christensen
3. Natasha Amran Laursen
4. Simon Kjær Simonsen
5. Vivi Mäkinen

Flash talk

6. Jonathan Baier
7. Majbritt Jeppesen
8. Mattias Hedegaard Kristensen
9. Søren Isidor

Oral presentation

10. Ditte Smed Kornum

Session 31

Pitch

1. Andreea-Alexandra Bach-Nielsen
2. Cecilia Majlund Hansen
3. Christian Lind Nielsen
4. Fredrika Magnuson
5. Martin Mølhave
6. Simon Storgaard Jensen

Flash talk

7. Johan Kløvgaard Sørensen
8. Josefine Beck Larsen
9. Martin Bækgaard Stisen

Oral presentation

10. Andreas Gammelgaard Damsbo

Session 32

Pitch

1. Fatemeh Yarmahmoudi
2. Leonardo Melo Rothmann
3. Sofie Dorset
4. Søren Hejgaard Elsborg
5. Yane Chaves

Flash talk

6. Jonas Holst Wolff
7. Louise Bendixen
8. Marvin Werner
9. Sujan Ravendran

Oral presentation

10. Camilla Eva Krænge

Session 33

Pitch

1. Bjarke Bøttger
2. David Haldrup
3. Ida Borreby Pedersen
4. Inger Lily Margrethe Jensine Hjuler Dorf
5. Julie Bondgaard Mortensen

Flash talk

6. Jelena Stankovic
7. Mai-Britt Skadborg
8. Nanna Sutter Rolighed
9. Theresa Møller Kynde

Oral presentation

10. Camilla Lundgreen Duus

Session 34

Pitch

1. Abarajitha Thiyagarajah
2. Melina Vejlø
3. Niwar Faisal Mohamad
4. Pelle De Deckere
5. Peter Andreas Andersen

Flash talk

6. Danni Chen
7. Josephine Olsen Kipp
8. Louise Elkjær Fløe
9. Nadia Iraqi

Oral presentation

10. Anders Guldhammer Skjerbæk

Session 35

Pitch

1. Laurits Kaaber
2. Muhammed Alparslan Gøkhan
3. Nicoline Larsen
4. Ruza Bjelovucic

Flash talk

5. Anika Kofod Petersen
6. Kathrine Bohn Faldborg
7. Mojdeh Mansoori
8. Yumi Chokyu Del Rey

Oral presentation

9. Sandra Thun Langsted

Session 36

Pitch

1. Ibrahim Alzaim
2. Ida Guldbrandt Kjær
3. Line Langberg Balsby
4. Saeideh Tavajoh

Flash talk

5. Alexandra Amalie Uglebjerg Pedersen
6. Casper Homilius
7. Frederik Bromer
8. Stig Henrik Andersen

Oral presentation

9. Andrea Lund

Session 37

Pitch

1. Emil Weissmann Jensen
2. Kirstine Bruun Viuf
3. Nina Haugbølle Bjerre Andersen
4. Trine Arnam-Olsen Moos

Flash talk

5. Astrid Becker-Larsen
6. Erik Perfalk
7. Malene Risager Lykke
8. Mette-Marie Zacher Kjeldsen
9. Sara Ellegaard Andreasen

Oral presentation

10. Victor Hvingelby

PHD DAY 2024

Abstracts

FOGH-NIELSEN COMPETITION

Care for persons with Bipolar Disorder in Low-Resource Settings: Psychoeducation in Rwanda

Caroline J. Arnbjerg, Department of Public Health, Center for Global Health

E. Musoni-Rwililiza, Center for Global Health, Department of Public Health, Aarhus University, Denmark; College of Medicine and Health Sciences University of Rwanda, Rwanda, 3Mental Health Department, University Teaching Hospital of Kigali, Rwanda; N.U. Rurangwa, College of Medicine and Health Sciences University of Rwanda, Rwanda; M.B Grønlund, Competence Centre for Transcultural Psychiatry (CTP), Mental Health Centre Ballerup, Denmark; C. Murekatete, Mental Health Department, University Teaching Hospital of Kigali, Rwanda; J. Carlsson, Competence Centre for Transcultural Psychiatry (CTP), Mental Health Centre Ballerup, Denmark; P. Kallestrup, Department of Public Health, Aarhus University, Denmark.

Introduction: While the efficacy of psychosocial interventions as an add-on treatment to pharmacotherapy is well documented in treating symptoms and relapse prevention in the Global North, the evidence is sparse in low-resource settings, with no psychosocial studies on relapse prevention from a low-income country. In this study, we aimed to assess the effectiveness of structured group psychoeducation versus a waiting list on relapse prevention for individuals with bipolar disorder in Rwanda, a low-income country.

Methods: This was a randomized controlled trial. Adults with bipolar disorder and no episode in the preceding four weeks were included from the two referral psychiatric hospitals in Rwanda and randomly assigned 12 sessions of group psychoeducation or a waiting list. The program was developed with patients and clinicians and contextualized to the Rwandan setting. Relapse was the primary outcome.

Results: From January to March 2021, 154 participants were assigned to either group psychoeducation or a waiting list. The retention rate was high, with only three participants opting to discontinue the psychoeducation after receiving one session. Although first-line pharmacotherapy was used sparingly, the psychoeducation program reduced the risk of hospitalization by 50% over the 12-month follow-up period.

Discussion: In resource-restrained settings, structured group psychoeducation for bipolar disorder demonstrated a beneficial impact on reducing relapse in adults with bipolar disorder, even in the presence of limited access to first-line pharmacotherapy. This is a scalable, effective, low-cost, and sustainable modality for the prevention of major psychiatric distress.

Themes: Mental health, Public health

Extending the Oncologist's Hand with AI in Radiotherapy

Mathis Ersted Rasmussen, Department of Clinical Medicine, Experimental Clinical Oncology

The ELAISA consortium: Kamal Akbarov, Egor Titowich, Katherine Wakeham, Jasper Albertus Nijkamp, Wouter Van Elmpt, A.F.M. Kamal Uddin, Ahmed Mohamed, Ben Prajogi, Brohet Kartika Erida, Catherine Nyongesa, Darejan Lomidze, Gisupnikha Prasiko, Gustavo Ferraris, Humera Mahmood, Igor Stojkovski, Isa Isayev, Issa Mohamad, Leivon Shirley, Lotfi Kochbati, Ludmila Eftodiev, Maksim Piatkevich, Maria Matilde Bonilla Jara, Orges Spahiu, Rakhat Aralbayev, Raushan Zakirova, Sandya Subramaniam, Solomon Kibudde, Uranchimeg Tsegmed, Stine Sofia Korreman, Jesper Grau Eriksen

Purpose: Global roll-out of artificial intelligence-assisted (AI-assisted) contouring has immense potential for the access and quality of care in radiotherapy. However, the current evidence is primarily from high-income countries.

The purpose of this study was to investigate contours' inter-observer variation (IOV), Similarity to Expert-Contours (SEC) and contouring time between radiation oncologists (ROs) in low- and middle-income countries (LMICs) doing either AI-assisted or manual contouring of organs-at-risk (OAR) in head-and-neck cancer for radiotherapy.

Materials and Methods: 97 ROs were invited to the study. They were randomized to either manual contouring or AI-assisted contouring of 8 common organs-at-risk of head-neck cancer. Deep learning-based auto-contours were made with MVision AI Oy, Helsinki, Finland. Contouring was performed online in EduCase™ (RadOnc eLearning Center, Inc). ROs were informed about the contouring guidelines used in the study and to “generate clinically acceptable contours”.

IOV was quantified with Dice-Sørensen Coefficient (DSC) between participants' contours and a median contour within groups and SEC with DSC between participants' contours and expert consensus contours. Contouring time was automatically recorded by EduCase.

Results: 89 ROs completed their case. AI-ssisted contouring as compared to manual contouring reduced IOV for 8/8 OARs, increased SEC for 5/8 OARs and reduced contouring time for 6/8 OARs.

Conclusion: AI-assisted contouring benefit contouring across multiple institutions located in LMICs globally. The results add a significant piece of evidence favoring further adoption of AI-assisted contouring worldwide.

Themes: Cancer, Diagnostics & technology
Keywords: Deep learning, Auto-contouring, Randomized trial

Acute myocardial infarction: Changes in prognosis

Pernille Gro Thrane, Department of Clinical Medicine, Cardiology

PG Thrane, Department of Clinical Medicine; KKW Olesen, Department of Cardiology, Aarhus University Hospital; T Thim, Department of Cardiology, Aarhus University Hospital; MB Mortensen, Department of Cardiology, Aarhus University Hospital; MK Hansen, Department of Clinical Medicine; N Stødkilde, Department of Clinical Medicine; C Gyldenkerne, Department of Clinical Medicine; SD Kristensen, Department of Cardiology, Aarhus University Hospital; M Mæng, Department of Cardiology, Aarhus University Hospital

Background: ST-segment elevation myocardial infarction (STEMI) is associated with a high early mortality that gradually declines over time. It is not known how long-term mortality relates to mortality in the general population.

Objectives: To assess excess mortality in STEMI patients treated with primary percutaneous coronary intervention (pPCI) compared to an age- and- sex-matched general population in landmarks periods (0-30 days, 31-90 days, 91 days to 10 years)

Methods: Using the Western Denmark Heart Registry, we identified consecutive patients undergoing first-time pPCI from January 2003 to October 2018. Each patient was matched by age, sex, and index year with 5 individuals from the Western Denmark general population. Excess mortality was expressed using stratified Cox regression.

Results: A total of 18,732 patients and 93,660 matched general population individuals were included (median age 64 years; 74% males). Baseline comorbidity burden was very similar in patients with STEMI and matched individuals. STEMI was associated with high mortality in the first 30 days compared to that of the general population (cumulative incidence: 6.0% vs 0.2%; hazard ratio (HR) 36.6, 95% CI 30.8-43.0), which declined from 31-90 days (0.93% vs 0.38%; HR 2.48 95% CI 2.11-2.91. In patients surviving the first 90 days, mortality out to 10 years was only slightly increased compared to that their matched peers (25.7% vs 23.7%; HR of 1.05, 95% CI 1.02-1.08).

Conclusions: If first-time STEMI patients survive the first 90 days after pPCI, their risk of dying is very close to mortality observed in an age- and sex-matched general population during 10-years of follow-up.

Themes: Cardiology, Epidemiology
Keywords: Acute myocardial infarction, Time trends, Mortality

First round of sessions

Session 1

Comparison of routes to cancer diagnosis across ethnic groups in Denmark: A population-based nationwide cohort study

Anne Dahl Sørensen, Department of Public Health, Research Unit for General Practice

L.F. Virgilsen, Research Unit for General Practice Aarhus; H. Jensen, The Danish Clinical Quality Program – National Clinical Registries; C. Wejse, Research Unit for Global Health, Aarhus University, and Department of Public Health, Aarhus University; G. Lyratzopoulos, Institute of Epidemiology and Health, University College London; P. Kallestrup, Research Unit for General Practice, Aarhus, Research Unit for Global Health, Aarhus University, and Department of Public Health, Aarhus University

Background: Studies on cancer diagnosis indicate that ethnic minority populations in developed countries have worse cancer prognosis than the background population. In general, the route to cancer diagnosis (RtD), e.g. fast-track referral vs. acute admission at the hospital, is strongly associated with the cancer prognosis. It is unknown whether cancer patients with ethnic minority background are diagnosed through less favorable routes than the background population.

Aim: We aim to 1) describe and compare the RtD's across ethnic groups in Denmark, and 2) investigate the association between ethnicity and 5-year overall survival across RtD's in Denmark.

Methods: We will conduct a population-based nationwide cohort study based on routinely collected Danish registry data. The study population comprises all cancer patients aged ≥ 18 years registered with a cancer diagnosis in the Danish Cancer Registry from 1 January 2014 to 31 December 2018 (n = 159,189). Ethnic groups will be defined according to 1) country of origin and 2) cultural dimensions as described in 'The Cultural Dimensions Theory' by sociologist Geert Hofstede.

Results: We will use multinominal logistic regression to assess RtD's for ethnic minority groups compared to ethnic Danes. Results will be presented as relative risk ratios with 'cancer patient pathway from primary care' as the reference. We will further present risk ratios for ethnic minority groups compared to ethnic Danes for being alive 5 years after cancer diagnosis across all RtD's.

Perspectives: Insights from the study will provide new knowledge on the diagnostic processes and cancer prognosis of ethnic minority patients in Denmark.

Themes: Cancer, Epidemiology
Keywords: Cancer diagnosis, Ethnic minority populations, Denmark

Feasibility of Weekly Cisplatin and Radiotherapy for Localized Anal Cancer – A Danish Anal Cancer Group report

Anne Vittrup Jakobsen, Department of Clinical Medicine, Health

C. Kronborg, Danish Centre for Particle Therapy, Aarhus University Hospital and Department of Clinical Medicine Aarhus University; R. Oksen, Department of Oncology, Vejle Hospital, University Hospital of Southern Denmark; B. Havelund, Department of Oncology, Vejle Hospital, University Hospital of Southern Denmark; K. Wind, Department of Oncology, Aarhus University Hospital; K.G. Spindler, Department of Oncology, Aarhus University Hospital and Department of Clinical Medicine Aarhus University.

Background: Standard treatment for squamous cell carcinomas of the anus (SCCA) is chemoradiotherapy (C-RT) with 5-FU and MMC. Compliance with treatment is crucial for locoregional control but treatment is associated with significant acute toxicity and treatment breaks. Weekly Cisplatin is an established treatment for other squamous cell carcinomas but has not been evaluated for SCCA.

Purpose: to investigate if RT with weekly Cisplatin is a feasible option for SCCA and to report the associated acute toxicity.

Methods: We identified patients with SCCA treated with curative RT and weekly Cisplatin from 1998-2020. Retrospective data from medical records and prospectively collected data from a Danish observational study were included. Disease-free survival (DFS) and Overall survival (OS) were estimated using the Kaplan-Meier method.

Results: We included 116 patients, 51 with prospective data. T-stage distribution was T1: 4%, T2: 71%, T3: 17%, T4: 8% and 47% had N+ disease. RT doses were 53.75Gy-64Gy to tumor. The mean cumulative Cisplatin dose was 307.5mg and the median overall treatment time was 43 days. 23 patients required hospitalization, 3 due to treatment-related febrile neutropenia. 89% of patients had complete response within 6 months after CRT. The median follow-up time was 4.5 years, and 20 patients were deceased at time of analysis of which 11 had died from anal cancer. The 5-year DFS and OS were 77.7% and 86.4%, respectively

Conclusion: Our results show that RT combined with weekly Cisplatin is an effective and safe treatment option in relation to outcome and acute toxicity compared to historical data.

Themes: Cancer, Epidemiology

Colon dysplasia and colorectal cancer in inflammatory bowel disease: Overall risk and evaluation of a novel biomarker to predict cancer development.

Jesper Winkler Andersen, Department of Clinical Medicine, Health, Aarhus University

F. Troelsen Department of Clinical Epidemiology

Presentation of project: As patients with inflammatory bowel disease (IBD) have an increased risk of colorectal cancer (CRC) Danish guidelines recommend regular CRC surveillance for IBD patients with certain risk factors.

We will conduct two register-based cohort studies to investigate the impact of clinical risk factors for developing CRC among IBD patients. These risk factors include, but are not limited to, age at diagnosis of IBD, extension of IBD, duration of IBD, IBD subtype, primary sclerosing cholangitis, characteristic findings at colonoscopy, medical treatments, and familial disposition. Knowledge could be transferred directly into clinical practice for IBD patients undergoing CRC surveillance and contribute to an improved identification of high-risk IBD patients. In the first study we look at all IBD cases with a possibility to compare with non-IBD cases. In the second study we investigate IBD patients with diagnosed LGD.

The group of IBD patients with LGD constitute a group of known high-risk individuals. Using copy number alterations (CNA) as a molecular biomarker for identifying which IBD patients with LGD who have a high risk of future high-grade dysplasia (HGD) or CRC-development show very promising preliminary results. However, numbers of patients and the pre-diagnosis selection in these studies do not yet justify clinical use. Therefore, we will setup a case-control study to investigate the sensitivity and specificity of CNA to predict HGD or CRC. If we demonstrate that CNA expression is a sensitive and specific biomarker for HGD and CRC development, it could become a valuable future tool in the management of IBD patients.

Themes: Cancer, Epidemiology
Keywords: biomarker, inflammatory bowel disease, colorectal cancer

Time to cystoscopy after initiation of aspirin and non-steroid anti-inflammatory drugs

Malene Andersen, Department of Clinical Medicine, KEA

M. Nørgaard, Department of Clinical Epidemiology, JB Jensen, Department of Urology; LD Andersen, Department of Molecular Medicine

Purpose: Hematuria is the most common sign of bladder cancer. Anticoagulant medication increases the risk of hematuria and might unmask silent bladder cancers. We tested this hypothesis for antiplatelet medication. We compared time until cystoscopy from first-time aspirin or NSAID initiation to the background population.

Methods: We conducted a cohort study of all Danish residents who were first-time initiators of aspirin and non-COX2-selective NSAIDs in 2005-2018 and had two or more redeemed prescriptions of the same exposure drug within 6 months. Unexposed individuals from the background population were matched 10:1 based on sex, age and municipality. We excluded individuals with prior cancers, bleeding disorders, urinary tract stones, cystoscopies, or antithrombotic/anticoagulant medications prescription redemptions. Analysis will be performed using Cox Proportional Hazard regression analysis with adjustment for sex, age, calendar year, prior arthropathies and Charlson comorbidity Index level (0,1-2, 3+). Data were gathered from the Danish health registries.

Results: In the preliminary analysis, we included 89.701 and 209.510 initiators of aspirin and NSAID, respectively. Within one year of follow up, 0,669% of aspirin initiators and 0,505% of NSAID initiators had a cystoscopy. Compared with the background population, this corresponded to an unadjusted hazard ratio of cystoscopy of 1.78 (95% CI, 1.64; 1.94) for aspirin and 1.94 (95% CI, 1.81; 2.07) for NSAID.

Importance: When evaluating if there is an association between bladder cancer and aspirin/NSAID use, an increased detection of bladder cancer due to antiplatelet function would be an important bias to consider.

Themes: Cancer, Epidemiology
Keywords: Hematuria, Cystoscopy, Antiplatelet

Data quality in the Danish Lung Cancer Registry

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Background: Since 2001, the Danish Lung Cancer Registry (DLCR) has monitored interventions and outcome of all Danish lung cancer patients with the intent to streamline and improve treatment and survival. The DLCR receives information from the Danish Patient Registries in addition to clinical information from the treating physicians. The past year alone, more than 50 papers have been published using DLCR as a data source. This study evaluates the validity of the information in the DLCR.

Methods: Patients diagnosed with non-small cell lung cancer from 2014 to 2016 and recorded in the DLCR were included, and a random sample of 1000 patients were selected for validation. Medical records (electronic files) were reviewed and were considered as the "gold standard" to which data listed in the DLCR were compared.

Results: Information was retrieved from medical charts for all 1000 patients. Agreement on stage at diagnosis was 90.1% (CI 88.0-91.9) and date of diagnoses was 96.1 (CI 94.7-97.1). Agreement on smoking status in pack years (+-5 pack years) was 87.8% (CI 85.0-90.2). PPV of treatment intent was 87.4 (CI 85.1-89.6).

Conclusion: The comparison of data from the DLCR with the medical records revealed overall high validity of the data in the registry. The results of this study are similar to validation of other clinical Danish cancer registries and the DLCR is considered useful for research purposes.

Themes: Cancer, Epidemiology
Keywords: Lung Cancer, Validation,

Cancer risk and survival in Danish patients with Neurofibromatosis 1

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Background: Neurofibromatosis 1 (NF1) is a rare genetic disease with an incidence of 1/2,500. It is inherited autosomal dominantly but around 50% of the variants occur de novo. The typical clinical features are multiple café-au-lait spots and cutaneous and plexiform neurofibromas. The syndrome has a cancer predisposition and individuals with NF1 have a decreased life expectancy, mainly due to deaths from cancer. Despite the increased risk for cancer, there are few population-based studies on the risk of cancer and survival in NF1.

Aim: The overall aim of this study is to estimate the cancer risk and survival in individuals with NF1 in Denmark.

Methods: The study is a retrospective cohort study with the biggest NF1 cohort known to date internationally. It includes 2,753 NF1 persons recruited from the Danish National Patient Registry and the clinical database RAREDIS. They were matched on sex and age with comparisons randomly selected from the Civil Registration System in a ratio 1:10. All individuals were linked to the Danish Cancer Registry to obtain information on cancer diagnoses. Hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated using a Cox proportional hazards model. Survival analyses were performed using the Kaplan-Meier method.

Results: There were significantly higher hazard ratios in most types of cancer in the NF1 such as brain tumour HR 18.2 (95% CI 12.4-27.0) and breast cancer HR 2.0 (95% CI 1.4-2.7).

Conclusion: From the results so far, we see significantly higher HRs for most types of cancer in the NF1 cohort. When this study is published, the results will help clinicians formulate national guidelines for when to screen NF1 patients.

Themes: Cancer, Epidemiology
Keywords: Neurofibromatosis type 1 (NF1), Cancer risk, Survival

Risk of primary liver cancer in patients with alcohol-related cirrhosis is similar in England and Denmark

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Background: Patients with alcohol-related cirrhosis (ALD cirrhosis) have an increased risk of primary liver cancer (hepatocellular carcinoma [HCC] or intrahepatic cholangiocarcinoma [iCCA]). Imaging-based surveillance for HCC is recommended in England, but not Denmark.

Methods: We included 17,085 English patients (2000-2016) and 22,121 Danish patients (1994-2022) with ALD cirrhosis using healthcare registries. We computed incidence rates (IR) and cumulative incidence of primary liver cancer (including HCC and iCCA separately) and, additionally, mortality from diagnosis of primary liver cancer.

Results: The IR of primary liver cancer per 100,000 person-years was 636 (95% CI 580-698) in England and 676 (630-726) in Denmark. The 5-year risk of primary liver cancer was 2.36% (2.12-2.63) in England (iCCA 0.07%, HCC 2.29%) and 2.37% (2.16-2.58) in Denmark (iCCA 0.05%, HCC 2.31%). In both countries, the risk of primary liver cancer was below 4% in all subgroups, increased in males and with increasing age. The 1-year mortality after a diagnosis of primary liver cancer was 56.7% (52.1-61.5) in England and 60.8% (57.3-64.4) in Denmark.

Conclusion: The risk of and the mortality with primary liver cancer is the same in English and Danish patients with ALD cirrhosis, thus questioning the impact of HCC surveillance guidelines. The risk of primary liver cancers increased with age and was higher for men. In both countries, HCCs constituted >97% of primary liver cancers.

Themes: Gastroenterology and hepatology, Epidemiology
Keywords: Epidemiology, Hepatology, Liver cancer

Efficacy of PD-L1 inhibition in recurrent head and neck cancer. A prospective multicenter study

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Aim of the study was to determine the real-life efficacy of single drug PD-1 inhibition comparing pembrolizumab to nivolumab in recurrent/metastatic head and neck squamous cell carcinoma (rmHNSCC). Data were collected at the five Danish head and neck cancer centers.

Descriptive statistics were used to describe patient, tumor and treatment. Endpoints were overall survival (OS) and progression-free survival (PFS), calculated from start of treatment to date of event/censoring. Survival was estimated by the KM method. Analyses were two-sided and $p<0.05$ were considered significant.

In total 375 pts were identified: 229 (61%) received pembrolizumab and 146 (39%) nivolumab. At baseline, the median age was 68 years for pembrolizumab and 63 years for nivolumab ($p<0.001$). A median of 5 treatment cycles were administered in both groups.

A median OS of 10 mo. [95% CI: 10-13] and a median PFS of 5 mo. [95% CI: 4-6] was observed for pembrolizumab. For nivolumab median OS was 10 mo. [95% CI: 9-12] and median PFS 3 mo. [95% CI: 3-4].

Patients with either WHO PS = 0-1 were compared to patients with WHO PS≥2. For pembrolizumab the HR=2.2 [95% CI: 1.5-3.2] ($p<0.001$) with endpoint OS while with endpoint PFS a HR=1.2 [95% CI: 0.9-1.7] ($p=0.3$) was found.

For nivolumab with endpoint OS a HR=4.4 [95% CI: 2.5-7.7] ($p<0.001$) d while with endpoint PFS HR=2.8 [95% CI: 1.6-4.7] ($p<0.001$).

For pembrolizumab PD-L1 TPS ≥ 20% or CPS ≥ 20, HR=0.8 [0.6-1.1] ($p=0.2$) was obtained for endpoint PFS while it for nivolumab was HR=0.6 [95% CI: 0.4-0.8] ($p=0.003$).

Overall, this national phase IV study comparing pembrolizumab to nivolumab showed no significant difference in efficacy in terms of either OS or PFS.

Themes: Cancer, Epidemiology
Keywords: Head and neck cancer, PD-L1, Palliative

Improved diagnosis of ovarian cancer

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Background: Preoperative differentiation between benign and malignant adnexal masses is a clinical challenge. Efficient diagnostic methods should ensure early referral of women with ovarian cancer to oncogynaecological treatment. Women with benign masses should be managed by minimally invasive surgery or expectantly. Primary diagnostic methods are non-expert ultrasonography combined with measurement of the biomarker CA 125. Second-line tools are Magnetic Resonance Imaging (MRI) and expert ultrasonography. Circulating tumor DNA (ctDNA) might present a future diagnostic tool. The diagnostic workup might be improved by implementation of ultrasound-based risk-models by the International Ovarian Tumor Assessment (IOTA) group in a low-risk population by different observers, systematic MRI-description, and by use of ctDNA as a biomarker.

Methods: Gynecologists and radiologists in the Central Denmark Region are introduced to IOTA terms for evaluation of ovarian masses. Ultrasonographic findings are recorded systematically by gynecologists according to IOTA terms. In consecutive women with suspected malignancy, ultrasonography by experienced observers is compared to systematic evaluation at MRI by radiologists. Detection of circulating tumor DNA in plasma samples is evaluated. Reference standard is histological diagnosis or follow-up.

Results: The area under the ROC curves, sensitivities and specificities, positive and negative predictive values of the methods will be compared in a total of 1798 currently included patients.

Conclusion: We aim to contribute with knowledge on a realistic optimal use of available imaging methods and the potential of ctDNA in diagnosis of ovarian cancer.

Themes: Gynecology and obstetrics, Cancer
Keywords: Ovarian cancer, Imaging, Diagnostic tools

SESSION 2

Soluble and Membrane Bound CD163 as a Biomarker in TKI-treated Metastatic Renal Cell Carcinoma Patients

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Renal cell carcinoma (RCC) is a cancer type with more than 400,000 new cases a year, worldwide. While ~25% is diagnosed with metastatic disease, further 20-50% of patients with localized disease develop metastatic renal cell carcinoma (mRCC) later, even after curative intended surgery.

The median 5-year survival of mRCC is currently ~30%, but survival vary depending on the International mRCC Database Consortium (IMDC) risk score, where patients are divided into either favorable, intermediate, or poor prognosis groups. 50% of patients fall into the intermediate prognostic group, where highly variable survival rates highlight the need for better prognostic biomarkers. The increasing number of different treatments for mRCC underscores the need for predictive biomarkers for these patients.

In a previous study, in patients receiving IL-2 and interferon-based treatment, we showed that both the soluble and membrane-bound hemoglobin-haptoglobin receptor CD163 may be an independent prognostic biomarker for mRCC, however, these data have not been validated in an independent patient cohort receiving tyrosine kinase inhibitors (TKI), which we here aim to do.

Using flow cytometry, we intend to analyze the expression levels of CD163 on peripheral blood monocyte subsets, and furthermore, using multiplex immunoassays we will characterize the cytokine profile before and during treatment, and at disease progression.

Thus, in this project we will investigate the potential of the mentioned blood-based biomarkers in mRCC patients, including the potential of measurements in pre-treatment and on-treatment samples to predict treatment response and, ultimately, survival for the patients.

Themes: Cancer, Molecular biology
Keywords: Renal Cell Carcinoma, Biomarkers, Cancer Immunology

Enhancing MRD Monitoring for Acute Myeloid Leukaemia-Myelodysplasia Related Patients using Multitarget, Stem Cell Based Approaches

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Acute myeloid leukaemia (AML), a malignant disease originating from the bone marrow, has a median survival after five years of less than 50%. The disease entity covers a range of diseases with related but distinct genetic backgrounds. The disease is monitored using measurable residual disease (MRD) during and after treatment to guide the physician's treatment choices and evaluate the patient's risk of relapse. MRD can be defined by residual leukemic cells indicated by certain genetic markers.

Current techniques for MRD monitoring are standardized to leukaemia specific single molecular markers, or require repeated bone marrow sampling. However, patients diagnosed with AML, myelodysplasia-related (AML-MR) are difficult to monitor with the standard MRD monitoring techniques, as they often lack single molecular markers, since these patients have a background of dysplastic cells with similar molecular variants as the leukemic cells.

We aim to enhance MRD monitoring for AML patients whereby a broader spectrum of AML subtypes can be followed precisely. To specify MRD monitoring we focus on the leukemic stem cells capable of generating a relapse. This will be done by isolation of stem cells from the samples prior to MRD measurement. Then, we will investigate the capability of error-corrected next generation sequencing (EC-NGS) to monitor MRD on a stem cell-based level. Additionally, we will explore how single cell analyses can improve MRD monitoring for AML-MR patients by unravelling genetic variations and immunophenotypes specific to the leukemic cells as well as explore the clonal dynamics.

Themes: Cancer, Molecular biology
Keywords: Acute myeloid leukemia, Measurable residual disease, Sequencing

Genome-wide methylome profiling of cell-free DNA enables prognostication of patients with advanced prostate cancer

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Castration-resistant prostate cancer (CRPC) is an incurable condition due to high rates of therapy resistance, and development of biomarkers to guide treatment decisions is urgently needed. Analysis of cell-free DNA (cfDNA) offers a promising strategy for biomarker discovery, as detection of tumor-derived cfDNA (ctDNA) in plasma has demonstrated prognostic value in various cancers. Here, we have established a methylation-based approach for detecting ctDNA (me-ctDNA) in CRPC plasma.

We generated cfDNA methylome profiles of a training cohort of 48 CRPC patients and 18 controls, using methylated cfDNA immunoprecipitation followed by sequencing. Based on a subset of the training cohort, we established a CRPC-specific methylation signature (cfMeCaP). Using the cfMeCaP methylation score of controls as cutoff, plasma samples were classified as me-ctDNA positive or negative, resulting in 100% sensitivity and specificity for detecting me-ctDNA in the full training cohort.

In a validation cohort of 85 CRPC patients 95.3% classified as me-ctDNA positive using the cfMeCaP signature. High cfMeCaP methylation levels correlated with significantly shorter progression-free and overall survival in both the training and validation cohorts. In earlier stage PC, me-ctDNA was detected in 17/37 (45.9%) patients using cfMeCaP. Here, me-ctDNA detection was associated with significantly shorter time to CRPC progression, suggesting that the prognostic potential of cfMeCaP is not limited to mCRPC patients.

These results highlight the promising potential of plasma me-ctDNA analyses across multiple stages of PC to identify high risk patients that may benefit from intensified treatment.

Themes: Cancer, Molecular biology
Keywords: Circulating tumor DNA, Epigenomics

The Role of Non-Coding RNAs and the Tumor Microenvironment in the Development of Bruton Tyrosine Kinase Inhibitor-Treatment Resistance in Mantle Cell Lymphoma

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Mantle cell lymphoma (MCL) is an aggressive B-cell non-Hodgkin lymphoma with a heterogeneous clinical and biological behavior. Bruton Tyrosine Kinase inhibitor (BTKi) is commonly used as a single-agent therapy for patients with relapsed MCL and has shown high response rates, however many patients eventually relapse due to various resistance mechanisms. Increasing evidence has demonstrated that the tumor microenvironment (TME) plays a critical role in the development of drug resistance, making the TME an interesting target for investigating acquired drug resistance in MCL. Non-coding RNAs (ncRNAs) constitutes a large group of RNAs that are non-protein coding but are identified to have various functions in gene regulations. While ncRNAs are reported to be involved in several diseases, including cancer, their role in B-cell malignancies and how they impact the TME have not been thoroughly investigated. Using RNA sequencing data from primary MCL samples from patients with various risk scores, as well as from healthy control samples, I will profile ncRNA expression patterns in MCL. Furthermore, I will investigate spatial expression of ncRNAs within the TME using single-cell spatial transcriptomics to examine BTKi-treated patient samples. Identifying potentially deregulated ncRNAs in MCL could elucidate important functions in the development and progression of MCL, thereby advance our knowledge of MCL. Furthermore, by mapping the spatial location of different cell types with the addition of in-depth transcriptomic characterization of the TME, could potentially identify drivers of TME-mediated drug resistance, leading to a better understanding of treatment responses in MCL.

Themes: Cancer, Molecular biology
Keywords: Non-Coding RNA, Mantle Cell Lymphoma, Spatial Transcriptomics

CRISPR/dCas9 induced DNA De-methylation of cg20803293 in the GSTM5 promotor upregulates gene expression

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Background: Osteosarcoma (OS) is the most common type of bone cancer and affects primarily children. Previously, we have performed a screening of the epigenome in samples from 97 OS patients. Among the results, Glutathione S-Transferase mu5 (GSTM5) was found to be hypermethylated at the cg20803293 site, and the genes' expression rate was decreased. However, site-specific demethylation of the CpG and its relation to transcription remains unexplored.

Purpose: To validate a causal association between hyper-methylation of the GSTM5 promoter and decreased expression, we aim to remove DNA methylation in this specific location by utilising the sgRNA-directed CRISPR/dCas9 system linked to ten-eleven translocation (TET) dioxygenase1.

Materials and Methods: The relationship between GSTM5 promotor hypermethylation and its transcription was examined using targeted demethylation of cg20803293 in HEK293T cells using the catalytically inactive CRISPR/dCas9 system. The methylation status was measured by Methylation-Sensitive High-Resolution Melting (MS-HRM) analysis of bisulfite-converted cellular DNA. Expression of mRNA was measured by qPCR.

Results: Hypermethylation of the GSTM5 promotor correlates with downregulated transcription in HEK293T cells. MS-HRM analysis shows that target-specific demethylation of cg20803293 is achieved using the CRISPR/dCas9 system and this will restore transcription as measured by qPCR analysis.

Conclusion: Hypermethylation of the GSTM5 promotor correlates with the downregulation of transcription. Demethylation of cg20803293 restores gene expression

Themes: Cancer, Genetic engineering
Keywords: CRISPR, Methylation, Cancer

Improved therapy of Multiple Myeloma by harnessing the Tumor Immune Micro-Environment: Turn Back TIME

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Multiple myeloma (MM) is a malignancy arising from plasma cells in the bone marrow. It is the second most common hematological malignancy worldwide and despite of recent advances in treatment, the disease remains incurable to date. The development and progression of MM is supported by an immunosuppressive microenvironment in the bone marrow with anti-inflammatory (M2-like) macrophages as key orchestrators.

We have developed a lipid nanoparticle (LNP)-based drug targeted towards the CD163 receptor which is highly expressed on anti-inflammatory (M2-like) macrophages. The LNPs encapsulate an inhibitor of the transcription factor STAT3, which has been shown to be overactivated in CD163-positive macrophages in the bone marrow of MM patients and is known to induce a pro-tumoral phenotype of macrophages. We have shown that this drug can inhibit STAT3 in human monocyte-derived macrophages with increased effect in CD163-positive macrophages. We will use these CD163-targeted STAT3-inhibitory LNPs to further investigate the role of STAT3 in the tumor microenvironment, especially focusing on how targeted STAT3 inhibition affects macrophage phenotype and function.

Importantly, this drug delivery system is versatile and can be used to manipulate other central de-regulated pathways in specific macrophage subsets. As part of this project, we aim to identify such de-regulated pathways in bone marrow from myeloma patients using single cell RNA-sequencing and flow cytometry. In perspective, this may lay the foundation for novel personalized treatment of MM and potentially other cancers, where macrophages play a similar role in the tumor biology.

Themes: Cancer, Immune diseases
Keywords: Multiple Myeloma, Tumor-associated macrophages, Immunotherapy

Lipid nanoparticles as vector for delivery of CRISPR-Cas9 targeting RUNX1-RUNX1T1 in AML with t(8;21)(q22;q22.1)

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Acute myeloid leukemia (AML) with t(8;21)(q22;q22.1) resulting in the fusion oncogene RUNX1-RUNX1T1 is a well-described subtype of AML. Associated with a favorable prognosis, the main cause of mortality remains relapse, occurring in 30% of patients. Previous research has established that an intron-targeting dual-gRNA approach can disrupt the RUNX1-RUNX1T1 fusion oncogene, leading to inhibited leukemic cell growth and proliferation, suggesting its potential as a future therapeutic in the treatment of AML. In this study, we investigated lipid nanoparticles (LNPs) as a potential vector for delivery of gene therapy for AML. Human AML cell line Kasumi-1 was used for in vitro experiments. Primary patient bone marrow mononuclear cells (BM-MNCs) from 1 patient with AML and 1 patient with myelofibrosis were used. LNPs were synthesized using NanoassemblrTM Ignite®. The LNPs were packed to contain: (i) GFP-mRNA; (ii) gRNA; or (iii) Cas9-mRNA. Flow cytometry was utilized for analysis of GFP expression and evaluation of transfection efficiency. PCR was used for validation of CRISPR mediated disruption of RUNX1-RUNX1T1. High GFP expression was detected in Kasumi-1 cells corresponding > 90% expression. Treatment of primary patient BM-MNCs demonstrated LNP capacity for transfection of both monocytes, granulocytes as well as leukemic blasts. Treatment of Kasumi-1 cells with CRISPR technology targeting the RUNX1-RUNX1T1 fusion gene resulted in consistent disruption of the fusion gene at various dosages when delivered in LNPs. Collectively, our data indicates that LNPs are potential vectors for delivery of CRISPR-Cas9 technology to myeloid cells including malignant leukemic blasts.

Themes: Cancer, Molecular biology
Keywords: Leukemia, CRISPR, Delivery

Tumor Immune MicroEnviroment (TIME) in Renal Cell Carcinoma: Identification of Prognostic Markers and Design of Targeted Treatment

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Treatment of metastatic renal cell carcinoma (mRCC) has been markedly improved with the introduction of immune checkpoint inhibitors (ICIs). However, ~40% of patients do not respond adequately to the treatment and no biomarkers for treatment selection currently exist.

In mRCC, tumor-associated macrophages (TAMs) are known to play pivotal roles in tumor cell proliferation and survival, tumor angiogenesis, suppression of anti-tumor immunity, and treatment resistance. These alterations in the tumor immune microenvironment (TIME) skew tumor infiltrating lymphocytes (TILs) towards an exhausted phenotype and this decrease in proliferation and effector functions is at least in part mediated by an increased expression of immune checkpoint molecules e.g., Programmed cell Death protein (PD-1). Still, how the interactions between TAMs, TILs, and cancer cells impact treatment response remain elusive.

Re-programming of TAMs towards a pro-inflammatory state may improve treatment response for the ~40% of non-responders to ICI treatment, where macrophage targeted lipid-nanoparticles (LNPs) containing relevant siRNA may unleash effective anti-tumor immunity from resident TILs.

The aim of this study is to identify and validate biomarkers (sCD163, sCD206, and PD-1), as a part of the NORDIC SUN clinical trial, whereby identifying non-responding patients up front or early into the treatment. Further, we aim to establish an in vitro model of the TIME in RCC to investigate the effect of the macrophage targeted LNPs as a possible future early add-on to conventional ICIs to overcome treatment resistance.

Themes: Cancer, Molecular biology
Keywords: Tumor Immune MicroEnvironment, Renal cell carcinoma, Biomarkers

HDR-based gene correction in HSPCs by co-delivery of Cas9/sgRNA RNPs and donor sequence in 'all-in-one' lentivirus-derived nanoparticles

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Genome editing using CRISPR/Cas9 allows targeted restoration of disease-causing genes and is particularly promising for treatment of monogenic disorders. However current standard delivery approaches do not comply with safe in vivo delivery. By adapting the properties of lentiviruses to package proteins, we have developed a CRISPR/Cas9 delivery technology in which we package Cas9/sgRNA as ribonucleoprotein (RNP) complexes in lentivirus-derived nanoparticles (LVNPs) for efficient knockout. Here, we explored the capacity of LVNPs to co-deliver RNPs and an RNA donor molecule, which is converted to double-stranded DNA by reverse transcription, for editing by homology-directed repair (HDR). In HeLa and K562-derived reporter lines, we observed targeted HDR-based knockin of the mCherry gene in more than 60% of the cells treated with such 'all-in-one' LVNPs. Notably, potent knockin was dependent of the DNA-PK inhibitor M3814, suggesting that restriction of repair by nonhomologous end-joining was required for effective HDR. We used this approach to efficiently tag the LMNA gene with a full-length eGFP gene (38% in HeLa; 13% in K562) and to introduce the E6V HBB gene variant causing sickle-cell anemia (up to 35% efficiency in K562, 34% in HUDEP-2 and 23% in HSPCs). Interestingly, under conditions supporting similar on-target indel formation in the HBB locus using either standard RNP nucleofection or LVNP-directed RNP delivery, cutting in a known off-target site was markedly reduced in LVNP-treated cells compared to nucleofected cells. Our results provide proof-of-concept for the use of LVNPs as delivery agents for complete HDR genome editing with reduced off-target effects.

Themes: Genetic engineering, Molecular biology
Keywords: CRISPR/Cas9 delivery, Homology directed repair, Gene editing

SESSION 3

Cholesterol-associated CYP27A1 tumor expression and prognosis in premenopausal breast cancer

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Introduction: Obesity, hypercholesterolemia, and breast cancer (BC) are associated and an important link between hypercholesterolemia and BC prognosis may be the cholesterol metabolite, and selective estrogen receptor modulator, 27-hydroxycholesterol catalyzed by the CYP27A1 enzyme. CYP27A1 is differentially expressed in BC with proposedly opposite prognostic value depending on menopausal status. This study aims to investigate the prognostic value of CYP27A1 expression in a large population-based premenopausal BC cohort.

Methods: Among 4,684 premenopausal Danish BC patients from the Predictors of Breast Cancer Recurrence (ProBeCaRe) cohort, diagnosed between 2002 and 2011, CYP27A1 expression was assessed by immunohistochemical stainings of tumor tissue arranged in 99 tissue microarrays. By use of digital image analysis tumor cells were visually separated from surrounding stroma, normal breast tissue and carcinoma in situ. Finally, CYP27A1 intensity was analysed in BC cells.

Preliminary Results: IHC stains were successfully established. A total of three Application Protocol Packages (APPs) were developed for this project.

APPs 1 and 2 have been used to visually separate tumor cells from surrounding tissue. APP3 has been developed for detection of staining intensity. Initial evaluation of tumor cores demonstrated that expression of CYP27A1 as expected varies between tumors.

Perspectives: CYP27A1 expression may serve as an independent, prognostic biomarker in BC, but the fact that previous studies found opposing prognostic effects of CYP27A1-expression in relation to menopausal status merits further investigation in a unique large-scaled cohort such as ProBeCaRe.

Themes: Cancer, Imaging techniques
Keywords: Breast Cancer, Cholesterol, CYP27A1

Benefit of respiratory gating in the Danish Breast Cancer Group Partial Breast Irradiation trial

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Background and purpose: Partial breast irradiation (PBI) has been the Danish Breast Cancer Group (DBCG) standard for selected breast cancer patients since 2016 based on early results from the DBCG PBI trial. During trial accrual, respiratory-gated (RG) radiotherapy was introduced in Denmark. This study aims to investigate the effect of RG on mean heart dose (MHD).

Patients and methods: From 2009-2016 the DBCG PBI trial included 230 patients with left-sided breast cancer receiving external beam PBI, 40 Gy/15 fractions/3 weeks. Localization of the tumor bed on the planning CT scan, the use of RG, coverage of the clinical target volume (CTV), and doses to organs at risk were collected.

Results: RG was used in 123 patients (53%). In 176 patients (77%) the tumor bed was in the upper and in 54 patients (23%) in the lower breast quadrants. The median MHD was 0.37 Gy (interquartile range 0.26-0.57 Gy), 0.33 Gy (0.23-0.49 Gy) for RG, and 0.49 Gy (0.31-0.70 Gy) for free breathing, $p<0.0001$. MHD was <1 Gy in 206 patients (90%) and <2 Gy in 221 patients (96%).

RG led to significantly lower MHD for upper-located, but not for lower-located tumor beds, however, all MHD were low irrespective of RG. RG did not improve CTV coverage or lower lung doses.

Conclusions: PBI ensured a low MHD for most patients. Adding RG further reduced MHD for upper-located but not for lower-located tumor beds but did not influence target coverage or lung doses. RG is no longer DBCG standard for left-sided PBI.

Themes: Cancer, Imaging techniques
Keywords: Breast cancer, Respiratory gating technique, Partial breast irradiation

Identifying Ovarian Cancer – Can We Do Better: Using New Advanced MRI Techniques and Metabolomic Biomarkers?

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Background Ovarian cancer ranks fifth in cancer deaths among women. 70% of the patients have advanced stage of disease at time of diagnosis. Pre-operative diagnostic imaging, evaluation and decision of treatment is challenging for both radiologists and specialists in nuclear medicine. The aim of this study is to investigate functional and metabolic MRI-techniques, and their ability to improve ovarian cancer diagnostics – in both correct diagnosis and disease severity. Methods Forty patients suspected of epithelial ovarian cancer and referred to the dept. of Gynaecology and Obstetrics, AUH and selected for an multidisciplinary team conference (MDT) will be recruitted and submitted to the conventional 18F-FDG PET/CT and MRI-protocol with the addition of an MR-research-package. The additional MR-research-package is performed prior to MDT and includes dynamic contrast enhaced (DCE) images of perfusion, diffusion images of cellular intretrigity (DKI), mitocondrial function (31P) and pyruvate metabolism (hyperpolarized 13C-pyruvate MRI). Biomarkers from NMR-metabolomics and hyperpolarized 13C-pyr MRI, DCE, DKI, 31P imaging will be analyzed to attepmt to create a diagnostic algorithm to support clinicians in classifying tumour spread of ovarian cancer and to predict treatment response. Results We expect better prediction of malignancy and resectability using the above techniques. Perspective This study has the potential to pave the way for larger clinical trials that could improve our understanding, diagnostics and treatment of ovarian cancer. Furthermore, the use of these novel imaging techniuques are bringing them closer to clinical translation.

Themes: Cancer, Imaging techniques
Keywords: Ovarian cancer, Multiparametric MRI, Diagnostics

Response to initial chemotherapy in 20 patients with limited disease small cell lung cancer

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Introduction: Limited disease small cell lung cancer (LD-SCLC) is treated with combined chemo-radiotherapy. Frequent local and distant recurrences are present despite treatment. This calls for a way of predicting more persistent tumors, to better outcomes for these patients (pts). Here done by evaluating the radiologic and metabolic response to initial chemotherapy (CTx), seen as changes in tumor volume and highest standard uptake value in 1cm3 (SUVpeak).

Materials and Methods: 20 pts with LD-SCLC treated in 2015-2016 was retrospectively examined. CTx regimen consisted of platinum/Etoposide. Radiotherapy (RT) was delivered as 45Gy/30fx/10week. All pts had diagnostic PET/CT-scans (dPCT) and planning PET/CT scans (pPCT) acquired for RT planning. Median time between scans were 1.5 months [1;4], during which, 1-4 series of CTx were administered. Gross tumor volumes for tumor (GTV-T) and lymph nodes (GTV-N) were delineated on pPCT and deformably transferred to dPCT followed by visual inspection and correction. Volume and SUVpeak were determined on all scans and changes calculated.

Results: At diagnosis median GTV-T and GTV-N volume were 112.0ml, [min; max] [1.7;452.2] and 42.9ml [2.3;247.8], and median SUVpeak were 10.8 [1.9;16.4] and 9.1 [2.8;15.4], respectively. After initial CTx the median volume decrease was 40.9% [1.0;93.3] for GTV-T and 42.6% [5.2;91.3] for GTV-N. The median decrease in SUVpeak was 41.2% [10.8;83.0] for GTV-T and 57.0% [17.7;85.1] for GTV-N.

Conclusion: All patients had a decrease in volume and SUVpeak after initial CTx. Responses varied within the group; this may guide us to deliver individualized RT with increased doses to patients with more persistent tumors.

Themes: Cancer, Imaging techniques
Keywords: Lung Cancer, Small Cell Lung Cancer, Early Response

Quality assurance of internal mammary node irradiation

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Aim: Internal mammary node irradiation (IMNI) is highly dependent on target volume delineations. Therefore, our aim is two-fold. First, compare internal mammary node (IMN) doses between the original and modern ESTRO delineations. Second, compare IMN doses in left and right-sided breast cancer patients.

Methods: From 2007-2014, locoregional radiotherapy to high-risk breast cancer patients included the regional nodes but only IMNI in right-sided patients, whereas IMNI was omitted in left-sided patients. From the DBCG RT Nation study, treatment plans were collected. The DBCG guidelines recommended that the clinical target volume (CTV) of the IMN was covered with 90% of the prescribed dose (V90%). The CTVn_IMN was only delineated in right-sided patients (IMN_old). Left and right-sided CTVn_IMN structures were auto-segmented with in-house developed deep learning following ESTRO delineations (IMN_new). Additionally, due to the cranial discordance, the IMN_new was separated into IMN_new_cranial and IMN_new_caudal. Differences between groups were tested with non-parametric test.

Results: Treatment plans for 2,893 (63.7%) patients were available. In right-sided patients, the median V90% IMN_old (91.5%) was higher than IMN_new (74.0%), $p<0.001$. Dose coverage in IMN_new_caudal was comparable to IMN_old. Comparing IMN_new_caudal by laterality, the median V90% was 94.0% in right-sided patients and 20.1% in left-sided patients, $p<0.001$.

Conclusion: Dose coverage in original IMN_old delineations was comparable to the caudal part of the IMN_new auto-segmentation. Using IMN_new_caudal, we found a significantly higher IMN dose coverage in right-sided patients than in left-sided patients.

Themes: Cancer, Imaging techniques
Keywords: Breast cancer, Radiotherapy, Quality assurance

Skin toxicity of FLASH proton radiation within the Spread-out Bragg Peak

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Introduction: The promising new radiation modality of FLASH radiotherapy has gained the wide interest. FLASH is radiotherapy delivered ultra-fast in a fraction of a second, which can reduce normal tissue toxicity compared to conventional treatments that can last several minutes. Most studies of proton FLASH investigate these effects within the entrance of the beam and not the most beneficial property of proton radiation; namely the Spread-out Bragg peak (SOBP). Our study aimed to determine the tissue-sparing effect of FLASH radiation on toxicity within a SOBP. To quantify this effect, we sought to produce full dose-response curves for acute skin toxicity.

Materials / methods: The right hindleg of unanaesthetised female CDF1 mice were irradiated with single-fraction doses between 30-65 Gy for FLASH (Field dose rate of 60 Gy/s) and between 20-50 Gy for conventional (CONV, 0.4 Gy/s) dose rates. The leg was placed in the middle of a SOBP generated from a single-energy beam using a 3D-printed static range modulator. Radiation-induced damage was assessed for acute skin toxicity monitored daily within 29 days post-treatment.

Results: Dose-response curves for early damage were produced from the percentage of mice reaching severe acute skin toxicity. The chosen doses comprise full dose-response curves for both CONV and FLASH radiation. Using SOBP proton FLASH radiation requires 29-43% higher dose to achieve the same toxicity as when irradiated with conventional dose rates.

Conclusion: We here illustrate FLASH radiation within the Spread-out Bragg peak performed on a skin-toxicity in vivo model. Radiation within the SOBP retains the normal-tissue-sparing effect of FLASH. The study is ongoing.

Themes: Cancer, Animal Models
Keywords: FLASH, skin toxicity, radiation damage

Dosimeter position reconstruction method for in vivo dosimetry during tandem+ring brachytherapy of cervical cancer

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To develop a method to reconstruct the position of the dosimeter when performing scintillator-based in vivo dosimetry (IVD) during pulsed dose rate (PDR) brachytherapy (BT) with a tandem ring (TR) applicator for cervical cancer.

At Aarhus University Hospital (AUH) in vivo dosimetry is routinely performed during BT treatments using an in-house developed detector system based on a ZnSe(O) scintillating crystal. For treatment of cervical cancer, a Varian TR is used. The scintillating crystal is placed inside the patient using an intracavitary BT needle in a holder near the base of the tandem part of the TR. The dose rate is then measured inside the patient for each dwell position during the treatment.

Prior to treatment, the dosimeter position is marked on an MRI image, but setup uncertainties can lead to deviations. A method was developed where the planned dwell positions in the ring were used in combination with the measured signal to perform a least-squares minimization fit of the theoretical dose rate. To test the method, a signal was simulated from the positions of the dosimeter and the source from the treatment plan. An additional random uncertainty was added from a Gaussian distribution with a standard deviation of 1%.

The accuracy (mean±1SD) of the reconstructed dosimeter position was 0.35 ± 0.81 mm. There was one outlier that showed a 5.3 mm deviation from the ground truth position. For this treatment only dwell positions in one half of the ring were used.

A method to reconstruct the dosimeter position was developed. The locations of the source positions inside the ring can influence the accuracy of the reconstruction.

Themes: Imaging techniques, Cancer
Keywords: Brachytherapy, Dosimetry, Quality Assurance

Preliminary results with hyperpolarized [1-13C] pyruvate MRI in hepatocellular carcinoma

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Introduction: Hepatocellular carcinoma (HCC) is the most common primary liver tumor and is one of the most common causes of cancer-related deaths worldwide. To offer patients curative treatment, it is important to diagnose HCC at an early stage. Today the diagnosis is based on characteristic radiological findings of tumors ≥ 10 mm which often are absent in tumors smaller than 10 mm. Therefore, there is a great need for a better diagnostic tool.

Material and Methods: Hyperpolarized (HP) Magnetic Resonance Imaging (MRI) enhances the signal by a factor of over 20.000 compared to normal MRI. Using HP 13C pyruvate as a MR contrast agent, metabolic conversion to lactate, alanine and bicarbonate can be quantified due to the chemical shift effect. Metabolic images were acquired in two patients with confirmed HCC.

Results and discussion: Lactate to pyruvate ratio (lac/pyr) was high in confirmed HCC tumors. however, lac/pyr were in both cases also increased in liver tissue near the HCC tumors. It is unclear whether the increase metabolism is origination from the tumor, an expression of an increased metabolism in the local environment near the tumor or metabolism from unrecognized cancer cells. Follow-up in the first patient revealed multifocal HCC in the right hemi liver. In the second patient histopathology showed intra hepatic HCC metastases in the resected hemi liver.

Conclusion: Preliminary results with HP [1-13C] pyruvate MRI shows promising in detecting metabolic alterations in the liver of patients with confirmed HCC.

Themes: Imaging techniques, Cancer

Clinical evaluation of deep learning based synthetic CTs from CBCTs for head-and-neck proton therapy

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Purpose/Objective: Proton dose calculation based on cone-beam CT (CBCT) is currently hindered by CT number inaccuracies and imaging artifacts. Deep learning has been shown to be superior to the traditional CBCT correction methods. This study evaluates synthetic CTs (sCTs) generated from CBCT using a 3D cycle-consistent contrastive-unpaired-translation generative-adversarial (CycleCUT) network.

Material/Methods: A total of 94 head-and-neck cancer patients were used to train and evaluate the performance of the CycleCUT network. For patients in the test set (12 patients), a CBCT was chosen with a criterion of being anatomically similar to a same-day repeat CT (rCT). The rCT was deformably registered to the corresponding CBCT to create a ground-truth rCT (gtrCT) to compare to the sCTs. The structure set was deformably propagated from the planning CT to both the sCT and gtrCTs, and the clinical proton plan was re-calculated on the sCTs and gtrCT. The proton dose distributions were compared in terms of target coverage and organ-at-risk (OAR) doses. Wilcoxon signed rank test was used to evaluate if the dose differences were statistically significant ($P \leq 0.05$).

Results: The sCTs generated using the CycleCUT network visually had a greatly reduced noise level compared to the CBCTs, with the image quality of the sCTs being comparable to the gtrCTs. No statistically significant differences were found between the dose distributions for the sCTs and the gtrCTs according to the Wilcoxon signed rank test.

Conclusion: The CycleCUT network was capable of generating sCTs from CBCT with an image quality comparable to gtrCT resulting in proton dose distributions comparable to those of regular CTs.

Themes: Cancer, Imaging techniques
Keywords: Adaptive proton therapy, Cone-beam computed tomography, Deep learning

SESSION 4

Targeting splenic endothelial immunosuppressive genes for anti-cancer therapy

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The spleen exhibits distinct characteristics and facilitates myeloid cell expansion, limiting their productive immune response during tumor development. The interaction of blood-borne tumor antigens with spleen-resident immune cells (ICs), is mediated by endothelial cells (ECs) that act as a selective barrier between blood and the underlying tissue. ECs in various tissues exhibit unique immunological features, beyond their role in IC recruitment. Tumor ECs are also found to hinder T cell activation and tumor infiltration. Moreover, identification of immune EC subsets in the lung in health and during cancer warrants further exploration of such ECs in other parts of the body, especially in crucial immune hubs such as the spleen, the more so given its accessibility as a promising therapeutic target site. However, the intricate tissue density and complexity of the spleen makes the elucidation of its discrete function during tumor immunity challenging.

This project aims to elucidate the complexity of splenic EC functions and immune-EC interactions that determine tumor response and to identify, using single-cell RNA sequencing, immunosuppressive target genes in spleen ECs as candidates for anti-cancer therapy.

Results: The single cell isolation of spleen ECs from a mouse orthotopic lung tumor model (with healthy controls) was optimized, and samples were further processed to create a 3' gene expression library for sequencing. The data obtained is being used to analyze the IC-EC interactions that are distinct to spleen in the context of cancer and to identify therapeutic candidate targets. This will be followed by target validation and experiments to unravel the mode of action.

Themes: Cancer, Omics
Keywords: Endothelial cells, Anti-cancer therapy

Brainstorming – Harnessing oncolytic viruses in the fight against high-grade brain cancers

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This research project explores the use of oncolytic viruses as a potential treatment for high-grade brain tumors. High-grade brain tumors such as glioblastoma are among the deadliest cancers, currently considered incurable. One promising and novel treatment approach are oncolytic viruses: Attenuated and genetically optimized viruses that specifically target tumor cells and spare healthy tissues. In this project, a selected group of clinically relevant oncolytic viruses are tested on patient-derived tumor samples ex vivo, aiming to determine their effectiveness in targeting and killing tumor cells. Combining in vitro data with NGS data and a thorough analysis of underlying brain tumor biomarkers, we aim to provide a novel predictive framework of tumor susceptibility to the respective oncolytic virus. Our study will provide valuable insights into the feasibility of oncolytic viruses as a novel therapeutic approach for high-grade brain tumors, with implications for personalized treatment strategies.

Themes: Cancer, Omics
Keywords: Onco-virotherapy, Brain cancer, Personalized medicine

Macrophage ”don’t eat me” checkpoints as biomarkers to monitor immunotherapy in bladder cancer

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Background: Bladder cancer (BC) is a common aggressive cancer type. It is in the early stages treated with one of the first types of immunotherapy, the Bacillus Calmette-Guerín (BCG) vaccine. However, new predictive biomarkers are needed as the treatment response varies among patients. We have recently described the presence of so-called “don’t eat me” checkpoint proteins in human serum and want to study these proteins as easily accessible biomarkers in bladder cancer.

The "don’t eat me" checkpoint receptors downregulate phagocytosis og activity of human macrophages. In a tumor environment, activation of these checkpoints can lead to tumor immune evasion and potentially immunotherapy failure.

Methods: We will establish and use thoroughly validated immunoassays to measure selected soluble versions of “don’t eat me” checkpoint proteins in serum and urine from the Bladder Cancer Tissue Biobank, MOMA, AUH. Levels of soluble checkpoint proteins will be associated with clinical data before and after immunotherapy and evaluated as predictive biomarkers. Tissue expression of checkpoint proteins will be investigated using multiplex immunostaining and a deep phenotyping of tumor-associated macrophages based on RNA sequencing data will be performed to characterize macrophage subtypes in BC. The effects of BGC on macrophage phenotype and expression of “don’t eat me” checkpoints will be studied in vitro.

Perspectives: We expect to identify new predictive biomarkers that can improve risk stratification and diagnostic precision in BC treatment. The characterization of macrophage subtypes in bladder cancer tumors may promote identification of new molecular targets for experimental therapy.

Themes: Cancer, Diagnostics & technology
Keywords: Oncology, Immunology, Biomarkers

Advancing the quality and clinical utility of ctDNA using synthetic reference material

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Worldwide CRC is the third most commonly diagnosed cancer and the second most frequent cause of cancer death. The standard of care for CRC patients with localized or regional disease (stage I-III) is surgical removal of the tumor, which can be followed by adjuvant chemotherapy (ACT). The decision to treat with ACT depends on the stage of the disease and different clinicopathological factors known to impact the risk of relapse. It is estimated that more than 60% of patients are treated unnecessarily with ACT after surgery and some patients without high-risk features recur nevertheless, and potentially could have benefited from post-operative ACT. Consequently, there is a need for a new and better risk marker. Circulating tumor DNA (ctDNA), shed from cancer cells, have the same genetic alterations as the cancer cell they originated from and thus have potential to be used as cancer markers. Currently all available ctDNA-based assays are for research-purpose only, and the implementation of ctDNA for clinical decision-making is of high interest. Well-validated quality control material for ctDNA detection is urgently needed to enable standardization and ensure consistent, interpretable, and comparable results. We have developed synthetic reference material for ctDNA detection, which we will use to conduct a national QA trial to increase the quality and harmonize ctDNA detection methods in Denmark. Furthermore, we will use the reference material for benchmarking, and clinical validation of the performance of available ctDNA diagnostic tests on CRC patients to bring ctDNA analysis closer to clinical implementation.

Themes: Cancer, Diagnostics & technology
Keywords: ctDNA, Reference Material, Benchmarking

Time-resolved in vivo dosimetry during proton Bragg peak FLASH irradiation of mice

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In pre-clinical mouse studies, ultra-high dose rate proton beams demonstrated reduced normal tissue toxicity while maintaining tumour control (FLASH effect). Proton therapy has the advantage that the beam stops at the depth of the tumour with no exit dose beyond Therefore, new mouse studies explored the FLASH effect in such a beam, focusing on acute skin toxicity and late effects (fibrosis around the foot joint).

A mouse's hind leg was irradiated with a 5cm spread-out Bragg peak (SOBP) generated from a 250 MeV proton beam. 28 mice received FLASH treatments with doses of 30 – 65 Gy, using a field with a 2cm x 3cm beam. Accurate dose delivery was validated with time-resolved in vivo dosimetry using a scintillation-based detector system with three probes. Those were placed close to the foot and joint and enabled both geometric and dosimetric validation.

Results showed small uncertainties in probe positioning. However, the mouse leg consistently aligned with the centre of the field. Dosimetric validation showed that the mouse foot target was within the high-dose area for all mice, while the joint target was closer to the field edge and received less than the planned dose.

In conclusion, the detector system was successfully calibrated for absolute dose measurements in the SOBP and provided time-resolved in vivo dose rate measurements for proton beam FLASH. This system allowed for the verification of accumulated dose and mouse leg positions in the treatment field.

Themes: Cancer, Diagnostics & technology
Keywords: Radiotherapy, FLASH, Dosimetry

Unlocking the Potential of the T-cell Receptor in Prostate Cancer

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Prostate cancer (PC) is the most diagnosed cancer among Danish men, with its diagnosis and subsequent monitoring still heavily dependent on the prostate specific antigen (PSA) test. The prognostic accuracy remains poor, leading to overtreatment of patients with non-aggressive cancer and undertreatment of those with aggressive cancer in need of immediate action. Recently, our research group documented the clinical value of tumor-infiltrating T-cells as markers of aggressive PC. We hypothesize that this signal can also be found in circulating T-cells isolated from the blood and used as proxy for the antitumoral immune response. While the prognostic potential of the T-cell receptor (TCR) repertoire remains in its infancy, promising results from other cancers indicate that a diverse repertoire composed of numerous unique T-cell clones correlates with improved survival.

Methods: This study utilizes a well-characterized cohort, encompassing 220 late-stage castration resistant (CR)PC patients with blood samples taken at the time of CRPC diagnosis with a subset of patients being sequentially sampled throughout the disease course. Additionally, blood samples from 30 healthy male donors and from 30 newly diagnosed PC patients are included.

Results: In an initial investigation, encompassing 8 patients with CRPC and 8 healthy males, we observed that the cancer patients had a higher proportion of hyper-expanded T-cell clones and a less diverse TCR repertoire compared to healthy controls.

Conclusion: While our initial findings are promising, we eagerly await the results from the larger study described above to establish the prognostic potential of the TCR repertoire in prostate cancer.

Themes: Cancer, Bioinformatics
Keywords: Prostate cancer, Liquid Biomarkers, T-cell receptor repertoire

Validity of self-reported night shift work among women with and without breast cancer

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Objectives: The objectives are to estimate the validity of self-reported night shift work among women with and without breast cancer and illustrate the consequences using quantitative bias analysis.

Methods: 225 women diagnosed with breast cancer and 1800 matched controls without breast cancer employed within the Danish hospital regions 2007-2015 participated 2015-2016 in a questionnaire-based survey. They reported night shift work status that was linked with objective payroll register day-by-day working hour data and the Danish Cancer Registry. For the breast cancer patients and their matched controls, we estimated sensitivity and specificity with the payroll data as the gold standard. We also estimated the impact on relative risk estimates for a hypothetical population by quantitative bias analysis.

Results: For breast cancer patients, we observed a sensitivity of night shift work of 86.2% (95% CI 77.3%-95.1%) and a specificity of non-night work of 82.6% (95% CI 76.4%-88.8%). For controls, the sensitivity was 80.6% (95% CI 76.9%-84.3%) and the specificity 83.7% (95% CI 81.7%-85.7%). Odds ratio for breast cancer in a hypothetical population decreased from 1.12 (95% CI 1.03-1.21) to 1.07 (95% CI 0.97-1.18) when corrected by the sensitivity and specificity estimates.

Conclusion: This study shows that female breast cancer patients slightly better recall previous night shift work than controls while breast cancer patients as well as controls recall previous non-night work with low specificity. The net effect of this misclassification tends to be a small over-estimation of the relative breast cancer risk.

Themes: Cancer, Statistics
Keywords: Validation, self-reported data, breast cancer

Diagnostic strategy in patients with an indeterminate nodule resembling hepatocellular carcinoma on multiphase contrast-enhanced CT

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Introduction: Magnetic resonance imaging (MRI) is often used secondary in patients evaluated for hepatocellular carcinoma (HCC) when multiphase contrast-enhanced computed tomography (ceCT) is inconclusive. The aim of this study was to investigate whether MRI as add-on provides a non-invasive conclusion or delays biopsy.

Methods: This single-institution study included 48 MRI scans of 44 patients due to suspicion of HCC on a multiphase ceCT scan. The MRI scans were conducted from May 2016 to July 2023. Information included indication and conclusion of MRI scan, decisions made at multidisciplinary team meetings evaluating liver tumors, and histology of liver biopsies.

Results: An MRI scan performed after a multiphase ceCT scan suspicious of HCC either confirmed or rejected the HCC diagnosis in 77 % of the cases. The patients without former HCC were later diagnosed with HCC in 18 % of the patients having an MRI scan rejecting the diagnosis. In cases with the MRI scan being also inconclusive, 73 % of the patients were diagnosed with a malignant disease within 26 months.

Discussion: MRI contributed to a final non-invasive diagnosis when HCC was suspected on a multiphase ceCT scan in 3/4 of the cases. However, a considerable number of patients having an MRI scan either rejecting HCC or being inconclusive were later diagnosed with HCC.

Themes: Gastroenterology and hepatology, Imaging techniques
Keywords: Hepatocellular carcinoma, Imaging

Exploring the Role of Secondary Particles in Quality Assurance using SOI Microdosimeters

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Quality assurance in proton therapy is crucial for high patient care standards. Relying solely on dose measurements for quality assurance offers a limited view of the proton beam, overlooking secondary particles. We used a Silicon On Insulator (SOI) microdosimeter to capture a wider energy spectra range, introducing the lineal energy spectrum as a new plan quality assurance dimension alongside dose.

A key question arises: how do these spectra differ when measured in an anthropomorphic phantom compared to a patient scenario? This study simulates a patient treatment plan using a CIRS head phantom. We focus on microdosimetric spectra's dependencies on material composition, exploring variations in secondary particle spectra concerning ICRP-defined materials (soft tissue, bone, skin) compared to epoxy resin used in anthropomorphic phantoms.

Strategically placing a physically accurate 10 µm SOI microdosimetric chip at critical clinical locations, such as adjacent to the brainstem, bones, and soft brain tissue, enables us to gain valuable insights into these discrepancies. The measurements were conducted at the Danish Centre for Particle Therapy, and simulations were performed using TOPAS V3.9. For the simulations, we observed no significant differences in lineal energy spectra between the epoxy materials and human tissue. Furthermore, the epoxy tissue spectra exhibited good agreement between measurements and simulations. This finding suggests that microdosimetry detectors can be used for quality assurance in proton therapy without significant deviations between QA and theoretical measurements in humans.

Themes: Cancer, Statistics
Keywords: microdosimeter, Quality assurance, proton therapy

Target coverage robustness with proton therapy for high-risk prostate cancer within the frame of a clinical trial

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Background and aim: Patients with high-risk prostate cancer are often treated with radiotherapy to the prostate and pelvic lymph nodes and may benefit from proton therapy due to the large treatment volume. However, this tumour site shows complex inter-fractional anatomical variations. The aim of this study was to evaluate target dose delivery robustness of proton therapy for high-risk prostate cancer within a pilot study before a randomised clinical trial.

Material and methods: Weekly repeated CT scans and treatment plans from ten patients included in the pilot phase of the PROstate PROTON Trial 1 (NCT05350475) were included in this study. Treatment plans were recalculated on a total of 69 repeated CT scans for the ten patients. The volume of the target structures that received 95% of the prescribed dose should be above 98%. This dose/volume criterion was evaluated for both the primary target (prostate) and the elective target (lymph nodes) for each recalculated treatment plan.

Results: Of the 69 recalculated treatment plans, the primary target dose/volume criterion was within the constraint level for 68 plans with the single marginal exception having a value of 97.6%. For the elective target, the equivalent results showed 63 of the recalculated treatment plans to be above the constraint level with four values above 95% and the remaining two at 93.1% and 91.8%.

Conclusion: The study showed that proton therapy treatment plans to the prostate and pelvic lymph nodes in high-risk prostate cancer patients are robust to inter-fractional anatomical variation in terms of target coverage. We are now including patients in the randomised phase of the PROstate PROTON Trial 1.

Themes: Cancer, Urology & Nephrology
Keywords: Prostate cancer, Proton therapy, Quality assurance

SESSION 5

Barriers and facilitators to multi-step prostate cancer screening interventions in Europe: stakeholder perspectives

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Prostate cancer (PCa) is diagnosed using a combination of prostate-specific antigen (PSA) levels and prostate biopsies. In an effort to mitigate over diagnosis and improve outcomes, the European Commission has proposed new multi-step PCa screening guidelines. Men should be screened via blood PSA testing followed by MRI, based on patients' risk. However, little work has been done into the stakeholder perspectives with regard to the proposed screening process. The objective is to investigate the perspectives of stakeholders with regard to the proposed multi-step prostate cancer screening protocol and their willingness/ability to implement it.Data will be collected in Poland, Lithuania, Ireland, and Spain. In sub-study 1, patients will be compared with others of similar criteria in order to determine the rates at which patients were prescribed the multi-step screening protocol. Sub-study 2 aims to investigate clinicians' opinions about the screening protocol just before starting to use the screening protocol and after a specified period of time. The data will be collected with questionnaires including questions based on the Theory of Planned Behavior. Sub-study 3 is a focus group study aiming to investigate stakeholders' attitudes toward multi-step screening, including epidemiologists, government healthcare officials, and clinicians. A framework analysis will be conducted to explore similarities and differences between sites. No results are available as the study is still preparing for data collection, anticipated to begin in 2024. Results and insights can be applied to other regions to help further the creation of new, feasible prostate cancer screening guidelines.

Themes: Cancer, Public health

Reduction of organ-at-risk doses by omission of selected elective target volumes in head and neck cancer radiotherapy

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Purpose: This study aimed to explore the potential for reducing irradiation of organs at risk (OAR) in head and neck cancer by omitting lymph node levels with low risk of sub-clinical disease.

Materials and Methods: Twenty patients with oropharyngeal cancer were retrospectively included. Three independent treatment plans were generated. Initially, a baseline plan (BP) was generated following current guidelines from DAHANCA. A second plan was generated in which lymph node levels with expected risk of sub-clinical disease of <10% were omitted (SP). Finally, a unilateral plan (UP) was generated where the whole contralateral region of the elective target volume (CTVe) was omitted. Mean dose to 12 OARs were reported, normal tissue complication probabilities (NTCP) and the spill-over dose for the remaining volume at risk >30Gy (V30GyRVR) was calculated.

Results: For UP, the mean dose to OAR were observed lower for 5/12 OAR in contrast to BP. SP showed little to no reduction in mean doses compared to BP. The NTCPs showed minimal variation in probability of xerostomia and dysphagia between BP and SP. However, a notable reduction was observed between BP and UP. Finally, a substantial decrease of V30GyRVRs was observed between BP and UP, whereas only a small reduction was seen between BP and SP.

Conclusion: Complete omission of contralateral regions in the CTVe in head and neck cancer achieves the highest reduction in mean doses to OAR and spill-over dose. Some reduction in both OAR and spill-over dose can be achieved through selected omission of low-risk lymph node levels. This study emphasizes the relevance of exploring methods to achieve benefits in reducing irradiation of OAR.

Themes: Cancer, Statistics
Keywords: Treatment Planning, Head and Neck cancer, Elective Target Volumes

IMMUNCIRC; Investigating the role of the immune system in immunotherapy response and the use of circulating tumor DNA-guided patient management in renal cancer

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The incidence of renal cell carcinoma (RCC) is increasing worldwide, with about a quarter of cases being diagnosed at an advanced disease stage and ~25% relapsing following curatively intendend treatment of their localized disease. Immunotherapy has markedly improved the treatment options for metastatic RCC, however which patients that benefit from this treatment and the underlying response mechanisms remain unclear. A few studies have proposed circulating tumor DNA (ctDNA) as a promising tool in RCC, but analyses have been challenged by the trace amounts of ctDNA shedded by RCC tumors. Moreover, the immune system's role in immunotherapy response warrants further investigation.

In this project we want to investigate the role of the T cells and bacteria composition in immuno-therapy response. Moreover, we aim to investigate the use of ctDNA as a more accurate risk stratification method and sensitive measure of relapse. ctDNA will be measured by looking at genomic and epigenomic variants using cfMeDIP-seq in plasma from 200 localized RCC patients. T cell clone composition in the blood and ctDNA levels will be measured longitudinally during treatment in 100 metastatic RCC patients and the role of the colonic microbiota in immunotherapy response will be determined from rectal swabs.

Overall, we aim to identify biomarkers that 1) more accurately risk stratify patients for recurrence, 2) predict immunotherapy response, and 3) detect residual disease following surgery or recurrence during treatment.

Results will benefit both patients and the health care system as expensive oncological treatment can be administered only to patients that need it and will benefit from it.

Themes: Cancer, Urology & Nephrology
Keywords: Renal cancer, ctDNA, Immunology

Psychosocial impact of multi-step prostate cancer screening in four European countries

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Background/Objectives: Prostate Cancer (PCa) is the most common cancer among European men, with approximately 450,000 new cases diagnosed annually. Currently, opportunistic screening using prostate specific antigen (PSA) testing has been found to be ineffective. This results in significant overdiagnosis, psychological harm and associated costs, without reducing mortality. To address these challenges, the EU project PRAISE-U aims to implement a systematic multi-step screening strategy that adds risk calculations and MRI to current strategies, with the objective of improving screening accuracy and reducing unnecessary biopsies. This PhD project aims to explore knowledge and attitudes towards PCa screening, the psychosocial impact at different stages in multi-step PCa screening and the experience of participants after risk stratification or biopsy.

Method: This study will include men aged 50-70 years. Recruitment will be tailored to five pilot sites in Ireland, Spain (Manresa and Galicia), Lithuania and Poland. Validated questionnaire will be used to address the objectives of this PhD, which will be administered either in paper-based or online formats. Participants will complete the questionnaires at baseline and when they have completed the screening process. Additionally, semi-structured focus group interviews will be conducted. To optimize recruitment and data collection strategies, we will engage local stakeholders in 'Collaborative User Boards,' allowing us to tailor these approaches to the pilot algorithm and local conditions.

Results: The study is currently in its preparation phase. Data collection will begin in April 2024.

Conclusion: This PhD study will provide information on the knowledge, attitudes, and the psychosocial impact of systematic multi-step PCa screening in men who participate in different screening modalities.

Themes: Cancer, Mental health
Keywords: Prostate cancer screening, Psychosocial impact, Mens perspective

Uncovering the expression landscape, functional roles and clinical potential of long non-coding RNAs in pediatric intracranial tumors

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Pediatric brain tumors (PBT) are one of the most frequent cancers diagnosed in children in Denmark. Clinical management is often challenging in part because the underlying pathobiology of the disease is poorly understood and only few molecular biomarkers have been identified. Current treatment consists of non-specific therapies often associated with long-term side effects related to impaired cognitive development and growth in children. Consequently, a better understanding of the underlaying pathobiology is urgently needed to find new avenues for improved therapeutic intervention. Long non-coding RNAs (lncRNAs) are an abundant subclass of RNAs that do not encode any protein. They are associated with the tumorigenesis of many cancers but have not yet been thoroughly studied in PBT.

In this project the landscape of lncRNA expression in PBT will be spatially resolved at single cell resolution using MERFISH or CosMx spatial transcriptomic technology. Specific lncRNAs will subsequently be validated using the RNA in situ hybridization technique RNAscope and functionally characterized using different in vitro model systems. Additionally, aberrant expression of lncRNAs will be identified by profiling of genome-wide lncRNA expression patterns in a nationwide patient cohort to elucidate the potential roles of lncRNAs in the disease. Finally, lncRNAs with prognostic value will be identified and validated using NanoString nCounter technology in randomized discovery and validation cohorts. Overall, this project will potentially improve the current knowledge of the underlaying pathobiology of PBT as well as provide new avenues for clinical management of the affected patients.

Themes: Cancer, Molecular biology
Keywords: Pediatric Brain Cancer, Non-coding RNA, Spatial transcriptomics

Sarcopenia – an overlooked prognostic indicator in lung cancer

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Background: Lung cancer stands as a leading global cause of mortality, with non-small cell lung cancer representing 80% of all primary lung malignancies. Early-stage non-small cell lung cancer is typically treated with surgical resection. Sarcopenia, characterized by muscle wasting and loss of muscle mass and strength, presents a worldwide health concern that diminishes quality of life and increases morbidity and mortality. Sarcopenia is a notable feature across various cancer diagnoses, including non-small cell lung cancer, and could serve as an independent prognostic indicator of poor short- and long-term outcomes. The overall objective of the present study is to investigate the prognostic significance and clinical consequences of pre- and post-operative sarcopenia in non-small cell lung cancer patients.

Method: This nationwide, population-based cohort study will be based on approx. 14.000 Danish patients diagnosed and surgically treated for non-small cell lung cancer between 2003-2020. Data will be provided from the Danish Lung Cancer Registry and Statistics Denmark and merged with body composition data from CT scans of all included patients. Specific software will be applied for automatic body composition analysis, preoperatively and during follow-up.

Perspective: This project holds the potential to improve the assessment of patients' overall health status and prognosis while assisting in the customization of individualized treatment plans, particularly in the context of pre- and postoperative rehabilitation.

Themes: Cancer, Surgery
Keywords: Lung cancer, Sarcopenia, Epidemiology

Comparative assessment of AI multi organ delineations tools of organ at risk in brain cancer patients

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Introduction: Finding the right compromise between tumor control and side-effect from radiotherapy (RT) in brain cancer requires accurate and systematic delineation of organs at risk (OARs). Current AI tools can accurately delineate larger OARs, but class imbalance makes delineation of smaller structures challenging. This study aims to investigate whether transformers can provide accurate delineations of small OARs in the brain.

Methods and materials: Two AI, deep learning models were trained for delineation of 9 OARs in brain: nnUNet and a transformer model. Both models were trained using k-fold on a dataset with 49 T1+contrast MRI scans of brain tumor patients and tested on 6 patients. Model performance was assessed using 1mm surface dice(SDSC).

Results: SDSC of the predicted delineations of OARs did not change for the large structures where nnUNet achieved median SDSC for Brainstem, of 0.65, Chiasm of 0.59 and Optic nerves R/L of 0.52/0.57 and transformer achieved 0.67 for Brainstem, 0.55 for Chiasma and 0. 0.48/0.57 for Optic nerves R/L.

However, the transformer model achieved a higher median SDSC of 0.65/0.66 for the R/L optics tracts compared to the nnUNet model, which acquired a median SDSC of 0.60/0.58, R/L.

Conclusion: There were no improvements in the SDSC, for Brainstem, Chiasm, or Optic nerves R/L. However, based on the results, there is an indication that transformers may provide an improvement for the smallest structures.

Themes: Cancer, Cancer
Keywords: Transformers, Neuro-oncology, segmentation

Commissioning of a pMBRT Slit Collimator for Preclinical Radiobiology Experiments at the Danish Centre for Particle Therapy

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Proton minibeam radiotherapy (pMBRT) has emerged as a promising technique in radiotherapy, offering potential improvements in treatment outcomes by minimizing toxicity. Prior to clinical adaptation, it is necessary to establish the efficacy of pMBRT through radiobiological studies.

Here, we develop a practical multi-slit collimator (MSC) for preclinical radiobiological studies of pMBRT. We achieve a homogeneous dose distribution within a PTV for in vivo studies with sharp contrast at the entrance, using a conventional PBS system-based treatment plan.

We used the Geant4 Monte Carlo simulation toolkit to investigate and refine various parameters, such as material selection, thickness, center-to-center distance (CTC), and throughput. A treatment plan was prepared using the Eclipse TPS, to deliver a uniform dose to the PTV (100 x 20 mm² wide, 55 mm to 85 mm deep). The dose distribution was experimentally validated with EBT3 radiochromic films at the DCPT's experimental beamline.

A 50 mm thick brass collimator can deliver the desired dose profile. Utilizing a CTC of 2.25 mm with a throughput of ~44%, a partly uniform dose distribution within the PTV is achieved while maintaining sufficient contrast at the entrance. The simulations exhibit reasonable agreement with the experimental findings. A slight misalignment of the collimator leaf of ~2.5 mrad had a pronounced impact on the dose profile.

We have developed an MSC with promising potential for pre-clinical pMBRT studies. A homogeneous dose distribution within the PTV can be achieved while maintaining sufficient contrast at the entrance. Validation against slit collimator modeling in the RayStation TPS is in progress.

Themes: Cancer, Cancer
Keywords: pMBRT, Collimator

The necessity of managing intra-fractional motion in stereotactic radiotherapy for central lung lesions

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Purpose: In the STRICT-lung trial (NCT05354596), central lung lesions are treated with stereotactic radiotherapy (SRT), using an inhomogeneous dose distribution to the target. A steep dose gradient between the target and nearby organs at risk (OAR) can with intra-fractional shifts lead to severe consequences. This study presents the dosimetric consequences of intra-fractional motion observed for STRICT-lung patients.

Material and Methods: Eighteen patients have been treated in/ad modum the STRICT-lung trial. The patients were set up based on daily cone beam CT (CBCT) soft tissue target match to the planning CT (pCT). After treatment delivery, a second CBCT image was obtained for investigation of intra-fractional target shifts. Retrospectively, the intra-fractional 3D target shift was calculated together with the difference in target mean dose and max dose to the OAR nearest the lesion.

Results: The median [range] target shift was 2.9mm [0.1, 14.2]. The target shifts were primarily in the cranial and dorsal directions. The median change in target mean dose was 0.44Gy [-14.11, 5.61], meaning that some of the patients received less target dose than planned due to intra-fractional target shifts. The OAR nearest the lesion was shifted towards the high-dose region for most patients. This resulted in it receiving a higher dose than planned.

Conclusion: Intra-fractional movements of the target and surrounding OAR can lead to an increased risk of toxicity and, in some cases, under-dosage of the target. To ensure safe SRT for centrally located lung lesions, monitoring and correcting intra-fractional target shifts during treatment is necessary.

Themes: Cancer, Cancer
Keywords: Image Guided Radiotherapy, Lung Cancer, SBRT

Treatment of bowel dysfunction following pelvic organ cancer

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Introduction: As cancer survival improves so does awareness on late sequelae and their impact on quality of life (QoL). The study aimed to report results on treatment of bowel dysfunction from our pelvic organ cancer late sequelae clinic.

Materials and methods: Patients with bowel dysfunction following treatment of pelvic organ cancer were offered treatment in a nurse-led clinic. Patients completed validated electronic patient-reported outcome measures assessing bowel function and QoL. Information on treatment modalities was recorded. Data collection is ongoing and is prospectively registered in an online database.

Results: In December 2021, 380 patients had started treatment for bowel dysfunction. The median (range) age was 66 (27-93) years with 55% women. Primary symptoms were faecal urgency (95%), fragmented defecation (93%), emptying difficulties (92%),

incontinence (flatus 89%, liquid stools 59%, solid stools 33%) and obstructed defecation (79%). At the time of analyses, 169 patients had completed treatment. At the end of treatment, 49% were treated with fibre supplement, 38% with anti-diarrhoeal medication, 24% with rectal emptying aids, 17% with oral laxatives and 24% with transanal irrigation. Five patients received a stoma and one patient sacral nerve stimulation. Significant improvements in all the primary symptoms ($p<0.001$), bowel-related QoL ($p<0.001$) and generic QoL ($p<0.001$) were observed.

Conclusions: Treatment of bowel dysfunction following pelvic organ cancer in our nurse-led clinic significantly improved the symptom burden and QoL. This encourages systematic screening for- and treatment of late sequelae following treatment of pelvic organ cancer.

Themes: Surgery, Cancer
Keywords: Bowel dysfunction, Pelvic organ cancer, Late sequelae

SESSION 6

Hospital-at-Home for older patients with frailty and acute disease – A protocol for a multi-method evaluation study

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Introduction: Hospital-at-Home (HaH) is an alternative to acute hospital admission for selected older patients. Older individuals face the potential risks of functional and cognitive decline, increased risk of delirium, and institutionalization when admitted to hospital. Previous studies have found that HaH reduces these risks. There is limited knowledge concerning HaH for older patients with frailty. We evaluate an existing geriatric-led, admission-avoidance HaH-service for older patients with frailty operated by a multi-disciplinary team. The aims are to describe the HaH service and explore the components of HaH that work, for whom, how, and in what circumstances.

Method: Initial review of HaH and the evaluation of complex interventions

Results: Theory-driven evaluation informed by the UK's Medical Research Council guidance will be conducted using multi-methods based on a program theory anchored in the local HaH-service:

1. Scoping review–examine research based on mechanisms in delivering HaH

2. Descriptive cohort study–describing patient and intervention characteristics and organisation

3. Qualitative study - gain an in-depth understanding of the practice of collaboration through interviews and observations

Conclusion: For HaH to evolve and impact the broader health system, a greater understanding of how the HaH model produces its outcomes is needed. The findings from this study are expected to generate contextually relevant evidence for improving the HaH integrated care model. With an understanding of how measures produce varying impacts in different circumstances, policymakers and practitioners will be able to successfully implement HaH in other settings.

Themes: Public health, Epidemiology
Keywords: Geriatrics, Acute Care, Organising Healthcare

Parental socioeconomic status and timing of puberty: a population-based cohort study within the Danish National Birth Cohort

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Background: Social inequality is demonstrated in most health outcomes, yet the influence of socioeconomic status on reproductive health, such as timing of puberty, is debated. Early puberty is a risk indicator for adult diseases, emphasizing the need to determine potential causes of earlier timing of puberty. The aim of this study was to investigate how parental socioeconomic status was associated with timing of puberty in girls and boys.

Methods: We studied 7890 girls and 7489 boys from the Puberty Cohort nested within the Danish National Birth Cohort (DNBC). Highest completed educational level among parents was used as the indicator of socioeconomic status. Information on pubertal development was obtained every six months throughout puberty. We estimated mean monthly differences for the average age at attaining multiple pubertal milestones using multivariable interval-censored regression models.

Pre-liminary results: When analyzing all pubertal milestones simultaneously, the pubertal milestones were on average attained earlier in girls of low-grade professional parents (-0.7 months [95% confidence interval (CI): −1.6; 0.2]), skilled parents (-1,4 (95% CI: −2.3; −0.4) and unskilled parents (-2,7 (95% CI: −3.8; −1.6) compared with girls of high-grade professional parents. Boys of unskilled parents attained the pubertal milestones earlier (-1,2 (95% CI: −2.3; −0.1) compared to boys of high-skilled professionals, but no clear association was observed for boys of low-grade professional or skilled parents.

Conclusion: Lower parental socioeconomic status was associated with earlier timing of puberty in both girls and boys.

Themes: Public health, Epidemiology
Keywords: Socioeconomic status, Epidemiology, Puberty

Mechanical exposures at work and development of severe low back disorders

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Introduction: Low back disorders (LBD) rank as the leading cause of years lived with disability and the primary driver of work absenteeism. Hence, LBD have garnered substantial attention in workplace prevention and management initiatives. However, these initiatives are challenged by the lack of robust evidence regarding both the relationship between mechanical work exposures (e.g., lifting) and LBD and the prognosis of work related LBD.

Therefore, we aim to examine the relationship between mechanical exposures at work and LBD and to describe the prognosis of work-related LBD.

Methods: This register- and population-based project follows a subset of the adult Danish population from 1976 to 2019 amounting to approx. 5 million people. LBD are identified in the Danish National Patient Registry while mechanical exposures are assigned yearly by linking job exposure matrices to job codes.

Under application of the target trial framework, Poisson regression including splines will be used to explore potential exposure-response relationships and threshold values for harmful exposure. In addition, risk and rate advancement periods will be used to examine potential acceleration of age-related LBD.

The prognostic part is limited to approximately 10.000 low back pain patients seen in departments of occupational medicine. Descriptive statistics and trajectory analysis will be used to explore the prognosis and identify subgroups within this population.

The results may yield:
- Recommendations on the acceptable level of mechanical exposures at work.
- Provide a more robust foundation for evaluating worker compensation claims.
- Offer improved medical guidance to individuals with work-related LBDs

Themes: Public health, Epidemiology
Keywords: Low back disorders, Mechanical exposures at work, Occupational epidemiology

Transition of Care in a Danish context: Translation, Cultural Adaptation, and Content Validation of CTM-15 and PACT-M

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Background: Transition of care from hospitalisation to home is a complex process with potential patient safety risks, especially for patients with multimorbidity. Insight into the patient's experience with a healthcare service can be provided through patient-reported experience measures (PREMs). The aim of this study was to translate, culturally adapt, and content validate two PREMs: Partners at Care Transitions Measure (PACT-M) and Care Transitions Measure 15 (CTM-15) for Danish-speaking patients with multimorbidity.

Methods: The translation procedure followed international guidelines. Patients, representing the target group, were systematically interviewed regarding the aspects of content validity; comprehension, relevance, and comprehensiveness. Healthcare professionals assessed each item of the instruments through questionnaires, allowing for the content validity index (CVI) to be computed at item level (I-CVI) and at instrument level (ave-CVI). Threshold for good I-CVI is ≥ 0.78 and for acceptable ave-CVI ≥ 0.90.

Results: The translation procedure and cultural adaptation were uncomplicated. Both the PACT-M and CTM-15 questionnaires were found to be relevant, comprehensive, and comprehensible to the target patient group. Based on responses from the healthcare professionals, the ave-CVI was 0.94 (I-CVI range 0.89-0.98) for the PACT-M and 0.88 (I-CVI range 0.60-0.98) for the CTM-15.

Conclusion: The CTM-15 and the PACT-M were successfully translated and culturally adapted into Danish. Both the CTM-15 and PACT-M demonstrated acceptable content validity among the target group patients, whereas in healthcare professionals the content validity was found to be lower for the CTM-15.

Themes: Public health, Epidemiology
Keywords: Patient reported outcome, validation, discharge

Pesticide exposure and adverse respiratory outcomes

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Background: The global consumption of pesticides is rapidly increasing and has led to concern on how the widespread use of these chemical compounds may affect public health. Research suggests that the inhalation of pesticides can lead to a range of respiratory problems and extend beyond occupational exposure. Individuals living near agricultural areas may face increased risk of respiratory diseases due to proximity to pesticide spraying.

Some of the most common respiratory diseases are asthma and chronic obstructive pulmonary disease (COPD), affecting hundreds of millions worldwide with an increasing prevalence. Existing literature suggests that exposure to pesticides could trigger asthma or COPD exacerbations.

Aim and methods: Regardless of the massive pesticide use on agricultural sites close to our homes, there are limited studies on the potential adverse effects from airborne chemical particles. Therefore, the aim of our studies is to examine the relationship between pesticide exposure in different life-stages and the risk of early onset asthma, late onset asthma and COPD exacerbations in a cohort including all Danish citizens from 2011 to 2021. To accomplish this, we will use data from the Danish registries, which provides detailed information on residencies, hospital admissions, prescribed medication, and proximity to agricultural pesticide use.

Themes: Public health, Epidemiology
Keywords: Pesticide exposure, Asthma, COPD exacerbations

Exploring multimorbidity patterns in the Danish population using Latent Class Analysis

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As multimorbidity grows in the population, healthcare must adapt. It is, therefore, important to know the disease pattern in the population. This study aimed to uncover and characterise different patterns of multimorbidity within the Danish adult population and assess their socio-demographic profiles and health-related quality of life (HRQoL).

We employed Latent Class Analysis to identify distinct and clinically meaningful disease patterns. Socio-demographic profiles were examined using bivariate analysis and multinomial logistic regression models. Differences in HRQoL across groups were analysed through Analysis of Variance. Data was derived from the 2021 Danish National Health Survey, covering information on education, cohabitation, work status, HRQoL, and 15 chronic diseases for respondents aged 16+ years (n=183,646; response rate=56.7%). Information on age, gender, ethnicity, and place of residence were obtained from register data.

The study identified seven disease groups (latent classes) within the population. One group, labeled "relatively healthy," included individuals with no or just one of the chronic diseases studied, representing 53% of the population. The remaining six groups displayed various multimorbidity patterns, distinct socio-demographic characteristics and HRQoL.

Our findings underscore substantial social inequalities in health and highlight the necessity for tailored healthcare interventions, strategies for workforce retention, and interdisciplinary cooperation. These insights are critical for adapting healthcare organisations and services to meet the evolving needs of a multimorbid population.

Themes: Public health, Epidemiology
Keywords: Multimorbidity, Social inequality, LCA

BMI development and risk of overweight and obesity after being enrolled in a Community-based Health Promotion and Obesity Prevention intervention in kindergartens

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Background: Almost 90% of children remain overweight or obese in adolescence if they were obese at three years of age or had an accelerated annual weight gain during preschool. Interventions targeting physical activity and dietary habits can attenuate overweight and obesity in preschool children, while the long-term effect of preschool interventions is unknown.

Objective: The present study aimed to investigate differences in attained BMI and the proportion of overweight and obesity at school entrance in children who attended kindergartens actively delivering a community-based health promotion and obesity prevention intervention (intervention group) compared to children who attended usual care kindergartens (no-intervention group).

Population: From September 2021 to June 2023, 2.037 children (6-year-olds) had their height and weight measured at school entrance (1.283 = intervention group), (754 = no-intervention group). A subset of 525 children in the intervention group had height and weight measured while in kindergarten at age 3- to 4.

Intervention: The intervention consists of a set of two hours training sessions in each kindergarten. The sessions were facilitated by community health nurses and with a participatory approach based on views and actions from the users of each kindergarten. The sessions targeted the employees, and the parents of children in the kindergartens, respectively. If a child was detected to have overweight or obesity, parents were offered a consultation with a community health nurse.

Perspective: The study will contribute to improving strategies targeted at obesity prevention and detection of unhealthy weight development in preschool children.

Themes: Public health, Epidemiology
Keywords: Obesity prevention, Childhood obesity, Participatory design

Improving partnership between researchers and patient partners in the research process

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Background: Research funding bodies, policymakers, researchers and patients increasingly require patients and their relatives to be engaged in research projects as patient partners. However, it remains unclear how researchers can best engage patient partners and what is the impact of their engagement. The aim is to develop an intervention to improve partnership between researchers and patient partners.

Method: We use the complex intervention framework to guide three studies, each answering a unique research question:

Study 1: How can patient partners effectively be engaged in the research process? A scoping review will be informed by Arksey and O'Malley's framework regarding how to engage patient partners and how to assess the impact of their engagement.

Study 2: What are barriers and facilitators for stakeholders when engaging patient partners in the research process? Two research projects where researchers engage patient partners will be investigated using interpretive description methodology.

Study 3: How can we improve researcher guidance for engaging patient partners in the research process? Interviews with patient partners and researchers will be conducted and a prototype intervention will be co-produced with patient partners and researchers. Patient partners and researchers will join a steering committee during the PhD project.

Perspectives: This project will generate novel knowledge to support researchers engaging patient partners and enhance the relevance of research based on partnership between researchers and patient partners. The results are expected to be generalizable to research within different patient groups and can form the basis for nationwide strategies.

Themes: Public health, Qualitative research
Keywords: Patient and Public Involvement, Patient partners, Scoping review

Development and validation of a machine learning model for prediction of type 2 diabetes in patients with mental illness

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Background: Type 2 diabetes (T2D) is approximately twice as common among individuals with mental illness compared with the background population, but may be prevented by early intervention on lifestyle, diet, or pharmacologically. Such prevention relies on identification of those at elevated risk (prediction). The aim of this study was to develop and validate a machine learning model for prediction of T2D among patients with mental illness.

Methods: The study was based on routinely collected data from electronic health records from the psychiatric services of the Central Denmark Region. A total of 74.880 patients with 1.59 million psychiatric service contacts were included in the analyses. We included 1343 potential predictors covering patient-level information on demographics, diagnoses, pharmacological treatment, and laboratory results. T2D was operationalized as HbA1c ≥48 mmol/mol, fasting plasma glucose >7.0 mmol/mol, oral glucose tolerance test ≥11.1 mmol/mol or random plasma glucose ≥11.1 mmol/mol. Two machine learning models (XGBoost and regularized logistic regression) were trained to predict T2D based on 85% of the included contacts. The predictive performance of the best performing model was tested on the remaining 15% of the contacts.

Findings: The XGBoost model detected patients at high risk 2.7 years before T2D, achieving an area under the receiver operating characteristic curve of 0.84. Of the 996 patients developing T2D in the test set, the model issued at least one positive prediction for 305 (31%).

Interpretation: A machine learning model can accurately predict development of T2D among patients with mental illness based on routinely collected data from electronic health records. A decision support system based on such a model may inform measures to prevent development of T2D in this high-risk population.

Funding: The Lundbeck Foundation, the Central Denmark Region Fund for Strengthening of Health Science and the Danish Agency for Digitisation Investment Fund for New Technologies.

Themes: Diagnostics & technology, Epidemiology
Keywords: Machine learning, Artificial intelligence, Type 2 diabetes

SESSION 7

Retinal oximetry as a dual-mode technique for studying retinal vascular disease

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Background: The introduction of retinal oximetry has provided new information about retinal vascular disease, but has also revealed unexplored potential applications. The validation of retinal oximetry has shown an inverse relationship between the oxygen saturation measured with retinal oximetry and the linear velocity of the blood. This methodological limitation might be used to measure retinal blood flow from the difference between the systemic oxygen saturation measured by pulse oximetry, and the velocity modified oxygen saturation measured by retinal oximetry. To explore this possibility, a method to quantify the linear velocity of the blood is needed, which can be achieved by Doppler Optical Coherence Tomography (Doppler OCT).

Purpose: To determine whether a combination of retinal oximetry and pulse oximetry can be used to measure the blood flow in larger retinal arterioles.

Methods: 30 healthy persons aged 18-40 will be examined with pulse oximetry in combination with Doppler OCT and retinal oximetry on the four arteriolar branches originating from the central retinal artery. The measurements will be performed at rest and during an intervention on the linear velocity (lifting a dumbbell) and oxygen saturation (breathing a hypoxic gas mixture).

Perspectives: This may potentially turn retinal oximetry into a dual-mode technique that can be used to study both retinal oxygen saturation and blood flow in a fast and non-invasive manner. This could provide valuable insight into the understanding of retinal vascular physiology and disease.

Themes: Imaging techniques, Neuroscience
Keywords: Retinal oximetry, Doppler OCT, Retinal blood flow

Advanced molecular imaging of cholestatic disorders in humans: pathophysiological characterization

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Background: Cholestasis is defined as the decreased flow of bile from the liver to the duodenum. Impaired function of the hepatobiliary system can lead to decreased intestinal uptake of lipophilic compounds. Medical causes of cholestasis are monitored by blood samples, which do not necessarily say much about the degree of cholestasis from a functional point of view. Position tomography (PET) with the tracer [N-methyl-11C]cholylsarcosine (11C-CSAR) can be used to track defects in the hepatobiliary system to quantify where the functional cause of cholestasis occurs. Using the tracer provides real-time measurements of the time-course of tissue concentrations of 11C-CSAR in liver tissue, bile ducts, and gallbladder by external detection.

Aim: The aim is to apply functional 11C-CSAR PET/CT scan to patients with genetic cholestatic disorders to gain new insight into the functional effects of genetic mutations and variations on the hepatobiliary handling of bile acids.

Methods: Patients with cholestasis will be recruited from the outpatient clinics in Aarhus and Viborg. A functional 11C-CSAR PET/CT scan will be performed while measuring blood concentrations of 11C-CSAR in arterial and hepatic venous blood.

We aim to include 15 patients with different cholestatic disorders.

Perspectives: This study will quantify the functional effects of genetic disorders and variations on hepato-biliary secretion of bile acids in vivo. This will improve our understanding of the defects and why some of them progress to structural diseases of the liver while others do not. The project will also demonstrate the clinical potential of applying 11C-CSAR PET/CT for clinical studies of patients.

Themes: Gastroenterology and hepatology, Imaging techniques
Keywords: Cholestasis, Hepato-biliary system, PET/CT

Explaining the Unexplainable Death by Introducing Ex-vivo Cardiac Imaging in Forensic Autopsies

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Background: In forensic medicine sudden death in presumed healthy individuals are in many cases presumed to have an underlying cardiac cause. But the forensic heart examination is based on microscopic examination guided by visual, gross anatomical inspection with an inherent risk of missing localized pathology and thereby missing the cause of death.

Aim: We aim at introducing post-mortem magnetic resonance imaging of ex-vivo whole hearts as an add-on to the forensic autopsy to improve the likelihood if finding a cardiac cause of death.

Methods: The hearts will be scanned in a clinical Philips Achieva 1.5T MRI system. We apply our previously developed imaging techniques for detailed three-dimensional assessment of the micro-structure of the entire myocardium. This includes high-resolution anatomical imaging with coronary angiography, fibrosis imaging, myocardial elastography, and diffusion tensor imaging. Areas of pathological interest in the heart can subsequently be subjected to conventional histological examination. The anatomical in-vivo appearance of the post mortem hearts will be preserved by filling the cavities with a water-based, MR-neutral polymer. The coronary arteries are visualized using a mixture of gelatin and contrast agents suitable for MRI.

Expected findings: By introducing the application of existing state-of-the-art imaging techniques, we expect to be able to provide hitherto inaccessible knowledge on the condition of the entire myocardium in three dimensions. This will aid the forensic scientist in locating sites of pathology, thereby increasing the chance of explaining a death that would previously have remained unexplained.

Themes: Imaging techniques, Diagnostics & technology
Keywords: Image guided autopsy, Forensic medicine

Multi-center and multi-vendor reproducibility of T1, T2 and ADC phantom data on 1.5T and 3T MRI scanners

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With the advent of quantitative magnetic resonance imaging, tackling the challenge of standardization and harmonization among vendors and centers has become a fundamental step for multi-center clinical studies involving MRI.

The aim of this international study was to assess multisite (six centers) and multi-vendor (three vendors) accuracy and reproducibility of typical MR biomarkers: T1, T2 and apparent diffusion coefficient (ADC). Field strength dependency was also taken into account by including both 3T and 1.5T scanners. T1 and T2 data were acquired on the NIST Essential System Phantom on two sets of vials, while ADC values were acquired on the Diffusion Phantom. Data was collected using the NIST approved protocols for each vendor: an Inversion Recovery sequence was adopted for T1 determination, a Multi Spin Echo sequence for T2 measurement and an EPI sequence with 4 b-values for diffusion measurements. Measured data were compared with NIST reference values at 20°. In each center reproducibility was assessed from two separate acquisitions.

Our study shows that multicenter MRI data obtained using the NIST approved protocol are comparable across sites and vendors. Some discrepancies (CV>5%) are present across sites especially for T1<250ms and T2 measurements on 3T scanners. ADC results show good comparability across sites, vendors and field strength. T1 and T2 data acquired on 1.5T scanners were more reproducible than those on 3T scanners.

These findings provide additional evidence in favor of the need of MRI harmonization across vendors to allow reliable multi-center MRI studies and ultimate transfer of MRI biomarkers to clinical practice.

Themes: Imaging techniques, Diagnostics & technology
Keywords: Quantitative MRI, Multi-center study, Phantom

Brain dynamics of improvisation

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Music is an integral part of human nature, reflecting a fundamental impulse that drives both listening and music creation. However, a clear distinction arises between performing pre-composed pieces and engaging in the spontaneous creative processes required for real-time music generation. Music improvisation involves the spontaneous creation of melodies and rhythms within a limited time frame. This unique form of musical expression demands the simultaneous management of intricate tasks, including generating and evaluating melodic and rhythmic sequences, coordinating with other musicians, and executing precise fine motor skills.

Despite the growing interest in studying this form of musical creativity, most studies struggle to capture the swift changes in brain activity, both during improvisation itself and the preparatory phase preceding it. To address this challenge, we propose a novel approach in the context of music improvisation and the spontaneous creative process. This approach involves combining the high spatial resolution of fMRI with the excellent temporal resolution of MEG to investigate the neural effects that emerge when individuals prepare for and engage in improvisation. Overall, this project aims to provide a more comprehensive understanding of music improvisation and, in a broader sense, the nature of creativity.

Themes: Neuroscience, Imaging techniques
Keywords: music improvisation, MEG, fMRI

Semi and fully Automatized image segmentation of Postmortem x-ray Computed Tomography scans.

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By now, medical imaging techniques such as x-ray computed tomography (CT) and magnetic resonance imaging (MRI) have become a fundamental part of clinical practices. Additionally, imaging is becoming an increasingly integrated research-tool in pre-clinical and basic research disciplines and postmortem scans are becoming a more common part of the modern autopsy.

Traditionally, qualitative interpretation of the images is performed by the radiologist but often lacks quantification. Imaging quantification is needed for e.g., measurement of organ size (traditionally obtained during autopsy). However, quantification is a time-consuming process often relying on image "segmentation", where anatomic structures are identified and isolated by clustering of the associated datapoints.

Currently, most image segmentation is at best semi-automatic and as such also semi-objective and therefore susceptible to human error. This study seeks to utilize Biomedisa (Lösel et al., 2020), a novel open access software specifically developed for image segmentation of biomedical and biological data, for the development of semi- and fully automatic organ segmentation of postmortem computed tomography scans. The goal of the project is to further integrate quantitative imaging as a part of the modern inquest and further establish forensic imaging as a helpful supplement to the traditional autopsy.

Themes: Imaging techniques, Imaging techniques
Keywords: Machine learning, PMCT, Forensic imaging

A proof of concept study: Imbalanced brain connectome as a possible mechanism underlying Bodily Distress Syndrome (BDSs), Multiple Chemical Sensitivity (MCS), and Long-COVID patients

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Bodily distress syndrome (BDSs) are characterized by persistent physical symptoms that cannot be explained by other somatic or psychiatric conditions. MCS is a non-allergic BDS characterized by odor intolerance, attributed to the influence of environmental chemicals in low, usually harmless doses. In recent decades, some different types of BDSs have been defined, with no clear explanation of their pathophysiology. The latest evidence of the long-covid diagnosis and strong overlaps with BDSs suggests the potential presence of new forms of somatoform disorders in the human population. Surprisingly, smell complaints were also one of the negotiable symptoms during the COVID-19 epidemic. Methods: This study included a test battery of questionnaires and paraclinical tests, including Sniffin' Sticks olfactory test, minimal mental state examination, and Sino-nasal outcome test 22. Accordingly, whole-brain computational modeling based on MRI-derived functional and structural connectomes has been employed using the 3T MR scanner. We have deliberately initiated the project with 6 MCS patients compared to 6 healthy subjects. Results: MCS group showed obvious brain structural differences in terms of 34 connectivities that were significantly different. Conclusion: Given the nature of these data, a study of brain connectivity including the main focus on the region of interest, combined with a test battery for potential biomarkers will be the next step in studying MCS, BDSs, and long-covid compared to control. We hope the method of this study can be used as a "fingerprint" in diagnosis and "treatment monitoring" by machine learning in BDSs and new diagnoses such as long-covid patients.

Themes: Imaging techniques, Neuroscience
Keywords: BDS, Long-COVID, Brain structural connectivity

Machine learning-assisted morphometrics for live/dead cell discrimination using imaging flow cytometry

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Imaging flow cytometry (IFC) is a high throughput, multiparametric technique that combines multicolor flow cytometry with fluorescence microscopy, thus integrating immunophenotyping with image analysis. Importantly, including a live/dead marker is needed to exclude dead cells that may otherwise cause false-positive results. As the number of detectors is limited, other reliable methods for viability determination could simplify IFC panels or possibly increase the extent of experiments. We propose that IFC combined with machine learning (ML) based on morphometrics offers a novel possibility to determine viability. A bone marrow sample was stained with the live/dead marker zombie green (ZG) and acquired using the ImageStream. Live and dead cells were gated based on ZG intensity and a total of 67 morphometric feature values were generated based on brightfield images. A logistic regression model was trained to predict the viability of cells using these morphometric feature values and class values based on ZG staining. Testing revealed a sensitivity of 96.2% and specificity of 95.6%. Also, principal component analysis was tried out and enabled clear separation of two cell populations. Future experiments will focus on testing the ML models further using other sample types and live/dead markers. If proven reliable, the need for a live/dead stain in IFC may become redundant, enabling simplification of IFC panels, or creating room for an additional marker.

Themes: Imaging techniques, Bioinformatics
Keywords: ImageStream, Cell viability, Machine learning

Seeing is believing: studying immunological processes in the living organism

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Lymphocytes are key players during cellular immune responses, including those in autoimmunity. Interplay of different lymphocytes takes place in so-called germinal centers (GCs). In the light zone of GCs, marked by follicular dendritic cells (FDCs), B cells are activated, selected, and regulated by different follicular T cells. The effect of this lymphocyte interplay on GC organization is poorly understood, as GC changes occur slowly and are thus difficult to capture.

We therefore developed and verified a method to study individual autoreactive GCs in the spleen in the same animal longitudinally for 15 days through an implanted abdominal imaging window (AIW) and serial intravital microscopy (IVM). Regulatory T cell reporter mice were treated with an inflammatory mediator (Resiquimod) inducing an autoimmune-like phenotype. Treatment was interrupted after 4 weeks to initiate a remission phase in autoimmune disease and the AIW was implanted to investigate GC dynamics associated with the remission.

During the remission, autoimmune-induced splenomegaly was reversed and intravital labeling of the FDC-network revealed reduction of FDC-network volume over two weeks, indicating GC contraction.

To our knowledge, this is the first study ever to use serial IVM of the spleen. We show that the gradual process of GC contraction can be detected, and upcoming analyses will clarify the disputed timing of T regulatory cell participation in GC contraction. For proof-of-principle, we benchmark our results against selected observations made by Flow Cytometry and conventional imaging analyses in cohort series.

Themes: Immune diseases, Imaging techniques
Keywords: autoimmunity, lymphocytes, 2-photon microscopy

SESSION 8

Development of the Nordic Nutrition Recommendations 2023 diet score and its association with all-cause, cancer-, and cardiovascular mortality in two Swedish cohorts

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Background: The Nordic Nutrition Recommendations (NNR2023) were updated in 2023 (NNR2023) and now encompass both human and planetary health. It is important to conceptualize these new dietary guidelines as a tool for research and to explore whether following the new guidelines is associated with lower mortality.

Objective: Develop a diet score quantifying adherence to NNR2023 guidelines and investigate the association between adherence levels and the risk of all-cause, cancer-specific, and cardiovascular-specific (CVD) mortality.

Method: Based on the NNR2023 guidelines, the diet score encompassed fifteen food groups. Food components were scored proportionally to a score ranging from 0 to 1, where 0 indicates no adherence and 1 indicates full adherence. Associations with mortality will be investigated in the Cohort of Swedish Men (n = 48,850), men aged 45-79, and the Swedish Mammography Cohort (n = 39,984), women aged 48-83. Detailed dietary and lifestyle information was collected in 1997, 2008/2009, and 2018/2019. Mortality data will be obtained from the Swedish National Patient Register and the Cause of Death Register. Cox proportional hazards regression models, with age as the underlying timescale, will estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between NNR2023 adherence and all-cause, cancer, and CVD mortality.

Perspectives: Developing a quantifiable diet score based on NNR2023 guidelines, offers a practical tool to provide crucial insights and a nuanced exploration of how different dietary patterns impact mortality rates, aligning with the broader goals of moving in a more sustainable direction and improving public health.

Themes: Epidemiology, Health Education
Keywords: Dietary guidelines, Epidemiology, Sustainable diet

Non-specific effects following COVID-19 vaccination

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Background: The national post-licensure surveillance of adverse events following COVID-19 vaccination solely captures information on non-specific symptoms experienced by vaccinated individuals. While most of these non-specific symptoms, such as fatigue, muscle pain, headache, impaired memory, and nausea are common and often do not lead to specific diagnoses, it is unknown whether these symptoms occur more frequently among vaccinated individuals than expected from background rates in the general population. A similar situation happened when the human papillomavirus (HPV) vaccine was introduced and the consequences for vaccine uptake were immense. Thus, to ensure people opt for vaccines, this PhD project aims to investigate the associations between COVID-19 vaccines and non-specific symptoms.

Materials: The project is based on data from the population-based Danish BiCoVac Cohort in conjunction with data from the national registries. A random sample of 911,613 Danish citizens between the ages of 16 and 65 was invited to participate. Data were collected in four questionnaires spanning from May 2021 to August 2022. The baseline survey was distributed before the general population was offered the vaccine to obtain information on lifestyle, health, and well-being as well as pre-vaccination symptoms. The follow-up questionnaires focused on COVID-19 vaccination, COVID-19 infection, and non-specific symptoms. Non-specific symptoms were identified using the 25-item Bodily Distress Syndrome (BDS) Checklist.

Results: Pending.

Perspective: The project will be a valuable add-on to the spontaneous registration of adverse events conducted by the Danish Authorities.

Themes: Epidemiology, Public health
Keywords: COVID-19 vaccination, Non-specific symptoms, Epidemiology

Stroke severity and other predictors of venous thromboembolism in stroke patients – a population-based cohort study

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Introduction: Venous thromboembolism (VTE) frequently occurs after stroke, particularly within the first 3 months after diagnosis, and post-stroke VTE is associated with increased mortality. Stroke severity is a known predictor of an adverse prognosis. However, its ability to predict VTE is uncertain. Moreover, knowledge on other predictors of post-stroke VTE is sparse.

Methods: In a population-based cohort study, we identified patients (≥ 18 years and free of recent VTE) with first-time ischemic stroke (N = 129.345) or intracerebral hemorrhage (N = 16.887) from 2004 to 2021. In separate analyses for each stroke subtype and follow-up periods (7 days and 3 months), we computed cumulative incidence proportion and unadjusted subdistribution hazard ratios (SHRs) for VTE for each potential predictor. Specifically for stroke severity, measured by Scandinavian Stroke Scale, we calculated adjusted SHRs in two multivariable models including (1) age and sex, and (2) predictors identified in the univariable analyses.

Results: In univariable analyses, the SHRs for stroke severity, active cancer and previous VTE ranged from 2 to 5 for both stroke subtypes and both follow-up periods. Multivariable analyses, adjusting for age, sex, and a selection of predictors, showed no substantial alterations in the estimates for stroke severity.

Discussion: Stroke severity, active cancer and previous VTE strongly predict post-stroke VTE in stroke patients within 7 days and 3 months following diagnosis. Stroke severity remains an independent predictor of VTE after adjustments and may be used to identify patients at higher risk of VTE in whom thromboprophylaxis should be considered.

Themes: Epidemiology, Cardiology
Keywords: Stroke, Venous thromboembolism, Stroke severity

Deep learning approach to integrate continuous glucose monitoring in cardiovascular risk assessment for people with diabetes

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Background: Diabetes Mellitus is a growing public health challenge globally, and is associated with a significant burden of complication, including cardiovascular diseases (CVD). An association is established between glycemic variability and cardiovascular health. However risk assessment tools to predict CVD risk in people with diabetes do not accommodate the rise in wearable technologies such as continuous glucose monitoring (CGM) devices. New analytical methods are needed to exploit the full potential of data. Deep learning plays a crucial role in this, but transferring knowledge from epidemiological cohorts to clinical cohort studies has not been exploited to date.

Aim: This project aims to unravel clinically relevant associations between glycemic control and cardiovascular (CV) risk and to translate this knowledge into risk assessment tools for people with diabetes.

Methods: We will investigate the current glucose prediction models and transfer learning, i.e. the reuse of models across different tasks, from the perspective of algorithmic fairness. Novel patterns in CGM data associated with CV risks will be studied, by repurposing models and using explainable artificial intelligence methods. We will analyse longitudinal predictors and to predict CVD incidence in people with type 1 diabetes. Furthermore, we will predict blood glucose spikes in order to tailor diet recommendations and assist risk assessments of CVD in people with type 2 diabetes.

Perspectives: The proposed project will contribute with valuable insight in how CGM data can be used in CVD risk assessments and show the potential in knowledge transfer between studies.

Themes: Epidemiology, Statistics
Keywords: Diabetes, Continuous Glucose Monitoring, Machine Learning

Integration of fundus photographs in risk assessment of cardiovascular disease using deep learning

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This PhD project develops deep learning methods to predict cardiovascular disease (CVD) risk in type 1 diabetes patients, incorporating retinal fundus photographs into the risk assessment process. The Steno T1 Risk Engine estimates CVD risk using traditional statistical methods based on demographic, lifestyle factors, and clinical measurements. However, it cannot process longitudinally collected images. The PhD project aims to predict CVD risk markers and incidence using fundus photographs and extend the Steno T1 Risk Engine with explainable artificial intelligence methods. Additionally, the project evaluates the fairness of the developed models and applies transfer learning and synthetic data generation to address potential biases. The PhD project combines deep learning and classical epidemiological methods on data sources from a Dutch cohort and a Danish diabetes clinic, complemented with register-based information. This research aims to enhance the integration of diverse data sources in clinical CVD risk assessment.

Themes: Epidemiology, Statistics
Keywords: Cardiovascular disease risk, Deep learning, Diabetes

Impact of self-reported health on the risk of opioid use after total hip arthroplasty in patients with osteoarthritis

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Background: Opioids are commonly used for short-term post-surgical pain management after total hip arthroplasty (THA), however, some patients continue to use opioids for up to one year after THA. We examined the association between preoperative self-reported health (SRH) and the risk of continued opioid use after THA in patients with osteoarthritis.

Materials and Methods: We used data from several Danish medical registries. Information on SRH (either good or poor) among 4,155 THA patients (2010-2018) was available from the Danish National Health Survey. Opioid use was defined as the redemption of ≥2 prescriptions 1-12 months after THA. We calculated prevalences of opioid use with absolute differences and prevalence ratios (aPR) (with 95% confidence interval) using log-binomial regression adjusting for sex, age, comorbidities, and education. Furthermore, we calculated the morphine milligram equivalent (MME) dose in the year after THA. Analyses were performed overall and by preoperative opioid use (defined as ≥1 opioid dispensing 0-6 months before THA).

Results: 3,283 patients reported good SRH and 872 reported poor SRH. Prevalence of opioid use was overall 13% for good SRH vs. 36% for poor SRH (aPR: 2.37, 2.04-2.76). For preoperative non-users, the prevalence was 6% for good SRH vs. 14% for poor SRH (aPR: 2.22, 1.63-3.04). For preoperative users, the prevalence was 31% for good SRH vs. 54% for poor SRH (PR: 1.66, 1.40-1.98). The median MME dose was 600 for good SRH vs. 1200 for poor SRH.

Conclusion: Patients with poor SRH were not only at higher risk of continued opioid use but also tended to consume a noticeably higher MME dose in the year after THA than patients with good SRH.

Themes: Epidemiology, Pharmacology
Keywords: Inequality, Osteoarthritis, Opioid

Cardiovascular safety of using non-steroidal anti-inflammatory drugs for gout: A Danish nationwide case-crossover study

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Objective: In patients with gout, non-aspirin non-steroidal anti-inflammatory drugs (NSAIDs) could be both cardiovascular beneficial, due to their anti-inflammatory actions, and cardiovascular hazardous, due to their prothrombotic, hypertensive, and proarrhythmic side effects. We, therefore, examined the risk of cardiovascular events associated with NSAID use in patients with gout.

Methods: We conducted a nationwide, population-based case-crossover study of all Danes ≥18 years of age with first-time gout during 1997–2020, who experienced a cardiovascular event (myocardial infarction, ischemic stroke, congestive heart failure, atrial fibrillation/flutter, or cardiovascular death) (n=59,150). The exposure was use of NSAIDs, overall and according to type (ibuprofen, naproxen, or diclofenac). We used the dates 300, 240, 180, and 120 before the outcome date as reference dates. We used the Mantel-Haenszel method to calculate odds ratios (ORs) with 95% confidence intervals (CIs) of the association between NSAID use and cardiovascular events.

Results: NSAID use was overall associated with 12% decreased odds of a cardiovascular event (OR=0.88, 95% CI: 0.85–0.91). This decreased odds ratio was observed for the use of ibuprofen (OR=0.92, 95% CI: 0.88–0.97) and naproxen (OR=0.85, 95% CI: 0.74–0.97), but not for the use of diclofenac (OR=0.97, 95% CI: 0.90–1.05). NSAID use overall was associated with decreased odds of all the individual components of the composite outcome.

Conclusions: NSAID use was not associated with an increased cardiovascular risk when used in patients with gout. Ibuprofen and naproxen appeared to have better cardiovascular risk profiles than diclofenac.

Themes: Epidemiology, Cardiology
Keywords: NSAIDs, Cardiovascular risk, Gout

Cardiovascular autonomic dysfunction association with arterial stiffness: The Maastricht study

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Background: The association between cardiovascular autonomic dysfunction (CAN) and increased arterial stiffness is well-documented among persons with diabetes. This study investigated the association between cardiovascular autonomic function and arterial stiffness in a population at different levels of diabetes risk.

Methods: CAN assessments by heart rate variability (HRV) measures were obtained from 1801 participants at the baseline examination of the Maastricht study. HRV indices were: standard deviation of inter-heartbeat intervals (SDNN) during 24-hour electrocardiogram recordings. Aortic stiffness and carotid stiffness were assessed by carotid-femoral pulse wave velocity (PWV) and carotid artery distensibility (carDC), respectively. We performed a cross-sectional analysis based on multiple linear regression. Model 1 was adjusted for age, sex, education, mean arterial pressure, and diabetes status. In model 2, we further adjusted for physical activity, smoking, alcohol, body mass index, HbA1c, triglycerides, total-to-high density lipoprotein cholesterol ratio, lipid-modifying- and antihypertensive medication.

Results: Forty-eight per cent of the study population were women. The median (25th & 75th percentile) age was 61 years (55; 66), while the median SDNN, PWV and carDC were 131 ms (107; 156), 8.56 m/s (7.44; 10.00), and 13.8 10^-3/kPa (10.7, 17.4), respectively. For each 10 ms lower SDNN, an association with 0.5 % (CI: 0.77; 0.33) higher PWV and 0.86 % (CI: 0.47, 1.23) lower carDC was seen. Associations did not change materially upon adjustment for the confounders in model 2.

Conclusion: CAN, measured as lower HRV, is associated with higher aortic and carotid stiffness.

Themes: Epidemiology, Cardiology
Keywords: Diabetes complication

Faecal microbiota transplantation for patients with diabetes mellitus type 1 and severe gastrointestinal neuropathy: a randomised, double-blinded safety and pilot-efficacy study.

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Background: Diabetes mellitus type 1 (DM1) is often complicated by gastrointestinal symptoms such as diarrhea, nausea, vomiting, abdominal pain, constipation, and faecal incontinence. These may be caused by intestinal neuropathy which predisposes to abnormal amount and composition of microbiota in the gut. Fecal microbiota transplantation (FMT) from a healthy donor to a patient could potentially change the microbiota in the gut and reduce gastrointestinal symptoms.

Methods: The study includes 20 patients with DM1 and chronic diarrhea. It is a 4-week, randomized, double-blinded, placebo-controlled pilot trial of oral FMT versus placebo. This is followed by open label FMT for an additional 4 weeks.

Results: We aim to evaluate if oral intake of FMT capsules is safe and well tolerated in patients with DM1, including those with prolonged gastric emptying and small intestinal transit. Furthermore, we want to access if FMT changes the microbiota of the colon and whether FMT is superior to placebo in reducing episodes of diarrhea. The last patient visit has been completed in October 2023 and results from the project are being analyzed.

Conclusion: This study will help evaluate the feasibility and safety of FMT against chronic diarrhea in patients with DM1.

Themes: Gastroenterology and hepatology, Endocrinology
Keywords: FMT, Diabetes type 1, Microbiota

Periodontitis: An Underappreciated Diabetes-related Complication

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Background: This study aimed to examine the clustering of periodontitis with other diabetes-related complications and explore pathways linking diabetes-related complications with common risk factors.

Methods: The sample included 2,429 U.S. individuals across 3 cycles of the National Health and Nutrition Examination Survey (NHANES). The structural equation modelling (SEM) approach included direct and mediated pathways from risk factors to diabetes-related complications, a latent construct comprising periodontitis, cardiovascular diseases, proteinuria, and hypertension. Covariates included age, sex, socioeconomic status, smoking, physical activity, healthy diet, alcohol consumption, haemoglobin A1c (HbA1c), dyslipidemia, and body mass index (BMI). Sensitivity analyses were performed considering participants with overweight/obesity and restricting the sample to individuals without diabetes.

Results: Periodontitis was found to be clustered with other diabetes complications. Higher HbA1c levels and BMI, older age, healthy diet, and regular physical activity were directly associated with the latent variable diabetes-related complications. A healthy diet and BMI had a total effect on diabetes-related complications. Sensitivity analysis considering participants with overweight/obesity and without diabetes showed consistent results.

Conclusion: Periodontitis co-occurs with multiple diabetes-related complications. For dentists, the presence of oral diseases may serve as a screening tool for other complications. For other health professionals, patients with diabetes-related complications should be encouraged to undergo an oral health screening for inflammation-related diseases.

Themes: Epidemiology, Dentistry
Keywords: Diabetes

SESSION 9

Pubertal development and social anxiety disorder in adolescents

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Background: For decades, the onset of puberty has declined for girls and probably also in boys. Age at onset of puberty might be associated with social anxiety disorder (SAD). SAD emerges in early adolescence, affecting 3-7% of males and 3-11% of females. We hypothesize that earlier and faster pubertal development are associated with higher risks of SAD due to increased self-awareness, fears standing out from peers, and hormonal and neurological changes.

Methods: The study population is the Puberty Cohort, a sub-cohort of the Danish National Birth Cohort (DNBC) children born from 2000-2003 (N=15,819) with information on pubertal markers from years 11-18 and modelled by individual non-linear mixed effect growth models. Of these 5,203 girls and 3,388 boys participated in the 18-year DNBC follow-up and responded to the Spence Children's Anxiety Scale subscale. SAD diagnoses and psychotropic treatment are retrieved for the entire cohort from Danish registries. Multiple linear regression and Cox regression are used to relate pubertal development to SCAS subscale scores for SAD, SAD diagnosis and treatment, adjusted for maternal age at delivery, maternal age at menarche, maternal worries in pregnancy, parental psychiatric disease, socioeconomic status, adverse events, and child emotional problems at age 7.

Conclusion: The results will provide insight into whether earlier and faster puberty might increase risk of SAD. Identifying adolescents at higher risk of SAD, underscores the need to address modifiable causes of altered puberty. This is particularly important given the challenging nature of treating SAD once it has developed.

Themes: Epidemiology, Mental health
Keywords: Pubertal development, Adolescence, Social anxiety disorder

Genetic ancestry impacts the predictive accuracy of family history and polygenic scores

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Background: Family history (FH) and polygenic scores (PGS) have received attention for their potential to enhance the precision of clinical prediction models. However, recent studies revealed that the accuracy of PGS decreases significantly when applied to individuals of non-European or admixed genetic ancestries. Generally, FH measures are considered to be more robust.

Methods: Our study aims at assessing the predictive power of PGS and two metrics of FH for various psychiatric disorders across the genetic ancestry continuum in Denmark. Data was obtained from Danish registers, the iPSYCH2015 and the ANGI-Denmark cohort. Family genetic liabilities (FGL) were estimated for 7 psychiatric disorders. The predictive performance of PGS, binary FH and continuous FGL were compared in relation to the genetic distance from individuals of Danish genetic ancestry.

Results: On average, the prediction accuracy of PGS decrease significantly by 91% when applied to individuals most genetically distant from the Danish centre (compared to individuals of Danish genetic ancestry). The precision of binary FH experienced a minor decline of 2% in individuals with the greatest genetic distance from individuals of Danish genetic ancestry. Only the continuous metric FGL exhibited a modest increase in predictive power; rising by 15%.

Conclusion: Our findings confirm that genetic diversity affects the predictive power of PGS for psychiatric disorders. Furthermore, our results provide new insight into the impact of genetic heterogeneity on FH. It is essential to continue investigating the impact of genetic ancestry on prediction models to develop more robust prediction models not suffering from racial bias.

Themes: Epidemiology, Mental health
Keywords: Genetic epidemiology, Genetic ancestry, Prediction accuracy

Mortality in Myasthenia Gravis: A nationwide population-based cohort study over 35 years

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Background: Myasthenia Gravis (MG) is an autoantibody-mediated neuromuscular disease characterised by neuromuscular transmission impairment. This results in variable degrees of muscle fatigability with a possible fatal outcome. Advanced specialized diagnostics and novel treatment modalities have presumably improved MG prognosis. However, it remains unclear, if patients with MG still carry an excess mortality rate compared to the background population.

Aims: To determine if patients with MG have an increased mortality rate compared to the background population. Further, we aim to study underlying causes of death and determine if death is due to disease itself, associated treatment complications or comorbidities.

Methods: We will study the mortality rate in the MG case population compared to the mortality rate in the corresponding control population, individually matched 1:10 on age, sex and diagnostic index date, based on individual-level linkage of data from nationwide health registries from 1985 to 2020. In earlier Danish studies, the diagnosis of MG has been found to have a high positive predictive value of 92.9% (CI 84.3-97.9). Everyone will be followed from the diagnostic index date in the case group until death, emigration, or end of study period, whichever occurs first. Cox regression analysis will be used to calculate hazard ratios of death with 95% confident intervals by total follow-up time after diagnostic index date. Comorbidities will be considered and level of comorbidity addressed with the Charlson Comorbidity Index.

Results: The results are impending and will be presented in 2024.

Themes: Epidemiology, Neuroscience
Keywords: Myasthenia Gravis, Mortality, Epidemiology

Loneliness, social isolation and all-cause mortality among persons with type 2 diabetes: A 5-year Danish population-based prospective cohort

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Background: Loneliness and social isolation represent distinct aspects of social disconnectedness, both of which are associated with excess mortality. However, the effects of loneliness and social isolation on mortality in persons with type 2 diabetes remain unclear. This study aims to investigate how loneliness and social isolation predict all-cause mortality in persons with type 2 diabetes.

Design: A 5-year prospective cohort study linking representative data from the 2017 Danish National Health Survey (n=129.319) with administrative records. An algorithm developed by Steno Diabetes Center Copenhagen Data will be used to identify persons with type 2 diabetes. Exposure to loneliness and social isolation are derived from survey data using the Three-Item Loneliness Scale and a modified version of the Valtorta Social Isolation Index. The final analytical sample will be approximately 7.500 observations.

Methods: Cox proportional hazards regression will be used to examine the longitudinal relationship between loneliness, social isolation, and excess mortality. The models will be adjusted for sex, age, education, comorbidity and duration of type 2 diagnosis. Stratified analyses will investigate differences on sex and age, and interaction will be used to detect any synergetic association between loneliness and social isolation on excess mortality.

Expected results: A meta-analysis by Holt-Lundstad and colleagues suggests that loneliness increases the risk for all-cause mortality by OR=1.26 [95 % CI: 1.03-1.53] and the effect of social isolation on all-cause mortality is OR=1.29 [95 % CI: 1.06-1.56]. We anticipate similar estimates in our study of persons with type 2 diabetes.

Themes: Epidemiology, Mental health
Keywords: Social disconnectedness, Type 2 diabetes, All-cause mortality

Boosting legume consumption in Denmark: the impact of information

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The 2021 Danish Dietary Guidelines for health of people and the planet recommend 100 g of precooked legumes daily; a sharp contrast to the estimated 2 g/day of legumes consumed today. A survey conducted by Aarhus University in 2021 revealed that the intention to increase legume consumption in the future was primarily hindered by a lack of knowledge about legumes. Public mass information campaigns on the Danish dietary guidelines have historically been employed to educate consumers, but low adherence persists. The daily inclusion of 100 g of legumes aims to mitigate diet-induced diseases and reduce the environmental impact of foods. However, it remains uncertain whether Danes are inclined to increase their legume consumption if they receive more information on health and climate benefits of legume consumption. In 2023, we therefore conducted a survey similar to that from 2021, but with the major difference that participants were randomized to receive information on 1) the health benefit of legumes, 2) the climate impact of legumes, or 3) no additional information before answering the survey. We aimed to evaluate the impact of providing information about legumes on participants' intentions to increase their legume consumption in the future. We sampled 1022 participants to replicate the distribution of specified demographic factors in the general Danish population. The survey included questions on sociodemographic, generic food habits, and consumption of and knowledge about legumes including barriers and drivers for consumption. Data collection concluded on August 8, 2023, and preliminary results will be presented at the 2024 PhD-Day.

Themes: Epidemiology, Public health
Keywords: National dietary guidelines, Dietary pulses, Consumers behavior

Prevalence and Patient Characteristics of Ectodermal Dysplasias: a nationwide population-based study

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Background: Ectodermal dysplasias (ED) constitute a group of rare genetic disorders with hypodontia, hypotrichosis, and hypohidrosis as cardinal features. To date, population-based studies into the epidemiology of ED are lacking. We aimed to identify a large cohort of ED patients to study the prevalence and characteristics.

Methods: We performed a nationwide, registry-based study identifying patients with ED. We applied a three-level search of the Danish National Patient Registry for diagnosis codes indicative of ED from Jan 1, 1995 to Aug 25, 2021. We also included the RareDis Database, the Danish Database of Genodermatoses, and local databases. Searches were followed by diagnosis validation and data collection through medical chart reviews, resulting in the final nationwide ED patient cohort.

Results: We identified 844 patients suspected of ED, of whom 791 (93.7%) had medical records available for review. We included 396 (50.1%) reviewed cases in the final cohort. The combined positive predictive value for ED-specific ICD-10 codes was 67.0% (95% CI: 62.7–71.0%). During 1995–2011, the estimated birth prevalence per 100,000 live births was 14.5 for all EDs and 2.8 for X-linked hypohidrotic ED. A genetic diagnosis was available for 241 (61%) patients, including EDA (n=100), IKBKG (n=55), WNT10A (n=21), TRPS1 (n=18), and other rare genetic causes.

Conclusions: We identified and characterized a validated nationwide cohort of ED patients with detailed clinical and molecular data, providing a unique resource for future ED research. The low PPVs of the search algorithms emphasize the importance of diagnosis validation. Our prevalence estimates are lower than previously reported.

Themes: Epidemiology, Paediatrics
Keywords: Ectodermal dysplasia, Genodermatoses, Population-based studies

Associations between social disconnectedness and subsequent medical conditions, and the role of co-existing mental disorders

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Background: Social disconnected individuals are at substantially increased risk of developing several medical conditions, but the current evidence base is limited by a narrow focus on specific diseases. Additionally, sample sizes restraints have hindered investigation of sex differences and the role of co-existing mental disorders. Therefore, we aim to provide a comprehensive overview of the associations between three distinct aspects of social disconnectedness and 11 broad categories of medical conditions with investigation of potential sex differences and potential interaction with co-existing mental disorders.

Methods: We will conduct a cohort study of participants from the Danish National Health Survey in 2013 or 2017 with follow-up until 2021. Survey data on social disconnectedness (loneliness, social isolation, and low social support) will be linked with register data on medical conditions in 11 broad categories (mental disorders; all-cause dementia; circulatory, endocrine, pulmonary, gastrointestinal, urogenital, musculoskeletal, hematologic, and neurologic conditions; and cancer). We will apply Poisson regression to estimate incidence rate ratios and incidence rate differences using marginal standardization after adjustment for age, sex, calendar year, country of birth, educational level, income, and wealth.

Results: We will report incidence rate ratios, incidence rate differences, potential sex differences, and potential interaction with co-existing mental disorders.

Conclusion: This study may lead to identification of relevant target groups for preventive interventions and provide knowledge on the disease burden associated with social disconnectedness.

Themes: Epidemiology, Public health
Keywords: Social epidemiology, Disease incidence,

Physical activity patterns in Danish parous women. A population-based survey linked to Danish national registries

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Background: Regular physical activity (PA) is linked to numerous health benefits for mothers as well as their children. Nonetheless, assessments of PA patterns among parous women are still largely unexplored.

The aim of the present study was to examine the proportion of parous and nulliparous women adhering to the PA guidelines established by the World Health organization (WHO) and if there was a difference between the two groups. Furthermore, to show the habitual PA profile divided into vigorous, moderate, light, and sedentary PA in the two groups.

Methodology: In this cross-sectional population-based study, a sample of 27,668 women aged 16 to 40 years was drawn from the 2021 Danish National Health Survey and linked with childbirth data obtained from the Danish National Birth Registry. The primary outcome was weekly hours of moderate to vigorous PA. The secondary outcome was four distinct PA profiles. Data analysis involved binomial regression models using STATA software.

Results: Of the 27,668 women, a total of 20,026 was included; 9,338 (46.6%) parous women and 10,591 (53.1%) nulliparous women. The prevalence proportion of parous and nulliparous women who did not adhere to the PA guideline recommended by the WHO was 63.8% and 51.3%. This corresponds to an absolute difference of 12.5 percentage points (95% CI: 11.1;13.8). Secondary, 66.2% of parous women had light PA as their habitual PA.

Perspectives: Danish parous women exhibit lower adherence to the international PA guideline and engage in less moderate and vigorous PA compared to nulliparous women. This highlights the need for future research to develop strategies for promoting increased PA among parous women.

Themes: Epidemiology, Gynecology and obstetrics
Keywords: Postpartum, Physical Activity, Parous women

School well-being and academic performance of children with juvenile idiopathic arthritis – a national register-based study

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Objectives: We aimed to investigate how school well-being (SWB) and academic performance of children with juvenile idiopathic arthritis (JIA) compare to their peers on a national level using the Danish national registers. Further, we investigated the potential influence of socioeconomic status (SES).

Methods: A population wide, register-based, cross-sectional study was performed. We compared the results of children with and without JIA in the Danish National Well-being Questionnaire (DNWQ), the National Danish School Testing (NDST), and the 9th grade final school marks in Danish and mathematics.

The results were analysed using adjusted ordinal logistic regression (SWB) and linear regression (tests and marks).

Results: We included in separate cohorts a total of 1,313,378 DNWQs (505,340 unique children), 2,882,148 NDST results (812,461 unique children), and 9th grade final marks of 581,804 children. Of these children 1,042, 1,541 and 1,410 children respectively fulfilled the criteria of JIA.

Children with JIA reported SWB comparable to their peers except for the question “Do you perform well in school?” (OR=0.89 [95% CI 0.81; 0.99]). In the NDST the children with JIA did just as good as their peers except for slightly lower scores in 6th grade mathematics (adjusted mean difference -1.73 [95% CI -3.33; -0.13]). We found no differences in the 9th grade final marks in neither Danish nor mathematics.

Stratifying the analyses on SES showed no significant differences in the associations.

Conclusion: Overall, children with JIA report SWB comparable to that of children with no JIA and perform equally well in school as children without JIA.

Themes: Paediatrics, Epidemiology
Keywords: Juvenile idiopathic arthritis, School well-being, School performance

SESSION 10

Comparing parent and child cognition in families with parental schizophrenia or bipolar disorder: a developmental perspective from the child was 7 to 11 to 15 years of age

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Background: Neurocognitive deficits are core features of both schizophrenia (SZ) and bipolar disorder (BP). Research has found that cognitive impairments are early vulnerability markers for these disorders. Children at familial high risk (FHR) for SZ or BP show cognitive impairments that lie in between the respective patient group and healthy controls.

Heritability of general cognitive ability increases significantly and linearly with age, suggesting a genotype-environment correlation. However, the intergenerational transmission of cognitive abilities is still an under-researched field both in general and in families with severe mental disorders.

By using longitudinal data from the child was 7 to 11 to 15 years of age, this study aim to assess the transmission of intelligence, processing speed and verbal working memory from both biological parents to their offspring in families with parental SZ or BP, or none of these disorders.

Methods: This study is part of The Danish High Risk and Resilience Study – VIA, a longitudinal nationwide cohort of children with no (PBC; 200), one or two parents diagnosed with SZ (FHR-SZ; 202) or BP (FHR-BP; 120). At age 7, 522 children and both biological parents were assessed (VIA 7). Parents and children underwent the same battery of tasks from validated neurocognitive measures. At age 11, the children were

assessed again (VIA 11). Now at age 15, the children are assessed for the third wave of the study (VIA 15).

Results: Data collection for VIA 15 is ongoing and will be finalized in the spring of 2024.

Themes: Mental health, Epidemiology
Keywords: Familial High Risk, Longitudinal Study, Cognition

Health Anxiety in the Danish Population: Is health anxiety associated with reduced heart rate variability?

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Background: Health anxiety (HA) is characterised by preoccupation with and an intensive fear of having a serious illness, despite showing no objective medical signs of illness. Heart rate variability (HRV) is a reflection of balance in the autonomous nervous system, and is found to be decreased in persons with different forms of anxiety. Having a reduced HRV is asscociated with an increased risk of cardiovascular disease. The association between HA and HRV is yet to be studied in large population studies.

Method: Data from DanFunD study with 9656 participants will be used – 2199 of which partook in measurement of HRV. HA cases will be identified using Whiteley-6-R, and SCL-90 to identify other types of anxiety. Both will be verified using diagnostic interview data. Relevant variables of HRV will be analysed to measure the function of the autonomic nervous system.

The aim of the project is to 1) examine the prevalence of HA in a large Danish cohort from the general population, and 2) explore possible associations between functions of the autonomous nervous system (HRV) and HA. We aim to compare individuals with HA to a) individuals without HA and b) to individuals with other types of anxiety.

Hypotheses:

- 3-4% of the examined population will fulfil criteria for moderate to severe HA
- Individuals with HA have reduced HRV compared to participants without HA
- Individuals with HA have reduced HRV to the same extent as individuals with other types of anxiety

Significance: Knowledge of HRV in HA patients will allow for a more nuanced understanding of the physiological mechanisms of HA, which may eventually contribute to better treatment.

Themes: Mental health, Cardiology
Keywords: Health anxiety, Heart rate variability, Autonomous nervous system

Experiences with End-of-life (EOL) for Patients with Pre-Existing Severe Mental Disorders – An Interview Study

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Introduction: The end-of-life (EOL) period causes suffering for patients and their relatives. For patients with severe mental disorder (SMD) complex psychosocial challenges are likely to add to the demanding situation.

The aim of this study is to investigate patients', relatives', General Practitioners' (GPs) and Specialised Palliative Care (SPC) professionals' experiences with EOL trajectories.

Methods: The study consists of semi structured interviews with 6-10 patients, their relatives, GPs, and SPC professionals in palliative teams or in hospice in Central Region Denmark. Hence, between 24 and 40 interviews are planned. A thematic analysis finding main themes in participants voices and wishes for EOL are planned.

Results: Until now, four interviews with patients, one interview with a relative and four interviews with SPC professionals have been conducted. Preliminary analysis show that patients want transparency in the information about expected remaining lifetime and that they want to plan their EOL period in advance. Some of them experienced that SPC professionals did not ask about their SMD, although every patient wanted to talk openly about their psychiatric diagnose with SPC professionals. The professionals experienced a lack of knowledge about SMD which create uncertainty. They all expect complex trajectories when the patient had an SMD.

Perspectives: The data collection will be ongoing until data saturation. Interviews will cover further challenges and strengths and hopefully provide insight into how to improve the quality of EOL to patients with SMD.

Themes: Mental health, Qualitative research
Keywords: End of Life, Quality of care, Psychiatry

Antidepressant use in parents having a child with Down syndrome.

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Background: Down syndrome (DS) is associated with cognitive challenges and increased morbidity, and thus poses significant challenges for new parents. The role of the healthcare system in supporting these parents is crucial, but is difficult to design and examine. As a proxy of parental wellbeing, we examined the mental health of Danish parents raising children with DS.

Aim: This project aims to assess antidepressant usage, as an indicator of mental health, in parents with a child with DS compared to the general population.

Method: This population-based cohort study used Danish health registries to analyse parents of children with DS born from 1995 to 2018, comparing them to parents of children without DS from the same period. The primary outcome was two or more redeemed prescriptions for antidepressants within two years after the child's birth. We did separate assessments of mothers' and fathers' antidepressant usage and we excluded parents with prior antidepressant prescriptions.

Results: Mothers exhibited age-adjusted unaffected odds ratios (ORs) of 1.0 (95% CI: 0.6-1.4), whereas fathers had increased ORs of 1.8 (95% CI: 1.1-2.6) for antidepressant use within two years of the child's birth when the child had DS, compared to the cohort.

Discussion: This study sheds light on the impact of having a child with DS on parental mental health, with an emphasis on potential gender differences. Knowing that fathers of children with Down syndrome are at particular risk of depression is new important knowledge for health providers and society.

Themes: Mental health, Epidemiology
Keywords: Down syndrome, Mental health, Parenting

Can health anxiety be differentiated from other anxiety phenomena in adolescence?

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Health anxiety is characterized by excessive rumination about the possibility of having a serious disease. In this study we explored if health anxiety differed from other anxiety phenomena in adolescence regarding depressive and physical symptoms, bodily dissatisfaction, the use of health care services and health-related quality of life (HRQoL).

Data from the 16/17-year follow-up (16-17 years old, N = 2521) from the general population-based Copenhagen Child Cohort 2000 was used. Self-report questionnaires were used to assess health anxiety, anxiety, depressive and physical symptoms, bodily dissatisfaction, and HRQoL together with register data on health care utilization. Four groups were created: 1) no health anxiety or anxiety, 2) only health anxiety, 3) only anxiety, and 4) both health anxiety and anxiety. Differences between the four groups regarding depressive and physical symptoms, bodily dissatisfaction, health care use and HRQoL were examined using general linear models.

A total of 10.4% adolescents were defined as having high health anxiety, and among these almost half (4.6%) reported having only high health anxiety without other anxiety symptoms. The health anxiety group (group 2) displayed significantly more physical symptoms, fewer depressive symptoms and higher health care utilization compared to group 3.

Our results suggest that health anxiety can be recognized as a separate construct in adolescence, associated with several negative health-related aspects. Research is needed to ensure adequate identification and treatment of health anxiety in this age group.

Themes: Mental health, Epidemiology
Keywords: Health anxiety, Psychiatry, Adolescents

Somatic Health Challenges and Social Factors in Forensic Psychiatric Patients: A Study on Health Inequities and Health Literacy

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Introduction: Ethnic minority groups face unique systemic barriers that impact mental and physical health. This study aims to investigate the impact of ethnicity on GP relationship and various health metrics within a Danish forensic psychiatric context.

Methods: 75 forensic psychiatric inpatients from Central Region Denmark were recruited for the study. 57 patients were of Western ethnicity (primarily of Danish descent) and 18 of non-Western ethnicity (primarily immigrants). Data was gathered through health questionnaires, clinical records, and -tests to examine a range of variables including family history, self-rated health, GP relationships, and key health indicators such as weight, smoking habits, HbA1c, and D-vitamin status.

Results: The study found notable ethnic disparities across various metrics. Patients of non-western ethnicity reported poorer self-rated health and less favorable relationships with their GPs compared to their Western counterparts. In terms of health indicators, non-western patients had lower mean weight, fewer daily smokers, but elevated levels of HbA1c and lower D-vitamin statuses.

Conclusion: Despite making up only 24% of the sample, the high prevalence of non-western ethnicities is noteworthy, given their estimated 8.9% representation in the broader Danish population. Our findings suggest a complex interplay of factors, including systemic barriers and cultural considerations, affecting mental health and healthcare experiences among these groups.

This study points to the need for greater emphasis on ethnic minorities in research exploring the complex interplay between mental health and healthcare.

Themes: Mental health, Epidemiology
Keywords: Health inequity, Forensic psychiatry, Ethnicity

Social inequality in mental health among Danish 15-year-olds

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Background: In Denmark, adolescents' use of medication, mental disorder diagnosis, and self-reported poor mental health have increased during the last decades. A social gradient in mental health is well-known. However, little is known about the changes over time in the association between social status and mental health in adolescents.

Method: In two cohorts, VestLiv and FOCA, depressive symptoms were measured with a 4-item version of the Center for Epidemiological Studies-Depression scale in 2004 and 2017. Subjective social status (SSS) was measured with the MacArthur Scale and socioeconomic status (SES) was measured as parents' educational level and household income.

The prevalence of depressive symptoms was stratified on sex, SSS and SES, and the association between SSS and depressive symptoms was analysed with logistic regression.

Results: The prevalence of depressive symptoms increased from 2004 to 2017 in females (39% to 62%) and males (30% to 44%). In adjusted analyses, associations between SSS and depressive symptoms showed a social gradient in both 2004 and 2017 when comparing adolescents rating middle SSS with low SSS (OR= 2.61(95% CI: 1.90; 3.57) and 2.26(95% CI: 1.88; 2.71)) and high SSS (0.79(95% CI: 0.64; 0.98) and 0.68(95% CI: 0.61; 0.75)). Further adjusted analyses, including register data on SES, medication use and mental disorder diagnosis, will be conducted before the conference.

Conclusion: The prevalence of depressive symptoms in two different cohorts increased from 2004 to 2017, especially among females. A strong association was found between SSS and depressive symptoms. Further associations between social status and mental health are yet to be explored.

Themes: Mental health, Epidemiology
Keywords: Mental health, Adolescents, Epidemiology

Increased Perceived Stress Levels and Social Disparities in Stress: A Comparative Study of 15-Year-Old Adolescents

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Background: Both internationally and nationally, there has been a substantial increase in individuals reporting high levels of stress, especially among young persons. This is a challenge since stress poses a threat to both the individual and society.

The aim of this study is to examine and compare stress levels among adolescents in two cohorts of 15-year-old adolescents from 2004 and 2017, respectively, in relation to social status.

Methods: Stress was measured using Cohen's Perceived Stress Scale, and subjective social status (SSS) was assessed with the MacArthur Scale from two youth cohorts: "VestLiv" (2004) and "FOCA" (2017). Objective measures of socioeconomic status (SES) were obtained from Statistics Denmark and included parental income, education and labour market participation (LMP).

Results: The average level of perceived stress has increased from 2004 to 2017 from 14.1 to 15.8 among females and from 12.2 to 12.6 among males (range: 0-40). Associations between low social status and high levels of stress were found, with both SES and SSS measures. Nonetheless, a much stronger association was observed when utilizing SSS as opposed to SES. Maternal education had the strongest association with high levels of stress among girls, while for boys, paternal education. An association with LMP was found, but in girls, only paternal LMP.

Conclusion: Levels of perceived stress have increased from 2004 to 2017, especially among females. Associations between low SES and high levels of stress were found, but the associations between low SSS and high levels of stress was markedly stronger.

Themes: Mental health, Epidemiology
Keywords: Perceived stress, Adolescents, Social inequality

Psychometric properties of the Danish version of Diabetes Eating Problem Survey Revised

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The aim of this study was to examine the psychometric properties of the Danish translation of Diabetes Eating Problem Survey – Revised (DEPS-R) among adolescents with type 1 diabetes. A total of 131 adolescents with type 1 diabetes aged 11-19 years old completed DEPS-R and Youth Eating Disorder Examination Questionnaire (YEDE-Q). Additional anthropometrical, biochemical, and medical data were obtained from medical records. Exploratory Factor Analysis was performed to examine the factor structure of DEPS-R. DEPS-R was found to have good internal consistency (Cronbach α=0.87) and was significantly correlated with YEDE-Q (r=0.80; p<0.01), HbA1c (r=0.32; p<0.01), zBMI (r=0.35; p<0.01) and age (r=0.20; p<0.05), indicating high construct validity. The mean DEPS-R score was 12.6 (±10.7) for the entire sample, however significantly different between males (8.4 [±9.1) and females (16.4 [±10.6]). Factor analysis revealed a 3-factor structure accounting for 58% of the variance, and suggested elimination of item 4. Adjustments lead to a higher Cronbach α, while maintaining construct validity of the 15 item DEPS-R with similar correlations on all variables. This study confirms DEPS-R to be a valid screening tool to detect symptoms of disordered eating in adolescents with type 1 diabetes but proposes a reduced version by deleting item 4. Future research is needed on updating the original DEPS-R including sensitivity analysis of DEPS-R in detecting serious eating disorder related behavior in type 1 diabetes.

Themes: Mental health, Paediatrics
Keywords: Eating Disorders, Screening, Diabetes

SESSION 11

The SORL1 p.Y1816C Variant Causes Impaired Endosomal Dimerization and Autosomal Dominant Alzheimer's Disease

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Truncating genetic variants of SORL1, encoding the endosome recycling receptor SORLA, have been accepted as causal of Alzheimer's disease (AD). However, most genetic variants observed in SORL1 are missense variants, for which it is complicated to determine the pathogenicity level because carriers come from pedigrees too small to be informative for penetrance estimations. Here, we describe three unrelated families in which the SORL1 coding missense variant rs772677709, that leads to a p.Y1816C substitution, segregates with Alzheimer's disease. Further, we investigate the effect of SORLA p.Y1816C on receptor maturation, cellular localization and trafficking in cell-based assays. Under physiological circumstances, SORLA dimerizes within the endosome, allowing retromer-dependent trafficking from the endosome to the cell surface, where the luminal part is shed into the extracellular space (sSORLA). Our results showed that the p.Y1816C mutant impairs SORLA dimerization in the endosome leading to a strong decrease in trafficking to the cell surface, resulting in decreased sSORLA shedding. Furthermore, we find that iPSC-derived neurons with engineered p.Y1816C mutation have enlarged endosomes, a defining cytopathology of AD.

Our studies provide genetic as well as functional evidence that the SORL1 p.Y1816C variant is causal for AD.

Themes: Neurodegenerative disorders, Molecular biology
Keywords: Alzheimer's Disease, SORL1, Dimerization

Can high-intensity exercise be used to treat fatigue in Parkinson´s Disease?

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Fatigue has been reported to be the non-motor symptom that, if improved, would make the most marked difference to the daily life of persons with Parkinson's disease (pwPD). Nonetheless, no studies have investigated if exercise holds the potential to decrease fatigue in clinically fatigued pwPD as observed in related populations.

A randomized controlled trail with follow up was designed. The primary purposes of the study are to test the hypotheses that pwPD receiving 12 weeks of aerobic exercise will show superior effects on fatigue (i.e., clinically relevant reductions) when compared to a control group (primary hypothesis), and that these effects are sustained after 12 weeks follow up (secondary hypothesis).

The results may hold the potential to establish aerobic exercise as a safe, accessible, and low-cost treatment of the most disabling PD non-motor symptom, fatigue. Accumulation of fatigue has profound consequences for pwPD and their relatives, making this study of great importance.

Themes: Neurodegenerative disorders, Rehabilitation
Keywords: Parkinson's disease, Rehabilitation, Exercise therapy

Freezing of Gait in Danish patients with Parkinson's disease assessed with wearable accelerometer: a cross-sectional validation study

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Introduction: Freezing of gait (FoG) is a debilitating symptom in patients with Parkinson's disease (PD) characterised by a sudden inability to move forward despite the intent to walk. The symptom often becomes more frequent during disease progression with an estimated prevalence range from 5-85% depending on disease stage. FoG leads to lower quality of life and potentially disabling falls. As FoG can be fluctuating it may be challenging to describe for the patient and to assess by the neurologist. This study aims to validate the use of a home-worn accelerometer as a measure of FoG among PD patients.

Methods: A total of 40 PD patients will be recruited from the Department of Neurology, Aarhus University Hospital, Denmark. Patients will on visit answer the New Freezing of Gait Questionnaire and have their symptoms assessed according to the Movement Disorder Society Unified Parkinson's Disease Rating Scale. Subsequently, they will wear the STAT-ON Holter (Sense4Care, Barcelona, Spain) for one week while keeping a gait diary. Sensitivity and specificity of FoG detection is estimated by relating the number of FoG episodes reported by the sensor compared to patients' self-reporting.

Conclusion: This study may provide the evidence that this waist-worn accelerometer is a valuable tool for accurately detecting and phenotyping FoG, thus providing an objective, biometrical marker for FoG in a Danish clinical setting that may guide personalised treatment. This could be of great importance when fine-tuning medication dosage or deciding on surgical therapies.

Themes: Neurodegenerative disorders, Diagnostics & technology
Keywords: Parkinson's disease, Freezing of Gait, Wearable devices

REVIVING EXHAUSED MUSCLE STEM CELLS IN DUCHENNE MUSCULAR DYSTROPHY (DMD)

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Duchenne Muscular Dystrophy (DMD) is a severe progressive X linked genetic disorder characterized by muscle degeneration. In boys, symptoms may become evident as early as 3 years of age. Dystrophin links the intracellular actin-based cytoskeleton network to the transmembrane components of the Dystrophin- glycoprotein complex (DGC) and the absence of dystrophin protein causes myofiber breakdown. Due to the myofiber breakdown, muscle stem cells (MuSCs) become activated leading to transition from quiescent to proliferative state. The activated MuSCs will start to regenerate the muscle. However, since the newly formed muscle cells lack the dystrophin protein the breakdown will continue. It remains unclear whether MuSCs express the DMD gene. As a result, it remains unresolved whether any functional change in DMD MuSCs is due to a dysfunction intrinsic to the MuSC (due to a lack of DMD expression), or due to a response to a diseased environment. To address this question, we purified MuSCs from DMD mice and wild-type controls and performed in vitro activation and differentiation time courses. By measuring RNA and protein levels using primer pairs and antibodies that cover the entire transcript and protein, respectively, we provide a first assessment of Dystrophin expression in MuSCs. In future experiments, we will delve deeper into the expression patterns of Dystrophin in MuSCs and further characterize the functional differences in DMD MuSCs.

Themes: Neurodegenerative disorders, Molecular biology
Keywords: Muscle Stem Cells, Muscular Dystrophy, Dystrophin

Unravelling the role of Cullin3-linked protein degradation in the development of neuromuscular disorders

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Neuromuscular disorders are typically associated with impaired protein degradation. In striated muscle, the ubiquitin-proteasome system degrades the majority of old and unwanted proteins via the addition of a polyubiquitin tag to the target by E3-ubiquitin ligases. Cullin3 (Cul3) is an E3-ubiquitin ligase and acts as a scaffold by interacting simultaneously with other proteins e.g., target adaptor proteins of the BTB domain–containing protein family. Recent studies conducted in mice showed that global loss of Cul3 is embryonic lethal whilst depletion of Cul3 specifically in skeletal muscle results in postnatal lethality characterized by a severe myopathy. Around 180 BTB domain-containing adaptor proteins are used by Cul3 to determine target specificity. Mutations in adaptors, such as Klhl9, Klhl40, Klhl41 or Kbtb13 in humans are linked to several neuromuscular disorders. To further unravel the role of Cul3 and its binding partners in muscle development, we performed a high throughput siRNA screen to identify Cul3 adaptors essential for the myogenic program and muscle cell maturation. Specifically, we used high-throughput image analysis to quantify the effect of Cul3 adaptor knockdown on muscle cell fusion index and morphology, focusing on parameters associated with muscle cell maturity. Our screen identified Klhl30, Klhl38 and Zbtb43 as adaptor proteins with previously unknown roles in muscle differentiation. Currently, we are validating the precise molecular functions of these newly identified adaptors during muscle development.

Themes: Neurodegenerative disorders, Molecular biology
Keywords: Neuromuscular Disorders, E3-ubiquitin Ligases, Muscle development

Using Basigin receptor as target for transport of Biotherapeutics across the blood-brain-barrier

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The use of biotherapeutic antibodies for CNS disorders are emerging worldwide. Newly published clinical studies show that up to 1% of administered mAbs reaches the brain parenchyma but it can be debated whether this fraction of mAbs is enough to reach sufficient target engagement. Further research is needed to optimize the transport of therapeutic mAbs into the brain.

The reason for this restricted passage can be found within the blood-brain-barrier (BBB) which is characterized by specialized endothelial cells creating tight junctions within the brain capillaries. Targeting a highly expressed receptor within these capillaries is a way to overcome this issue how-ever finding a receptor facilitating profound transcytosis at the BBB is difficult.

This project aims to evaluate the Basigin receptor as a potential target for transporting biotherapeutic drugs into the brain. Studies with transferring receptor antibodies have shown avidity and affinity are crucial for the intracellular transport and transcytosis. Thus, we are looking into the use of monovalent and bivalent Basigin mabs with variating affinities to disclose how this impact Basigin receptor mediated transcytosis. Our preliminary data indicates that the use of a low affinity monovalent Basigin mAb expresses a significant higher transcytosis compared to its bivalent counterpart. These findings can also be translated into vivo brain accumulation in a transgenic human Basigin mouse model.

Themes: Neuroscience, Pharmacology
Keywords: Blood-brain-barrier, Basigin, Transcytosis

The REVEAL study.

A Magnetic REsonance Spectroscopy Study InVestigating Cortical HyperExcitability in ALS

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BACKGROUND: Amyotrophic Lateral Sclerosis (ALS) is a rare devastating neuromuscular disease that results in severe disability and ultimately death within 2-4 years from the time of diagnosis. There is no cure and only very limited treatment available. No paraclinical investigations have been able to establish the diagnosis, which is therefore still based on the clinical examination. This delays timely diagnosis. In addition, ALS is difficult to differentiate from other neuromuscular diseases that have far more favorable prognosis.

The pathogenesis remains unclear. The main hypothesis is brain cortical hyperexitability due to a mismatch between the neurotransmitters glutamate (Glu) and GABA. A few studies using brain MR spectroscopy (MRS) have investigated this. However the studies have been limited by; Availability of 7T scanners and the 3T MRS systems ability to separate Glu from glutamine while simultaneously measuring GABA.

AIMS: To show that routine clinical 3T MRS can be used as biomarker that aids in:

1) Faster diagnosis and differentiating ALS from mimic diseases, by detecting altered levels of Glu/GABA in ALS patients compared to ALS mimics and healthy controls

2) Monitoring disease progression, by detecting elevated Glu turnover 6 months from baseline

3) Treatment response by detecting normalization of Glu levels after treatment with the glutamate antagonist Riluzole.

METHODS: Brain 3T 1H-MRS with the novel sequence 'SPECIAL' in healthy controls (n=20) and subjects (n=40) suspected of having ALS during the diagnostic work-up and after 6 months. If diagnosed with ALS the subject will also undergo MRS 4 weeks after initiation of Riluzole treatment.

Themes: Neurodegenerative disorders, Imaging techniques
Keywords: Amyotrophic Lateral Sclerosis, Motorneuron Disease, MR Spectroscopy

The aging vasculature in hippocampus

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The cerebral vascular network is responsible for delivering oxygen and nutrients to maintain normal brain function. Substrate delivery depends on local regulation of cerebral microvasculature to adjust cerebral blood flow (CBF) and the distribution of capillary transit times. Compromised microvasculature impairs capillary flow and increases capillary transit-time heterogeneity (CTH), limiting oxygen availability and resulting in neuronal degeneration and cerebral atrophy. Age-related vascular dysfunction is associated with disturbances of capillary flow dynamics and often precedes cognitive impairment. This study investigates capillary flow dynamics in the hippocampus of aging mice to understand how capillary mechanisms are regulated to reduce CTH and maintain oxygen availability. Steady state hippocampal hemodynamics were investigated using awake-restrained two-photon microscopy (TPM) and laser speckle contrast imaging (LSCI) through a chronic hippocampal cranial window. Capillary flow dynamics were measured using intravascularly (IV) fluorescent dyes, and blood-brain barrier disruption was determined by measuring the leakage of dye through vessels. Estimates of IV partial pressure of oxygen (PO2) and tissue oxygen tension (PtO2) were achieved using an oxygen-sensitive dye. Pulsatility index was estimated using LSCI during steady state. The study expects to reveal age-related changes in microvascular hemodynamics in the hippocampus of young and aged mice and their association with spatial learning and memory. Results of the study contribute to our understanding of the role of age-induced vascular disturbances on cognitive changes.

Themes: Animal Models, Neurodegenerative disorders
Keywords: Aging, Optical imaging, Microvasculature

The Role of Sortilin in Retinal Neurodegeneration

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The multifunctional receptor sortilin is studied in animal models of retinal neurodegeneration. The localization of sortilin and its co-receptor, the p75 neurotrophin receptor (p75NTR), was determined using immunofluorescence on retinal sections from human diabetic patients and streptozotocin-induced diabetic C57BL/6J male mice. In diabetic mice, levels were further quantified using WB and qPCR. Therapeutic studies have been performed in diabetic mice and mice subjected to optic nerve crush (ONC) using intravitreally injected anti-sortilin antibodies. Neuroprotection was evaluated in vivo by optical coherence tomography and by quantification of retinal ganglion cells (RGCs) in retinal flat mounts.

Sortilin levels are increased in human and murine diabetic retinas compared with non-diabetic controls. Sortilin is highly localized to retinal Müller cells and co-localizes with p75NTR in diabetic retinas. A significant protective effect of sortilin inhibition on inner retinal cells was observed in diabetic mice. At eight weeks following diabetes-induction, inner retinal thickness was reduced by 9.7% [-12.7%; -6.6%] ($p < 0.0001$) in the control group compared with the anti-sortilin injected group. Similarly, the RGC density was reduced 20.5% [-30.8%; -10.2%] ($p = 0.0009$) in the control group.

In conclusion, sortilin is upregulated in the diabetic retina, and activation of the p75NTR/sortilin complex seems essential to the loss of retinal neurons in experimental diabetes. The potential roles of sortilin in other models of retinal neurodegeneration are under ongoing investigation.

Themes: Neurodegenerative disorders, Animal Models
Keywords: Retinal disease, Neuroprotection, Animal models

Diagnostic and sensory changes in DPN in type 2 diabetes. A 5 year-follow-up

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Background: Diabetic polyneuropathy (DPN) is a common, debilitating complication of type 2 diabetes (T2D) caused by progressive damage to the peripheral nerves which causes a variety of sensory symptoms and signs. There are few cohort studies that have tracked the progression of DPN in detail and it is not known how sensory changes in DPN evolve over time.

Aim: To study the development of DPN in T2D-patients over time and describe the natural history of sensory changes that occur during the course of the disease.

Methods: Originally, 389 patients with newly diagnosed T2D were recruited to establish the diagnosis of DPN. For this study all participants from the baseline study were invited a 5-year follow-up examination and diagnosed according to international consensus criteria.

Results: 184 diabetes patients completed follow-up (follow-up rate 47 %). Median follow-up time was 5.1 years and median diabetes duration was 5.9 years and 11.0 years at baseline and follow-up, respectively. Prevalence of DPN was 56 % at baseline and 58.7 % at follow-up. There were significantly more patients in the confirmed DPN-group (36 vs 51 %) and significantly less in the probable DPN-group (27 vs 14 %) at follow-up compared to baseline. DPN-patients had developed more pronounced sensory changes across all sensory modalities from baseline to follow-up. Confirmed DPN patients developed significantly more pronounced hyposensitivity for all tested modalities and probable DPN patients had for brush and warmth from baseline to follow-up.

Conclusion: In our cohort prevalence of DPN was unchanged but more patients were in the confirmed DPN group and they had more pronounced sensory changes.

Themes: Neuroscience, Endocrinology
Keywords: Neuropathy, Diabetes, Clinical research

SESSION 12

LATIES - Late window thrombolysis in acute ischemic stroke

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Claus Z. Simonsen

Introduction: Acute ischemic stroke (AIS) is a leading cause of death and disability, and tissue plasminogen factor (tPA) is an effective treatment.

When symptom onset is known, tPA is given within 4.5 hour in Denmark. Patients with unknown symptom onset are scanned with diffusion weighted magnetic resonance imaging to select them for tPA on the WAKE-UP criteria.

European guidelines mention an option to treat with tPA after 4.5 hour, up to 9 hours, but it requires advanced imaging with perfusion weighted imaging (PWI), which is only available in few hospitals. These guidelines are based on the EXTEND-criteria and also include patients with unknown onset, stating that these late-window patients can be treated, if the PWI shows viable tissue surrounding the ischemic core.

In the Central Denmark Region, it is planned to begin performing PWI on patients with symptoms of AIS in the late window (unknown onset and known onset in the 4.5-9 hour-window).

Aim: to follow-up on all late window patients scanned in the Central Denmark Region after implementation of PWI and widened time window from 4.5 to 9 hours.

Methods: a prospective cohort study from 2023-25.

Focus: primary outcome: number of patients treated with tPA on EXTEND, WAKE-up or both criteria. The number needed to screen for the EXTEND criteria to identify one eligible patient to tPA. Secondary outcomes: neurological disability measured at the Modified Ranking Scale after 3 months, presented as an odds ratio. Risk of symptomatic intracranial haemorrhage after tPA presented as odds ratio and risk ratio.

Themes: Neuroscience, Imaging techniques
Keywords: Acute ischemic stroke, Late window thrombolysis, Perfusion imaging

Post-traumatic headache: Phenotyping, exploring pathophysiological insights and novel treatment strategies

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Background: Nearly 20,000 Danes suffer from mild traumatic brain injury (mTBI), also known as concussion, each year. 10-15% of these patients continue to suffer from persistent post-concussion symptoms (PCS). Headache associated with mTBI, post-traumatic headache (PTH), is one of the most common and persistent symptoms following mTBI. Between 30-90% of mTBI patients develop headache, of which 18-22% develop persistent (> 3 months) PTH. PTH is highly disabling and has high socioeconomic costs. However, PTH is poorly characterized, has unknown pathophysiology, and no adequate treatment options.

Aim: To advance the knowledge on the characterization and pathophysiology of PTH with an impact on the ability to diagnose and manage PTH effectively. The aim is also to evaluate the efficacy of repetitive transcranial magnetic stimulation (rTMS), a novel intervention on PTH.

Methods: Phenotyping of PTH will be performed using a comprehensive headache questionnaire. A randomized, placebo-controlled clinical trial will be conducted to assess the effect of rTMS on PTH frequency and intensity after intervention, 1 month- and 3 months after the intervention. Patients with PTH will receive 5 sessions of either active- or sham rTMS treatment. Blood samples will be taken prior to intervention, after intervention, and 1 month after the intervention. Blood samples will be examined for biomarkers associated with PTH and PCS.

Perspectives: To facilitate multidimensional outcome assessments and better treatment strategies in order to reduce the long-term disability in patients with PTH.

Themes: Neuroscience, Rehabilitation
Keywords: Post-traumatic headache, Concussion, rTMS

Intermittent hypoxic therapy as novel treatment of activity-related headache in migraineurs

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Objective: To Investigate personalized intermittent hypoxic therapy (IHT) in activity-related headaches (ARH) associated with migraines. The primary objective is to assess pain, disability, and headache severity using MIDAS and HIT-6 questionnaires. The Secondary objective is to evaluate physiological and molecular markers, quality of life, vascular perfusion, mitochondrial function, and cerebral artery flow velocity in ARH patients post-IHT.

Background: Migraines and exertional headaches impact life and productivity. ARH results from a metabolic-workload mismatch, potentially due to energy and vascular issues. IHT raises the headache threshold through mitochondrial and vascular adaptations. The paradoxical ARH and exercise link makes IHT a promising ARH symptom-reducing approach.

Methods: Proof-of-concept study with ARH patients and controls. Baseline data will be collected, followed by IHT at SANA Medical Systems consisting of one hour treatment every week for 8 weeks in total. Post-treatment physiological measurements will be obtained 2 weeks after ended treatment. Blood samples will be taken before and after exercise test, both at baseline and after ended treatment. Participants will fill out MIDAS, HIT-6, and SF-36 questionnaires for a follow-up period of six months after ended treatment. Statistical analyses compare measurements over time and between groups.

Significance and Contribution: This research addresses ARH's mechanisms, profoundly affecting patients' lives and economics. Investigating IHT as a non-pharmacological treatment offers valuable insights into ARH management and advances scientific understanding.

Themes: Neuroscience, Omics
Keywords: Migraine, Hypoxia, Intermittent hypoxic therapy

The effect of Locus Coeruleus ablation on neurovascular coupling

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Neurovascular coupling is an essential mechanism for brain health, as it increases the brain's energy supply in response to increased neuronal activity. This process is achieved through the release of vasodilating agents from neurons and astrocytes, leading to an increase in cerebral blood flow (CBF). Vascular resistance mostly stems from the capillary bed, where contractile pericytes can adjust capillary diameter to alter CBF. This control builds on a constant tone generated by the capillary pericytes. A primary contributor to this ongoing tone is the release of noradrenaline (NA) from axons originating from the Locus Coeruleus (LC) in the brain stem. With age, the risk of neurovascular dysfunction increases and precedes cognitive impairment. Likewise, age is the most significant risk factor for developing Alzheimer's disease (AD), where the LC is one of the earliest brain regions to degenerate. Despite well-known neurovascular dysfunction in AD and observed degeneration of the LC prior to AD onset, the impact of NA-LC ablation on neurovascular coupling is not understood. Therefore, this study aims to investigate capillary flow dynamics in NA-LC ablated transgenic pericyte mice to better understand the interplay of NA-LC, pericytes, and the consequences of NA-LC ablation on neurovascular coupling. Using two-photon microscopy to perform awake-restrained imaging, we will acquire measured estimates of oxygen tension and capillary flow dynamics and determine the severity of NA-LC ablation on the brain's neurovascular coupling ability.

Themes: Neuroscience, Neurodegenerative disorders
Keywords: Animal model, Neurovascular function, Brain energetic

Understanding the neuroprotective role of the novel HCO3– sensor RPTPγ in disease severity of ischemic stroke

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Background: Stroke is a leading cause of death and disability. Inadequate cerebral blood flow relative to metabolic demand lowers tissue oxygenation and causes acute ischemic damage followed by delayed secondary injury due to vasospasm and inflammation. Under physiological conditions, local acid-base-triggered mechanisms match cerebral blood flow to metabolic demand. These mechanisms are compromised during a stroke.

The novel extracellular HCO3– sensor RPTPγ is expressed by neurons, microvascular endothelial cells, and immune cells. The molecular mechanisms whereby RPTPγ regulates cardiovascular function remain largely unknown, however, there are some identified targets from other cell types that are known mediators of cerebral ischemic damage. Loss-of-function RPTPγ variants are associated with a 7-fold increased stroke risk in humans.

Aim: This study aims to investigate the role of the HCO3– sensor RPTPγ in translating acid-base disturbances in the extracellular environment of stroke lesions into altered intracellular signaling events that may confer neuroprotection.

Methods: I will induce brain ischemia in mouse models with disrupted expression of RPTPγ and explore the consequences for cerebral blood flow, neuronal metabolism, and ultimately stroke severity.

Perspective: The therapeutic interventions available during an ischemic stroke are limited. Exploring RPTPγ in ischemic stroke will provide new insights into the pathophysiological and molecular processes involved. Further, it will open new possibilities for therapies and treatments that could improve patient care.

Keywords: Cerebrovascular disease, Animal models/disease models, Laboratory Science

Themes: Neuroscience, Cardiology
Keywords: Cerebrovascular disease, Animal models/disease models, Laboratory Science

Threshold Tracking TMS and Neurofilament Light Chain as Biomarkers in ALS

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Background: There is a need for sensitive biomarkers in ALS to enable earlier diagnosis and to help assess potential treatments. The main objective of this study was to compare two potential biomarkers, threshold-tracking short-interval cortical inhibition (T-SICI), which has shown promise as a diagnostic aid, and neurofilament light chains (NfL).

Methods: Ninety-seven patients with ALS (mean age 67.1 ± 11.5) and 53 ALS mimics (aged 62.4 ± 12.9) were included. Mean disease duration was 14 months ± 14.1. Mean revised ALS functional rating score (ALSFRS-R) was 41.6 ± 4.7. Among the ALS patients, Fifty-five had spinal onset and 42 had bulbar onset. Patients were evaluated with ALSFRS-R, Penn upper motor neuron score (UMNS), muscle strength (MRC) score and examined with T-SICI, quantitative electromyography (EMG) and NfL measured in spinal fluid.

Results: In patients, NfL increased with UMNS evidence of neurodegeneration (rho=0.45, $p<0.001$) while T-SICI paradoxically increased towards normal values (rho=0.53, $p<0.001$). However, these two measures were uncorrelated, and neither correlated with ALSFRS-R or MRC score. Discrimination between all ALS patients and mimics was best for NfL (area under ROC curve 0.842) compared with T-SICI (0.675). For the patients with no UMN signs, NfL discriminated best (0.884) compared with T-SICI (0.811). Better discrimination, however, was achieved when combining T-SICI and NfL (0.922).

Conclusion: Both T-SICI and NfL correlated with upper motor neuron involvement, and combined they provided a strong discrimination between ALS patients and ALS mimics. Longitudinal studies are needed to assess their potential for detecting disease progression.

Themes: Neurodegenerative disorders, Neuroscience
Keywords: Amyotrophic lateral sclerosis, TMS, Neurofilament light chain

Comparative Study of High-Efficacy, Disease Modifying Treatments of Relapsing Multiple Sclerosis (CoSHED RMS)

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Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system, typically presenting in young adults.

Historically, MS was considered a T-cell-mediated disorder, but evidence has accumulated that B cells have been found to play a central role.

In recent years, antibodies to CD20 have been widely used. The first-in-class of these antibodies was rituximab (Rituxan™), subsequently several other candidates have been introduced. These B cell-depleting therapies reduce relapse rate and disease progression.

A national Danish investigator-initiated phase-III study of the effect of ocrelizumab versus rituximab in patients with active MS (DanNORMS: Danish Non-inferiority study of Ocrelizumab and Rituximab in MS NCT0488788).

In parallel with this study, we will initiate a prospective clinical non-randomized open-label multi-center follow-up study CoSHED (Comparative Study of High-Efficacy Disease-modifying treatment in relapsing MS) of the DanNORMS patients versus ofatumumab treated patients. Forty patients are included in each of the three treatment groups, ocrelizumab, rituximab and ofatumumab and will be compared to an age and gender matched control group. We will register aspects of both immunological, virological, and epigenetic responses and relate these findings to the relative efficacy of the three treatments, and the course of disease for the patients.

With this study we aim to increase our understanding of the mechanism of action of the three B cell-depleting treatments, and the pathogenic mechanisms in MS. The aim is to optimize personalized medicine for MS patients.

Themes: Neuroscience, Immune diseases
Keywords: Multiple Sclerosis, B cell depleting therapy, Ebstein Barr Virus

Cerebral pulsatility index in a mouse model of acute ischemic stroke.

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Introduction: Pulsatility index (PI) is used as a proxy for downstream arterial resistance during acute ischemic stroke in the clinic, with PI measurements from the contralateral hemisphere serving as baseline. We hypothesize that PI and cerebral blood flow change in both hemispheres during acute ischemic stroke, and aim to investigate these changes in a mouse model of acute ischemic stroke.

Methods: Cerebral blood flow and PI were measured with laser speckle contrast imaging in one C57BL/6 female mouse (age = 23 weeks). The right middle cerebral artery (MCA) was compressed with a glass micropipette for 69 minutes. Blood flow and PI were measured at baseline, during occlusion, after pipette retraction, and daily for 7 days after occlusion. Cylinder test was used to assess neurological deficits. Cerebral infarction was visualized with triphenyl tetrazolium chloride staining. Blood flow and PI changes are described as percentage of baseline level.

Result: During MCA occlusion, blood flow was reduced by 48.9% in right and by 7.9% in left MCAs. At 48h after occlusion, it remained reduced by 26.9 % in the right and by 3.8% in the left MCAs. At 120h after occlusion, blood flow increased by 26.7% in the right and by 18.6% in the left MCAs. PI was increased with 50.83% in right and reduced by 25.8% in left MCAs during occlusion. During follow-up, PI was reduced by 4.9% in right and by 37.5% in left MCAs at 48h after occlusion, and was reduced by 8.3% in the right and 16.6% in the left MCAs at 120h after occlusion.

Conclusion: MCA blood flow and PI change bilaterally during and after MCA occlusion

Themes: Neuroscience, Animal Models
Keywords: Acute ischemic stroke, Cerebrovascular hemodynamics, Pulsatility index

Living with Myotonic dystrophy type 1: A scoping review.

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Background: Myotonic dystrophy type 1 (DM1) is a multisystemic neuromuscular disease, causing progressive physical and cognitive impairment. People with DM1 experience difficulties performing daily activities and the disease affects their participation levels. Additionally, caregivers to people with DM1 experience an increased caregiver burden. The aim of the study was to identify the existing literature on experiences of living with adult onset DM1 according to people with adult onset DM1, their caregivers and health care professionals.

Methods: A scoping review guided by the framework of Arksey and O'Malley was conducted. A literature search was performed in five databases in October – November 2022. The Mixed Methods Appraisal Tool was used for critical appraisal. Key findings were categorized using the International Classification of Functioning, Disability and Health (ICF).

Preliminary results: 11 out of 1842 studies were included, of which five had a quantitative design, five had a qualitative design and one study had a mixed methods design. The studies reported on multiple factors which affected the lives of people with adult onset DM1 and their caregivers. All components of the ICF were represented among the included studies. Activity and participation and personal factors were the most reported components, followed by body functions and structures, environmental factors, and not definable concepts.

Conclusion: Adult onset DM1 have a great biopsychosocial impact on the lives of people with DM1 and their caregivers.

Themes: Qualitative research, Rehabilitation
Keywords: Neuromuscular disease

Dopaminergic dysfunction predicts disease course in isolated REM sleep behaviour disorder

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Objectives: Isolated REM sleep behaviour disorder (iRBD) is a parasomnia that can precede neurodegenerative diseases such as Parkinson's disease (PD) and dementia with Lewy bodies (DLB). Although more than 90% of patients with iRBD develop PD, DLB or Multiple System Atrophy over time, it is not possible to predict the course of disease progression. The dopaminergic function of the striatum is affected early in patients with iRBD, and [18F]-DOPA positron emission tomography (PET) can examine brain dopaminergic function in vivo. This study aimed to investigate striatal dopaminergic dysfunction in patients with iRBD as a possible predicter of forthcoming progression to a parkinsonian disorder.

Methods: Twenty-one patients with polysomnography-confirmed iRBD had [18F]-DOPA PET and were subsequently followed for eight years to detect progression to a parkinsonian disorder. Comparisons of baseline imaging were made between phenoconverters and non-phenoconverters.

Results: A total of 17 patients had baseline [18F]-DOPA PET scans and successful follow-up. Phenoconverters were diagnosed with PD or DLB (n=8) and had significantly lower baseline tracer uptake in the putamen of both the most and least affected hemisphere ($p<0.001$ and $p<0.001$, respectively) compared with non-converters. Correction for iRBD disease duration at baseline did not influence these findings.

Conclusions: This study suggests that dopaminergic dysfunction in the putamen assessed by [18F]-DOPA PET could predict which patients with iRBD are closest to developing a parkinsonian disorder. This predictor may be important in future trials of treatments when selecting the study population.

Themes: Neurodegenerative disorders, Neuroscience
Keywords: REM sleep behaviour disorder, Predictors, PET imaging

SESSION 13

Genome-wide association study of Borderline Personality Disorder accounting for age at diagnosis and family history in iPSYCH

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Borderline Personality Disorder (BPD; ICD-10 F60.3x) is characterized by marked instability in emotions, self-image, and interpersonal relationships. Individuals with BPD make up a large proportion of the patient population in psychiatric hospital services. To develop more effective treatment options and aid early intervention, we must improve our understanding of BPD etiology. Previous twin and family studies have reported a heritability of 60–75%, but genome-wide association studies (GWAS) of BPD have been underpowered to detect significantly associated genetic variants to date.

To investigate how common genetic variation influences the likelihood of developing BPD, we conducted a GWAS BPD liability in the iPSYCH2015 sample, accounting for age at diagnosis and family history. iPSYCH is a nationally representative case-cohort study of all individuals born in Denmark 1981–2008 and diagnosed with a major psychiatric disorder by 2015 (i.e., cases) and individuals randomly selected from the population for the cohort. The sample for this study consisted of ~7K individuals with BPD from the entire iPSYCH sample and ~46K individuals without BPD from the cohort. We applied the extended liability threshold model conditioned on family history (LT-FH++) method to estimate each individual's liability to develop BPD in the study sample and conducted a linear GWAS of BPD liability with the first ten genetic principal components and genotyping array as covariates.

Variants at the 5q21 locus between NIHCOLE and RNU6-334P were significantly associated with BPD liability. This is the largest single-sample GWAS of BPD to date, and the first to find any significant hits.

Themes: Mental health, Omics
Keywords: Psychiatry, Epidemiology, Genomics

Course of neurocognitive development in children at familial high risk of schizophrenia or bipolar disorder: A prospective cohort study from 7 to 15 years of age. The Danish High Risk and Resilience Study – VIA 15

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Background: Schizophrenia (SZ) and bipolar disorder (BP) are severe mental disorders with shared and distinct clinical, cognitive, and genetic risk factors. These risk markers are also present in offspring, who have an increased risk of developing severe mental illness.

SZ is a neurodevelopmental disorder and neurocognitive impairments are presenting years before the manifestation of overt clinical symptoms. Findings regarding premorbid neurocognitive impairments in BP are less conclusive. Investigating the course of neurocognitive development before illness offers insights into both shared and illness-specific vulnerability markers.

The results from previous assessments of the presented cohort showed stable neurocognitive deficits in children at familial high risk (FHR) of SZ and stable neurocognitive functioning in children at FHR-BP that were comparable to population-based controls (PBC).

The aim is to study the neurocognitive development in children at FHR-SZ and FHR-BP compared with PBC from age 7 to 15.

Methods: The Danish High Risk and Resilience Study (VIA) is a population-based cohort of 522 children (202 FHR-SZ, 120 FHR-BP, and 200 PBC). They were assessed at baseline at age 7 (VIA 7) and at first follow-up at age 11 (VIA 11) with a retention rate of 89%. VIA 15 is

the second follow-up at age 15. Neurocognitive functioning was assessed with a comprehensive neurocognitive test battery of validated tasks.

Results: Data collection will be finalized in the spring of 2024.

Perspectives: Examining the development of neurocognitive deficits in children at FHR-SZ and FHR-BP will elucidate shared and distinct endophenotypes and help differentiate the pathophysiology of SZ and BP.

Themes: Mental health, Epidemiology
Keywords: Neurocognitive development, Familial high-risk, Schizophrenia and Bipolar

Longitudinal assessment of brain atrophy in patients with isolated REM sleep behaviour disorder

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Isolated rapid-eye-movement behaviour disorder (iRBD) is a parasomnia strongly associated with Parkinson's disease (PD) and other alpha-synucleinopaties that can manifest years before the onset of motor symptoms. Previous studies have shown structural changes in the brains of iRBD patients using Voxel based morphometry (VBM), however not consistently.

In this study, we wanted to examine the extend of atrophy in iRBD patients compared to a group of 19 healthy controls (HC) and how that progressed over the three-year follow-up period, using VBM. We analysed high-resolution MRI scans of a group of iRBD patients who had a baseline scan (N=20) and a follow-up scan (N=9) three years later.

Whole brain VBM analysis showed a cluster of significant decreased grey matter (GM) density in the cuneus/precuneus area in the patients at baseline compared to HC. Region of interest (ROI) analysis confirmed significant reductions in GM density at baseline in Calcarine sulcus, precuneus and cuneus. Interestingly, the ROI analysis also showed significant reduction in the caudate nucleus in the iRBD patients. When comparing the

baseline and the follow-up scans there was a significant reduction in GM density in the right cuneus and precuneus, as well as in the right caudate and bilateral putamen.

These results support the previous findings of significant atrophy in iRBD patients when compared to HC and suggests that there is a measurable progression of atrophy over a relative short follow-up period, including striatal areas highly relevant to Parkinsonism.

Themes: Neurodegenerative disorders, Imaging techniques
Keywords: Parkinson's disease, REM sleep behaviour disorder, Voxel based morphometry

Participation in structured leisure-time activities among people living with Spinal Cord Injuries – A cross-sectional study.

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Background: Spinal cord injury (SCI) impacts health and presents substantial daily life challenges. The transition to home after hospital rehabilitation entails adapting to new daily routines and roles. Engaging in leisure-time activities can aid individuals in achieving and sustaining an active, social, and meaningful life. This study aims to: 1) assess the prevalence of structured leisure-time activities among individuals with SCI and 2) investigate the associations between leisure-time activities and self-perceived activity and participation, mental well-being, and quality of life.

Methods: We conducted postal and online surveys, enrolling participants aged 18 or older who had been admitted to the Spinal Cord Injury Center of Western Denmark after 2013, regardless of the cause of the injury. We employed a custom questionnaire, refined with input from individuals with SCI, to evaluate structured leisure-time activities. General activity and participation were assessed using the USER-P questionnaire, while quality of life and mental well-being were measured using the International Spinal Cord Injury Data Sets Quality of Life Basic and the WHO-5 Well-Being Index. Demographics and structured leisure-time activities will be presented in terms of frequency. Regression analysis will be used to explore associations between main variables, adjusted for covariates.

Perspectives: Exploring the potential benefits of non-healthcare, community-based activities as a part of rehabilitation may aid in the creation of novel and sustainable pathways that bridge the gap between healthcare and the community, alleviate capacity issues, and enhance local reintegration.

Themes: Rehabilitation, Mental health
Keywords: Neurorehabilitation, Community participation, Spinal Cord Injury

Improving mental health in patients with type 2 diabetes in general practice

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Background: Type 2 diabetes (T2D) is linked to mental health issues, with unknown prevalence in general practice. Reduced mental health affects diabetes treatment outcomes, prompting national guidelines to recommend increased focus on mental health in patients with T2D. The International Diabetes Federation suggests using the WHO Well-being Index (WHO-5) to identify patients with impaired mental health, but at present there's a lack of established screening tools for systematic mental health assessment in patients with T2D.

Aim: Our objective is to assess the mental health of patients with T2D in general practice and investigate whether it is sufficient to ask the patients how they are (with a single-item mental health question) or if WHO-5 would be a useful addition as a systematic screening tool.

Methods: This cross-sectional study surveyed 230 patients with T2D in Danish general practices from May to December 2023. Enrollment occurred at their annual chronic care consultation. The questionnaire included four validated screening tools for general well-being (WHO-5), depression (PHQ-9), anxiety (GAD-7) and diabetes distress (PAID-5) and a single-item mental health question.

Preliminary results: Among 133 patients, 48 individuals (34%) experience some sort of impaired mental health. Notably, WHO-5 identifies 25 of cases (52%), while the single-item mental health question identifies only 8 (17%). It is important to highlight that patients identified by both the WHO-5 and the single-item question display statistically significant poorer mental health compared to the remaining patients.

Themes: Mental health, Diagnostics & technology
Keywords: Mental health, Type 2 Diabetes, Screening tools

The Impact of Individual Factors and Preferences on Music for Sleep.

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Since ancient times, music has been used as a sleep aid. Lullabies share common ground and are rooted in cultural traditions around the world (Mehr et al., 2019). Sleep problems are highly prevalent in modern society and today, with the 24-hour access to music, many adults report using music for sleep (Bjorvatn, Waage, & Saxvig, 2023; Brown, Qin, & Esmail, 2017; Morin, LeBlanc, Daley, Gregoire, & Mérette, 2006). Still, the research in this field is limited, the characteristics of people using music for sleep remain unknown, and the features of music used for sleep are not clear.

The first part of my Ph.D. project focuses on investigating these characteristics. The first study will consist of an online survey where participants listening to music for sleep will answer questions about their demographics, their preferences in music for sleep, and psychological factors. The survey will be distributed through posts on social media and on websites, to reach as many participants as possible. The purpose of the survey is to understand what type of music is used for sleep, and how personal variables, music preferences, and psychological factors may influence the choice of this music. To investigate this, Music Information Retrieval and Machine Learning techniques will be used. This study would ultimately lead to the creation of a dataset of music for sleep, to be used in the development of more individualized solutions and treatments for sleeping disorders.

Themes: Neuroscience, Public health
Keywords: Music, Sleep, Individual characteristics

Mind the Heart - Paving the way for timely assessment and treatment of mental health disorders in children and adolescents with congenital heart defects

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Objective: Congenital heart defects (CHD) affect approximately 1% of new-borns. Compared to children without CHD, these children have a 50% higher risk of requiring special education assistance and higher rates of autism and ADHD have been reported. Studies on other types of mental health disorders (MHD) are sparse, with conflicting results and mainly limited to those with severe CHD. Early recognition of MHD is pivotal, however often overlooked in children with somatic conditions. The aim of this study is to test the feasibility of an online screening programme (SDQ and DAWBA) for MHD in children with CHD and to systematically describe the proportion with an MHD as well as the number of specific subtypes of MHD and their potential predictors.

Methods: All young patients (5-17 years), in Denmark diagnosed with CHD (N ~ 4800) and their parents will be identified through Danish national registries and invited to participate via e-boks in a stepwise manner according to type of CHD. Parents and children ≥ 11 years will complete the SDQ and DAWBA and a feasibility questionnaire. Descriptive statistics will be used for attrition analysis. Data on feasibility, the proportion of overall MHD and the frequency of specific subtypes of MHD will be reported as total numbers and percentages with 95% CI. Regression analyses will be used to explore if subgroups of MHD are associated with specific subtypes of CHD or sociodemographic factors.

Results and conclusion: The results will be ready during 2024/2025. We expect this project to provide new knowledge on the use of online screening measures of MHD in children with CHD, which may constitute a resource saving collaborative care model.

Themes: Mental health, Cardiology
Keywords: congenital heart defects, mental health, psychiatry

Mobile app-assisted behavioural treatment for children and adolescents with tic-disorders:

- A pilot randomised controlled clinical trial

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Background: Chronic tic disorders are neurodevelopmental disorders that occur relatively frequently in childhood. Tics can have significant impact on the child, both academically and socially. Clinical guidelines recommend behaviour therapy as the primary approach, but limited resources may pose challenges to its implementation. International research suggest that digital interventions may be effective in treating tic disorders, although additional clinical trials are necessary to confirm these findings.

Methods: This is a pilot study preceding a randomised clinical superiority trial comparing the efficacy of app-assisted tic training versus app-assisted tic learning. The study evaluates the feasibility and acceptability of the app-based treatment and participants are randomized to either this treatment or treatment as usual (TAU) delivered by video sessions. Both interventions implement strategies from the well-documented manual "Niks to tics," utilizing a combination of Habit Reversal Training (HRT) and Exposure and Response Prevention (ERP). Thirty-three participants aged 9-17 years were included, fourteen of whom were assigned to the app-treatment group while the remaining nineteen were assigned to the TAU group. Two dropouts were observed in each group.

Perspectives: The study suggests that the recruitment process is feasible and with satisfactory adherence to the treatment. A clinically significant reduction in total tic severity score was observed in both groups, and the acceptability of the app intervention indicates satisfaction with the treatment itself and the outcome. Furthermore, data was used for power calculations in the randomised clinical superiority trial.

Themes: Mental health, Paediatrics
Keywords: Tourette, digital therapy, feasibility

Experiences of receiving internet-based treatment (“One step at a time”) for multi-system functional somatic disorder: Preliminary findings from qualitative interviews

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Background: Functional somatic disorders (FSDs) of the multi-system type are prevalent and may impair patients' quality of life. Effective treatments are available, but access to treatment is limited. Internet-based therapy is becoming increasingly popular and is a cost-effective alternative. As part of evaluating the effectiveness of the internet-based therapist-assisted cognitive behavioral treatment "One step at a time", we conducted qualitative interviews with users. Preliminary results are presented here.

Methods: Semi-structured qualitative interviews with 5 patients were conducted after a follow-up consultation at 4 months after treatment. Interviews of 30-60 min based on an a priori developed interview guide were recorded and transcribed, and the results were analyzed using thematic analysis.

Results: Analysis resulted in 5 main themes: Getting better, which describes patient’s experiences of the treatment, 2) The therapeutic process, which describes how patients worked with the program and what was useful, 3) Barriers to treatment describes the various obstacles to achieving patient’s therapeutic goals, 4) The importance of the social context describes the importance placed on the therapist and the longing for meeting other patients, and 5) Benefits and limitations of internet-treatment describes the experienced advantages and disadvantages of receiving the treatment over the internet.

Conclusion: Preliminary findings from the interviews showed that most patients experienced the treatment as meaningful and helpful. Nevertheless, there were several barriers for engaging fully with the treatment, which limited patients in achieving their treatment goals.

Themes: Mental health, Rehabilitation
Keywords: Functional Somatic Disorder, Internet-based treatment, Cognitive Behavioral Therapy

Towards personalized explanation for functional somatic disorders: a participatory design study

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Background: Functional somatic symptoms (FSS) are a feature of a range of common health conditions. FSS are distinct in that they are not amenable to explanation by linear causal processes and fall between the gaps in mainstream medical epistemology. The result is often a lack of appropriate explanation and treatment for patients seeking help for these problems. Relevant, accessible and integrated explanations for complex symptoms are a necessary foundation to empower people towards recovery.

Methods: Utilising engaged scholarship methods, over the course of a year, we have co-created an open-access, interactive online explanatory model of FSS (bodysymptoms.org). The starting point was a mixed methods study which thematized the explanatory models for FSS in current clinical use across specialist European treatment centers, and a systematic review of relevant aspects of medical explanation. Through iterative participatory design, it has been ensured that the final symptom explanations developed have clinical utility and face-value relevance to end users. Personalized navigation of the model was prioritized in development, so that explanations could relate to the heterogeneity of symptom experience in FSD.

Results and conclusion: To explain functional symptoms there is a need to make room for new ways to understand the body and the ways it can become unwell. The body can be understood as a complex system that adapts in personal ways to result in states of ill health with transdiagnostic validity. New forms of knowledge can come from bringing diverse perspectives together in dialogue. This project demonstrates how the power of research can be harnessed to create shared value.

Themes: Health Education, Public health

SESSION 14

Virtual Reality: Relaxation in an Acute Environment

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Background: Sedation has been shown to increase time on mechanical ventilation, length of stay and mortality rates in intensive care unit (ICU) patients. This has prompted changes in sedation strategies, making less sedation standard treatment. Sedation was used to keep patients comfortable in an unfamiliar and technical environment with continuous disturbances, high noise levels and clinical surroundings. Consequently, conscious patients experience discomfort, sleep disturbances and anxiety during admission. Virtual reality (VR) is used in other hospital settings for distraction to reduce discomfort and anxiety. Existing knowledge deems VR safe and feasible to use in the ICU population; however, its effect has yet to be established.

Purpose: This project aims to identify and evaluate a VR intervention to reduce patients' discomfort and anxiety during ICU admission.

Methods: The project is guided by the Medical Research Council's framework for developing/identifying and evaluating complex interventions.

A suitable VR intervention is identified through stakeholder involvement, focusing on acceptability and usability. The evaluation combines a quasi-experimental pre-post-test and interviews with participants to capture diverse perspectives on the intervention.

Perspectives: This study will contribute to the scarce knowledge of the effect of VR on the ICU population. VR has the potential to be expanded for other uses, i.e., early rehabilitation and sleep promotion and could be an easy and cheap intervention reducing ICU survivors' burden of ill health.

Themes: Public health, Rehabilitation
Keywords: Complex interventions, Critical Care, Virtual Reality

Interdisciplinary collaboration between general practice and sickness benefits office in return to work processes

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Background: Effective collaboration among stakeholders is essential in supporting return to work (RTW) of individuals on sick leave. Two pivotal stakeholders are sickness benefits offices and general practice. However, existing literature indicates that their collaboration is currently limited and not functioning optimally. This has adverse effects on both professionals, and individuals on sick leave, the latter experiencing being the messenger between professionals.

Aim: To improve future collaboration between these two stakeholders it is imperative to gain a deeper understanding of their current collaborative practices. Thus, the aim of this PhD project is to a)investigate activities taking place in the collaboration between general practice and sickness benefits office in RTW processes and b)identify underlying conditions influencing possibilities for collaboration.

Method: This project consists of three studies; a scoping review followed by a case study design including two empirical studies. The first empirical study focus on activities occurring between the two stakeholders, while the second study focus on underlying conditions for collaboration, eg differences in legislation, cultures and/or economy.

Institutional theory and the concept of boundary spanning underpins the project theoretically. Qualitative methods including interviews, observations and document analysis will be employed.

Perspective: Results obtained from this project will offer valuable insights for development of interventions aiming to improve future collaboration between general practice and sickness benefits office in RTW processes, ultimately contributing to more efficient RTW processes.

Themes: Public health, Qualitative research
Keywords: collaboration, sick leave, boundary spanning

MOVE your Lungs: Chronic Obstructive Pulmonary Disease - Physical Activity and Pulmonary Rehabilitation

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Introduction: Denmark is among the European countries with the highest point prevalence and mortality of chronic obstructive pulmonary disease (COPD). Non-pharmacological interventions are crucial in the process of increasing the health and well-being of patients with COPD. All Danish municipalities offer pulmonary rehabilitation (PR) programmes for patients with COPD. PR can potentially increase physical capacity and quality of life and reduce the risk of exacerbations and hospitalizations. Unfortunately, patients with COPD struggle to sustain their level of physical activity following PR, and the beneficial effects of PR frequently diminish after a period of 6-12 months.

Aim: This project investigates new potential benefits of a pulmonary rehabilitation (PR) programme and how to help patients with COPD stay physically active after PR.

Methods:

1. A quantitative study will explore the effects of PR on musculoskeletal pain levels, COPD symptoms, physical capacity, and quality of life.

2. A qualitative study using semi-structured interviews will explore motivation and barriers to physical activity in patients with COPD who have recently completed a PR programme.

3. A feasibility study will evaluate the feasibility and acceptability of individualized guidance to assist patients with COPD towards peer-based physical activities in the local community following PR.

Perspectives: If we can assist patients with COPD to stay physically active after PR, patients with COPD may be able to maintain the achieved benefits in physical capacity and quality of life.

Themes: Public health, Rehabilitation
Keywords: COPD, Physical activity, Rehabilitation

Potentiation of general anesthesia by local blockade of the peripheral vagus nerve

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Background: General anesthetics are used extensively in modern medicine, but the associated cardiopulmonary risks and chronic neural effects pose a growing issue to aging patient populations. Anesthetic premedication presents a promising method to reduce the risks associated with high-dose general anesthesia.

Methods: The present study was designed to probe the anesthetic sparing properties of acute vagus nerve blockade in mice. To this end, we treated the vagus nerve with either bupivacaine or saline (control) via a pre-installed neck catheter one hour prior to isoflurane gas anesthesia. We assessed the anesthetic potency by computing the anesthetic induction time using a deep learning-based method for pose estimation.

Results: When preceded by vagus nerve blockade, the induction time of isoflurane gas anesthesia decreased by 22% (-15 seconds, $P < 0.05$), consistent with anesthetic potentiation. In addition, vagus nerve blockade exhibited hemodynamic stabilizing effects. Potential confounders, such as age, had minor significance.

Conclusion: Vagus nerve blockade may be an effective general anesthetic adjuvant with hemodynamic stabilizing effects. Further research is needed to confirm the findings presented in this preliminary study, e.g., using targeted vagus nerve blockade and extensive hemodynamic monitoring.

Themes: Neuroscience, Surgery
Keywords: vagus nerve stimulation, locus coeruleus, neural network simulations

Are Sexual assaults a risk factor for functional somatic disorders?

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Background: An increasing number of sexual assaults (SA) are being reported. The consequences of being a victim of SA are unclear. Some studies have implied associations between SA and functional somatic disorders (FSD). This study investigated associations between the severity of SA and the symptom severity of FSD, conceptualized as bodily distress syndrome (BDS).

Methods: 7.493 individuals from the population-based Danish Study of Functional Diseases (DanFund) completed questionnaires on SA, FSD, poor mental health, other traumatic experiences, and sociodemographics. Comparisons between groups were performed by means of χ^2 test. Risk ratios (RR) for FSD and poor mental health were estimated in statistical models with sexual assault as the primary exposure by generalized linear models. We adjusted for: age at examination, self-rated social status, sex, education, and adverse childhood environment.

Results: The results showed that SA was associated with single-organ FSD (RR=1.51; 95%CI=1.22–1.87), multi-organ FSD (RR=3.51; 95%CI=1.89–6.49), and emotional distress (RR=1.75; 95%CI=1.21–2.54). SA showed a higher prevalence and more severe somatic symptoms across all organ systems compared to individuals not exposed to SA. Adjusting for physical and emotional abuse did not change the observed associations. No interactions with poor mental health were found.

Conclusions: Our results suggest that SA is a unique risk factor for FSD, indicating that SA is not solely a risk factor for somatic symptoms centered in the pelvic or gastrointestinal area, but also emerges from and affects the whole body. Due to the cross-sectional study design, further studies are required.

Themes: Public health, Epidemiology
Keywords: Sexual Assaults, Functional Somatic Disorders, Bodily Distress Syndrome

Patient-reported harm following surgery cancellation: a cross-sectional study

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Background: Cancellation of planned surgery poses an ongoing challenge to the healthcare system. Delay in care of a scheduled appointment is described as an example of harm that may negatively impact patients.

Objectives: To estimate the prevalence of harm following surgery cancellation.

Design: A cross-sectional study to measure patient-reported harm following surgery cancellation. The study was conducted at Aarhus University Hospital among patients from various surgical specialties. Data were collected between the 1st of December 2021 to the 1st of June 2022 among patients (>18 years) who had experienced cancellation of planned surgery due to organizational reasons. A constructed survey was emailed to all identified patients in June 2022.

Results: A total of 436 patients (55.5%) replied the survey. Of those, physical worsening was reported by 42% and emotional strain by 48%. A longer waiting period (>30 days) was associated with higher risk of reporting physical worsening than a shorter waiting period (≤30 days). One third of patients had a need of a stronger or higher dose of analgesics in the extended waiting period. New-onset insomnia was reported by 29% of patients. Several patients feared deterioration of their disease (44%) and 9% reported anxiety of dying from their disease.

Conclusion: Harm following cancellation of planned surgery was found to be evident among approximately half of the respondents. Hence, the study directs attention to a need for the development of systems that seek to reduce patient harm when cancellation occurs.

Themes: Public health, Mental health
Keywords: Surgery cancellation, Patient safety, Emotional harm

The validity of instruments to measure knowledge in population-based cancer screening – a systematic review

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Introduction: Relevant knowledge forms the basis of an informed choice of (non)participation in cancer screening. However, general recommendations on measuring individuals' knowledge are lacking, and meta-analysis is hampered by heterogeneity of instruments used. This systematic review evaluates the measurement properties of existing instruments for measuring individuals' knowledge on population-based cancer screening.

Materials and Methods: A literature search was undertaken in PubMed, PsycINFO, Embase, CINAHL, Scopus and Web of Science. The review included any study reporting one or more measurement properties of the instrument or sub-scale used measuring knowledge of cancer screening including breast, colorectal and/or cervical cancer screening. The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) were used to evaluate the methodological quality of the included studies and the measurement properties of the instruments.

Results: Currently, titles and abstracts of 4,602 studies were screened and 355 papers read in full-text. In total 82 studies were included and 28 studies were evaluated using COSMIN. All included studies were assessed as having an inadequate content validity including PROM development. Additional assessment of the measurement properties of the studies were not proceed.

Conclusion: This systematic review will map existing instruments and evaluate their quality. The results indicate a lack of a common understandig of what constitutes relevant knowledge and a need for a well-documented and validated instrument for the measurement of knowledge about cancer screening.

Themes: Public health, Cancer
Keywords: Informed Choice, Questionnaire technique

The Brief Health Literacy scale for Adults: Adaptation and validation of the Health Literacy for School-Aged Children questionnaire

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Background: Health literacy is acknowledged as an important determinant of health. The Health Literacy for School-Aged Children (HLSAC) is a brief, generic instrument measuring self-reported health literacy among school-aged children. Given its brevity and broad conceptualization of health literacy, the HLSAC is a potentially valuable measuring instrument also among adults.

Aim: This validation study aimed to adapt the HLSAC questionnaire to fit an adult population through assessment of content validity and subsequently determine the construct validity of the adapted instrument, the Brief Health Literacy scale for Adults (B-HLA).

Methods: The content validity of the HLSAC was assessed through interviews with respondents and experts, and the structural validity of the adapted instrument (B-HLA) was evaluated using Rasch analysis.

Results: The content validity assessment (n=25) gave rise to adjustments in the wording of five items. The B-HLA demonstrated overall misfit to the Rasch model (n=290). Items 6 and 8 had the poorest individual fits. We found no signs of local dependency or differential item functioning concerning sex, age, education, and native language. The B-HLA demonstrated unidimensionality and ability to discriminate across health literacy levels (PSI=0.80). Discarding item 6 or item 8 resulted in overall model fit and individual fit of all items.

Conclusions: The B-HLA appears to be a valid and reliable instrument for assessing health literacy among adults. However, the instrument would benefit from further refinement of specific items followed by a new assessment of content validity, construct validity, and convergent validity.

Themes: Public health, Public health
Keywords: Health literacy, Patient-reported outcomes, Rasch analysis

The efficacy of blood flow restriction EXercise before total Knee arthroplasty on sit-to-stand function 3 months postoperatively (EXKnee): A randomized controlled trial.

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Objective: To compare eight weeks of preoperative low-load blood flow restricted resistance training (BFR-RT) to preoperative standard care before total knee arthroplasty (TKA) on changes in the 30 seconds chair stand test (30STS) from baseline to three months after TKA as the primary outcome.

Methods: Eighty-six patients scheduled for TKA were randomized to 8 weeks preoperative BFR-RT 3x/week or preoperative usual care. Primary outcome: 30seconds sit-to-stand test. Secondary outcomes: Knee injury and Osteoarthritis Outcome Score (KOOS) subscales Pain, Symptoms, Activities of Daily Living, Sport & Recreation, and Quality of Life, 1repetition maximum (RM) leg press strength on the affected and unaffected leg, exercise adherence, and surgery-related complication.

Results: Intention-to-treat analysis of 86 patients did not reveal significant between-group changes from baseline to three months after surgery on 30STS performance 0.01(95%CI -1.7;1.7). No between-group changes were observed for KOOS subscales. Significant between-group changes in 1RM leg press strength were observed prior to surgery and three months after surgery for both legs favoring BFR-RT. Exercise adherence was 90.6%, and 36 patients completed >80% of the sessions. No differences were observed in surgery-related complication. Two patients declined TKA after engaging in BFR-RT.

Conclusion: Eight weeks of preoperative BFR-RT yielded no superior effects on functional performance or patient-reported outcomes three months after surgery. However, BFR-RT group can induce significant gains in leg press strength lasting up to three months after surgery. Two patients in the BFR-RT group cancelled surgery due to improvements in knee joint pain and symptoms following the intervention period.

Themes: Rehabilitation, Public health
Keywords: Rehabilitation, Physiotherapy, Total Knee Arthroplasty

SESSION 15

The effect of maternal and child BCG scarring on disease severity: An observational hospital-based study from Guinea-Bissau

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Background: The Bacillus Calmette-Guérin (BCG) vaccine against tuberculosis has beneficial non-specific effects, lowering all-cause child mortality. These effects may be amplified if the mother is BCG-vaccinated as well, suggesting maternal priming.

Objectives: To assess the overall and age-specific effects on in-hospital mortality if both child and mother have BCG scars ("double scar") compared with the combined group of just one scar (either child or mother), or no scars ("mono-/no scar").

Methods: Observational study conducted at the main pediatric ward in Guinea-Bissau, examining the overall and age-specific case-fatality of children aged 2-59 months from 2017 - 2023. Data was analyzed in binomial logistic regression models adjusted for child's weight for age and maternal educational level.

Results: BCG scar data was available for 4,017 children; 1,939 were in the double scar group and 2,078 were in the combined group of either mono or no scar (Only child:1,138, Only mother: 457, Neither had a scar: 483). 6.2% (249/4,017) died during admission; 7.4% (153/2,078) in the combined mono-/no scar group and 5.0% (96/1,939) in the double scar group. The overall aRR of dying for mono-/no scar vs. double scar was 1.31 (1.02-1.68). The effect declined with age, being 1.54 (1.03-2.30) from 2-8 months, 1.35 (0.90-2.02) from 9-23 months and 0.89 (0.52-1.51) from 24-59 months.

Conclusion: Corroborating findings from previous studies, children with mono- or no scar tended to have higher risk of in-hospital death compared to children with double scar. These findings suggest further investigation into the priming effect of maternal BCG vaccination.

Themes: Epidemiology, Paediatrics
Keywords: BCG vaccine, Non-specific vaccine effects, Maternal priming

Does co-administration of BCG with Pentavalent vaccine reduce morbidity compared with Pentavalent vaccine only? A natural experiment in Guinea-Bissau

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Background: Vaccines may impact infection susceptibility beyond the specific targeted pathogen through non-specific effects in the immune system. The most recent vaccine has the strongest effect. Studies indicate that co-administration of BCG (scheduled at birth) and the Pentavalent vaccine (diphtheria-tetanus-pertussis-h.influenza type B-hepatitis B (Penta); scheduled after 6, 10 and 14 weeks) is beneficial compared with Penta alone.

In Guinea-Bissau, a BCG shortage 2020-21 caused a natural experiment where delayed BCG vaccines were frequently given with subsequent doses of Penta.

Objectives: To assess whether co-administration of BCG and Penta is associated with a 30% lower risk of health center consultation compared with Penta alone as the latest received vaccine.

Methods: Bandim Health Project (BHP) runs a health and demographic surveillance system. We followed infants between 6 weeks - 9 months of age between 01 Jan, 2021 and 30 Jun, 2023, tracking their vaccination- and health status at bimonthly home visits. Health center consultation rates will be compared for Penta+BCG vs Penta-alone using a Cox hazard model with age as underlying timescale. Baseline characteristics will be adjusted for based on a change in estimate criterion (affect the hazard rate by >10 %). Moreover, we will calculate propensity scores and use inverse probability treatment weights to estimate an average effect.

Results: A total of 2205 children contribute with 4230 observation periods. Final data cleaning and analyses are ongoing.

Conclusion: Investigating whether BCG with Penta is beneficial to child health may identify possibilities to improve immunization programs in low-income countries.

Themes: Infectious Diseases, Public health
Keywords: Childhood Immunization Program, Morbidity, BCG Vaccine

Human papilloma virus prevalence and feasibility of urine- and vaginal self-sampling as cervical cancer screening modalities in HIV-infected women in Guinea-Bissau

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Background: The prevalence and distribution of high-risk human papillomavirus (hrHPV) genotypes are poorly described among women living with HIV (WLWH) in Guinea-Bissau, a country without cervical cancer (CCU) screening despite high burdens of HIV and CCU. Knowledge on hrHPV prevalence and the acceptability of first-void urine and vaginal self-sampling for hrHPV testing among WLWH is essential to contribute to CCU screening policy development.

Objectives: To estimate hrHPV DNA prevalence and -genotype distribution and evaluate acceptability and preferences between two hrHPV self-sampling methods among WLWH.

Methods: WLWH aged 18-64 years were enrolled to self-collect paired first-void urine and vaginal specimens for hrHPV testing, using the AllplexTM HPV HR assay (Seegene, Seoul, Korea), and allows detection of 14 individual hrHPV genotypes. Acceptability and preferences regarding the two sampling methods were assessed using questionnaires.

Results: Data collection is on-going with the aim of enrolling 500 WLWH. Among 448 women both devices were well-accepted, though the urine device was significantly easier (97.8% vs 92.0% $p<0.01$) and more comfortable to use (96.4% vs 92.9%, $p=0.023$). Sample preference was 43.1% (38.6-47.7%), 28.1% (24.1-32.5%) and 27.5% (23.5-27.8%) for urine-, vaginal- and both methods, respectively. Among 30 vaginal samples 66.7% (49.6-82.3%) were hrHPV positive and out of those, 60% (36.1-80.9%) were multiple-infected.

Conclusion: Self-sampling was well-received, with urine being the preferred screening modality. This suggests hrHPV self-sampling could act as a potential CCU screening modality in Guinea-Bissau.

Themes: Infectious Diseases, Cancer
Keywords: HPV self-sampling, Cervical Cancer Screening, HPV DNA testing

Pomalidomide as an immune-enhancing agent for the control of HIV: An investigator-initiated phase I/IIb clinical trial in people living with HIV on ART and during analytical treatment interruption.

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Antiretroviral therapy (ART) suppresses HIV replication and prevents the development of AIDS, but lifelong treatment is required. Persistence of HIV in latently infected CD4+ T cells remains a major barrier to a cure. Other obstacles include the dysfunctional immune responses associated with chronic HIV infection. A key component of future HIV cure strategies could therefore be the use of immune-modifying drugs to re-invigorate dysfunctional HIV specific immune responses.

Pomalidomide is an immune-modulating drug that is licensed for the treatment of cancer. Preliminary data has shown that pomalidomide reduced the frequency of dysfunctional NK cells in samples from people with HIV (PWH) treated ex vivo, whilst increasing NK cell polyfunctionality. Furthermore, pomalidomide drove an expansion of HIV-specific CD8+ T cells and increased CD8+ T cell-mediated HIV-specific lysis ex vivo. Collectively, this data substantiates the evaluation of pomalidomide as an immune-enhancing agent to treat HIV.

Pomalidomide will be investigated in a randomised, placebo-controlled clinical trial. PWH will be randomised 1:1 to receive pomalidomide 2mg or placebo for three treatment cycles, each consisting of 21 days on and a minimum of 7 days off. In phase I, participants will receive cycle I while on suppressive ART. In phase II participants will receive cycle II and III in the setting of an analytical treatment interruption. Primary outcomes are safety and time to viral rebound. Targeted enrolment is 16 per arm.

In conclusion this clinical trial will inform the use of pomalidomide as an agent to reinvigorate anti-HIV immunity and may support immunological control of HIV in the absence of ART.

Themes: Infectious Diseases, Immune diseases
Keywords: HIV cure studies, Immune modifying drugs, Clinical trial

Optimized diagnosis of Tuberculosis in an African HIV cohort

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Background: Guinea Bissau is a country with a high burden of both tuberculosis (TB) and HIV and co-infections occur regularly. This poses a significant challenge as these patients often have atypical presentations and increased risk of extrapulmonary and disseminated TB which complicates diagnostics.

Objectives: To assess the diagnostic efficacy of routine implementation of the Bandim TBscore on treatment naïve HIV patients to enhance the diagnostics of TB. Moreover, assessing the sensitivity of Xpert MTB/RIF when applied on urine samples compared to applying it on sputum samples only.

Methods: Patients ≥15 years were included and examined using the Bandim TBscore and urine samples was collected from all. Patients who scored ≥3 on the Bandim TBscore returned with sputum samples. Sputum and urine samples was analyzed using GeneXpert MTB/RIF. Positive patients were started on TB treatment.

Results: Data collection is on-going with the aim of enrolling 300 new HIV patients. Amongst 231 patients, 24 (10.4%) were positive. Of these 6 (25.0%) were positive on the urine and the sputum samples, 15 (62.5%) were only positive on sputum sample, 3 (12.5%) positive on urine samples only. By implementing the Bandim TBscore and urine samples, an additional 9 (37.5%) patients were identified that were not suspected of TB when following the local guidelines. Six (25.0%) of these were found by using the Bandim TBscore, 3 (12.5%) by urine samples.

Conclusion: Implementation of this approach has so far identified 24 positive patients. Adding urine samples and the Bandim TBscore to the diagnostic algorithm has increased the TB diagnostics with 37.5% (18.8-59.4%). Final results are still pending.

Themes: Infectious Diseases, Diagnostics & technology
Keywords: Tuberculosis, HIV, Guinea-Bissau

PET/MRI fails to detect suppressed Staphylococcus aureus prosthetic vascular graft infection (PVGI) in a rat model

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Background: Infections remain a serious complication to the usage of vascular grafts. This study aimed to investigate the natural course of infection and response to treatment through PET/MRI and ex vivo bacterial quantification in a rat model of PVGI.

Methods: Rats received a PTFE graft implanted in a. carotis communis. Prior to insertion, implants were inoculated with Staphylococcus aureus or left sterile. Rats were scanned on day 10 (n=6 S. aureus/sterile), day 20 (n=5 S. aureus, n=6 sterile) and day 31 (n=14 S. aureus, n=8 sterile) post-surgery in a Mediso nanoScan® PET/MRI. Post-scan, animals were euthanized, and implants retrieved for CFU enumeration. N=8 S. aureus rats received daptomycin and rifampicin on day 20-29.

Results: S. aureus rats exhibited a stable infection with an increase in median log CFU/implant (range) over the study period from 6.8 (6.1–7.2) at day 10, to 7.7 (7.3–8.8) at day 31 ($p=0.001$, Mann-Whitney test). Animals treated with daptomycin/rifampicin had a load of 1.8 log CFU/implant (0.0–2.5), which was lower than untreated S. aureus ($p<0.01$), but higher than sterile ($p=0.03$).

SUVmax was highest for all groups at day 10 and exhibited a similar decline over time for all groups. At all timepoints, median SUVmax was significantly higher in S. aureus rats compared to all other groups. At day 31, SUVmax was comparable between sterile and treated rats.

Conclusion: PET/MRI could distinguish between infected and sterile rats but was ill-suited to monitor natural course of S. aureus infection, as SUVmax fell significantly while CFU remained stable/rose. Further, SUVmax was similar between animals with suppressed infection and sterile animals.

Themes: Infectious Diseases, Animal Models
Keywords: Implant-associated infections, Bacteriology, PET/MRI

Time to Clearance of SARS-CoV-2 Infections in Immunocompromised Patients

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Evidence suggests that immunocompromised (IC) individuals are at greater risk of COVID-19-related mortality compared to immunocompetent individuals. Data indicate that SARS-CoV-2 infections can persist for prolonged periods in IC individuals with highly varying disease outcome and symptom profile. There is a need for further characterization of the complex immunological mechanisms contributing to diverging disease outcomes in IC patients with identification of factors associated with time to viral clearance (TTC).

We established a patient cohort of 43 SARS-CoV-2 PCR positive IC patients. Study visits were repeated with 4-8 weeks intervals until viral clearance was confirmed, with collection of blood and pharyngeal swab samples. The cohort consists of 27 patients with hematological malignancy (HM), 11 solid organ transplanted patients, and 5 patients with other immunocompromising conditions. We assessed TTC and found no significant difference among the groups, although the HM group generally had longer TTC. We further sub-stratified the HM group to reveal a significantly longer TTC among the remaining HM patients compared to all other groups when subtracting the multiple myeloma patients as a separate group. We measured serum antibodies against SARS-CoV-2 nucleocapsid at visit 2 and found that IC patients had significantly lower antibody levels compared to immunocompetent individuals, and antibody levels correlated with TTC. Furthermore, levels were significantly lower among patients who previously received B-cell depleting antibodies as well as these patients having significantly longer TTC. Deep characterization of cellular immunity and its role in TTC is ongoing.

Themes: Infectious Diseases, Immune diseases
Keywords: SARS-CoV-2, Immunocompromised patients, COVID

Factors influencing time to viral rebound during analytical treatment interruption in clinical HIV trials

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Background: Human immunodeficiency virus (HIV) continues to be a challenge worldwide. Antiretroviral therapy (ART) is effective in controlling the virus but if ART is stopped, the virus rebounds within weeks, necessitating people living with HIV to adhere to a daily ART regimen throughout life.

Hypothesis: A functional cure characterized by effective HIV-specific immunity controlling the viral burden can remove the need for continuous ART. In the search for a functional HIV cure, both viral and host factors influencing time to rebound (TTR) are of highest importance. To identify these factors effect on TTR, clinical HIV trials, including an analytical treatment interruption (ATI), are valuable.

Methods: A meta-analysis based on six prospective clinical HIV trials will be conducted. All clinical trials were conducted or partially conducted at Department of Infectious Diseases, Aarhus University Hospital. The trials included people living with HIV and an ATI was part of the study design. One of the outcomes was TTR. All trials have been published from 2014 to 2023. For this meta-analysis variables are extracted, and statistical analysis are made for comparison.

Perspectives: A functional cure will enhance quality of life for people living with HIV and expenses related to management and treatment will decrease.

Themes: Infectious Diseases, Immune diseases
Keywords: HIV, Functional cure, Time to viral rebound

Clinical significance, species distributions and temporal trends of nontuberculous mycobacteria isolates in Denmark from 1991 through 2022: a nationwide study of microbiology data

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Introduction: Nontuberculous mycobacteria (NTM) can lead to a wide spectrum of clinical manifestations depending on the degree of exposure, species virulence, host immunity, and infection site.

We aimed to describe the clinical significance, species distribution, and temporal trends of NTM infections in Denmark.

Methods: In a nationwide register-based study, we included all individuals with a positive NTM isolate in Denmark from 1991 to 2022 and used microbiological data to assess the clinical significance of pulmonary NTM. Using a validated method, patients were categorised as definite disease, possible disease, or colonization. Temporal trends were evaluated using a Poisson regression model.

Results: Most patients had definite disease (n=2158, 52%) while 26% (n=1060) had possible disease and 22% (n=905) had colonization. The species most often associated with definite pulmonary NTM disease were Mycobacterium malmoense (55.4%), M. kansasii (45.5%), and M. avium complex (36.1%). When combining definite and possible disease, M. kansasii (86.4%), M. malmoense (81.0%), and M. szulgai group (78.4%) were the most significant species. Across disease categories and locations, M. avium complex was highly predominant. The incidence rate of a positive NTM culture per 100,000 individuals increased throughout the period.

Conclusion: NTM infections, particularly pulmonary, are increasing in Denmark. M. malmoense, M. kansasii, M. szulgai, and M. avium complex are the most clinically significant. M. avium complex is of greatest relevance due to the high prevalence.

Themes: Infectious Diseases, Epidemiology
Keywords: Nontuberculous mycobacteria, Clinical significance, Temporal trends

Treating tuberculosis-driven malnutrition with a protein-rich nutritional supplement improved tuberculosis treatment adherence but not weight gain: a multicenter, open-label, cohort randomized controlled trial

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Introduction: Tuberculosis (TB) disease causes malnutrition due to reduced appetite, malabsorption and altered metabolism. In resource-poor and food insecure settings it is important to treat malnutrition alongside TB infection to improve treatment outcome. The aim was to evaluate the effect of a protein-rich nutritional supplement on anthropometric measures and treatment outcome in patients with TB living in Guinea-Bissau, West Africa.

Methods: A multicenter, open-label, cohort randomized controlled trial was conducted between July 2017 and August 2022. Patients ≥18 years with newly diagnosed drug-susceptible TB and BMI <20 kg/m2 were included in the study from four TB treatment sites. The intervention group received a daily protein shake comprising 62.5g whey protein powder (245 kcal, 47.5g protein, Lacprodan DI-8090®) for 6 months i.e. duration of TB treatment.

Results: Out of 232 patients, 114 were assigned the control group and 118 the intervention group. No differences in anthropometric measures were observed between the groups after 6 months. Patients in the intervention group were less likely to have an unsuccessful treatment outcome (treatment failure, lost-to-follow-up (LTFU) and death), OR 0.63 (95% CI 0.31–1.25), and significantly less likely to be LTFU during treatment, HR 0.48 (95% CI 0.24–0.98).

Discussion: While the nutrition therapy did not further improve anthropometric measures, it did improve treatment adherence and reduced the number of patients LTFU. This could potentially result in a reduced number of relapse cases and new drug-resistant TB cases.

Trial registration: ClinicalTrials.gov ID: NCT3302949

Themes: Infectious Diseases, Public health
Keywords: Tuberculosis, Malnutrition, Nutrition Intervention

SESSION 16

Can high maternal vitamin D levels positively affect prenatal neurodevelopment in obese pregnancies?

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Background: Overweight and obesity among pregnant women is a global health problem, associated with neurodevelopmental, metabolic, and cardiovascular health issues in the children. Maternal overweight/obesity increase macrophage presence in the placenta indicating increased placental inflammation, and animal studies show that placental inflammation may cause adverse effects in the offspring. During fetal development, the placenta supports brain development by supplying neurotrophic signals including brain derived neurotrophic factor (BDNF) and inflammatory cytokines.

Vitamin D plays an important role in the function of the immune system and in brain development. Notably, vitamin D deficiency is common among pregnant women worldwide.

This study aims to investigate if obesity and high vitamin D serum levels during pregnancy affects prenatal neurodevelopment determined by the inflammatory status and the BDNF levels of the placenta.

Methods: Women are recruited at Randers Regional Hospital as part of a larger randomized clinical trial investigating the effect of increased vitamin D supplement during pregnancy (10µg vs. 90µg). Umbilical cord blood samples and placental samples are collected within five hours after birth. Gene and protein expression of pro-inflammatory cytokines and BDNF will be analyzed with qPCR and ELISA.

Results: The study is ongoing.

Primary outcome: Neurotrophic levels in umbilical cord blood.

Secondary outcome: Inflammatory status in placental tissue.

Conclusion: We expect that this study will provide new insight on how maternal obesity affects the placenta and whether increased vitamin D supplementation during pregnancy can ameliorate such adverse effects.

Themes: Gynecology and obstetrics, Neuroscience
Keywords: Vitamin D, Obesity, BDNF

Artificial sweeteners in pregnancy and childhood overweight

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Background: Artificial sweeteners (AS) are becoming increasingly popular as a way of decreasing caloric intake, and the sweeteners are believed to be a safe alternative to sugar. However, previous studies suggest that AS consumption during pregnancy can affect the offspring's weight in childhood.

Objective: We wished to examine the association between prenatal exposure to AS and overweight from birth to 11 years of age, in the Danish National Birth Cohort (DNBC).

Methods: 101,042 mother-child dyads were enrolled in the DNBC from 1996-2002. 72,821 women completed a Food Frequency Questionnaire in gestational week 25 reporting frequency of consumption of beverages sweetened with AS (ASB) or sugar. Anthropometric measurements of the singleton children were obtained at birth, 5 and 12 months, 7 and 11 years. We performed multivariate logistic regression to obtain the odds ratio (OR) for overweight in relation to maternal consumption of ASB. The analyses were adjusted for parental and early life risk factors for childhood overweight, including maternal pre-pregnancy body mass index (BMI), Healthy Eating Index, smoking and physical activity in pregnancy, duration of breastfeeding, parental socioeconomic status and paternal BMI.

Results: We found an increased odds of overweight at 7 and 11 years in children, whose mothers reported drinking ≥1 ASB daily during pregnancy compared to never consumption (7 years: adjusted OR (aOR) 1.16 (95% confidence interval (CI) 1.05-1.29) and 11 years: aOR 1.19 (95%CI 1.05-1.34)).

Conclusion: We found that in utero exposure to AS increases the risk of overweight in later childhood, but not at birth or in infancy in a Danish population.

Themes: Gynecology and obstetrics, Epidemiology
Keywords: Artificial Sweeteners, Childhood Obesity, Prenatal Exposures

Can increased vitamin D supplementation reduce obesity-related inflammation in pregnancy?

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Background: Obesity and overweight during pregnancy have become a major clinical concern. In Denmark, one out of every three pregnant women suffer from overweight or obesity, thereby increasing pregnancy complications. Mechanistically, overweight is associated with chronic inflammatory activity, impacting both the mother and placenta. This association has been linked to adverse effects on the next generation, including an increased risk of cardiovascular disease, obesity, and neurodevelopmental challenges in the offspring. It is well-known that vitamin D (VD) is important for macrophage function as VD reduces inflammatory activity by suppressing the pro-inflammatory M1 macrophage fraction. Furthermore, VD affects lipid- and glucose metabolism by stimulating insulin production and affecting β-cell response to inflammation.

The aim of this study is to characterize the inflammatory activity during the third trimester of pregnancy concerning overweight and investigate if increased dose of maternal VD supplementation affects the inflammatory profile.

Methods: The GRAVITD trial is a double-blinded randomized clinical trial investigating the effects of increasing VD supplementation during pregnancy. From this cohort, a total of 156 maternal third trimester serum samples were obtained. Multiplex ELISA were performed targeting MCP-1, IL-17, IL10, IL1beta, IL4, IL13, IL6, and TNF-alpha. Samples were also analyzed for 25(OH)D using HPLC-MS/MS at Department of Biochemistry at Aarhus University Hospital.

Results: The study is ongoing; results will be presented.

Themes: Gynecology and obstetrics, Molecular biology
Keywords: Inflammation, Vitamin D, Obesity

The impact of Maternal Scanning Outreach in rural Sierra Leone on the referral of women with high-risk births to Masanga Hospital.

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Background: Sierra Leone has some of the highest maternal and perinatal mortality rates in the world. Many women, living in rural areas, give birth outside hospital facilities with severe or fatal consequences especially for women with high-risk pregnancies and their unborn child. We hypothesize that an antenatal Maternal ultrasound Scanning Outreach programme (MSO) increases the prevalence of women with high-risk pregnancies who give birth at Masanga Hospital and provides better birth outcomes for the mother and the babies. The aim of this study was to assess the effect of MSO in rural Sierra Leone.

Method: The study compared the prevalence of high-risk births, perinatal deaths and severe maternal complications related to birth at Masanga Hospital before and after the implementation of MSO. All women giving birth at the hospital one year before and after the implementation of MSO were included. Data was manually extracted from medical records at Masanga Hospital.

Results: The prevalence of high-risk births at Masanga Hospital was increased by 7 % after the implementation of MSO (RR = 1.07 (95% CI [0.97 ; 1.19]). The prevalence of maternal near-miss events among high-risk births decreased (RR = 0.74, 95%CI [0.57 ; 0.97]), and the prevalence of intrapartum perinatal deaths among high-risk singleton births decreased (RR = 0.45, 95%CI [0.06; 1.06]).

Conclusion: Although not statistically significant, more women with high-risk pregnancies gave birth at the hospital and these had better maternal and perinatal outcomes after the implementation of MSO. This study will yield novel insights into the value of antenatal ultrasound offered in an outreach program in rural Sierra Leone.

Themes: Gynecology and obstetrics, Public health
Keywords: Antenatal ultrasound, Rural Sierra Leone, Maternal and child health

Impact of surgery on fertility among patients with deep endometriosis

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Objective: Aim of the study was to investigate pregnancy and live birth rate after surgical resection of rectosigmoid deep endometriosis (DE) and assess if complications affect these rates.

Study design: Case series of 193 women with rectosigmoid DE and pregnancy intention undergoing a rectosigmoid resection for DE from January 2009 to May 2019. All surgeries were performed at the Department of Obstetrics and Gynecology, Aarhus University Hospital, Denmark. Surgical and fertility outcome data were obtained through patient files.

Results: 117 women became pregnant postoperatively with a pregnancy and live birth rate of 60.6% and 53.9%, respectively. 39 women (20.2%) became pregnant spontaneously and 78 women (40.4%) by intrauterine insemination or assisted reproductive technologies. Median time to pregnancy after surgery was 12.4 months (range: 0.4–58). Clavien-Dindo complication grade III (none grade IV) was registered among 16.6%. These women had pregnancy and live birth rates of 50%, not statistically significantly different from those without complications.

Conclusions: Informing women with bowel endometriosis and pregnancy intention regarding treatment choice is not easy. Our results indicate that the risk of complications does not seem to affect either chance of pregnancy or live birth rate. Further research is necessary in this field to achieve enough evidence to inform this group of women sufficiently.

Themes: Gynecology and obstetrics, Surgery
Keywords: Endometriosis, Endometriosis surgery, Pregnancy

Insulin resistance in gestational diabetes mellitus

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Background: Gestational diabetes mellitus (GDM) is one of the most common pregnancy disorders affecting around 5% of the Danish pregnant population. Women diagnosed with GDM in one pregnancy have increased risk of developing GDM in following pregnancies and a lifelong increased risk of diabetes. A complication to GDM is excess fetal growth caused by maternal hyperglycemia. Intermittent blood glucose monitoring is used to tailor the treatment, but despite well-regulated blood glucose excess fetal growth occurs. Continuous glucose monitoring, when used in the treatment of Type 1 Diabetes, reduces maternal hyperglycemia and glycemic variability resulting in reduced frequencies of large newborns.

Aim: The aim of this study is to examine the glycemic variability monitored by continuous glucose monitoring in GDM pregnancies as a predictor for large for gestational age fetuses.

Methods: A prospective cohort study will be performed, analysing data from 14 days of continuous glucose monitoring from 100 women with GDM. All women will wear a blinded continuous glucose monitor and an activity tracker for 14 days and continue fingertip measurements of blood glucose.

Perspectives: We wish to apply the use of continuous glucose monitoring in a GDM setting to investigate if fetal growth is better predicted from continuous glucose measurements rather than single point measurements of blood glucose.

Gaining knowledge on the consequences of glucose excursions during GDM will help clinicians to tailor the best possible treatment and hopefully contribute to alter the course of GDM.

Themes: Gynecology and obstetrics, Endocrinology
Keywords: Gestational Diabetes Mellitus, Diabetes in pregnancy, Continuous glucose monitoring

ABCB1 expression is increased in human first trimester placenta from pregnant women classified as overweight or obese

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Worldwide, millions of pregnant women are affected by obesity. Placental function is essential for pregnancy outcome. The transporter proteins P-glycoprotein (P-gp), encoded by the gene ABCB1, and Breast Cancer Resistance Protein (BCRP), encoded by the gene ABCG2, are important for trans-placental transport of endogenous substances including cortisol and sugars. Importantly, they also protect the fetus from xenobiotics (e.g. pharmaceuticals). Animal studies suggest that maternal nutritional status can affect expression of placental transporters, but little is known about the effect on the human placenta, especially in early pregnancy.

We investigated if overweight and obesity in pregnant women altered the mRNA expression of ABCB1 encoding P-gp or ABCG2 encoding BCRP in first trimester human placenta. With informed consent, 75 first trimester placental samples were obtained from women voluntarily seeking surgical abortion (< gestational week 12). Maternal BMI was defined at the time of termination of pregnancy. Compared to normal-weight pregnancies (BMI 18.5–24.9 kg/m2, n = 34), ABCB1 mRNA expression was significantly increased in placenta samples from women classified as overweight (BMI 25–29.9 kg/m2, n = 18) ($p = 0.040$) and women classified as obese (BMI ≥ 30 kg/m2, n = 23) ($p = 0.003$). The mRNA expression of ABCG2 was unaffected by maternal obesity ($p = 0.291$).

In conclusion, maternal BMI affects ABCB1 but not ABCG2 mRNA expression in first trimester human placenta, indicating obesity-induced placental changes in the early pregnancy. Further studies should determine the potential consequences for placental-fetal interaction, e.g. in case of medication during pregnancy.

Themes: Pharmacology, Gynecology and obstetrics
Keywords: P-glycoprotein, Placental-fetal interactions, Placental transporter

Placental mosaicism for autosomal trisomies: a registry-based study of Danish cases 1983-2021

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Background: Mosaicism is defined by the presence of two or more cell lines within the same tissue and is found in 2-4% of placental samples (CVS). Most often the mosaic cell line is confined to the placenta (CPM), but the risk of fetal involvement varies with the involved chromosome. In this study we aimed to identify all cases of placental mosaicism in Denmark from 1983 to 2021 and estimate chromosome-specific risk of fetal involvement and to examine if this risk is affected by maternal and/or pregnancy characteristics.

Methods: The Danish Cytogenetic Central Registry (DCCR) was searched for cases of singleton pregnancies diagnosed with mosaicism in the placenta between 1983 and 2021. Cases with XX/XY were excluded. Ascertained cases from DCCR from 2008-2018 were then coupled with data from the Danish Fetal Medicine Database. All cases were manually reviewed.

Results: 1,063 cases of placental mosaicism with follow-up analyses (amniocentesis and/or fetal tissue) were identified. Of these 512 were mosaics for autosomal trisomies. The overall risk of true fetal mosaicism (TFM) involving any autosome was 13.1% (95%CI: 10.3;16.3) with great variation across chromosomes, e.g. trisomy 7: 0% (97.5%CI: 0;6.6) and trisomy 21: 42.5% (95%CI: 27.0;59.1).

Conclusion: When mosaicism for an autosomal trisomy is detected in CVS, the risk of fetal involvement varies greatly between chromosomes, from 0% (trisomy 7) to 42.5% (trisomy 21), and risk estimates should be chromosome specific when counselling pregnant couples.

Themes: Gynecology and obstetrics, Epidemiology
Keywords: Fetal diagnostics, Genetics, Mosaicism

Fetal membrane cells in maternal blood after rupture of membranes

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BACKGROUND: In both term and preterm pregnancies, rupture of the fetal membranes (ROM) is preceded by fetal membrane inflammation, cellular senescence, and microfractures. We hypothesize that this damage is associated with shedding of fetal membrane cells into the maternal blood, and that their concentration constitute a biomarker for threatening ROM. The aim of this study was to evaluate whether it is possible to isolate fetal membrane cells in maternal blood after ROM at term. The perspective is that their concentration is increased at threatening preterm prelabor rupture of the fetal membranes (pPROM), as this condition is characterized by a more pronounced fetal membrane damage.

METHODS: Blood samples (30 mL) were drawn from 20 term pregnant women (GA>37) with ROM. Fetal cells were isolated by a combination of Magnetic Activated Cell Sorting (using a pool of 12 cell-surface antibodies) and Florescent Activated Cell Sorting (using a pool of 12 fluorescent-labeled cytoplasmic antibodies). The fetal origin of the isolated cells were verified by Short Tandem Repeat analysis.

RESULTS: Fetal cells were identified in 10 of 20 blood samples (50%). Their numbers ranged from 1 to 12 cells. The median time between ROM and blood sampling was 2.8 h (95%CI [1.5;5.5]) for samples with fetal cells and 9.9 h (95% CI [5.1;19.1]) for samples without fetal cells (median ratio = 3.5 (95% CI [1.4;8.9]), $p < 0.02$).

CONCLUSION: After ROM at term, it is possible to isolate fetal cells in maternal blood, and these cells are likely to be of fetal membrane origin because: 1) they are isolated by using antibodies highly expressed in fetal membrane cells, and 2) their presence correlates with time after ROM.

Themes: Gynecology and obstetrics, Diagnostics & technology
Keywords: Fetal membranes, Preterm birth, Biomarkers

SESSION 17

Equal access to HPV-vaccination: Preliminary results of a cross-sectorial intervention of School-based HPV-education and -vaccination.

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Background: Human Papillomavirus (HPV)-related cancer diseases can be prevented with vaccination. Despite free access to vaccination through the Danish Childhood Vaccination Program, children with ethnic minority background attend substantially lesser than native children (65% vs. 93%).

Practical as well as emotional barriers regarding sexuality and cultural taboos, need to be accommodated, to achieve increased participation. In collaboration with multiple stakeholders, we developed a culturally adapted intervention aiming to improve HPV-vaccination coverage by 10%-point for ethnic minority children.

Methods: The study is a non-randomized implementation study. The cross-sectorial intervention was developed and conducted according to Complex Interventions Framework.

The intervention was implemented throughout school year 2022-23 and consisted of three school-based core elements: 1) parental HPV-education, 2) pupil HPV-education, and 3) HPV-vaccination at school.

Intervention group: 670 nine-13-year-old pupils at five schools in the Municipality of Aarhus, with proportion of pupils with ethnic minority background varying from 26% to 91%.

Control group: 3000 children comparable in age and community.

Results: Analysis of quantitative and qualitative results are ongoing, and preliminary results will be presented. Primary outcome is difference in HPV-vaccination coverage between intervention and control group. The intervention has been qualitatively evaluated in 10 focus-group interviews.

Conclusion: The study has potential to increase attendance in HPV-vaccination by breaking down barriers to participation. It may serve as a means, to obtain equity in HPV-related cancer prevention.

Themes: Gynecology and obstetrics, Health Education
Keywords: Complex intervention, HPV-vaccination, Equity in health

Perceived stress and the risk of spontaneous abortion

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Spontaneous abortion (SAB), defined as pregnancy loss <22 weeks of gestation, occurs in 15-25% of all pregnancies. Experiencing an SAB can be emotionally and physically exhausting. Stress is common in women of reproductive age. However, limited evidence exists of the association between stress and SAB. This study aims to investigate the association between preconception stress and the risk of SAB in two Danish preconception cohorts.

We used self-reported questionnaire data from two preconception cohorts of >16000 women trying to conceive (SnartGravid.dk and SnartForældre.dk cohorts) in combination with registry data from The Danish National Patient Registry and The Danish National Birth Registry to assess stress and identify SABs. Participants completed questionnaires on sociodemographic, reproductive, and behavioral factors at baseline and at follow-up every 8 weeks until pregnancy or for up to 12 months. Psychological stress was assessed with the Perceived Stress Scale 10. SABs were identified via self-report in questionnaires and through registry data allowing us to identify early and late SABs.

The analytic sample consisted of 8082 participants who reported a pregnancy within 12 months of study entry with a median perceived stress score of 13 (IQR 9-17). We identified 1433 SABs with a median gestational age of 7 weeks (IQR 6-9).

We will use Cox proportional hazards regression models with gestational weeks as time scale to compute hazard ratios and 95% confidence intervals for associations between stress and SABs. The models will be adjusted for possible confounding factors such as socioeconomic status, age, and behavioral factors. Analyses are ongoing.

Themes: Epidemiology, Gynecology and obstetrics
Keywords: Preconception, Perceived Stress, Spontaneous Abortion

Self-reported sleep quality correlates with infection risk: results from the Danish Blood Donor Study

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Objectives: Sufficient sleep quality is important for maintaining immune system homeostasis and, thus resistance to infections. However, its impact on all-cause infections in generally healthy populations remains insufficiently studied. The present study investigated the association between self-reported sleep quality and the risk of all-cause infections among healthy blood donors with no known comorbidities.

Methods: In this prospective cohort study, we included 71,287 blood donors from the Danish blood donor study (DBDS) who had completed a questionnaire on sleep quality, lifestyle factors, and health-related items. Questionnaire data were linked with health registry data on redeemed prescriptions of antimicrobial agents, a proxy for acute infections. Sex-stratified hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using multivariable Cox proportional hazard analysis adjusted for relevant confounders.

Results: A total of 15,291 (22.8%) participants redeemed at least one antimicrobial prescription within 12 months after inclusion. Participants reporting chronic insomnia, daytime fatigue, or short sleep duration had an increased risk of redeeming an antimicrobial prescription; estimated HR 1.13 (95% CI: 1.08 –1.18) in females; 1.10 (95% CI: 1.05–1.16), in males. Antimicrobial use also appeared to increase with number of reported sleep problems.

Conclusion: Poor sleep quality was associated with increased risk of antimicrobial prescription redemption in a large cohort of healthy individuals without known comorbidities. These findings highlight the importance of sleep quality for infection risk, even among healthy individuals.

Themes: Epidemiology, Infectious diseases
Keywords: Blood donors, Sleep, Infectious disease

Physical Activity and Risk of Spontaneous Abortion in a Danish Preconception Cohort

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Background: Spontaneous abortion (SAB) affects about 15-30% of all pregnancies, making it one of the most common pregnancy complications. The causes of SABs are multifactorial, but the evidence on whether and how physical activity (PA) influences the risk of SAB has been inconsistent.

We aim to quantify the association between replacement of pre-pregnancy sedentary time with different intensities of PA and the risk of SAB in a Danish preconception cohort.

Methods: We included 4,724 participants who conceived after entry in the SnartForældre.dk cohort from 2011 to 2023. Information was collected via baseline and bi-monthly questionnaires linked with Danish registries. The International Physical Activity Questionnaire was used to measure PA before conception and pregnancy outcomes were identified through follow-up questionnaires, the Danish National Patient Registry, and the Medical Birth Registry.

We used Cox proportional hazards regression models to calculate hazard ratios (HR) and 95% confidence intervals (CI), using gestational weeks as the time scale. Isotemporal substitution modeling was used to examine the effect of replacing fixed durations of sedentary time with walking, moderate and vigorous intensity PA.

Preliminary results: SAB risk was 18% and median gestational weeks at loss was 7 (interquartile range: 5-9 weeks). The HR for replacing 30 minutes of sedentary time/day with 30 minutes of walking, moderate or vigorous PA were 1.00 (95% CI 0.99-1.02), 1.05 (95% CI 0.96-1.15), and 1.00 (95% CI 0.88-1.13), respectively.

Conclusion: Substitution of 30 minutes of sedentary time/day with the same duration of different intensities of PA were not associated with risk of SAB.

Themes: Epidemiology, Gynecology and obstetrics
Keywords: Physical activity, Spontaneous abortion, Preconception cohort

Time trends in incidence of pilonidal disease from 1996 – 2019 - A Danish population-based cohort study

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Background: Pilonidal disease (PD) is a condition commonly encountered in the clinic. Studies indicate a surge in occurrence over the past decades. However, current knowledge is based on small studies with few patients, selected age groups, or primarily men. The aim of the present study is to assess time trends in incidence and age distribution in a nationwide Danish setting.

Metode: Using nationwide data from the Danish National Patient Registry and the Civil Registration System (1996-2019), we identified a cohort of 41,031 patients recorded with diagnostic or surgical procedure codes representing PD. We computed the incidence rate, incidence rate ratio (IRR) and, median age in 5-year intervals.

Results: The overall incidence of PD has increased from 27.3 (95% CI: 26.7-27.9) /100,000 PY in 1996-2000 to 39.8 (95%CI: 38.9-40.7) /100,000 PY in 2015-2019. For men, the incidence has increased from 38.2(95%CI: 37.1 – 39.2) to 57.1 (95%CI: 55.5 – 58.7) /100,000 PY and for women the incidence has increased from 16.7(95% CI: 16.0 – 17.4) to 22.6 (95% CI: 21.6 – 23.7) /100,000 PY. Comparing men to women, the IRR increased from 2.3(95%CI: 2.2 – 2.4) in 1996-2000 to 2.5(95%CI: 2.4 – 2.7) in 2015-2019. The median age at first contact has decreased at the same time-period from 27 to 25 years in men and from 25 to 23 years in women.

Conclusion: Since 1996, the PD incidence has increased significantly, notably affecting males the most and widening the gender gap. Simultaneously, median age at first contact has decreased. The increased burden of disease and surgery is not reflected within the literature and more studies are warranted to further our understanding of this condition.

Themes: Surgery, Epidemiology
Keywords: Pilonidal disease, Incidence, Abscess

Recurrent ischemic stroke in patients with atrial fibrillation on oral anticoagulants: a nested case-control study in Denmark

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Background: Atrial fibrillation (AF) is an important risk factor for ischemic stroke (IS). Treatment with oral anticoagulants (OAC) reduces the risk of IS. However, patients may still suffer an IS or recurrent IS (re-IS) in spite of OAC treatment.

Aim: We aimed to estimate the cumulative incidence for re-IS in patients with AF starting or continuing OAC after an index stroke, and the incidence rate of re-IS for both OAC initiators and restarters after index stroke (cohort analysis).

In addition, to describe characteristics of patients with re-IS including stroke severity and short-term mortality of re-IS, and to estimate the risk of re-IS associated with OAC discontinuation (nested case-control analysis).

Methods: We conducted a nationwide register-based cohort study and a nested case-control study within the study cohort. The study period began January 2014 and ended June 2022. We used the Danish registries (The Danish Stroke Registry, The Danish National Patient Register, The Danish Prescription Register and The Danish Civil Registration System) to identify the cohort of AF patients admitted for IS (index stroke) who initiated or restarted OAC treatment after their index stroke. We followed this group of patients for re-Is.

Results: pending – data is being analyzed and will be presented on phd-day 2024.

Conclusions: pending.

Themes: Neuroscience, Epidemiology
Keywords: Stroke, Atrial fibrillation, Oral anticoagulation

Validation of a Classification system for Periprosthetic Joint Infections.

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Background: Periprosthetic Joint Infection (PJI) is the most feared complication of hip and knee joint arthroplasty. A classification system has been proposed to stratify the complexity of PJI. This study aimed to validate this classification system in a large prospectively collected Australian microbiological confirmed PJI cohort.

Methods: We applied an adapted version of the JS-BACH classification of PJI complexity to the Prosthetic Joint Infection in Australia and New Zealand, Observational (PIANO) cohort. The PIANO cohort consists of 653 patients from 27 hospitals, with large joint arthroplasty, 2 years follow-up, and a stringent definition of success. Patients were classified into 3 categories with increasing treatment complexity. Treatment success was assessed based on survival, prosthetic function, infection resolution, and absence of antibiotic use.

Results: The cohort was classified into "1- uncomplicated" (n=268), "2- complex" (n=330), and "3- limited options" (n=55). We found similar demographics with the original JS-BACH population but a difference in category distribution with more DAIR procedures, less one and two-stage procedures, and a higher proportion of uncomplicated patients. We found significant differences in treatment outcomes with odds ratio for category 1 vs. 2 was 1.75 (95% CI: 1.24 – 2.47), and for category 1 vs. 3, it was 7.12 (95% CI: 3.42 – 16.02).

Conclusion: The adapted JS-BACH classification system proves valuable in evaluating the risk of treatment failure for PJI in hip and knee arthroplasties within PIANO cohort. However, its clinical significance for orthopaedic surgeons remains uncertain and an area that warrants further exploration.

Themes: Surgery, Epidemiology
Keywords: Ortopædkirurgi, Proteseinfektion, Klassifikationssystem

Danish translation, modification, and validation of the Eustachian Tube Dysfunction Questionnaire

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Introduction: The Eustachian tube is a connection between the nasopharynx and the middle-ear cavity. It mainly has three functions: ventilation and pressure-equalization, removal of secretion from the middle-ear cavity and protection against retrograde infections from the nasopharynx. When this function is impaired, a condition called Eustachian tube dysfunction (ETD) occurs. ETD consists of a variety of symptoms including otalgia, fullness and hearing impairment. No test or symptom can single-handedly diagnose ETD. A patient-reported symptom score called the Eustachian Tube Dysfunction Questionnaire (ETDQ-7) was developed in 2012. Due to the need for clarification of the clinical usefulness of ETDQ-7 in a Danish ear-nose-throat setting, the aim of the study is to translate, modify and validate ETDQ-7 into Danish.

Methods: ETDQ-7 was filled out by 75 patients with ETD who were referred to the Ear-Nose-Throat Department, Regional Hospital West. 20 patients repeated this after four weeks. Tympanostomy was performed on the affected ear/ears to normalize middle-ear pressure. ETDQ-7 was completed again for both ears with open tympanostomy tube(s). 75 age- and gender matched controls filled out ETDQ-7.

Results: Test-retest showed good reliability ($p=0.19$). Mean ETDQ-7 score in the symptomatic ears was 32.0, receding to 16.5 after tympanostomy ($p<0.000$). Mean ETDQ-7 score in asymptomatic ears in ETD patients was 10.2 compared to 9.4 in controls ($p=0.20$).

Conclusion: ETDQ-7 is a helpful tool, that can aid clinicians diagnosing ETD and evaluate the effectiveness of a treatment.

Themes: Surgery, Diagnostics & technology
Keywords: Eustachian tube, Ear-nose-throat, Questionnaire

Target and failure pattern in SCC-HNCUP: a prospective phase-4 study from DAHANCA

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Purpose or Objective: The Danish national guidelines for head and neck squamous cell carcinoma of unknown primary (SCC-HNCUP) is from 2013. The guideline recommends bilateral elective neck irradiation. Elective mucosal areas typically include pharynx and larynx. Depending on affected neck node levels, nasopharynx is omitted in some cases and in other cases, only the oral cavity and oropharynx are irradiated. Trends towards a more individualized treatment approach with unilateral irradiation are emerging.

Aiming to assess compliance to treatment guidelines, a comparative matching of radiation treatment (RT) plans with guidelines was performed. Regional failures were described in relation to planned CTV's (unilateral/bilateral) to evaluate whether the recurrences occurred in prophylactic irradiated areas.

Material and Methods: All patients who received RT as part of treatment for SCC-HNCUP in Denmark between 2014 and 2020 were included. Elective mucosal clinical target and elective nodal clinical target volumes from RT plans were obtained and compared with the topography of any ipsilateral or contralateral loco-regional failures.

Results: A total of 193 patients received curative radiotherapy as part of their treatment; 80 with primary (C)RT and 113 with adjuvant (C)RT. Concomitant chemotherapy was cisplatin (40 mg/m2 weekly). Seventy percent of patients treated with primary (C)RT received concurrent nimorazole. Patients were predominantly treated with IMRT (97%). A subfraction (17%) received elective neck irradiation unilaterally for unilateral neck disease. After a median (IQR) follow-up time of 3.1 (1.4 to 5.1) years, 10% had an in-field recurrence on the irradiated side of the neck. No patients treated unilaterally had a recurrence contralaterally. Seven percent had bilateral neck node disease. All of these were treated with bilateral RT, and 7% of these had regional in-field recurrence. Sixty-seven percent of mucosal failures occurred within the elective target volume. 5-year loco-regional failure rate was 19%.

Conclusion: We present the largest failure pattern analysis on a complete national cohort of SCC-HNCUP patients to date. Loco-regional failures are described in relation to planned CTVs. The loco-regional control was acceptable and comparable to primary head and neck SCC in other sites.

Themes: Cancer, Epidemiology
Keywords: head and neck cancer, failure, squamous cell carcinoma

SESSION 18

Development and evaluation of a cross-sectoral cognitive rehabilitation program for critically ill patients

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Introduction: Nearly 90% of all patients are discharged from the Intensive Care Unit (ICU) in Denmark due to improved medical treatment and advanced technology. However, many ICU survivors show significant long-lasting cognitive impairments.

Objectives: We aim to develop and evaluate a rehabilitation program to support ICU patients' cognitive function throughout the care pathway from ICU to home.

Methods: This PhD study is conducted according to the Medical Research Council's guideline for developing and evaluating complex interventions, in the following three phases:

1) Development of the intervention, entailing a workshop, a Delphi process and expert meetings, with involvement of both health professionals and former patients and relatives.

2) Pilot study: To evaluate applicability and feasibility of the study design, the number of eligible patients (reasons for ineligibility), recruitment (reasons for refusal), the measurement instruments and the timing of the assessments (reasons for possible barriers and missing assessments), and fidelity of the cognitive rehabilitation program.

3) Randomized controlled trial (RCT): Patients admitted in the ICU, will be allocated to either; a) Intervention In-ICU group and Post-ICU group, b) Intervention In-ICU or c) Usual care.

We hypothesize that patients in group a will achieve the greatest reductions in cognitive impairment compared to group b and c.

Perspective: The results from this study will have the potential to impact on how we support ICU survivors in the rehabilitation pathway.

Themes: Rehabilitation, Public health
Keywords: Cognitive function, Rehabilitation, Intensive Care

Early individualised nutritional intervention to prevent malnutrition in patients with cancer receiving palliative chemotherapy

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BACKGROUND: 30-50% of patients with cancer are malnourished, resulting in poorer prognosis, increased toxicities, reduced quality of life, and reduced physical function. Nevertheless, cancer-related malnutrition remains largely unrecognized and undertreated in clinical practice.

AIM: To examine the effect of an early individualised nutritional intervention on body weight, quality of life, survival, muscle mass, performance status, physical function, nutritional risk, and treatment tolerance in patients with cancer receiving palliative chemotherapy.

METHODS: An intervention study with a historical control cohort. Participants are newly diagnosed patients with lung, pancreatic, ovarian, or colorectal cancers recruited at initiation of palliative chemotherapy. The control group followed current clinical practice. The intervention group receives an individualised nutritional intervention delivered by a clinical dietitian from treatment initiation and throughout the treatment trajectory. The intervention is tailored to the participant's nutritional needs, food preferences, nutrition impact symptoms, and smell- and taste disorders. The primary endpoint is change in body weight. Secondary endpoints include quality of life, survival, muscle mass, performance status, physical function, nutritional risk, and treatment tolerance. Data are collected at baseline and after 12 and 24 weeks.

PERSPECTIVES: The project will provide new knowledge on the effects of individualised nutritional interventions for patients with cancer receiving palliative chemotherapy, and the potential to improve quality of life, treatment tolerance, and survival.

Themes: Cancer, Rehabilitation
Keywords: Nutrition, Cancer, Dietetics

Adherence to secondary prevention of Atherosclerotic Cardiovascular Disease - Identify barriers and facilitators

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This project aims to identify barriers and facilitators for adherence in secondary prevention of atherosclerotic cardiovascular disease (ASCVD). International studies found that only 33% of patients with ASCVD achieve the reduction of LDL-cholesterol recommended in the 2019 European Guidelines. In addition, over half of the Danish patients qualified for cholesterol-lowering therapy do not receive it.

The PhD project consists of 4 studies. The first study, will identify barriers and facilitators for adherence to European Guidelines among clinicians working with ASCVD. An existing questionnaire will be translated, validated and send out to clinicians in Central Denmark Region (CDR). In the second study, we will develop a Patient Reported Outcome questionnaire (PRO) for Danish patients in secondary prevention of ASCVD in CRD, based on the COSMIN guidelines. In the third study, we will analyse the results of the PRO questionnaire and identify barriers for patient's adherence to the 2019 European Guidelines. In the fourth study, we will use the results from study 1 and 3 to identify organisational barriers and facilitators in ASCVD treatment.

Perspective: Barriers among patients and clinicians will be identified to improve adherence to secondary prevention of ASCVD. This knowledge will be central to reduce disease burden due to ASCVD from a patient and society perspective.

Themes: Cardiology, Rehabilitation
Keywords: Atherosclerotic, Adherence, Patient-Reported Outcome

Rehabilitation and return to everyday life for patients with long COVID

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Background: A new group of patients with post-viral syndromes have emerged from the COVID-19 Pandemic: patients with long-term symptoms after COVID-19 (long COVID). These patients may experience severe disabilities, leading to distinct rehabilitation needs. Nationally and internationally, evidence on the effects and functioning of long COVID rehabilitation interventions are scarce.

Methods: The overall purpose of the PhD project is to optimise rehabilitation for patients with long COVID in order to improve functioning and return to work. It comprises three evaluations following the Medical Research Council's framework for evaluation of complex interventions:

1) A non-randomised controlled clinical trial with 12-month follow-up aiming to evaluate the effectiveness of a structured rehabilitation intervention, The Long COVID Rehabilitation Intervention, with both individual and group sessions compared to less structured rehabilitation interventions with primarily individual sessions. A total of 950 patients are included.

2) An economic evaluation alongside the clinical evaluation aiming to evaluate the cost-utility and cost-effectiveness of The Long COVID Rehabilitation Intervention. It will be performed from a societal perspective, including costs of the interventions, use of healthcare services and productivity loss.

3) A realistic process evaluation aiming to explore and evaluate implementation, mechanisms of impact and the context of The Long COVID Rehabilitation Intervention using both quantitative and qualitative methods.

Perspectives: This PhD project offers a unique chance to generate important knowledge in the rehabilitation field of Post-Viral Syndromes on a global scale.

Themes: Rehabilitation, Public health
Keywords: Complex interventions, Rehabilitation, Long COVID

Gastrointestinal stimulation as a treatment of postoperative ileus following cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (STIMULATE) - A clinical feasibility study

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Background: Postoperative ileus (POI) is a frequent complication following cytoreductive surgery (CRS). No efficient treatment exists. Recent preclinical studies have shown a beneficial effect of electrical stimulation of the gastrointestinal tract on the length of POI.

The aim of the study is to evaluate the safety and feasibility of electrical stimulation of the stomach in patients undergoing CRS.

Methods: Patients undergoing CRS were eligible for participation. At the end of surgery, before the abdomen is closed, a pace wire is attached to the stomach, exteriorized through the abdominal wall, and connected to a pacemaker. A 1:1 randomization is performed. The pacemaker is turned on in the intervention group and turned off in the control group.

Once a day during admission, patients are asked to fill out a patient diary on gastrointestinal function. When normal gastrointestinal function was restored, the pace wire was removed.

Results: 27 patients were eligible, and 12 patients accepted participation (44%). Three was excluded per operatively. Nine patients completed the intervention so far, 4 in the control group and 5 in the intervention group.

The pace wires were easily removed in all patients.The treatment was well tolerated. In both groups patients reported short intervals of intraabdominal muscle spasm.

In the intervention group median number of days till first stool was 3,5 (range: 2-5), in the control group it was 5 (range: 4-5).

Conclusion: This study found that it is feasible and safe to mount a pace wire on the stomach and connect it to an external pacemaker. This study forms the basis for further clinical studies of electrical stimulation as a treatment of POI.

Themes: Surgery, Diagnostics & technology
Keywords: Postoperative ileus, Electrical stimulation, Abdominal surgery

IMPACT OF COLONIC DIVERTICULOSIS ON DAILY LIFE. THE DIVIPACT STUDY.

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Colonic diverticulosis may impact quality of life due to altered bowel function, pain, hospitalizations, and surgery. We aimed to characterize subjects with diverticulosis, to investigate the impact of diverticulosis on daily life, and to identify potential risk factors for hospitalizations and surgery.

Online surveys were sent to subjects diagnosed with colonic diverticulosis (K572-9) at least one time from 2010 through 2022 in The Central Denmark Region. Exclusion criteria included a diagnosis of colorectal cancer and dementia. The survey was comprised of questions regarding background information, daily life, and several validated questionnaires concerning quality of life, bowel function, urinary function, and sexual function. Additionally, subjects were asked to accept review of their medical records to further investigate their hospital contacts.

We identified 29,624 eligible subjects of whom 21,932 (74%) responded to the survey and 20,135 (68%) consented to medical record review. Responders had a median age of 70 years (IQR 62-76) and males constituted 48%. Of those who consented to medical record review 79% (n = 15,837) had diverticulosis with only out-patient contact, 19% (n = 3,947) had been hospitalized with no surgery performed, and 2% (n = 351) had been hospitalized and had surgery performed. Surgery was most often performed at first admission (65% of all surgery performed). In conclusion, we have established a cohort of 21,932 subjects with diverticulosis. Subjects have answered a comprehensive survey, and based on this, we will further investigate symptom burden and quality of life in subjects with diverticulosis.

Themes: Surgery, Gastroenterology and hepatology
Keywords: Diverticulosis, Patient-reported outcomes, Quality of life

Feasibility of intratracheal tracheostomy sealing

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Background: Tracheostomy decannulation after prolonged mechanical ventilation therapy leaves the patient with an open upper airways channel. Improper tracheostomy wound sealing leads to pulmonary dysfunction and reduced voice quality. The prevailing tracheostomy wound sealing method involves using a bandage to seal the tracheostoma, but this approach often proves ineffective. In response to this challenge, we have recently introduced an innovative, promisinig concept for intratracheal tracheotomy sealing. This study aims to investigate the feasibility of intratracheal tracheostomy sealing immediately normalizing physiological airway conditions, hereby improving pulmonary function and voice quality.

Material and methods: Fifteen tracheostomized patients were included. Upon decannulation, a temporary intratracheal tracheostomy sealing disc was inserted and spirometry was conducted to measure forced vital capacity (FVC), forced expiratory volume in first second (FEV1) and peak expiratory flow (PEF) as indicators of airway flow. Voice recordings were assessed using an equal appearing interval scale.

Results: After insertion of the sealing disc, mean FVC increased by 51% ($p<0.001$); FEV1, by and 30% ($p<0.001$). PEF increased statistically non-significantly by 7%. Voice quality increased by 51% ($p<0.001$).

Conclusion: This feasibility study disclosed improved FVC, FEV1 and voice quality for decannulated patients immediately after insertion of an intratracheal tracheostomy sealing disc. We consider this new treatment promising for optimization and restoration of pulmonary function and voice quality after prolonged ventilation therapy.

Themes: Surgery, Animal Models
Keywords: Tracheostomy, Respiratory Insufficiency, Spirometry

Quantitative Comparison of a Hand-Sewn Anastomosis and Stapled Anastomosis using Laser Speckle Contrast Imaging, an Experimental Setup in a Porcine Model

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Colorectal surgery relies on maintaining optimal microcirculation(MC), up until now, has been subjectively evaluated by the surgeon. Laser speckle contrast imaging (LSCI) offers an objective image-based approach for quantifying MC in bowel ends. We aim to explore the relationship between MC and anastomosis(AM) in an open surgery porcine model using LSCI.

Ten healthy female pigs underwent midline laparotomy. We then created four AM, 2 hand-sewn and 2 stapled, so that both the small intestine and colon featured one of each. LSCI measurements on all four AM and a segment of untouched small intestine and colon. We recorded baseline values before AM creation, immediately after, and after a one-hour rest period. Thereafter, we induced hypotension by aspirating blood, achieving a MAP of 50-60 mmHg, LSCI measurements were made in hypotensive conditions. To restore and maintain a MAP between 85 and 100 mmHg, we initiated continuous norepinephrine(NE) infusion. After 30 minutes, we repeated LSCI measurements.

In the untouched intestine, we observed no statistically significant changes between baseline and during surgery. However, when we induced hypotension, MC decreased and when MAP was restored with NE infusion, MC declined further, dropping 25% for the colon and 20% for the small intestine.

As for the AM, a reduction was seen in MC upon their formation, with a drop of up to 60% across all AM types. While a significant improvement was seen after the rest period, MC declined once more following hypotension and NE administration. This decline stagnated.

LSCI serves as a quantitative, real-time, and non-contact method for detecting microcirculatory changes in and around the AM

Themes: Surgery, Animal Models
Keywords: laser speckle contrast imaging, microcirculation, Intestinal surgery

Hip strengthening exercise dosage is not associated with clinical improvements after total hip arthroplasty – a prospective cohort study (the PHETHAS-1 study)

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Purpose: Postoperative rehabilitation exercise is commonly prescribed after total hip arthroplasty (THA), but its efficacy compared to no or minimal rehabilitation exercise has been questioned. Preliminary efficacy would be indicated if a dose-response relationship exists between performed exercise dose and degree of postoperative recovery. Thus, the objective was to evaluate the preliminary efficacy of home-based rehabilitation exercise (HRE) based on the association between performed exercise dose and change in gait speed from 3 to 10 weeks after surgery.

Methods: A prospective cohort study was conducted. Following primary THA, patients were prescribed HRE using elastic bands. Performed exercise dose (repetitions/week) was objectively measured using attached sensor technology. Primary outcome was change in gait speed (40m fast-paced walk test). Secondary outcomes included patient-reported hip disability. In the primary analysis, a linear regression model was used.

Results: Ninety-four patients (39 women) with a median age of 66.5 years performed a median of 339 exercise repetitions/week. Across outcomes, participants significantly improved from 3 to 10-week follow-up. The association between performed exercise dose and change in mean gait speed was 0.01 m/s [95% CI: -0.01; 0.02] per 100 repetitions.

Conclusions: We found no indication of preliminary efficacy of HRE using elastic bands, as no significant and clinically relevant associations between performed exercise dose and changes in outcomes were present. Trials comparing postoperative rehabilitation exercise with no exercise early after THA are warranted.

Pre-registration: NCT03109821, pre-print doi:10.1101/2023.07.12.23292442

Themes: Rehabilitation, Surgery
Keywords: Exercise therapy, Dose-response, Hip arthroplasty

SECOND ROUND OF SESSIONS

SESSION 19

Effect of butyrate treatment on myocardial ischemia in a rat model

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Introduction: Congestive heart failure (CHF), most commonly caused by myocardial infarction (MI) is a leading cause of morbidity and mortality in the world. Preventing the damage by MI may lower scar burden and hinder the development of heart failure.. We have recently observed that the ketone body ß-hydroxybutyric acid possess mitochondrial preservation capabilities during ischemic stress. However, the impact of increased butyrate levels during acute myocardial ischemia is unknown.

Aim: The aim of this study is to investigate the effect of Tributyrin and butyrate supplementation as a treatment strategy in the isolated perfused heart model and the in-vivo rat model.

Method: Male Sprague Dawley rats will be used for experimental study. In-vivo MI will be induced. The heart will be excised and transferred under continuous perfusion to an isolated perfused heart system. Tributyrin containing higher plasma concentration of butyrate, will be administered orally mixed in a liquid diet at a dose of 1000 mg/kg in vivo.

Results: This research year study is ongoing since 1 September 2023.

Perspective: The present study proposal will contribute with essential knowledge on the effects of butyrate treatment on myocardial infarction. Specifically, the impact on hemodynamics and mitochondrial function of this compound will be assessed both in an in vivo and in an ex vivo experimental animal model of ischemic heart disease

Themes: Cardiology, Cardiology
Keywords: Heart Failure, Ischemia, Butyrate

Cardiopulmonary Resuscitation Quality during Basic- vs. Advanced Life Support during In-hospital Cardiac Arrest

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Introduction: High-quality chest compressions with minimal pauses are essential to improve survival following in-hospital cardiac arrest (IHCA). Knowledge on cardiopulmonary resuscitation (CPR) quality during IHCA is limited. We aimed to compare basic- and advanced life support CPR performance during IHCA resuscitation attempts.

Methods: This cohort study compared CPR performance during IHCA extracted from recordings of defibrillator impedance signals from Automated External Defibrillators (AEDs) utilized by ward staff to initiate basic life support and manual defibrillators utilized by advanced life support providers in 5 hospitals in the Central Denmark Region. We measured chest compression fraction, the longest chest compression pause duration, and chest compression rate. CPR performance during basic- and advanced life support was compared using multivariate regression adjusted for defibrillation.

Results: From May 2017 through April 2022, we identified 327 IHCAs (30 AEDs, 297 manual defibrillators) with data on CPR performance. The median chest compression fraction was 78 (73;82)% for basic life support and 81 (76;86)% for advanced life support (difference: 4.6%, 95% CI: 1.1-8.2, p=0.01). The median duration of the longest chest compression pause was 18 (13;25) sec. vs. 16 (9;27) sec. (difference: 1.4 sec., 95% CI: -7.0-9.8, p=0.75) and the median chest compression rate was 111 (106;116) per minute vs. 118 (112;124) per minute (difference: 6.9 compressions per minute, 95% CI: 3.4-10.4 compressions per minute, p<0.001) for basic- vs. advanced life support, respectively. There was not a statistically significant higher proportion of IHCAs with mean chest compression rate within guidelines range of 100-120 compressions per minute for basic life support (OR: 0.51 (0.22-1.18), p=0.11).

Conclusion: Basic life support was associated with a lower chest compression fraction and chest compression rate when compared to advanced life support during IHCA.

Themes: Cardiology, Health Education
Keywords: In-hospital cardiac arrest, Advanced life support, Basic life support

Heart Transplantation: Optimization of Hearts from Circulatory Dead Donors in a Porcine Real-life Model

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Background: Heart transplantation (HTx) remains the gold standard treatment for end stage heart failure. A serious limitation is shortage of donor organs and every year patients die on the waiting list. An alternative to expand the donor pool has recently emerged in the form of donation from circulatory dead donors (DCD).

Aim:
1. To examine whether infusion with ketone body sodium-3-hydroxybutyric acid in the DCD donor during NRP can improve primary graft function after standard cold storage and subsequent HTx.
2. To examine whether it is possible to transplant DCD hearts and regain good contractile graft function after 24 hours of preservation with hypothermic machine perfusion.
3. To examine whether it is possible to establish a clinically relevant biomarker for surveillance of the machine perfused DCD heart.

Method: Our porcine model of DCD and HTx is well established, including cross pig transplantation. Pressure-volume catheters will measure contractility, ejection fraction, and diastolic function of both ventricles. Microdialysis allows for continuous sampling of ischemic metabolites. Biopsies from the left ventricle will be analyzed ex vivo for mitochondrial respiration by oxygraphy.

Perspective:
1. Ketone bodies may reduce the risk of primary graft failure and improve outcomes.
2. Longer periods of cold machine perfusion will make it possible to expand donor collaboration with organ offers from centers that requires longer transport time than normal.
3. Finding a reliable clinically relevant marker for surveillance of organ damage, will support the surgeon's decision whether to use a donor heart, and reduce the number of unnecessarily discarded hearts.

Themes: Cardiology, Animal Models
Keywords: Heart Transplantation, Circulatory Dead Donors, Ketone Bodies

Low-density lipoprotein cholesterol, coronary artery disease severity and cardiovascular disease events across the age-spectrum: Novel insights from 85.000 individuals undergoing computed tomography angiography from the Western Denmark Heart Registry

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Background: LDL cholesterol (LDL-C) is a well-known central driving force for development of atherosclerosis. Yet, important questions remain regarding the role of LDL-C as a risk factor for coronary artery disease (CAD) and atherosclerotic cardiovascular disease (ASCVD) events across the age spectrum.

Aim: To assess if LDL-C levels are associated with more severe CAD and higher risk for developing future ASCVD events in all ages. Secondly, to assess the association of on-treatment LDL-C and risk of future ASCVD events. Thirdly, to provide deep insights into the association of LDL-C with CAD severity, by performing new advanced coronary plaque analyses to obtain unprecedented information on coronary atherosclerosis phenotypes.

Methods: We include 85.000 patients undergoing Coronary Computed Tomography Angiography (CCTA) between 2008 and 2022 from Western Denmark Heart Registry (WDHR). CCTA provides information on the coronary atherosclerosis burden and presence of stenoses. Information on cholesterol values, medication use and development of ASCVD events are collected using Danish Registries.

Additionally, we will perform advanced plaque imaging in 2000 patients using new imaging software to provide deep insights into the association of LDL-C with atherosclerosis development.

Perspectives: As the proportion of individuals on lipid-lowering treatment are increasing, especially among those aged over 70 years, our study will yield clinically important data regarding LDL-C as a risk factor for CAD and ASCVD.

Themes: Cardiology, Epidemiology
Keywords: LDL-cholesterol, Coronary Artery Disease, CT Angiography

Phenotyping and characterization of a Danish Wild-type Transthyretin Amyloidosis Cardiomyopathy cohort: A cross-sectional study

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Background: Wild-type transthyretin cardiac amyloidosis (ATTRwt-CM) is a progressive cardiomyopathy leading to heart failure, reduced quality of life (QoL) and poor prognosis in elderly patients. ATTRwt-CM is caused by amyloid fibril deposition in the myocardium, amyloid fibrils form due to misfolding and aggregation of transthyretin (TTR).

Hypothesis: We hypothesize that more severe ATTRwt-CM stages lead to poorer QoL. We expect that misfolded (misTTR) and fragmented (fragTTR) TTR can be decected in patients with ATTRwt-CM and that they correlate with disease severity based on clinical, biochemical, and diagnostic imaging parameters.

Aims: 1° To examine QoL measures in a contemporary ATTRwt-CM cohort and its relation with disease severity according to clinical characteristics and prognostic disease stage markers. 2° To assess the feasibility of measuring misTTR and fragTTR in patients with ATTRwt-CM and their correlation with ATTRwt-CM severity.

Design: Prospective cross-sectional study

Setting: 100 consecutive ATTRwt-CM patients representing all disease stages according to the National Amyloid Center system will be included from the out-patient amyloidosis clinic at Aarhus University Hospital. A control cohort of 20 patients without ATTR disease will be included for comparison of mis-/fragTTR values.

Perspectives: This study will provide comprehensive insights into ATTRwt-CM and its impact on QoL. MisTTR and/or fragTTR show promise as a simple and harmless method for evaluating clinical disease progression of ATTRwt-CM. Overall, providing novel insights to guide future personalized treatment strategies and contributing to improve the prognosis of patients with ATTRwt-CM.

Themes: Cardiology, Diagnostics & technology
Keywords: Cardiac amyloidosis, Quality of life, Disease monitoring

The use of problem analysis and evidence synthesis prior to a Ph.D. study.

Simon Graff, Department of Public Health, Forskningsenheden for almen praksis

Flemming Bro

How do you prepare for the development of a complex intervention in a Ph.D.? This pitch introduces how our project group progressed from problem analysis and evidence synthesis to the program theory for our Ph.D. project.

Our project is based on the MRC framework for the implementation of complex interventions and aims to improve the detection of patients with undiagnosed familial hypercholesterolemia (FH) in general practice in Denmark. To avoid developing an 'ideal' intervention in the planning phase that is difficult to implement, we wanted to investigate the behavior of stakeholders (doctors, staff, and patients) before identifying and prioritizing solutions.

We based our problem analysis and evidence synthesis on MRC and O'Cathain's guidelines; first, we formed an expert group; discussed the issue and brainstormed ideas; conducted a literature review, recognizing a lack of insight into the Danish general practice context, and subsequently conducted a pilot study to examine the clinical behavior of stakeholders in the detection of FH.

The pilot study included 40,000 patients, of which 6.6% had potential FH, as they had an LDL cholesterol ≥ 5 mmol/L, and a detailed journal audit was conducted on 29 of these patients.

We gained insight into the current approach to FH identification. We discovered knowledge gaps, organizational barriers, and uncertainty regarding national guidelines and referral criteria.

Insights from the pilot study provided new knowledge about the current detection of FH. These new insights contributed to the development and refinement of our final program theory for the Ph.D. project. Our process underscores the importance of a thorough preparation phase.

Themes: Cardiology, Public health
Keywords: Complex interventions, General Practice, Mixed Method

The effects of proposed bicarbonate sensor RPTPγ on exercise performance

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Receptor Protein Tyrosine Phosphatase (RPTP)γ is associated with risk of ischemic disease in humans, but the underlying mechanism is not fully understood. The current understanding is that RPTPγ impacts endothelial function through sensing of extracellular HCO_3^-. Exercise is a physiological challenge that disturbs pH, pCO_2, and $[HCO_3^-]$ locally and systemically. This study aims to investigate the importance of RPTPγ in the adaptation to exercise.

To investigate the response to voluntary exercise, wild type and RPTPγ knockout mice had continuous access to angled running wheels for 6 weeks, whereas the non-exercised control group had access to a dummy wheel. We evaluated adaptations to exercise through exercise capacity tests on a treadmill, heart hypertrophy measured as heart weight to body weight ratio, and body composition by MRI scans.

During the 6-week exercise period, RPTPγ knockout mice ran 11.1±0.4 km/day, which was significantly less than wild type mice (14.6±0.5 km/day). In the exercise capacity test, both RPTPγ knockout and wild type mice improved their performance after exercise (from 22.9±1.5 to 35.1±2.7 min and 30.5±1.3 to 44.6±3.5 min, respectively). Wild type mice showed exercise-induced heart hypertrophy with an increase in heart weight to body weight ratio from 7.6±0.4 mg/g to 8.6±0.3 mg/g and no change in body fat percentage (from 8.6±0.4% to 8.4±0.4%). The RPTPγ knockout mice showed no heart hypertrophy (7.5±0.2 mg/g to 7.3±0.2 mg/g) but they developed an increased body fat percentage (from 9.0±0.4% to 10.6±0.4%) during the exercise period.

We propose that HCO_3^- sensing via RPTPγ optimizes physical performance and physiological adaptations to exercise.

Themes: Cardiology, Animal Models
Keywords: Exercise, Cardiovascular physiology, Bicarbonate-sensing

Oximetry guided versus rapid deflation: impact of radial artery occlusion and time to hemostasis when performing radial interventions – A randomised study

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Background: Patients suspected of coronary heart disease most often is referred for an angiogram to have their arteries examined for potential restriction in blood flow. When performing coronary angiography and angioplasty, it is well documented that radial access is associated with fewer complications and better outcome compared to femoral access. However, complications such as radial artery occlusion (RAO), hematoma, pain and development of nerve damage remains an issue.

Methods: We randomized 3600 patients between two hemostatic techniques. The standard handling of the transradial device (TR band) used for achieving hemostasis of the artery, "rapid deflation" (group A) compared to "oximetry-guided patent hemostasis" (group B). We also randomised between sheath size 5 and 6 French. Rapid deflation was defined as deflation of 1/3 ml of air every 20 min. and Oximetry guided as fully deflation after 60 min. The Primary endpoints were time to hemostasis and the rate of RAO at discharge.

Results: Time to hemostasis differed significantly between the two deflation groups. Also between sheath sizes we found a significant benefit on time to hemostasis of smaller sheath size. We found an extremely low rate of RAO however no difference in number of RAO between groups.

Conclusion: Oximetry guided deflation is associated with earlier hemostasis and removal of the TR band. A strategy of partial deflation every 20 min is no longer recommended and removal of the TR band should be individualizes. The very low incidences of RAO in both groups indicate that short and light compression time is crucial in preserving the radial artery after coronary artery interventions.

Themes: Cardiology, Cardiology
Keywords: Radial angiography/angioplasty, Closure device, Radial artery occlusion

Eligibility and preventive potential for semaglutide in real-world overweight and obese patients with myocardial infarction

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Background: The Semaglutide Effects on Cardiovascular Outcomes in People with Overweight or Obesity (SELECT) trial found a 20% reduction in major adverse cardiovascular events (MACE).

Objectives: To determine the prevalence of first-time myocardial infarction (MI) patients meeting SELECT trial inclusion criteria and to estimate the preventive potential of semaglutide if allocated in a real-world Western European cohort.

Methods: The SELECT trial inclusion and exclusion criteria were applied to patients with first-time MI and documented coronary artery disease (CAD) by coronary angiography. SELECT-eligibility included a body mass index ≥27 kg/m2 and no diabetes. Main outcome was MACE, a composite of MI, ischemic stroke, and cardiovascular death. We estimated the prevalence of SELECT-eligible patients, the incidence of 5-year MACE, and the corresponding number needed to treat to prevent one MACE (NNT5).

Results: Between January 1, 2010, and December 31, 2021, we identified 34,405 patients with first-time MI and CAD. Among these, 31% (10,769) were SELECT-eligible to treatment with semaglutide. The incidence of 5-year MACE was 10.7% (95% confidence interval 10.0-11.3) for SELECT-eligible patients. Applying a 20% relative risk reduction of MACE as reported in the SELECT trial, 5-year risk of MACE would be reduced to 8.6% with an estimated NNT5 to prevent one MACE of 47 patients.

Conclusions: One in three patients with a first-MI meet SELECT trial criteria with a NNT in 5 years of ≈50 for preventing one MACE. These results are of paramount importance to regulatory authorities and clinicians when implementing semaglutide in clinical practice.

Themes: Cardiology, Epidemiology
Keywords: Prevention, Myocardial infarction, Obesity

The short-chain fatty acid butyrate is an inotropic agent with vascular and cardioprotective properties

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The heart can metabolize the microbiota-derived short-chain fatty acid butyrate. Butyrate may have beneficial effects in heart failure, but the underlying mechanisms are unknown.

We tested the hypothesis that butyrate elevates cardiac output by mechanisms involving direct stimulation of cardiac contractility and vasorelaxation in rats. We examined effects of butyrate on 1) in vivo hemodynamics using parallel echocardiographic and invasive blood pressure measurements 2) isolated perfused hearts in Langendorff systems under physiological conditions and after ischemia and reperfusion (IR), and 3) isolated arteries mounted in isometric wire myographs. We test adding Na-Butyrate to injection solutions or physiological buffers and compared effects with NaCl at equimolar concentrations. Butyrate at plasma concentrations of 0.6 mM increases cardiac output by 48.8±14.9%, stroke volume by 38.5±12.1%, left ventricular ejection fraction by 39.6±6.2% and lowers total peripheral resistance by 33.5±6.4% without affecting blood pressure or heart rate. Butyrate shows concentration dependent (0.1-5 mM) increments in left ventricular systolic pressure by up to 23.7±3.4% in isolated perfused hearts and by 9.4±2.9% following IR, while reducing myocardial infarct size by 27.2±7.5%. Butyrate relaxes isolated coronary septal arteries concentration dependently with an EC50=0.68 mM.

We conclude that butyrate elevates cardiac output through mechanisms involving increased cardiac contractility and vasorelaxation. This combined mechanism may entail that inotropic stimulation by butyrate does not induce adverse myocardial damage as butyrate reduced myocardial damage during ischemia and reperfusion.

Themes: Cardiology, Animal Models
Keywords: Cardiovascular system, Metabolism, Small-chain fatty acids

SESSION 20

Investigating Mammary Gland Functionality: Insights into Lactation and Calcium-Mediated Secretion in Murine Models.

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Lactation is the foundation of mammalian life, ensuring the survival and healthy development of the growing neonate(s). However, the mechanisms guiding milk production, enrichment, and secretion by the mammary epithelial cells (MECs) remain incompletely understood. One signaling pathway that has proven important for maintaining MECs function during lactation is calcium (Ca2+). During lactation, an increased expression of Ca2+ channels transport vast amounts of the ion into intracellular stores, mainly by store-operated calcium entry (SOCE). Depletion of SOCE Ca2+ channels in mice stalls milk ejection and results in the inability to fully nourish the neonates. SOCE may also play a role in regulating the production and secretion of milk in MECs; however, this mechanism has not been fully investigated. This study aims to explore the role of calcium signaling in governing milk quality and quantity in MECs during lactation. Here, we developed genetically modified mouse models to investigate the role of specific SOCE mediators during lactation. This study assesses lactation by recording pup weights, milk composition, and gland development. Functional analyses, including the evaluation of milk ejection and oxytocin-induced contraction of the mammary secretory unit, are conducted using advanced 3D ex vivo live imaging techniques. Findings will not only shed light on functional diversity in milk secretion but other secretion pathways in biology as well. Ultimately, results of the study can improve our understanding of nursing, leaving a significant impact on the health of mothers and infants.

Themes: Animal Models, Molecular biology
Keywords: Mammary Gland, Lactation, Calcium Signaling

A comparison of the C57BL/6JRj and SWISS mice strains as a murine model of glucocorti-coid induced osteopenia and skeletal muscle atrophy.

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Background and aim: Glucocorticoids (GC) may have a negative impact on the musculoskeletal system. The aim of this study was to compare the applicability of two mice strains, C57BL/6JRj (C57) and SWISS, as a murine model of GC-induced loss of bone and muscle mass.

Methods: 32 female mice, 14 weeks-old, of each strain were stratified into four groups: (n=8 pr. group): 1) Control; 2) Methylprednisolone (MP), 15 mg/kg/day; 3) MP, 22.5 mg/kg/day; and 4) MP, 30 mg/kg/day. The mice were sacrificed after 4 weeks. Muscle volume and muscle cell cross sectional area (CSA) were determined. For bone, areal bone mineral density (aBMD), bone microstructure, and bone strength was evaluated.

Results: All doses of MP resulted in a significant loss of muscle volume for both strains, and a significantly lower muscle cell CSA in SWISS mice, but not in C57 mice. Femur aBMD was significantly lower in SWISS mice receiving 22.5 and 30 mg/kg/day MP, but not in C57 mice. At the femoral mid-diaphysis, cortical thickness was significantly lower for all doses of MP in C57 mice, but not in SWISS mice. At the distal femoral metaphysis, SWISS mice receiving 30 mg/kg/day MP had a significantly lower trabecular thickness while C57 mice did not differ from controls. Contrarily, for vertebra L4, bone volume fraction was significantly higher for all doses of MP in C57 mice, but not in SWISS mice. Bone strength of femur and L4 did not differ from controls in neither SWISS nor C57 mice.

Conclusion: MP leads to loss of muscle mass in both SWISS and C57 mice, however, the present doses of MP did not result in loss of bone mass in any of the two strains. A higher dose of MP may be needed.

Themes: Animal Models, Endocrinology
Keywords: Glucocorticoid, Osteopenia, Sarcopenia

Understanding the Role of Megalin in Retina: Insights from a Mouse Model Study

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Patients with megalin gene variants present a high myopic phenotype, and ablation of retinal megalin leads to severe retinal dystrophy, primarily affecting the light-sensing photoreceptor cells. Megalin, an endocytic receptor, is known for its role in kidney function by mediating the reabsorption of plasma proteins. Its role in the eye remains unclear, although previous studies in our group suggest that megalin deficiency affects visual cycle enzymes.

My project aims to investigate megalin's role in the eye. I utilize a megalin knockout mouse model to examine the role of megalin for normal function of visual cycle proteins and enzymes as well as for megalin interaction partners.

I will assess this using electron microscopy, immunohistochemistry, and co-immunoprecipitation while analyzing the abundance and activity of visual cycle enzymes (e.g., RPE65, LRAT, RDH5) and cellular transport proteins (CRBP1, CRALBP) via immunofluorescence, western blotting, and ELISA.

The results reveal that the retina experiences gradual degeneration in the megalin knockout model, leading to a significant loss of photoreceptor cells and, consequently, blindness.

The analyses of retinoid composition show that retinyl esters accumulate in the retina of megalin knockout mice, indicating delayed generation of 11-cis retinol – a critical step in the visual cycle catalyzed by RPE65. Additionally, RPE65 gene expression is reduced in the mice, suggesting that megalin influences the visual cycle by interacting with RPE65, potentially acting as a scaffold protein.

I will further employ this model to investigate the role of megalin and pathogenic changes in the retina during retinal dystrophy.

Themes: Molecular biology, Animal Models
Keywords: Megalin, Retinal dystrophy, Visual cycle

A translational pig model for high-dose Methotrexate pharmacokinetics in CNS

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Background: In treating pediatric cancer, optimizing therapeutic strategies is paramount. This study investigates the pharmacokinetics and toxicity of high-dose Methotrexate (HDMTX) in the brain, with a focus on pediatric patients with central nervous system (CNS)-involved acute lymphoblastic leukemia and malignant brain tumors. While Methotrexate (MTX) is essential in treating these cancers, our understanding of its CNS pharmacokinetics remains incomplete. Our objective is to offer insights to enhance treatment efficacy while minimizing toxicity in HDMTX treatment regimens.

Methods: We developed a translational juvenile pig model, replicating pediatric cancer therapy conditions. Anesthetized 15 kg juvenile pigs received 5 g/m2 HDMTX intravenous standard dose infusion. We employed microdialysis for frontal lobe extracellular MTX assessment and serial collection of cerebral spinal fluid (CSF). Liquid chromatography mass spectrometry (LC-MS) was applied for simultaneous measurement of MTX and its metabolites in microdialysate, CSF, urine, and plasma.

Perspective: Preliminary results demonstrate successful sample collection and quantification of MTX in sedated juvenile pigs, across plasma, microdialysate, CSF, and urine. This foundational work paves the way for future studies to explore MTX concentrations with increased dosing, coupled with measures to protect against systemic toxicity. Furthermore, metabolomics analysis via LC-MS will uncover potential causes of MTX-induced CNS toxicity. Our research is a critical step in refining MTX dosing strategies, with the potential to enhance survival prospects and reduce long term side effects for children with brain cancer.

Themes: Animal Models, Cancer
Keywords: Methotrexate, Metabolomics, Toxicity

Personalized Surgery – introducing medical 3D print technology in orthopaedic oncology

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Background:In the last decades, 3D printing (3DP) has undergone tremendous development. Patient-specific 3D models enables surgeons to take preoperative planning from screens into physical space and it has been demonstrated that this can aid surgeons in challenging cases. More promising is the use of patient-specific instruments (PSI) and customized implants. Recently a 3DP center has been launched at Aarhus University Hospital (AUH) and in collaboration with the Danish Technological Institute (DTI), custom-made 3D metal implant manufacturing will be able to happen in-house. The objective of this study is to assess the osseointegration of various surface types on 3DP titanium implants provided by DTI through a rigorously validated randomized animal study.

Methods: 20 skeletally mature sheep were used. Stable, non-weight-loaded, test-implants were inserted into the left humerus, femur, and tibia for a total of 3 implants per sheep. Sheep were randomly assigned a number and 3DP titanium implant with a rough surface, or a smooth surface was randomly implanted into the humerus. Same procedure was performed with the femora and tibiae with implants with different porosity and coating. After 4 weeks of observation all sheep were euthanized, and samples were collected and are undergoing preparation. The specimens will be cut into blokes, each containing an implant and surrounding tissue. Each block will then be cut into a 3 mm high block for mechanical test, closest to the surgical entry site, and a 6 mm block for histomorphometrical evaluation. Biomechanical testing will be performed as push-out test. Histomorphometry will be used for the evaluation of implant osseointegration.

Themes: Animal Models, Surgery
Keywords: 3D printing, Custom-made implant, Orthopaedic

Soluble macrophage-mannose receptor, CD206 (sCD206): A potential non-invasive biomarker for idiopathic pulmonary fibrosis

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Objectives: Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive fibrotic lung disease known to be driven by pro-inflammatory and pro-fibrotic pulmonary macrophages (PMs). It was recently discovered that the soluble macrophage mannose receptor CD206 (sCD206) is associated with IPF severity, whereas another soluble macrophage receptor CD163 (sCD163) does not seem to predict disease progression. The purpose of this study was to confirm these findings in a large validation cohort and to investigate the usefulness of another macrophage biomarker, the soluble signal-regulatory protein α (sSIRPα).

Materials & Methods: Quantification of three macrophage biomarkers, sCD206, sCD163 and sSIRPα, was assessed in blood samples from 150 IPF patients using in-house enzyme-linked immunosorbent assays (ELISAs). Quantification of additional biochemical parameters was assessed using automatised analysers.

Results: Unlike sCD163 and sSIRPα, sCD206 demonstrated repeated significant correlations to biochemical parameters (lactate dehydrogenase, p=0.0096; albumin, p=0.0027; haemoglobin, p=0.0141; C-reactive protein, p=0.0004) as well as the 6-minute walking test (p=0.0002). Linear regression between sCD206, forced vital capacity and shortness of breath was also statistically significant (p=0.0182 and p=0.0199, respectively). Interestingly, patients with sCD206>0.357 mg/L had a significantly higher mortality rate than patients with sCD206<0.357 mg/L (p=0.0030).

Conclusion: The study confirms that the macrophage biomarker sCD206 (unlike sCD163 and sSIRPα) is associated with both IPF disease severity and mortality. Further studies are needed to fully evaluate its clinical applicability.

Themes: Immune diseases, Infectious diseases
Keywords: Macrophages, Idiopathic pulmonary fibrosis, Biomarker

Sustaining fibrotic injury in animal models of idiopathic pulmonary fibrosis

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The murine in-vivo model of bleomycin-induced Idiopathic Pulmonary fibrosis (BLEO-IPF) is considered a standard model in drug discovery. However, treatment responses in the model are not sufficiently predictive for therapeutic benefit in clinical trials. In contrast to IPF patients, lung fibrosis spontaneously resolves over time in BLEO-IPF mice, this results in reduced clinical translatability and predictive validity of the model. This PhD project aims to develop and validate an optimized disease model of IPF that more faithfully recapitulates hallmarks of human IPF.

To get a better understanding of the model, a time-course study was conducted with the aim to investigate disease progression in the BLEO-IPF model and to determine at which point the fibrosis starts resolving. In the current study, BLEO-IPF animals were euthanized, 7-42 days after intratracheal BLEO instillation and compared to saline-administered control mice. Bleomycin was found to progressively increase lung inflammation (%-area of galectin-3 staining) and fibrosis (% area of Col1a1 and Col3). Moreover, bleomycin increased semiqiuantitative Ashcroft fibrosis scores (lung fibrosis). For all histological endpoints investigated, a gradual, consistent decline was observed from day 14 post-dosing. Subsequently standard of care (nintedanib and pirfenidone) was tested against an antifibrotic TGFβ-ALK5 inhibitor (ALK5i). Interestingly, only ALK5i treatment improved lung histological endpoints in the model.

In conclusion, the spontaneous resolution of fibrosis in the model was found to occur from day 14 post-dosing and out of all the tested compounds, only ALK5i improved the lung histological endpoints.

Themes: Animal Models, Animal Models
Keywords: Idiopathic Pulmonary Fibrosis, Animal model, Time-Course Study

Posterior mitral valve reconstruction using 2-ply vacuum pressed small intestinal submucosa extracellular matrix: Acute in vivo evaluation

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Objective: Employing MRI scans of healthy pigs, we planned to propose a patch design for reconstructing the posterior mitral valve with 2-ply vacuum-pressed small intestinal submucosal extracellular matrix and evaluate its utility in an acute porcine model.

Materials & Methods: Five healthy pigs were subjected to MRI scans, and subsequent geometrical measurements were taken to suggest a patch design. The patch was fashioned from a double-layered vacuum-pressed small intestinal submucosal extracellular matrix. Posterior mitral valve reconstruction was performed in an acute 80-kg porcine model (n = 7). Pressure and echocardiography assessments were conducted both before and after the intervention.

Results: The reconstructed mitral valve was fully competent without any signs of regurgitation. Baseline peak left atrial pressure vs reconstruction: 9.9 ± 1.1 mmHg, p = 0.676; mean pressure difference across mitral: 4.5 ± 2.3 mmHg vs 4.1 ± 2.3 mmHg, p = 0.063.

Conclusion: Utilizing our patch design composed of 2-ply vacuum-pressed porcine small intestinal submucosal extracellular matrix, we succeeded in reconstructing the posterior mitral valve in an acute 80-kg porcine model. The reconstructed mitral valve was fully competent; no signs of mitral valve regurgitation, stenosis, or systolic anterior motion were found.

Themes: Animal Models, Surgery
Keywords: Mitral valve, Posterior reconstruction, Bio scaffold

A Porcine Model of Human-like Chronic Thromboembolic Pulmonary Disease

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Background: Chronic Thromboembolic Pulmonary Disease (CTEPD) is a long-term complication after acute pulmonary embolism (PE). Untreated, CTEPD can lead to right sided heart failure. The pathophysiology is unknown but is believed to be multifactorial.

Aim: We aimed to develop a porcine model of chronic thromboembolic lesions that was comparable with CTEPD patients.

Methods: Twelve pigs were randomized (1:1) into: PE group and SHAM. PE group received infusion of autologous blood clots while SHAM received saline infusion.

After one month, the pigs were evaluated with hemodynamics, Computed Tomography Pulmonary Angiography (CTPA), pressure volume recordings, and samples of the pulmonary arteries were collected. The samples from PE group were compared with samples from CTEPD patients who underwent pulmonary endarterectomy.

Results: One month after intervention, pulmonary arterial pressure (PAP) had decreased in both groups compared to baseline (PE group: 19.3+/-3.1 mmHg vs. 12.7+/-0.52 mmHg, p=0.03, SHAM: 17.8+/-3.4 mmHg vs. 12.3+/-2.1 mmHg, p=0.009). Right ventricular (RV) ejection fraction (EF) and RV-PA coupling had normalized in PE group (RV EF: 72+/-7 % vs. 78+/-11 %, p=0.2, RV-PA coupling: 1.4+/-0.5 vs. 2.0+/-1.1, p=0.1) while SHAM was unaltered (RV EF: 75+/-8 % vs. 82+/-5 %, p=0.2, RV-PA coupling: 2.3+/-1.6 vs. 2.3+/-0.8, p=0.98). PE group had visible clots on CTPA after one month. Histological samples from PE group showed organized thrombus with fibrotic tissue, macrophages, neointima formation and recanalization comparable to CTEPD patients.

Conclusion: Induction of large autologous PE in pigs induced chronic thromboembolic human-like lesions without pulmonary hypertension.

Themes: Animal Models, Cardiology
Keywords: CTEPD, Pulmonary Embolism, Animal Model

Neuroplastic effects of subthalamic Deep Brain Stimulation in a parkinsonian minipig model

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Background: Deep Brain Stimulation (DBS) of the subthalamic nucleus (STN) is an effective neurosurgical treatment for Parkinson's disease (PD) adjunct to medical treatment. However, the underlying mechanisms of STN DBS are still obscure including the role of neural plasticity.

Methods: We investigated the neuroplastic effects of STN DBS in 11 female minipigs (age 7-11 months). We induced unilateral PD by 6-OHDA microinjections in the right medial forebrain bundle (n=8) and compared with saline controls (n=3). All had DBS leads implanted in the right STN. Some animals received chronic stimulation, whereas others were sham PD/controls. The motor function was continuesly quantified by gait mat analysis. Using Golgi-Cox tissue impregnation, the structural plasticity was assessed by comparing dendritic spine densities of the affected vs. unaffected primary motor cortex (M1) in Layer 2/3 and Layer 5.

Results: The motor function decreased following both PD induction and DBS implantation but resurged after stimulation onset. We found layer specific spine density alterations in the basal dendrites of M1. Layer 2/3 differences were predominant in the PD animals where spine densities tended to decrease, however, less so with DBS treatment. Layer 5 differences were mainly detected in the stimulated animals regardless of disease.

Discussion: Our results indicate the underlying mechanisms of DBS to involve a layer specific structural plasticity in M1. Specifically, PD was found to affect the spine density in Layer 2/3, which could partly be rescued by STN DBS, whereas DBS seemed to induce altered spine densities in L5. The latter may be facilitated by antidromic hyperdirect pathway activation.

Themes: Neuroscience, Animal Models
Keywords: Deep Brain Stimulation, Neuroplasticity, Minipigs

SESSION 21

Handover of information from ward staff to the cardiac arrest team during in-hospital cardiac arrest: Identifying deficiencies and building a new model

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Background: Survival after in-hospital cardiac arrest (IHCA) depends on identifying the cause of arrest, which requires appropriate handover of patient information from the ward staff to the cardiac arrest team. About 90% of cardiac arrests occur outside of the intensive care units in Scandinavian countries and the survival prognosis is poor ranging from 15-30 %. Improper handover of patient information from ward staff to the cardiac arrest team has been described as an important barrier for in-hospital resuscitation.

Purpose: This study aims to investigate handovers from ward staff to the cardiac arrest team, identify which information being requested by the cardiac arrest team, and to develop a tool for structured handover during IHCA.

Materials and methods: This is a clinical cohort and mixed methods study. We will investigate clinical in-hospital resuscitation attempts at Randers Regional Hospital by equipping all cardiac arrest team members with body cameras in order to collect video recordings of in-hospital resuscitation attempts. We will analyze the data from the video recordings and questionnaires using a qualitative and quantitative approach. The main analysis will be a qualitative assessment of which information that is being handed over by the ward staff and requested by the cardiac arrest team. We will utilize themes and elements from video recordings to make a consensus study among task force members in the International Liaison Committee on Resuscitation to make a new model for structured handovers to cardiac arrest teams.

Themes: Qualitative research, Cardiology
Keywords: In-hospital cardiac arrest, Cardiopulmonary resuscitation, Handover of information

Developing a model for end-of-life care in transitional care for community dwelling older adults

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Background: Most patients wants to spend the last part of their lives at home, but older adults often end up spending much of it in hospitals, receiving unwanted and futile treatment and eventually die in hospital. Concerns about being a burden to the family or lack of symptom relief can change their preferences when the time of death approaches in favor of hospitalization. Studies have indicated that patients who had discussed their end-of-life preferences were more likely to spend their end-of-life time at their preferred place.

The aim of the project is to develop a model to support health care professionals to comply with the end-of-life preferences of community dwelling older adults.

Methods: The overall framework is British Medical Council's Complex Interventions. The first study is a scoping review on advance care planning in older adults (2023). The second study will be a Delphi study involving healthcare professionals, older adults and relatives in developing a model for advance care planning in community dwelling older adults (2024). Third study will be a feasibility test of the model (2025). Partners in the project are Randers Regional Hospital, Norddjurs Municipality and general practice.

Results: In winter 2023 we will be able to present preliminary results of the scoping review.

Conclusion: The perspectives of the project is that the model can support health care professionals in meeting older adults' preferences towards place of death, life prolonging treatment, hospitalization and resuscitation and secondly to reduce unplanned hospitalizations. The project will contribute to evidence-based knowledge on advance care planning in geriatric care.

Themes: Qualitative research, Public health
Keywords: end-of-life care, older adults, transitional care

The value of patient-reported outcome measure assessment and circulating tumor DNA to detect early relapse during surveillance in women with vulva cancer

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Purpose: Vulva cancer (VC) is a rare disease often diagnosed in elderly women. Treatment of VC is mutilating, and despite a curative intent, 25-40% will experience a recurrence. Today, evidence on intervention and prevention of a VC recurrence is limited, and valid biomarkers for risk stratification are lacking. Detection of circulating tumor DNA (ctDNA) may represent a novel technological breakthrough for personalized risk assessment and treatment allocation. Additionally, systematic assessment of patient-reported outcome measures (PROMs) may represent a valid method for early detection of recurrence. The overall aim of the present PhD study is to optimize the current surveillance program for VC.

Methods: We will conduct a prospective cohort study with a mixed method research design. We will collect liquid biopsies to identify ctDNA in women with VC at the time of diagnosis and prospectively during surveillance. Further, we will collect and analyze PROM data during surveillance in women with VC to evaluate symptomatology which may trigger early clinical check-up.

Results: Patient enrollment is expected to start in 2024 and will run for 5 years. We expect to include 250 patients.

Conclusion: Our results will contribute with new knowledge to the field of individualized surveillance programs for women with VC. In-time detection of recurrence is crucial to offer curative treatment with as limited need for mutilating surgery as possible. Follow up data from the two parallel studies will investigate if a combination of ctDNA monitoring and PROM assessment at the time of diagnosis and over time improves treatment allocation, recurrence detection, survival, and quality of life.

Themes: Gynecology and obstetrics, Cancer
Keywords: Vulva cancer, Surveillance, Patient-reported outcomes

A multi-component transition program targeting to support newly graduated nurses in their transition to become skilled nurses – a feasibility study

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Background: Nurse shortage is a huge global problem, and the intention to leave the profession is high, especially among young, newly graduated nurses. Thus, efforts are needed to increase the retention of nurses. The transition from nurse student to graduated nurse can be difficult; therefore, a transition program to support newly graduated nurses could be a strategy. The study aims to assess the feasibility of a 2-year transition program tailored to newly graduated nurses employed in a medical ward at a regional hospital.

Methods: The framework of developing and evaluating complex interventions from the Medical Research Council is followed. An expert group of stakeholders has been involved from the outset. A descriptive design assesses the feasibility through six areas: acceptability, demand, implementation, practicality, integration and limited efficacy. The study will investigate the feasibility of each element of the transition program e.g. supervision, stay in outpatient clinics, fellowship, life lab, skills training and simulation. Data are collected through semi-structured qualitative interviews with 12 newly graduated nurses, five who have left the program, five who have completed the program and two who are currently in the program. 12 program providers including preceptor nurses, are also interviewed. The study is deductive, and directed content analysis is used.

Results: Pending

Conclusion: Anticipated outcomes include a refined understanding of how a tailored transition program can empower newly graduated nurses in demanding clinical environments. The findings are expected to uncover crucial program elements and shed light on the ideal timing of their integration.

Themes: Qualitative research, Health Education
Keywords: Transition program, Newly graduated nurses, Feasibility study

Use of opioid analgesics 3 and 12 months following primary knee arthroplasty

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Surgical intervention with knee arthroplasty has proven a successful and effective treatment for osteoarthritis of the knee. Most patients require treatment with strong analgesics (opioids) in the first days to weeks after surgery for sufficient pain relief and rehabilitation. However, prolonged use of opioids increases the risk of dependence and addiction as well as a more complicated postoperative course after knee arthroplasty.

The main objective of this analytic follow-up study is to evaluate the use of opioids 3 and 12 months after primary knee arthroplasty. The study is based on prospectively collected patient-reported data from the Silkeborg Knee Replacement Cohort Study (SIKS). In total, 1225 patients are included in the cohort: 1025 patients undergoing total knee arthroplasty (TKA) and 200 undergoing unicompartmental knee arthroplasty (UKA). The two types of knee arthroplasty will be examined individually.

The cohort will be divided at baseline based on self-reported opioid use before surgery as the exposure of interest: group 1) use of opioids (opioid-tolerant) and group 2) no use of opioids (opioid-naïve). The prevalence of the primary outcomes – self-reported use of opioids 3 and 12 months after primary knee arthroplasty – will be estimated and compared in the two groups. Moreover, the self-reported cause and frequency of the prolonged opioid use will be evaluated.

The preliminary results will be presented at the PhD Day 2024.

Themes: Surgery, Epidemiology
Keywords: Orthopedic surgery, Knee arthroplasty, Opioid analgesics

Feasibility of Early Remote Rehabilitation after Cardiac Surgery in a Primary Health Care Setting

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Introduction: An increasing number of elderly patients are undergoing heart surgery, leading to functional decline and impaired quality of life post-discharge, despite successful surgery outcomes. Cardiac rehabilitation (CR) has demonstrated effectiveness in countering this decline and enhancing physical capacity, independence in activities of daily living, and quality of life. However, due to sternal precautions, current CR initiation is delayed for weeks following open heart surgery.

The advent of mobile health technologies presents an opportunity to provide immediate coaching and personalized exercise regimens at home via mobile apps, potentially bridging the care gap between hospital discharge and the commencement of center-based CR.

Aim: This study aims to assess the feasibility of early home-based mobile CR supervised by physiotherapists (PTs) from the municipal rehabilitation center.

Methods: The study will be conducted as an explorative qualitative feasibility study in Aalborg municipality. Patients will be introduced to a mobile app incorporating accelerometry-based sensors for remote, individualized guidance on physical activity, along with feedback on training progress.

Post-discharge, patients will receive phone calls from municipal PTs for exercise adaptation, general guidance, and information on center-based rehabilitation. Approximately six weeks after surgery, patients will be invited to commence the center-based rehabilitation program.

Data will be collected through a group interview with the PTs, and telephone interviews with patients regarding their experience with the intervention. Participation rates in CR will be collected through journals.

Themes: Rehabilitation, Qualitative research
Keywords: Cardiac Rehabilitation

Can simulation-based team training improve working conditions among healthcare professionals

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Background: Burnout and mental health disorders issues are prevalent among healthcare professionals, leading to increased instances of sick leave. Research has demonstrated that simulation can enhance job satisfaction and mental well-being in healthcare professionals. Simulation involves replicating real-life clinical scenarios and creating authentic environments to practice specific clinical situations. Thus, the implementation of simulation-based team training is considered a valuable tool supporting healthcare professionals. This PhD project investigates whether the adoption of simulation-based team training can effectively reduce sick leave and support working conditions among healthcare professionals.

Methods: From April 2023 to April 2024 a simulation-based team training intervention will be implemented across four pediatric departments in Denmark. Another four pediatric departments will serve as the control group. A total of 1,200 participants were included in the project. The intervention implies healthcare professionals engaging in simulation-based team training at a higher quantity and frequency.

Outcomes and analysis: To evaluate if the intervention supports healthcare professionals, we plan to conduct two studies. Study 1 investigates if simulation-based team training can reduce sick leave among healthcare professionals. Study 2 explores if the simulation intervention has an impact on patient safety culture. A difference-in-difference analysis will compare sick leave and patient safety culture between hospital sites (intervention versus control) and across time periods (before versus after the intervention).

Conclusion: Pending

Themes: Health Education, Paediatrics
Keywords: Simulation-based team training

The doctors' perception of skin diseases in general practice in Denmark, with emphasis on atopic dermatitis – A descriptive study

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Introduction: Skin diseases are a common reason for consulting a medical doctor, e.g. a general practitioner (GP) in countries where GPs function as gatekeepers. Despite this, GPs have very sparse dermatological training in their Residency program. The aim of this study was to investigate management of and challenges with skin diseases in general practice from the GPs' point of view.

Methods: This is a questionnaire study developed in collaboration between specialists in dermatology and family medicine. The questionnaire has been developed specifically for this study and tested and validated on three separate populations of GPs. It was sent out to all 298 GPs in the North Region of Denmark on 5th of April 2022 and data collection continued until 8th of June 2022

Results/hypotheses: A total of 94 GPs (31.5%) responded to the survey. Sixty-four percent of the GPs reported, that 5-10% of their consultations concerned dermatology, and 25% reported that in more than 10% of their consultations, patients have a secondary skin problem. Top three most frequent skin diagnoses were rated to be seborrheic keratoses, children with AD, and acne.

Discussion/perspectives: Consultations for skin diseases are very common in general practice, and very often, patients bring up their skin issue secondary to another problem. 43% of GPs in our study had taken postgraduate training in dermatology, which underlines the need for more dermatological education in the GPs' residency program.

Themes: Health Education, Public health
Keywords: Dermatology, General practice

Conducting ward rounds with older patients living with frailty: A modified Delphi study

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Background: Conducting ward rounds is a core medical skill. Frailty, an age-related condition, increases ward round complexity. Despite ward rounds with older patients living with frailty is a common task, no consensus exists on how such ward rounds should be conducted. Therefore, we aimed to identify consensus-based key content items for conducting ward rounds for older patients with frailty.

Methods: A focus group qualified a modified five-round Delphi study. Experts in geriatric medicine and medical communication were invited to participate. Through panellists' comments and an iterative and thematic approach, content items were identified and refined before panellists assessed for consensus. Consensus was defined as 75% of panellists voting 7-9 on a 1-9 Likert scale. Items without consensus returned to the next Delphi-round. Items were eliminated if consensus was not reached after the second assessment.

Results: Eight experts in geriatric medicine qualified the Delphi study. Overall, 35 experts in geriatric medicine and medical communication participated in the Delphi study. Response rates were 74%, 81%, 86%, 72%, and 85% in Delphi rounds 1-5, respectively. A total of 108 items reached consensus. Items were organized into four overall elements: 1) preparation, 2) conduction, 3) competencies required, 4) patient characteristics.

Conclusions: The identified content items for conducting ward rounds with older patients with frailty included four themes on preparation, conduction, competencies required, and patient characteristics. Future work will investigate effect of including the identified content items in the curriculum for postgraduate medical education.

Themes: Health Education, Qualitative research
Keywords: Curriculum Development, Patient-centered communication, Patients living with frailty

Being permanently infertile and the ‘choice’ of surrogacy – an interdisciplinary, qualitative study

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Introduction: Gestational surrogacy, in which an infertile couple contract with a woman to carry a fetus that the intended parents will raise, increases worldwide, and offers a route to parenthood for individuals and couples who otherwise have limited options. However, the situation in Denmark is that surrogacy with the help of healthcare professionals is illegal and adoption is on the decline. This paper addresses the issues of the permanently infertile couples with special attention to their experiences of surrogacy.

Methods: A qualitative in-depth semi-structured interview study was performed between May and September 2022. Fourteen Danish permanently infertile couples participated, and they were in different stages of using surrogacy. The interviews were transcribed and analysed using systematic text condensation.

Results: This study expanded on the term ‘reproductive exile’ by identifying four different forms of exile: the exiled Danish couple, the gestational carrier in exile, exile at home and, finally, the reproductive body in exile. The interviews took place in the wake of the Covid-19 pandemic and at the start of the war in Ukraine, thus, the couples' experience of acting in international surrogacy, crossing borders, elucidated the complications that arise when the whole world shuts down.

Discussion: The interviews gave a Danish perspective on the lived lives of the permanent infertile couples and the implications of the current Danish law on surrogacy. The war and Covid-19 pandemic highlighted the vulnerability of the situation for all parties involved. The results may serve as guidance for Danish legislators and ethicists in their future decision making on surrogacy.

Themes: Gynecology and obstetrics, Qualitative research
Keywords: Surrogacy, Infertility, Medical ethics

SESSION 22

Simple method for isolation and selective cultivation of primary porcine retinal endothelial cells and pericytes

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Background: Diabetic retinopathy (DR) is a common complication of diabetes mellitus and a leading cause of visual impairment in the Western world. DR is a complex neurovascular disorder, and little is known about the underlying pathology. Changes in the microvasculature is a hallmark of DR pathophysiology with loss of pericytes and formation of microaneurysms as early events, but degeneration of retinal ganglion cells (RGCs) is increasingly recognized as pivotal to the pathogenesis. Therefore, the complex composition of the neurovascular unit - a concept describing the connection between RGCs, vascular cells and glial cells in the retina - must play a crucial role in the disease development, which is why the relationship between neurodegeneration and microvasculature damage is rising as an important study area. This project aims to investigate the difference between the diseased and the healthy retina, with an emphasis on the integrity and function of the retinal vasculature.

Perspectives: For in vitro investigations of the retinal vasculature, primary cells are the optimal choice. However, only a few protocols exist on how to isolate primary vascular cells from the retina. Even fewer protocols describe how to achieve monocultures of retinal endothelial cells and pericytes simultaneously. We have attempted to develop a simple and adaptable method that hopefully will result in consistent selective isolation of endothelial cells and pericytes, thereby providing the basis for further exploration of the retinal vasculature.

Themes: Molecular biology, Endocrinology
Keywords: Diabetic Retinopathy, Laboratory science, Primary cells

Vascular and metabolic dysfunction in adipose tissue: a dangerous duo in obesity

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Adipose tissue (AT) functionality is dependent on a continuous exchange of nutrients and hormones, which is regulated by the AT vascular barrier and AT blood flow (ATBF). The ATBF is controlled by innervation as well as by an interplay between adipocytes (among other AT cells), and the cells constituting the AT vasculature. Importantly, in people living with obesity and/or insulin resistance, the ATBF is disturbed during fasting and in the post prandial state, which exacerbates cardiometabolic complications. We hypothesize that impaired cellular crosstalk within AT drives ATBF dysregulation and cardiometabolic complications in people living with obesity.

The aim of this project is to identify cellular determinants of ATBF functionality and investigate their correlation with clinical features like obesity. We will thoroughly analyse transcriptomic data, captured at the single-cell level, from human AT samples that showcase both functional and dysfunctional AT states. Our study groups include individuals with insulin resistance, those with normal glucose tolerance, those assessed for ATBF (obese both before and after lifestyle intervention), and a control lean and obese group. Key determinants of ATBF, identified either in clinical studies or in the transcriptomic data, will be further explored in primary in vitro cellular models (endothelial cells, smooth muscle cells, and pericytes) and ex vivo myograph assays on vessels isolated from human AT. In short, we plan to elucidate the molecular mechanisms and cellular crosstalk that governs the ATBF.

Themes: Molecular biology, Pharmacology
Keywords: Adipose tissue blood flow, Dysfunctional adipose tissue, Vascular biology

The mechanism and regulation of aggrephagy

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In a healthy organism, cytoplasmic protein aggregates are recognized and degraded by the autophagy-lysosome pathway, in a selective process known as aggrephagy. Impairment of this process can lead to cytotoxicity, which in turn can cause neurodegeneration when occurring in the brain. One example hereof is Parkinson's disease, which is characterized by the presence of alpha-synuclein-containing aggregates. Despite its relevance in preventing neurodegenerative diseases, the underlying mechanism of aggrephagy in physiological as well as in pathological situations is largely unknown. Therefore, I aim at understanding of how cytoplasmic aggregates are recognized and how these aggregates can be eliminated. For my investigations, I will use a chemically inducible system based on particles induced by multimerization (PIM), in which I have tetracycline-dependent expression of a construct in which GFP and RFP are fused in tandem to several FKBP domains. Exposure to rapalog2 results in the formation of aggregates that are targeted by aggrephagy. The GFP-RFP tag enables tracking their aggregate formation in a fluorescence microscope and the conversion from a yellow to a red fluorescence signal over time due to the low pH in the lysosome allows to examine their lysosomal degradation as turnover kinetics. In parallel, I also have the same system expressing the PIM-APEX2 fusion protein, which allows conducting proximity biotin labelling. Both strategies will be used to perform co-immunoprecipitation experiments followed by proteomics analyses to identify aggrephagy players. Those will be validated by a siRNA-based counter screen and their role in aggrephagy will be further investigated.

Themes: Molecular biology, Neurodegenerative disorders
Keywords: Autophagy, Protein aggregates, Chemically inducible system

Importance of proper post culture cell handling of a cryopreserved human adipose derived mesenchymal stem cell therapy product

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BACKGROUND: The regenerative and anti-inflammatory abilities of adipose derived mesenchymal stem cells (AD-MSCs) make these cells an intriguing asset for clinical use. Cryopreservation (cryo) of AD-MSCs prior to therapy enables off-the-shelf availability. Reformulation of an AD-MSC product to remove cytotoxic cryo-preservative is favored when administrating to a purity demanding anatomical site. This study aimed to identify a simple and clinically adaptable post-cryo AD-MSC procurement approach.

METHODS: The entire AD-MSC refinement process from thawing to reformulation and storage was tested on expanded and cryo human AD-MSCs using isotonic solutions (phosphate buffered saline (PBS), Ringer's acetate and saline with or without 2% human serum albumin (HSA)). AD-MSC numbers and viability were analyzed with flow cytometry.

RESULTS: When thawing cryo AD-MSCs the presence of protein in the thawing solution was essential as up to 50% of the AD-MSCs were lost in the protein-free solutions. The reformulation and storage of AD-MSCs in culture medium and PBS showed poor cell stability, resulting in >40% cell loss and <80% viability after 1 hour at room temperature. However, employing saline for reformulation seemed to offer an alternative for post-thaw storage. This approach showed no cell loss and maintained viability at >90% for at least 4 hours.

CONCLUSION: This study identified a simple and clinically compatible post-cryo procurement method of AD-MSCs using saline with 2% HSA for thawing and pure saline for reformulation and storage for several hours at room temperature. This significantly eases the logistics between the cellular production facility and the treatment site.

Themes: Molecular biology, Pharmacology
Keywords: Mesenchymal stem cells, Cellular therapy, Cell viability

Complement fragment C3d in B cell activation and antigen transport

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The salient feature of any adaptive immune response is the antigen-specific reaction of select lymphocytes. To activate B cells, intact antigen must be transported to the lymph node or spleen where most naive B cells reside. When pathogens are attacked and potentially destroyed by complement, they are covered in C3 fragments. The complement fragments act as a signal of danger and bind complement receptors on subcapsular sinus macrophages, B cells, and follicular dendritic cells that all aid in either the transport or long-term storage of antigens. To become activated, B cells must recognize antigen with their B cell receptors, but their activation can be enhanced through simultaneous engagement of the B cell co-receptor, complement receptor 2. To study the role of the terminal C3 fragment C3d in B cell activation and antigen transport, we are using an RNA nanostructure. The nanostructure is called the “four-way junction” and as the name suggests it has four arms to which molecules can be conjugated in a stoichiometrically controlled fashion. This allows us to couple B cell and/or T cell antigens to a specific number of C3d molecules. The methods we are employing are in vitro calcium-flux assays of B cell activation, in vivo vaccination studies, and two-photon imaging of lymph nodes to follow antigen transport intra vitally. Understanding the details of antigen transport an B cell activation will increase our knowledge of current vaccines and aid in the design of new vaccines.

Themes: Molecular biology, Immune diseases
Keywords: Complement system, Lymphocytes

Monitoring the effect of inflammation in an in vitro stroke model

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Kim Ryun Drasbek, Department of Clinical medicine

Acute ischemic stroke (AIS) is the second leading cause of death globally and one of the major causes of long-term disability worldwide. Therapeutic treatments following stroke must be provided within 4.5-6 hours. Thus, there is an urge to find a therapy that extends the treatment window while providing long-term neuroprotection.

Remote Ischemic Conditioning (RIC) is a promising non-invasive treatment that seems to enhance the outcome of stroke. Upon RIC treatment, extracellular vesicles (EVs) and cargo micro-RNAs (miRNAs) are released into the bloodstream and promote cell-to-cell communication. Intercellular signalling regulated by vesicular miRNAs holds the potential to attenuate stroke's devasting consequences.

In AIS, inflammation can compromise the blood-brain barrier (BBB), resulting in severe tissue damage and lasting neurological impairments. Human brain microvascular endothelial cells (HBMEC) and their surrounding glycocalyx, are implicated in maintaining BBB integrity. However, when the inflammatory cascade is initiated, the glycocalyx gets disrupted. As a result, HBMECs start to express ICAM-1, which can enhance the recruitment of leukocytes, and subsequently the inflammatory response. Thus, investigating the impact of RIC-miRNAs on HBMECs, may provide valuable insight into their protective potential against inflammation and BBB breakdown.

In the future, RIC-miRNAs could be used as new biomarkers for the treatment and diagnosis of stroke. Further, by detecting the most protective RIC-miRNAs we aim to contribute to the advancement of a novel therapy designed to address both the immediate and long-term consequences of AIS.

Themes: Neuroscience, Molecular biology
Keywords: Acute Ischemic stroke (AIS), Remote ischemic conditioning, microRNA (miRNA)

Autoantibodies against TRIM21 and its individual domains in autoimmune disease

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Anti-SSA-autoantibodies are common in patients with rheumatologic disease, especially Sjögren's syndrome, systemic lupus erythematosus and rheumatoid arthritis. They consist of both autoantibodies towards Ro60 and Ro52, the latter also known as TRIM21. TRIM21 is an intracellular protein consisting of four domains; PRY/SPRY, Coiled-Coil, B-box and RING. The aim of this study was to establish an indirect ELISA detecting autoantibodies towards both the full-length TRIM21 protein and its four domains. We expressed the five constructs, created, and validated indirect ELISA protocols for each target using plasma from anti-SSA positive patients and healthy controls. Our findings were validated to the clinically used standards. We measured significantly higher levels of autoantibodies towards our full-length TRIM21, and the PRY/SPRY, Coiled-Coil and RING domains in patients compared to healthy controls. No significant difference in the level of autoantibodies were detected against the B-box domain. Our setups had a signal to noise ratio in the range of 30 to 184, and an OD between 2 and 3. Readings did not decline using NaCl of 500 mM as wash, affirming the high binding affinity of the autoantibodies measured. Our protocols allow us to further study the different autoantibodies of anti-SSA positive patients. This creates the possibility to stratify our patients into subgroups regarding autoantibody profile and specific pheno- or endotype.

Themes: Immune diseases, Molecular biology
Keywords: Autoantibodies, Autoimmune disease, Anti-Ro52

Unraveling the features of extracellular vesicles derived from mouse peripheral nerves

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Extracellular vesicles (EVs) are cell-secreted nanosized particles delineated by a lipidic bilayer and carrying a wide range of molecules, such as proteins and RNAs, thus mediating crucial roles in intercellular communication. In the last decades, research on EVs has arisen exponentially because of their relevance to basic biology, as well as their potential utilization as diagnostic biomarkers. The isolation and analyses of EV populations are challenging because of their biophysical complexity and heterogeneity, in particular when the EV source is a solid tissue. However, tissue-derived EV characterization is important for validation of results obtained from cell cultures and for a better understanding of EVs roles in biologically complex conditions. In peripheral nerves, Schwann cells (SCs) envelop the axons and support the normal neuronal functionalities. Inspired by published protocols for extraction of EVs from solid tissues, we aim to optimize a workflow allowing efficient and reproducible isolation of EV populations from mouse peripheral nerves; by using a reporter mouse line expressing a specific tag in SC-derived EVs, our final goal is to specifically isolate and characterize the SC-derived EVs population. We provide preliminary characterization of the isolated EVs by means of Western Blotting, Nanoparticle Tracking Analysis and Cryogenic Electron Microscopy, searching for general and tissue/cell-specific EVs features.

Themes: Neuroscience, Molecular biology
Keywords: Extracellular vesicles, Peripheral nervous system, Schwann cells

Paragenetic inheritance of autoimmunity and downstream neuropsychiatric sequelae

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Systemic lupus erythematosus (SLE) is a chronic autoimmune disease, targeting multiple organs, including the kidneys, skin, and lungs. However, up to 75% of patients experience neuropsychiatric manifestations ranging from headache to cognitive impairment and psychosis. This is proposed to be caused by cross-reactive autoantibodies targeting the cells of the CNS.

Particularly children of autoimmune mothers are at high risk, since maternal transfer of autoantibodies, combined with genetic predisposition, can negatively impact the development and health of the offspring. Here, we used embryo transfers to examine the maternofoetal transfer of autoantibodies and immune activation in offspring; hereby, uncoupling environmental and genetic factors.

Normal C57BL/6J embryos were transferred to either 564Igi females, a murine strain presenting with SLE-like disease due to an autoreactive B cell receptor knock-in, or to healthy C57BL/6J females as controls.

Maternal transfer and endogenous production of both total and autoreactive antibodies were measured using time-resolved immunofluorometric assays (TRIFMA). Immune cell populations were analysed by flow cytometry, and the cortical microglia morphology were visualized using an immunohistochemical Iba1 stain and confocal microscopy and subsequently assessed via an image analysis pipeline.

Increased maternally transferred and endogenously produced (auto)antibody levels were detected in offspring born to autoimmune mothers, along with increased B cells in lymph nodes and splenic plasma cell and -blast populations. However, no significant change in microglia morphology was observed between embryo transfer offspring, mothers, or controls.

Themes: Immune diseases, Animal Models
Keywords: Autoimmunity, Maternal antibody transfer, Neuroimmunology

Endothelial metabolism regulates STING-driven inflammation

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Introduction: Endothelial cells (ECs) play a crucial role in the onset of inflammation by mediating the adhesion and subsequent transmigration of immune cells from the circulation. Immune cell trafficking requires activation of ECs, an energy demanding process often associated with a shift in their metabolism. As targeting EC metabolism could lead to normalization of the vasculature during pathophysiological situations, exploring the interplay between EC metabolism and inflammation, particularly STING-mediated inflammation, is of our interest.

Results: The activation of endothelial STING increased the expression of chemokines, pro-inflammatory cytokines and cell adhesion molecules in addition to junctional rearrangements in vitro. Similar observations were made in different murine inflammatory models in vivo. Moreover, these observations were abrogated in STINGKO ECs and in STINGECKO mice.

Additionally, this inflammatory signature was dependent on IRF3 nuclear translocation and was found to be associated with metabolic rewiring of ECs. Transcriptomic and metabolomic analysis of IRF3-activated ECs revealed increased expression of genes related to oxidative phosphorylation (OXPHOS). Indeed, OXPHOS inhibition in vitro and in vivo impaired EC inflammatory responses upon IRF3 activation.

Conclusion: The inflammatory signature of ECs upon STING pathway activation requires metabolic rewiring, leading to increased oxidative phosphorylation. Mechanistically, these alterations depend on IRF3 transcriptional activity. These results suggest that the modulation of EC metabolism can modify the inflammatory manifestations of diseases.

Themes: Molecular biology, Immune diseases
Keywords: Endothelial cell biology, Metabolism, Inflammation

SESSION 23

Efficient in vitro and in vivo mRNA and CRISPR delivery with lipid nanoparticles

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Gene editing with CRISPR-Cas9 offers hope for treating genetic disorders, yet efficient delivery of the CRISPR components remains a hurdle in therapeutic applications. Lipid nanoparticles (LNPs) have emerged as a robust and safe strategy for delivery, offering high encapsulation efficiency and cargo protection. To advance LNP-based mRNA and CRISPR therapy, we systematically evaluate LNP delivery efficiency in in vitro, ex vivo, and in vivo settings.

Our approach involves microfluidic mixing of ionizable lipids, helper lipids, cholesterol, and PEGylated lipids to achieve a uniform nanoparticle size distribution. To assess delivery efficiency, we encapsulate EGFP mRNA in LNPs. Our preliminary results demonstrate the effective delivery of EGFP mRNA to various cell types, including primary cells like human fibroblasts, Schwann cells, primary cortical neurons, and iPSC-derived astrocytes and

microglia. Furthermore, we successfully target challenging cell types such as human endothelial cells.

LNP-mediated mRNA delivery also performs well in ex vivo mouse brain slice cultures and in vivo via subretinal injection. Moreover, we achieve efficient non-homologous end joining and homology-directed repair gene editing using LNP-mediated delivery of Cas9 mRNA, synthetic gRNA, and single-stranded oligodeoxynucleotide templates in cultured cells.

While improvements are needed, our results show that LNP is a promising delivery strategy for advancing CRISPR/Cas9-mediated gene editing and RNA therapeutics. The project is supported by the Lundbeck Foundation (R396-2022-350), aiming to investigate the possibility of utilizing LNP-CRISPR technology for Duchenne Muscular Dystrophy.

Themes: Genetic engineering, Neurodegenerative disorders
Keywords: Lipid Nanoparticles, CRISPR, Delivery

Characterization of an inflammation-driven chronic kidney disease model using human precision-cut kidney slices

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Chronic Kidney Disease (CKD) affects about 10% of the adult population. A major contributor to CKD progression is low-grade inflammation, which promotes fibrosis, leading to gradual loss of kidney function. To date, there remains a need for reliable and translational human models of inflammation-driven CKD that can enhance our understanding of the mechanisms linking inflammation and fibrosis in CKD pathogenesis. Therefore, our aim was to establish a novel model of inflammation-driven CKD using human precision-cut kidney slices (PCKS).

Human PCKS were prepared from macroscopically healthy kidney tissue obtained from tumor nephrectomies. The PCKS were cultured for 24h or 48h with or without TNFα stimulation/inhibition. The subsequent inflammatory response in the slices was characterized by qPCR, cytokine membrane array and fluorescence microscopy.

Expression of the proinflammatory markers TNF, IL1B, CCL2 and IL6 spontaneously increased during incubation of human PCKS, which could be inhibited by Etanercept (TNFα inhibitor) treatment. On the other hand, TNFα stimulation further increased the gene expression of the tested proinflammatory markers. In addition, a cytokine membrane array revealed that 17 different cytokines and chemokines were secreted by the slices, with levels varying based on incubation time and TNFα stimulation. Lastly, immunofluorescent staining demonstrated an increase in a marker of immune activation (HLA-DR) after TNFα stimulation.

This study utilized human PCKS to model inflammation-driven CKD development. Importantly, the established model holds promise as a pre-clinical drug screening platform, specifically for anti-inflammatory CKD treatments.

Themes: Urology & Nephrology, Molecular biology
Keywords: Chronic kidney disease, Ex vivo human model, Inflammation

Acute retinal necrosis upon VZV infection in a patient with a splice-site mutation in ZC3HAV1 suggests an important antiviral role for ZC3HAV1 in VZV infections

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Varicella zoster virus (VZV) is an α-herpesvirus causing varicella in primary infected individuals. Thereafter, the virus remains latent in sensory ganglia until reactivated, causing zoster. In rare cases, VZV causes severe infections in the central nerves system (CNS) including encephalitis, meningitis and acute retinal necrosis (ARN). Previous studies have already reported key molecules of immunity against severe VZV infections. However, the exact pathogenesis remains incompletely understood. Therefore, we aim to identify novel inborn errors in patients with severe CNS infections upon VZV to discover new key molecules playing a role in controlling these infections. Whole exome sequencing (WES) in a patient with ARN due to VZV revealed a splice-site variant in ZC3HAV1 (Zinc Finger CCCH-Type Antiviral Protein 1) (c. 1994-2A>T), causing exon-skipping of exon 9. ZC3HAV1 encodes the protein ZAP which is shown to exhibit direct antiviral activity by mediating the degradation of viral mRNA. Besides that, it is suggested to negatively regulate interferon (IFN) signaling to prevent an excessive immune response. RT-qPCR on PBMC's after VZV infection showed increased viral mRNA levels and slightly increased IFN-β mRNA levels in the patient compared to controls. Also, ZAP KO HEK293FT cells showed increased viral mRNA expression and increased IFN-β expression after VZV stimulation compared to WT HEK293FT cells. These results suggest that ZAP plays an important role in the control of VZV which has not been shown before.

Themes: Infectious Diseases, Immune diseases
Keywords: Antiviral immunity, Innate immunity, Inborn errors

Exploring associations of single nucleotide polymorphisms in endoplasmic reticulum aminopeptidases (ERAPs) and susceptibility to multiple immune-mediated inflammatory diseases

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Background: Single nucleotide polymorphisms (SNPs) in the endoplasmic reticulum aminopeptidase 1 (ERAP1) and ERAP2 genes have been associated with susceptibility to several immune-mediated inflammatory diseases (IMIDs), primarily in genome-wide association studies.

We here take advantages of the unique cohort from the National Centre for Autoimmune Diseases (NCAD) to investigate the association of specific SNPs in ERAP1 and ERAP2 with the presence of two or more IMIDs. We further aim to clarify whether these SNPs, alone or in combination with the known risk allele HLA-C*06:02, are associated with multiple IMIDs occurrences.

Methods: The study population compromises 171 patients with two or more IMIDs. Using real time PCR allelic discriminations method, we genotyped two SNPs in ERAP1 (rs30187, rs27524) one SNP in ERAP2 (rs2248374) and the HLA-C*06:02 risk allele (rs4406273).

Results: We observed no overrepresentation of a specific risk allele in either ERAP1 or ERAP2 when considering the entire study population. However, a significantly higher proportion of homozygote ERAP1 rs30187 TT and ERAP1 rs27524 AA genotypes among HLA-C*06:02 positive patients were seen than among HLA-C*06:02 negative patients.

Our dataset confirms the known associations between the HLA-C*06:02 allele and psoriasis, and the HLA-B*27 allele and spondyloarthritis.

Conclusion: These preliminary results from this unique yet heterogenous population suggest an interaction between HLA-C, ERAP1 and ERAP2. This interaction, when combined, may represent a profile predisposed to autoimmunity, resulting in the development multiple IMIDs.

Themes: Immune diseases, Molecular biology
Keywords: Dermatology, Inflammation, Psoriasis

The dysbiosis of the acne skin microbiome and its decline after isotretinoin treatment

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Acne vulgaris is a complex skin condition, and the onset of the disease involves various factors, including the skin microbiome. However, knowledge of the skin microbiome in acne, as well as the impact of isotretinoin (ISO), the most efficient treatment of severe acne, remains limited. This study compared the skin microbiomes of acne patients and healthy individuals and assessed the effects of ISO treatment. Skin swabs were collected from healthy individuals, pre-ISO acne patients and post-ISO acne patients. The analysis included target-specific amplicon-based sequencing to assess the general bacterial, staphylococcal and C. acnes composition, as well as droplet digital PCR for absolute quantification. The analysis revealed that pre-ISO acne patients had reduced diversity in the C. acnes population with an increase in relative abundance of IA1 strains and a decrease in type II strains. The staphylococcal population showed increased diversity, notably an increased relative abundance of potentially harmful Staphylococcus aureus. Both staphylococcal and C. acnes populations decreased in quantity. Post-ISO treatment, staphylococcal and C. acnes populations significantly decreased. Overall, the dysbiosis of the acne microbiome involved changes in both the C. acnes and staphylococcal populations with ISO treatment primarily affecting C. acnes. Other organisms could -to some extent- take over the space; Streptococcus, Corynebacterium and Micrococcus had increased relative abundances, in a patient-specific manner. Results suggest a potential benefit from skin probiotics for timely restoration of the healthy skin microbiome in acne patients treated with ISO.

Themes: Infectious Diseases, Molecular biology

Lipid nanoparticle-induced gene expression for antiviral therapy against SARS-CoV2 and Influenza A infections

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Viral infections with influenza A virus (IAV) and SARS-CoV2 are major causes of morbidity and mortality worldwide. The development of effective vaccines based on mRNAs encoding SARS- CoV2 antigens was recently made possible due to breakthrough developments in mRNA delivery technology. Here, ionizable cationic Lipid-Nano-Particles (LNPs) encapsulate and protect mRNA from enzymatic degradation and thus allow for efficient cellular uptake with subsequent protein expression in vivo. If this technology can be used to protect against virus infection by the direct delivery of mRNAs that encode anti-viral genes into airway epithelium is not yet established.

We have identified a novel network of NRF2-dependent genes with high anti-viral potential towards IAV and SARS-CoV2. With this project, we aim to test if the LNP technology can be exploited to induce infection protection by delivering mRNAs and sgRNAs to induce the expression of these new anti-viral genes. Through distinctive combinations of LNP components, we have optimized mRNA/sgRNA delivery to human airway epithelia and human hepatic cell lines which now enables us to genetically manipulate the expression of the anti-viral gene network. We will determine the antiviral capacities by LNP delivery of the NRF2-dependent gene network ex vivo in a stratified primary human airway epithelium model and in- vivo in a mouse model of IAV and SARS-CoV2 infection. This project will determine if LNP-based delivery of the NRF2-inducible anti-viral genes can elicit antiviral control at physiologically relevant epithelial surfaces during infection with Influenza A virus and SARS-CoV2.

Themes: Infectious Diseases, Infectious diseases
Keywords: Lipid nanoparticle delivery, Airway infections, Anti-viral genes

The role of ER-phagy in virus infections

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ER-phagy is the selective autophagy of the endoplasmic reticulum (ER), through which ER fragments are delivered into lysosomes for degradation. Besides its function to ensure cell homeostasis, ER-phagy appears to be a cellular mechanism against pathogens, including viruses. Some ER-phagy-specific genes have been associated with viral infections, suggesting that ER-phagy and viruses interact for pro-viral or anti-viral effects. However, only two direct interactions have been described in molecular detail, i.e., the one between the ER-phagy receptors FAM134 and ATL2 and SARS-CoV-2, and the one between FAM134B and Dengue and Zika viruses. To investigate the extent to which ER-phagy and viruses interact, we designed a siRNA library targeting individually or in combination each gene associated to date with the ER-phagy machinery. We knocked down these genes in two human cell lines and studied the effect of these depletions in the replication of six viruses from six different families using virus strains that express luciferase as the reporter gene. Our screen identified several ER-phagy-related genes that seem to promote or prevent viral replication. The results show that ER-phagy may play a role in the life cycle of herpes simplex virus 1 and coxsackievirus B3, while specific genes may have ER-phagy-unrelated functions in the life cycle of the other tested viruses. We are currently validating and following up on the most interesting hits. We aim at providing new insights into the role of ER-phagy and its related proteins during viral infections as well as the subversion strategies of specific viruses. This knowledge could be key for the future development of anti-viral drugs.

Themes: Infectious Diseases, Molecular biology
Keywords: Selective autophagy, Endoplasmic reticulum, Viral hijacking

A biomarker of the S100A9 subunit; Cpa9-HNE is decreased in response to adalimumab treatment in axSpA

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Background: 5-10% of patients with axial spondyloarthritis (axSpA) are diagnosed with co-morbid inflammatory bowel disease (IBD), however 22%-69% of all axSpA patients have microscopic gut inflammation. Persistent gut inflammation is prognostic for progression to ankylosing spondylitis. Fecal calprotectin was previously successful in identifying gut inflammation in patients with axSpA.

Objective: We measured Cpa9-HNE, a protein fragment of the S100A9 subunit of calprotectin generated by human neutrophil elastase (HNE), in serum of axSpA patients initiating adalimumab treatment (the INTASAH study). Serum was sampled at week 0 (baseline), and after 12 and 52 weeks of treatment. Patients were stratified based on fecal calprotectin at week 0 into two groups indicating patients without (<50 mg/kg, n = 11) and with (>100 mg/kg, n = 10) gut inflammation.

Results: Cpa9-HNE was detected in all patients. Patients with <50 mg/kg fcal had similar levels to patients with >100 mg/kg, meaning that Cpa9-HNE did not correlate with fecal calprotectin levels. From week 0 to 12, there was a significant decrease in Cpa9-HNE in both the <50 mg/kg group (p=0.0358) and >100 mg/kg group (p=0.0027). A number of patients increased in Cpa9-HNE from week 12 to 52. There was no significant difference in the <50 mg/kg group from week 0 to 52 (p=0.0822), as well as >100 mg/kg group (p=0.0526).

Discussion: Cpa9-HNE may indicate lowered gut inflammation in response to adalimumab treatment, however serum Cpa9-HNE is not a tissue-specific measure of gut inflammation. Future studies include measuring a larger panel of tissue degradation fragments and associations with gut involvement and treatment outcome.

Themes: Immune diseases, Gastroenterology and hepatology
Keywords: Axial spondyloarthritis, Gut inflammation, Calprotectin

Solvent effect on the self-assembly of α-helical phenol-soluble modulin peptides

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Members of the Staphylococcus aureus phenol-soluble modulin (PSM) family peptides are secreted as functional amyloids that serve diverse roles in pathogenicity, e.g., as the structural scaffold in the biofilm formation. Many literatures emphasize that self-assembly and crystallization of amyloidogenic peptide play important roles in the physiological environment, considering that high ordered crystal state is the thermodynamically favorable state. In vitro, the self-assembly of these small and amphiphilic peptides will be affected by external conditions in the environment, e.g., temperature, ion strength and solvents. Here, we focus on the control of dimethyl sulfoxide (DMSO) to PSMα3 crystallization, as DMSO is vital in biological research for protein treatments. To explore the possible changes both in the morphology and secondary structures during the self-assembly process, we utilize various biophysical techniques (e.g., TEM, AFM, CD, optical microscope).

Themes: Infectious Diseases, Imaging techniques

The CES genes are silent protecters against influenza in our airways

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NRF2 is a transcription factor that regulates the expression of antioxidant genes and inflammatory responses. We focus on the Carboxyl Esterase (CES) family of genes, a NRF2 subset highly expressed in airway epithelia, which demonstrate potent antiviral activity against Influenza A virus (IAV). Employing CRISPR activation, we successfully diminish IAV replication by overexpressing CES genes in Huh7 cells. Additionally, intriguing connections between CES genes and IFITM3 shed light on potential antiviral pathways.

Utilizing air-liquid interface cell cultures, we observe a substantial increase in CES genes expression, both at the RNA and protein levels, as airway cell cultures mature.

This study enriches our understanding of NRF2's pivotal role in airway defence, underscoring CES genes as formidable antiviral allies against Influenza A virus.

Themes: Infectious Diseases, Molecular biology
Keywords: Airway immunity, Innate immunology, Influenza infection

SESSION 24

Renal Aquaporin-2 and Protein Kinase A localization following cAMP increase

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Short-term renal water handling for fine-tuning urine concentration is mediated by arginine vasopressin (AVP), which regulates the trafficking of renal aquaporin-2 (AQP2) between intracellular vesicles and the plasma membrane. AVP triggers an increase in cAMP, leading to Protein Kinase A (PKA) activation and subsequent phosphorylation of AQP2 at serine 256. Phosphorylation of AQP2 at S256 leads to AQP2 vesicle exocytosis.

Dysregulation of AQP2 trafficking is associated with multiple water balance disorders, which manifest as either urinary concentration defects or water retention. Therefore, studying the molecular mechanism of AQP2 vesicle exocytosis is crucial for developing targeted treatments for common water balance disorder.

This study investigates the subcellular localization of AQP2 and PKA before and after an increase in cAMP. MDCK cells were stimulated with forskolin to elevate cAMP levels and fixed at various time points (0, 5, 10, 15, and 30 minutes) after stimulation. The localization of PKA and AQP2 was visualized through immunofluorescence imaging. In DMSO treated cells, AQP2 and PKA were mainly localized on large intracellular vesicles in the perinuclear region, with some co-localization of AQP2 and PKA observed. Upon forskolin treatment, AQP2 translocated to the plasma membrane, and PKA displayed a more diffuse distribution. We aim to employ Expansion Microscopy to enhance resolution and facilitate imaging of endosomes and subdomains, thus allowing us to visualize if PKA clusters on AQP2 vesicles in response to cAMP increase. This will bring us closer to unravelling the mechanism of AQP2 trafficking and its significance in maintaining body water balance.

Themes: Urology & Nephrology, Imaging techniques
Keywords: Nephrology, Cell biology, Fluorescence Microscopy

The renal urinary concentration mechanism: Towards a detailed model of Aquaporin 2 shuttling

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Aquaporin water channels (AQPs) play a critical role in water homeostasis by facilitating water transport across cellular membranes. AQP2 is vital in the urinary concentration mechanism. It is located in the apical plasma membrane and subapical intracellular vesicles in the principal cells of the renal collecting duct. Upon dehydration, the hormone Arginine Vasopressin (AVP) is released which binds to the basolateral membrane of the principal cells. This binding leads to phosphorylation and relocation of AQP2 from the cytoplasm to the apical membrane, increasing water permeability and thus reabsorption. Mutations in AQP2 or the AVP receptor, lithium-induced nephrogenic diabetes, congestive heart failure, and chronic kidney disease can all lead to dysregulation of AQP2 shuttling. In this project, we aim to use a variety of stimuli known to affect AQP2 shuttling, AQP2 phosphorylation and employ expansion microscopy to increase resolution to visualize the AQP2 vesicular population. We have successfully expanded both cells and tissue and by using spinning disk microscopy coupled with deconvolution and image processing, we can image the AQP2 vesicular population to a resolution of approximately 40 nm. A better understanding of the shuttling mechanism of AQP2 could provide new insight that could lead to new treatment options and an improvement in the quality of life of patients affected by AQP2 dysregulation.

Themes: Urology & Nephrology, Imaging techniques
Keywords: Water balance, Microscopy, Aquaporin 2

mRNA THERAPY DURING NORMOTHERMIC MACHINE PERFUSION OF DONOR KIDNEYS - **CANCELLED**

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Introduction: Development of fibrosis in the donor kidney after transplantation remains a challenge, leading to a reduction in graft function. Normothermic machine perfusion (NMP) of the donor kidney prior to transplant allows ex vivo drug delivery with limited adverse effects. Synthetic messenger RNA (mRNA) encoding anti-fibrotic therapeutic proteins combined with NMP, has great potential to prevent early fibrosis development of renal grafts. Therefore, the aim of this study is to evaluate the feasibility of mRNA therapy during ex vivo kidney-NMP.

Methods: As a proof-of-concept, mRNAs encoding for a secretive protein (human erythropoietin, hEPO) and an intracellular red fluorescent protein (mCherry) were used. Porcine kidneys (n=3) were perfused in pairs on NMP using a red blood cell-based perfusate for 6.5 hours. Then, randomized to treatment with lipid nanoparticles (LNPs) carrying 150 µg mRNA or control. Perfusate, urine and tissue were obtained and analyzed for hEPO levels with ELISA.

Results: Perfusion characteristics and functional markers were not affected by ex-vivo LNPs-mRNA treatment. In kidneys treated with hEPO mRNA, hEPO protein was detected in the perfusate and urine about 1 hour after mRNA delivery. hEPO levels increased in perfusate and urine during NMP reaching 4-6 IU/mL after 6 hours. The delivery of mRNAs encoding mCherry is currently tested.

Conclusion: mRNA therapy during ex vivo kidney-NMP was shown feasible. To aid clinical translation, the strategy will be proven in a porcine auto-transplant model and human discarded kidneys, including the use of mRNAs encoding anti-fibrotic proteins.

Themes: Urology & Nephrology, Urology & Nephrology
Keywords: mRNA, NMP, Transplantation

Bile Acids as a Mediator of Renal Injury in Non-Alcoholic Fatty Liver Disease

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Rikke Nørregaard, Henricus Antonius Maria Mutsaers

Numerous studies demonstrate a higher prevalence of chronic kidney disease (CKD) among non-alcoholic fatty liver disease (NAFLD) patients (20-55%) compared to the general population (5-30%). The precise link between these conditions remains unclear, however, growing attention centers on bile acids (BA), which are known to induce renal inflammation, oxidative stress, and cellular damage. My study aims to investigate the pathophysiological mechanisms of NALFD- and BA-mediated renal injury. Firstly, I will evaluate the expression profile of bile acid receptors (BAR) in the kidney from both humans and rats. Next, the impact of BAs on BAR expression will be investigated in Human Renal Fibroblast (HRF) cells and human Precision-Cut Kidney Slices (hPCKS) as well as in kidney tissue from rats with NAFLD and cirrhosis. In addition, I will evaluate markers of renal injury, inflammation, fibrosis, oxidative stress, and liver injury in both rat models. This will be complemented by measurements of cell injury, inflammation, fibrosis, and oxidative stress in HRF cells and hPCKS exposed to pathological concentrations of BAs. Subsequently, attempts will be made to reverse the effects of the BAs in HRF cells, hPCKS, and both rat models through the administration of BAR agonists or antagonists, for example, obeticholic acid. Lastly, single-cell RNA sequencing (scRNAseq) will be used to analyze the transcriptional changes in hPCKS as well as kidney tissue from NAFLD and BDL rats. We expect that this study will unveil why NAFLD and CKD frequently exist together, including the influence of systemic BAs on the kidneys.

Themes: Urology & Nephrology, Molecular biology
Keywords: Chronic Kidney Disease, NAFLD, Bile acids

Effects of Exogenous Ketosis on Renal Function, Renal Perfusion and Sodium Excretory Capacity in Healthy Subjects (KETO)

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BACKGROUND: Renewed interest in the physiological role of ketone bodies (KB) has emerged. Previously KB have been negatively associated with diabetic ketoacidosis. However, it has become clear that there are also beneficial effects. For example, a Danish study has shown, that infusion of KB in heart failure patients induced a significant improvement in cardiac output and perfusion.

Only few studies have examined renal effects of ketosis. A study suggested that infusion of KB lead to increased renal blood flow (RBF) and glomerular filtration rate (GFR). KB is reabsorbed in the proximal tubule along with sodium, suggesting that KB may influence sodium excretion. However, there are no human studies dealing with the effects of ketosis on sodium- and water balance. Thus, further studies on renal effects of ketosis are needed.

HYPOTHESIS: Ketosis increases RBF and GFR and decreases 24-hour blood pressure

METHODS: We are conducting a randomized, placebo-controlled, double-blinded crossover study in 15 healthy subjects who are randomized to receive either a ketone vehicle (ketone ester) or placebo vehicle (taste and volume matched drink) for five days in addition to a standardized diet. RBF (determined by [15O]-H2O PET/CT), GFR (determined by Tc99m-DTPA clearance) and remaining effect variables, will be measured on the last day of the interventions.

PERSPECTIVES: Study completion is expected in spring 2024. The results will provide hypothesis generating data on possible effects of ketosis on renal function and blood pressure. Based on the findings we will carry out two other studies in patients with hypertension and chronic kidney disease.

Themes: Urology & Nephrology, Endocrinology
Keywords: Ketosis, Nephrology, Metabolism

Obstructive sleep apnea in chronic kidney disease: an overlooked risk factor for cardiovascular and renal disease progression

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Background: Moderate to severe OSA is very common in CKD patients (25-40% prevalence) and it has been associated to contribute to increase extracellular volume and total body sodium retention. Na accumulation stored in connective tissues can induce a pro-inflammatory state and endothelial disfunction, leading to faster decline in eGFR in patients with chronic kidney disease, accelerated vascular calcification and higher aortic stiffness. OSA might also be linked to deterioration of kidney function due to renal hypoxia.

Aim: Renal hemodynamic effects in CKD patients with OSA and the occurrence of renal hypoxia have not been evaluated yet. We aim to assess the impact of OSA on cardiovascular risk factors in chronic kidney disease (CKD), evaluate sodium and water retention as potential contributors to OSA, analyse the effects of intensified diuretic therapy on OSA severity and shed light on whether hypoxia periods are associated to accelerated kidney function loss.

Methods: The present study involves recruiting around 300 advanced CKD patients which will be screened for OSA. Coronary and aortic CT, echocardiography and determination of biomarkers will be assessed. Moreover, 23Na MRI on soft issue and MRI renal perfusion and oxygenation will also be performed. An interventional trial stage will assess changes in tissue sodium content and apnoea-hypopnea index when applying an intensified diuretic treatment.

Expected results: This research project aims to demonstrate the contribution of OSA to kidney function loss and progression of cardiovascular risk factors in CKD patients. Moreover, we expect to advance our understanding of how OSA and sodium tissue retention are related.

Themes: Urology & Nephrology, Imaging techniques
Keywords: Chronic Kidney Disease, Obstructive Sleep apnea, Cardiovascular risk factors

The testicular microvasculature in Klinefelter syndrome is immature with compromised integrity and characterized by excessive inflammatory crosstalk

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Klinefelter syndrome (KS; 47,XXY) is a rare congenital condition in males with a supernumerary X chromosome. The phenotypic presentation is variable, but generally includes infertility and hypergonadotropic hypogonadism. Recent studies exhibit microvascular dysfunction in the testes of males with KS, in addition to an increased intratesticular testosterone concentration. With this study we aim to investigate the implication of the testicular microvasculature in the hypogonadism observed in males with KS.

We analyzed publicly available single-cell RNA sequencing data of testicular cells from males with KS (n = 6), non-obstructive azoospermia (n = 5), cryptozoospermia (n = 3) and controls (n = 15). The integration of these datasets allowed us to analyze gene expression profiles and communication patterns among testicular cell types.

Rooted in changes at the single-cell level, our study demonstrates a shift in gene expression within the testes of males with KS. We identified genes uniquely dysregulated in capillary endothelial cells, indicating enhanced capillary endothelial cell activation and disorganized vessel formation, leading to impaired vessel maturation and increased EC barrier permeability. This was accompanied by altered cellular communication, revealing increased inflammatory cross-talk and pro-inflammatory responses.

This study offers novel insights into the testicular pathophysiology in KS and underscores the potential contribution of microvascular dysfunction to the hypogonadism and infertility observed in males with KS, yet the precise connections to testosterone deficiency and testicular atrophy remain to be fully elucidated.

Themes: Endocrinology, Omics
Keywords: Klinefelter syndrome, Single-cell RNA sequencing, Testosterone

Isotope-guided metabolomics dissects kidney arginine metabolism

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Background-Aim: L-arginine is a key amino acid for organism detoxification, protein metabolism, and kidney and cardiovascular health. This study aims to detect arginine uptake and its metabolic fate in kidney in vivo and ex-vivo models by metabolic flux analysis.

Method: Healthy mice were fed with normal and 13C6-15N4-arginine diet. Extracted metabolites from kidneys were analyzed with UHPLC/QQQ-based mass spectrometry targeting arginine-related pathways including the urea cycle, polyamines, the nitric oxide pathway, arginine/proline/glutamate interconversion, and modified forms of arginine. In addition, isolated glomeruli, cortical tubules and nephron segments from healthy mice were incubated with 13C6-arginine and analyzed accordingly.

Results: Isotope tracing revealed arginine fate in the common arginine-related pathways in the kidney of the arginine diet fed animals. The ex vivo experiments confirmed that all nephron segments, except for the thin ascending limp of the loop of Henle, take up and metabolize arginine. More specifically, ornithine was found in all segments apart from the collecting duct (CD). Agmatine was formed in the proximal straight tubule (PST) and the CD, whereas arginine contributed to the proline and glutamine formation in the glomeruli, the proximal convoluted tubule and the CD. Methylated forms of arginine were observed in the PST and the distal convoluted tubule.

Conclusion: This study allowed for the detection of basic arginine-related metabolites in the kidney and the specific metabolic fate of arginine in each nephron segment. The detailed isotope-based arginine metabolic flux and its role in kidney disease models will be determined next.

Themes: Urology & Nephrology, Omics
Keywords: kidney metabolism, arginine metabolism, kidney disease

Thrombocytes constitute an effective clearance system for uropathogenic Escherichia coli in a murine model of urosepsis

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Urosepsis is a life-threatening host reaction to uropathogenic bacteria in the blood, associated with reduced microperfusion and tissue hypoxemia. Thrombocytopenia, one of the diagnostic criteria for sepsis, is a distinct negative prognostic marker for survival. Interestingly, our preliminary data in a murine model of urosepsis reveal that the thrombocyte number falls prior to intravascular coagulation. Here we investigate the fate of circulating thrombocytes during urosepsis.

All experiments were carried out in anaesthetised male Balb/cJRj mice (8-10 weeks). E. coli (O6:K13:H1) 330·10^6 were administered iv.

We detected an early thrombocyte reduction of about 37%, already 30 min after E. coli injection compared to mice receiving vehicle. Correspondingly, we observe a short transient increase in thrombocyte activation after 30 minutes of E. coli exposure compared to vehicle control, independent of intravascular coagulation. Thrombocytes are known to form complexes with neutrophils or monocytes. However, the number of these complexes remained constant during the early fall in thrombocyte number and, thus, cannot explain the drop in circulating thrombocytes. Interestingly, we found that the number of bacteria in the blood fell by 69% in parallel with the thrombocytes 30 minutes after injection. By image-enhanced flow cytometry, we were able to show that the GFP-expressing E. coli instantly and primarily is scavenged by circulating thrombocytes and that these complexes are acutely removed from the circulation.

The data strongly suggest that circulating thrombocytes constitute the most important cell type for fast scavenging and clearance of invading bacteria during urosepsis.

Themes: Infectious Diseases, Urology & Nephrology
Keywords: Urosepsis, E. coli, Thrombocytes

Minimal Change Disease at debut and relapse

– a retrospective description of treatment strategies and changes throughout time

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Background: Minimal change disease (MCD) has traditionally been treated with prednisolone monotherapy based on clinical evidence. With the introduction of new drugs and awareness of the severity of prednisolone side effects, treatment strategies may have evolved. The aim was in a retrospective design to describe if treatment strategies and clinical outcomes have changed over time. Methods:

Health records from 239 Dutch and Danish adult patients with nephrotic syndrome and biopsy verified MCD from 13 hospitals were reviewed and treatment at onset of disease and at relapse were described, as well as clinical outcome.

Results: Primary treatment with Prednisolone monotherapy was initiated in 205 patients, and 169 gained remission within a median of 46 days. In 30 patients' additional immunosuppression were added, mostly calcineurin-inhibitors (CNI), Cyclophosphamide or a combination and 21 gained remission within a median of 235 days. In 27 patients no treatment was given. Overall, 93.2% gained remission and 55.9% relapsed, with 68% in the first year following remission. At 1st relapse Prednisolone monotherapy was mostly used both before and after 2010 (68.8% and 45.3%). At 2nd relapse Prednisolone + CNI was preferred after 2010. Rituximab was introduced after 2010, whereas the use of Cyclophosphamide decreased. Remission rates were high at all strategies. 30% of patients experienced more than 1 relapse.

Conclusion: The primary therapeutic approach with prednisolone monotherapy is unchanged predominant over time with high rates of remission. Treatment of relapse has changed over time increasing the use of CNI, introducing Rituximab, and reducing the use of Cyclophosphamide.

Themes: Urology & Nephrology, Immune diseases
Keywords: Minimal change disease

SESSION 25

B cells and Tertiary Lymphoid Structures: Implications for Liver Cancer Progression

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Introduction: Tertiary lymphoid structures (TLS) are observed in various pathologies including chronic inflammation and various types of cancer, where they affect the course of illness. In recent years, the presence of TLS in relation to cancer has been increasingly studied as TLS in the tumor milieu correlates with increased survival rates in patients with some cancers. However, conflicting data has emerged regarding liver cancer, and this project aims to investigate B cell differentiation in relation to liver cancer progression.

Methods: Mouse models of liver cancer will be utilized to investigate the presence of TLS. This includes a model of a "hot" liver tumor generated with a carcinogen and a "cold" liver tumor generated by CRISPR. Additionally, mice with a specific loss of T-bet in B cells will be generated, as B cells with loss of T-bet exhibit reduced serum IgG2 levels and inflammatory cytokines which have been associated with liver cancer progression.

Results: Analysis of TLS formation in mice with liver cancer shows an increased amount of TLS with tumor progression. The formation of TLS is not restricted to cancer, as mice with steatosis also develop TLS albeit with reduced size compared to mice with liver cancer. Interestingly, reduced TLS size is observed in STING-deficient mice with liver cancer, indicating that lack of innate immunity reduces TLS size.

Future perspectives: The implications of T-bet-deficient B cells on tumor progression will be assessed in mice with liver cancer. The two models of liver cancer will be compared, and the presence of TLS will be evaluated. TLS will be assessed in terms of fully developed structures, cytokines, and IgG2 production.

Themes: Cancer, Animal Models
Keywords: B cells, Liver cancer, Immunotherapy

Hyperglycemia during treatment in children and adolescents with acute lymphoblastic leukemia and lymphoma

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Background and aims: Medication induced hyperglycemia is an adverse event to treatment with dexamethasone and PEG-asparaginase in children and adolescents with acute lymphoblastic leukemia (ALL) and lymphoma. Hyperglycemia during treatment increases the risk of infections and is associated with metabolic syndrome and type 2 diabetes later in life.

The incidence and severity of hyperglycemia is not well known and the pattern of hyperglycemia during treatment is not well characterized.

The aims of the study are to investigate the incidence and severity of hyperglycemia and to map out the pattern of hyperglycemia during different treatment phases.

Methods: A continuous glucose monitoring (CGM) system is used to collect glucose data during specific treatment phases involving dexamethasone and PEG-asparaginase. The study population consist of all children and adolescents between 1 and 17 years with newly diagnosed ALL or lymphoma and treated at one of the four Danish pediatric oncology sites.

Results: The study is ongoing. Results are pending.

Perspectives: Data from the study can contribute to new guidelines for when to monitor blood glucose during treatment and when to start treatment.

Themes: Paediatrics, Cancer
Keywords: acute lymphoblastic leukemia, hyperglycemia, continuous glucose monitoring

Exploring ROCK1 Activation in Invasive NF1-Deficient Glioblastoma

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Glioblastoma (GBM) is a malignant and aggressive brain tumor derived from astrocytes. The overall survival is poor, even with the standard treatment of surgical resection, radiation and TMZ. Neurofibromin (Nf1) loss occurs in 14% of GBM cases, often leading to features resembling epithelial-to-mesenchymal transition. A subgroup of Nf1-deficient tumors exhibits a diffuse morphology, complicating surgical resection. In this project we aim to elucidate the mechanisms underlying the transformation of glioblastoma into the diffuse phenotype seen in Nf1-deficient tumors.

We have established a mouse model of GBM using CRISPR through stereotaxic delivery of AAV particles or primary cell lines to the striatum. Hereby, tumors with deficiencies in Nf1 or Rb1 and Pten, P53 were generated.

Histological examination of NF1-deficient tumors revealed a diffuse morphology compared to Rb1-deficient tumors, which reflects the mesenchymal subtype of human GBM. A screening for 350 kinases activity showed significant differences between Rb1 and Nf1-deficient tumors. Of these, ROCK1 was significantly increased in Nf1 deficient tumors and tumor derived cell lines. ROCK1 is associated with cell migration, and we hypothesize that increased ROCK1 activity could drive phenotypic changes towards the diffuse morphology. To explore the function of ROCK1 in morphological changes, we have generated tumors with loss of ROCK1 using CRISPR in combination with loss of Pten, P53, and Nf1. Preliminary data shows, that loss of ROCK1 in the tumor leads to a more dense morphology. Future work will explore the molecular mechanism of ROCK1 on morphology alterations in the glioma and possible interventions.

Themes: Cancer, Genetic engineering
Keywords: Glioblastoma, Animal Models, CRISPR

Investigation of tumor microenvironment in immunotherapy response in bladder tumors

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BACKGROUND: Immunotherapy is administered to treat both non-muscle-invasive (NMIBC) and muscle-invasive bladder cancer (MIBC), in the form of intravesical instillations of BCG and immune checkpoint inhibitors, respectively. Despite their pervasive role in bladder cancer treatment and initial promising response rates, recent data indicates that the long-term effectiveness of immunotherapeutic drugs falls short of expectations.

OBJECTIVE: The mechanisms of immune activation through immunotherapy are far from fully understood and predictive biomarkers for immunotherapy response are urgently needed. The objective of this project is to utilize novel spatial molecular profiling technologies to explore the immune-cancer cell microenvironment and its potential association with immunotherapy response.

METHODS: Data from two clinically well-annotated cohorts will be analyzed in this study; one with patients diagnosed with NMIBC, treated with BCG instillations, and the other with patients diagnosed with MIBC, treated with neoadjuvant chemotherapy before cystectomy and atezolizumab (anti-PD-L1) upon metastatic relapse.

We will characterize the tumor microenvironment of the two cohorts by high-plex spatial and molecular RNA and protein analysis using the GeoMx Digital Spatial Profiler and single cell spatial proteomics using imaging mass cytometry. A predictive treatment response model will be constructed using integrative data analysis.

PERSPECTIVES: This project will help delineate the biological mechanisms of the immune system for patients suffering from bladder cancer and in this way enhance our understanding of immunotherapy response and pave the way for biomarker-based treatment.

Themes: Cancer, Urology & Nephrology
Keywords: Bladder cancer, Spatial transcriptomics, Immunotherapy

T Cell Recovery after Chemotherapy in Children, Adolescents and young Adults with Acute Myeloid Leukemia

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Background: Intensive myelosuppressive therapy is essential to obtain permanent cure in acute myeloid leukemia (AML). Despite high complete remission (CR) rates of induction therapy leukemic cells may persist and expand into relapse. T cells exert anti-leukemic activity, but current treatment regimens may affect recovery of T cell function. Children mainly recover T cells from thymic output whereas adults maintain T cells by peripheral proliferation. Optimal T cell reconstitution may constitute a pivotal part in avoiding relapse.

Hypotheses & aims: We hypothesize that T cell function is affected by AML therapy, and that optimal T cell reconstitution after AML therapy is age dependent. We will explore the differences in T cell recruitment through thymic output versus peripheral cell expansion after AML therapy according to age, and the association between impaired immune reconstitution and risk of relapse. Further, we will investigate recovery of T cell receptor repertoires after AML therapy compared to age-normalized values in an immunological healthy cohort.

Patients & Methods: Patients between 0-50 years of age diagnosed with de novo AML in CR at the end of chemotherapy are eligible. Blood sampled at monthly intervals from AML patients have already been collected. Sixty-two children and eight adults are included. Immunologically healthy children undergoing orthopedic surgery constitute the control group (n=30).

Thymic output and peripheral T cell expansion after AML therapy is being assessed by T cell receptor excision circles (TRECs) measurements and spectral flow cytometry. T cell receptor repertoires will be investigated by a high-throughput RNA-based multiplex Next Generation Sequencing method.

Preliminary results & perspectives: We observe an age-dependent variation with lower TRECs levels in increasing age for children after chemotherapy.

With this study we aim to uncover the importance of optimal immune function and recovery after AML therapy.

Themes: Paediatrics, Cancer
Keywords: Acute Myeloid Leukemia, Immune Reconstitution, Pediatrics

Using overlapping reads to model sequencing errors enables accurate calling of low-frequency somatic mutations

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Calling rare somatic variants from Next Generation Sequencing (NGS) data is a more challenging task than calling high frequency germline variants. Imprecise calls of rare variants are mainly caused by the low allele frequency that becomes similar to the frequency of artifactual errors. However, all bases produced by NGS sequencing do not have equal error rates. Therefore, enhancing the accuracy of rare somatic variant calling necessitates an accurate estimate of the error rate of a specific base in a specific read. The BetterBaseQualities (BBQ) tool utilizes information from overlapping sequencing reads to estimate sequence context and mutation-type-specific error probabilities.

We tested the effect of the estimated error probabilities on variant detection by analyzing cell-free DNA (cfDNA) sequencing data from individuals with cancer. The error rates of alternative alleles observed in matched tumor biopsy were compared with those not seen in the primary tumor data. In addition, variant calls made based on the improved error probabilities were compared with the variants called with the state-of-the-art tool Mutect2.

We observed lower estimated error probabilities for bases where the alternative alleles are also seen in the primary tumor than for alternative alleles not seen in the tumor. In addition, variants called with BBQ had improved precision compared to variants called with Mutect2.

These results demonstrate that rare somatic variant calling can be improved by estimating base-specific error probabilities with models applying information from overlapping reads and sequence context.

Themes: Bioinformatics, Cancer
Keywords: Bioinformatics, cfDNA, mutation calling

Potentially inappropriate drugs in older patients with acute illness: Preliminary data from a Delphi-process

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Background: Adverse drug events (ADE) cause 10% of all acute hospitalizations in older patients and affect 19% of all older patients during hospital stay.

However, there needs to be a clear consensus as to what constitutes a potential inappropriate prescription (PIP) in older patients with acute illness. In this study, we used a Delphi-technique to establish consensus on the subject.

Methods: The study was conducted as a 3-round Delphi process:

In Round 1, a list of PIPs, obtained from the literature and clinical experience, was presented to an expert panel with doctors from geriatrics, pharmacology and emergency medicine specialities. Each expert would rate their agreement with each PIP on a 5-point Likert Scale from "Strongly disagree" to "Strongly agree". They were also asked for feedback on each PIP and could suggest new PIPs for inclusion.

All PIPs for which consensus had yet to be reached and the suggestions from the panel were presented to the panel in Round 2.

Any PIP that had yet to reach consensus was presented to the panel in the final Round 3.

Results: The panel consisted of 23 experts (10 from geriatrics, 6 from pharmacology, and 7 from emergency medicine).

In Round 1, 70 PIPs were presented and consensus was reached for 53 of them (76%). The remaining 17 PIPs and 62 new suggested by the panel were presented in Round 2. Consensus was reached on 62 (78%), and the remaining 17 were presented to the panel in Round 3.

We hope to have the data from Round 3 by December 2023.

Conclusion: It was possible to reach a consensus among experts on what constitutes a PIP in older patients with acute illness. Our findings can contribute to reducing ADEs in this patient group.

Themes: Pharmacology, Diagnostics & technology
Keywords: Geriatrics, Delphi-process, Emergency medicine

T cell receptor repertoire and diversity are associated with outcome in bladder cancer

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Cancer-specific T cells express receptors (TCRs) specific for cancer neoantigens, and the expansion of these is believed to be an early response to malignancy. Our objective was to characterize the TCR repertoire in patients with bladder cancer (BC) and explore correlations with disease outcome.

We analyzed the TCR repertoire in blood samples from 119 patients with muscle-invasive BC using ultradeep amplicon-based sequencing of the TCR beta chain. Overall T cell fractions were inferred from whole exome sequence data of blood DNA. The T cell subtype composition in tumor and blood was investigated in four patients using the Chromium Single Cell kit from 10X Genomics.

We found that low peripheral TCR diversity was associated with a worse outcome in BC, particularly when combined with a low fraction of circulating T cells. The low-diversity TCR repertoires were characterized by large expanded T cell clones that were persistent over time. We found that these clones were likely cytotoxic T cells with an exhausted phenotype and unlikely cancer-specific. Conversely, the smaller clones were presumably naive T cells.

We suggest that high TCR diversity and high T cell fraction are markers of general immune competence, reflecting the ability to combat cancer and other diseases. Our findings underline the crucial role of the immune system in determining disease outcome and highlight the potential for improving immune health as a promising approach for future treatment and prevention.

Themes: Cancer, Urology & Nephrology
Keywords: Biomarker, Immune Cells, Bladder Cancer

Doxorubicin concentrations in bone tumour relevant tissues after bolus and continuous infusion – a randomized porcine microdialysis study

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Background: Doxorubicin is a widely used chemotherapeutic drug that can be administered intravenously as both a bolus infusion and a continuous infusion. The latter is believed to lower the risk of cardiotoxicity, which is a critical long-term complication in relation to Doxorubicin treatment. The local tissue concentrations of Doxorubicin will be reflected on both treatment efficacy and the toxicity, but very limited information is available. The aim of this study was to measure the concentration of Doxorubicin after continuous and bolus infusion in tumour relevant tissue.

Methods: Sixteen pigs (female, Danish Landrace, mean 77 kg) were randomized into two groups of eight. Both groups received an intravenous infusion of 150 mg Doxorubicin; Group 1 received a bolus infusion (5-15 min), and Group 2 received a continuous infusion (6 h). Prior to infusion, microdialysis catheters were placed intravenously and in 4 bone tumour relevant tissue compartments (cancellous bone, subcutaneous tissue, synovial fluid of the knee joint and muscle tissue). Sampling was done (n=13) over 24 h, and venous blood samples were collected as reference.

Results: No significant variation was found regarding area under the concentration time curve (AUC0-24h) between the two groups, while peak drug concentration (Cmax) was significantly higher in three compartments in Group 1 compared to Group 2. Overall, the unbound tissue concentrations were extremely low with values below 0.20 ug/mL.

Conclusion: The pharmacokinetic profile for Doxorubicin in the investigated tissues is very similar when comparing bolus and 6 h continuous infusion.

Themes: Pharmacology, Cancer
Keywords: Microdialysis, Doxorubicin, Pharmacokinetic

SESSION 26

PEAR1: A potential biomarker for aspirin treatment response in patients with coronary artery disease

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Background: Aspirin is standard therapy to prevent cardiovascular events, yet reduced antiplatelet effect of aspirin has been reported. Limited research suggests that genetic variation in PEAR1, a platelet surface receptor, is associated with platelet activation and aggregation. However, no studies have explored the importance of PEAR1 for the antiplatelet effect of aspirin in patients with chronic coronary syndrome (CCS). The aim of this study is to examine whether a high expression of PEAR1 is associated with reduced antiplatelet effect of aspirin.

Methods: This is an observational cross-sectional study, which will include patients diagnosed with chronic coronary syndrome and in daily treatment with 75 mg aspirin. Upon inclusion, blood samples will be taken once from every patient. Flow cytometry will be used to quantify the expression of PEAR1 on platelets, and the platelet aggregation potential will be measured by using whole blood impedance aggregometry.

Results: The study is at its initial phase and the results are yet to be obtained. Preliminary results will be presented if available.

Perspective: Previous studies have shown that treatment with low-dose aspirin reduces the risk of major cardiovascular events with 20-25% in high-risks patients. Despite this, some researchers suggest that inadequate inhibition of platelet aggregation in vitro may be associated with reduced cardiovascular protection. This study will provide new knowledge and understanding of the interplay between the expression of PEAR1, platelet function and antiplatelet effect of aspirin, which may facilitate improvement of the current secondary prevention strategy in patients with CCS.

Themes: Cardiology, Diagnostics & technology
Keywords: Cardiovascular Disease, Platelet function, Antiplatelet therapy

Using machine learning in early detection of cancer among patients with mental illness

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Late detection of cancer is a key challenge contributing to the inequality in life expectancy of people suffering from severe mental illness compared to the general public. Detection of early signs of cancer in individuals diagnosed with mental illnesses is a complicated matter, as the underlying effects are likely complex and interdependent. Success in identifying early warning signs, therefore, requires sophisticated techniques that are capable of identifying subtle latent factors in large quantities of data. This project proposes to develop and apply state-of-the-art deep learning techniques from the field of Natural Language Processing (NLP) to identify early indicators of cancer among individuals with mental disorders. This will be done using transformer-based model architectures to extract dense, context-dependent representations of patients and detect subtle indicators and complex patterns in electronic health records (EHRs). The dataset for this project consists of EHR data from 130.000 patients from the PSYchiatric clinical outcome prediction (PSYCOP) cohort. If successful, the project allows detection of warning signs of cancer with sufficient precision and accuracy to allow for early detection and identification of at-risk individuals. Detecting early warning signs will enable initiation of treatment in time and improve prognosis, hopefully leading to enhanced life quality and life span among individuals suffering from mental illness.

Themes: Statistics, Diagnostics & technology
Keywords: Machine Learning, Predictive modeling

Pharmacogenomics in Psychiatry: Optimizing identification of high-risk patients for the development of serious cardiac events

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QT prolongation is an important risk factor for malignant arrhythmias and sudden cardiac death. Common psychotropic drugs can be pro-arrhythmic by causing prolonged ventricular repolarization (drug-induced long QT syndrome, diLQTS). This rare but serious complication may contribute to excess mortality in children and adults with mental illness. Due to inter-individual variability in drug response and significant heritability of the QT interval, a pharmacogenomic (PGx) testing tool could help identify patients at high risk of diLQTS. The project aims to reduce morbidity and mortality related to pro-arrhythmic drugs through optimized identification of high-risk patients using PGx in combination with sociodemographic and clinical factors while accounting for interactions between genes, pro-arrhythmic drugs, and concomitant drug use. The project is based on secondary use of existing biobank and register data from Denmark, Estonia, and the UK to increase our understanding of the complexity of cardiac side effects, drug-drug-gene interactions, and genetics' role in psychotropic drug use.

Themes: Omics, Pharmacology
Keywords: pharmacogenomics, personalised medicine, psychotropic drugs

Non-invasive Assessment of Skin Vascularization, Blood Perfusion, and Micro-morphology in Patients with Atopic Dermatitis and Psoriasis

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Background: Atopic dermatitis and psoriasis are chronic skin conditions that significantly impact the physical, psychological, and social well-being of affected individuals. Current techniques for studying dermal microvasculature are limited in scope and invasiveness. Optical coherence tomography (OCT) and laser speckle contrast imaging (LSCI) offer non-invasive, high-resolution alternatives to better understand the microstructural and vascular changes in these skin diseases.

Aim: We aim to evaluate the feasibility of employing OCT and LSCI as non-invasive imaging techniques for patients with atopic dermatitis and psoriasis. Furthermore, it seeks to establish whether quantitative measures of blood perfusion and vascular density correlate with questionnaire outcomes, pain thresholds, and histological findings obtained through biopsy-based assessments.

Methods: This feasibility study involves recruiting 20 atopic dermatitis patients, 20 psoriasis patients, and 20 matched control subjects. The research protocol includes questionnaire assessments, pain threshold tests, OCT imaging, LSCI imaging, and skin biopsies. After the initial assessment, patients will undergo three months of systemic treatment and then undergo a follow-up assessment.

Expected results: This research project aims to advance our understanding of atopic dermatitis and psoriasis, offering potential non-invasive alternatives to invasive biopsy procedures while shedding light on the microstructural and vascular changes in these skin diseases.

Themes: Diagnostics & technology, Paediatrics
Keywords: Dermatology, Optical Coherence Tomography, Laser Speckle Contrast Imaging

Atrioventricular block with pacemaker indication as a marker of transthyretin amyloidosis among elderly patients? – Protocol for ATTRAB-study

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Background: Incidence of transthyretin amyloidosis (approximately 300-400 new patients annually in Denmark) is increasing due to improved diagnostics, better clinical awareness and change in demographics with more elderly inhabitants in the population. However, there is still a considerable diagnostic delay in transthyretin amyloidosis from start of symptoms until the diagnosis is reached. Specifically, up to 15-30% of patients with transthyretin amyloidosis already have an implanted pacemaker before the time of diagnosis.

Therefore, we want to investigate the prevalence and potential clinical markers of transthyretin amyloidosis at the time of pacemaker implantation due to advanced atrioventricular block.

Method: In a prospective, multicentre, observational cohort study, we will investigate 170 patients >65years with advanced atrioventricular block and a requirement of pacemaker treatment for the presence of transthyretin amyloidosis. We will investigate the study cohort with cardiac biomarkers, echocardiography, clinical history of red flags for transthyretin amyloidosis and perform a DPD-scintigraphy to evaluate for transthyretin amyloidosis.

Results: Pending as inclusion are ongoing since start 2023.

Perspective: This study will provide valuable clinical knowledge of the prevalence of transthyretin amyloidosis among patients with pacemaker-requiring new-onset atrioventricular block and the clinical parameters suggestive of transthyretin amyloidosis in the study cohort.

Themes: Cardiology, Diagnostics & technology
Keywords: Amyloidosis, Diagnosis, Heart Failure

Incidence of Non-sustained Ventricular Tachycardia And Arrhythmic Disease Progression In Hypertrophic Cardiomyopathy - Cancelled

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Forty-eight-hours Holter monitoring (HM) is recommended to identify non-sustained ventricular tachycardia (NSVT) in patients with hypertrophic cardiomyopathy (HCM). This study aims to estimate the 48-hours-incidence of NSVT in HCM patients and to analyze arrhythmic disease progression. We retrospectively evaluated HCM patients enrolled in the Registry for Hereditary Cardiovascular Diseases from 2011 to 2019. A total of 145 patients met the inclusions criteria to be a proband with HCM or a relative with hypertrophy ≥13mm. A cross sectional analysis was done in 131 patients with at least one available HM. A follow-up HM was available in 97 patients. Of 145 patients, the mean age was 54±15 years and 98 (68%) were male. The proportion of patients free of NSVT were 66% after 48-hours HM (n=131). Fifteen percent of NSVTs occurred from 36 to 48 hours into the HM. The mean follow-up time between first and latest HM (n=97) was 4.3 (±2.5) years. The proportion of patients free of NSVT was 69% and 63% in the first and latest HM, respectively (p=0.17). There was no difference in number of ventricular cycles or the calculated frequency analyzing the first episode of NSVT in each HM. There was no significant difference in event rates of NSVT between first and latest HM (HR 0.84, 95% CI 0.26-2.70, p=0.77) and no association between age and NSVT (HR 1.03, 95% CI 0.83-1.28, p=0.80). In conclusion, NSVT occurred with an incidence rate of 34% per 48-hours HM. An important part of NSVTs was identified in the last 12 hours of monitoring. The was no significant progression in the incidence rate nor the characteristics of NSVT during follow up. Age had no effect on the incidence of NSVT.

Themes: Cardiology, Diagnostics & technology
Keywords: Hypertrophic cardiomyopathy, Ventricular tachycardia, Monitoring

Vascular pulsatility in the ageing brain

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Increased vascular stiffness and consequently pulsatility increase the risk of developing Alzheimer's disease and several cardiovascular diseases, but the exact pathways are still a mystery. Most of our knowledge on the in-vivo effects of increased stiffness comes from the large vessels, while capillaries are expected to play the most significant role in cognitive decline. Using Laser Speckle Contrast Imaging (LSCI), we investigated how the microvascular pulsatility changes with age in wild-type mice (C57BL/6).

Twelve mice aged 10 (n=5), 35 (n=3), and 57 (n=4) weeks, respectively, were imaged at 5 separate time points, 4 weeks apart. To access the cortical microvessels, we used LSCI in awake-restrained mice with a chronic cranial window over the left middle cerebral artery (MCA) and its branches. After finishing in-vivo experiments, the MCA was isolated, and mounted on a wire myograph and tone was recorded to assess the physiological changes of ageing in the vasculature.

The blood flow and pulsatility index in veins, arteries and parenchyma did not change with age and remained constant throughout the experiment. The pulse-associated relative diameter dilation remained constant in veins, but in arteries, it began to increase after 65 weeks of age; from 0.0986 arb. unit at 65 weeks to 0.1580 arb. unit at 81 weeks (60.2 %, p= 0.0521). These results are supported by the myograph results, indicating an age-related increase in compliance of the MCA.

Themes: Diagnostics & technology, Imaging techniques
Keywords: Blood flow imaging, Animal models/disease models, Medical technology and diagnos

Why do patients develop in-hospital cardiac arrest? A prospective observational study (WHY-IHCA)

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Introduction: In-hospital cardiac arrest (IHCA) is common and carries a poor prognosis. Often, the aetiologies of IHCA are unclear. The objective of this study is to describe the feasibility of a protocolised investigation aiming at describing the aetiologies of IHCA in survivors as well as non-survivors.

Methods: The study is a prospective observational study. Inclusion started on April 1st, 2023, and will continue until February 1st, 2025. A total of 150 patients are expected to be included corresponding to an inclusion rate of 6.8 patients per month. All cases of adult IHCA without an obvious cause are included and will undergo a protocolised investigation consisting of blood laboratory values, echocardiography, and radiographic imaging.

Results: During the first 6 months of inclusion, 44 patients have been included in the study corresponding to an inclusion rate of 7.3 patients per month. Of the 44 patients, 22 are included as non-survivors and 22 are included as survivors. Blood laboratory values were obtained in 15 of 22 non-survivor cases. All non-surviving patients underwent post-mortem radiographic imaging. In surviving patients, blood laboratory values were obtained in all 22 cases. Twenty of 22 patients underwent radiographic imaging, and 19 of 22 patients had an echocardiographic survey performed.

Conclusions: Thus far, the expected inclusion rate for the timely completion of the study is met. The protocolised investigation is relatively feasible; however, there is a significant amount of missing data especially on blood laboratory values in non-surviving patients. This might be addressed by informing and teaching clinicians continuously of their roles in the study.

Themes: Cardiology, Diagnostics & technology
Keywords: Intensive Care Medicine, Anaesthesiology, Cardiac arrest

A user independent denoising method for x-nuclei MRI and MRS

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X-nuclei MRI (also called non-proton MRI) are limited by the intrinsic low signal-to-noise ratio as compared to conventional proton imaging. Clinical translation of x-nuclei examination warrants the need for a robust and versatile tool improving image quality for diagnostic use. In this work, we compare a novel denoising method with fewer inputs (tMPPCA) to the current state-of-the-art denoising method (GL-HOSVD). Denoising approaches were compared on human acquisitions of sodium (23Na) brain scans, deuterium (2H) brain scans, carbon (13C) heart and brain scans, and simulated dynamic hyperpolarized 13C brain scans, with and without additional noise. Noise-removal was quantified by residual distributions, and statistical analyses evaluated the differences in mean-square-error and Bland-Altman analysis to quantify agreement between original and denoised results of noise-added data. GL-HOSVD and tMPPCA showed similar performance for the variety of x-nuclei data analyzed in this work, with tMPPCA removing ~5% more noise on average over GL-HOSVD. The mean ratio between noise-added and denoising reproducibility coefficients of the Bland-Altman analysis when compared to the original are also similar for the two methods with 3.09 ± 1.03 and 2.83 ± 0.79 for GL-HOSVD and tMPPCA, respectively. The strength of tMPPCA lies in the few-input approach, which generalizes well to different data sources. This makes the use of tMPPCA denoising a robust and versatile tool in x-nuclei imaging improvements and the preferred denoising method, which could help facilitate the use of x-nuclei MRI in a clinical setting.

Themes: Imaging techniques, Diagnostics & technology
Keywords: Denoising, MRI, x-nuclei

SESSION 27

Cutting-Edge AI diagnostic Tool for Penile Lesions: Distinguishing Benign from Malignant Cases

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Introduction & objectives: Penile lesions are rare and many doctors are unfamiliar with them. Even amongst professionals, distinguishing between benign and malignant can be challenging.

We aim to develop an AI-based image recognition software to assist health professionals in evaluating penile lesions. The AI will be accessible to healthcare professionals, aiding them in identifying unusual changes, determining biopsy strategies and deciding when referral to an appropriate treatment facility is required.

We expect the study to attain roughly 3,000 pictures before February 2026, and which time a working prototype will be ready. Collection of images and validation are ongoing.

Materials & methods: This is a clinical prospective data collection study conducted at three urological departments at large Danish hospitals. In late 2023, more sites will be included.

After obtaining written consent, digital images are collected securely . These images are then entered into the AI learning platform and retrospectively validated based on histology or clinical course. The morphology recognition application, developed by our collaborator Jacob Elmose Jensen from Cystotech, will be customized for the study's needs. Training the AI will involve collaboration with software engineers and domain experts.

Results: As of October 2024, 7 months into the project, 951 pictures from 140 men have been collected. Of these, 9 men presented with carcinoma, 9 with PeIN, 40 with benign lesions and 72 are normal variants. Ten are awaiting pathology results.

Conclusion: The study is well underway, the setting works well and the prospect of obtaining 3,000 images before February 2026 seems feasible.

Themes: Urology & Nephrology, Cancer
Keywords: AI, Penile lesions, Diagnostics

The Association Between Type 2 Diabetes and Melanoma Stage and Prognosis

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Background and Importance: In individuals with type 2 diabetes, the leading diabetes-related cause of death in high-income countries has transitioned from cardiovascular diseases to cancer. Therefore, more knowledge is needed to assess the impact of diabetes on site-specific cancers.

Aims: This study aims to assess the impact of type 2 diabetes on the prognosis of individuals diagnosed with melanoma, examining parameters such as tumour stage, melanoma recurrence, melanoma-specific mortality, and overall survival.

Methods: A nationwide cohort was conducted, including all melanoma-diagnosed individuals in the Danish Cancer Registry from 2004 to 2019. Diabetes status was determined from prescription records, hospital diagnoses, blood samples, and diabetes-specific podiatrist services. Participants were followed from their melanoma diagnosis, and key outcomes were melanoma stage, mortality, and recurrence. We employed multivariable generalized linear models and Cox proportional hazard regressions in our analyses, adjusting for sex, age, cancer stage, and socioeconomic factors.

Results: Preliminary results show a significant sex difference in the impact of type 2 diabetes on melanoma aggressiveness factors. Furthermore, men with early-stage melanoma and type 2 diabetes were found to have increased melanoma-specific mortality compared to individuals without diabetes.

Significance and Future Perspectives: We aspire that our findings may serve as a foundation for further research and drive alterations in clinical practices, with the ultimate objective of enhancing the individual patient journey for patients with melanoma and comorbid type 2 diabetes.

Themes: Cancer, Endocrinology
Keywords: Melanoma, Type 2 diabetes, Cancer

GreenBladder - Early detection of bladder cancer in residents in Greenland using a urinary biomarker and a mobile cystoscopy unit

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The incidence of bladder cancer (BC) in Greenland is significantly lower than in Denmark. However, a disproportionately high mortality rate indicates a potential underdiagnosis and diagnostic delay of BC in Greenland. This may partly be explained by the limited access to specialized healthcare services and the non-specific symptoms associated with BC. Early detection and treatment of BC are vital, emphasizing the need for novel diagnostic strategies. A proposed alternative to cystoscopy is the utilization of urinary biomarkers.

Objective: This study aims to evaluate the utility of a urinary biomarker as a selection tool for cystoscopy referral in patients exhibiting potential BC symptoms, including hematuria, particularly in areas with limited access to urological services.

Materials and methods: Citizens of Greenland above the age of 18 years referred for cystoscopy are invited to participate in an observational study. A BC-specific urinary biomarker test (Xpert Bladder Cancer Detection) will be performed at the time of cystoscopy at the patient's local health care center or hospital.

Results: By October 2023, 109 patients have been enrolled in the study. While study inclusion is still ongoing, preliminary observations indicate long waiting times for cystoscopy, extending up to several years from referral.

Conclusion: With selected investigations by a sensitive urinary marker, patients with bladder tumors will potentially be selected to earlier diagnosis compared to the current non-selected investigations with the inherent logistic and economical challenges. With this strategy, we aim at improving the current poor prognosis for bladder cancer patients in Greenland.

Themes: Urology & Nephrology, Cancer
Keywords: Bladder Cancer, Urinary Biomarkers, Early cancer detection

Optimizing diagnosis and primary treatment of non-muscle invasive bladder cancer by use of artificial intelligence

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Background: Bladder cancer is the 10th most common cancer type when considering both sexes. In non-muscle-invasive bladder cancer (NMIBC), intravesical recurrence and progression pose a challenge in the management of patients.

In Denmark, approximately 40% of patients with NMIBC experience recurrence within the first year. Missed lesions and incomplete resection are both possible causes for this. Therefore, better identification of tumors and pathology during resection could potentially improve recurrence free survival.

Methods: This study is a prospective randomized controlled trial using a convolutional neural network (CNN) artificial intelligence as a supportive tool for detecting lesions in the bladder. 712 patients suspected of NMIBC will be randomly allocated 1:1 into two groups. The control group will receive standard diagnosis and treatment with conventional transurethral bladder resection (TURB). In the intervention group, a real-time artificial intelligence software will live-track bladder lesions during the primary TURB. All patients will receive standard follow-up regime according to Danish guidelines. After 12 months, recurrence rates in both groups will be analyzed to compare the efficiency of use of the artificial intelligence program with standard care during first TURB.

Aim and hypotheses: We aim to investigate the use of a CNN-based artificial intelligence software, to increase detection efficiency and enhance surgical decision making during the primary TURB. We hypothesize that the CNN-software will increase detection of bladder lesions, thus lowering the annual recurrence and progression rates.

Themes: Urology & Nephrology, Diagnostics & technology
Keywords: Artificial Intelligence, Bladder cancer, Diagnostics

How effective is mammography screening on the reduction of breast cancer mortality among breast cancer survivors and chronically ill.

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Introduction: The Danish breast cancer screening program rely on age-based criteria. However, the risk of breast cancer varies among women, leading to ongoing trials exploring risk-based screening strategies. Unfortunately, these trials overlook the fact that there is no evidence on how well mammography screening reduces breast cancer mortality among women at high risk. We will estimate this reduction among two high risk groups.

Methods: We evaluate the benefits of mammography screening in two subgroups: breast cancer survivors and chronically ill women, using an old method that compare invited/participated survivors in Fyn and Copenhagen to those not invited/not participated survivors in the rest of Denmark (Study 1/2). Additionally, we account for healthy user bias. The new method will be tested by comparing mortality rates between chronically ill participants and non-participants (Study 3).

Preliminary Findings for study 1: The Fyn survivor groups each comprised 1758 invited breast cancer survivors. Of those, 309 survivors died from breast cancer. Control groups, consisting of non-invited survivors in other Danish counties, included 17878 survivors, with 3895 breast cancer deaths. Preliminary results indicate a 17.5% (95%CI: 7%- 26%) reduction in breast cancer mortality among invited survivors in compared to non-invited counterparts.

Discussion: Receiving an invitation to Breast cancer mammography screening results in a significant reduction in breast cancer mortality rates. This might suggest that the current mammography screening program is effective to some degree for survivors. However, it is not as effective as for general population.

Themes: Cancer, Public health
Keywords: Screening, Breast cancer, Risk-based

Cancer recurrence: Detection and diagnostic intervals in Danish general practice

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Background: Cancer recurrence (CR) is frequently detected outside of scheduled follow-up visits. The general practitioner (GP) is presumed to facilitate most of these diagnostic pathways. However, little is known about CR detection in general practice. We aim to examine diagnostic intervals (DIs) and actions taken by the GP for patients presenting symptoms of CR in general practice.

Methods: We conduct a retrospective, national cohort study based on questionnaire data linked to register data at the individual level. Patients diagnosed with CR of melanoma, lung, breast, colorectal, bladder, ovarian and endometrial cancer between Jan 2022 and May 2024 are included. Patients are identified consecutively using validated, register-based algorithms. The affiliated GP is invited to complete a questionnaire on the diagnostic pathway. Danish health registers provide information on CR diagnosis date, general practice affiliation, comorbidity, education, sex, and age.

Results: The proportion of diagnostic pathways initiated by the GP was 33%, hospital-based follow-up was 44%, and other routes were 23%. The median DI was 42 days when the GP initiated the diagnostic pathway. The DI was 26 days longer (95% CI: 15 to 36) at the median if the GP did not initiate the diagnostic pathway. At the 90th percentile the DI was 35 days shorter (95%CI: -45 to -24) if the diagnostic pathway was initiated outside of general practice.

Conclusions: One third of diagnostic pathways for CR was initiated by the GP between scheduled follow-up visits or after ended follow-up. At median the CR diagnosis was delayed almost four weeks if the GP did not initiate the diagnostic pathway.

Themes: Cancer, Public health
Keywords: Cancer recurrence, General practice, Detection

Record-based frailty and Days Alive and Out of Hospital within 90 days after radical cystectomy in older patients with bladder cancer: Preliminary results from a retrospective cohort study

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Objective: The aim of this study is to examine the association between frailty and Days Alive and Out of Hospital (DAOH) 90 days postoperatively, in older patients with muscle-invasive bladder cancer undergoing radical cystectomy (RC). DAOH is a valid marker for cumulative morbidity and mortality after RC. Frailty increases risk of adverse events after RC, and comorbidity is an independent risk factor for reduced DAOH, but the association between frailty and DAOH following RC has not yet been investigated.

Materials and methods: Patients aged ≥65 years with MIBC and undergoing RC in 2018-19 at Aarhus University Hospital were rated according to a level of frailty by the record-based Multidimensional Prognostic Index (r-MPI), a validated retrospective frailty assessment tool, using data from electronic patient records. DAOH and Length Of hospital Stay (LOS) were dichotomized according to the median. The current data are preliminary, unadjusted results.

Results: In total, 95 patients were assessed. 60 (63%) patients were categorized as non-frail, 35 (37%) as frail. Mean age was 77 years (SD±5.3) for the frail group and 74 years (SD±5.6) for the non-frail group (p=0.01). 71% were males. Median overall DAOH was 81 days (IQR 75-83), and median LOS 7 days (IQR 7-9). Patients who were frail had a significantly increased risk of lower DAOH (RR 2.2 (95% CI 1.4-3.4), p<0.01) and higher LOS (RR 1.2 (95% CI 1.01-1.51), p=0.04) compared to non-frail.

Conclusion: Preliminary results indicate that the level of frailty might be associated with reduced DAOH in older patients undergoing RC. Thus, modification of preoperative frailty could potentially increase DAOH.

Themes: Urology & Nephrology, Cancer
Keywords: Frailty, Bladder Cancer

Prehabilitation in prostate cancer patients prior to nerve sparring radical prostatectomy

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Background: Localized prostate cancer is commonly treated with radical prostatectomy (RP). Following surgery, adverse effects as urinary incontinence and erectile dysfunction are common. Literature shows the benefit of interventions prior to surgery to enhance treatment success, known as prehabilitation (PREHAB).

Aim: To examine whether a four-week PREHAB intervention program consisting of physical exercise, pelvic floor exercise, a diet intervention and stress management is feasible in prostate cancer patients prior to RP.

A secondary purpose is to collect preliminary data on patient-reported outcomes, physical performance and urinary incontinence.

Design: Feasibility randomized clinical trial.

Methods: The MRC-Framework for developing and evaluating complex interventions was used for development of the PREHAB program.

A total of 40 patients referred to RP, are randomized to the intervention or the control group. The control group receives standard intervention. The intervention group receives PREHAB.

Outcome: The primary outcome is to determine adherence, recruitment-rate, safety and adverse events.

Statistical analysis: Descriptive statistics will be used to describe the sample. Measures in outcome efficacy will be measured in the difference between groups and a power calculation of the final RCT study will be performed.

Results: We have so far recruited 30 out of 40 in total.

Perspective: RP is highly effective looking at survival. Side effects can be severe, and negatively affect the patient's quality of life. PREHAB is associated with fewer side effects, increased coping with the side effects, earlier discharge from hospital and improved long-term health condition.

Themes: Cancer, Rehabilitation
Keywords: Prehabilitation, Prostate cancer, Complex intervention

Electronic patient reported outcome measures (ePROM) collected through smartphone text messages.

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Background: The use of patient reported outcome measures (PROM) for measuring healthcare data is rapidly increasing and might be the golden standard within the next decade. The use of PROM in treatment of cancer patients has proven to increase quality of life and satisfaction with care and survival.

Electronic PROM (ePROM) has proven to be superior to paper diaries in some cases. A new emerging electronic platform for ePROM is text messages.

Objectives: To assess the feasibility of using smartphone text messaging to collect ePROM in a large-scale multicenter, multinational randomized clinical trial.

Methods: Participants in the North-REG Dwell Time study receives daily questionnaires during the study regarding side effects (SE) caused by BCG treatment. When activated an email containing the patient's phone number are sent to an external company that then converts the email to a text message. The text messages include a link to a unique questionnaire. When answered the answers are returned directly back. In total, a participant can receive a total of 98 text messages over a one-year period. The text messages include both daily questionnaires regarding SE and 4 quality of life (QoL) questionnaires.

Results: In total, 13,504 text messages were sent to 169 study patient between February 2021 and July 2023. We found an overall response rate at 95% when smartphone text messaging was used to collect ePROM. Daily questionnaires regarding SE and QoL questionnaires had a response rate at 96% and 87%, respectively. There was no significant difference in received text messages or response rate, between the intervention and control group.

Conclusion: This relatively new way of collecting ePROM has proven to be feasible. It was associated with an extremely high response rate. Moreover, it can be regarded as effective for both participants and healthcare professionals as answers are entered "live" and directly into a database with low risk of input errors, recall bias or underreporting of SE.

Themes: Urology & Nephrology, Cancer
Keywords: ePROM, Text messages, Bladder cancer

SESSION 28

Can Swede score improve the diagnostic accuracy of cervical cancer and precancer?

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Introduction: Colposcopy and cervical biopsies are gold standard to detect cervical cancer and precancer. Studies have shown considerable intra- and interobserver variability in colposcopy, even among experienced colposcopists. A standardized colposcopic scoring tool, Swede score, has been developed to find or exclude high grade lesions in the histopathology of cervical intraepithelial neoplasia grad 2 or higher (CIN2+). The aim is to explore, whether the implementation of Swede score can improve diagnostic accuracy of cervical cancer and precancer.

Materials and methods: A prospective multicentre, non-randomized intervention study with five public colposcopy clinics and two private colposcopy clinics in Central Region Denmark and Southern Region Denmark. Enrolment began in May 2023. Colposcopies with Swede score (intervention clinics) will be compared with colposcopies without Swede score (reference clinics) in detecting CIN2+. Characteristics of the women will be collected from medical records. From the Danish Pathology Databank, we will collect data on previous screening history, cervical biopsies and/or cervical excisions. The sensitivity, specificity, the negative and positive predictive value of the Swede score for CIN2+ detection will be estimated and compared with reference clinics. ROC curves will be made.

Results: Not available.

Conclusion: The study will provide important knowledge on the value of using a standardized scoring tool for colposcopic examination in Denmark, potentially improving the detection of cervical cancer and precancer. Hopefully, we can improve the diagnostic accuracy, and hereby prevent cervical cancer and precancer in Danish women.

Themes: Gynecology and obstetrics, Cancer
Keywords: Cervical cancer and precancer, Diagnostics

Unlocking Precision Surgery: A Randomized Controlled Trial Investigating Selective Nerve Root Block's Diagnostic Potential in Lumbar Degenerative Disease

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Background: Radiculopathy is a prevalent painful condition. Affection of the lower extremities is common with an incidence of approx. 5 per 1000 person years. It is often the result of a herniated disc or stenosis, causing mechanical compression. It is the most common indication for spine surgery with an estimated annual cost for surgery in the US of 15 billion USD. Unfortunately, 20-25% do not achieve the minimal clinical important difference in pain reduction post-operatively.

Method: The study is a prospective multicenter randomized controlled trial evaluating the effect of adding the outcome of a selective nerve root block (SNRB) to the surgical decision making. Patients will either be offered standard of care or standard of care + SNRB. Patients referred to our departments with radiculopathy and radiological evidence of root compression are eligible for inclusion.

Results: Patient recruitment commenced October 2023, and our goal is to include 160 patients over the next 2 years; 80 undergoing surgery with prior SNRB and 80 without. Study sites are Aarhus University Hospital, and Private Hospital Mølholm.

Conclusion: SNRB's are currently used by clinicians. However, the existing evidence base is limited, and it remains uncertain whether patients selected for surgery with the aid of SNRB experience different outcomes compared to those receiving standard care. If the SNRB group demonstrates superior outcomes, it may warrant consideration of incorporating SNRB into the diagnostic evaluation for all patients with nerve root compression. On the other hand, if results are suboptimal, limiting the use of SNRB would spare future patients from an unnecessary procedure.

Themes: Surgery, Diagnostics & technology
Keywords: Spine, Surgery, Diagnostics

Pneumothorax is common in patients with emphysema treated with endobronchial valves in the upper lobes and results in prolonged hospital admission and more complications

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Background: Endobronchial valve treatment has emerged as a treatment option for a selected group of patients with chronic obstructive pulmonary disease. Pneumothorax is the most common and serious adverse event of this treatment. The aim is to compare pre-operative characteristics of patients with and without postoperative pneumothorax, and to describe the immediate post-operative consequences of pneumothorax.

Method: Patients treated with endobronchial valves between august 2021-23 were prospectively included. Information on demographics, BMI, pulmonary function, MRC and complications were collected from the medical records.

Results: A total of 49 patients were included. The pneumothorax rate was 10/49 corresponding to 20.8%. The median time to drain treatment were 2.6 hours (range 1-50) and median drain treatment duration were 13 days (range 8-63). Patients with pneumothorax had significantly higher MRC (4.3 vs. 3.7, p = 0.0188) and BODE-index (6.7 vs. 5.5, p = 0.0092), while there was no difference in FEV1, FVC, TLC, RV, BMI or age. The risk of pneumothorax after upper lobe treatment were 39.1% and significantly higher compared to 3.85% in the lower lobes, risk ratio 10.17 (CI 1.39-74.3, p = 0.003). Median duration of admission in patients with pneumothorax was 13 days compared to 2 days without pneumothorax (p= 0.00). The risk of hospital-acquired pneumonia was significantly higher in the pneumothorax group with 70% compared to 23% (p 0.008)

Conclusion: Pneumothorax is more commonly experienced in patients with a high symptom burden or if valves are placed in the upper lobes and causes prolonged hospital admission and risk of hospital-acquired pneumonia.

Themes: Surgery, Diagnostics & technology
Keywords: Emphysema, Pneumothorax, Endobronchial Valves

A highly responsive bioassay for quantification of glucocorticoids

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Measurement of total cortisol levels in serum samples is currently based on immunoassays or liquid chromatography-mass spectrometry (LC-MS/MS). However, measurement of bioavailable cortisol is laborious, unreliable and inconvenient for the patient. Therefore, a new versatile assay with the ability to measure both total and bioavailable cortisol from serum represents an important supplement to the current methods. We have generated a cell based glucocorticoid reporter assay (HEK293F-GRE). The assay was validated for cell line stability, accuracy by dilution linearity, precision, repeatability, reproducibility, and specificity. Additionally, the assay was tested for measuring both total and bioavailable cortisol in serum. The assay showed linearity at five dilution levels with R2 = 0.98 and an accuracy between 0.8-1.2. Precision (CV <20 %) was validated down to 3-6 nM dexamethasone and estimation of total cortisol concentration was comparable to cortisol immunoassay and LC-MS/MS in most serum samples. Moreover, the assay estimated the bioavailable cortisol fraction in serum samples to a level that agreed with the literature. The HEK293F-GRE assay holds the potential to be a complementary method for estimating cortisol in clinical practice. The ability to quantify bioavailable cortisol directly from serum samples is alluring and provides an opportunity for monitored and personal dose regimens of exogenous glucocorticoids.

Themes: Diagnostics & technology, Endocrinology
Keywords: Glucocorticoids, Luminescence assays

Impact of elective target and nodal boost on acute gastrointestinal toxicity in cervical cancer: EMBRACE-II findings

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Purpose: To assess acute gastrointestinal (GI) toxicity incidence in locally advanced cervical cancer (LACC) patients and association with external beam radiotherapy (EBRT)

nodal boosting and elective target volume selections in the prospective international EMBRACE-II study.

Methods: In EMBRACE-II (2016-2021) patients received EBRT, chemotherapy, and MRI-guided brachytherapy. EBRT included a prescription of 45Gy/25 fractions to elective targets and a recommendation of 55-65Gy for positive nodes. Patients with baseline (BM), 4th week of treatment (RT4W) or end of treatment (RTEND) GI toxicity (CTCAE v3.0) assessments were included. To evaluate the impact of EBRT, patients were grouped based on lymph node (LN) boosting and elective irradiation.

Results: Among 1302 eligible patients, GI toxicity peaked at RT4W and declined at 3 months follow-up (3M). At RT4W, 15.5%, 6.4% and 2.4% of patients experienced grade 2 or worse (G≥2) diarrhea, abdominal pain/cramping and proctitis, respectively, while at 3M incidences were 2.5%, 3.3%, and 0.3%. Node negative (Group1) and node positive (N1) up to two boosted pelvic nodes patients (Group2) had comparable GI toxicity. Pelvic+para-aortic (PAN) elective field in N1 patients without boosted para-aortic nodes (Group3) led to similar or slightly higher GI toxicity. Pelvic+PAN elective irradiation combined with para-aortic node boosting (Group4) was associated with higher GI toxicity, but tolerable with rare severe events (G≥3) compared to other groups.

Conclusion: Acute GI toxicity was higher at RT4W and decreased at 3M, with rare G≥3. Pelvic+PAN elective irradiation with para-aortic node boosting was associated with a higher GI toxicity.

Themes: Cancer, Gynecology and obstetrics
Keywords: AcuteGastrointestinal Toxicity, Cervical Cancer, EMBRACE-II Study

Effects of Percutaneous Transluminal Renal Angioplasty for Atherosclerotic Renal Artery Stenosis in High-Risk Patients – A Danish Nationwide, Double-blinded, Randomized and Sham-controlled Study. (The DAN-PTRAII trial)

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Background: Atherosclerotic renal artery stenosis (ARAS) can result in atherosclerotic renovascular disease (ARVD) characterized by resistant hypertension, ischaemic nephropathy and episodes of heart failure/flash pulmonary oedema. Despite optimal medical therapy, ARVD carries a significant cardiovascular risk with an expected poor outcome. Percutaneous transluminal renal angioplasty (PTRA) with stent placement provides an alternative treatment option to medical therapy alone.

PTRA is currently controversial because randomized trials have not demonstrated any clear advantage of PTRA over optimal medical therapy. However, the randomized trials have been criticized for their exclusion of high-risk patients, potentially denying those who might have derived the most substantial benefits.

Aim: To investigate the effects of PTRA compared with optimal medical therapy alone for selected high-risk patients with severe ARAS.

Methods: DAN-PTRAII is a Danish nationwide, double-blinded, randomized and sham-controlled trial. We aim to randomize 80 patients receiving optimal medical therapy to either PTRA or sham with a follow-up period of 6 months.

To be eligible, patients must exhibit at least one clinical ARVD manifestation and have a renal artery stenosis of minimum 70%.

The primary outcome is changes in systolic blood pressure based on a nurse administered 24-hour ambulatory blood pressure monitoring at baseline and 6 months after PTRA/sham.

Results: Study completion is expected in 2025/2026.

Perspective: The proposed study is powered to demonstrate the superiority of PTRA over medical treatment alone, with the potential to profoundly shape our approach to treating patients with ARVD.

Themes: Urology & Nephrology, Surgery
Keywords: Renovascular disease

Management of Unilateral Craniofacial Microsomia with Orthopedic Functional Appliances: A systematic literature review.

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Introduction: The study aimed to summarise current knowledge regarding use of orthopedic functional appliances (OFA) in managing unilateral craniofacial microsomia (UCM).

Methods: Eligibility criteria review: 1)Assessing OFA as a stand-alone treatment and 2)OFA in combination during or after MDO. The PICO (population, intervention, comparison, and outcome) format formulated clinical questions with defined inclusion and exclusion criteria. No limitations concerning language and publication year applied.

Information sources:Literature search of Medline, Scopus, Embase, Cochrane Central Register of Controlled Trials, Web of Science databases without restrictions up to 30 September 2022. Risk of bias was assessed.

Syntheses of results: According to Cochrane and PRISMA guidelines,2 independent authors conducted data extraction. The level of evidence for included articles was evaluated based on Oxford evidence-based medicine database. Due to heterogeneity of studies and insufficient data for statistical pooling, meta-analysis not feasible. Therefore, results synthesised narratively.

Results: A total of 437 articles were retrieved. Of these,9 met inclusion criteria: 5 assessing OFA and 4 assessing OFA during or after MDO.

Discussion: Limited evidence to suggest, stand-alone and combination treatment with OFA is beneficial for treating mild-to-moderate UCM-related dentofacial deformities in shortterm. No studies assessed burden of care.

Conclusion: In management of UCM, there is insufficient evidence supporting efficacy of OFA as standalone treatment or when combined with MDO. Additionally, there is lack of evidence regarding treatment protocols and effect on condyles and TMJ.

Themes: Diagnostics & technology, Dentistry
Keywords: craniofacial syndromes, Rare diseases, functional appliances

Femoral arterial cannulation and invasive blood pressure measurement in out-of-hospital cardiac arrest – a feasibility study

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Background: Prolonged out-of-hospital cardiac arrest (OHCA) has a dismal prognosis. Cardiopulmonary resuscitation (CPR) is normally delivered as an algorithmic, same-for-all treatment.

Chest compressions may improve coronary perfusion pressures thereby possibly restoring cardiac activity. Rate, depth, and location of chest compressions can be optimized using intra-arrest invasive blood pressure (IBP) as a target.

The aim of this study is to assess the feasibility of femoral arterial cannulation (FAC) and establishing IBP during CPR.

Methods: The study is conducted in the Central Denmark Region's Prehospital Emergency Medical Services' (EMS) physician-staffed rapid response vehicles.

Physicians experienced in ultrasound-guided vascular access can participate.

Inclusion criteria:

1) Adult, non-traumatic cardiac arrest
2) CPR indicated beyond initial drug administration and airway management OR
3) Return of spontaneous circulation in unconscious patients

Exclusion criteria: Previous study participation and do-not resuscitate orders.

The personnel undergo systematic training for FAC during CPR.

The primary outcome is the rate of FAC in eligible patients.

FAC is considered feasible if attempted in 75% of eligible patients and completed in 75% of attempts. The study period is July 1st, 2023, to June 30th, 2024.

Physicians', patients' and FAC attempt details are retrieved from medical records and monitor data. The study was approved by the EMS board of directors as a quality development project.

Perspectives: Optimized and individualized CPR may increase cardiac arrest outcomes in patients not otherwise salvageable. This feasibility-study may enable the EMS to use IBP-guided CPR in prolonged OHCA.

Themes: Diagnostics & technology, Health Education
Keywords: cardiac arrest, femoral arterial cannulation, invasive blood pressure

Exploring Mechanisms Behind Thrombosis in Systemic Lupus Erythematosus

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Objective: This comprehensive review seeks to survey existing literature concerning systemic lupus erythematosus (SLE)-related thrombosis risk mechanisms within six pro-coagulable categories: autoantibodies (including antiphospholipid antibodies (aPL)), the complement system, platelets, the endothelium, the coagulation system, and fibrinolysis. Patients with SLE face an approximately 50% thrombosis risk after diagnosis, However, the underlying mechanisms are intricate, and anticoagulation recommendations are lacking.

Methods: The review was conducted on the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statements. PubMed and Embase were searched without time restrictions to identify studies evaluating mechanisms of thrombosis based on the six mentioned pro-coagulable categories in SLE.

Results: Thirty-one studies were included. Thirty studies employed in vitro investigations utilizing a case-control design, and one animal study was identified. Autoantibodies (mainly aPL) were the subject of investigation in 80% of studies. Ten studies identified cross reactivity between aPL and other SLE autoantibodies. There is a paucity of studies exploring the impact of anti-inflammatory or anti-thrombotic treatments within the investigated mechanisms.

Conclusions: The thrombosis risk mechanisms mediated by aPL in SLE are well-documented. These mechanisms may also be shared with other autoantibodies in SLE, potentially explaining the increased thrombosis risk observed in aPL-negative SLE patients. Further research is warranted to elucidate the effects of different treatments on thrombosis mechanisms in SLE.

Themes: Immune diseases, Diagnostics & technology
Keywords: Autoimmunity, Systemic Lupus Erythematosus, Thromboembolism

Evaluation of transglutaminase 2 inhibition in fibrotic human precision cut kidney slices

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Chronic kidney disease is characterized by progressive fibrosis which is not directly targeted by current treatment strategies. Transglutaminase 2 (TG2) is involved in fibrotic processes such as excess matrix deposition. Studies of TG2 inhibition in animal models have demonstrated antifibrotic effects of pharmacological TG2 inhibition, but data in human tissue is lacking. We investigated the antifibrotic effect of TG2 inhibition in a model of human kidney slices (HKS) exposed to TGF . HKS from 11 patients were unstimulated or stimulated with TGF (10 ng/ml) for 48 hours in the presence of the TG2 inhibitors LDN27219 or Z-DON. ATP concentration measurements were used to assess tissue viability. mRNA and protein expression of collagen 1α1 and 3α1, fibronectin, α-smooth muscle actin (αSMA) and TG2 were assessed. TG2 activity was slides were stained with picrosirius red. Paired t-test against the TGF control was used. TG2 activity was decreased with the inhibitors even though TG2 protein expression remained unchanged. Neither LDN27219 nor Z-DON prevented mRNA upregulation of fibronectin and collagen 1α1, but LDN27219 decreased mRNA expression of αSMA compared to the TGF control. However, TGF did not affect the fibrotic markers at a protein level and no increased collagen deposition was detected. Although TG2 inhibition had no effect on mRNA expression its involvement in protein expression remains to be studied in a model with a fibrotic setting. αSMA mRNA downregulation with the TG2 inhibitor LDN27219 confirms a role of TG2 in myofibroblasts formation. The HKS model holds promise for developing antifibrotic treatments that act through mRNA degradation pathways.

Themes: Pharmacology, Urology & Nephrology
Keywords: Kidney, Fibrosis, Transglutaminase 2

SESSION 29

Feasibility of Assessing the Abnormal Paediatric Airway using Rotational Optical Coherence Tomography - The OCT Air Study

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Background: Abnormalities in the paediatric airway are usually diagnosed by a computerized tomography (CT)-scan and diagnostic dynamic bronchoscopies (DDB). However, these methods have several limitations in the airway; CT-scans use a high dose of ionizing radiation, which generally should be avoided in children. Additionally, the CT-output is not dynamic, thus compromising the output due to the impact of the respiratory motion on the airway's format and volume. Even though the DDB output is dynamic, it is not quantifiable, creating a risk of interobserver variability when grading stenoses.

This create a demand for an alternative measuring method that is both quantifiable and with the ability to obtain dynamic cross-sectional images of the airway.

The catheter-based methods Optical Coherence Tomography (OCT) and Optical Frequency Domain Imaging (OFDI) can obtain dynamic cross-sectional images by using light close to the infrared range. The methods are already implemented within other medical fields.

Aim: To investigate whether OCT/OFDI are feasible methods regarding diagnosing and assessing the diseased paediatric airway.

Methods: OCT/OFDI of the airway was performed on nine paediatric subjects in relation to DDB due to severe respiratory symptoms. The obtained data was subsequently analysed using the analysis software QCU-CMS (Leiden University, NL), before data was compared to the DDB- and CT-output.

Results: OCT/OFDI show promising results as a diagnostic tool in the paediatric airway. The results of the study align with prior research in cardiology and ophthalmology, demonstrating that the methods can enhance procedural outcomes by improving accuracy of measurements.

Themes: Paediatrics, Imaging techniques
Keywords: Airway Malformations, OCT/OFDI, Feasibility

The effect of methylphenidate for giggle incontinence in children

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Introduction: Giggle incontinence (GI) is a rare form of urinary incontinence that occurs during or immediately after laughing due to involuntary and complete bladder emptying. Few studies in the literature report that methylphenidate can be effective in treatment of this condition.

Objective: The aim of this study is to characterize children with GI and evaluate their response to methylphenidate, as well as describe treatment duration, dosage of methylphenidate, relapse rates after discontinuation of medication, and side effects.

Methods: Medical records and 48-h frequency-volume charts from children treated with methylphenidate for GI in the period January 2011–July 2021 were retrospectively analyzed.

Results: Eighteen children were diagnosed with GI and fulfilled inclusion criteria. Fifteen patients were included in analysis, as 3 out of 18 children decided not to take the methylphenidate that was prescribed. In total, 14 out of the 15 GI patients treated with methylphenidate experienced clinical effect. All patients included in the study had methylphenidate prescribed in a dose range

of 5–20 mg daily. Treatment duration ranged from 30 to 1001 days, with a median of 152 days (IQR 114, 243.5). Ten children experienced complete response and two of those reported symptom relapse after discontinuation of the methylphenidate. Only mild and short-lasting side effects were reported by two patients.

Discussion: Our study demonstrates that methylphenidate is an effective treatment in children diagnosed with GI. Side effects are mild and uncommon.

Themes: Paediatrics, Urology & Nephrology
Keywords: Giggle incontinence, Methylphenidate, Urinary incontinence

Lung Volumetry In Fetuses With Transposition Of The Great Arteries

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Fetuses and children with complex congenital heart defects (CHD) are at risk of smaller brain volumes, likely because of the altered distribution of oxygenated blood during fetal life. Knowledge about growth of other organs during fetal life is limited. Few studies suggest that CHD with restricted pulmonary blood flow could result in decreased fetal lung volumes. No studies have, to our knowledge, reported organ volumes in fetuses with CHD that supply normal or higher amounts of oxygen and blood to the pulmonary circulation. We examined the organ volumes in fetuses with transposition of the great arteries (TGA) compared to healthy fetuses using fetal magnetic resonance imaging (MRI).

Eleven fetuses with TGA, without other known diseases or chromosomal abnormalities, and 22 healthy fetuses were scanned 1-3 times during pregnancy at gestational age 27 through 38 weeks. The MRI scans were conducted on a 1.5 Tesla Siemens scanner with a 14-17 second scan time, a slice thickness of 2mm, and a voxel size of 0.8x0.8x2.0mm^3. A blinded observer (EK) measured total intracranial-, lung-, liver-, and kidney volumes and compared the measurements from those with and without TGA using differences in mean volume, regression modeling including estimated fetal weight (EFW), and sex.

Preliminary data indicates no significant difference in lung volumes through gestational ages 27 to 38 weeks between fetuses with and without TGA after adjusting for EFW and sex. Mean lung volume was 99.7cm^3, 95% Confidence interval (CI): [83;116]cm^3 and 93.7 cm^3, 95%CI: [83;105]cm^3 for fetuses with and without TGA, respectively. Ongoing data analysis with full results is expected to be presented on the PhD day.

Themes: Cardiology, Paediatrics
Keywords: Congenital heart defect, Fetal organ growth

MYELODYSPLASIA-RELATED CYTOGENETIC ABNORMALITES IN CHILDHOOD ACUTE MYELOID LEUKEMIA – A 20-YEAR I-BFM-AML COLLABORATIVE DATABASE STUDY

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Background: The leukemogenesis of childhood acute myeloid leukemia (AML) with myelodysplasia-related cytogenetic abnormalities is unknown. Childhood AML harbor cytogenetic aberrations related to myelodysplastic syndrome (MDS). Monosomy 7 occurs in 25-40% childhood MDS and <5% of childhood AML. CK occurs in 15-20% of childhood MDS and 15% of childhood AML. Childhood AML may have developed from antecedent MDS.

Aim: Our aim is to describe the AML with myelodysplasia-related cytogenetic abnormalities (AML-MDSk) in childhood at diagnosis.

Methods: Approximately, 1.000 children within the I-BFM-AML diagnosed with AML-MDSk between 2000-2022 are eligible for inclusion. Characteristics including leukemic blasts in peripheral blood (PB) and bone marrow (BM), white blood cell count (WBC), and FAB classification at diagnosis are reported. CK is defined as at least three unrelated cytogenetic abnormalities.

Results: Thirty-six children were included. Preliminary results show a median age at diagnosis of 3 years (range: 0-18). Three children had a history of prolonged cytopenia prior to diagnosis. At diagnosis, median blasts in PB and BM were 32% (range: 0-100%) and 62% (range: 13-100%), respectively and median WBC was 14 x 109/L (range: 0.9 – 308 x 109/L). FAB M7 (n=12) and FAB M5 (n=6) were the most frequent morphological subtypes. Trisomy 8 was the most frequent numerical cytogenetic abnormality (n=9). Monosomy 7 was present in 3 children. CK was present in 21 children.

Conclusion: Our study is expected to provide insight into whether AML-MDSk constitutes a distinct subgroup of AML or represents MDS evolving to a higher blast count.

Themes: Paediatrics, Cancer
Keywords: Acute Myeloid Leukemia, Clinical Characteristics, Myelodysplastic syndrome

Atopic dermatitis in childhood and subsequent pubertal development: A nationwide cohort study

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Background: Although atopic dermatitis could delay pubertal development through several mechanisms, empirical evidence is still lacking.

Objective: To investigate the association between atopic dermatitis and pubertal development.

Methods: The Puberty Cohort, a sub-cohort within the Danish National Birth Cohort, consists of children born between 2000–2003. Mothers provided self-reported information on doctor-diagnosed atopic dermatitis when the children were six months, 18 months, and seven years old. The National Patient Registry identified hospital-diagnosed atopic dermatitis. From 11 years, the children reported half-yearly information on pubertal development. We estimated the mean age difference in months at attaining Tanner stages 1–5 and the development of axillary hair, acne, first ejaculation, voice break, and age at menarche using an interval-censored regression model.

Results: In total, 15,538 children were included, 22 % had self-reported doctor-diagnosed atopic dermatitis, and 0.3 % had hospital-diagnosed atopic dermatitis. Boys but not girls with hospital-diagnosed atopic dermatitis tended to have later pubertal development, with the average difference in age at attaining all puberty milestones being 6 months (95 % confidence intervals: -3; 14). No association was found for girls or boys with self-reported doctor-diagnosed atopic dermatitis.

Conclusion: Our study suggests that boys with hospital-diagnosed atopic dermatitis had later pubertal development than their unaffected peers, although the results were imprecise, with confidence intervals crossing the null.

Themes: Epidemiology, Paediatrics
Keywords: Atopic dermatitis, Puberty, Cohort study

NURSING INTERVENTIONS FOR PEDIATRIC PATIENTS WITH CANCER AND THEIR FAMILIES: A SCOPING REVIEW

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Objective: The objective was to develop a comprehensive overview of the nursing interventions available for pediatric oncology patients and their family members, outline the interventions characteristics, and identify potential knowledge gaps.

Methods: This review was conducted in accordance with the JBI guidelines. Citations was retrieved in the databases Scopus, PubMed, CINAHL, PsycINFO, and Embase following inclusion criteria: Peer-reviewed studies written in English, Danish, Norwegian, or Swedish from year 2000, refer to pediatric patients with cancer, and/or family members of a pediatric patient with cancer, who have received non-pharmacological and non-procedural nursing interventions provided by a pediatric oncology hospital service. The identified studies were screened based on title and abstract, as well as full text by 2 independent reviewers. Critical appraisal was done using the Mixed Methods Appraisal Tool.

Results: Out of 2762 references, 26 studies meet the inclusions criteria comprising 24 unique nursing interventions. 88,5 % was published from 2013 and onward, reflecting the rapidly changing landscape within pediatric oncology treatment. 35,6 % was qualitative, 57,7 % was quantitative and 7,7 % was mixed method. Intervention content, components, timing and delivery mode varied widely. 61,5 % of the interventions was targeted at parents and mothers were highly overrepresented (66,4 %). Most interventions had an educational focus provided in the diagnostic phase and only few had a family-centered focus.

Conclusion: There is a clear need for interventions with a genuine family-centered focus.

There is a great gap in reporting the characteristics of the interventions components, timing and delivery.

Themes: Paediatrics, Qualitative research
Keywords: Childhood cancer, Nursing interventions, Scoping Review

A complex couplet care intervention: Effects on length of stay, skin-to-skin contact, breast stimulation and wellbeing among infants and their parents in a neonatal intensive care unit – a quasi-experimental trial

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Background: Zero separation between mother and infant after birth is related to positive health outcomes, however it is not common practice when both mother and infant are sick. Sick mother-infant dyads are separated due to a division of medical specialties into neonatal – and maternal care. The implementation of couplet care is becoming increasingly common, but little is known about the effect of this new practice, where both mother and infant are admitted together and jointly card for.

Objective: To evaluate the effect of a couplet care intervention based on family nursing care on infant and maternal length of stay, skin-to-skin contact, breast stimulation and wellbeing among infants and their parents in a neonatal intensive care unit.

Methods: This study is a non-blinded quasi-experimental pretest – posttest trial with two groups of families with a sick mother and infant. The intervention group (n = 232) receives couplet care defined as both mother and infant are admitted in one unit and jointly cared for by neonatal nurses. In contrast, control group families (n = 232) receive usual care defined as current practice where mother and infant are separated and admitted into two units. Comparison of intervention and control group will be done by linear regression, chi-squared test and by logistic regression.

Implication for practice: This study examines the effect of a couplet care intervention and whether it may improve health and wellbeing among infants and their parents. The results may inform future models of care that best support and enhance family outcomes as well as recommendation of implementing couplet care in other neonatal intensive care units

Themes: Paediatrics, Gynecology and obstetrics
Keywords: Couplet care, Complex intervention, Quasi experimental

ALL-STAR Lungs: Late pulmonary adverse effects; pulmonary function and symptomatology in children and adolescent survivors of acute lymphoblastic leukemia (NOPHO ALL2008 cohort)

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The most common childhood cancer, acute lymphoblastic leukemia (ALL), affects approximately 40 children and adolescents in Denmark each year. Childhood ALL survival rates have risen from 50% to 90% in developed countries within the past three decades as recently established in the contemporary treatment protocol cohort, the NOPHO ALL2008. Studies have also revealed a severe toxicity rate of 50% during treatment. Pulmonary function deficits (PFD) and obstructive respiratory disorders grade 3-5 occur in 9 % and 10 % of childhood ALL survivors respectively. Previous studies fall short because they study irradiation, now obsolete and known to cause PFD, other older treatment regimens, they lack controls or have register-based data as reference. Forgoing these shortcomings, we aim to uncover late pulmonary adverse effects by examining pulmonary function in childhood NOPHO ALL-2008 survivors.

This national cross-sectional study includes a childhood NOPHO ALL-2008 protocol treated cohort (N=317) and matched controls undergoing physical examination, lung function testing, and questionnaires. The primary outcome is mean pulmonary function in ALL survivors compared with controls.

Status reveals a recruitment rate of 70% of eligible survivors (N=293). 206 survivors (≧1 lung test, N= 191) and 215 (≧1 lung test, N= 206) controls has participated. Data collection completes within 2023 and results are analysed for publication in 2024.

The study will provide national results regarding pulmonary function and symptoms in childhood ALL survivors, expectedly leading to an optimization of current national follow-up management in regard to prevention, earlier diagnosis, and treatment of LPAE.

Themes: Paediatrics, Cancer
Keywords: Paediatrics, Leukemia, Pulmonology

Variation in content of cannabinoids in cannabis tea dependent on cannabis product and preparation method used – A comparison of three products included in the Danish medicinal cannabis pilot programme

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Background: A pilot programme including medicinal cannabis plant products was implemented in 2018 in Denmark. Intake as tea is the recommended administration route for several of the products. The aim of this study was to elucidate the content of the cannabinoids tetrahydrocannabinol (THC), THC-acid (THC-A), cannabidiol (CBD) and CBD-acid (CBD-A) in cannabis tea depending on cannabis product used, and preparation method.

Methods: A standard cannabis tea was prepared from three products with a labeled content of 6.3%, 14%, and 22% THC + THC-A, respectively, according to manufacturer's instructions. Additionally, preparations with added coffee creamer were made. Quantification of cannabinoids were performed by UPLC-MS/MS in tea and plant material.

Results: The content of cannabinoids in plant material was between 62% and 92% of the labeled content. The content of THC in standard tea was 9.0 (SD = 6.4), 22 (SD = 11), and 40 (SD = 15) µg/ml, respectively, when prepared from products with a labeled content of 6.3, 14, and 22% THC + THC-A, respectively. In standard tea, THC-A and CBD-A were present in higher concentrations than THC and CBD. Adding coffee creamer prior to boiling induced a significant increase in THC and THC-A content for two of the three cannabis products, whereas adding coffee-creamer after boiling did not make significant changes in the cannabinoid content. Coffee creamer did not change the content of CBD and CBD-A.

Conclusion: Cannabis tea varied in concentrations of cannabinoids when the same preparations were repeated and dependent on plant product and preparation method used. In standard tea, THC-A and CBD-A were the most abundant cannabinoids.

Themes: Pharmacology, Urology & Nephrology
Keywords: Medical cannabis, Cannabis tea, Cannabinoids

SESSION 30

Polyamine treatment in elderly patients with coronary artery disease – a randomized controlled trial. From a Cardiovascular perspective.

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Life expectancy has increased tremendously over the past century and as populations age, chronic diseases such as cardiovascular disease and diabetes have become more prevalent. Healthy aging is therefore of paramount importance to further promote longevity and quality of life.

In humans, a high concentration of whole-blood spermidine is associated with longevity, and individuals with a high dietary spermidine intake have improved cardiovascular health and less obesity. Spermidine is essentially a polyamine found in all plant-derived foods, particularly in whole grains, soybeans, nuts, and fruit. Its favorable effects may act via several mechanisms. In an experimental model of hypertensive heart disease, spermidine reduced cardiac hypertrophy and improved diastolic and mitochondrial function. Spermidine also induces cytoprotective autophagy in skeletal muscle and alters body fat accumulation by metabolically modulating glucose and lipid metabolism.

The clinical data on spermidine dietary supplementation are scarce. In elderly subjects with cognitive problems, spermidine supplement was well tolerated and had potential blood-pressure-lowering effects. The reported beneficial effects of spermidine raise the question whether elderly patients with cardiovascular disease can benefit from a dietary supplement of this polyamine.

The aim of the study is to investigate the effects of daily oral polyamine dietary supplement versus matching placebo over a 12-months treatment period in elderly patients with cardiovascular disease.

Themes: Cardiology, Endocrinology
Keywords: Cardiovascular ageing, Dietary supplementation, Clinical trial

An evaluation of transdermal versus oral estrogen replacement therapy in Turner syndrome through deep-mining of all accessible data sources in the BI warehouse

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Background: Turner syndrome is a rare genetic disease caused by an absolute or partial lack of one of the two X chromosomes. Females with Turner syndrome might present with varying phenotypes with some of the key indicators being short stature, hypergonadotropic hypogonadism, poor development of secondary sex characteristics and infertility. The main focus of treatment is estrogen replacement therapy, either via transdermal or oral route of administration.

Aim: Our aim is to clarify whether there are any discrepancies between patients with Turner syndrome who receive transdermal versus oral estrogen replacement therapy. Additionally, this project seeks to examine how utilization of data mining might impact the process of data collection in data-heavy studies such as this.

Methods: The project will be formatted as a multi-year retrospective study including relevant patients from Region Midt. Collection of data will be conducted via the Business Intelligence (BI) data-warehouse, which extracts data from a multitude of the region's systems, containing information regarding electronic patient journals, medicine use, laboratory work and much more. This allows the user to customize and automatize data extraction, thereby decreasing the need for manual data collection. Examined parameters will include sex hormone levels, liver function, blood pressure, anthropometric measurements and more.

Perspectives: The results obtained from this project can be utilized when discussing treatment with patients, thereby ensuring the best possible care of the syndrome. Further, the experience gathered from using data mining as a form of data collection can be applied to other similar projects.

Themes: Endocrinology, Epidemiology
Keywords: Turner syndrome, Estrogen replacement therapy

Treatment with Zoledronate Subsequent to Denosumab in Osteoporosis 2 (ZOLARMAB2)

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Background: Treatment for osteoporosis with denosumab (DMAb), an antibody against receptor activator af nuklear factor kappa-B-ligand, markedly increases bone mineral density (BMD) and reduces the risk of fractures. The suppression of bone resorption ceases when DMAb is discontinued, and bone turnover does not merely return to pretreatment level but increases above in what has been termed "rebound activation of bone turnover". This phenomenon leads to rapid and substantial bone loss and increased risk of multiple vertebral fractures. Zoledronate has a biological half-life of years and suppresses bone turnover.

Aims:
1) to investigate if multiple infusions of zoledronate can prevent the rebound activation of bone turnover and the subsequent bone loss in patients previously treated with DMAb and if there is difference between infusing zoledronate at fixed time-points or when bone turnover is increased.
2) to investigate the effect of DMAb discontinuation on muscle mass and -strength.
3) to investigate the underlying pathophysiological mechanisms.

Method: This study is a multi-center randomized open label, interventional study in 200 postmenopausal women, randomized to treatment with zoledronate at fixed time-points (group 1) or when bone turnover is increased (group 2). Outcomes will be investigated by DXA, bone turnover markers, and muscle function tests.

Perspective: This study will show if BMD can be maintained by administrating zoledronate repeatedly during the first 6 months after discontinuing DMAb.

If BMDcan be maintained by zoledronate, potential long-term side effects of denosumab can be prevented and costs associated with life long DMAb treatment can be saved.

Themes: Endocrinology, Pharmacology
Keywords: Osteoporosis, Denosumab, DXA

Metabolic effects of four-week lactate-ketone ester supplementation

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Background and aim: Recent research reveals intriguing results concerning the role of exogenous lactate and the ketone body 3-hydroxybutyrate (3-OHB) as energy sources and signaling molecules. Applications are multiple in health and disease, including altering metabolic parameters related to obesity and fueling the heart. Thus, separate oral administration of lactate and 3-OHB influences appetite and satiety, alter concentrations of the hunger hormones ghrelin and GLP-1, and slow gastric emptying, while they both appear to inhibit lipolysis. 3-OHB administration have shown direct insulin sensitizing effects. The heart is one of the largest energy-consuming organs in the body, utilizing both lactate and ketone bodies as metabolic substrates. Separate infusion of 3-OHB and lactate has shown beneficial hemodynamic effects in patients with heart failure, dramatically increasing cardiac output.

We hypothesize that chronic co-administration of lactate and 3-OHB, as a novel lactate-ketone ester administered twice daily for 28 days, may ameliorate various metabolic endpoints related to obesity and the heart.

Material and methods: Design: 10 healthy, obese (BMI 30-40) subjects without diabetes will be examined on four separate occasions within a double-blind placebo-controlled randomized crossover design.

Intervention: 4-week period drinking either lactate-ketone ester (LaKe-ester) or placebo twice daily.

Outcome measures: Insulin sensitivity, echocardiographic measurements, weight, body composition, lipolysis, gastric emptying, appetite sensation scores, tolerability, and changes is plasma concentrations of free fatty acids, insulin, and hunger hormones.

Themes: Endocrinology, Cardiology
Keywords: Ketone bodies, Lactate, Exogenous administration

The Optimised Use of Romosozumab

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Background: Romosozumab (ROMO) is a monoclonal antibody that binds and inhibits sclerostin, with a dual effect of increasing bone formation and decreasing bone resorption. ROMO was recently introduced as a standard treatment of osteoporosis in postmenopausal women with a recent fragility fracture for 12 consecutive months. Studies demonstrate that the bone anabolic effect of ROMO is observed within the first 6 months of treatment, however, there is evidence to suggest that the anabolic response may reappear after an interval with antiresorptive or no treatment with a second course of ROMO.

Aim: Optimising the clinical use of ROMO in patients with osteoporosis and fractures by demonstrating if ROMO treatment results in higher gains in bone mineral density (BMD) if administered for 6 months before and after anti-resorptive treatment than observed with the current treatment regimen, and whether shorter treatment with ROMO followed by antiresorptive treatment results in similar gains in BMD as observed with current practice.

Methods: A 2-year, randomized, open-label intervention trial. We enroll 270 postmenopausal women, randomizing in three groups: Group 1; ROMO for 12 months, followed by Zoledronate (ZOL) for 12 months; Group 2; ROMO for 6 months, ZOL for 12 months, and ROMO for 6 months; Group 3; ROMO for 6 months, followed by ZOL for 18 months.

Perspectives: If repeated treatment with ROMO is superior in increasing BMD, this may have implications for clinical practice. Furthermore, if ROMO treatment for a shorter duration has a similar effect on BMD as observed with full-length of treatment, future clinical management may include a shorter duration of ROMO treatment.

Themes: Endocrinology, Pharmacology
Keywords: Osteoporosis managment, Romosozumab

Effect of colchicine on cardiovascular target organ damage in patients with type 2 diabetes

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Background and aim: Chronic low-grade inflammation has been suggested to play a pivotal role in the atherosclerotic processes ultimately leading to diabetic vascular complications. Indeed, administration of the anti-inflammatory drug colchicine has recently been demonstrated to reduce the risk of cardiovascular events. However, the mechanisms underlying the cardioprotective effects of the drug remain to be elucidated.

Increased arterial stiffness and endothelial dysfunction are important contributors to the unfavorable cardiovascular prognosis seen in patients with type 2 diabetes. The effect of colchicine on arterial stiffness, endothelial function and vascular inflammation remains to be elucidated.

Material and methods: We are carrying out a randomized placebo-controlled trial aimed at elucidating the effect of colchicine on cardiovascular target organ damage in patients with type 2 diabetes and established CVD. Participants will be randomized to 6 months treatment with colchicine or placebo. Specific aims are to test effect of colchicine on (1) arterial stiffness assesses as carotid-femoral pulse wave velocity, (2) endothelial function assessed by peripheral arterial tonometry and (3) vascular inflammation assessed with arterial 18fluorodeoxyglucose-positron emission tomography of the aorta.

Results: We expect to have results on the primary outcome (arterial stiffness) December 2023.

Conclusion and perspectives: Insights to the mechanisms of cardiovascular risk reduction may help lay ground for future clinical use of colchicine in secondary prevention of CVD.

Themes: Endocrinology, Pharmacology

Pulmonary infection with gram-negative bacterial pathogens before and two years after elexacaftor/tezacaftor/ivacaftor introduction: Results from the Danish National Cystic Fibrosis Cohort

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Background: Cystic fibrosis pulmonary disease is caused by mucus obstruction due to cell membrane protein channel malfunction leading to infection, biofilm establishment, chronic inflammation, cyst formation, fibrosis, and respiratory insufficiency. Several gram-negative bacterial pathogens cause pulmonary infection leading to accelerated lung function loss and decreased survival. Novel Elexacaftor/tezacaftor/ivacaftor (ETI) therapy modulates protein channel function and significantly improves prognosis. Studies of pulmonary infection are essential for development of rational culture regimens and future antibiotic strategies. The objective of this study is to assess change in gram-negative pulmonary pathogens before and 2 years after ETI initiation.

Methods: The study includes Danish cystic fibrosis patients ≥12 years of age initiating ETI therapy in a nation-wide prospective cohort study. Demographic and clinical data, airway secretion culture, biochemistry and serology results are collected in the Danish Cystic Fibrosis Registry. Pulmonary pathogens included are P. aeruginosa, Achromobacter, and Burkholderia species. Descriptive statistical analysis is used to assess patient characteristics and infection status as well as change in prevalence of cystic fibrosis pulmonary pathogens.

Results: Baseline clinical and microbiology data was successfully collected and validated. Patients with minimum 24 months follow up were included. Data are currently undergoing analysis and results will be presented.

Themes: Infectious Diseases, Infectious diseases
Keywords: Cystic fibrosis, Pulmonary infection, CFTR modulator therapy

Preliminary results: Characterizing Regional Pulmonary Gas Transfer using Hyperpolarized 129-Xenon MRI in Fibrosing Interstitial Lung Disease

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Introduction: Progressive Fibrosing Interstitial Lung Disease (PF-ILD) is a diverse group of diseases characterized by formation of fibrous tissue in the lung parenchyma resulting in progressively restricted ventilation and disrupted gas diffusion. Currently, the total gas transfer capacity of the lungs is measured using the single-breath carbon monoxide uptake in the lung (DLCO). This measure is global, and regional changes in gas transfer may not be detected.

Materials and Methods: Hyperpolarized 129-Xenon (HP 129Xe) gas is a novel MRI contrast technique providing information about key aspects of pulmonary physiology. As the gas is inhaled it dissolves in lung tissue and binds to haemoglobin, similarly to oxygen. The MR signal shifts and allows distinction between whether the signal arises from gas-phase, from dissolved-phase in lung tissue (M) or bound to the Red Blood Cells (RBC). The ratio RBC:M is interpreted as pulmonary gas transfer, and we aim to image and quantify this in patients with PF-ILD.

Results and discussion: This is an ongoing study; patients are currently included. In two patients, preliminary data shows whole lung RBC:M (mean ± SD) of 0.17 ± 0.05 with basal areas of the lung showing relatively lower RBC:M 0.14 ± 0.02. For reference, RBC:M data from healthy controls found in the literature range from 0.30 to 0.50. Comparing to available literature we also find a close correlation between DLCO measurements and RBC:M ($R^2 = 0.98$).

Conclusion: Hyperpolarized 129-Xe MRI can image regional pulmonary gas transfer. It shows regional differences in accordance with known disease patterns and show a strong correlation with currently applied clinical methods.

Themes: Imaging techniques, Diagnostics & technology
Keywords: Respiratory diseases, Pulmonary Fibrosis, Hyperpolarized MRI

Bioelectric impedance analysis (BIA)-derived parameters following exercise in individuals with type 2 diabetes

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Aim: This exploratory substudy will investigate how exercise and changes in insulin sensitivity affect bioelectric impedance analysis (BIA)-derived parameters in individuals with type 2 diabetes (T2D).

Background: BIA is a safe and non-invasive technique that measures the passive opposition (i.e., impedance) provided by the body against a weak, externally applied alternating current. BIA is often used in for instance gyms to assess body composition. The impedance can be described as an electric circuit with a resistor Re (representing the extracellular fluid) parallel with a serial circuit of a resistor Ri (representing the intracellular fluid) and a capacitor Cm (representing cell membranes). Currents with low frequencies cannot cross cell membranes, therefore only Ri contributes to the measurements. At high frequencies currents can pass cell membranes and Re will also contribute. In bioelectric impedance spectroscopy (BIS) a wide range (>200) of frequencies are used, making it possible to estimate Re, Ri and Cm.

Cm is regarded as a measure of cell membrane integrity but has scarcely been studied in a clinical setting. Re and Ri reflects hydration status. Other parameters (e.g., face angle) correlate in numerous clinical fields with health status, disease status and prognosis. However, BIA has scarcely been studied in relation to T2D.

Materials and methods: 40 individuals with T2D will be randomized to either 12 weeks of moderate bike exercise thrice weekly or no exercise. Before and after the intervention BIA parameters will be estimated with BIS, insulin sensitivity will be measured with the insulin suppression test and body composition will be assessed with DEXA scan.

Themes: Endocrinology, Diagnostics & technology
Keywords: Type 2 diabetes mellitus, Bioelectric impedance analysis, Insulin sensitivity

A randomised, double-blind, sham-controlled, multicentre study investigating the effect of transcutaneous vagal nerve stimulation on gastrointestinal symptoms in individuals with diabetic gastroenteropathy

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INTRODUCTION: Diabetic gastroenteropathy frequently causes debilitating gastrointestinal symptoms. Previous uncontrolled studies have shown that transcutaneous vagal nerve stimulation (tVNS) may improve gastrointestinal symptoms. To investigate the effect of cervical tVNS in individuals with diabetes suffering from autonomic neuropathy and gastrointestinal symptoms, we conducted a randomised, double-blind, sham-controlled study.

METHODS: This study included adults with type 1 or 2 diabetes, gastrointestinal symptoms, and autonomic neuropathy. Active cervical tVNS or sham stimulation was self-administered over two successive study periods: 1 week of 4 daily stimulations and 8 weeks of 2 daily stimulations. The primary outcomes were gastrointestinal symptom changes using the Gastroparesis Cardinal Symptom Index (GCSI) and the Gastrointestinal Symptom Rating Scale (GSRS). Secondary outcomes included gastrointestinal transit times and cardiovascular autonomic function.

RESULTS: In study period 1, active and sham tVNS resulted in similar symptom reductions (GCSI: -0.26 (SD 0.64) versus -0.17 (SD 0.62), P=0.44; GSRS: -0.35 (SD 0.62) versus -0.32 (SD 0.59), P=0.77). In study period 2, active stimulation also caused a mean symptom

decline comparable to sham (GCSI: -0.47 (SD 0.78) versus -0.33 (SD 0.75), P=0.34; GSRS: -0.46 (SD 0.90) versus -0.35 (SD 0.79), P=0.50). The tVNS was well-tolerated.

CONCLUSION: Cervical tVNS, compared to sham stimulation, does not improve gastrointestinal symptoms among individuals with diabetes and autonomic neuropathy.

Themes: Gastroenterology and hepatology, Endocrinology
Keywords: Diabetic gastroenteropathy, Vagal nerve stimulation, Gastrointestinal symptoms

SESSION 31

The nordic rectal prolapse study - a multicenter international cohort study

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On behalf of the Nordic Rectal Prolapse study group

Background: Rectal prolapse (RP) significantly affects quality of life. Surgical management of RP lacks consensus, and the need for evidence-based practice has increased, especially due to aging populations equivalating a higher number of procedures and controversies surrounding mesh usage. Patient reported outcomes such as symptom control and quality of life are crucial for RP surgery. Large-scale international trials with long-term follow-up are needed to assess the effectiveness of different surgical procedures.

Objectives: The primary aim is to determine whether well established procedures for external RP are non-inferior to the preferred operation, laparoscopic ventral mesh rectopexy. Secondary aims include the impact of different procedures on constipation symptoms, patient identified endpoints, short-term harms, response to interventions based on baseline characteristics, costs, quality-adjusted life years and recurrence rates.

Methods: The study follows a prospective multicenter international cohort design. Patients with full thickness RP are included, and any type of type of surgery for RP is allowed. Primary endpoint is change in quality of life at 6 months postoperative. Secondary outcome parameters involve patient reported outcome measures assessing quality of life, bowel function, urinary and sexual function, pain, and global satisfaction. Group size calculation aims for 90% power to demonstrate non-inferiority with a two-sided 95% confidence interval, targeting a recruitment of 430 participants. Long-term safety and recurrence will be addressed separately through consent for 1-, 3- and 5-year follow-up.

Themes: Surgery, Qualitative research
Keywords: Rectal prolapse, Surgery, PROMs

The interaction effect between multimorbidity and hip fracture on infection risk: a nationwide registry-based study of 92,599 patients with hip fracture

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Background: Infection is a frequent and serious complication after hip fracture (HF) surgery. Multimorbidity in HF patients is associated with elevated infection risk. It is unclear whether multimorbidity interacts with HF to increase infection risk beyond their individual effects.

Methods: Using nationwide Danish registries, we identified 92,599 patients ≥65 years surgically treated for HF between 2004 and 2018. Matched on age, sex, and surgery year, a comparison cohort from the general population without HF (n=462,993) was randomly collected.

Multimorbidity was defined using the Charlson Comorbidity Index in categories no (score 0), moderate (score 1-2) or severe (score >=3). We computed incidence rates (IR) of any hospital-treated infection with 95% confidence intervals and estimated the interaction contrast based on the difference in IRs.

Results: The 30-day IR of infection was 181 (176-176) per 100 person years (PY) in HF patients with no multimorbidity and 9 (8-9) in the comparison cohort. The IR increased to 240 (234-246) in HF patients and 17 (16-18) in the comparison cohort with moderate multimorbidity. The corresponding interaction contrast of 51 (43-59) showed that 21% of IR was explained by the interaction. This interaction contrast was 99 (87-111) in person with severe multimorbidity, thus 33% of IR was explained by the interaction.

Conclusion: There is a biological interaction between multimorbidity and HF that leads to a substantial increased infection risk. The interaction effect increased with multimorbidity burden. Future studies should test pre- and postoperative interventions in HF patients with multimorbidity to reduce their infection risk and mortality.

Themes: Epidemiology, Surgery
Keywords: Hip fracture, Infection, Multimorbidity

Testing the strength and healing of interlocking laser osteotomies

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Background: The surgical treatment of sarcomas is an essential part of a comprehensive management since sarcomas are particularly resistant to both chemo- and radiotherapy. Nonunion is the main complication after sarcoma resection and biological reconstruction using a fibula graft. Currently, osteotomies are performed using handheld, oscillating saws that cause debris, heat generation and microfractures that increase the risk of nonunion. Studies on cutting the bone with laser have reported less bone injury and improved bone healing. Furthermore, laser osteotomes have almost no geometrical limitations, and are therefore capable of cutting geometrical patterns that interlock, increase the initial stability and decreases the risk of nonunion.

Aim: This study examines the mechanical properties and healing of interlocking laser osteotomies fixated with a biodegradable screw compared to osteotomies performed with an oscillating saw and fixated with a metal plate and screws.

Methods: The osteotomies will be performed in the tibia of rabbits. The animals are randomized into either interlocking laser osteotomies, or a transverse osteotomy with an oscillating saw and conventional internal fixation. The rabbits will be euthanized after 6 weeks. The amount of newly formed bone will be assessed by micro-CT scans. The visibility of the osteotomy line will be evaluated, the mineral density and compositional properties of the callus will be determined with regards to both total callus volume and the mineralized callus volume. The mechanical properties will be evaluated in terms of shear strength by a destructive load test and the osteotomy segments will be tested until failure.

Themes: Surgery, Cancer
Keywords: Interlocking osteotomies, Sarcoma, Robotic surgery

Comprehensive evaluation of gastrointestinal function in patients with Neurogenic Bowel Dysfunction (protocol abstract)

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Abstract of protocol, for Ph.d Day January 2024, with project: "Comprehensive evaluation of gastrointestinal function in patients with Neurogenic Bowel Dysfunction"

Background: Neurogenic Bowel Dysfunction (NBD) is a common condition following spinal cord injury- or disease (SCI/D), and multiple sclerosis (MS). Symptoms include constipation, fecal incontinence, and difficult/prolonged bowel emptying, often in combination. It ensues restricted social life, increased admissions, and correlates with poor quality of life. Transanal irrigation (TAI), is a safe and often effective method for treating NBD, however it is not efficient in all cases.

Structural research of NBD is scarce, and treatment is primarily empirical. Therefore, further clinical research, is called upon, to optimize treatment of NBD.

Methods: Patients are recruited from Aarhus University Hospital. After screening, information and written consent, patient participate in baseline examinations. These consist of validated questionnaires regarding severity of condition, autonomic function, and bowel symptoms. Then, a specially designed bowel MRI, and an examination of transit time through the gastrointestinal tract, using the Motilis 3D transit time medical equipment, are performed. Patients with indication for TAI, will undergo treatment for a minimum of 30 days, after which examinations are repeated, and study is completed. Patients where TAI is not indicated, study participating is completed after baseline examinations.

Results: Study is currently in a patient recruitment/examining state; hence results are not available.

Conclusions: Pending due to ongoing study.

Themes: Gastroenterology and hepatology, Neurodegenerative disorders
Keywords: Neurogenic bowel dysfunction, Transanal irrigation, Clinical research

Optimizing post-tonsillectomy morbidity: a multicenter, double blinded, randomized controlled trial comparing surgical instruments

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Importance: Tonsillectomy, a common surgical procedure, is associated with significant morbidity, including postoperative pain and post-tonsillectomy hemorrhage. There is a pressing need for further research to reduce these complications.

Objective: To investigate whether tonsillectomies performed with the impedance-dependent tissue sealer device, BiZact™, resulted in a lower post-tonsillectomy hemorrhage rate and reduced postoperative pain compared to the traditional cold steel technique.

Design: A multicenter, double-blinded, RCT was implemented. Pre- and postoperative patient data were collected using the Danish Tonsil Database.

Setting: The study enrolled patients at five ENT departments in Denmark.

Participants: The study included elective and acute patients undergoing tonsillectomy for benign indications, patients above four years of age, and a weight above 16 kilograms. Exclusion criteria comprised specific medical conditions and patient age and weight restrictions.

Exposure: Participants were randomized to tonsillectomy with cold steel or BiZact™.

Main Outcomes and Measures: The primary outcomes assessed included post-tonsillectomy hemorrhage, postoperative pain, and perioperative variables. Secondary outcomes comprised complications to tonsillectomy, unscheduled healthcare contacts, and patient-reported outcomes.

Conclusion: We anticipate that BiZact™ is noninferior or better than the cold steel technique in terms of post-tonsillectomy hemorrhage and postoperative pain, potentially challenging the gold standard status of the cold steel technique. This research seeks to

ensure more favorable, less painful, and less costly postoperative period after tonsillectomy.

Themes: Surgery, Public health
Keywords: Tonsillectomy, Postoperative complications, Randomized controlled trial

The Impact of Somatic and Psychiatric Multimorbidity, Lifestyle Factors, and Socioeconomic Markers on the Risk of Reoperations following Osteoporosis-Related Hip Fracture

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Background: In Denmark, 8,000 people sustain new osteoporosis-related hip fractures every year. Mortality is almost 10% within 30 days. Reoperation is a common complication, and about 9% of patients are reoperated within 1 year. Risk factors for reoperation have predominantly revolved around surgery-related factors. Implementation of knowledge from these studies had limited impact on reoperation risk, implying other factors may play a role.

Aim: The PhD project aims to identify potential modifiable risk factors for reoperation, focusing on chronic somatic and psychiatric disorders, mobility and BMI, and socioeconomic position markers.

Methods: Using medical registries, such as the Danish Multidisciplinary Hip Fracture Registry and the Danish National Patient Registry, we will create a population-based cohort of patients operated due to an acute hip fracture during 2005-2022. We expect the inclusion of at least 100,000 patients. We will use the Kaplan-Meier method for net reoperation risk, in addition to the competing risk method for crude reoperation risk. Cox regression will be used to estimate cause-specific hazard ratios to assess the association between potential risk factors and reoperation.

Perspectives: The PhD project will promote the identification of a patient subgroup that requires additional pre- and postoperative evaluation, screening, optimization, and community-based follow-up program. Results will have the potential to improve treatment and outcome of hip fracture patients both nationally and internationally. In the long term, the results may help to develop and validate a clinical model for predicting reoperations using machine learning algorithms.

Themes: Epidemiology, Surgery
Keywords: Hip Fracture, Reoperation, Inequality in Healthcare

The effect of the popliteal plexus block on postoperative opioid consumption, pain, muscle strength and mobilization after total knee arthroplasty - a randomized, controlled, blinded study.

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Background and aim: Peripheral Nerve Blocks (PNB) in multimodal pain treatment for total knee arthroplasty (TKA) reduce acute postoperative pain and opioid consumption. Ideally, a PNB primarily anaesthetise pain-transmitting nerves while preserving muscle strength and mobility. To date, this has only been achieved by Femoral Triangle Block (FTB) and Adductor Canal Block (ACB) which anaesthetise nerves from the front of the knee capsule. Popliteal Plexus Block (PPB) is a novel PNB designed to anaesthetise nerves from the rear knee capsule. We aimed to explore PPB's potential as a valuable PNB for TKA.

Methods: We enrolled 165 TKA patients in a fast-track setup at Silkeborg Regional Hospital, randomly assigning them to three groups: Group A (PPB + FTB), Group B (FTB), and Group C (ACB). The primary outcome was 24-hour postoperative accumulated opioid use. Secondary outcomes included preoperative muscle strength tests (pre- and post-block), repeated assessment of pain scores at rest and during 90 degree active knee flexion, and a postoperative mobility test 5 hours postoperative.

Result and perspectives: The results are currently being analysed and will be presented at the PhD day 2024. We hope to demonstrate that adding PPB to a multimodal pain treatment for TKA substantially reduces postoperative opioid consumption without adversely affect muscle strength or patient mobility. Further research should reproduce the findings, optimize local anaesthetic dosages for PPB, and explore potential benefits in other knee surgical procedures.

Themes: Surgery, Rehabilitation
Keywords: Postoperative pain, Peripheral Nerve Block, Anaesthesiology

Minimal important change of the Western Ontario Osteoarthritis of the Shoulder (WOOS) index

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Introduction: The Minimal Important Change (MIC) for patient-reported outcomes measures is the value that describes the smallest improvement considered worthwhile by patients. To the best of our knowledge, no MIC of the Western Ontario Osteoarthritis of the Shoulder Index (WOOS) score or the Disabilities of the Arm Shoulder and Hand (DASH) has been reported using the anchor-based predictive modeling approach based on patients with glenohumeral osteoarthritis or rotator cuff tear arthropathy.

The aim of this study was to determine the MIC for WOOS and DASH in patients with glenohumeral osteoarthritis or rotator cuff tear arthropathy treated with a total shoulder replacement.

Materials and methods: Data on 231 patients were collected at four hospitals in Denmark and Finland. Data were collected at baseline and 12 weeks after surgery. At 12 weeks, the patients were asked about their perceived overall improvement after surgery measured by the Patient Global Impression of Change (PGI-C). The MIC was estimated for the WOOS and DASH using the adjusted predictive modelling approach with the PGI-C as an anchor.

Results: Of the 231 included patients, 104 was included in the MIC analysis. Patients had a mean age of 71 years and 56% were women. The estimated adjusted MIC for the WOOS score was 13.3 (-6.2; 23.3) and 7.2 (12.8; 1.7) for DASH.

Conclusion: For patients with glenohumeral osteoarthritis or rotator cuff tear arthropathy treated with a TSA or RSA, the estimated MIC for WOOS were higher than shown in previous studies . The estimates show wide confidence intervals , which could be due to the low sample size but could also indicate a large heterogeneity within the patient group.

Themes: Surgery, Rehabilitation
Keywords: Minimal important change (MIC), Patient reported outcome measu, Total shoulder replacement

Exploring needs, barriers to, and facilitators of rehabilitation following revision hip replacement - a grounded theory study

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Background: Current evidence on rehabilitation after revision total hip replacement (THR) is inadequate and development of rehabilitation interventions is warranted. Even so, little is known about patients' experiences with revision THR rehabilitation.

Aim: This study aimed to explore patients' rehabilitation experiences after revision THR and to develop a substantial theory about the factors influencing patients' use of rehabilitation after revision THR.

Materials and Methods: Using constructivist grounded theory, we conducted semi-structured qualitative interviews with 12 patients with completed rehabilitation programs after revision THR. Patients were recruited from Aarhus University Hospital. Data collection and analysis were a constant comparative process conducted in three phases; initial, focused, and theoretical.

Results: From the data, we generated a substantial theory of the participant's circumstances and ability to integrate rehabilitation into their everyday life after revision THR. Four categories were constructed based on patients' experiences in different contexts: hesitance, fear avoidance, self-commitment, and stamina.

Conclusion: This study highlighted that patients' expectations, past experiences, attitudes, trusts, motivation, and circumstances interact to influence engagement and adherence to rehabilitation and described four categories relating to the integration of THR rehabilitation into their everyday life. Clinicians should be aware of and account for these categories during rehabilitation. Tailored individual rehabilitation interventions and clinician approaches to optimize commitment and adherence are needed among patients with revision THR.

Themes: Rehabilitation, Surgery
Keywords: Rehabilitation, Orthopaedic Surgery, Experiences

Persistent low physical activity after stroke and risk of new vascular event or death

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Background and aims: Physical activity (PA) reduces cardiovascular risk. We aimed to investigate the relation between low PA before and after stroke and long-term risk of vascular events or death.

Methods: We assessed pre- and post-stroke PA in patients with first-ever ischemic stroke using the Physical Activity Scale for the Elderly (PASE) questionnaire at stroke admission and after 6 months, respectively. Covariates includes clinical data, stroke severity and functional status prestroke. Main outcome was a composite endpoint of new cardiovascular events (myocardial infarction, stroke or transient ischemic attack) or any cause of death from 6 months after stroke. Main exposure was PASE-score in the lowest quartile both pre- and post-stroke (low-PA-group). Data was analysed using a multivariate Cox proportional-hazards model.

Results: In total, 490 patients with available PASE-scores were included from The Efficacy of Citalopram Treatment in Acute Ischemic Stroke (TALOS) trial. Median age (interquartile range) was 68 (58; 76), 170 (35 %) were female, and 48 (9.8 %) patients were in the low-PA-group.

In the median follow-up period of 6.9 (5.7; 7.7) years, 11.3 events per 100 patient years occurred in the low-PA-group vs 4.66 among the rest (adjusted hazard ratio: 1.72 (confidence interval: 1.07; 2.77).

Conclusion: Patients with continued low levels of PA before and after stroke were at a higher long-term risk of composite outcome of new cardiovascular events or death compared to patients with changed PA level or continuously higher levels. This low-PA-group may constitute a special group for future interventional trials.

Themes: Rehabilitation, Neuroscience
Keywords: stroke, physical activity

SESSION 32

Inhibition of PI4KIIIα as a Novel Potential Approach for Parkinson's Disease Treatment

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Parkinson's Disease (PD) is a complex neurodegenerative disorder with various underlying causes, predominantly linked to α-synuclein aggregation and dopaminergic neuronal death in the substantia nigra. Phosphatidylinositols, particularly PI4KIIIα, play a critical role in membrane structure and trafficking, with emerging studies suggesting a potential connection between PI4KIIIα inhibition and α-synuclein reduction. Our pilot studies indicate a possible relationship between PI4KIIIα inhibition using Phenylarsine oxide (PAO) and decreased intracellular α-synuclein levels, resulting in increased cell viability. This study aims to further investigate the impact of PAO and other PI4KIIIα inhibitors, such as GSK-A1, Quercetin and PIK93, on α-synuclein levels through various experiments, including spatial transcriptomics and protein analysis on mouse tissue, primary neurons and SH-SY5Y and PC12 cell cultures. The study's goal is to provide insights into gene and protein dysregulation in PD and identify key proteins and pathways involved in the downregulation of intracellular α-synuclein following PI4KIIIα inhibitor administration, potentially leading to novel therapeutic targets for neurodegenerative symptoms.

Themes: Neuroscience, Neurodegenerative disorders
Keywords: Parkinson's disease, PI4KIIIa, α-synuclein

Decoding Addiction Through DNA Methylation and Neuroimaging: A Longitudinal Study on Developmental Predisposition

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The development of Substance Use Disorders (SUD) is still unclear. Broadly, we propose that susceptibility to SUD originates from epigenetic variations and neural changes during youth. Then, external influences during adulthood accentuate these foundational susceptibilities. Therefore, taking advantage of two independent longitudinal cohorts, we expect to provide novel information on SUD development and in the neuroscience field by looking at their longitudinal neurodevelopmental and epigenetic trajectories from childhood to adulthood using the Neuroimaging Epigenetics (NiE) approach - the interplay of epigenetics, environmental factors, and brain and behavioral patterns.

The first cohort is the Coccaine Study: a unique longitudinal biopsychosocial study of Brazilian adults with severe Cocaine Use Disorder (CUD) that aims to investigate neurobiological changes in CUD over time with an ongoing second wave (N<168). The second is the Brazilian High-Risk Cohort Study (BHRC). BHRC is a rich longitudinal biopsychosocial dataset of school-age children (now adults) from Brazil that aims to investigate typical and atypical trajectories of psychopathology over development. BHRC has a 3-wave of data collection (N<700). BHRC and Coccaine performed a comprehensive cognitive, clinical, and environmental assessment. Also, Magnetic Resonance Imaging (MRI) and blood were collected. Longitudinal trajectories within each cohort will be estimated using mixed and structural equation modeling to analyze the individual and joint effects on primary outcomes. DNA methylation and MRI data across cohorts will be normalized utilizing the same pipelines with categorical and strategic adjustments.

Themes: Neuroscience, Bioinformatics
Keywords: Addiction, Neurodevelopment, Neuroimaging-Epigenetics

Base editing of chronic granulomatous disease-causing mutations in CYBA and CYBB

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Chronic granulomatous disease (CGD) is a monogenic inborn error of immunity resulting from phagocyte dysfunction. The only curative treatment for CGD is allogeneic hematopoietic stem cell (HSC) transplantation. However, this carries the risk of severe adverse effects. Therefore, ex vivo gene editing of autologous human HSCs is being studied. DNA double-strand break (DSB)-independent gene editing technologies such as base editing have been developed to circumvent the challenges of DSB-dependent gene editing. Here, we present ongoing work using base editing to correct CGD-causing variants in the CYBA and CYBB genes. We generated clonal K562 cell line models carrying the pathogenic variants CYBA c.371C>T, CYBB c.252G>A and CYBB c.625C>T. Furthermore, we have acquired patient-derived CYBA c.371C>T peripheral blood mononuclear cells (PBMCs) as well as PBMCs and CD34+ hematopoietic stem and progenitor cells (HSPCs) from a healthy donor heterozygous for the CYBB c.252G>A variant. For the CYBB c.625C>T variant, base editing correction efficiencies of up to 99% was reached in the K562 cells. In the patient-derived CYBA c.371C>T PBMCs, editing efficiencies of more than 90% was obtained with minimal indel formation and bystander editing. Furthermore, we were able to successfully edit CD34+ HSPCs heterozygous for the CYBB c.252G>A variant reaching up to 76% alleles carrying the wild type variant. These results demonstrate the high efficiency and product purity of base editing and support further exploration of base editing for treatment of CGD. Future studies will include safety validation of the bystander edits, off-target analyses and engraftment studies of base edited CD34+ HSPCs.

Themes: Genetic engineering, Immune diseases
Keywords: Gene editing, Base editing, Chronic Granulomatous Disease

Adenine feeding leads to uremia in mice

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Chronic kidney disease (CKD) elevates the risk of cardiovascular disease (CVD) development. Unfortunately, conventional CVD treatments have limited effectiveness in patients with concurrent CKD. Research have linked a group of metabolites, uremic toxins (UTs), with endothelial dysfunction and ventricular hypertrophy, making these UTs potential targets for CVD intervention in CKD patients. We aimed to characterise plasma and urine metabolome of adenine (Ad)-treated mice with various stages of kidney injury.

Male mice received a diet enriched with 0.2% Ad to induce kidney injury and divided into 5 groups: control group, 2 weeks (w) of Ad diet, 4 w of Ad diet, 4 w of Ad diet and 1 w without and 4w of Ad diet and 2 w without. Urine was collected the day before termination and blood and kidneys at termination day. Urine and plasma metabolomes were analysed by LC-MS. Gene expression of transporters in kidney tissue was determined by qPCR.

We found high plasma and a low urine levels of amino acid derivatives after 2 and 4 w with Ad diet. The metabolic profiles in urine and plasma after 1 and 2 w of washout had a intermediate profile. We saw elevated levels of UTs, incl. indoxyl sulfate, p-cresyl sulfate, and kynurenic acid, in the plasma after 2 and 4 w of treatment that were restored after a 2-w washout. We found that gene expression of proximal tubule influx transporters decreased, while the expression of efflux transporters increased after 2 and 4 w and returned to baseline after 2-w washout.

Ad diet induced uremia in mice due to dysregulation of proximal tubule transporters. However, after 2 w of washout, transporter levels fully recovered, partially restoring the uremic state.

Themes: Omics, Animal Models
Keywords: Chronic kidney disease, Metabolomics, Uremic toxins

Establishing a treatment-resistant depression model for study the resolution of inflammation

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About 30-50% of patients with Major Depression Disorder fail to show a substantial clinical response to conventional antidepressant therapy. Among the various etiological hypotheses of depression, there are the theory of neuroinflammation and the dysregulation of the hypothalamus-pituitary-adrenal (HPA) axis. The aim of this first part of the project is standardize an animal model for TRD that can be used for further analysis, mainly to screen the specialized lipid pro-resolving mediators (SPM) profile and look for the relation between these compound and depressive-like behavior, since they have a very important active profile for ending neuroinflammation. It is our hypothesis that a repeated treatment with ACTH (30 or 100 ug/mg for 21 days) can mimic this condition in balb/c male mice and, in a first moment, have a predictive validity to TRD. Imipramine (IMI, 30ug/kg) was used for positive control for the last 7 days as well as Ketamine (KET, 20 ul/kg) one hour before the behavioral experiments. For the quantitatve analysis, it was performed the forced swin test and tail suspension test and the imobility time in both was count as a parameter for depressive-like behavior. The data show that the repeated treatment with ACTH: 1) induced a depressive-like behavior with 30ug/mg dose; 2) IMI disrupted this behavior decreasing the immobility time in FST; and 3) KET was not able to disrupted the depressive-like behavior. The repeated treatment with ACTH at 100ug/mg was not able to induce depressive-like behavior. Since the aim is to work with TRD, the ACTH strategy for this was not an effective model.

Themes: Neuroscience, Pharmacology
Keywords: Depression, Neuroinflammation, Lipids

Prime editing of human CD34+ hematopoietic stem cells for correction of GATA2 deficiency and X-linked chronic granulomatous disease

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Ex vivo gene editing of autologous human hematopoietic stem cells is currently being developed as a treatment for inborn errors of immunity (IEI), but the current gene editing platform relying on Cas9 and the use of rAAV6 as a donor for homology-directed repair is challenged by indel formation, off-target editing and toxicity in hematopoietic stem cells. Thus, there is a need for versatile genome editing strategies in hematopoietic stem cells that do not require delivery of a donor template and works without generating DNA double-strand breaks (DSB). Here, we present ongoing work using the DSB-independent prime editing technology to correct several patient-derived IEI-causing mutations. We optimized prime editing guide RNAs (pegRNAs) to efficiently correct mutations in a panel of disease genes, including GATA2 and CYBB, causing GATA2 deficiency and X-linked chronic granulomatous disease, respectively. We also optimized nicking sgRNAs (ngRNAs) for both GATA2 and CYBB and found that editing efficiencies were highly dependent on the ngRNA, with prime editing rates in model K562 cell lines varying between 20% and 80% with alternative ngRNAs. In vitro transcribed PEmax mRNA as well as synthetic pegRNAs and ngRNAs were co-delivered to patient-derived peripheral blood mononuclear cells as well as CD34+ hematopoietic stem and progenitor cells (HSPCs) from healthy donors, yielding prime editing rates of 20% and 35%, respectively. Notably, while prime editing generally resulted in less editing than conventional HDR-based gene editing, prime edited HSPCs showed superior viability and significantly increased colony-forming potential. This indicates an increased fitness compared to traditional CRISPR-based gene editing approaches, supporting the further exploration of prime editing to treat IEI.

Themes: Genetic engineering, Molecular biology
Keywords: Gene editing, Hematopoietic stem cells, Inborn errors of immunity

Orthogonal and multiplexed transcriptional modulation and gene editing using orthologous CRISPR/Cas9 systems

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Gene-specific transcriptional modulation can be induced by CRISPR/Cas-based activation (CRISPRa) and interference (CRISPRi) by recruitment or direct fusion of transcriptional regulators to nuclease deficient Cas9 (dCas9). Here we expand the emerging area of CRISPR mediated transcriptional modulation though In Vitro Transcribed (IVT) mRNA delivery by cloning, producing, and testing different combinations of dCas9 and transcriptional modulators for IVT mRNA delivery. We utilize dCas9 from both S. aureus and S. pyogenes, and a mix of full length and truncated sgRNAs to perform multiplexed transcriptional modulation as well as orthogonal CRISPRa, CRISPRi, and knockout (KO). Our findings show that the direct fusion activation domain, VPR, allows for the most efficient upregulation across all tested targets compared to the truncated VPR variant, VPRmini, and recruitment-based SunTag systems. The KOX1 KRAB domain for CRISPRi outperformed KOX1-MeCP2 and ZIM3 KRAB constructs for both dSaCas9 and dSpCas9 fusions for transcriptional repression. Using dSpCas9-VPR mRNA with truncated sgRNAs for CD123 activation, dSaCas9-KRAB mRNA and sgRNAs for CD5 repression, and SpCas9 and sgRNA targeting the TRAC locus for TCR KO, we perform genetic engineering with transient up- and downregulation of two genes while knocking out a third. We found that while substitution of full length CRISPRa sgRNAs for truncated sgRNAs allows for orthogonal activation and KO using the same Cas9 variant, the Cas9 protein:sgRNA ratio is crucial for balancing KO and CRISPRa efficiency. These studies demonstrate the versatility and potential of CRISPR-based transcriptional modulation for complex genetic engineering.

Themes: Genetic engineering, Molecular biology
Keywords: CRISPR, transcriptional modulation

Recurrent lymphoid meningitis in heterozygous IRF7 deficiency

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Monogenic inborn errors of immunity (IEIs) can underlie recurrent lymphoid meningitis (RLM, Mollaret's meningitis) caused by HSV-2 infection. Such IEIs usually result in impaired ability of brain resident cells to control viral replication, analogous to IEIs causing herpes simplex encephalitis. Here, we report a RLM patient carrying a heterozygous null mutation in IRF7, the master regulator of interferon expression. This IRF7 Q185X mutation resulted in a truncated protein when expressed in vivo. Peripheral blood mononuclear cells (PBMC) from the patient expressed reduced amounts of full-length IRF7 protein and showed greatly reduced interferon (IFN) expression in response to intracellular nucleotides and TLR9 stimulation. IFN expression was further impaired upon HSV-1, HSV-2, and IAV infection of PBMCs. In vitro generated plasmacytoid dendritic cells (pDCs) with heterozygous IRF7 knock-out will be evaluated for their ability to express IFNA upon HSV-2 infection. Fibroblasts from the patient will be used to investigate the dependence on IRF7 in the control of viral replication. This study highlights the role of IRF7 in controlling recurrent HSV-2 infection. We point to a previously underappreciated role of peripheral immune cells in the immune response against viruses in the brain.

Themes: Immune diseases, Infectious diseases
Keywords: innate immunology, HSV, inborn errors of immunity

Exploring CRISPR-Mediated Gene Correction Strategies as a Definitive CURE for DOCK8 Deficiency

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DOCK8 deficiency manifests during childhood resulting in recurrent infections, atopic diseases, and malignancies, leading to significant morbidity and mortality. Allogeneic hematopoietic stem cell transplantation faces challenges such as lack of HLA-matched donors and risk of graft-versus-host disease. This emphasizes the need for alternative treatment options. Here, we develop an ex vivo CRISPR/Cas9-mediated gene therapy for DOCK8.

We conducted site-specific gene editing in DOCK8 deficient THP-1 clones using three distinct strategies: 1)CRISPR/Cas ribonucleoprotein complex delivery to induce a site-specific double-strand break, while simultaneously delivering a repair template by adeno-associated virus serotype 6 for integration of a corrective partial cDNA, 2)The same as 1), but delivering single stranded oligonucleotide (ssODNs) as HDR repair template, and 3)Correcting gene variants by the new gene editing tool “Prime Editing”.

Locus-specific modification was achieved across all strategies, with editing ranging from 50 to 100%. The AAV-based strategy exhibited the lowest editing efficiency, while the ssODN approach demonstrated the highest. Correction of patient-specific variants using ssODN repair templates for HDR has shown partial reconstitution of DOCK8 mRNA and protein expression, reaching up to 70% of the wildtype.

Our preliminary findings support the feasibility of DOCK8 gene editing and its potential therapeutic application. However, optimization of AAV and prime editing strategies is warranted to assess their potential. Furthermore, assessment of functional immune cell restoration and efficiency in hematopoietic stem cells are crucial for clinical translation.

Themes: Genetic engineering, Immune diseases
Keywords: DOCK8 immunodeficiency, Gene editing, Prime Editing

Spatial summation and lateral inhibition of thermosensation

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Spatial summation (SS) and lateral inhibition (LI) are thermosensory processes that impact how we perceive temperature. SS describes a relationship between stimulation surface area and perceived temperature intensity. An increase of stimulation surface area will cause a sub-additive increase in perceived temperature intensity. LI encompasses the inhibition of neighbouring neurons and underlies spatial acuity. How are these processes affected differently by warm and cold temperatures?

16 participants completed a thermosensory task in which they perceived warm and cold stimuli of variable size (SS condition) or variable distance (LI condition). Participants were asked to indicate if they felt the stimulus as warm or cold and subsequently rate the temperature intensity on a visual analogue scale.

Results showed that the participants responded faster to cold and also rated the cold stimuli as more intense. Hierarchical Drift Diffusion Modelling of the response times indicated larger and wider drift rates for cold vs. warm area sizes, which indicated that SS had a bigger effect on the cold stimuli than the warm. Additionally, LME indicated a weak LI effect for both cold and warm perception.

Our findings suggest that SS works differently for cold and warm perception and demonstrate the occurrence of LI during innocuous temperatures. We are planning to study these mechanisms, and how they are changed by aging and neuropathy. Additionally, we will investigate if the differences in warm and cold SS could underlie the thermal grill illusion.

Themes: Neuroscience, Statistics
Keywords: Thermosensation, Pain, Computational modelling

SESSION 33

Improvements in daily Activity and exercise in Children with overweight: The Act-Child study

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An increasing proportion of Danish children do not meet the national guidelines of recommended daily physical activity. Physical inactivity in children is associated with obesity, increased risk of lifestyle diseases and impaired quality of life (QoL).

In this study, we aim to investigate the long-term effect of a community-based lifestyle intervention including physical activity for children living with obesity. The outcomes are changes in daily physical activity, QoL and weight during a 5-year follow-up period.

The study is a clinical trial investigating physical activity in a population of 300 children with obesity from Randers and Aarhus municipality. The children will participate in a family-centered lifestyle intervention, whereof 100 children will be randomized to an add-on intervention, which includes high intensity interval training (HIIT).

This study will provide insight into the long-term effects of lifestyle interventions either with or without HIIT-add-on regarding daily physical activity and improvements in QoL.

Themes: Endocrinology, Paediatrics
Keywords: Overweight, Physical activity, Quality of Life

Effects of extensive Weight loss on Insulin resistance and Lipid-kinetics in people with obesity, fatty liver Disease.

The WILD study

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Background: Dyslipidemia is primarily driven by the secretion of Very-Low-Density Lipoproteins and Triglycerides (VLDL-TG) from the liver. Although studying VLDL-TG kinetics has been challenging, our research group has developed a safe and sophisticated tracer technique to facilitate this investigation.

To gain a deeper understanding of the pathophysiology behind the resolution of Non-alcoholic Fatty Liver Disease (NAFLD) and dyslipidemia, we aim to explore the relationship between hepatic VLDL-TG particle secretion, other circulating fatty acids, insulin resistance, and the severity of NAFLD in women with obesity and NAFLD during and after extensive weight loss.

Aim: The primary objective of the study is to investigate changes in VLDL-TG kinetics during and after extensive weight loss in women with obesity and fatty liver disease treated with either Roux-en-Y Gastric Bypass (RYGB) or a high dose of Glucagon Like Receptor 1-receptor agonist (GLP-1ra). Secondly, we will study impacts on the immune system and microbiota, in relation to the improvement of fatty liver, insulin resistance, and changes in VLDL-TG kinetics.

Design: This study is i) a study on the natural history of VLDL-TG kinetics during extensive weight loss, and ii) a randomized, open-label, single-center trial conducted at Steno Diabetes Center Aarhus, Aarhus University Hospital, Denmark. We intend to recruit 24 women, eligible for bariatric surgery and randomly assign them to receive either RYGB or GLP1ra, 12 in each treatment group. Participants will undergo examinations at three time points: before treatment initiation, after achieving a weight loss of 10% from baseline, and 8 months after treatment initiation.

Themes: Endocrinology, Gastroenterology and hepatology
Keywords: Obesity, NAFLD, Dyslipidemia

INfluenza VaccInation To mitigate typE 1 Diabetes (INVITED trial) – a randomized, double-blinded, placebo-controlled clinical trial in children and adolescents with recent-onset type 1 diabetes

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Background: In type 1 diabetes (T1D) preservation of β-cell function eases the burden of T1D, stabilizes blood glucose excursions and reduces the need for insulin administration, which is highly desirable. Influenza vaccination, considered a novel candidate for immune modulation, holds promise for attenuating the autoimmune destruction of β-cells through the induction of a protective cytokine response. Our study aims to assess the efficacy of influenza vaccination in preserving β-cell function in children with recent-onset T1D.

Methods: One hundred patients aged 7-17 years with recent-onset T1D will be randomized in 1:1 ratio within 14 days of diagnosis to receive either standard influenza vaccine or placebo. The primary outcome is difference in mean change (baseline to 12 months) in mixed-meal stimulated C-peptide response between groups during a 2-hour tolerance test. Secondary and exploratory outcomes include mean change (baseline to 6 months) in mixed-meal stimulated C-peptide response, hemoglobin A1c, insulin requirements, glucose sensor metrics, diabetes antibodies, inflammatory markers and serum hemagglutinin inhibition antibody titers against influenza viruses.

Discussion: The preservation of β-cell function remains a critical goal in T1D management. Currently no immunotherapeutic treatments are available for β-cell preservation. Influenza vaccination is an inexpensive intervention with documented mild side effects. A positive study outcome could lead to immediate implementation of influenza vaccination in routine care for pediatric patients with recent-onset T1D.

Trial registration: ClinicalTrials.gov NCT05585983

Themes: Endocrinology, Paediatrics
Keywords: Type 1 Diabetes, Immunomodulation, Influenza Vaccination

Genomic and clinical aspects of fetuses with sex chromosome aneuploidies

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Background: Sex chromosome aneuploidies (SCAs) are disorders characterized by either complete or partial loss or gain of sex chromosome. SCAs affect 1:400 newborns. SCAs are associated with increased morbidity, including congenital malformation. Epigenetic mechanisms (e.g. DNA methylation) regulate the activity of our genes, and these mechanisms have profound impact on health and disease. Adult SCA patients exhibit distinct and tissue-specific epigenomes, but while the fetal period is critical for establishing the epigenome, limited epigenomic data during SCA embryogenesis exists.

Objectives: This study aims to elucidate how altered sex chromosome dosage impacts the methylome and epigenetic gene regulation in placentas and fetuses with SCAs, and how these changes lead to the fetal phenotype and influence morbidity in childhood and adulthood.

Methods: In this case-control study, we aim to enroll 120 pregnant women, who have decided to terminate pregnancy: 80 carrying fetuses with a SCA (cases) and 40 carrying genetically normal fetuses (controls). Comprehensive clinical examination and tissue sampling of the placenta and the fetus will be done directly after elective abortion and during fetal autopsy. Tissue samples will be analyzed using genomic methods, including single-nuclei RNA sequencing, spatial transcriptomics, DNA sequencing with methylation analysis, and RNA sequencing. Genotype-phenotype associations will be explored using weighted correlation network analysis and AI-driven "deep phenotyping".

Perspectives: This study will increase our understanding of SCAs and the link between genotype and phenotype, potentially leading to improved patient care in the future.

Themes: Endocrinology, Omics
Keywords: Sex chromosome aneuploidies, Epigenetic modifications, Embryonic development

Increased risk of metabolic dysfunction-associated steatotic liver disease in individuals with low birth weight – a case-control and reversibility study

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BACKGROUND: Metabolic dysfunction-associated steatotic liver disease (MASLD) is associated with insulin resistance as well as the metabolic syndrome. Steatosis can cause inflammation and secondly steatohepatitis. Globally, MASLD affects around 32% of the adult population. Low birth weight (LBW) is a risk factor for developing type 2 diabetes explained by the thrifty phenotype hypothesis and recent findings suggest that LBW individuals also have a higher risk of undiagnosed MASLD. In this project we aim to validate the increased MASLD risk in LBW individuals and subsequently investigate the potential reversibility of the disease.

METHODS: Study I is a case-control screening study in early middle-aged non-obese individuals born with LBW (n=250) and normal birth weight (NBW) (n=50), respectively. Examinations include anthropometrics, blood samples, body composition (DXA), liver fat content, liver stiffness and adipose tissue biopsies.

Study II is a deep phenotyping intervention study where LBW individuals with MASLD (n=12) and NBW (n=12) will be recruited from study I. The intervention is four weeks of time restricted eating limiting food intake to an 8-hour window during the day. Examinations include assessment of 24-hour energy expenditure, respiratory quotient and substrate oxidation as well as examination of glucose and lipid metabolism using stable tracer infusion.

PERSPECTIVES: Firstly, this project will elaborate on MASLD and associated dysmetabolic traits in individuals born with a LBW, and secondly, identify a group of individuals who may benefit from preventive strategies, including targeted screening and possibly caloric restriction for MASLD reversibility.

Themes: Endocrinology, Gastroenterology and hepatology
Keywords: Low birth weight, Steatotic liver disease, Metabolism

Impact of glucocorticoid exposure on skeletal muscle function: experimental study in human subjects

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Background and aim: A notorious and dreaded adverse effect of glucocorticoids (GC) is muscle wasting and visceral obesity. The mechanisms of muscle wasting upon GC exposure are not clarified. Within the last decade, muscle-resident multipotent mesenchymal stem cells called fibro-adipogenic progenitors (FAPs) have been identified as master regulators of skeletal muscle homeostasis and are located in the interstitial space of resting or regenerating muscle. Aberrant accumulation and function of FAPs cause loss of skeletal muscle mass and function.

Utilizing a human data set, we study the effects of GC exposure on skeletal muscle structure and function in healthy older subjects. We hypothesize that muscle stem cells and FAPs mediate GC-induced myopathy.

Material and methods: Healthy participants older than 50 years of age are randomized to receive placebo or prednisolone (37,5mg) for 5 days. Muscle stem cells and FAPs will be analyzed in biopsies from skeletal muscles and further characterized using single cell RNA-sequencing and Fluorescence-Activated Cell Sorting (FACS). Body composition including muscle mass (DXA scan), muscle strength, spontaneous physical activity, diet registration, and glucose homeostasis are also recorded.

Conclusion (and perspectives): We combine translational and in vivo human research to elucidate the pathophysiology of GC excess, which is of clinical interest since 3% of the Danish population receives GC treatment.

Themes: Endocrinology, Pharmacology
Keywords: Myopathy, Glucocorticoid, Skeletal muscle

Can Pravastatin improve Insulin Sensitivity in Renal Transplant Recipients and Patients with Chronic Kidney Disease? The INSTA-study

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Background: Insulin resistance (IR) and associated disorders of glucose metabolism (GM) such as type 2- and post-transplant diabetes (DM) are highly prevalent in patients with chronic kidney disease (CKD), including renal transplant recipients (RTRs). Cardiovascular disease (CVD) risk is significantly increased in these populations and augmented by IR. Statins are cholesterol lowering drugs used in CVD prophylaxis; evidence indicates adverse effects of statins on GM, with increased IR and risk of DM, albeit with significant differences across statin types and doses. The pharmacological properties of pravastatin separate it from other statins; these may lead to neutral or beneficial effects of this drug on GM. Under the hypothesis that pravastatin improves insulin sensitivity in CKD patients, we initiated the INSTA study.

Methods: A double-blinded, placebo-controlled, cross-over study is conducted in 10 non-DM RTRs and 10 non-DM CKD patients, respectively. Both groups undergo two sequence-randomized treatment phases of 12 weeks Pravastatin 40 mg daily or placebo, separated by a 4-week wash-out phase. The primary outcome is insulin sensitivity measured with a hyperinsulinaemic euglycaemic glucose clamp at the end of each treatment phase. Secondary outcomes include insulin secretion, markers of GM, insulin signalling and gene/protein expression in muscle and adipose tissue, and faecal microbiotic composition. Currently, 10 RTRs and 9 CKD patients have been enrolled.

Perspectives: Improvement of the metabolic profile of patients with impaired kidney function without a concomitant increase in risk of DM, with the aim of ameliorating CVD risk in these populations.

Themes: Endocrinology, Urology & Nephrology
Keywords: Insulin Resistance, Post-transplant Diabetes, Cardiovascular Disease

Faecal Microbiota Transplantation against chronic diarrhea in Patients with Systemic Sclerosis - a randomized, double-blinded, safety and pilot-efficacy study.

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Aim: In this investigator-initiated 9-week, randomised, double-blinded placebo-control pilot trial we aim to investigate the safety and pilot-efficacy of faecal microbiota transplantation as an adjuvant treatment against chronic diarrhea in patients with Systemic Sclerosis (SSc).

The study results will provide crucial insights into the potential and benefits of faecal microbiota transplantation by evaluating symptom relief and subsequent improvement in quality of life. Additionally, the study aims to investigate the underlying factors contributing to these symptoms in patients with SSc; whether gastrointestinal symptoms for these patients are caused by changes in microbiome, physiological conditions of the gut, or a combination thereof. Moreover, monitoring the influence of capsule faecal microbiota transplantation on patients' SSc will be another important aspect of this trial.

Design: This study is a of capsule-FMT. The study is designed to have two intervention periods, the first is 5 weeks and the second is 4 weeks. 20 patients will be included, and a series of investigations will be made at baseline. Subsequently, patients undergo a 1:1 randomisation for either active FMT or placebo during their initial intervention of two components. Patients receive either Active FMT on both components given in the first intervention or placebo capsules for both components. Four weeks later the first intervention period ends, and investigations from baseline are repeated before the second intervention, which is treatment with a third component of active FMT for all 20 patients. After another four weeks, the second intervention period ends with a repeat of investigations.

Themes: Gastroenterology and hepatology, Gastroenterology and hepatology

Working-life exposome and COPD

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Background: Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide with 3.3 million deaths annually. Several exposures, such as tobacco smoking, occupational dust and fumes, and ambient air pollution, are known to increase the risk of COPD. Most individuals are exposed to multiple exposures, thus assessing the total burden of exposure is crucial. Taking an exposome approach allows us to explore combined exposures and unravel the importance of specific exposures.

The aim of this study is to investigate the association between working-life exposome and COPD.

Method: The study population (n=13,160) consists of two population-based cohorts, the European Community Respiratory Health Survey (ECRHS)) and the French Constances cohort. Clinical information on COPD is available at multiple time points, together with a full job history. Several Job exposure matrices including EUROJEM will be applied to assess individual cumulative occupational exposures. Based on address information ambient air pollution is assessed from the EXPANSE exposome surfaces. Correlation analyses will be followed by a two-step approach. 1) using an ExWAS approach, logistic regression will be applied to study the associations between each exposure and COPD, after adjusting for sex, height, weight, pack-year during the follow-up period, and early-life disadvantages. Variables with a p-value>0.2 will be left out. 2) The retaining variables will be analysed using e.g., Bayesian Kernel Machine Regression, and/or Lasso.

Conclusion: Insights into how working-life exposome affects the risk of COPD may lay the ground for an evidence-based preventive strategy.

Themes: Epidemiology, Public health
Keywords: Exposome, Respiratory diseases, working-life

The Efficacy of Salt Restriction in Patients with Hypertension and the Predictive Value of Salt Blood Test

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Lowering salt intake has shown to decrease blood pressure (BP), though the response varies among individuals. This might be due to differences in sodium (Na) storage capacity. The Salt blood test examines this capacity of the red blood cells and could be related to blood pressure response to a lower salt intake.

This study aimed to test the effect of a four-week salt restricted diet on BP and study the association between change in BP and salt intake. The salt-blood test was examined as a possible predictor of decrease in BP.

Seventy-two patients with hypertension were included and randomized 2:1 to either salt restriction or a control group for a 4-week study period. Blood samples, 24-hour BP monitoring and 24-hour urine collection were performed before and after. Two-sample t-test and linear regression analysis were performed.

Change in Na-excretion from baseline to follow-up was -61.9 mmol in the intervention group compared to 4.6 mmol in the control group ($p<0.0001$) and 42 out of 48 in the intervention group managed to lower their salt intake.

Change in systolic 24-hour BP was found to be significantly different between groups (-7.3 mmHg in interventions vs 1.5 mmHg in control, $p=0.0001$). Change in BP was correlated with higher systolic BP at baseline ($p=0.0001$, $R2=0.2870$) and lower Na excretion after the intervention ($p=0.0012$, $R2=0.2048$). No association between decrease in BP and Salt-blood test was found ($p=0.3157$, $R2=0.0229$).

In conclusion, four weeks of salt restriction decreased 24-hour BP significantly. Predictors of response were higher BP at baseline and low Na-intake after the intervention. Salt blood test, however, did not seem to predict decrease in BP.

Themes: Urology & Nephrology, Cardiology
Keywords: Hypertension, Sodium

SESSION 34

The effect of Fremanezumab on pain in patients with Complex Regional Pain Syndrome: a randomized, double-blind, proof of concept, placebo-controlled trial

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BACKGROUND: Complex Regional Pain syndrome (CRPS) is a debilitating primary pain condition in the limbs which can develop after a trauma. The treatment of CRPS is challenging. Clinical and preclinical studies suggest that the neuropeptide Calcitonin Gene-Related Peptide (CGRP) is both a mediator of pain and inflammation in CRPS which makes CGRP a possible target for a mechanism-based treatment. Recently, drugs targeting CGRP including Fremanezumab have become available and have been shown to be effective in the treatment of migraine.

OBJECTIVES: To compare the change in pain intensity from baseline to the last week of Fremanezumab treatment with placebo in CRPS patients. Other objectives are to assess pain relief and differences in clinical signs and function between the groups and if the effect can be predicted by CRPS biomarkers.

METHODS: This is a randomized, double-blind, proof-of-concept, placebo-controlled study where 60 adult patients with CRPS with disease lasting from 3-18 months will be randomized to treatment for eight weeks with Fremanezumab 225 mg or placebo (Isotonic saline) at 1:1 rate. Study procedures will include patient-reported outcome measures such as pain diary, physical examination, quantitative sensory testing, CRPS severity score, blood samples (Inflammatory markers), skin biopsies and measurement of cutaneous blood flow.

TIME FRAME: The study is expected to begin in November 2023 with last patient, last visit in July 2025.

PERSPECTIVES: This study will hopefully elucidate the pathogenesis of CRPS, and the assessment of the efficacy of Fremanezumab may result in a mechanism-based treatment option for patients with CRPS.

Themes: Neuroscience, Pharmacology
Keywords: Complex Regional Pain Syndrome, Pain, Drug therapy

Modeling the Influence of Cannabinoids on effort, fatigue and interoception

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Many countries are moving towards the legalization of cannabis for medicinal and recreational use. Medicinal cannabis has been proposed as treatment for several disorders like depression and anxiety. However, research on the effects of cannabinoids on the human brain and body are few and suffer from many limitations, such as using uncontrolled 'natural' cannabis. Studies using controlled cannabis are typically clinical trials focused on the efficacy of medicinal cannabis for specific diseases. Consequently, there is a gap in our fundamental understanding of the underlying neurocognitive mechanisms through which cannabinoids influence and affect the healthy, adult body and brain.

This project will investigate how cannabinoids influence our perception of effort, fatigue and interoception. In this double-blind within-subject study, 50 participants will take part in three sessions during which they will receive either THC, CBD or placebo (one per session). During each session, participants will undergo fMRI scans while completing an adapted version of the Effort Learning Task. This task probes how people learn about effort and reward. After the scan they will also complete two tasks, investigating their interoceptive sensitivity in the cardiac and respiratory domain.

Overall, the aim of this study is to enhance our understanding of THC and CBD's effects on the body, the brain, and their interaction in healthy individuals. The study will give us insight into how these compounds might alter the ability to learn about effort and reward. This in return might give direction for future studies on the treatment of depression, anxiety, and schizophrenia with medicinal cannabis.

Themes: Neuroscience, Pharmacology
Keywords: Cannabinoids, Effort Learning, Interoception

Impact of Noradrenaline vs. Phenylephrine on Brain Circulation, Organ Blood Flow, and Tissue Oxygenation in Anesthetized Patients with Brain Tumors: A Randomized Controlled Trial

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Background: Perioperative hypotension can lead to cerebral and organ ischemia, impacting patient outcomes. Vasopressors are commonly used to maintain blood pressure, but their effects on organ circulation and oxygenation vary. This randomized controlled trial aims to compare the impact of noradrenaline and phenylephrine on brain circulation, organ blood flow, and tissue oxygenation in patients with brain tumors.

Methods: This single-center, double-blinded trial will enroll 40 adult patients with supratentorial brain tumors. Patients will be randomized 1:1 to receive either noradrenaline or phenylephrine infusion during surgery. Positron emission tomography (PET) will be used to assess cerebral and multi-organ blood flow and oxygen consumption parameters at various time points. Primary and secondary endpoints include changes in cerebral blood flow, brain energy consumption, tissue oxygen saturation, and organ-specific blood flow and oxygen consumption. Statistical analyses will be conducted to detect significant differences between the two vasopressors.

Discussion: This study aims to enhance our understanding of how noradrenaline and phenylephrine affect organ circulation and oxygenation in patients with brain tumors. The results will contribute to evidence-based clinical practice for choosing vasopressors in perioperative and acute care settings, ultimately optimizing patient outcomes. Ethical approval and informed consent have been obtained, and the study is expected to provide valuable insights into vasopressor therapy's impact on organ circulation during anesthesia.

Themes: Neuroscience, Pharmacology
Keywords: Noradrenaline vs Phenylephrine, Brain and organ circulation, Positron emission tomography

The role of dopamine in the pleasurable urge to move to music, rhythm perception and production

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Music's profound ability to move us physically and emotionally is rooted in the fundamental connection between music and movement in the brain. Humans experience the pleasurable urge to move to music (PLUMM) in response to rhythmic patterns with moderate complexity, which evoke a more pronounced PLUMM experience than low or high complex rhythms, following an inverted U-shaped pattern. Previous studies have explored the role of dopamine in musical experience, suggesting its significant involvement in the mechanisms that elicit PLUMM.

Neuroimaging studies have shown that PLUMM engages motor and limbic basal ganglia (BG) networks which overlap with cortico-striatal and mesolimbic dopaminergic pathways. Moreover, Parkinson's disease, a neurodegenerative disorder in the BG alters PLUMM, flattening the inverted U curve and shifting preferences to simpler rhythms, reinforcing the potential role of dopaminergic systems. However, a direct dopamine-PLUMM link remains unestablished.

In a double-blind, placebo-controlled study, we aim to establish this connection. This study has two arms: one focusing on behavior and the other on fMRI neuroimaging. In both studies, participants will perform three tasks after receiving levodopa, risperidone, or a placebo. The first task assesses PLUMM through rhythmic pattern ratings. The second task explores harmony likability, and finally a series of tapping tasks. We hypothesize that dopamine influences the inverted U-shaped PLUMM curve through alterations in beat perception, production, and general pleasure. This study will help us understand the role of dopamine in musical reward and the brains' reward system in general.

Themes: Neuroscience, Pharmacology
Keywords: Music, Dopamine, Behaviour

Neuropathic pain and sensory disturbances in spinal cord injury and peripheral nerve root lesions.

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Background: Pain caused by a lesion or disease in the somatosensory nervous system is known as neuropathic pain. Nerve compression, neuropathy, and spinal cord injury can lead to neuropathic pain, but the underlying mechanisms are incompletely understood. Syringomyelia is a rare disease characterized by a fluid-filled cavity in the spinal cord, a syrinx, that causes damage to surrounding neuronal tissue. Syrinx development may complicate several disease conditions, and abnormal cerebrospinal fluid flow is perceived as a central mechanism for pathogenesis and progression. Damage to nociceptive pathways, specifically spinothalamic tract fibers, is implicated, but not in itself sufficient to cause neuropathic pain, prompting further investigation into underlying mechanisms beyond pathway integrity. Hence, only a subset of patients suffering from syringomyelia develop neuropathic pain. Additionally, lesions affecting nerve roots, e.g., a herniated disc, may cause peripheral neuropathic pain in the arms or legs, and knowledge of these patterns, known as dermatomes, form an integral part of clinical neurological diagnosis and decision making.

Methods: We will examine patients with syringomyelia and single nerve root lesions. Patients will undergo pain assessment, neurological examinations, and quantitative sensory testing. In syringomyelia patients, we will examine the pathoanatomical syrinx features using magnetic resonance imaging (MRI) as well as cerebrospinal fluid flow dynamics using 2D phase contrast MRI. Using neurophysiological examinations, we will investigate the function of nociceptive pathways as well as spinal cord dorsal horn excitability.

Themes: Neuroscience, Neurodegenerative disorders
Keywords: Neuropathic Pain, Syringomyelia, Clinical

Socioeconomic inequalities in excess mortality and life years lost associated with mental disorders: a nationwide cohort study in Denmark

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Background: Mental disorders are associated with elevated mortality rates and shorter life expectancy, but few studies to date have examined the role of socioeconomic position (SEP) in these associations.

Methods: We designed a cohort study including all persons living in Denmark on January 1, 2000 (N 5.2 million) and followed them up until December 31, 2020. Information on mental disorders, individual SEP, and mortality was obtained from national registers. We estimated mortality rate ratios (MRR) and population attributable fractions (PAF) of deaths for each diagnosis, and calculated the average reduction in life expectancy as life years lost.

Results: In preliminary analyses, we observed that mental disorders are associated with elevated all-cause and cause-specific mortality rates regardless of SEP level. Specifically, in the bottom SEP quintile, MRR comparing people with and without mental disorders was 2.16 (95%CI 2.11-2.20) for all-cause mortality, 3.57 (3.26–3.91) for external causes and 2.10 (2.06–2.15) for natural causes, and PAFs were 9.1%, 18.2%, and 8.7%, respectively; whilst the corresponding MRRs in the top SEP quintile were 3.28 (3.17–3.40), 9.52 (8.30–10.91), and 3.07 (2.96–3.19) and PAFs were 5.7%, 18.3%, 5.2%. The gap in life expectancy for people with mental disorders in the top SEP quintile was 8.30 years (75.91 vs. 84.21 years), whereas this difference was 5.97 years in the bottom SEP quintile (73.16 vs. 79.13 years).

Conclusion: This study provides a comprehensive analysis of effect modification by SEP in the associations between specific types of mental disorders and cause-specific deaths, presenting mortality risks on both absolute and relative scales.

Themes: Mental health, Public health
Keywords: Psychiatric epidemiology, Mortality, Socioeconomic inequalities

Anterior shoulder instability during apprehension-relocation test measured with radiostereometry

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Background: Anterior shoulder instability can be treated with the Latarjet procedure in patients with glenoid bone defects. Apprehension-relocation test is the preferred preoperative clinical test to evaluate shoulder instability with a dichotomous outcome.

Aim: To quantify the shoulder kinematics during an apprehension-relocation test in patients scheduled for the Latarjet procedure compared to their contralateral healthy shoulder.

Patients and methods: Twenty patients scheduled for the Latarjet procedure, and a healthy contralateral shoulder (HE) were included. Radiostereometric (RSA) image recordings of the patient's shoulders were performed during a repeated apprehension-relocation test. Bone volume models were generated from computed tomography scans of both shoulders and aligned with the RSA recordings. The contact center of the glenohumeral joint and the distance to the anterior and inferior glenoid rim were calculated. The paired differences between the injured (INJ) and HE shoulder were presented.

Results: During apprehension, the contact center of the INJ shoulders was 1.57 mm ($p=0.01$) more anterior and 1.69 mm ($p<0.01$) more inferior than the HE shoulders. For apprehension and relocation, the contact center was 3.99 mm ($p <0.01$) and 2.94 mm ($p<0.01$) closer to the anterior glenoid bone rim for the INJ shoulders compared to the HE shoulders, respectively. For apprehension, the contact center was 2.05 mm ($p=0.01$) closer to the inferior glenoid rim for the INJ shoulders compared to HE shoulders.

Conclusion: The contact center and the distance to the glenoid rim were more anterior and inferior during apprehension for the INJ shoulders compared to the HE shoulders.

Themes: Surgery, Imaging techniques
Keywords: Anterior shoulder instability, Radiostereometry, Apprehension-relocation test

CASEMED

Cancer Patients with pre-existing Severe Mental Disorders

Development and pilot test of a collaborative care model

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BACKGROUND: Cancer patients with pre-existing severe mental disorders (SMD), including moderate to severe depression, bipolar disorder and schizophrenia, are known to have reduced life expectancy and are less likely to get recommended cancer treatment. The aim of this study is to develop and pilot test a collaborative care model, to enhance the cancer care.

METHODS: Four workshops with 5 nurses, 4 oncologists, 3 psychiatrists, 2 general practitioners (GPs), 1 psychologist, and 16 patient representatives were conducted to develop a prototype. Afterwards a pilot test, with 13 patients were carried out. During this process, we made continuous adaptations to the prototype. The qualitative data were analysed focusing on acceptability, feasibility, mechanisms of impact and key uncertainties.

RESULTS: The final CASEMED cancer care model included: Early identification of psychiatric comorbidity, engagement of caregivers, education of the healthcare professionals, securing continuity among staff and enhanced collaboration between sectors. The last was achieved through an online psychiatric multidisciplinary team conference (pMDT) where the patient's GP, a project psychiatrist and the patient's oncologist participated.

Thirteen patients agreed to participate and eight pMDTs were conducted. The pMDT was able to suggest optimisations in treatment in 6 out of 8 cases, including changes in prescribed medications (50%), referral to psychiatric ward (37%) and supplementary consultants (50%).

CONCLUSION: This study indicates that the CASEMED cancer care model has a high potential to optimise treatment for cancer patients with pre-existing SMD. A larger feasibility study is currently being conducted.

Themes: Cancer, Mental health

Interscan reproducibility of CT derived coronary plaque measurements using a semi-automated analysis software

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Background: Coronary computed tomography angiography (CCTA) is a well-established non-invasive imaging modality, offering detailed anatomical information of the coronary tree. Furthermore, CCTA allows quantification and characterization of certain atherosclerotic plaque features. However, studies on interscan reproducibility of coronary plaque quantification are limited.

Aims: To evaluate interscan reproducibility of coronary artery plaque burden quantification from CCTA using a semi-automated plaque analysis software.

Methods: A total of 103 patients with known coronary artery disease recruited from three Danish sites underwent 2 CCTA scans within one hour time span. Repeated scans were conducted using the same acquisition protocol. All scans were blindly reviewed by one reader using a semi-automated plaque analysis software (AutoPlaque, version 3.0) to assess plaque burden. For each patient, plaque components were measured in absolute volumes (mm3) for the following plaque subtypes: total plaque (TP), calcified plaque (CP), non-calcified plaque (NCP), and low-density non-calcified plaque (LD-NCP). LD-NCP was defined by an attenuation <30 Hounsfield units (HU). Statistical analyses have not been performed yet.

Perspectives: This study represents the most expansive investigation of interscan reproducibility of coronary plaque quantification thus far. It is evident that the effectiveness of semi-automated tools in evaluation of coronary plaque hinges on their capacity to deliver consistent and replicable results, especially when the potential purpose is to monitor progression of coronary artery disease.

Themes: Cardiology, Imaging techniques
Keywords: Coronary CTA, Coronary plaque

Substantial deficits and differences exist across measures of walking capacity in patients with multiple sclerosis

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Background: Walking capacity is important not only to persons with multiple sclerosis (pwMS), but also to clinical practice and research. The present study aims to compare the extent of impairments (relative to healthy controls (HC)) across three commonly used walking capacity outcomes in pwMS.

Methods: In a two-hospital cross-sectional study, walking capacity was assessed using the timed 25-foot-walk-test (T25FWT; "walking speed"), the six-minute-walk-test (6MWT; "walking endurance"), and the six-spot-step-test (SSST; "walking balance and coordination"). Data were compared to normative reference data in HC.

Results: A total of 228 pwMS (68% females) were involved in the study; age 53.7±11.6 yrs (range 26–81 yrs), patient determined disease steps (PDDS) 2.9±1.9 (range 0–7), time since diagnosis 12.6±9.9 yrs (range 0-49 yrs), MS-phenotype (RRMS/SPMS/PPMS) 146/39/41. Compared to HC, deficits were observed across all walking capacity outcomes ($p<0.001$); T25FWT -26 [-30;-23] %, 6MWT -36 [-39;-32] %, and SSST -44 [-47;-40] % Deficits differed across walking capacity outcomes ($p<0.001$).

Conclusion: Altogether, pwMS performed substantially worse than HC across all three walking capacity outcomes. The results showed, that the SSST was superior to T25FWT and 6MWT in detecting walking capacity impairments in pwMS.

Themes: Rehabilitation, Neurodegenerative disorders
Keywords: Multiple sclerosis, walking capacity, outcome measures

SESSION 35

Low-dose, standard and high-resolution CBCT for alveolar bone measurements (and digital model making)

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Objective: To assess the impact of dose-lowering Cone-Beam Computed Tomography (CBCT)-protocols in diverse CBCT-units on linear bone measurements in the posterior mandible when planning dental implants. The hypothesis is that bone measurements performed in low-dose (LD) CBCT-scans are not different from those performed in standard (SD) and high dose (HD) protocols.

Materials and methods: Twenty-six human cadaveric and partially edentulous mandible specimen were chosen to identify sites to be restored with dental implants (42 sites).

Each specimen was examined in three CBCT-units (Viso G7, Planmeca, Finland; Axeos, Dentsply-Sirona, Germany; and X1, 3Shape, Denmark), three times on each, using a LD, SD, and HD protocol with a fixed and smallest possible field-of-view (FOV).

The datasets were imported into dedicated software (OnDemand 3D, Cybermed, Korea) and the region of interest defined by one operator. Each site was localized based on visibility of the mandibular canal and neighboring teeth. For each site the most appropriate coronal and sagittal image were chosen and exported as a PNG (Portable Network Graphic format) file. The exported images (two for each site for every protocol) will be randomized and measurements of bone height and width will be performed on each image by three calibrated and blinded observers. Twenty percent of the measurements will be repeated, to allow assessment of intra-observer agreement.

Results: The results will focus on the inter- and intra-observer agreement, as measured by intra-class correlation coefficients, and on the comparison of the diverse bone measurements for each protocol, within each CBCT-unit and observer-wise, also using dedicated statistical analyses.

Themes: Dentistry, Imaging techniques
Keywords: Low-dose, CBCT, Alveolar bone measurements

Truth or myth? Ability of dairy proteins to reduce capsaicin-induced oral burning pain and possible clinical implications

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Background: Many disorders can cause burning pain in the oral mucosa, e.g., Burning Mouth Syndrome. Milk proteins have been claimed to reduce capsaicin-induced oral burning pain.

Aim: Assess the role of milk proteins in reducing capsaicin-induced oral burning pain.

Methods: 24 healthy participants were recruited for a double-blinded, placebo-controlled cross-over study consisting of three sessions. During each session, mucosal pain was evoked by exposing each participant's tongue to 0.075% capsaicin crème for 8 min. The level of the perceived burning intensity and unpleasantness was scored on two different numerical rating scales every 30 s. After capsaicin exposure, the participants rinsed their mouth with a different solution during each session (5% whey, 5% casein and tap water). Scoring of unpleasantness and burning intensity continued after rinsing. To assess temperature and somatosensory changes on the tongue mucosa, a thermographic image was taken and sensory testing was performed trice during each session.

Results: No differences were found between sessions when comparing unpleasantness and burning intensity after rinsing ($P>0.772$) or the duration of the perceived unpleasantness and burning intensity ($P>0.117$). No difference was found between sessions for tongue surface temperature and somatosensory changes ($P>0.053$)

Conclusion: We observed no significant difference in the relief provided by rinsing with 5% whey and 5% casein solutions compared with water. The relieving effect associated with consuming milk products after capsaicin consumption could instead be associated with other milk constituents or a synergistic effect between different constituents.

Themes: Dentistry, Neuroscience
Keywords: Oral Mucosa, Capsaicin, Pain

A comparative study of interdental osteotomies performed with robotic controlled laser osteotome or a piezoelectric saw

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Background: Maxillary arch segmentation is a common practice to improve occlusion in patients with dentofacial deformities. However, it's occasionally avoided due to the challenge of performing interdental osteotomies without causing iatrogenic root perforation. This comparative study aims to evaluate the potential, feasibility and precision of interdental osteotomies performed with a Cold Ablation Robot-guided Laser Osteotome (CARLO) compared to osteotomies performed by an experienced maxillofacial surgeon.

Materials and Methods: Prior to surgery 10 human cadaver maxillae were computed tomography (CT) scanned. Virtual surgical plans (VSP) of 20 interdental osteotomies between canine and lateral incisor were made in a split-mouth design. Half of the osteotomies were performed by CARLO, while experienced maxillofacial surgeons used a piezoelectric saw for the other half. Both CARLO and the surgeon were asked to follow the VSP. CT scans of the maxillae were obtained post-surgery, and the osteotomy paths were compared with the VSP.

Preliminary results: Initial visual inspection showed CARLO-made osteotomies deviated due to parallel shifts from the VSP, while surgeons' divergent osteotomies resulted from altered osteotomy angle. CARLO consistently maintained the angulation specified by the VSP.

Conclusion: With CARLO, it is indeed possible to perform interdental osteotomies with the correct osteotomy angulation. However, in some cases, there can be a parallel displacement of the osteotomy path. This indicates that while CARLO offers promise, there are still challenges to address in ensuring precise osteotomies.

Themes: Surgery, Dentistry
Keywords: Robotic surgery, Computer-Assisted Surgery, Dentistry

Dental Students' Attitudes on Cardiopulmonary Resuscitation Training via Virtual Reality: An Exploratory Study

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Introduction: Cardiac arrest is a major public health issue, with around 300,000 cases occurring in Europe each year. Dentists need to maintain their CPR skills and training to prevent cardiac arrest. Traditional face-to-face training is expensive and difficult to coordinate, but Virtual Reality (VR) offers a promising alternative. This preliminary research study aims to investigate dental students' attitudes towards integrating VR technology into CPR training.

Materials and methods: We recruited 120 dental students who participated in their annual CPR training course. The students were divided into two groups: one received conventional CPR training with manikins and the other received VR CPR training using a VR emergency simulation. Both groups underwent a basic life support presentation. After training, the VR training group completed a questionnaire assessing their experience.

Results: A study of 120 dental students found that 88 had never used VR before, but found it valuable for CPR training. They viewed VR as an educational tool, but some found the simulated hospital setting less significant. They recommended incorporating VR into dental education, but noted the need for tailored scenarios.

Conclusion: Further research is needed to explore the impact of virtual environments like dental clinics or hospitals on the proficiency and effectiveness of CPR administered by dental students and professionals, aiming to determine if this digital environment enhances learning outcomes and improves CPR quality in dental settings.

Themes: Dentistry, Diagnostics & technology
Keywords: virtual reality, dental students, CPR

Keypoint detection and representation for automated comparison of intraoral 3D photoscans

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Forensic odontology identification (comparative dental analysis) is one of the three primary identifiers in disaster victim identification. With the addition of intraoral 3D photo scans to dental records, a new level of detail awaits implementation in the identification process. Such implementation requires development of a matching algorithm. For such an algorithm to be useful in a forensic setting, distinguishment between 3D photo scans from the same individual, opposed to scans from different individuals, is fundamental.

The aim of this study was to explore possible constructions of a matching algorithm using combinations of keypoint detection and different keypoint representation techniques.

Intraoral 3D photo scans of 6 jaws were used for testing the combination of methods. For keypoint detection, keypoints were found using Difference of Curvature (DoC). For keypoint representation, five representation methods were explored: Unique Signatures of Histograms (USC), Signature of Histograms of OrienTations (SHOT), Equivalent Circumference Surface Angle Descriptors (ECSAD), Rotational Projection Statistics (RoPS), and Signed Feature Histogram (SFH). Further, combinations of the methods were carried out.

SHOT representation, and three combination methods, were able to unambiguously separate matches from mismatches. The best performing separation was done using SHOT as the keypoint descriptor, since the separation margin was not increased by combining representation methods.

We conclude that an algorithm comprising a combination of DoC keypoint detection and SHOT representation when working with 3D photo scans could be applicable in forensic odontology identification.

Themes: Bioinformatics, Dentistry
Keywords: 3D dental photo scans, Keypoint representation, Keypoint detection

A Study in Healthy Volunteers to Improve Methods for Detection of GHB in Drug Rape Victims

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The date rape drug, gamma-hydroxybutyrate (GHB), poses a challenge in forensic detection due to its short detection window of less than 6 hours in blood and less than 12 hours in urine. GHB is a short chain fatty acid and is used medically for narcolepsy treatment. As a degradation product of the neurotransmitter GABA, it exists endogenously, complicating exogenous detection. This study aims to enhance legal certainty in drug-facilitated sexual assault cases by identifying GHB metabolites with extended detectability and exploring alternative detection matrices like saliva, dental calculus, hair, and sweat.

A randomized, double-blinded, placebo-controlled clinical trial involving 30 healthy volunteers administered a single 50 mg/kg dose of GHB (as sodium oxybate) or placebo has been conducted. Blood, urine, and saliva samples were collected over 5 days, with sweat samples taken after 24 hours and dental calculus and hair samples after 4 weeks.

Untargeted metabolomics analysis will be applied to blood and urine samples to identify GHB metabolites that can serve as biomarkers to extend the detection window. Concentrations of GHB and potential biomarkers will be quantified using LC-MS/MS in blood, urine, and saliva. Additionally, LC-MS/MS will be employed in an attempt to detect GHB in sweat, dental calculus, and hair.

This research represents a crucial step towards developing more effective methods for GHB detection, thereby aiding forensic investigations in drug rape cases.

Themes: Omics, Pharmacology
Keywords: Toxicology, Metabolomics, Pharmacology

Adolescent Dietary Quality as a Risk Factor for Painful TMD and Headaches in Young Adults

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Painful temporomandibular disorder (P-TMD) is a common orofacial pain condition often associated with headaches. We investigated the association between adolescents' diet quality and the presence of P-TMD and headaches in young adulthood.

Diet quality of 33,412 individuals from the Danish National Birth Cohort (DNBC) at age 14 was assessed using the Healthy Eating Index (HEI) encompassing eight domains. Among these, 11982 participants completed the TMD Pain Screener and responded to headache-related queries at age 18. Utilizing logistic regression and ordinal logistic regression, we analyzed HEI and dietary domains as potential risk factors for P-TMD and headaches.

HEI scores were divided into quartiles, with quartile four indicating higher diet quality. Quartile four showed higher odds of P-TMD (OR=1.13, P=0.02), but after adjustment and including inverse probability weighting (IPW) results were no longer significant but estimate almost unchanged (OR=1.12 [95% CI, 0.96-1.30], P=0.11). Overall diet quality showed no significant associations with headaches. However, specific dietary domains - fiber, sodium, and added sugar - displayed associations with headaches but not P-TMD, even after adjustment.

In summary, overall diet quality during adolescence did not exhibit a significant link with P-TMD or headaches in young adulthood after adjustments. Notably, some specific dietary domains exhibited significant associations with the risk of developing headaches. These findings underscore the interplay between diet and pain disorders, calling for further research to unveil the underlying pathophysiological mechanisms connecting lifestyle, P-TMD, and headaches.

Themes: Dentistry, Epidemiology
Keywords: Painful TMD, Dietary quality, Headache

pH-FISH: a combined analysis of microscale pH and microbial architecture in biofilms

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Dental caries is caused by acid production in bacterial biofilms that form on the tooth surface. These biofilms display considerable pH gradients and contain localized acidic pockets that drive the disease process. pH gradients in dental biofilms may, in part, be the result of distinct spatial arrangements of specific bacteria. pH ratiometry and fluorescence in situ hybridization (FISH) are well-established methods to investigate the biofilm pH and microbial composition at the microscale, respectively. In this study, we develop a new method, pH-FISH, to concomitantly map biofilm pH and bacterial distribution in structurally intact biofilms. As a proof-of-concept, the method is used to study the interplay between pH and bacterial microarchitecture in in situ-grown biofilms from healthy and caries-active participants.

Biofilms are grown for two days on glass carriers with laser-marked microscopic fields of view (FOVs) in individual intraoral splints. Thereafter, the biofilm pH response to sucrose is monitored in the marked FOVs using the ratiometric dye C-SNARF-4. Biofilms are then fixed in a mix of agarose and paraformaldehyde to preserve their three-dimensional microarchitecture. FISH is performed using oligonucleotide probes specific to the dominant bacterial genera in the biofilms, as determined by 16S rRNA gene sequencing. The correlation between local pH and the abundance and distribution of specific genera in the marked FOVs is assessed by digital image analysis. pH-FISH is a powerful method to explore the relationship between biofilm microarchitecture and virulence, and it will contribute to uncover new targets for caries-preventive therapies.

Themes: Dentistry, Dentistry
Keywords: dental biofilms, dental caries, confocal microscopy

Strategy for Prompt and Effective Thoracentesis in the Emergency Department (SPEEDTAP):

A Multicenter Randomized Clinical Trial

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Introduction: Shortness of breath due to pleural effusion often leads to the Emergency Department (ED) admission. Typically, thoracentesis is performed in the radiology department. However, thoracentesis in the ED may reduce treatment delays. Currently, fluid drains passively into a collecting bag post-pigtail catheter insertion. An alternative option is active removal of fluid using a syringe. Currently, no one has investigated the effectiveness thoracentesis with active drainage in an ED setting. The aim of this study is to investigate how active fluid removal in the ED compared to the standard thoracentesis performed by radiologists affects time to complete pleural effusion drainage.

Methods: This is a prospective, randomised, investigator-initiated, multicenter, clinical superior trial investigating thoracentesis methods in four EDs in Central Denmark Region. Patients are randomised to either active fluid removal in the ED or insertion of pigtail catheter in the radiology department (control). Primary outcome: time from clinical indication to complete drainage. Key secondary outcomes include length of stay, ED admission to ED discharge and safety end-points. The trial begins in January 2024 and the primary results will be reported after 30-day follow-up, anticipated in autumn 2024.

Discussion: The results will clarify the impact of ED manual fluid drainage on drainage time, length of stay and patient satisfaction and potentially change clinical practice.

Themes: Diagnostics & technology, Cardiology
Keywords: Emergency medicine, Thoracentesis, Treatment method

SESSION 36

Human Adipose Tissue Blood and Lymphatic Endothelial Cell Heterogeneity in Health and Disease

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White adipose tissue is a highly plastic organ, which dysfunction is implicated in the development of metabolic diseases and associated cardiovascular deterioration. While the healthy adipose tissue is highly vascularized, obesity is associated with vascular rarefication and malfunction. Nevertheless, an endothelial cell-centered analysis of the effects of obesity and diabetes on human adipose tissue endothelial cells (AdECs) at the single cell transcriptomic level is lacking. The transcriptomes of paired human visceral and subcutaneous adipose tissue from six donors were profiled using single nucleus RNA sequencing. The validation of a previously un-recognized AdECs subcluster was performed on cultured human derived AdECs. The presented adipose tissue atlas comprises a total of 16,819 vascular and lymphatic AdECs, distributed over six distinct subpopulations, from six donors including lean, obese, and obese diabetic subjects. We report pronounced AdECs heterogeneity and identify in addition to canonical AdECs cellular subtypes, including arterial, venous, capillary, and lymphatic AdECs, novel AdECs

cellular subtypes including AdECs with a partial mesenchymal transcriptome and immune-modulating AdECs. We further characterize AdECs with a partial mesenchymal transcriptome and demonstrate that human-derived AdECs undergo endothelial-to-mesenchymal transition in response to pro-fibrotic and pro-inflammatory stimulations. Our analysis demonstrates the heterogeneity of human AdECs and the occurrence of previously unrecognized cellular populations, which participation in the homeostasis of the adipose tissue and the pathogenesis of obesity requires further investigation.

Themes: Endocrinology, Omics
Keywords: Adipose tissue vasculature, Endothelial cells, Obesity

Effect of methylprednisolone on the synthesis of glycerol-3-phosphate in adipose tissue from female mice

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Obesity is a major healthcare problem and mechanisms controlling fat distribution are of key interest. In white adipose tissue (WAT) fatty acids (FAs) are esterified with glycerol-3-phosphate (G3P) to form triglyceride (TG) and G3P can be synthesized from glucose and via glyceroneogenesis. In both cases, glycerol-3-phosphate dehydrogenase (cGPDH) plays a role.

Use of glucocorticoids is associated with central obesity and is suggested to reduce the esterification of FAs in WAT by inhibiting the synthesis of G3P via glyceroneogenesis.

Based on this we hypothesize that glucocorticoids influence the synthesis of G3P in WAT in a depot specific manner.

Female SWISS mice (n = 24) were divided into 3 groups: Controls or mice injected with methylprednisolone (Solu-Medrol); 15 mg/kg/day or 22.5 mg/kg/day for 4 weeks. Bodyweight was monitored and visceral and subcutaneous WAT were removed for analysis.

The final bodyweight did not differ between groups after 4 weeks of treatment ($p = 0.164$). However, the relative change in body weight was significantly higher in the 22.5 mg/kg/day than in the 15 mg/kg/day group ($0.8 \pm 1.5\%$, $-3.0 \pm 1.4\%$, $5.0 \pm 2.3\%$, $p = 0.02$). Our analysis suggest that methylprednisolone had no impact on the relative protein expression of cGPDH in visceral WAT (1.0 ± 0.1, 1.3 ± 0.2, 1.5 ± 0.4, $p = 0.73$). Further analysis will include the expression of other proteins relevant for the synthesis of G3P in visceral and subcutaneous WAT.

In conclusion, our preliminary results show no significant impact of 4 weeks of methylprednisolone treatment on bodyweight or the abundance of cGPDH in visceral WAT.

Themes: Endocrinology, Molecular biology
Keywords: Adipose tissue, Glyceroneogenesis, Methylprednisolone

Lymphedema, low-grade inflammation, and the vasculature in Turner syndrome

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Background: Turner syndrome (TS) is caused by complete or partial X monosomy in some or all cells, causing a myriad of complication including reduced final height, estrogen deficiency, infertility, lymphedema, and cardiovascular disease.

Aim: Our aim is to evaluate the lymphatic and cardiovascular system in a cohort of adult women with TS to elucidate any defects, abnormalities or dysfunctions that may explain the complications related to TS and link these finding to the epigenetic changes in TS.

Methods: 100 women with TS and 50 controls will be included. To evaluate the cardiovascular system, we will use MRI of the heart and aorta to assess both function and morphology. Using 4D-flow measurements we will estimate the risk of aortic wall rupture and dissection. Furthermore, we will use an FDG-PET/CT to detect otherwise undetectable low-grade inflammation in the vascular system which may contribute to the development of cardiovascular complications such as dissections. Also, we will examine the lymphatic system using ICG(indocyanine green)-lymphography and MRI to evaluate the lymphatic system, grade dysfunction, and detect subclinical lymphedema. Lastly, we will collect blood, muscle, skin, fat, buccal and urothelial samples to associate the epigenetic changes with the phenotypic features of TS.

Perspectives: The potential of these analyses is that we could be able to identify patients at high risk and need for medical or surgical intervention at an early stage and thus prevent or minimize this acute life-threatening complication of TS. Furthermore, we wish to increase our understanding of the association between the genetic modifications and the phenotype of TS.

Themes: Endocrinology, Imaging techniques
Keywords: Turner Syndrome, Lymphedema, Cardiovascular

Exploring Inflammatory Resolution Pathways to Attenuate Cardiometabolic Diseases

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Background & aim: Approx. 30% of obese individuals appear protected against diabetes, dyslipidemia, and hypertension. We aim to elucidate pathways that differentiate healthy and unhealthy cardiometabolic phenotypes, focusing specifically on inflammatory resolution. We hypothesize that the ability to regulate inflammatory resolution determines susceptibility to cardiometabolic diseases.

Material & methods: Lean, overweight, or obese volunteers are categorized as metabolically healthy or unhealthy, aiming to recruit 20 males and 20 females in each of these 6 groups. Anthropometric measurements and biologic samples (e.g. blood, urine, saliva, feces, skin, muscle, adipose tissues) are collected. We study the inflammatory resolution capacity of the patients, by blood FACS analyses coupled to a "blister model" or acute/resolving inflammation. Using explants, we also assess the therapeutic potential of the pro-resolving lipid lipoxin.

Results: To date, we have recruited 137 patients, with a median age of 68 years and evenly split between genders. Obese and overweight individuals had higher CRP levels than their lean counterparts. In addition, the obese metabolic unhealthy group had significantly higher levels of leukocytes and neutrophils than the lean healthy group.

Conclusion: This study investigates the molecular pathways underlying cardiometabolic phenotypes and their association with inflammatory resolution. By examining these factors, we strive to deepen our comprehension of metabolic diseases and explore potential therapeutic interventions for resolution of inflammation.

Themes: Endocrinology, Molecular biology
Keywords: Cardiometabolic diseases, Obesity, Inflammation

Characterizing coronary atherosclerotic plaques using Magnetic Resonance imaging

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Background: Assessing coronary plaque composition in addition to traditional luminal stenosis evaluation is essential in predicting events in patients with coronary artery disease (CAD). A high burden of lipid-rich plaques has been linked to increased risk of coronary events and mortality. Coronary Magnetic Resonance Angiography (CMRA) is a non-invasive and contrast-free method for visualization of the coronary arteries. A state-of-the-art CMRA scan, utilizing T1-weightening, has emerged for detecting lipids in coronary plaques, visualized as high-intensity plaques.

Objectives: To correlate plaque characteristics observed on T1-weighted CMRA to those visualized on coronary CT angiography (CCTA).

Methods: In the study, 78 patients who had previously undergone CCTA and exhibited at least one proximal coronary non-calcified plaque were recruited and underwent CMRA. Coronary plaques on CMRA were identified as high signal intensity areas as compared to the surrounding myocardium. CCTA were analysed using software to determine plaque characteristics such as non-calcified plaque and calcified plaque volume.

Results: In a preliminary analysis of 42 patients, 28 patients had high-intensity plaques in the coronary arteries on CMRA, corresponding to non-calcified plaques on CCTA. Analysis of the full cohort, and an assessment of plaque signal intensity on CMRA compared to plaque characteristics on CCTA is pending.

Conclusion: T1-weighted CMRA may feasibly identify coronary plaques with high-risk plaque features, albeit further refinement of the scanning protocol is required. However, CMRA holds potential to enhance CAD risk assessment without the need for ionizing radiation or contrast agents.

Themes: Cardiology, Imaging techniques
Keywords: Coronary artery disease, Atherosclerosis, Magnetic Resonance Imaging

Ketone body 3-hydroxybutyrate increases cardiac output through systemic vasorelaxation and enhanced cardiac contractility

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The ketone body 3-hydroxybutyrate (3-OHB) increases cardiac output and myocardial blood flow without affecting arterial blood pressure in humans, including patients suffering from heart failure with reduced ejection fraction. However, the cardiovascular sites of action remain unclear. In this project, we test the hypothesis that 3-OHB acts directly on blood vessels to lower afterload and directly on the heart to enhance contractility. We test effects of 3-OHB on (a) hemodynamics using invasive blood pressure measurements and echocardiography, (b) isolated arteries and veins in wire myographs, and (c) isolated perfused hearts in Langendorff systems. We compare Na-3-OHB to equimolar NaCl added to injection- and saline solutions. At plasma levels of 2–4 mM, 3-OHB increases cardiac output (by 28.3±7.8%), stroke volume (by 22.4±6.0%), left ventricular ejection fraction (by 13.3±4.6%) and lowers systemic vascular resistance (by 30.6±11.2%) without affecting heart rate or blood pressure significantly. Beginning at 1–3 mM, 3-OHB relaxes isolated coronary, cerebral, femoral, mesenteric, and renal arteries as well as brachial, femoral, and mesenteric veins by up to 60% of the pre-contraction level. In isolated perfused hearts, 3-OHB (3-10 mM) increases left ventricular developed pressure by up to 26.3±7.4 mmHg and coronary flow rate by up to 20.2±9.5%. We conclude that systemic vasorelaxation and increased cardiac contractility can explain the elevated cardiac output observed during 3-OHB administration.

Themes: Cardiology, Endocrinology
Keywords: Physiology, Hemodynamics, Metabolism

The effect of anti-activin receptor type IIA/IIB antibodies on muscle, bone, and blood in healthy and in immobilization-induced osteopenic and sarcopenic mice

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Introduction: Anti-activin receptor type IIA/IIB antibodies (αActRIIA/IIB ab) are one of a series of recently discovered drugs that target the activin receptor pathway. Inhibiting this pathway leads to skeletal muscle cell hypertrophy, bone formation, and increased hematopoiesis. The aim of this study was to investigate the effects of αActRIIA/IIB ab on muscle, bone, and blood in both ambulating mice and in mice suffering from sarcopenia and osteopenia.

Methods: Sarcopenia and osteopenia were induced by injecting botulinum toxin A in the right hindlimb of the mice causing muscle paralysis and thereby immobilization. Muscle was analyzed for mass, size, and histological appearance. Bone was analyzed for bone mineral density, bone structural properties, bone strength, and histological properties. Whole blood was analyzed for cell count, cell volume, and differential count.

Results: αActRIIA/IIB ab caused a large increase in muscle mass in both ambulating (+21.4%) and sarcopenic (+12.2%) mice. Furthermore, αActRIIA/IIB ab increased bone volume fraction for both ambulating (+64.9%) and osteopenic (+44.3%) mice at the distal femoral metaphysis. At the femoral mid-diaphysis, αActRIIA/IIB ab caused a significant increase in bone area (+5.7%) for osteopenic mice. No effect was found of αActRIIA/IIB ab treatment on hematopoiesis after either 48 hours or 7 days.

Conclusion: Treatment with αActRIIA/IIB ab caused a significant increase in skeletal muscle mass in both healthy and sarcopenic animals but did not seem to affect hematopoiesis. Moreover, αActRIIA/IIB ab treatment caused a significant bone formation in trabecular bone, while this was less pronounced in cortical bone.

Themes: Endocrinology, Animal Models
Keywords: Osteoporosis treatment, Activin pathway inhibitor, Translational medicine

Mapping niche dynamics at single-cell resolution to boost the regenerative potential of aged skeletal muscle

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Ageing is characterized by a decline in skeletal muscle mass, strength, and regenerative capacity. The condition is known as sarcopenia and leads to loss of mobility and quality of life in the aged population. Muscle regeneration is driven by muscle stem cells (MuSCs). However, MuSCs do not act alone. During muscle regeneration, the immune system plays a key role in orchestrating the rapid transition from an inflammatory to a regenerative phase. Previous studies have shown that during ageing, MuSC function declines and hematopoietic stem cells show bias toward the myeloid lineage. This suggests that immune imbalance with ageing might be impacting the MuSCs function. Here, we employed single-cell mass cytometry (CyTOF), which allows for detection of up to 50 surface or intracellular markers per single cell, to study the role of immune cells in muscle regeneration. We investigated the composition of immune cells in skeletal muscle from young and aged mice during homeostasis and through an acute injury. High-dimensional analysis utilizing X-shift software for unsupervised clustering, revealed significant differences in the proportion of several immune subpopulations between young and aged skeletal muscle. Future research will broaden our understanding of these differences and provide key insights into immune mechanisms that regulate muscle regeneration, and how they are affected by ageing. Potentially, it will support the development of new therapeutic strategies to boost muscle regeneration in the elderly population.

Themes: Omics, Public health
Keywords: Muscle stem cells, Muscle immunobiology, Inflammation

Impact of Transient Steatosis on Liver Regeneration and Post-Hepatectomy Liver Failure in Rats

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Background and aim: Transient steatosis becomes evident shortly after partial hepatectomy (PH) in rodents. This study aimed to elucidate the influence of hepatic lipid accumulation on the processes of liver regeneration and the development of post-hepatectomy liver failure (PHLF).

Methods: Rats were randomly assigned to one of the three groups: 90% PH, sham operation with midline laparotomy, or no surgery. We compared rats with fatal PHLF with rats without PHLF (recovering rats) at 24 hours after PH, as fatal PHLF was evident at this point. Proteomics and Western blotting were utilized to assess variations in protein expressions among rats with and without fatal PHLF, while stereological methods were applied to quantify the hepatic lipid content.

Results: The lipid metabolism was significantly up-regulated in rat suffering from PHLF compared to recovering rats ($p<0.001$). All rats undergoing 90% PH had an increase in hepatic lipid content relative to sham- and non-operated rats. The accumulated hepatic lipid proportion was twice as high in recovering rats (61% of the hepatocyte volume, 95% CI: 49-73%) compared to rats with fatal PHLF (29% of the hepatocyte volume, 95% CI: 19-40%). The mean lipid volume in recovering rats was measured at 2715 µm3 (95% CI: 2267-3162), whereas rats with fatal PHLF exhibited a mean lipid volume of 1611 µm3 (95% CI: 1049-2172).

Conclusion: Transient hepatic steatosis appears to serve as a promising prognostic marker for regeneration and prevention of PHLF.

Themes: Animal Models, Gastroenterology and hepatology
Keywords: Post-hepatectomy liver failure, Liver regeneration, Rat study

SESSION 37

Thriving or Surviving? A Longitudinal Inquiry into Early Career Academics' Development of Teacher Identities within the Health Sciences Education

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Research is often perceived as valued over teaching in the university context. Additionally, in the health sciences, academics typically identify more strongly with their role as researchers or practitioners (e.g., clinicians), and new academics, who are trained to do research, often remain less prepared for the teaching role. During the early career phases, academics face many challenges and tensions in shaping their professional identity. Understanding the formation of teacher identity—that is, their own ideas of "how to be", "how to act", and "how to understand their work"—in this period, is crucial in developing excellent teachers and a strong teaching culture. Therefore, the main purpose of this PhD project is to investigate the processes and critical circumstances in which early career academics develop their teacher identity in health sciences education. One study will collect experienced teachers' narratives through 7 expert interviews, to understand the critical events and circumstances that have shaped strong teacher identities within the health sciences. Another study will collect 10-15 early career academics' solicited audio diaries over a period of three semesters combined with focus group interviews in between semesters. This study will scrutinize the processes and critical conditions that are part of the academics' teacher identity formation in the early career phases. The project is expected to contribute new contextual knowledge valuable to individual teachers, as well as guidelines for educational developers and decision-makers to create proper support systems for early career academics to ensure quality teaching and retain talented teachers.

Themes: Health Education, Qualitative research
Keywords: Teacher identity, Health sciences education, Qualitative longitudinal study

Learning in a high-stake environment: how does your cognitive capacity affect surgical skills?

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Surgical residents need to acquire a vast variety of skills in high-stake environments with a high consequence of failure. Such environments require the resident to manage a high cognitive load. As cognitive capacity is limited, high cognitive load may compromise learning, surgical skills, and patient safety. However, little is known about how high-stake environments' influence cognitive load and surgical skills. By studying the association between learning environments, cognitive load, and surgical skills, the present study may guide the design of learning environments and inform how residents learn to cope with high cognitive load. Thus, we aim to study how learning environments affect learners cognitive load and their skill acquisition.

To study this, residents on a 3-day laparoscopy course are randomized to perform a suturing exercise in a high-stake or low-stake environment. The high-stake environment consists of stressors, including informing participants, that their surgical skills will be evaluated by experts, that they will be videotaped, and having an instructor observe their performance. Residents will be videorecorded while doing a suturing exercise. Recordings will be reviewed by experts to evaluate residents' surgical skills using the Objective Structured Assessment of Technical Skills (OSATS) tool. Cognitive load will be measured using the subjective self-report measures, NASA-TLX and Paas cognitive load scale. We hypothesize that residents in high-stake environments will have higher cognitive load and their surgical skills will decrease compared to low-stakes environments.

Preliminary data from three courses will be presented at the PhD-day.

Themes: Health Education, Surgery
Keywords: Medical Education, Cognitive Load, Laparoscopy

Introductory positions: How they influence postgraduate medical training and specialty choice

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Background: Specialty choice is an important step in a doctor's work life. Research on career choice has primarily focused on medical students' intentions. Much of the research is questionnaire-based and has revealed sociodemographic and life-style factors that predict preferences, but not the sense-making that takes place when the actual choice is made. In Denmark, the introductory position (IP) is a one-year employment in a specialty of interest that can be repeated in other specialties until the doctor applies for main specialist training. The objectives of the IP are described as allowing junior doctors to get familiar with a specialty before making their final choice and allowing the specialties to evaluate young doctors before accepting them.

Aims: We aim to investigate how the IP influences specialty choice and potentially identify other unanticipated benefits.

Methods. We use a qualitative, narrative approach based on document analysis, interviews, and focus groups. We will describe the background of the Danish postgraduate system by analysing documents from the national deciding bodies of postgraduate medical education. We will investigate the role of the IP in specialty choice and the road to main specialist training by interviewing junior doctors during IPs and conducting focus group interviews with doctors who have just started main specialist training.

Results: We expect to have an outline of the interview guide and theoretical framework to present in January 2024.

Conclusion: This PhD project will help redefine the purpose of the IP to best serve postgraduate medical education and recruitment to the specialties.

Themes: Health Education, Qualitative research
Keywords: Specialty choice, Postgraduate medical training, Narrative analysis

Suffering and well-being as experienced by adults with refractory epilepsy undergoing rehabilitation in a community setting and their next of kin - a qualitative study.

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Introduction: Adults with Refractory Epilepsy (RE) and their next of kin are influenced on their well-being after in-patient rehabilitation. Despite this knowledge, research on the challenges experienced by adults with RE and their next of kin is sparse, and further there is lack of knowledge on how professionals can support the well-being of both actors in the rehabilitation process in community settings.

Aim: To identify challenges faced by adults with RE and their next of kin with focus on their perceptions of suffering and wellbeing, and further to integrate this knowledge with the perspectives of rehabilitation professionals from the epilepsy field in the development of recommendations for rehabilitation care in community settings after discharge.

Methods: The project is based on a phenomenological-hermeneutic design. To gain significant insights into patients and next of kin's experiences during the rehabilitation process in a community setting the study will be based on individual in-depth research interviews with adults with RE, their next og kin and professionals.

Perspectives: The project will contribute with recommendations that promote well-being for adults with RE and their next of kin undergoing rehabilitation in community settings after discharge. The recommendations will be dedicated professionals involved in the community rehabilitation in order to bridge the in-patient rehabilitation and the community support after discharge with national and international value to both society, rehabilitation professionals, the adults with RE and their next of kin.

Themes: Qualitative research, Rehabilitation
Keywords: Phenomenology, Lifeworld-led care, Transition

Mental health of young female athletes

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In recent years, a large number of national and international elite athletes have reported on the dark side of life in elite sport and talked about problems thriving in highly competitive elite sport environments (e.g., in British cycling, Danish swimming and Danish soccer). At the same time, there has been a growing cultural and societal interest in well-being and mental health (Andersen et al. 2020; Katznelson et al 2022). Mental health in elite sport is in many ways threating virgin territory. Mental health is more than the absence of mental illness, and it is also more than an individual matter. Most research until now take a narrow approach and employ standardized test based on recognized diagnostic criteria, which fail to consider contextual variables (e.g., gender and culture) that influence the manner in which the mental ill health condition is expressed (Henriksen et al 2019). The purpose of this study is to contribute to our understanding of mental health in elite sport, especially in the context of the Danish talent development system. The study is designed as a short-term ethnographic study (Pink & Morgan 2013) following four young talented females in their everyday life. The fieldwork has moved between and connected different locations (e.g., the school, the training environment and the talents home). The design allowed us to see mental health as an alignment between the individual and the context and try to understand this complexity better. I am right now in the middle of data analyzing, but I will present some of my results on the PhD day 2024.

Themes: Qualitative research, Mental health
Keywords: Elite sport

Predicting involuntary admission in psychiatry using machine learning

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Background: Involuntary admissions (IA) to psychiatric hospitals are on the rise across Europe – including Denmark. These events can be traumatic for patients and are associated with substantial societal costs. If patients at elevated risk of IA could be identified, prevention may be possible.

Objectives: To develop and validate a prediction model for IA of patients with mental illness using machine learning trained on electronic health record (EHR) data.

Methods: EHR data from all adult patients who had been in contact with the Psychiatric Services of the Central Denmark Region between 2013 and 2021 were retrieved. From this EHR dataset, we derived ~700 structured predictors (covering e.g., diagnoses, medication, and coercive measures) and around 1200 predictors from free text using term frequency - inverse document frequency and sentence transformers. At every psychiatric inpatient discharge, we predicted IA 6 months ahead. XGBoost and Elastic Net regularized logistic regression models were trained on 85% of the dataset. Subsequently, the model with the best predictive performance will be tested on the remaining 15% of the data.

Results: The model was trained on ~36,000 prediction times distributed among ~14,000 unique patients, having ~1400 IA within 6 months distributed among ~700 unique patients. Based on training data the XGBoost model performed best, obtaining an area under the receiver operating curve of 0.783.

Conclusion: A machine learning model utilizing routinely collected EHR data can accurately predict IA. If implemented as a clinical decision support tool, this model may guide interventions aimed at reducing the risk of IA.

Themes: Mental health, Diagnostics & technology
Keywords: Psychiatry, Prediction, Machine learning

Can some childhood mental health disorders be prevented? Long-term risk of psychiatric disorders following neonatal, invasive Group-B Streptococcus disease.

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Background/ hypothesis: Invasive group B Streptococcus disease (iGBS) is the most common infection in early childhood, and can lead to several neurodevelopmental impairments. However, the risk of psychiatric disorders has not been investigated in infants with iGBS, especially iGBS sepsis. We aim to examine the association between infant iGBS (sepsis or meningitis) and the risk of psychiatric disorders from early childhood until adolescence.

Methods: A population-based cohort study using national health care data from 1997 through 2018 in Denmark. Exposed children had hospital-diagnosed iGBS during the first 89 days of life. A general population comparison cohort was sampled and matched 10:1 to the exposed cohort by sex, year of birth and gestational age.

Psychiatric disorders were defined by the International Classification of Diseases, Tenth Revision codes (ICD-10-codes). Cumulative risk (CR) of psychiatric disorder was calculated by treating death as a competing event. Cox proportional hazards regression was used to compute hazard ratios (HRs) and the associated 95% confidence intervals (CIs).

Results: The CR for the entire follow-up period (0-22 years) of any psychiatric disorder was increased in children with iGBS (22.6% (95% CI 19.4–25.9%)) compared with the comparison cohort (19.4% (95% CI 18–20.8%)). The adjusted HR for any psychiatric disorder was 1.42 (95% CI 1.22–1.66).

Conclusion: Our study finds an increased long-term risk of psychiatric disorders following neonatal iGBS. Our findings close another knowledge gap regarding neonatal, invasive infections and long-term mental health outcomes.

Themes: Epidemiology, Infectious diseases
Keywords: Group B Streptococcus, Paediatrics, Psychiatry

Early identification of postpartum depression: Possibilities of using information on personal and family history of psychiatric disorders to identify at-risk women

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Background: Postpartum depression (PPD) affects 10-15% of new mothers with negative consequences when untreated, thus early identification is essential. Personal and family history of psychiatry (PH, FH) are two of the most significant risk factors, often co-existing due to shared genes and environment. The aim of this study is to disentangle the contribution to PPD by the two risk factors and assess the potential of systematically using this information to identify women at risk.

Methods: A cohort study using Danish registers and the HOPE cohort will be conducted. From a total of 439,511 women giving birth to a liveborn child from 2015 to 2021, a subset of 170,218 women screened with the Edinburgh Postnatal Depression Scale (EPDS) will be included. Women with depression one year prior to delivery will be excluded. The exposures will be defined as any psychiatric disorder (ICD-10: F00-99) or psychotropic medication use (ATC: N05-06) in the index mother (personal history) and the index mothers' parents (family history). The outcome will be a) PPD symptoms defined as an EPDS score of 11 or above within 12 weeks postpartum, and b) PPD diagnosis defined as a depression diagnosis (ICD-10: F32-33) or redeemed antidepressant prescription (ATC: N06A) within 6 months postpartum. Descriptive characteristics of the population will be presented. Absolute and relative measures of risk will be presented for the association between PH and FH (alone and in combination) and PPD. Mediation analysis will be performed to examine the mediating effect of personal history of psychiatry on the association between family history of psychiatry and PPD.

Results: Expected at the presentation.

Themes: Mental health, Epidemiology
Keywords: Postpartum depression, Psychiatry, Mental health

Real-world effectiveness of faecal microbiota transplantation (FMT) for first or second Clostridioides difficile infection (CDI)

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Introduction: Clostridioides difficile infection (CDI) is a life-threatening disease with high mortality. Faecal microbiota transplantation (FMT) is established for recurrent CDI but its use for first or second CDI is investigational. We aimed to assess the effectiveness of FMT for early CDI in a real-world clinical setting.

Methods: This was a multi-site, cohort study including patients with first or second CDI treated with FMT in Denmark from June 2019 to February 2023. The primary outcome was cure of Clostridioides difficile associated diarrhea (CDAD) at week 8 following repeat FMT treatment. Secondary outcomes were cure at week 1 and week 8 following the first FMT treatment, and 90-day mortality following positive Clostridioides difficile test.

Results: 467 patients with median age 73 years (IQR 58-82 years) received FMT; 167 (36%) had antibiotics-refractory CDI, 262 (56%) had severe CDI, and 89 (19%) had fulminant CDI. Cure of CDAD following one or more FMT treatments was achieved in 367 patients (79%, 95% CI 75-82%). The 90-day mortality was 10% (95% CI 8-14%). Following the first FMT treatment, cure of CDAD was achieved in 353 patients at week 1 (76%, 95% CI 71-79%),

and 255 patients (55%, 95% CI 50-59%) had sustained effect at week 8 without further treatment.

Conclusion: FMT effectively treats first and second CDI. Repeating FMT improves the effect. The 90-day mortality rate is substantially lower than reported in comparable cohorts where FMT was not used regularly.

Themes: Gastroenterology and hepatology, Infectious diseases

Results of a Randomized clinical trial of MicruBurst Spinal Cord Stimulation in Parkinson's Disease (STEP-PD)

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Background: Gait impairment including Freezing (FoG), causes significant morbidity in Parkinson's disease (PD). We present the results of the first ever double-blind, placebo-controlled efficacy and feasibility clinical trial of paraesthesia-free MicroBurst spinal cord stimulation (SCS) for gait impairment in PD.

Methods: Twelve PD patients with gait impairment were enrolled as part of STEP-PD. Randomisation was 1:1 in two groups receiving either Microburst (40 Hz baseline, burst trains of 450 Hz – active group) or sham stimulation (stimulator OFF) for six months.

Main outcome was the postural instability and gait disorder subscale of the Movement Disorder Society Unified-Parkinson Disease Rating Scale (MDS-UPDRS). Further assessments were timed 20 meter walk, timed up-and-go (TUG), Berg Balance Scale and measurements from an accelerometer at baseline and at six months.

Results: We found minor improvement in the primary outcome in MicroBurst compared to sham at the end of the study period. This was not significant (ES 0.69 (95%CI interval –3.23;1.85 p=0.556). Episodes of freezing per 1,000 steps were similar in both MicroBurst and

sham groups at follow-up [ON: 0.27 (95% CI -1.24;1.78 p=0.686); OFF: -1.13 (95% CI -4.54;2.27 p=0.457): and Overall: 0.5 (95% CI -1.59;2.60 p=0.596)].

Conclusion: Results show little effect of MicroBurst on gait impairment and severity of FoG in PD at a follow-up of six months. We identified potential future means of improving outcomes, including targeted stimulation paradigms for specific sub-groups of patients. The entire cohort entered an ongoing, open label, active treatment phase for an additional six months.

Themes: Neurodegenerative disorders, Rehabilitation
Keywords: Parkinson's Disease, Neuromodulation, Rehabilitation

Co-chairs's abstracts

Incidence of type 2 diabetes after breast cancer treatment: a Danish matched cohort study

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Background: Increasing cancer survivorship means an increasing proportion of cancer survivors at risk of chronic conditions. We evaluated the impact of breast cancer (BC) and its treatments on the risk of incident type 2 diabetes (T2D).

Methods: Using Danish registries, we assembled a cohort of all Danish women aged 30 to 99 years diagnosed with incident early-stage BC during 1996-2021. We enumerated a matched comparison cohort including 5 women per BC case who were cancer- and diabetes-free, matched on age and index date. We followed both cohorts from 6 months after diagnosis to the first of T2D, emigration, death, or end of the study (December 31, 2022). We computed the incidence rate (IR) per 1000 person-years and used Cox regression to estimate hazard ratios (HR) and associated 95% confidence intervals (95%CI) of T2D, adjusting for confounding.

Results: Among 74,526 BC survivors and 372,630 matched controls, the IR of T2D was 8.0 (95%CI: 7.8-8.3) and 7.6 (95%CI: 7.5-7.6), corresponding to an adjusted HR (aHR) of 1.07 (95%CI: 1.04 – 1.10). Endocrine therapy (aHR 1.22, 95% CI: 1.16 – 1.29), chemotherapy (aHR 1.10, 95%CI: 1.03 – 1.17), and radiation therapy (right-sided; aHR 1.18, 95% CI: 1.09 – 1.27 and left-sided; aHR 1.24, 95%CI: 1.15 – 1.33) were associated with elevated risk of T2D. Among women treated with endocrine therapy, tamoxifen and aromatase inhibitors were associated with excess risk of T2D (aHR 1.08, 95%CI: 1.01 – 1.15 and aHR 1.23, 95%CI: 1.15 – 1.31, respectively).

Conclusion: BC survivors have increased risk of incident T2D compared with non-cancer controls. This excess risk is present following several cancer-directed treatment modalities.

Themes: Epidemiology, Cancer
Keywords: Breast cancer, Type 2 diabetes, Epidemiology

Interval cancer and screening outcomes at second round screening in the Danish FIT-based bowel cancer screening program

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Introduction: Colorectal cancer (CRC) screening participants with low-risk adenomas(LR) or a negative(Neg) Feacal Immunochemical Test(FIT) are recommended a new FIT after two years. However, from 2014-2017 screening intervals up till four years were allowed. This gave opportunity to evaluate screening intervals. We aimed at comparing second screening outcomes between groups and between early and late screened.

Methods: In a register-based cohort study we follow participants with LR or Neg screening results from their first CRC screening in March 2014 till June 2017 until second screening participation. We compared interval cancer(ICRC) incidence and FIT- and colonoscopy results at second screening across baseline results (Neg=ref) and across screening intervals (<2.5 vs >3years).

Results: Incidence of ICRC among 828,940 in the Neg group was 0.06% after two years, while 0.13% out of 11,698 in the LR group, RR 2.1 (1.27;3.55). A screening interval >3y nearly doubled the risk, Neg=RR 1.81(1.56;2.11), LR= RR 1.92(0.73;5.05). At screening interval <2.5y the FIT-pos rate was 4.24% rising to 4.53% at >3 years in the Neg group, while 14.7 rising to 15.59 in the LR group. The PPV for CRC was 4.03 and 4.35 at regular and late screening for the Neg group, while 2.52 and 3.53 for the LR group.

Discussion: The LR group had a twofold risk of ICRC as compared to the Neg group, which rise questions to the quality of their recent colonoscopy. ICRC nearly doubled in both groups at interval >3y, though absolute numbers were small. Increasing intervals seems reasonable if colonoscopy capacity is lacking, but requires that the LR group has received a high quality colonoscopy at first screening

Themes: Cancer, Epidemiology
Keywords: Colorectal cancer, Screening, early detection

Proteomic profiling differentiates classic Hodgkin lymphoma with and without skeletal involvement at the time of diagnosis

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Introduction: Classic Hodgkin lymphoma (cHL) is a highly curable disease, even in advanced stages. cHL is characterized by a unique tumor microenvironment (TME) consisting of few, scattered neoplastic Hodgkin and Reed-Sternberg (HRS) cells, embedded in an abundant background of reactive immune and stromal cells. When cHL disseminates, the new disease sites also contain both HRS cells and TME cells. Whether cases that present with bone lesions, harbour specific TME features is unknown.

Methods: Protein expression patterns in pre-therapeutic formalin-fixed, paraffin embedded lymph node lymphoma samples from 69 cHL patients diagnosed at AUH, DK between 2009-2018 were analyzed by nLC-MS/MS. FDG-PET/CT scans were reviewed specifically for bone involvement. The study cohort included 50 patients with nodal cHL (n-cHL) and no skeletal involvement, and 19 patients with both skeletal and nodal disease (s-cHL).

Results: We identified 2,298 proteins; comparison of the protein profiles between the s-cHL and n-cHL groups revealed 220 unique proteins significantly differentially expressed ($p<0.05$) and with a fold change of at least 25%. In hierarchical clustering based on 25 proteins with a p-value <0.001, two clusters were observed: (i) a skeletal-group comprising 12 s-cHL and 4 n-cHL samples; and (ii) a nodal-group of 46 n-cHL and 7 s-cHL samples. Of particular interest among the differentially expressed proteins, we identified IDH1 and WDFY4.

Conclusion: Our data show differential protein expressions in cHL lymph node tumor tissues that correlate with the presence or absence of concomitant bone involvement at diagnosis.

Themes: Cancer, Molecular biology
Keywords: classic Hodgkin lymphoma (cHL), proteomics,

EGLN1 is a druggable dependency in neural crest-like melanoma

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Melanoma cells can adopt transcriptional cell states that resemble different stages of embryonic development of melanocytes from the neural crest. Multiple studies have implicated a neural crest-like melanoma cell state in resistance to current therapeutic modalities, including BRAF/MEK inhibition, adoptive T cell transfer, and immune checkpoint blockade. Identification of therapeutic targets in neural crest-like melanoma cells could provide new strategies for limiting tumor cell state-related treatment resistance in melanoma. Here, we leveraged genome-wide CRISPR screen data from the Cancer Dependency Map (DepMap) to identify genetic dependencies unique to neural crest-like melanoma cell lines. DepMap analysis identified EGLN1, a key cellular oxygen sensor and regulator of the hypoxia response, as a novel dependency in neural crest-like melanoma cells. In vitro studies confirmed loss of fitness following EGLN1 deletion in neural crest-like melanoma cells, which was phenocopied with a small molecule pan-EGLN inhibitor (FG4592). Consistent with the known cellular function of EGLN1, both HIF1a and HIF2a are stabilized following either EGLN1 knockout or pharmacological inhibition, although the growth inhibitory effect of FG4592 was rescued with deletion of HIF1a, but not HIF2a. Characterization of FG4592 treated cells revealed HIF1a-dependent G0/G1 cell cycle arrest and metabolic rewiring with increased glycolysis and decreased oxidative phosphorylation. Collectively these findings suggest that targeting EGLN1 may represent a novel therapeutic strategy for neural crest-like melanoma cells to counteract the development of dedifferentiation-related treatment resistance.

Themes: Cancer, Molecular biology
Keywords: Cancer, Melanoma, EGLN1

Benefit of range uncertainty reduction in robust optimization for proton therapy in brain, head-and-neck and breast cancer patients

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Purpose: The primary cause of range uncertainty (RU) in proton therapy is the CT-based estimation of the stopping-power ratio relative to water. This study examined the dosimetric impact of reducing the RU in the robust optimization for a varied patient population and determined the level of RU that led to a clinically relevant reduction in dose to the organs-at-risk (OARs).

Methods: Treatment planning CT scans of 40 adult patients with brain (N=30), head-and-neck (HN; N=5) and breast (N=5) cancer were included in the study. Six new plans were robustly optimized for each patient with varying levels of RU (ranging from 3.5% in the original plan to 1.0%). All plans were based on the initial clinical treatment plan's beam directions and optimization objectives. The robust optimisation and evaluation included fourteen scenarios, combining setup and range errors. Each plan was optimized until a clinically acceptable plan was obtained for all setup and range scenarios. The dosimetric effect of a reduced RU was evaluated for the OARs near the target.

Results: Reducing the RU in the treatment plan slightly reduced the nominal dose to the surrounding tissue. For the body volume receiving 80% of the prescribed dose, a reduction in RU from 3.5% to 2.0% resulted in an average decrease of 6 cc for brain, 19 cc for HN, and 22 cc for breast cancer patients.

Conclusions: Reducing RU in robust optimization showed a reduction in dose to OARs. The clinical relevance depends on the affected organs and the clinical dose constraints.

Themes: Cancer, Imaging techniques
Keywords: Proton therapy, Robust optimization, Range uncertainty reduction

Combining checkpoint inhibitors with other established cancer therapies to improve effectiveness in solid tumors.

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Introduction: A ton of research is done to establish different combinations in clinics, where radiotherapy or chemotherapy is given to make the tumor more immunogenic. This is crucial for solid tumors, as they are largely known to be poor immunotherapy candidates. We want to see the effects of combining one of the inhibitors (anti-CTLA-4; cytotoxic T lymphocyte associated protein - 4) with medications that have been shown to have dual-purpose cell-killing mechanisms as well as influence tumor immunogenicity. These include proton radiation therapy and the blood vessel-distorting medication, OXi4503.

Objectives: To investigate the critical factors influencing tumor growth inhibition seen when we combine anti-CTLA-4 with either proton radiation, or OXi4503. Materials & Methods: All experiments used C3H mammary carcinoma grown in the right rear foot of CDF1 mice. Treatments were started when tumors were at specific size of 50-400 mm3. These included either proton radiation (5 - 20 Gy on day 0), or OXi4503 (50 mg/kg, injected i.p. on days 0, 3, 7, and 10) and was combined with anti-CTLA-4 (injected i.p. on days 1, 4, 8, and 11). The assay used was tumor growth time and number of days for tumors to reach 1000 mm3 was our endpoint.

Results & Conclusions: Our Tumor model is generally unresponsive to Anti-CTLA-4 as a single therapy agent. An enhanced response was obtained when it was combined with either proton radiation or OXi4503. With increasing tumor size, the enhancement decreases, indicating negative co-relation between tumor size and the resulting efficacy of the combination therapy. The enhancement is dependent on the extent of damage done prior to anti-CTLA-4 treatment.

Themes: Cancer, Animal Models
Keywords: Proton Radiation, Vascular Disrupting Agent, Checkpoint Inhibition Therapy

Targeting macrophage heterogeneity in ovarian cancer using a lipid nanoparticle-based system

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In ovarian cancer, macrophages are the most abundant non-cancerous cell in the tumor microenvironment, and these tumor-associated macrophages (TAMs) help orchestrate immunosuppression, angiogenesis, metastatic spread and many other aspects, which in turn, facilitates disease progression. However, pan-depletion of TAMs as a treatment strategy has shown limited efficacy in clinical trials, and single cell RNA-sequencing (scRNA-seq) has revealed extensive heterogeneity in the TAM compartment. This implies that utilizing macrophage heterogeneity is the key to unlocking the therapeutic potential of TAMs.

Combining scRNA-seq with high dimensional immunophenotyping of macrophages using spectral flow, we have identified Cx3cr1, F11r positive macrophages, that accumulate in the omentum as the tumor grows. Furthermore, this population peaks 5 weeks after inoculation, as the ovarian cancer starts spreading to the other organs in the peritoneal cavity. Moreover, the expression of F11r is induced by TGF-beta signaling, indicating that the population could have a pro-tumoral phenotype. Using our targeted lipid-nanoparticle based platform, we can deliver RNA based tools to modify the function, using siRNA, CRIPSRa or CRISPRi. This tool can be used to evaluate the effect of this Cx3cr1, F11r positive population in ovarian cancer, and how important signaling pathways, such as TGF-beta are involved in their phenotype.

Themes: Cancer, Molecular biology
Keywords: Cancer-immunology, Immunology, Lipid nanoparticles

Identification of extrachromosomal circular DNA in the blood of non-small cell lung cancer patients

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Introduction: In the last decade, a substantial focus has been on exploring circulating tumor DNA, ctDNA, in cancer research. However, it is important to note that not all tumor DNA is linear and located in the chromosome. The genomic instability associated with cancer can result in the formation of double-stranded circular DNA fragments that reside outside of the chromosomes, referred to as extrachromosomal circular DNA, eccDNA. The aim of this project is to use blood samples from non-small cell lung cancer, NSCLC, patients to detect and evaluate the potential of eccDNA as a biomarker.

Methods: Cell-free DNA was isolated from blood samples from 32 patients with NSCLC before start of treatment. The DNA was digested with a plasmid-safe ATP-dependent DNase to isolate eccDNA from linear DNA. The eccDNA was sonicated to shorter linear fragments and sequenced using short-read next-generation sequencing. The eccDNA was identified using the Circle_Finder tool, which detects unique circular fragments based on the identification of a junctional tag.

Results: A median number of 44,475 eccDNA (range 6,434 to 276,742) was identified. The eccDNA had lengths ranging from 33 to 244,825,049 base pairs, with a median of 354,5 base pairs and the majority of the eccDNA having a length below 2000 base pairs (92.7 to 99.8 % of the eccDNA). The eccDNA showed a distinct bimodal size distribution with peaks at 190 and 320 base pairs, corresponding to the length of one or two nucleosomes.

Conclusion: eccDNA is present in the blood of patients with NSCLC and can be detected using the Circle_Finder algorithm. Future studies will further investigate the potential of eccDNA as a biomarker in NSCLC.

Themes: Cancer, Omics
Keywords: Circulating tumor DNA, Extrachromosomal circular DNA, Non-small cell lung cancer

UNRAVELING THE SYNERGY BETWEEN FRACTIONATED STEREOTACTIC BODY RADIOTHERAPY (SBRT) AND HYPERTHERMIA IN A TUMOR BEARING MOUSE"

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Introduction. Stereotactic Body Radiotherapy (SBRT) is known for its superior cancer cells killing, inducing radiation resistance hypoxic cancer cells which are sensitive to hyperthermia. Combining SBRT with heat presents promising therapeutic outcomes. Our unpublished data showed positive results in tumor control using specific fractionated SBRT doses and hyperthermia (41.5°C for 1 hour with a 30-minute interval), preserving healthy tissues. This study aims at exploring the effects of 3 fractions of 15 Gy SBRT doses combined with hyperthermia at varying temperatures and intervals on tumor growth.

Methods: C3H mammary carcinomas were implanted in the rear legs of CDF1 mice and tumors treated at around 200 mm^3 with three 15 Gy fractions using photon or proton. Other animals received the same radiation doses plus a single hyperthermia treatment at temperatures of 40.5°C, 41.5°C, or 42.5°C for 1 hour, at 30, 90, or 180 minutes after the final irradiation fraction. Study ended as tumors reached three times their initial treatment volume (TGT3) or tumor control 90 days post-treatment. Student t test is used to compared various results with $P<0.05$ set as level of significance.

Results: Preliminary data shows that at shortest time interval between the application of SBRT and heat and at a higher temperature, tumors took longer days in animals to grow to 3 times their starting treatment volume for both photon and proton animal groups.

Conclusion: The combination of fractionated SBRT doses with a singular hyperthermia shows a synergistic effect in treating C3H mammary carcinoma in vivo. This synergy is most prominent at higher temperatures and shorter time intervals.

Themes: Cancer, Cancer
Keywords: Angiogenesis, Tumor Microenvironment, Hypoxia

Diagnosis and staging of hepatocellular carcinoma using biomarker-directed aptamer panels

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Background: Hepatocellular carcinoma (HCC) is the fourth leading cause of cancer-related death globally, and most tumors are detected at the late stages of the disease. Screening at-risk patients with ultrasound has acceptable sensitivity for detecting HCC at any stage but less so in detecting early stages. Thus, novel biomarkers are needed to detect early-stage HCC, as cure rates decrease with later stages.

Methods: We investigated the ability of a novel platform named APTASHAPE to develop protein biomarker-directed aptamer panels to stratify healthy individuals from individuals with HCC and distinguish individuals with HCC based on disease severity. We included 92 individuals with HCC and 24 healthy controls and divided them into a development and a test set.

Results: A panel developed to distinguish individuals with HCC based on their Tumor, Nodes, and Metastasis (TNM) stage accurately stratified healthy controls from TNM stages 1A, 1B, and 2 with an area under the receiver operating characteristics curve (AUC) value of 0.77 in the development set and 0.79 in the test set. In the panel developed to distinguish individuals based on their Barcelona Clinic Liver Cancer (BCLC) score, the distinction between healthy individuals and BCLC stages 0, A, and B had an AUC of 0.84 in the development set and 0.92 in the test set. Further, the panels discriminated early and late-stage HCC with AUC of 0.83 and 0.66 for TNM and 0.67 and 0.57 for BCLC in the development and test set, respectively.

Conclusion: In summary, the APTASHAPE platform is a promising unbiased tool to develop panels for identifying individuals with HCC and could potentially unveil novel protein biomarkers.

Themes: Gastroenterology and hepatology, Cancer
Keywords: Hepatocellular carcinoma, Aptamers,

The association between markers of socioeconomic position and risk of infection after surgery for hip fracture: a nationwide cohort study of 54,853 Danish patients

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Background: Infections are among the most frequent and serious complications after hip fracture surgery. Although markers of low socioeconomic position (SEP) are reported to be associated with elevated mortality after hip fracture, it remains unclear whether SEP is also associated with a higher risk of infections.

Method: Utilizing Danish population-based medical registries we obtained individual-level data on SEP markers (education, liquid assets, marital status, and cohabitation) of patients surgically treated for hip fracture (2010-2017). The outcomes were any hospital-treated infection and any community-treated infection, within 1 year of surgery. We computed cumulative incidences and used Cox regression to calculate adjusted hazard ratios (aHR) with 95% confidence intervals comparing patients within each SEP marker.

Results: The cumulative incidence of hospital-treated infection varied from 28.0% to 33.4%, whereas the cumulative incidence of community-treated infection varied from 55.0% to 64.4%, by SEP markers.

All markers of low SEP were associated with increased risk of both hospital-treated and community-treated infections. For instance, the aHRs for hospital-treated infections were 1.06 (1.00-1.12) for patients with low vs. high education, 1.25 (1.21-1.31) for low vs. high liquid assets, 1.29 (1.22-1.35) for divorced vs. married, and 1.11 (1.05-1.18) for living alone vs. cohabiting. The aHR for community-treated infection was 1.50 (1.44-1.57) for nursing home vs. cohabiting.

Conclusion: Not cohabiting, any unmarried status, low liquid assets, and low education were associated with increased risk of infection up to one year after hip fracture surgery.

Themes: Epidemiology, Public health
Keywords: Hip fracture, Infection, Socioeconomic position

Potentially prevetable hospital admissions – characteristics and potentials for prevention in the home care setting

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Background: The number of acute hospital admissions are rising. Recent years public and political attention has been drawn to health care providers in the municipalities and their role in prevention of hospitalisations for ambulatory care sensitive conditions (ACSCs). In Denmark, ACSCs include 9 conditions, e.g. urinary tract infection, pneumonia, and dehydration. Acute hospital admissions for these conditions are deemed preventable for people aged +65 years. However, multimorbidity increases the level of complexity in the efforts made in primary care, and the impact of multimorbidity on ACSCs is sparsely described.

Aim: This study aims to gain a comprehensive understanding of potentially preventable acute hospital admissions with a focus on municipal health care practices compared and related to patient and organisational characteristics. This is done by:

1) thoroughly describing patterns in a population of patients acutely admitted with ACSCs to a Danish hospital in the period 2013-2018 and the association between multimorbidity and readmissions in this population

2) exploring the practices in the home care setting to prevent or avoid admissions for ACSCs.

Method: Two quantitative register-based studies with data from the National Patient Registry, and one qualitative ethnographic study based on field observations from two Danish municipalities are carried out. Within a mixed-method framework inspired by Creswell, the studies are combined in a convergent design where finding from quantitative and qualitative studies are merged.

Themes: Public health, Epidemiology
Keywords: Acute hospitalisation, Multimorbidity, Prevention

Cross-dataset cancer detection from cell-free DNA fragment coverage correlations with open chromatin sites across hundreds of cell & tissue types

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Changes in cell-free DNA (cfDNA) fragmentation patterns have been used to detect and subtype cancers within single datasets. We present a novel cancer detection method that generalizes across multiple datasets and their differing cancer types. The method correlates bias-corrected fragment coverage across the genome with the presence of open chromatin sites for hundreds of different cell & tissue types and applies machine learning to the correlation coefficients. The generalization of the method is tested via cross-dataset-validation. Our work highlights the necessity and challenges of developing methods that generalize to out-of-cohort data, as required for future clinical use.

Themes: Bioinformatics, Cancer
Keywords: Cancer Detection, Cross-Dataset Generalization, Cell-Free DNA Fragmentomics

Longitudinal alcohol consumption trajectories and risk of breast cancer among postmenopausal women – a Danish cohort study

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Background: Despite alcohol consumption being an established risk factor for breast cancer (BC), few studies have evaluated how the dynamic nature of drinking behavior over the lifespan influences the risk of BC. This study aimed to estimate trajectories of alcohol consumption during adulthood and investigate their associations with risk of primary malignant BC among postmenopausal women.

Methods: At baseline, 28,720 women aged between 50-65 years from the Danish Diet, Cancer and Health Cohort recalled their average alcohol intake during the past 12 months and at the ages of 20, 30, 40, and 50 years. Alcohol consumption trajectories were estimated using latent class mixed models. To examine the association between alcohol consumption trajectories and BC, we fitted Cox proportional hazard models using data from 24,543 women weighted by the mean posterior probabilities of latent class membership and adjusted for potential confounding factors.

Results: We identified 4 distinct mean alcohol consumption trajectories. During a median follow-up of 16.5 years, 1,591 cases of BC occurred. An alcohol consumption trajectory characterized by a consistently high (>10g/day) alcohol intake with some variation in early adulthood was associated with risk of BC (HR: 1.24, 95%CI: 1.04-1.49) compared to a continuously low alcohol intake throughout adulthood. No association with BC was found for the remaining trajectory profiles.

Conclusion: In this large cohort, postmenopausal women who followed a consistently high alcohol consumption pattern throughout adulthood had a higher risk of BC compared to women with a consistently low intake of alcohol intake.

Themes: Epidemiology, Cancer
Keywords: Alcohol consumption, Breast cancer, Latent class mixed models

Polypharmacy in pregnancy on the rise: Study on 1.4 million Danish pregnancies from 1998 to 2018

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Introduction: Today more women enter pregnancy with preexisting comorbidity and therefore with potential exposure to polypharmacy (concomitant intake of more than one type of medication). This study aims to describe the temporal change of prescription medications in pregnancy in Denmark from 1998 to 2018 with special focus on polypharmacy, patterns of use, and the underlying demographics.

Methods: A Danish nation-wide historical registry study based on all clinically recognized pregnancies with a gestational age ≥ 10 weeks between 1998 and 2018. Medication use was estimated by redemption of prescriptions in pregnancy.

Results: Among 1 402 327 clinically recognized pregnancies, the redemption of at least one prescription medication in pregnancy increased from 56.9% in 1998 to 63.3% in 2018 parallel to polypharmacy (24.8% in 1998 to 35.2% in 2018). The use of medications for chronic conditions increased more than the use for occasional/short-time conditions. Redemption of prescription medications in pregnancy is mostly seen among pregnant women ≥ 35years of age, whereas the pregnant women <25 years experienced the biggest increase in use of medication during the study period.

Discussion: Use of prescription medication, including polypharmacy, increased from 1998 to 2008, possibly explained by an increased prevalence of pregnant women with pharmacologically treated chronic conditions and striking differences in medication use among maternal age groups over time. Future studies should investigate the risk of polypharmacy and its accompanying risk of harmful maternal and fetal risks.

Themes: Gynecology and obstetrics, Epidemiology
Keywords: Perinatal pharmacoepidemiology, Polypharmacy, Temporal trend

The association between airborne microbial diversity and load, and allergic respiratory diseases – a Northern European study

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Allergic diseases are on the rise and affect myriads of people worldwide. While studies have suggested a diverse and abundant airborne microbiome to reduce the risk of allergic respiratory diseases in children, this link has not yet been established in adults.

We aimed to investigate the association between the airborne microbiome and allergic respiratory diseases in adults. We hypothesized that decreased microbial diversity and load would be associated with a higher prevalence of allergic respiratory diseases.

In 2011-2014, 1038 participants from the follow-up of the European Community Respiratory Health Survey, ECRHS III, collected settled dust in their bedrooms. The dust samples were analyzed for microbiome composition and load by 16S rRNA sequencing and qPCR. Information on diseases was derived from questionnaires. Analyses were stratified by atopic status (from specific IgE and skin prick tests), and performed using logistic regression, adjusted for sex, age, smoking, and study center.

An increase in bacterial load was found to be associated with more non-allergic asthma, both active (OR per IQR 1.24 (1.02-1.46) and ever (1.18 (1.05-1.33)). The same was seen for non-allergic rhinitis (1.12 (1.01-1.25)), whereas an opposite association was seen for allergic rhinitis (0.87 (0.72-1.03)). These results were not found for bacterial richness or Shannon Index. There were no significant association between the microbial indices and chronic rhinosinusitis or atopic status.

The results suggest a link between bacterial load and allergic diseases for adults. The results were, however, not consistent.

Themes: Epidemiology, Public health
Keywords: Microbiome, Allergy, Respiratory health

Pre-pregnancy BMI and likelihood of reaching active phase of induced labor. Study protocol for a cohort study

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Background: In 2022, the Danish rate of labor induction was 22%. Obesity, defined as a Body Mass Index (BMI) ≥30 kg/m2, is associated with a high risk of complications in pregnancy and labor. In consequence, women with obesity are more likely to undergo labor induction. Labor induction includes medical or mechanical methods or a combination of both. The preferred method depends on different factors like parity and previous history, cervical ripeness, or local or national policies. When inducing labor, the effect of the induction procedure may vary. In some cases, individuals may not even progress into the active phase of labor, which is the threshold where the induction process itself is considered successful. It has been demonstrated that increasing BMI is associated with an increased risk of Caesarean delivery following labor induction. However, if maternal BMI is associated with the likelihood of reaching the active phase of labor remains unknown.

Objective: To investigate the association between maternal BMI and the likelihood of reaching active phase of labor.

Methods: This cohort includes term induction of labors in the Central Denmark Region from 2013 to 2022 (approx. 28,000 labors). To investigate a possible nonlinear association, a logistic regression analysis is performed. Data are modelled using restricted cubic spline analyses. The model is adjusted according to potential confounders.

Results: No results are available for presentation.

Perspectives: Results of this study provides knowledge about labor induction and adds key information to an on-going discussion of the overall effects of labour induction.

Themes: Gynecology and obstetrics, Epidemiology
Keywords: Induced labor, Obesity, Adverse pregnancy outcomes

Development and validation of a machine learning model for prediction of severe mental disorder in patients with mental illness

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Background: Schizophrenia and bipolar disorder are among the most debilitating mental disorders, strongly affecting the ability to lead a normal life. Though both disorders usually have their onset early in life it often takes years before a correct diagnosis is made, which delays adequate treatment and leads to a progressively worse prognosis for the patients.

Objectives: To develop and validate a prediction model for the transition to schizophrenia and bipolar disorder among patients initially diagnosed with less severe mental illness using machine learning trained on electronic health record (EHR) data.

Methods: EHR data from all adult patients who had been in contact with the Psychiatric Services of the Central Denmark Region between 2013 and 2021 were retrieved. From this dataset, we derived a large number of structured predictors (e.g. diagnoses, medication), as well as features derived from free text. Before every outpatient visit, we predicted the risk of transitioning to schizophrenia or bipolar disorder within the following two years.

Results: Analyses are currently ongoing and will be presented at the PhD Day.

Themes: Bioinformatics, Mental health
Keywords: machine learning, natural language processing, mental health

Challenges in nutritional and physical activity support for patients with COPD exacerbation: Insights from an observational study in Pulmonary Wards

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Background: Malnutrition and low muscle mass are frequent conditions for patients with Chronic obstructive pulmonary disease (COPD), leading to increased exacerbation of COPD, hospitalization, and early death. This project aims to develop a person-centred intervention that promotes nutritional and physical activity support to patients with COPD and their relatives during admission and after discharge. Identifying the current practices for nutritional and physical activity support for admitted patients with COPD is a part of the intervention development process.

Aim: To explore actions, factors, and interactions between the patients and the healthcare professionals that facilitate or hinder nutritional and physical activity support for admitted patients with acute exacerbation of COPD.

Methods: This study adheres to the Medical Research Council framework for complex interventions. Eighteen field observations were conducted across three pulmonary wards, complemented by eleven follow-up interviews with multiple healthcare professionals, conducted between November 2020 and November 2022. The collected data were coded using NVivo and analyzed through inductive qualitative content analysis.

Preliminary results: Nutritional and physical activity support during hospitalization rarely takes place. Patients, though motivated, lack proper assistance. Effective nutrition support occurs when healthcare professionals engage with patients about their meals. However, task delegation leads to a loss of patient-specific nutrition information and accountability in providing adequate nutrition and physical activity support during hospital stays.

Themes: Public health, Qualitative research
Keywords: COPD, Complex interventions, Person-centred support

R953C Mutation in SORL1 Gene Causes Functional Abnormality of the Protein

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Background: The SORL1 (Sortilin Related Receptor 1) gene encodes for an endosomal sorting receptor, SORLA, and recent genetic studies have shown that it is the gene most frequently affected in patients with Alzheimer's disease (AD). In the current study, we have identified a variant, R953C, (residing in the YWTD-domain of SORLA) in a family where it segregates with early-onset AD. We used cell biological assays to evaluate maturation and sorting defects of the mutant receptor.

Method: To investigate molecular consequences of R953C mutation, we transiently expressed SORLA-WT and SORLA-R953C in HEK293 and N2a cell lines. We analyzed the maturation and shedding of the receptor by Western blotting. Using flow cytometry, we determined the cell surface expression of the mutant compared to WT. Finally, the intracellular localization of the mutant was assessed by immunocytochemistry and confocal microscopy.

Result: We observed a significant decrease in the maturation and shedding of the mutant receptor, leading to an overall 80% reduction in soluble SORLA present in the culture media of cells transfected with R953C construct compared to WT. Our flow cytometry analysis demonstrated that in 80% of the cells expressing the mutant receptor, the SORLA protein is retrained intracellularly. In comparison, only 10-15% of cells expressing the WT receptor showed intracellular retention. Within the cells, the R953C mutant receptor was primarily localized to the endoplasmic reticulum (ER) whereas the WT was mainly localized to the endosomes, suggesting the retention of the mutant in the ER and uncovering possible defects in entering the endosomal sorting pathway.

Conclusion: In conclusion, we have elucidated some of the molecular mechanisms that appear to have a role in pathogenicity of R953C mutation.

Themes: Neurodegenerative disorders, Molecular biology
Keywords: SORL1, Alzheimer's disease, R953C

Airway Dynamics Affect Respiratory-Modulated Brain Oscillations

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In this study, we investigate the profound influence of airway modulation on the intriguing phenomenon of breath-brain coupling in human subjects. Utilizing state-of-the-art magnetoencephalography and concurrent breathing measurements, we conducted a comparative analysis of Respiratory-Modulated Brain Oscillations (RMBOs) during both oral and nasal breathing. Our results unequivocally demonstrate the pivotal role of nasal breathing in the generation of RMBOs. This finding sheds light on the physiological mechanisms underlying respiratory-brain interactions, emphasizing the importance of nasal breathing in modulating brain activity. This work contributes to a deeper understanding of the intricate connections between respiration and brain activity, with implications for both basic neuroscience research and clinical applications.

Themes: Neuroscience, Statistics
Keywords: Brain-Body-Interaction

Neurofilament Light Protein as Early Biomarker of Chemotherapy-Induced Peripheral Neuropathy.

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Chemotherapy-induced peripheral neuropathy (CIPN) is a chronic, disabling, and potential painful condition with no treatment seen in cancer patients treated with neurotoxic chemotherapy. Neurofilament light protein (NfL) is a structural protein found in nerve axons. Upon nerve damage NfL is released and detectable in blood.

The aim of the study was to examine the effect of oxaliplatin on NfL levels both on cellular level invitro and in blood samples from patients receiving oxaliplatin to evaluate the potential of NfL as an early biomarker of CIPN.

Human sensory neurons were developed from induced pluripotent stem cells and exposed to clinically relevant concentrations of oxaliplatin. Axonal damage was assessed using immunolabeling and high-content imaging. Following oxaliplatin exposure, the medium of the human sensory neurons was collected, and NfL levels were quantified using single-molecule array (SIMOA).

Patients diagnosed with colorectal cancer undergoing chemotherapy treatment with or without oxaliplatin were included. Symptoms of CIPN was documented and accumulative dosage and treatment regime was logged. Blood samples were taken; prior to, 3 months and 6 months after treatment start. NfL levels were analyzed using SIMOA.

In vitro oxaliplatin caused axonal damage to human sensory neurons in a concentration-dependent manner, and it correlated to NfL secretion from the neurons. In the clinical study, 20 patients treated with oxaliplatin and 10 without oxaliplatin were included and data suggest a correlation. Results from both setups will be presented at full at the PhD day 2024.

Themes: Cancer, Neuroscience
Keywords: Biomarker of CIPN, Neuropathy and pain, Neurofliament light protein

" We're the very bottom, so it's going to be hard to 'catch any fish' around here..." Understanding vulnerable Greenlanders' perspectives on cancer and barriers to screening in Denmark – A qualitative study

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BACKGROUND: Cancer poses global health challenges. Indigenous groups, like Greenlanders in Denmark, experience notable disparities in cancer risk, incidence, diagnosis, care, and outcomes. This study explores their cancer perceptions, screening barriers, and intervention potential, seeking to identify content and facilitators for higher screening participation.

METHODS: The study was based on a qualitative ethnographic design, utilising participatory observations and qualitative interviews. The sample comprised 46 participants from four distinct drop-in centres. Of these, 28 were vulnerable Greenlanders (19 women and 9 men), 9 were staff members (9 women and 3 men), and 6 were relatives (4 women and 2 men). The data were analysed through inductive content analysis.

RESULTS: Vulnerable Greenlanders in Denmark find it challenging to manage their own health and many depends on support from others. Fear of cancer and death shape their attitudes towards screening. However, participation in cancer screening programmes is positively viewed for most but can be challenging. Different intervention ideas raised by the Greenlanders, relatives and staff members can guide the development of strategies to increase participation rates.

CONCLUSION: This study is an important step towards reducing cancer disparities among vulnerable Greenlanders in Denmark. Despite facing a range of challenges, they recognised the benefits of early detection and overall expressed a desire to participate in screening. They emphasised the importance of regular awareness delivered through compassionate face-to-face interactions.

Themes: Cancer, Qualitative research
Keywords: Healthcare disparities, Vulnerable groups, Screening

Three birds with one stone: A cluster-randomised trial using breast cancer screening as an opportunity to offer self-sampled screening for cervical and colorectal cancer screening.

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BACKGROUND: The Danish breast cancer (BC) screening programme has a higher participation rate (83%) as compared to cervical cancer (CC) and colorectal cancer (CRC) screening (both 60%). Non-participation is often not a deliberate choice. The study aimed to evaluate an offer of self-sampling kits for non-participants in CC and CRC screening while attending BC screening.

METHODS: A cluster-randomised study was conducted from Sept. 2021 to May 2022. On 100 selected days, five Danish BC screening units were randomised 1:4 to serve as intervention or control units.

Women attending BC screening at the intervention unit were offered an administrative check-up on their screening status in CC (50-64 years) and CRC screening (50-69 years). Women overdue with CC and/or CRC screening were offered self-sampled screening.

Concurrently, a questionnaire to evaluate the intervention from a user-perspective was sent to women in both groups.

RESULTS: A total of 27,116 women were included in the trial with 5,618 and 21,498 in the intervention and control group, respectively.

Main outcome will be the difference in coverage between intervention and control group six months after the intervention, and difference in participation between intervention and control group for women overdue with CCU and/or CRC at breast cancer screening six months after the intervention

CONCLUSION: Offering self-sampling to women overdue with CC and CRC screening when attending BC screening was a feasible intervention. Final results of main outcomes will be presented at the PhD day.

Themes: Public health, Cancer
Keywords: Cancer screening, Preventive care, Randomised controlled trial

Distributed leadership in quality improvement collaboratives in health care

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Introduction: Distributed leadership (DL) has been suggested for describing patterns of influence in collaborative settings where health care services are performed across professions and organizations. This PhD sub-study explores how leadership in quality improvement collaboratives (QICs) within health care is characterized by aligned DL practices, and how these practices relate with experienced progress and achievements in the quality improvement (QI) work.

Methods: The analysis relied on a qualitative, multi-case study of two nationwide Danish QICs. Data consisted of 12 single-person and 21 group interviews with local QI teams and local and regional QIC coordinators (85 informants in total), participant observations of 34 meetings within the QICs, and collection of documentary material. Data was analyzed thematically with NVivo.

Results: Leadership practices in local QI teams are characterized by aligned DL, with leadership activities being widely distributed based on negotiated, emergent practices regarding the aims, roles, and scope of the QI work. Yet local coordinators play a pivotal role in facilitating the QI activities, and hierarchical support from formal managers is a precondition for the contribution of aligned DL to experienced progress and achievements in the QI work.

Discussion: To provide the best circumstances for robust QI, the emergent DL should be balanced by thorough consolidation of the practices. The active participation of formal managers and local coordinators is pivotal for this consolidation and is decisive for the increased potential for long-term achievements and sustainability of the QI work, particularly within complex QICs.

Themes: Qualitative research, Public health
Keywords: Quality improvement, Distributed leadership, Implementation

Heat shock protein 90 inhibition ameliorates atopic dermatitis-like inflammation in primary human keratinocytes and mice

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Heat shock protein 90 (HSP90) is a key protein that folds and promotes the activity of many client proteins. Recent studies suggest that inhibition of HSP90 may be a novel approach to treating inflammatory skin diseases, but this has not been investigated for atopic dermatitis. The aim of this study was to evaluate HSP90 as a novel drug target in atopic dermatitis. Primary human keratinocytes were stimulated with TNF/IFNγ or TNF/IL-4 to induce an atopic dermatitis-related gene expression (in vitro). In addition, MC903 (calcipotriol) was applied daily to the right ears of mice to establish an atopic dermatitis mouse model (in vivo). When measured by RT-qPCR in primary human keratinocytes, RGRN-305 (a HSP90 inhibitor) suppressed the gene expression of key cytokines and chemokines associated with atopic dermatitis (e.g., CCL17, CCL22, TSLP). In addition, using western blotting, RGRN-305 reduced the phosphorylation (i.e., activity) of STAT3 and STAT6. Furthermore, we discovered that topical and oral RGRN-305 ameliorated atopic dermatitis-like inflammation in mice by reducing the clinical findings of dermatitis (swelling and redness), gene expression of key cytokines (e.g., Il4, Il6, Il13) and skin infiltration of immune cells (T cells, mast cells, neutrophils,). RNA sequencing analysis of the skin tissue showed that RGRN-305 mitigated MC903-induced transcriptome alterations and suppressed genes implicated in inflammation and the JAK-STAT signalling pathway. In conclusion, HSP90 inhibition ameliorated inflammation in experimental models of atopic dermatitis, suggesting that HSP90 may be a novel drug target in atopic dermatitis.

Themes: Immune diseases, Animal Models
Keywords: atopic dermatitis, heat shock protein 90, novel drug target

siRNA-nanoparticles for knockdown of phagocytosis checkpoint genes in human macrophages

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Background: Macrophages are innate immune cells involved in important homeostatic functions such as host-defense, tissue repair, and phagocytosis. In cancer, macrophages often accelerate tumor progression and metastasis. Methods to regulate macrophage behavior could therefore provide new opportunities for immunotherapy.

Methods: We prepared siRNA-loaded lipid nanoparticles (siRNA-LNPs) against genes that regulate macrophage phagocytosis of tumor cells (SIRPα, LILRB1, and Siglec-10). We transfected human monocyte-derived macrophages in vitro and monitored gene and protein knockdown by RT-qPCR and flow cytometry.

Results: Transfection with siRNA-LNPs efficiently reduced target gene expression. Relative to untreated macrophages (100%), mean [95% CI] mRNA expression at 48 h after transfection was 2.99% [-7.27%;12.60%] for SIRPα, 9.71% [-0.52%;19.66%] for LILRB1, and 1.76% [-6.18%;9.54%] for Siglec-10. Combination treatments with multiple LNPs achieved comparable results to single treatments. For example, mean [95% CI] mRNA expression of LILRB1 at 48 h was 9.36% [-2.68%;21.40%] for single vs. 8.92% [1.48%;16.35] for combination treatment, while the median fluorescence intensity of LILRB1 protein at 72 h was 32.57% [20.36%;44.79%] for single vs. 21.40% [12.41%;30.38%] for combination treatment.

Conclusion: Our results suggest that siRNA-LNPs enable efficient knockdown of multiple genes in human macrophages. Future studies should determine their potential to modulate macrophage anti-tumor behavior and enable macrophage phagocytosis of tumor cells.

Themes: Cancer, Immune diseases
Keywords: Macrophages, Immunotherapy, Phagocytosis

End-of-Life Care at ICUs: A Survey among Scandinavian Intensivists

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BCKGROUND: Intensive Care Units (ICUs) are important locations for providing End-of-Life (EOL) Care for the dying patient. Current literature shows that geography, culture and religion may play a significant role in EOL strategies in ICUs around the world. We aimed to examine knowledge and attitudes of EOL care for dying patients among Scandinavian intensivists.

METHODS: A questionnaire was sent to approximately 200 ICU physicians in Denmark, Sweden, Norway, Iceland and Finland. The questionnaire consisted of: (1) Background information about respondents age, gender, experience, working institutions and existing guidelines in EOL care (local, regional and national), (2) ICU physicians' level of knowledge and confidence in performing EOL care in ICU and (3) Practical management of EOL care in the ICU.

RESULTS: Preliminary data from 115 (58%) respondents, shows that 29 (25%) of the respondents have a local guideline for EOL care in their ICU.

Seventy-five (64%) physicians felt very confident performing EOL care.

Sixty-nine (82%) physicians had morphine as their first-choice drug for pain-management and 55 (65%) had midazolam as first-choice drug for anxiety-management.

CONCLUSION: Our study shows that most Scandinavian ICU phycisians feel very confident in performing EOL care for the dying, but the EOL care are diverse and only twenty-five procent have a guideline for EOL care available in their department.

Themes: Health Education, Qualitative research
Keywords: Intensive Care Medicine, Palliative Medicine, End-of-Life Care

Hospital managers' perspectives on pregnancy policy and work adjustments – a cross-sectional study

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Background: Risk assessment and work adjustment safeguards pregnant employee. Knowledge on management perspectives in relation to implementation of protective measures is limited.

Objectives: Primary aim was to describe Danish hospital managers' engagement in pregnancy policy and work adjustment. Secondary, we aimed to investigate how managers' characteristics and the setting affect engagement and behaviour.

Methods: The study was a cross-sectional study with 212 managers. Outcomes were within dimensions of health promotion, pregnancy policy, work adjustment, collaboration, manager support, and sick leave.

Logistic and ordinal logistic regression models were applied to identify associations between background information and outcomes.

Results: Of the managers included, 84% arranged meetings and 76% conducted occupational risk assessment. Most managers (96%) engaged in dialogue with employees before sick leave. Most managers felt competent in providing guidance for pregnant employees and 99% considered work adjustment important, mainly to safeguard mothers and children.

The self-reported data showed positive associations between female managers and feeling competent to guide the employee. Further, management training was associated with meetings with pregnant employees. Seniority was associated with feeling competent to guide and dialogue. Midwifery support was associated with competence in guiding about risk factors.

Conclusion: Work adjustment and risk assessment are considered a priority by Danish hospital managers. Overall, managers feel competent guiding pregnant employees. However, managers experience midwifery support beneficial for the guidance of pregnant employees.

Themes: Gynecology and obstetrics, Public health
Keywords: management, pregnancy policy, health-care personnel

Are cardiac rehabilitation pathways influenced by diabetes: a cohort study

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Introduction: Cardiac rehabilitation (CR) is highly recommended for patients after acute coronary syndrome (ACS) due to its proven beneficial effects. A common comorbidity of ACS is diabetes, and CR patients who have both conditions appear to have a worse prognosis than those without diabetes. Unfortunately, this high-risk group is underrepresented in the successful completion of CR. However, it is not known where in the CR pathway, from hospital discharge to the end of CR, the barriers appear. This study aims to compare key aspects; referral, uptake, and completion along the CR pathway in diabetic ACS patients compared to non-diabetic ACS patients.

Methods: The study was carried out as a cohort study using national Danish registers. The study included patients (aged 18 or above) discharged after a diagnosis of ACS within the Central Denmark Region between September 2017 and August 2018. Diabetes information was obtained from three sources. Logistic regression models were used to examine the association between diabetes status and the three outcomes; non-referral, non-uptake, and non-completion. Results were reported as odds ratio (OR) with 95 % confidence intervals (CI).

Results: A total of 2,447 patients (88.5%) were eligible for the study, and 457 patients (18.7%) had diabetes. Non-referral was not statistically significant associated with having diabetes when adjusting for prespecified variables (OR = 1.11, 95% CI 0.87 - 1.41). Non-uptake was statistically significant associated to having diabetes (OR = 1.38, 95% CI 1.01 - 1.90). Non-completion was not statistically significant to having diabetes (OR = 1.06, 95%CI 0.73 - 1.53).

Conclusion: This study found that for patients with diabetes, uptake to CR was the main barrier to successful completion of the CR pathway. The findings suggest that patients with diabetes require further support and encouragement to attend CR to avoid the negative outcome of not successfully completing the programme.

Themes: Rehabilitation, Public health
Keywords: Rehabilitation, Acute coronary syndrome, Diabetes

Validation of diagnostic code DG61.8: Demyelinating Polyneuropathy with respect to Chronic Inflammatory Demyelinating Polyneuropathy and Multifocal Motor Neuropathy

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Background: Chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN) are autoimmune diseases where myelin damage of peripheral nerves leads to reduced nerve conduction and hence muscle weakness and sensory loss in arms and legs. Immunomodulatory or -suppressive treatment will recover function in most of these patients. However, identifying which patients have CIDP or MMN is challenging. Furthermore, the true incidence in Denmark is unknown. CIDP and MMN is diagnosed using the ICD-10 code DG61.8, however the positive predictive value (PPV) of this code is unknown, and hence cannot be used to calculate the incidence in Denmark.

Aim: To calculate the PPV of DG61.8 for CIDP and MMN and via this calculate the incidence of CIDP and MMN in Denmark.

Method: A complete list of patients diagnosed with DG61.8 in Denmark 01.01.1996 - 31.12.2020 (n= 1856) were obtained from the Danish Healthy Data Authority. Medical charts, blood workups, MR, CT, PET and neurophysiology reports from Odense University Hospital 2010-2020 (n=219) and Aarhus University Hospital 2011-2020 (n= 168) were obtained and are being validated using the EFNS/PNS 2010 diagnostic criteria for CIDP and MMN to validate the diagnostic code DG61.8. Based on this work, the PPV for CIDP and MMN of DG61.8 will be calculated. The incidence of CIDP and MMN in the Central Danish Region (2011-2020) and The Region of Southern Denmark (2010-2020) is calculated. The national incidence of CIDP and MMN in Denmark 1996 - 2020 is estimated by multiplying the PPV to the no. of cases not already validated (n=1469).

Results: Work in progress. Data analysis is expected to be complete in January 2024.

Themes: Neuroscience, Epidemiology
Keywords: CIDP

Ischemic stroke modeling in Mice: A comparative analysis of middle cerebral artery occlusion methods.

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Ischemic stroke due to cerebral artery occlusion is a significant challenge, with high risk of subsequent futile reperfusion. Stroke research has resulted in a variety of animal models, among which microfilament-induced large middle cerebral artery (MCA) occlusion is widely used. While this model allows permanent or temporary MCA occlusion, it also involves permanent ligation of the carotid artery, with substantial infarction, progressive edema, and risk of arterial rupture followed by subarachnoid hemorrhage. Additionally, the model has been criticized regarding its fidelity in mimicking clinical thrombectomy procedures rather than clinical stroke.

In 2021, Erdener et al. introduced a redeveloped approach, involving transient distal MCA occlusion (tMCAO) in mice, by a blunt mechanical compression of the distal M1 segment. The model avoids permanent ligations, ensures controlled recanalization, and targets ischemic core development within the cortex. We further extended the approach to a high survival-rate stroke model, enabling simultaneous real-time monitoring of both hemispheres, an improvement to the original single-hemisphere paradigm.

Our aim is to characterize this innovative tMCAO model in mice and compare it to the conventional microfilament model in a longitudinal perspective. We showed that the conventional method affects cerebral blood flow prior to tMCAO initiation due to initial carotid artery ligation, questioning baseline comparisons. Conversely, this relationship is not seen in our tMCAO model, and we thereby suggest that this model is more advantageous for dynamic changes in blood flow and research on delimited cortical ischemic core development.

Themes: Animal Models, Surgery
Keywords: Ischemia, Reperfusion, Modeling

Safe and beneficial use of fluorescence during thyroidectomy to predict hypoparathyroidism.

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Background: Total thyroidectomy is a common surgical procedure and carries a risk of postoperative hypoparathyroidism (hypoPT). To predict the risk of postoperative hypoPT, we evaluated parathyroid glands with injection of indocyanine green (ICG) during surgery. The aim was to examine the potential of fluorescence to predict the risk of hypoPT and its potential safety issues.

Method: In this prospective cohort from Aarhus University Hospital, we included patients undergoing total thyroidectomies from May 2021 to June 2023. All patients had ICG injections during surgery, and each visible parathyroid gland was scored according to the fluorescent output from 0 – 2 with a higher score corresponding to a greater blood supply.

HypoPT was defined as the need for alfacalcidol following surgery. Biochemistry was measured before and after all operations.

Results: A total of 124 patients were included. At discharge, treatment with alfacalcidol was needed in 38% (n=6) of patients with a gland score less than 2, whereas alfacalcidol was only needed in 8% (n=9) of patients with a gland score of 2 (p-value = 0.004). After 2 months, 25% (n=4) of patients with a score less than 2 needed alfacalcidol, and 6% (n=7) with a score of 2 needed alfacalcidol (p= 0.036). No increase in Alat was measured after two months. Mean creatinine levels increased in all patients from 66.3 µmol/L to 71.8 µmol/L (p=0.001). Sub-analysis revealed that patients with hypoPT had a larger increase in creatinine mean 13.1 µmol/L vs 4.6 µmol/L (p=0.008).

Conclusion: The use of fluorescent ICG injections during total thyroidectomy does not fully exclude hypoPT following surgery, it appears to be a promising approach for predicting the risk of postoperative hypoparathyroidism. By enhancing the intraoperative identification and preservation of parathyroid glands, ICG improves immediate feedback to the surgeon about vitality of each parathyroid gland. No risk was associated with the use of ICG. However, Creatinine did increase for all patients postoperatively, but significantly more in hypoPT patients.

Themes: Surgery, Endocrinology
Keywords: Hypoparathyroidism, Fluorescence, Total thyroidectomy

Serial changes and prognostic implications of myocardial work indices in subtypes of aortic stenosis undergoing transcatheter aortic valve replacement

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Background. Evaluation of left ventricle (LV) systolic function in patients with aortic stenosis (AS) undergoing transcatheter aortic valve replacement (TAVR) is challenging, as ejection fraction (LVEF) and global longitudinal strain (LV GLS) does not take afterload into account. Myocardial global work indices (GWI) estimate the work of the left ventricle assessing contractility with strain analysis and afterload with blood pressure and aortic valve mean gradient.

We aimed to evaluate changes in LV myocardial work in subgroups of AS from before TAVR to one-month after TAVR, and to assess the prognostic value of LV GWI.

Methods. We included 473 patients undergoing TAVR from 2016 to 2018. GWI was estimated using speckle tracking strain imaging and by adding the aortic valve mean gradient to the systolic blood pressure, as a non-invasive estimate of pressure in the LV. The primary event was all-cause mortality.

Results. Patients with preserved LVEF (>50%) decreased in GWI from preoperative assessment to one-month follow-up across all subgroups (high gradient; low flow, low gradient and normal flow, low gradient). Patients with reduced LVEF (<50%) GWI increased in all subgroups of AS. In multivariate analysis, each 100 mmHg% increase in GWI was associated with improved prognosis (HR 0.95 [95% CI: 0.91-0.99], p=0.014).

Conclusions. LV GWI increases in patients with reduced LVEF across subgroups of AS patients due to increased contractility. LV GWI decreases in patients with preserved LVEF due to stationary contractility and decreased afterload after TAVR. Preoperative assessment of LV GWI in AS patients undergoing TAVR offers additional prognostic implications beyond LVEF and GLS.

Themes: Cardiology, Imaging techniques
Keywords: Aortic stenosis, Echocardiography, Systolic function

The Impact of Sex and Age On Long-term Outcome After Percutaneous Coronary Interventions – A Pooled Analysis Of The Randomized Controlled SORT OUT Trials

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Background: Sex-related long-term outcome in patients treated with percutaneous coronary interventions (PCI) are contradicting. We aimed to investigate the sex-related difference in outcome five years after PCI in a randomized all-comer population.

Methods: A pooled analysis with individual patient data of the SORT OUT III, V, VI, VII, VIII and IX trials were performed. The SORT OUT trials were multicenter, single-blinded, non-inferiority trials randomizing all-comer populations to receive either of two drug-eluting-stents. Primary endpoint was a composite major adverse cardiac event (MACE) at five years, defined as all-cause mortality, spontaneous myocardial infarction (MI) and target lesion revascularization (TLR). Secondary endpoints were target lesion failure (TLF) and the individual components of MACE and TLF. TLF was defined as cardiac death, target vessel MI and TLR. Exposure was biological sex at baseline. Outcome were assessed at five-years by an independent clinical event committee.

Results: From January 2006 to April 2017, 15,278 (24.4% women) were included in the MACE analysis and 10,078 (23.7% women) in the TLF analysis. Women were older (67.8 10.7 vs 64.8 11.0 years) and had more cardiac risk factors besides a lower rate of previous revascularization and MI compared to men. No difference in Acute coronary syndrome (ACS) was found (50.4% in women vs 51.4% in men). Difference in MACE was IRR 95% CI 0.91 (0.84-0.99), and TLF was 0.81 (0.70-0.93) with male sex as reference.

Conclusions: In a pooled analysis of all-comer patients in the SORT-OUT trials MACE, TLF and cardiac death were significant lower in women compared to men five-years after treatment with PCI.

Themes: Cardiology, Cardiology
Keywords: coronary artery disease, chronic total occlusion,

Cognitive dysfunction in early experimental non-alcoholic fatty liver disease is associated with systemic and neuroinflammation

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Background: Cognitive dysfunction is an increasingly recognised manifestation of non-alcoholic fatty liver disease (NAFLD), but the mechanistic link remains unclear. The aim of this study was to investigate the hypothesis that experimental NAFLD in rats leads to cognitive dysfunction as a consequence of both systemic and neuroinflammation.

Methods: Twenty male Sprague Dawley rats were randomized to a high-fat, high-cholesterol (HFHC) NAFLD diet, or a standard diet (n=10 per group), for 16 weeks. Assessments included characterization of: NAFLD (histology), neurobehaviour, hepatic and systemic inflammation, brain microglia and astrocyte activation, and synaptic density.

Results: The HFHC diet induced NAFLD with extensive steatosis and lobular inflammation without fibrosis. Several plasma cytokines were elevated (CXCL1, IL-6, IL-17, MIP-1α, MCP-1, IL-10; all $p < 0.05$) and correlated with corresponding increases in hepatic chemokine gene expression. In the prefrontal brain cortex, we observed a 19% increase in microglial activation confirmed by both Iba1 immunohistochemistry ($p = 0.03$) and 3H-PK11195 autoradiography ($p < 0.01$). In parallel, synaptic density was reduced to 92%, assessed by 3H-UCB-J autoradiography ($p < 0.01$). NAFLD animals exhibited impaired memory of previously encountered objects in the Novel Object Recognition test ($p = 0.047$). They also showed depression-like behaviour evidenced by increased immobility time ($p < 0.01$) and reduced swimming time ($p = 0.03$) in the Forced Swim Test.

Conclusion: Experimental, non-fibrotic NAFLD, as a model to reflect the early stage of human disease, results in cognitive impairment and depression-like behaviour. This NAFLD model gives rise to an inflammatory profile in liver, plasma, and the brain, resulting in neuroinflammation and diminished synaptic density, which we suggest provides the pathogenic link between liver disease and cognitive dysfunction in NAFLD.

Themes: Animal Models, Gastroenterology and hepatology
Keywords: Fatty liver disease, Cognitive dysfunction, Neuroinflammation

The Effects of Elevated Maternal BMI on Offspring Cortisol Metabolism

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Background and aims: In Denmark, one in three women fulfils the WHO criteria for obesity at the beginning of their pregnancy. Obesity affects the hypothalamic-pituitary-adrenal (HPA) axis, regulating cortisol levels. Cortisol is essential for organs and brain maturation and an inadequate or excessive level among pregnant women may modify the fetal HPA axis. This project aimed to investigate how maternal BMI modifies placental cortisol metabolism, particularly the placental enzymes HSD11B1 and HSD11B2 controlling the transfer of cortisol from mother to fetus and the long-term effects on children's HPA axis.

Materials and methods: First-trimester placental tissue was collected with informed consent from 75 legal abortions (<12 gestational weeks) performed on maternal request. The mRNA expression of HSD11B1 and HSD11B2 and the cortisol receptor NR3C1 was determined.

To evaluate the potential long-term effect of maternal BMI, we performed a systematic review and identified 15 studies investigating the effect on placental cortisol metabolism at birth, and offspring HPA axis functioning up to 25 years of age.

Results: In early pregnancy, high maternal BMI levels were associated with higher expressional levels of both HSD11B2 and NR3C1. The effect on HSD11B2 was most pronounced among girls. The literature search revealed that high maternal BMI levels down-regulated placental HSD11B2 activity at term, with a hyper-activated cortisol stress response in young childhood that led to a flattered cortisol response in later life.

Conclusion: Maternal BMI affects HSD11B2 and NR3C1, which potentially influences the offspring's HPA axis functioning.

Themes: Gynecology and obstetrics, Molecular biology
Keywords: Cortisol, Maternal BMI, HPA axis

The influence of vagus-mediated immune modulation in the progression of Parkinson's disease and its hypothesized subtypes

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In Parkinson's Disease (PD) intraneuronal aggregated alpha-synuclein (ASYN), induces neuronal dysfunction and death, affecting predominantly substantia nigra, but also other neurons in the central and peripheral nervous system (CNS & PNS). In parallel to neurodegeneration, central and peripheral immune changes occur in PD, an inflammatory process where ASYN plays a central role in influencing neuronal health. Borghammer's team recently proposed two PD subtypes based on the initiation site of ASYN pathology: 1) a body-first subtype that starts in the gut and enters the brainstem bilaterally via the vagus nerve (VN); these patients show a faster PD progression than 2) the brain-first subtype of milder progression. Brain-first PD is proposed to spread unilaterally from the forebrain toward the lower brainstem and finally the periphery. In both subtypes, the VN is affected albeit at different time points. The VN exerts an anti-inflammatory modulation (inflammatory reflex), that might be disrupted by ASYN pathology promoting inflammation and contributing to the faster progression in the body-first subtype. To investigate this, we have mimicked aspects of the body-first PD subtype in rats by a) performing a vagotomy followed by injection of preformed fibrils (PFF) of mouse ASYN into the brain, b) induced overexpression of ASYN in the VN, and c) injections of PFFs into the gut. The preliminary data shows the expected degeneration of peripheral and central innervation in gut-injected rats, as well indication of an early immune response in the CNS in PFF-injected animals compared to PBS-controls

Themes: Neurodegenerative disorders, Neuroscience
Keywords: Parkinson's Disease, Immune response, Animal models

Complement activation is associated with radiographic spinal progression in axial spondyloarthritis

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Background: Radiographic axial spondyloarthritis (r-axSpA) is an inflammatory disease with elusive pathogenesis. Animal models have shown inhibition of complement to diminish structural changes in axSpA. Our aim was to investigate complement and radiographic progression in axSpA-patients recruited from the longitudinal CONSUL cohort.

Methods: All patients had risk factors for radiographic spinal progression (BASDAI≥4, elevated CRP and/or ≥1 syndesmophyte(s)). Serum samples were collected at baseline (n=96) and after 108 weeks (n=89) of TNF inhibition (TNFi) therapy. They were analyzed by immunoassays for complement proteins (L-ficolin, M-ficolin, H-ficolin, CL-L1, MBL, MASP-1, MASP-2, MASP-3, and MAp44) and the complement activation product C3dg. X-rays were performed at baseline and after 108 weeks and read blinded by three independent expert readers.

Results: In total, 19 patients developed new bone formation at week 108. Baseline levels of MASP-1, MASP-2, and C3dg were elevated in patients developing new bone formation, whereas MASP-3 levels were decreased (all $p<0.05$). Baseline MASP-1, MASP-3, and C3dg

predicted the development of new bone formation in a univariate regression analysis, and MASP-1, MASP-3, and C3dg remained significant in a multivariate analysis. L-ficolin and C3dg levels at week 108 were elevated in patients with new bone formation.

Conclusions: In this study, complement activation (C3dg), MASP-1 and MASP-3, prior to TNFi therapy, predicted the development of new bone formation at week 108. Elevated levels of C3dg and L-ficolin at week 108 were associated with new bone formation. Our findings suggest an involvement of complement in new bone formation in r-axSpA.

Themes: Immune diseases, Molecular biology
Keywords: Axial spondyloarthritis, The Complement System, The Lectin Pathway

Discovery of SARS-CoV-2 neutralizing antibodies

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Despite development of effective SARS-CoV-2 vaccines, a sub-group of vaccine non-responders depends on therapeutic antibodies or small-molecule drugs in cases of severe disease. However, perpetual viral evolution has required continuous efficacy monitoring as well as exploration of new therapeutic antibodies, to circumvent resistance mutations arising in the viral population. During this study, the immune response from 203 COVID-19 convalescent participants was characterized, to identify 15 individuals with potential potent SARS-CoV-2 neutralizing antibodies. SARS-CoV-2-specific B cell sorting and subsequent single-cell sequencing was performed on patient material, resulting in the screening of 455 monoclonal antibodies for SARS-CoV-2 variant binding and virus neutralization. Using the antibody potency data to reflect back on single cell analysis, a cluster of activated B cells highly enriched for SARS-CoV-2 neutralizing antibodies was identified. The transcriptomic signature of activated B cells harboring broadly binding neutralizing antibodies with therapeutic potential identified here, may be a guide in future efforts of rapid therapeutic antibody discovery. Epitope binning and Cryo-EM structure analysis identified the majority of neutralizing antibodies having epitopes overlapping with the ACE2 receptor binding motif (class 1 binders). Extensive functional antibody characterization identified two potent neutralizing antibodies, one retaining SARS-CoV-1 neutralizing capability, while both bind major common variants of concern and display prophylactic efficacy in vivo.

Themes: Infectious Diseases, Immune diseases
Keywords: SARS-CoV-2, Neutralizing Antibody, Discovery

Does SGLT2i improve renal hemodynamics? A randomized, double blinded, placebo controlled trial

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Background: Sodium-Glucose- Cotransporter-2-Inhibitors (SGLT2i), an antidiabetic medication, have revolutionized the treatment of chronic kidney disease (CKD), reducing risk of cardiovascular death and end-stage renal disease by 30% in patients with and without concomitant type 2 diabetes (DM2). However, the underlying mechanisms of action are unknown.

Glomerular hypertension is an important pathophysiological feature in both DM2 and CKD. Conversely, SGLT2i is thought to alleviate glomerular hypertension by causing a decrease in renal blood flow (RBF), leading to a decrease in glomerular filtration (GFR). Animal models seem to support this, but in human studies results have been conflicting and the renal hemodynamic effects of SGLT2i have never been examined in patients with CKD

Hypotheses: SGLT2i decreases RBF and GFR in patients with DM2 with and without CKD as well as in patients with non-diabetic CKD.

Methods: A randomized, double blinded, placebo controlled cross over study including 3 different patient groups with 15 patients in each group. The 3 groups are:

1) Patients with DM2 and preserved kidney function (eGFR> 60 ml/min)

2) Patients with DM2 and CKD (eGFR 20-60 ml/min)

3) Patients with non-diabetic CKD (eGFR 20-60 ml/min)

Each participant is randomized to 4 weeks of SGLT2i treatment (empagliflozin 10 mg) or matching placebo. After a 2-week wash out period, each participant is crossed over to 4 weeks of the opposite treatment. At the end of each treatment period, RBF is measured with an Rb82-PET-scan and GFR is measured with single-sample Tc99-DTPA-clearence.

Results: Studies are completed. Data analysis is on going . Preliminary results will be presented if available.

Themes: Urology & Nephrology, Imaging techniques

Development and clinical implementation of a national AI based model for automated delineation in breast cancer radiotherapy

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Background: In breast cancer radiotherapy (RT), delineation of the targets for irradiation, i.e. breast and involved lymph nodes, is performed manually in CT-scans and determines optimization of the radiation dose. Due to low visibility in images, there are large variations between clinicians, and national standardization is desired. We investigate use of artificial intelligence (AI) for automation of the delineation process.

Methods: A national workshop was arranged in the Danish Breast Cancer Group with 21 experts from all eight Danish RT centres. More than 300 workhours were contributed to create two high quality delineation data sets (298 patients).

A set of 278 patients was used to train nnUNet models to delineate the internal mammary nodes and upper lymph node levels. In a separate test set, predicted structures were generated using the trained models.

Predicted structures were compared with expert delineations for Dice similarity coefficient (DSC), cranial-caudal length (CC) and width.

A qualitative study is scheduled for November '23 followed by national implementation in a clinical trial.

Results: The models showed good results with a median DSC=0.7 for the internal mammary nodes and DSC=0.8 and for the upper lymph node levels (a DSC of 1 is a perfect match).

The internal mammary node model showed a CC average of 115±10 mm (expert delineations 111±14 mm) and an average width of 14±2.6 mm(expert delineations 14±1.8 mm).

Conclusions: We developed a national AI model for automated target delineation in breast cancer radiotherapy. The model will be implemented nationally for practice changing fast consistent delineation process ensuring equal treatment for all patients.

Themes: Cancer, Imaging techniques
Keywords: Breast cancer, National AI model, automation of delineation

Proteomic profiling identifies apoptotic deregulation predictive of histological transformation in follicular lymphoma

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Follicular lymphoma (FL) is characterized by the t(14;18) translocation and subsequent upregulation of anti-apoptotic BCL2 protein. While generally indolent of nature, FL remains incurable. Furthermore, histological transformation (HT) to a high-grade lymphoma remains the leading cause of FL-related death.

We performed a large-scale mass spectrometry-based proteomics study on diagnostic FL biopsies, in which proteins predictive of HT were identified. Of interest, proteins involved in apoptotic regulation, namely CASP3, MCL1, BAX, BCL-xL, and BCL-rambo, were differentially expressed in comparison with HT. Protein expression levels in pre-therapeutic lymphoma biopsies from FL patients, either with (subsequently-transforming FL (st-FL); n=20) or without (non-transforming FL (nt-FL); n=33) subsequent transformation, and in paired high-grade biopsies from the transformed lymphomas (transformed FL (tFL); n=20) were evaluated by immunohistochemistry.

At time of initial diagnosis, samples from st-FL patients had higher expression levels of CASP3 ($p<0.001$), MCL1 ($p=0.015$), BAX ($p=0.003$), BCL-xL ($p=0.025$), and BCL-rambo ($p=0.057$) compared with samples from nt-FL patients. Shorter transformation-free survival (TFS) was significantly associated with high expression levels of CASP3 ($p<0.001$), MCL1 ($p=0.002$), and BAX ($p=0.007$). Combining the five markers to a risk score based on expression levels showed inferior TFS with increasing numbers of markers with high expression levels.

Our data show differential protein expression in FL lymphoma tissues, here with focus on biomarkers that indicate apoptotic deregulation in relation to FL-patients subsequent experience of HT.

Themes: Cancer, Omics
Keywords: Lymphoma, Proteomics, Apoptosis

Sequential MRI Evaluation of Lymphatic Abnormalities over the Course of Fontan Completion

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Purpose: In the single ventricle population, abnormal lymphatic architecture relates to poor outcomes. It is uncertain if these abnormalities progress following Fontan surgery. This study aimed at evaluating potential changes and relating them to outcomes.

Materials and Methods: We retrospectively reviewed lymphatic imaging performed from June 2012 to February 2023. All individuals with imaging before and after Fontan surgery were included. Lymphatic abnormalities were classified into four types based on the amount and location of lymphatic vessels. Classifications were compared between stages and related to clinical outcomes.

Results: Forty-three subjects were included in the study. Lymphatic abnormalities progressed in 19 out of 43 individuals (p-value=0.04). Subjects progressing to a high-grade lymphatic classification had longer post-operative drainage (9 vs 17 days, p-value=0.04) and hospitalization following Fontan completion (13 vs 26 days. P-value 0.03) compared to those displaying no progression. Furthermore, during a median 8 (5-9) years of follow-up, they were more likely to have developed chylothorax (12% vs 75%, p-value<0.01) and/or PLE (0% vs 38%, p-value<0.01). Progression to any grade was not associated with any increased risk of adverse events.

Conclusions: Lymphatic abnormalities progress in half of single ventricle individuals following Fontan completion. Progression of abnormalities to a high-grade classification relates to worse postoperative outcome. One-time lymphatic imaging for risk assessment in the single ventricle population may be insufficient, as lymphatic abnormalities may progress over time.

Themes: Imaging techniques, Cardiology
Keywords: Congenital heart disease, Lymphatic system, Single ventricle

The impact of atrial fibrillation on [15O]H2O PET myocardial perfusion imaging

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Background: Ongoing atrial fibrillation (AF) is associated to reduced myocardial perfusion. We aimed to determine the impact of ongoing AF on the precision of myocardial blood flow (MBF) estimated by 15O-H2O PET myocardial perfusion imaging (MPI) to guide subsequent early revascularization in patients with angina and previously diagnosed AF.

Methods and results: We prospectively included 346 patients with angina and persistent or paroxysmal AF referred for 15O-H2O PET MPI prior to possible angiography and revascularization. Patients were scanned either during ongoing AF or sinus rhythm (SR). Patients were analysed in groups based on cardiac rhythm and prior coronary artery disease (CAD): SR-noCAD, AF-noCAD, SR-CAD or AF-CAD. As expected, MBF was substantially affected by prior CAD and ongoing AF [MBF (mL/min/g): 2.82 (SR-noCAD) vs. 2.12 (AF-noCAD) vs. 2.22 (SR-CAD) vs. 1.80 (AF-CAD). Ongoing AF was independently associated to reduced hyperemic MBF. Furthermore, a 0.1 mL/min/g incremental decrease in vessel specific MBF was independently associated to a 23% increase in odds of early revascularization. ROC-analysis of vessel specific hyperemic MBF to predict early revascularization yielded the following area under the ROC curve (AUC): SR-noCAD: 0.95; AF-noCAD: 0.79; SR-CAD: 0.78; AF-CAD: 0.88.

Conclusion: Ongoing AF was independently associated to reduced global hyperemic MBF. Despite this, in this single-site setting, the capabilities of vessel specific hyperemic MBF by 15O-H2O PET MPI to predict subsequent early revascularization for AF patients with angina were exceedingly high and only moderately reduced in the presence of either ongoing AF or previously documented CAD.

Themes: Imaging techniques, Cardiology
Keywords: Myocardial Perfusion Imaging, Coronary Artery Disease, Atrial Fibrillation

PCSK9 targets megalin in the kidney proximal tubule and aggravates proteinuria in nephrotic syndrome

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Proteinuria is a prominent feature of chronic kidney disease (CKD). Interventions that reduce proteinuria slow CKD progression and the associated risk of cardiovascular disease (CVD). We here propose a mechanistic coupling between proteinuria and the CVD-risk protein PCSK9 involving the receptor megalin. We find that PCSK9 undergoes glomerular filtration and is captured by megalin, the receptor responsible for driving protein reabsorption in the proximal tubule. Accordingly, megalin-deficient mice and patients carrying megalin pathogenic variants are characterized by elevated urinary PCSK9 excretion. Interestingly, PCSK9 knockout mice displayed increased renal megalin while PCSK9 overexpression resulted in its reduction. Furthermore, PCSK9 promoted trafficking of megalin to lysosomes in cultured proximal tubule cells, suggesting that PCSK9 is a negative regulator of megalin. This effect is potentially accelerated under disease conditions as genetic destruction of the glomerular filtration barrier in mice, and minimal change nephropathy in humans, resulted in markedly increased tubular PCSK9 uptake and urinary PCSK9 excretion. Pharmacological PCSK9 inhibition increased renal megalin, while reducing urinary albumin excretion and kidney injury markers in nephrotic mice. In conclusion, glomerular damage increases filtration of PCSK9 and concomitantly megalin degradation, resulting in escalated proteinuria. Targeting PCSK9 may be beneficial to attenuate proteinuria-induced kidney injury in CKD.

Themes: Urology & Nephrology, Cardiology
Keywords: Chronic kidney disease, PCSK9 inhibitors, Megalin

Identifying safe diagnostic algorithms for sentinel lymph node mapping in high-risk endometrial cancer: the SENTIREC-endo study - **CANCELLED**

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Introduction: Sentinel lymph node (SLN) mapping is suggested to be a safe staging method for women with high-risk endometrial cancer (EC). The current staging with pelvic (PLD) and paraaortic (PALD) lymph node dissection is associated with prolonged surgical time and risk of complications. However, approximately 20-45% of women have failed mapping, leaving a need for consensus on the surgical algorithm in case of non-mapping. We aimed to assess the safety of SLN-mapping algorithms in women with high-risk EC.

Methods: We undertook a national prospective diagnostic accuracy study of SLN-mapping in women with high-risk EC from March 2017- January 2023. A power calculation was based on the negative predictive value (NPV). Women underwent SLN-mapping, pelvic (PLD) and paraaortic (PALND) lymph node dissection besides removal of any FDG/PET–positive lymph nodes.

Results: We included 216 women; 170 women underwent SLN mapping, PLD and PALND and were included in the analyses. 42/170 (24.7%) had nodal metastasis. The algorithm SLN+PLD in case of failed mapping demonstrated a sensitivity of 88% (95% CI 74-96) and an NPV of 96% (95% CI 91-99). The sensitivity increased to 93% (95% CI 81-99) and the NPV to 98% (95% CI 93-100) if PLD was combined with removal of any PET-positive lymph nodes. PLD+PALND in non-mapping cases achieved a sensitivity of 95% (95% CI 84-99), NPV 98% (95% CI 95-100).

Conclusion: SLN-mapping is a safe staging procedure in women with high-risk EC if strictly adhering to a surgical algorithm, including removing any PET-positive lymph nodes and PLD in failed mapping cases. PLD+PALND obtains similar accuracy in case of failed mapping if FDG/PET-CT is not available.

Themes: Cancer, Gynecology and obstetrics
Keywords: Endometrial cancer, Surgical staging, change of guidelines

Early child predictors of functional somatic symptoms in adolescence - Cancelled

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Background: Current explanatory models describing factors underlying the development of Functional somatic symptoms (FSS) emphasize complex interactions between early child- and parental-specific predictors. We examined the effect of infancy regulatory problems (i.e. sleeping, feeding and tactile reactivity), emotion (dys)regulation, and contact problems in infancy on FSS throughout adolescence.

Methods: Standardized behavioral assessments and self-report questionnaire data from assessment waves at ages 0-1-, 11-12- and 16-17 years of the population-based Copenhagen Child Cohort (CCC2000) were linked with covariate data on maternal psychiatric illness and family adversity from Danish national registers. Multiple regression analyses adjusting for covariates were performed to examine the effect of predictors on FSS during pre-, late, and throughout adolescence, categorized into persistent (high FSS at age 11-12 and 16-17), remission (high FSS only at age 11-12), incident (high FSS only at age 16-17) or no FSS (no FSS at age 11-12 and 16-17).

Results: Infancy regulatory problems significantly predicted preadolescent FSS (b = 0.38, p = .002). A comparable yet statistically non-significant pattern was found on FSS during late adolescence. These regulatory problems were significantly associated with the remittent FSS course pattern throughout adolescence (i.e. high levels of FSS at pre- but not late adolescence) (OR = 3.19, p = .001).

Conclusion: A combination of infant regulatory problems could represent early impairments in sensory reactivity and dysfunctional processing of sensory input, potentially contributing to aberrant somatic symptom expression in preadolescence.

Themes: Epidemiology, Mental health
Keywords: Functional Somatic Symptoms, infancy regulatory problems, maternal psychiatric illness

Local intraoperative zoledronic acid decreases migration of cementless total knee arthroplasty by suppression of bone resorption.

A randomized, double-blinded RSA study of 55 patients with 5 years follow-up

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Introduction: Cementless tibial implants migrate initially until osseointegration. Bisphosphonates inhibit osteoclast activity and reduce bone resorption.

Methods: A prospective, double-blinded, randomized study including 55 patients operated with a cementless total knee arthroplasty. Patients were randomized to either soaking of the cut tibia plateau for 60 seconds with ZOL (0.6 ml ZOL (0.8 mg/ml) in 1.4 ml NaCl (ZOL group) or 2 ml NaCl (9mg/ml) (placebo group) or. We measured migration (subsidence) of the tibial implant by Radiostereometry Analysis (RSA), bone turnover markers in blood samples (CTX, P1NP) and periprosthetic Bone Mineral Density (p-BMD) by dual-energy X-ray absorptiometry (DXA). RSA, DXA, and blood samples were obtained postoperative and at follow-up at 2, 6, 12, and 24 weeks and at 1, 2, and 5 years.

Results: The ZOL group had significantly less tibial implant subsidence than the placebo group. At 5 years follow-up, mean implant subsidence was -0.01 mm (95% CI: -0.22; 0.20) in the ZOL group and -0.51 mm (95% CI: -0.72; -0.31) in the placebo group (p=0.001). Bone resorption (CTX) was lower at 2 weeks follow-up in the ZOL group (p<0.001), bone formation (P1NP) was similar between groups (p>0.05) and p-BMD was higher in the ZOL group than in the placebo group (p=0.031).

Conclusion: ZOL application decreased tibial implant migration and increased periprosthetic BMD, which may be explained by suppression of bone resorption. Local intraoperative ZOL application on the tibial bone provides a clinically significant medical improvement of early cementless tibial implant fixation, which increases the likelihood of longer knee arthroplasty survival.

Themes: Surgery, Endocrinology
Keywords: Total Knee Arthroplasty, Bone remodelling, Radiostereometric Analysis

Elevated Cobalt and Chrome Levels in Metal-on-Polyethylene Knee Megaprostheses: A Prospective 1-Year Study of 56 Patients

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Background: Megaprostheses are commonly used in the treatment of bone tumors and extensive bone defects. Concerns have emerged regarding elevated levels of chromium and cobalt in patients with metal-on-metal megaprostheses. Elevated cobalt and chrome levels have been associated with chromosomal aberrations, hypersensitivity reactions, nephrotoxicity, and potential teratogenic effects. Some cases have reported organ failure and death due to cobalt toxicity. This prospective study aims to identify systemic cobalt and chrome levels in metal-on-polyethylene knee and hip megaprostheses and their associations with other factors.

Methods: A total of 56 patients underwent knee or hip megaprosthesis surgery. Serum cobalt and chrome levels were measured preoperatively and at three intervals within the first year using Inductively Coupled Plasma Mass Spectrometry.

Results: A significant increase in serum cobalt levels was observed after knee megaprosthesis surgery compared to preoperative levels. An association between younger age, higher eGFR and increased cobalt levels were observed. No significant correlations were found between ion levels and resection length or the number of modular connections.

Conclusion: The study reveals elevated serum ion levels in Metal-on-Polyethylene knee megaprostheses in contrast to Metal-on-Polyethylene hip megaprostheses. Furthermore, a significant positive correlation between Co and Cr levels and Co and eGFR were identified. This study highlights the importance of monitoring systemic cobalt and chrome levels in patients with megaprostheses and underscores the necessity for guidelines to effectively address these elevated systemic ion levels.

Themes: Surgery, Cancer
Keywords: Megaprostheses, Systemic ion levels

Characterization of variants of uncertain significance by CRISPR/Cas-induced knock-in

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Alexander Rafael LaVilla Labial, Emil Aagaard Thomsen, Kristian Alsbjerg Skipper, and Jacob Giehm Mikkelsen

Rapid advancements in next-generation sequencing (NGS) have paved the way for molecular profiling of various cancers. Global initiatives like The International Cancer Genome Consortium (ICGC), The Cancer Genome Atlas (TCGA), and PanCancer Analysis of Whole Genomes (PCAWG) have identified numerous genetic variants potentially linked to cancer diagnosis and prognosis. However, the clinical relevance of many of these variants, often called 'variants of uncertain significance' (VUS), remains uncertain. There's an urgent need for genetic methods to elucidate the functional importance of these VUS and expedite diagnostic insights.

Our project endeavors to establish an experimental platform based on CRISPR/Cas technology, which aims to accelerate the assessment of the clinical significance of genetic variants uncovered through NGS in patients. This platform involves the precise introduction of a VUS of interest into the correct genetic locus within a cell line. This is achieved through the process of nucleofection using synthetic Cas9 protein, complexed with synthetic single guide RNA (sgRNA) and the presence of donor DNA. In parallel, we introduce a neutral control variant that closely mimics the wild-type sequence but carries a silent mutation. By comparing the frequencies of the two introduced genetic variants through NGS, we can expediently gauge their impact on relevant cellular phenotypes, such as cell growth.

We're also creating cellular model systems to study the effects of VUS on cell growth and DNA repair.

Themes: Cancer, Genetic engineering
Keywords: CRISPR, Variants of uncertain specific, Next-Generation-Sequencing

Interrogating endothelial cell heterogeneity and dysfunction in health and metabolic diseases by CRISPR gene editing and single-cell RNA sequencing

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Endothelial cells (ECs) lining the blood vessels have vital functions in regulating tissue metabolism and homeostasis. Dysfunction of ECs are associated with the pathogenesis and progression of many human diseases and nearly all metabolic disorders. Thus, targeting ECs is considered a promising diagnostic and therapeutic biomarker. However, the heterogeneity and functions of disease-associated EC subtypes are not fully studied and genetic modification technologies in ECs are poorly developed, hindering the development of EC-based clinical applications. To overcome this, we first developed a highly efficient and selection-free genetic manipulation method (approx.100%) in primary cultured ECs1. Using pigs as a model, we further illustrated the single-cell transcriptome signatures and functional specialization for EC subtypes in various tissues and discovered functionally an important EC subtype undergoing the endothelial-to-mesenchymal transition in adipose tissues2. Furthermore, we explored the circulating ECs and immune cells as possible biomarkers for diabetes eye complications by single-cell RNA sequencing of human PBMCs from 1) patients with diabetes and newly diagnosed PDR (n=10), 2) patients newly diagnosed diabetic maculopathy (n=10), 3) diabetes patients without eye disease (n=10), and 4) healthy individuals (n=10). Initial results revealed disease-associated cell composition changes and functional alterations. Further investigations with advanced data analysis and experimental validation are being performed to identify ECs and immune molecules as diagnostic markers or therapeutic targets for diabetic eye complications like PDR.

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Themes: Omics, Genetic engineering
Keywords: Endothelial cell heterogeneity, scRNAseq + CRISPR gene editing, Discovery of biomarkers

Socioeconomic disparities in dementia diagnostics among stroke patients

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Background: Though dementia risk after stroke is high, dementia diagnosis rate among stroke patients is low. Low socioeconomic status (SES) is a risk factor for dementia, however patients with low SES may be underdiagnosed. With this study we aim to investigate if there are socioeconomic disparities in dementia diagnostics among stroke patients.

Methods: This was a nationwide register-based study including all patients with incident ischemic or haemorrhagic stroke in Denmark from 2010-2020. Socioeconomic status was defined by pre-stroke income, employment status, and educational level. Patients were followed until dementia diagnosis, death, or end of follow-up. Incidence rates of dementia diagnoses were compared between groups using Poisson regressions.

Results: In the study period, 98953 patients with incident stroke were identified. Median [IQR] age was 72 [62-80], 55.9% were male and 89.1% had ischemic stroke. Dementia was diagnosed in a total of 5675 patients a median of 2.4 [0.89-4.8] years after stroke (incidence rate = 12.1/1000 person years). Patients with low income had similar diagnosis rates as patients with high income (incidence rate ratio (IRR) = 1.04 (0.94-1.15)). Patients with low educational level had only slightly higher diagnosis rates than those with high education (IRR = 1.11 (1.03-1.20)). Unemployed had higher diagnosis rates than those who were employed before stroke (IRR = 1.47 (1.29-1.66)).

Conclusion: Overall dementia diagnosis rate among stroke patients is low. Patients with low income and low educational level may be underdiagnosed.

Themes: Neuroscience, Epidemiology
Keywords: Stroke, Dementia, Socioeconomic status

Stepping into an era of personalized exercise in MS – elucidating the influence of muscle strength and aerobic capacity on lower extremity physical function

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Introduction: To prescribe a personalized and thus more optimal exercise program for persons with multiple sclerosis (pwMS) having limited physical function, it is important to understand the extent of impairments in the two main contributing physiological systems. The latter comprise the neuromuscular system (~muscle strength) and the cardiovascular system (~aerobic capacity).

Two of the most applied tests of physical function are the five times sit to stand (5STS) and the six-minute walk test (6MWT),

Objective: To investigate how aerobic capacity and lower limb muscle strength independently influence physical function (5STS and 6MWT).

Methods: Knee extensor muscle strength (MVC; isokinetic dynamometry), aerobic capacity (VO2; incremental exercise test), 5STS and 6MWT were evaluated. Multiple linear regression was used to evaluate associations.

Results: One-hundred and fifty pwMS (45 ± 8.8 years) were enrolled and completed evaluation of VO2 (25.8 ± 7.5 [range 7.6;48.5] mlO2/min/kg), MVC (1.80 ± 0.61 [range 0.33;3.99] Nm/Kg), 5STS (11.3 ± 4.1 [range 5.09;30.5] s), and 6MWT (545 ± 133 [range 97;776] m). With 5STS as dependent variable an R2 = 0.16 was observed with both VO2 (std β -0.16) and MVC (std β -0.28) contributing as independent variables, corresponding to VO2 explaining 36% and MVC, 64%. With 6MWT as dependent variable an R2 = 0.37 was observed with both VO2 (std β 0.44) and MVC (0.24) contributing as independent variables, corresponding to VO2 explaining 65% and MVC 35%.

Conclusion: Whilst muscle strength and aerobic capacity both contribute to explain physical function, 5STS is preferentially linked to muscle strength and 6MWT linked to aerobic capacity.

Themes: Rehabilitation, Neurodegenerative disorders
Keywords: Multiple Sclerosis, Exercise, Rehabilitation

Non-Classical GABAergic neurons

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Neurovascular coupling (NVC) mechanisms are constantly adjusted to provide oxygen and energy to the brain during high metabolic demands. Excitatory neuronal activity modulates the release of vasoactive molecules that target the neurovascular unit, regulating the capillary and arteriole blood flows. "Non-classical" inhibitory gamma-aminobutyric acid (GABA)ergic interneurons (INs) are also enriched with vasoactive substances. INs have close associations with cerebral capillaries, yet their role in regulating capillary flows during NVC remains poorly understood. In this study, we examine the role of a recently described neocortical layer 1 population of INs (NDNF-INs) in regulating capillary flows.

We aim to correlate cell activity with changes in capillary flow dynamics and their role during NVC. We will test cell activation using two-photon Ca2+ imaging of transfected NDNF cells with GCaMP8m in awake transgenic mice. We will also evaluate capillary hemodynamics during activation of INs combining single-cell two-photon optogenetic stimulation and single capillary scans. Last, we will examine changes in tissue oxygenation during the activation of NDNF cells and correlate them to cell activity and capillary hemodynamic changes.

Preliminary findings indicate that a whisker stimulation of 2 s at 3 Hz activates approximately 10% of NDNF-INs. Our research underscores the significance of INs in neurovascular coupling, shedding light on the diverse functional roles of L1 NDNF-INs.

Themes: Neuroscience, Neurodegenerative disorders
Keywords: Neurovascular couplling, Blood flow, inhibitory

Quantitative lung and lobar perfusion from dual-source, dual-energy CTPA in chronic thromboembolic pulmonary hypertension and acute pulmonary embolism.

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Background: Guidelines on severity assessment of chronic thromboembolic pulmonary hypertension (CTEPH) and acute pulmonary embolism (PE) rely on hemodynamic and clinical parameters, imaging, and laboratory findings. Pulmonary perfusion is not widely considered, as no reliable and quick evaluation methods for quantification of perfusion have been validated. Dual-energy computed tomography pulmonary angiography (DE-CTPA) can provide automated, user-independent, quantification of pulmonary perfusion concurrent with CTPA images for diagnosis.

Methods: Patients diagnosed with acute PE or CTEPH (n=162) between 2019 and 2023 underwent DE-CTPA at the time of their diagnostic work-up. The images from 81 PE patients and 81 CTEPH patients were processed using the machine-learning based eXamine DE Lung Isolation software to obtain quantitative lung and lobar perfusion data. Clinical data was retrieved from electronic patient journals.

Results: Whole lung blood volume was lower ($p<0.001$) in PE patients (median 3399 mL [2554, 4284]) than in CTEPH patients (median 4094 mL [3397, 4818]). The same was observed at single lung and lobar level. Multivariate comparison encompassing all lobar blood volumes showed a difference between the two groups ($F = 11.4$, $Pr>(F) = 0.001$). We found poor correlation ($r<0.3$) between clinical and hemodynamic parameters for both patient groups.

Conclusion: Lung and lobar perfusion are lower in patients with acute PE than patients with CTEPH as highlighted by differences in DECT-derived pulmonary blood volume parameters. This might be explained by the differences between an acute, decompensated disease phenotype and a chronic, compensated disease phenotype.

Themes: Cardiology, Diagnostics & technology

Erosive Progression Assessed by High-resolution Peripheral Quantitative Computed Tomography Compared to Conventional Radiography in 359 Patients with Established Rheumatoid Arthritis: A One-year Cohort Study

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Introduction: High-resolution peripheral quantitative computed tomography (HR-pQCT) is a sensitive imaging technique to assess erosive disease in rheumatoid arthritis (RA). The objectives were to investigate the ability of HR-pQCT to detect erosive progression during one year compared to conventional radiography (CR) in a cohort of patients with RA.

Methods: This prospective cohort study included consecutively 359 patients with RA (disease duration≥5 years) at the Dept. of Rheumatology, Aarhus University Hospital between 2018 and 2020. HR-pQCT and CR were obtained at inclusion and at one-year. Erosive assessment was performed at the second and third metacarpophalangeal joint using HR-pQCT. Erosive progression was defined as an increase in erosion number≥1 or an increase in erosive volume>least significant change. Sharp/van der Heijde scoring was applied using CR of hands, wrists and feet. Erosive progression was defined as a 1.1-point increase in erosion score according to the smallest detectable change.

Results: Erosive progression was identified in 35/331 (11%) patients using CR and in 40/310 (13%) patients using HR-pQCT. In complete paired analyses, progression was identified by both CR and HR-pQCT in 7 patients, meaning that HR-pQCT identified 33/310 (11%) patients not detected by CR. Patients with progression identified only on CR (23/310, 7%) had primarily progression in the feet or in other joints not undergoing HR-pQCT.

Conclusion: A substantial number of patients with RA might be overlooked using CR only to monitor erosive progression. The added value of high-resolution CT might improve patient outcomes through accurate disease assessment and individualized therapy.

Themes: Immune diseases, Imaging techniques
Keywords: Rheumatoid arthritis, High-resolution peripheral CT, Erosive progression

Fibroblast Activation Protein in Patients with Growth Hormone Deficiency: Before and After Treatment

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Background: Growth hormone deficiency (GHD) has detrimental effects with metabolic implications e.g. insulin resistance and dyslipidemia. These effects are reversed by growth hormone (GH) therapy. Fibroblast activation protein-α (FAPα) can cleave collagens and is expressed almost only under pathological conditions such as fibrosis. FAPα also inactivates fibroblast growth factor 21 (FGF21) which is a hormone with potent beneficial effects on metabolism. Despite their related involvements, data on the interaction between GH, FGF21 and FAPα are scarce.

The aim of the present study is to measure circulating FAPα, FGF21 components and biomarkers of collagen turnover in patients with GHD compared to a control group.

Materials and methods: Serum samples from 9 control patients and 16 patients with adult-onset GHD before and after GH treatment have been analyzed using immunoassays for FAPα concentration and activity, and FGF21.

Results: Serum levels of FAPα (ng/mL) significantly increase in the GHD patients after GH treatment [135.6 (111.6-163.8) vs 168.5 (107.3-233.9), $P<0.05$], and FAPα activity (RFU/min) in serum likewise increase [719.0 (467.3-1104.2) vs 1277.8 (668.9-1609.4), $P<0.05$], [median (IQR)]. Total FGF21 remain unchanged after GH treatment. In the control group, FAPα concentration and activity as well as FGF21 remain unchanged. This study is ongoing and data on biomarkers of collagen turnover are pending at time of abstract submission.

Conclusion: Circulating FAPα concentration and activity increase in response to GH treatment in patients with adult-onset GHD, whereas FGF21 does not change in response to GH treatment. This study is ongoing and more data are pending.

Themes: Endocrinology, Immune diseases
Keywords: Fibrosis, Adipose tissue, Growth hormone

Integration of cell-free DNA end motifs and fragment lengths can identify active genes in liquid biopsies

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Multiple studies have shown that the plasma cell-free DNA (cfDNA) from cancer patients differ in both fragment length and fragment end motif (FEM) from healthy individuals. Yet, there is a lack of understanding on how the two factors combined are associated with cancer and gene transcription. In this study, we evaluate cfDNA fragmentomics in plasma from lung cancer patients (n = 12) and healthy individuals (n = 7) using targeted sequencing. A personal gene expression profile is established from plasma using H3K36me3 cell-free chromatin immunoprecipitation sequencing (cfChIP-seq) and short cfDNA fragments (<150 bp) are isolated using in vitro size-selection. The genes with the highest expression display enrichment of short cfDNA fragments (median = 19.99%, IQR: 16.94% – 27.13%, P < 0.0001) compared to the genes with a low expression. Furthermore, distinct GC-rich FEMs are enriched after cfChIP. Combining the frequency of short cfDNA fragments with the presence of distinct FEMs resulted in an even further increase in enrichment of the highest expressed genes (median = 37.85%, IQR: 30.10% - 39.49%, P < 0.0001). In vitro size-selection of < 150 bp cfDNA could also isolate cfDNA representing active genes and in the vitro size-selection enrichment correlated with the cfChIP-seq enrichment (Spearman r range: 0.499-0.882, P < 0.0001). This study expands the knowledge regarding cfDNA fragmentomics and sheds new light on how gene activity in the cells og origin is associated with both cfDNA fragment lengths and distinct end motifs.

Themes: Omics, Bioinformatics
Keywords: Liquid Biopsies, Fragmentomics, Lung cancer

Deciphering the impact of a missing or an extra X chromosome – studies of candidate genes in zebrafish models

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Turner syndrome (TS; 45,X) and Klinefelter syndrome (KS; 47, XXY) are common sex chromosome aneuploidies affecting females and males, respectively. TS is associated with a partial or complete loss of one X chromosome in females while KS is due to one or more extra X chromosomes in males. Both TS and KS are associated with increased mortality and morbidity. TS and KS individuals have a higher risk of developing psychiatric disorders (e.g., autism spectrum disorder, attention-deficit/hyperactivity disorders (ADHD), anxiety, depression, and schizophrenia). Some TS and KS individuals develop several disorders while other individuals are almost unaffected, showing a clinical heterogeneity of TS and KS. The mechanisms leading to the clinical phenotype is still not clear. However, our research group have identified several candidate genes that may be implicated in the phenotype of TS and KS.

In this project, 5 candidate genes will be investigated in zebrafish models of TS and KS. We have established the first knockout zebrafish models of TS using CRISPR/Cas9. Our knockout strategy has been to create mutant genes with a major deletion of the coding region or a premature termination codon leading to loss-of-function. Later on, we will generate overexpression zebrafish models of KS using the Tol2 transposon system. For each model, social behavior, ADHD, autism spectrum disorder, and anxiety-like behavior will be investigated using behavioral testing.

The aim of this study is to decipher the genetics behind the neuropsychiatric phenotype of TS and KS and identify novel therapeutic targets which may be used for developing new, better, and personalized medicine for these patients.

Themes: Endocrinology, Neuroscience
Keywords: Animal Model, Turner Syndrome, Behavioral Testing

Power training in older people with multiple sclerosis – the PoTOMS study

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Introduction: Approximately one-third of all persons with multiple sclerosis (pwMS) are older, i.e., having an age ≥ 60 years. Whilst aging and MS separately elicit deteriorating effects on brain morphology, neuromuscular function, and physical function, the combination of aging and MS may pose a particular challenge. To counteract such detrimental changes, power training (i.e., a type of resistance exercise focusing on high velocity muscle contractions) presents itself as a viable and highly effective solution. Power training is known to positively impact physical function, neuromuscular function, as well as brain morphology. Existing evidence is promising but limited to young and middle-aged pwMS, with the effects of power training remaining to be elucidated in older pwMS.

Methods: The presented 'Power Training in Older MS patients (PoTOMS)' trial is a national, multi-center, parallel group, randomized controlled trial. The trial compares 24 weeks of usual care to 24 weeks of usual care and power training. The primary outcome is whole brain atrophy rate. The secondary outcomes include changes in brain micro and macro structures, neuromuscular function, physical function, cognitive function, bone health, and patient reported outcomes.

Results: The results are pending the completion of the trail summer 2024.

Themes: Rehabilitation, Public health
Keywords: Exercise, Multiple sclerosis, Aging

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