PHD DAY
HEALTH

ABSTRACTS

20 JANUARY 2023

AARHUS
UNIVERSITY

PHD DAY 2023 PROGRAMME

20 JANUARY 2023, 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)**
Michael Winterdahl, Associate professor, Department of Clinical Medicine, Aarhus University
Luisa S. Cassiano, PhD student, Chair of the PhD Association at Health, Aarhus University

8.25 **Keynote lecture by Dr. Sarah Hill, research psychologist and professor at Department of Psychology at TCU in Fort Worth, Texas**
Introduced by Michael Winterdahl, Associate professor, Department of Clinical Medicine, Aarhus University

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

9.40 **Fogh Nielsen Prize Competition** (45 min)
Per Kirkeby, The Lakeside Lecture Theatres

10.35 **Oral sessions**
The Lakeside Lecture Theatres

12.05 **Break with lunch and networking**

12.50 **Flash talk presentations and Poster presentations**
The Lakeside Lecture Theatres, Anatomy (build. 1231), Samfundsmedicinsk Auditorium (build. 1262/101), and building 1264 (209 and 310)

14.30 **Break with coffee/tea and cake**

14.50 **Flash talk presentations and Poster presentations**
The Lakeside Lecture Theatres, Anatomy (build. 1231), Samfundsmedicinsk Auditorium (build. 1262/101), and building 1264 (209 and 310)

16.20 **The programme for the day ends**
On different locations

18.30 **Dinner and award ceremonies**

Centralværkstedet, Aarhus C.

Festive speech: TBA

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.
- E-posters will be available through padlet before the PhD Day and on 20 January as well. You'll receive more information about this in January.
- 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 2023

- Michael Winterdahl, Associate professor, Department of Clinical Medicine, Chair PhD Day 2023
- Luisa Schertel Cassiano, PhD student, Department of Dentistry and Oral Health, Co-chair 2023

- Anders Etzerodt, Associate professor, Department of Biomedicine
- Annika Haarbye Jensen, PhD administrator, Graduate School of Health
- Bente Pedersen, PhD administrator, Graduate School of Health
- Charlotte Hansen Gabel, PhD student, Department of Public Health
- Fernando Valentim Bitencourt, PhD Student, Department of Dentistry and Oral 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
- Luisa Schertel Cassiano, PhD student, Department of Dentistry and Oral Health
- Merete Bjerrum, Associate professor, Department of Public Health
- Peter Carøe Lind, PhD Student, Department of Clinical Medicine
- 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

Oral sessions	Poster sessions	Flash talk sessions
10.35-12.05	12.50-14.30 and 14.50-16.20	12.50-14.30 and 14.50-16.20

10.35-12.05

Oral session 1:	Lakeside Lecture Theatre, **Per Kirkeby Auditorium**
Oral session 2:	Lakeside Lecture Theatre, **Merete Barker Auditorium**
Oral session 3:	Lakeside Lecture Theatre, **Jeppe Vontilius Auditorium**
Oral session 4:	Lakeside Lecture Theatre, **William Scharf Auditorium**
Oral session 5:	Lakeside Lecture Theatre, **Eduard Biermann Auditorium**

12.50-14.30

Poster session 1:	Anatomy (Building 1231), 2nd floor, **Room 214**
Poster session 2:	Anatomy (Building 1231), 2nd floor, **Room 216**
Poster session 3:	Anatomy (Building 1231), 2nd floor, **Room 220**
Poster session 4:	Anatomy (Building 1231), 2nd floor, **Room 224**
Poster session 5:	Anatomy (Building 1231), 2nd floor, **Room 228**
Poster session 6:	Anatomy (Building 1231), 2nd floor, **Room 232**
Poster session 7:	Building 1264, 2nd floor, **Room 209**
Poster session 8:	Building 1264, 3rd floor, **Room 310**

Flash talk session 1:	Lakeside Lecture Theatre, **William Scharf Auditorium**
Flash talk session 2:	Lakeside Lecture Theatre, **Eduard Biermann Auditorium**
Flash talk session 3:	Lakeside Lecture Theatre, **Jeppe Vontilius Auditorium**
Flash talk session 4:	Lakeside Lecture Theatre, **Merete Barker Auditorium**
Flash talk session 5:	Lakeside Lecture Theatre, **Per Kirkeby Auditorium**
Flash talk session 6:	Anatomy (Building 1231), 4th floor, **Small Anatomy Auditorium**
Flash talk session 7:	Building 1232/115, **Big Anatomy Auditorium**

14.50-16.20

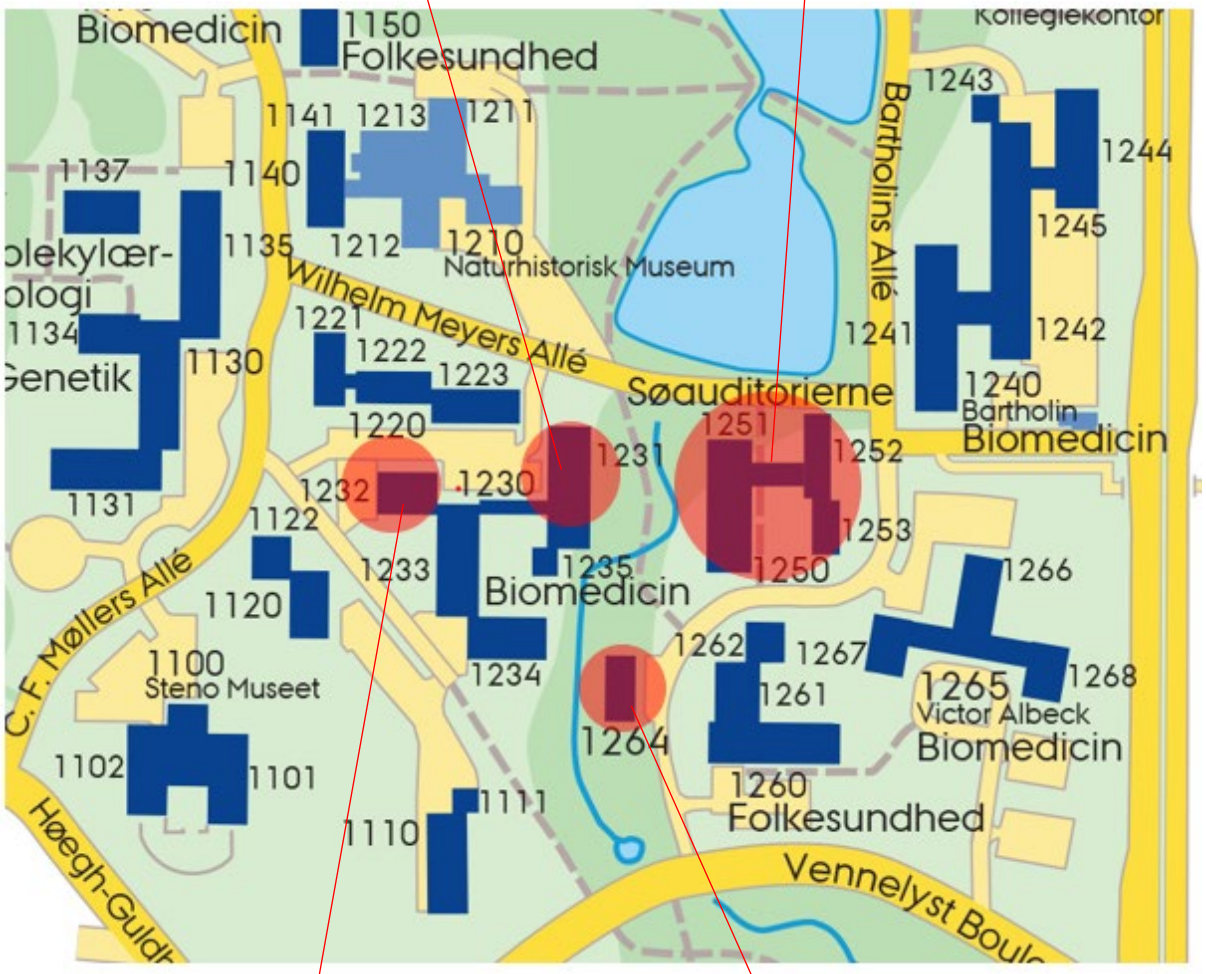
Poster session 9:	Anatomy (Building 1231), 2nd floor, **Room 214**
Poster session 10:	Anatomy (Building 1231), 2nd floor, **Room 216**
Poster session 11:	Anatomy (Building 1231), 2nd floor, **Room 220**
Poster session 12:	Anatomy (Building 1231), 2nd floor, **Room 224**
Poster session 13:	Anatomy (Building 1231), 2nd floor, **Room 228**
Poster session 14:	Anatomy (Building 1231), 2nd floor, **Room 232**

Flash talk session 8:	Lakeside Lecture Theatre, **William Scharf Auditorium**
Flash talk session 9:	Lakeside Lecture Theatre, **Eduard Biermann Auditorium**
Flash talk session 10:	Lakeside Lecture Theatre, **Jeppe Vontilius Auditorium**
Flash talk session 11:	Lakeside Lecture Theatre, **Merete Barker Auditorium**
Flash talk session 12:	Lakeside Lecture Theatre, **Per Kirkeby Auditorium**
Flash talk session 13:	Anatomy (Building 1231), 4th floor, **Small Anatomy Auditorium**
Flash talk session 14:	Building 1232/115, **Big Anatomy Auditorium**
Flash talk session 15:	Building 1264, 2nd floor, **Room 209**
Flash talk session 16:	Building 1264, 3rd floor, **Room 310**

BUILDING LOCATIONS

Anatomy Building
2nd floor: Poster sessions 1-6 and 9-14
4th floor: Flash talk sessions 6 and 13

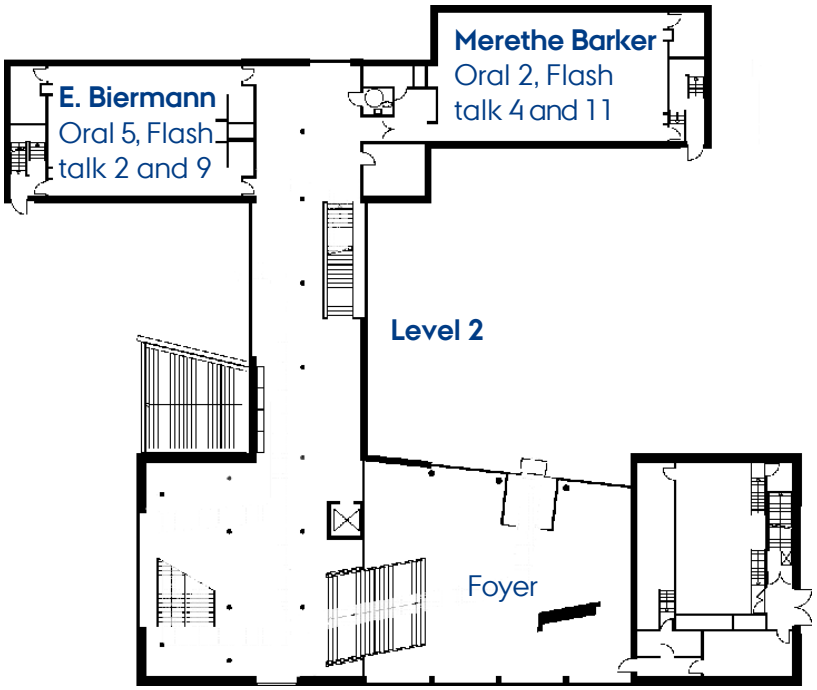
Lakeside Lecture Theatres
Oral sessions 1-5
Flash talk sessions 1-5 and 8-12

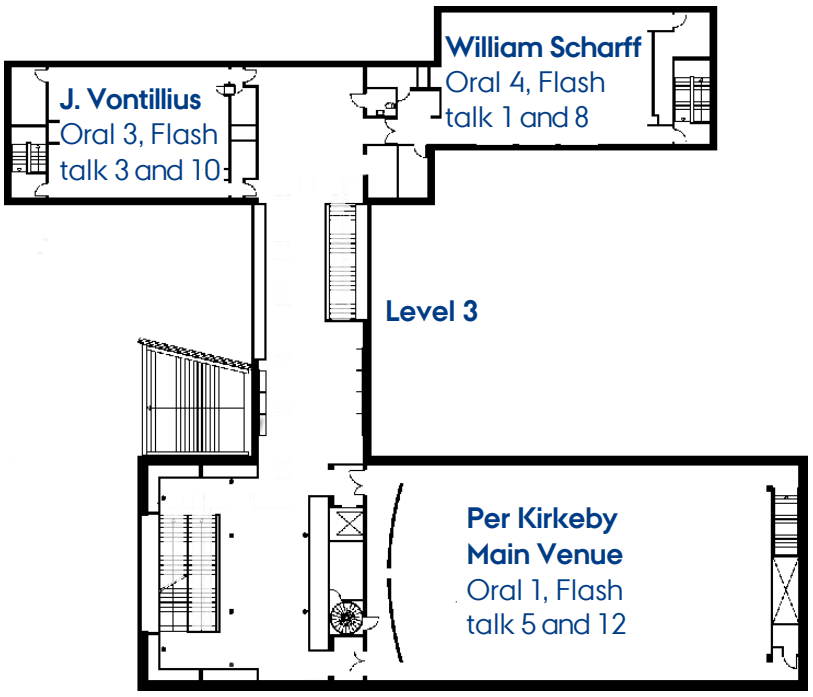


Building 1232
Flash talk session 7 and 14

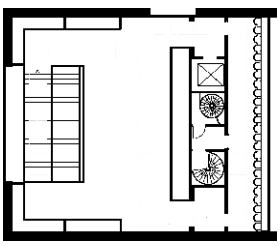
Building 1264
Poster sessions 14-15
Flash talk sessions 14-15

Lakeside Lecture Theatres





Level 4



Anatomy Building (1231, 2nd and 4th floor)
- Poster session 1-6 and 9-14
- Flash talk 6 and 13

Big Anatomy Aud. (Building 1232/115)
- Flash talk 7 and 14

Building 1264 (2nd and 3rd floor)
- Poster session 7-8
- Flash talk 15-16

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

NorDoc

is going to launch its

6th Nordic PhD Summer School

At Uppsala University and Karolinska Institutet,
16 - 18 August 2023

Find more information about the Summit **very soon** at the NorDoc website:
https://www.nordochealth.net/

Keep an eye on PhD courses in the NorDoc network

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

It was great fun in Aarhus in 2019!

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

AARHUS UNIVERSITY

AU Career PhD & JR

Career services for PhDs and junior researchers




We provide support and knowledge about non-academic career paths, career development as well as how to transition from academia to industry/public sector jobs.

Our services include:

- Individual career counselling
- Mentor programme
- Career events and workshops
- Website with advice, tools and career path descriptions

As a PhD supervisor, it is increasingly essential to discuss career paths and career development with your PhD students who in many cases seek jobs outside of academia. This can be challenging and we are here to help.

AU Career PhD & JR is a service that you can refer your PhD students to when they have questions regarding careers outside academia.

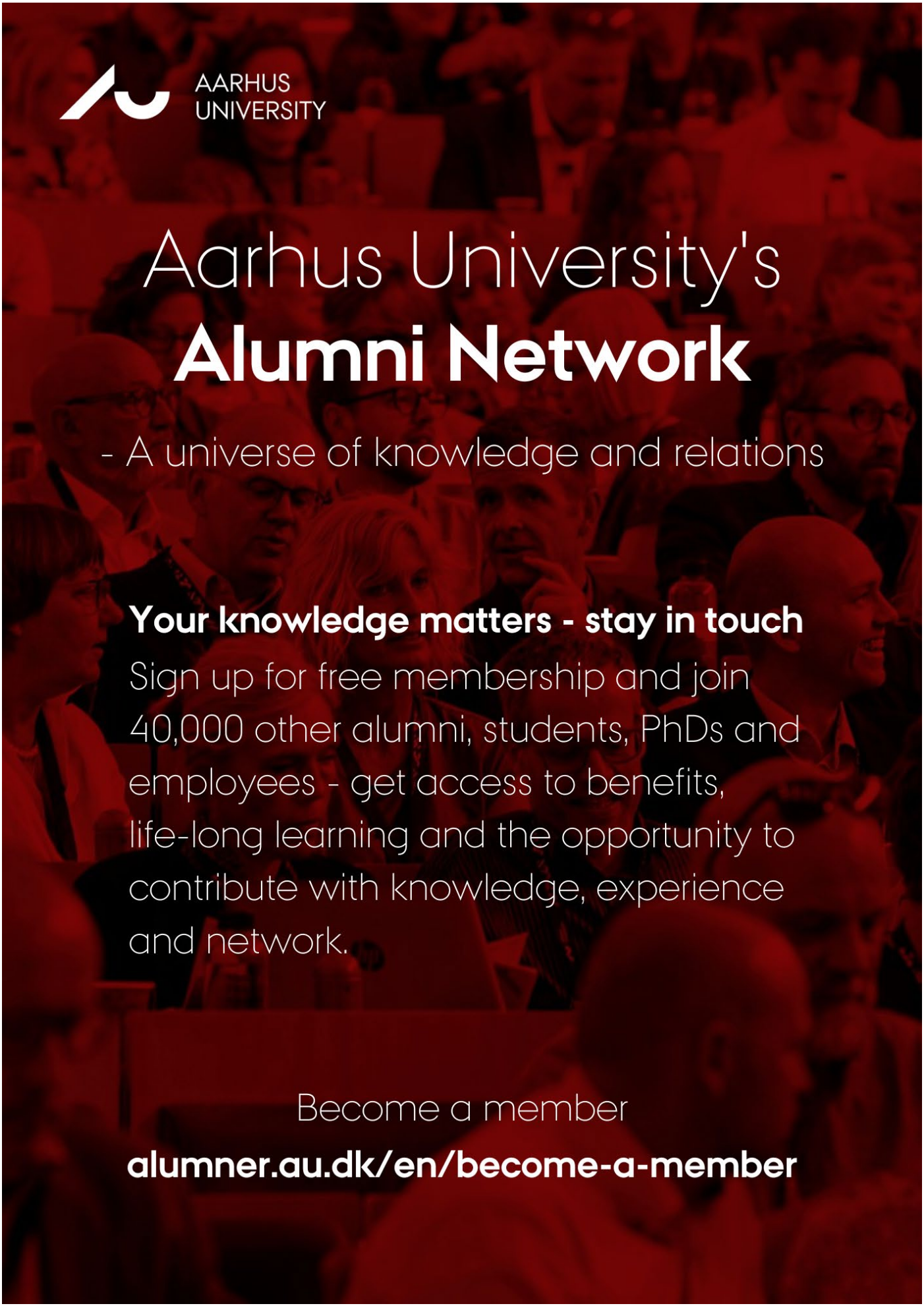
Contact us if you have any further questions and/or read more: **talent.au.dk/career**

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

Miriam Kobberømed
Ph.D. Career Consultant
Phone: +45 9352 2564
Email: mkob@au.dk

/AUCareerPhDandJR

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
Victor Albeck Building
Vennelyst Boulevard 4
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.

library.au.dk

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Royal Danish Library

DO YOU NEED FUNDING FOR YOUR RESEARCH?

Research Support Office has collected some of the most **useful tips** on how to write an **effective grant proposal** on our website

www.au.dk/fse

Here you can:

- Find help and advice on how to write your project description and tools to present your CV and budget.
- Sign up for workshops, courses and events and gain knowledge on grant writing, funders etc.

To get started and find relevant funding for your project visit:
www.researchprofessional.com

Technology Transfer Office

Technology Transfer Office (TTO) is your commercial partner at Aarhus University.

We bring your inventiontions to market

Our services include:

- IPR protection
- Business modelling
- Investor relations
- Licensing

TTO has **experience with over 1000 inventions filled by employees** and offers a designated commercial contact person for your inventions.

The contact person manages the commercialisation process from initial meetings with industry contacts through to potential final contract.

If you have any questions please contact one of our business development managers.

We are ready to help and support further dialogue.

Au.dk/TTO

Linkedin.com/company/au-techtrans

AARHUS UNIVERSITY

AARHUS UNIVERSITET
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

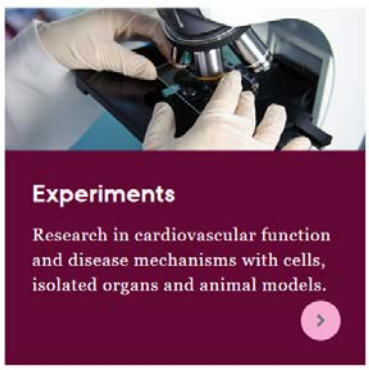
Development of talents within cardiovascular research

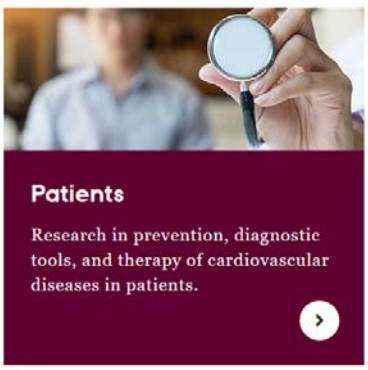
WHAT DO WE OFFER?

- 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 are the most prevalent causes of death worldwide. As a society, we need more knowledge about the correlation between e.g. inflammation and development of autoimmunity and cancer, biomarkers and molecular mechanisms of infectious & inflammatory diseases. In the Inflammation Network, we collaborate across disciplines in order to ask the right questions and to find answers.

We comprise a wide range of researchers with interest in, among others, immune-mediated diseases, diagnostic methods, epidemiological data, inflammatory markers, intracellular immune pathways, human genetics, and the understanding of cell populations and tissue structures. Our steering committee also includes two **PhD student representatives:** Fernando Valentim Bitencourt and Lotte Lindgreen Eriksen.

Scan this to join via our website

What´s in it for early career researchers?

The Inflammation Network offers you an opportunity to expand your research network, which may ultimately lead to development of long-lasting professional relationships that your future research projects could benefit from. Researchers of all career stages, including those who are still under education, contribute to the Inflammation Network. **PhD student** Morten Kelder Skouboe, who is member of a research group at Dept. of Biomedicine, says:

"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".

Mark your calendar and sign up!

Our **3rd Inflammation Network Day** is scheduled for March 8th – a day of outstanding talks bridging basic and clinical research in inflammation, infection and autoimmunity. The program features excellent keynotes on infection immunology, the microbiome, tumor immunology, autoimmunity, and numerous talks from junior researchers.

Scan this to read more and register for 3rd 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

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

UNIVERSITETET I OSLO · Université Paris Cité · Università di Pisa · universität wien

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

Are you an early career researcher within the research fields of diabetes, metabolism and/or endocrinology, and are you seeking funding for your research, world-class educational activities or new collaborations? Then check out the Danish Diabetes and Endocrine Academy.

The Danish Diabetes and Endocrine Academy collaborates with national and international universities, university hospitals, and the life science industry to foster early-career research talent through education and talent development, networking and collaboration, and grants.

The Danish Diabetes and Endocrine Academy offers:

- PhD courses, Postdoc courses and symposia
- Workshops, networking and collaboration activities
- PhD Scholarships, Postdoc Fellowships and Visiting Professorships.

National and international early-career researchers within diabetes, endocrinology, and metabolism will have open and unlimited access to our activities.

You can follow us on Twitter, LinkedIn and Instagram at Danish Diabetes and Endocrine Academy, where you can stay up to date with all the latest news and get to know us better. You can also visit our website ddeacademy.dk and stay updated with our events.

Kind regards,

Tore Christiansen
Managing Director
Danish Diabetes and Endocrine Academy

PHD DAY 2023

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 – 9.40 to 10.25

Søren Kragh Moestrup as chair.

Co-chair: Luisa Schertel Cassiano

Oral Sessions – 10.35 to 12.05

Senior chair – name	Oral session
Jakob Christensen	1
Chihiro Nakamoto	1
Christian Wejse	2
Helle Prætorius Øhrwald	2
Claus Gravholt	3
Anne Højager Nielsen	3
Johan Palmfeldt	4
Lisbeth Frostholm	4
Esben Søndergaard	5
Cathrine Hjorth	5

Co-chairs – name	Oral session
Mads Ebbesen	1
TBD	2
Omeed Neghabat	3
Ellen Steffensen	4
Stine Høvring Godsk	5

Poster Sessions – 12.50 to 14.30 and 14.50 to 16.20

Senior chairs – name	Poster session
Hans Jürgen Hoffmann	1
Oleguer Plana-Ripoll	2
Lars Rolighed	3
Dorte Rytter	4
Palle Villesen	5
Morten Nørgaard Andersen	6

Cecilie Nørby Lyhne	7
Brita Sørensen	8
Break	
Deirdre Cronin Fenton	9
Sâmia Joca	10
Pall Karlsson	11
Julie Schmidt	12
Rubens Spin-Neto	13
Poul Henning Jensen	14

Co-chairs – name	**Poster session**
Lene Nyhus Andreasen	1
Marie Bodilsen Nielsen	2
Bjørn Kristensen Fabian-Jessing	2
Rasmus H Gantzel	3
Thorkild Terkelsen	3
Anna Louise Vestergaard	4
Tina Birkeskov Axelsen	4
Johanna Laura Heinz	5
Frederik Holm Rothemejer	5
Mette Pedersen	6
Vivi Just-Nørregaard	7
Lisa Carlson Hanse	8
Break	
Martin Petri Bækby	9
Anne Gaml-Sørensen	9
Katia Soud	10
Lina Bukowski	10
Sarah Bisgaard Olesen	11
Jemila Peter Gomes	11
Cathrine Bang Overgaard	12
Sia Viborg Lindskrog	12
Lau Amdisen	13
Xin Lai	14
Laura Linnea Määttä	14

FLASH TALK SESSIONS – 12.50 TO 14.30 AND 14.50 TO 16.20

Senior chairs – name	Flash talk session
Vivi Schlünssen	1
Jasper Nijkamp	2
Tina Wang Vedelø	3
Cecilia Ramlau-Hansen	4
Christian Vægter	5
Bent Winding Deleuran	6
Zeynep Yilmaz	7
Break	
Stinne Greisen	8
Anna Halling Folkmar Andersen	9
Kristine Raaby Gammelgaard	10
Christiane Gasse	11
Jacqueline Herold	12
Nanna Rolving	13
Renee van Der Sluis	14
Birgitte Mønster Christensen	15
Alma Pedersen	16

Co-chairs – name	Flash talk session
Mikkel Oxfeldt	1
Jakob Wang	1
Camilla Ejlertsen	2
Camilla Gaarsdal Uhrbrand	3
Xiaoyu Zhou	3
Anna Sofie Koefoed	4
Karina Binda	5
Karen Maria Juul Sørensen	5
Morten Bjørn Jensen	6
Ankur Razdan	7
Break	
Tine Lauritsen	8
Peter Georgi	8
Mathias Kaas Ollendorff	9
Eleni Kanouta	10
Lasse Knudsen	11
Maiken Bay Ravn	12

Wenfeng Ma	12
Lola Qvist Kristensen	13
Nanna Steengaard Mikkelsen	14
Marie Høst Pahus	14
Jean-Claude Kresse	15
Morten Madsen	15
Lisa Tønning	16
Signe Janum Eskildsen	16

Session Overview

Find abstract titles and abstracts by searching your name or session (Ctrl+F)

Fogh-Nielsen Competition – 9.40 to 10.25

1. Shokouh Arjmand
2. Cecilie Siggaard Jørgensen
3. Nikolaj Bøgh

Oral Sessions – 10.35 to 12.05

Oral session 1

1. Anne Behrndtz
2. Tatyana Fedorova – **CANCELLED**
3. Nana Christensen
4. Thien Vinh Luong
5. Niels Okkels

Oral session 2

1. Vinni Faber Rasmussen
2. Claudia Jaensch
3. Frederik Husum Mårup
4. Lena Rosvig
5. Emilie Hasager Bonde

Oral session 3

1. Andreas Nielsen Hald
2. Anita Dittrich
3. Eva Bølling-Ladegaard
4. Hjalte Gram
5. Britt Borg

Oral session 4

1. Peter Preben Eggertsen
2. Anders Breinbjerg
3. Kristoffer Kjærgaard
4. Line Raunsbæk Knudsen
5. Louise Hermann

Oral session 5

1. Louise Engelbrecht Buur
2. Jesper Berg Nors
3. Kevin Marks
4. Kasper Bonnesen
5. Zixiang Wei

Poster Sessions – 12.50 to 14.30 and 14.50 to 16.20

Poster session 1

1. Jonathan Baier
2. Andreas Nielsen
3. Emilie Grarup Jensen
4. Layla Pohl
5. Sofie Fonager – **CANCELLED**
6. Kristian Antonsen
7. Olivia Wagman
8. Bjarke Hviid-Vyff
9. Anne Poder Petersen
10. Ali Abdul-Hussein Abood
11. Signe Bergliot Nielsen

Poster session 2

1. Anne Søjbjerg
2. Oskar Jefsen
3. Eva Skovslund Nielsen
4. Yifan Tan
5. Judit Prat Duran
6. Sandra Hummelgaard
7. Sarah Kelddal
8. Camilla Lundgreen Duus
9. Steffen Flindt Nielsen
10. Ninna Kjær Nielsen
11. Rikke Vilsbøll Milling

Poster session 3

1. Luana Domingos
2. Ole Andersen
3. Helene Bandsholm Leere Tallaksen
4. Anders Mellemkjær
5. Karen Hesseldal
6. Mikkel Breinholt Kjær
7. Mikkel Lundbech
8. Gencer Kurt
9. Andrea Lund

10. Tua Gyldenholm
11. Henrik Lynge Hovgaard – **CANCELLED**

Poster session 4

1. Ina Marie Dueholm Hjorth
2. Emmeli Mikkelsen
3. Magnus Leth-Møller
4. Sarah Bjørnholt
5. Marie Anneberg Brahe
6. Chloe Saunders
7. Signe Vogel
8. Camilla Rahr Tatari
9. Emma Davidsen
10. Helen Højgaard
11. Tanja Sofie Hansen

Poster session 5

1. Anette Bjerregaard Alrø
2. Katrine Bjørnshave Bomholt
3. Stine Fjendbo Galili
4. Morten Kelder Skouboe
5. Nanna Johnsen
6. Jacob Storgaard
7. Anne-Mette Iversen
8. Tone Rubak
9. Kirstine Hymøller
10. Demi van Der Horst
11. Kristoffer Skaalum Hansen

Poster session 6

1. Priyanshu Sinha
2. Mette Brogård
3. Casper Dueholm Vestergaard
4. Imaiyan Chitra Ragupathy
5. Pernille Thordal Larsen
6. Asta Mannstaedt Rasmussen
7. Marie Beck Enemark
8. Kasper Kjærgaard
9. Sofie Tilbæk
10. Rikke Kongsgaard Rasmussen
11. Demet Özcan

Poster session 7

1. Amanda Paust
2. Charlotte Tornøe Ekkelund Nørholm
3. Maja Thøgersen

4. Anne Dorte Lerche Helgestad
5. Maiken Meldgaard
6. Kathrine Synne Weile
7. Dalia Karzoun
8. Rasmus Møller Jørgensen
9. Søren Lomholt
10. Malthe Jessen Pedersen
11. Sandra Langsted
12. Søren Sperling

Poster session 8

1. Gregory Wood
2. Jonathan Nørtoft Dahl
3. Anders Pedersen
4. Anders Dahl Kramer
5. Jacob Seefeldt – **CANCELLED**
6. Maja Fuhlendorff Jensen
7. Diana Sharysh
8. Simon Madsen
9. Julie Axelsen
10. Katrine Berg
11. Salma Raghad Karim

Poster session 9

1. Jannik Wheler
2. Pernille Gro Thrane
3. Philip Vestergaard Munch
4. Marie Mathilde Christensen
5. Christian Skødt Antoniussen – **CANCELLED**
6. Henrik Schou Pedersen
7. Mette Søeby
8. Nadia Roldsgaard Gadgaard
9. Lina Muenker
10. Frederik Pagh Kristensen
11. Anna Melgaard

Poster session 10

1. Pia Boxy
2. Kathrine Hyldig Bjerre
3. Rasmus West Knopper
4. Vitalii Dashkovskyi
5. Ole Borup Svendsen
6. Gemma Fernández Rubio
7. Jannick Maesen
8. Elnaz Fazeli
9. Johannes Bech Steinmüller
10. Ole Ahlgreen

Poster session 11

1. Simon Bøggild Hansen
2. Camilla Blunk Brandt
3. Lotte Lina Nielsen
4. Anders Stouge
5. Amanda Bæk
6. Mathias Thygesen
7. Nichlas Christensen
8. Ludvig Renbo Olsen
9. Thomas Wisbech Skov
10. Maya Pedersen

Poster session 12

1. Saga Elise Eiset
2. Kim Hochreuter
3. Ester Ellegaard Sørensen
4. Rasmus Klitgaard
5. Christina Truelsen
6. Christoffer Trier Månsson
7. Simone Stensgaard
8. Nadine Vatterodt
9. Folefac Charlemagne Asonganyi
10. Gustav Alexander Poulsgaard

Poster session 13

1. Cristina R Exposto
2. Pernille Rikvold
3. Fernando Valentim Bitencourt
4. Jane Lauridsen
5. Karoline Kærgaard Hansen
6. Mette Amalie Nebsbjerg
7. Suzanne Olivia Foster Vander Elst
8. Stig Holm Ovesen
9. Yixin Lin
10. Maria Vlachou

Poster session 14

1. Jasper Carlsen
2. Helga Haahr-Lillevang
3. Alberte Seeberg
4. Uwe M. Pommerich
5. Peter Kolind Brask-Thomsen
6. Miriam Højholt Terkelsen
7. Ida Stisen Fogh-Andersen
8. Maja Husted Hubeishy

9. Susanne Lillelund
10. Tobias Gœmelke

Flash Talk Sessions – 12.50 to 14.30 and 14.50 to 16.20

Flash talk session 1

1. Anitha Tind
2. Stina Bollerup
3. Theresa Møller Kynde
4. Marie Hauge Pedersen
5. Amanda Marie Somer Christesen
6. Mojdeh Mansoori
7. Morten Daniel Jensen
8. Thomas Valsamidis
9. Mathias Klarlund
10. Sarah Cecilie Tscherning
11. Iben Strøm Darfelt
12. Ida Bergholdt Jul Christiansen
13. Kristin Allergodt

Flash talk session 2

1. Marjolein L.e
2. Mattias Hedegaard Kristensen
3. Mette Haldrup Jensen
4. Amalie Asmind Rosendal
5. Akila Aiyar
6. Anika Kofod Petersen
7. Katrine Johannsen
8. Anne Kraushaar Martensen
9. Uffe Kjærgaard
10. Rupan Ralf Paramasivam
11. Louise Schmidt Grau
12. Lene Holst Andersen
13. Jesper Staulund

Flash talk session 3

1. Josefine Tang Rørbech
2. Caroline Bækmann Jeppesen
3. Marie Tholstrup Philipsen
4. Mette Vestergård Pedersen
5. Michella Bjerregaard
6. Simon Horsholt Thomsen
7. Nanna Svensson
8. Sonja Izquierdo Meyer
9. Anders Schram
10. Pernille Bach Steen

11. Sofie Sejer Skoubo
12. Catalina Hartmann Skovsgård
13. Peter Lægdsmand

Flash talk session 4

1. Karen Marie Albrecht Olesen
2. Karen Omann Binderup
3. Katharina Skovhus Prior
4. Ane-Kersti Skaarup Knudsen – **CANCELLED**
5. Cecilie Møller Rønfeldt
6. Dina Overgaard Eriksen
7. Eske Glud
8. Nina Nordtorp Deacon
9. Ninna Lund Larsen
10. Sine Jacobsen
11. Solvej Videbæk
12. Stine Birkebæk

Flash talk session 5

1. Anna Rønnest Bomholt Poulsen
2. Kristyna Safrankova
3. Andreas Gammelgaard Damsbo
4. Anna Bystrup Jacobsen
5. Camilla T. Erichsen
6. Emil Peters
7. Line Amalie Hellemose
8. Matti Bock Guldager
9. Signe Mikkelsen
10. Sigrid Breinholt Vestergaard
11. Jacob Drachmann
12. Pelle De Deckere
13. Johanne Aarup Lauritsen

Flash talk session 6

1. Tobias Stemann Lau
2. Rikke Nicoline Stokholm
3. Laura Krogh Herlin
4. Cathrine Elgaard
5. Maria Danielsen
6. Yumi Chokyu Del Rey
7. Sissel Due Jensen
8. Ida Marie Marquart Løber
9. Lukas Ridder
10. Kathrine Bohn Faldborg
11. Laura Stenbro
12. Laura Andersen

Flash talk session 7

1. Kirsten Woolpert
2. Anne Juhl Nielsen
3. Anne Sofie Baymler Lundberg
4. Bayan Sardini
5. Malene Lykke
6. Elisabeth Solmunde
7. Fie Langmann
8. Lisbeth Mølgaard Laustsen
9. Nicoline Stidsen
10. Ina Grønkjær Laugesen
11. Jesper Medom Vestergaard
12. Ulrik Bak Kirk

Flash talk session 8

1. Mie Wolff Kristensen
2. Simon Nyberg Thomsen
3. Henriette Mathiesen
4. Nanna Kristjánsdóttir
5. Nina Lykkegaard Gehr
6. Oliver Kjærlund Hansen
7. Jakob Holsting
8. Johannes Frasez Sørensen
9. Stine Bogetofte Thomasen
10. Vanaja Kumarasegaram
11. Villads Lundsteen Jacobsen

Flash talk session 9

1. Kristian Savstrup Kastberg
2. Jamal Bousamaki
3. Emil Winkel
4. Frederik Skov
5. Louise Bendixen
6. Tobias Wang Bjerg
7. Mikkel Dahl-Jessen
8. Adriano Chaves
9. Anders Tobias Frederiksen
10. Yan Hu
11. Stig Henrik Andersen

Flash talk session 10

1. Karolina Klucznik
2. Kasper Grooss
3. Anders W. Mølby Nielsen
4. Klara Lanng
5. Anja Gouliaev Kirkeby

6. Asbjørn Kjær
7. Carmen Oroperv
8. Line Kristensen
9. Emil Leth Lauridsen
10. Fanny Asmussen
11. Louise Elkjær Fløe

Flash talk session 11

1. Julie Løye Hejl
2. Laura Omann
3. Astrid Becker-Larsen
4. Astrid Ibsen Bruun
5. Charlotte Duholm
6. Christine Leonhard Birk Sørensen
7. Danni Chen
8. Ellen Bjerre-Nielsen
9. Maria Louise Jöhnk
10. Frida Hæstrup
11. Stinne Eika Rasmussen

Flash talk session 12

1. Maria Bolther Pælestik
2. Lise Filt Jensen
3. Christina Shen-Zhuang Nielsen
4. Gitte Stokvad Brix
5. Louise Bjerregaard
6. Christel Gry Aagren Nielsen
7. Anne Mohr Drewes
8. Katrine Dorn Brodersen
9. Alexandra Amalie Uglebjerg
10. Henrik Bjerre
11. Peter Carøe Lind

Flash talk session 13

1. Nadia Iraqi – **CANCELLED**
2. Jacob Hartmann Søby
3. Søren-Haldur Bülow Rasmussen
4. Thomas Skaarup Godsk
5. Mohab Basem Abdallah
6. Julie Stengaard Brewer
7. Casper Homilius
8. Anne Louise Jensen
9. Lise Lykke
10. Malene Kærslund Hansen
11. Didde Kidmose Kristensen

Flash talk session 14

1. Marvin Werner
2. Cecilie Siem Bach-Nielsen – **CANCELLED**
3. Majbritt Jeppesen
4. Emma Falling Iversen
5. Fredrikke Dam Larsen
6. Qian Liu
7. Jonas Holst Wolff
8. Vibeke Klastrup
9. Sujan Ravendran
10. Victor Næstholt Dahl
11. Xiangning Ding

Flash talk session 15

1. Camilla Mains Balle
2. David Haldrup
3. Emma B. Johannsen
4. Jelena Stankovic
5. Thomas Stax Jakobsen
6. Mathias Hänel
7. Frederik Søholm Gillesberg
8. Mai-Britt Skadborg
9. Maria Chrysopoulou
10. Sidse Høyer
11. Pernille Duedahl

Flash talk session 16

1. Laura Houstrup Matthiesen
2. Ida Marie Melsen
3. Niels Holm
4. André Sejr Klenø
5. Martin Bækgaard Stisen
6. Tine Rasmussen
7. Anette Viftrup
8. Malene Blumenau Pedersen
9. Chenghao Gu
10. Helle Christiansen
11. Sara Ellegaard Andreasen

PHD DAY 2023

Abstracts

FOGH-NIELSEN COMPETITION

Sex, estrous cycle, and ketamine in depression: A path to a novel mechanism of action for ketamine

Shokouh Arjmand, Department of Clinical Medicine, Translational Neuropsychiatry Unit

M.V. Pedersen, Department of Clinical Medicine; N.R. Silva, Department of Biomedicine; C. Biojone, Department of Biomedicine; C.R. Cecchi, Department of Biomedicine; S. Joca, Department of Biomedicine; A.M. Landau, Department of Clinical Medicine; H. Kaastrup Müller, Department of Clinical Medicine; G. Wegener, Department of Clinical Medicine

While holding a great promise for treating the subgroups of depressed patients who do not respond adequately to antidepressants, discrepancies among the findings of preclinical studies as well as a dearth of disaggregation of the outcomes of clinical studies in males and females, and of females in different stages of the menstrual cycle, have limited personalized prescription of ketamine. Here, in a translational approach, the behavioral sensitivity to an acute subanesthetic dose of ketamine in freely cycling female and male Flinders Sensitive Line (FSL) rats was examined. To evaluate the effects of the estrous cycle on depressive-like behaviors, baseline depressive- and anxiety-like behaviors were assessed during physiological fluctuations of ovarian sex hormones. Next, the hypothesis of the possible direct interaction of ketamine with sex steroid receptors (ERα, ERβ, GPR30, PRs) was explored *in silico*. Using a battery of behavioral tests, we first demonstrated that ketamine has antidepressant-like effects in FSL rats. Within our study power, we could not detect any sex- or estrous-cycle-specific different antidepressant-like responses to ketamine. We conclude that physiological oscillations of ovarian sex hormones neither amplify nor diminish the behavioral antidepressant-like effect of ketamine in FSL rats. In addition, such hormonal fluctuations do not predispose female animals to exhibit enhanced or reduced depressive-like behaviors. In parallel, molecular docking simulations revealed preliminary evidence that ketamine might exert a rapid antidepressant activity by directly interacting with estrogen receptors alpha and beta, as well as progesterone receptors, but not GPR30.

Keywords: Psychiatry, psychology and mental health, Animal models/disease models, Pharmacology

Pathogenesis of enuresis - impact on treatment

Cecilie Siggaard Jørgensen, Department of Clinical Medicine,

C. S. Jørgensen, Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital, Aarhus; J. P. Thirstrup, Department of Biomedicine, Aarhus University, Aarhus, Denmark; B. Walters, deCODE genetics/Amgen, Reykjavík, Iceland; A. S. Breinbjerg, Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital, Aarhus; C. Albiñana, National Centre for Register-based Research, Department of Economics and Business Economics, Aarhus University, Aarhus, Denmark; D. Demontis, Department of Biomedicine, Aarhus University, Aarhus, Denmark; J. Grove, Department of Biomedicine, Aarhus University, Aarhus, Denmark; B. J. Vilhjálmsson, deCODE genetics/Amgen, Reykjavík, Iceland; H. Stefánsson, deCODE genetics/Amgen, Reykjavík, Iceland; E. Agerbo, National Centre for Register-based Research, Department of Economics and Business Economics, Aarhus University, Aarhus, Denmark; A. Børglum, iPSYCH, The Lundbeck Foundation Initiative for Integrative Psychiatric Research, Aarhus, Denmark; T. D. Als, Department of Biomedicine, Aarhus University, Aarhus, Denmark; S. Rittig, Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital, Aarhus, Denmark; K. Kamperis, Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital, Aarhus, Denmark; K. Stefánsson, deCODE genetics/Amgen, Reykjavík, Iceland; J. H. Christensen, Department of Biomedicine, Aarhus University, Aarhus, Denmark.

Introduction:

Nocturnal enuresis (NE) is a highly hereditary disorder. Recently, we have shown that common genetic variants play a substantial role in NE risk and pointed at the first genome-wide significant loci. Here we present an updated genome-wide association study (GWAS) of NE.

Methods:

NE cases (5-25 years of age) were identified within iPSYCH2015, which is a large population-based Case–Cohort sample, based on ICD-10 diagnoses and redeemed desmopressin prescriptions. The GWAS was based on unrelated individuals and a genetically homogenous sample and performed using logistic regression including relevant covariate. Polygenic risk scores (PRS) were analyzed for association with NE.

Results:

The GWAS included 7,971 NE cases and 65,795 controls. We confirmed previously identified NE loci on chromosome (chr) 6 and chr13 (rs11155041 (chr6), P=1.78x10-18 and rs6563038 (chr13), P=3.96x10-12). Furthermore, we identified novel independently associated variants at chr6 (rs6908136 (lead variant), P=4.11x10-9) and a variant at chr 20,

which was borderline significantly associated with NE (rs6112794, P=5.11x10-8). The findings were replicated in an Icelandic sample. PRSs for ADHD and BMI were associated with NE (P<0.05).

Conclusion:

We hereby confirmed the role of common genetic variants in NE risk and point at novel genomic loci for NE. Among the new potential NE risk genes mapped, we highlight the HCRTR2 gene encoding the Orexin receptor type 2. Of relevance to NE pathoetiology, the orexin/hypocretin system is essential in the regulation of sleep and arousal. An orexin receptor antagonist (Suverexant) has in a case report been shown to be effective in NE treatment.

Keywords: Paediatrics, Nephrology, Urology

Metabolic MR of the brain - from basic shuttles to clinical translation

Nikolaj Bøgh, Department of Clinical Medicine, MR Research Center

N Bøgh, CW Rasmussen, LB Bertelsen, ESS Hansen, C Laustsen. The MR Research Center, Dept. of Clinical Medicine

MRI with hyperpolarized [1-13C]pyruvate enables in vivo detection of the conversion of pyruvate to lactate and bicarbonate, representing a key metabolic cross-section. A one-cell model is often used in hyperpolarized MRI; but, in fact, the brain's metabolism is compartmentalized as hypothesized in the astrocyte-neuron lactate shuttle model. In this somewhat controversial framework, pyruvate is converted to lactate in astrocytes and shipped to neurons for oxidation to bicarbonate. We hypothesized that bicarbonate detection is sensitive to depletion of MR-signal of lactate, suggesting shuttling of lactate from glial cells to neurons.

We imaged rats (n = 13) using hyperpolarized [1-13C]pyruvate on a 3T system. In a cross-over fashion, each rat was scanned twice, only altering the lactate flip-angle (0° or 90°) – effectively preserving or destroying the signal available for conversion to bicarbonate. In 8 rats, we performed imaging of the brain. Subsequently, we performed imaging of the heart, liver, and kidneys in 5 rats.

In the brain, bicarbonate signal-to-noise ratio (SNR) increased ~65% when lactate was not excited. The pyruvate SNR was equivalent between experiments, indicating negligible differences in perfusion or polarization. In the heart, kidney, and liver, we observed no effects of lactate excitation.

In MRI with hyperpolarized [1-13C]pyruvate of the brain, the bicarbonate SNR was decreased when the MR-signal was destroyed while in the lactate pool. This effect was isolated to the brain. Our findings provide a new line of evidence for shuttling of lactate from astrocytes to neurons.

Keywords: Basic neuroscience, Molecular metabolism and endocrinology, Clinical neuroscience

Oral sessions

Oral session 1

Can Helicopters solve the Transport Dilemma for Patients with Symptoms of Large-Vessel Occlusion Stroke in Intermediate density Areas?

A simulation model based on real life data

Anne Behrndtz, Department of Dentistry and Oral Health

A. Behrndtz, R. Beare2, S lievlieva2, G. Andersen1, J. Mainz1, M. Gude3, H. Ma2, V. Srikanth2, C.Z. Simonsen1, T. Phan2

1Aarhus University Hospital, Neurology, Aarhus, Denmark, 2Monash University, Stroke and Ageing Research, Department of Medicine, School of Clinical Sciences at Monash Health, Melbourne, ACT, Australia, 3Department of Clinical Medicine, Prehospital Department, Aarhus N, Denmark

Background: This modeling study aimed to determine if helicopters may optimize transportation of patients with symptoms of large vessel stroke in "intermediate density" areas like Denmark, by bringing them directly to comprehensive stroke center.

Methods: We estimated time to treatment for patients requiring endovascular therapy or intravenous thrombolysis under four configurations: "drip and ship" with and without helicopter and "bypass" with and without helicopter. Time delays, stroke numbers per municipality, and helicopter dispatches for four helicopter bases from 2019 were obtained from the Danish Stroke and Helicopter Registries. Discrete event simulation (DES) was used to estimate the capacity of the helicopter fleet to meet patient transport requests, given the number of stroke codes per municipality.

Results: The median onset-to-needle time at comprehensive stroke center (CSC) for the bypass model with helicopter was 115 minutes (interquartile range (IQR): 108, 124); the median onset-to-groin time was 157 minutes (IQR: 150,166). The median onset-to-needle time at the primary stroke center (PSC) by ground transport was 112 minutes (IQR: 101, 125) and the median onset-to-groin time when primary transport to the PSC was prioritized was 234 minutes (IQR: 209, 261).

Linear correlation between travel time by ground and the number of patients transported by helicopter (rho = 0.69, p< 0.001) indicated that helicopters are being used to transport more remote patients. DES demonstrated that an increase in helicopter capture zone by 20 minutes increased the

number of rejected patients by only 5%.

Conclusions: Our model calculations suggest that using helicopters to transport stroke patients

Keywords: Clinical neuroscience, Work environment and organisation, Other

Evaluation of 11C-donepezil as a biomarker for parasympathetic denervation and possible applications in early Parkinson's disease

Tatyana Fedorova, Department of Clinical Medicine

L Seidelin, Dept. of Clinical Medicine; K Knudsen, Dept. of Nuclear Medicine; EH Danielsen, Dept. of Neurology; DJ Brooks, Dept. of Clinical Medicine; P Borghammer, Dept. of Clinical Medicine.

Background

Parkinson's disease (PD) is a debilitating disorder that affects 1% of people over 60 years of age. The primary features of PD are motor symptoms including bradykinesia, tremor, postural instability, and rigidity. However, non-motor symptoms such as constipation, sleep disturbances and psychological problems have gained visibility in recent years. Unfortunately, we have yet to develop a robust method to detect and follow PD progression in the periphery. Here we aim to investigate the use of a positron emission tomography (PET) tracer, 11C-donepezil, as a potential biomarker for peripheral parasympathetic denervation.

Methods

We included 19 PD patients with a mean disease duration of 1.5 years, 12 vagotomised patients and 16 age- and sex-matched controls. High-resolution CT-scans and PET 11C-Donepezil images of abdomen and thorax were obtained from all subjects. PMOD software was used to manually define volumes of interest based on anatomical CT scans and functional PET scans using a modified version of previously described methodology.

Results

11C-donepezil PET signal in PD patients was decreased by 14 % (p=0.04) in the small intestine and 22 % (p=0.002) in the colon compared to healthy controls. In vagotomised patients the decrease in PET signal was even more pronounced with a decrease of 33% in the small intestine (p=0.0004) and 22 % in the colon (p=0.003).

Conclusion

In conclusion, our work established the presence of parasympathetic degeneration in early PD and the relevance of 11C-donepezil PET as a marker of damage to peripheral parasympathetic neurons. These findings will allow for future studies of peripheral parasympathetic degeneration in prodromal PD.

Keywords: Clinical neuroscience, Medical technology and diagnostic techniques, Basic neuroscience

Repeated measurements of lower leg skeletal muscle perfusion using 15O-H2O PET/CT

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J. Sørensen, Department of Nuclear Medicine & PET Centre, Aarhus University Hospital, Aarhus K. Bouchelouche, Department of Nuclear Medicine & PET Centre, Aarhus University Hospital, Aarhus

M.A. Madsen, Department of Nuclear Medicine & PET Centre, Aarhus University Hospital, Aarhus

L.P. Tolbod, Department of Nuclear Medicine & PET Centre, Aarhus University Hospital, Aarhus

Introduction: 15O-H2O PET/CT is the gold standard for non-invasive measurements of tissue perfusion and can potentially play a future role in the diagnosis and treatment of peripheral artery disease. We aimed to measure the variation of normal resting perfusion in calf muscles between individuals and between repeated measurements in the same individual.

Methods: 10 healthy subjects underwent two identical 15O-H2O PET/CT scans of the calves, separated by a 5-min. break, where they were taken out of the scanner and asked to walk a few steps. Low-dose CT was followed by an injection of 400MBq 15O-H2O and a 6-min. dynamic PET scan. We defined volumes of interest (VOIs) in different muscles (gastrocnemius(GAS),soleus(SOL),tibialis anterior(TA), and peroneus longus(PL)) of each subject for quantitative measurements of 15O-H2O. Kinetic analysis was performed using in-house developed software. K1 (ml/100ml/min) was estimated using a 1-tissue compartment model.

Results: Resting K1 values ranged from 0.13-0.73 ml/100ml/min (median 0.26). Variation was observed in the muscle groups, with median K1 values of 0.32(GAS), 0.24(PL), 0.37(SOL), and 0.25(TA) ml/100ml/min in the first scan. Repeated measurements of 15O-H2O PET/CT perfusion in calf muscles showed a strong correlation of K1 values (slope:1.02,r=0.90) and the blood input function did not change between the repeated scans.

Conclusion: Normal resting perfusion in four muscle groups of the calf ranged from 0.13-0.73 ml/100ml/min in healthy subjects. The largest variation was seen between individuals, with a smaller variation between muscle groups. Repeated measurement of resting blood flow yielded a strong overall correlation of K1.

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Other

Does a three week ketogenic diet have an impact on whole-body metabolism and cardiac parameters?

Thien Vinh Luong, Department of Clinical Medicine, Department of Nuclear Medicine and PET-Centre & Steno Diabetes Center Aarhus

L.C. Gormsen, Department of Nuclear Medicine and PET-Centre, Aarhus University Hospital; E. Søndergaard, Steno Diabetes Center Aarhus, Aarhus University Hospital; N. Møller, Steno Diabetes Center Aarhus, Aarhus University Hospital

Background. Ketone bodies (KB) are produced in the liver as a fuel when blood glucose levels are low, as can be seen with a ketogenic diet (KD) or prolonged fasting. Our group has demonstrated that infusion of ketone salts increases cardiac output by 2 l/min and ejection fraction by 8% in heart failure patients, and that ketosis promotes a metabolic shift away from glucose and fatty acid oxidation towards the less oxygen requirering ketone body oxidation.

Purpose. To investigate whether a KD affects metabolic and cardiac parameters compared to a standard diet (SD).

Methods. A randomized, crossover study of 11 obese individuals aged 50-70 years. Each individual underwent three weeks of both a KD and a SD. After each period, a study day containing blood samples, biopsies, indirect calorimetry and hyperinsulinemic euglycemic clampand an evaluation of cardiac parameters with positron emission tomography scans were performed.

Preliminary results. Metabolic measurements showed a slightly higher M-value during a KD compared to a SD ($p=0.14$). The respiratory exchange ratio was lower during the KD under clamp conditions ($p<0.05$). Myocardial fatty acid esterification ($p<0.05$) and oxidation ($p<0.05$) were significantly different. The coronary flow reserve in the heart increased significantly ($p=0.01$).

Conclusion. The KD creates a shift towards fatty acid and KB oxidation on whole-body level, even during infusion of insulin and glucose, and a tendency towards an increase in insulin sensitivity. For the heart, a KD significantly increases the myocardial blood flow and an increase in myocardial fatty acid esterification, as expected, but a lower myocardial fatty acid oxidation.

Keywords: Cardiovascular system, Molecular metabolism and endocrinology, Medical technology and diagnostic techniques

Distribution of Cholinergic Nerve Terminals in the Elderly Human Brain Measured with [18F]FEOBV PET

Niels Okkels, Department of Clinical Medicine

N. Okkels, Department of Nuclear Medicine and PET, Aarhus University Hospital; J. Horsager, Department of Nuclear Medicine and PET, Aarhus University Hospital; M. Labrador-Espinosa, Unidad de Trastornos del Movimiento, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Seville, Spain; F.O. Hansen, Department of Nuclear Medicine and PET, Aarhus University Hospital; K. Andersen, Department of Nuclear Medicine and PET, Aarhus University Hospital; T. Fedorova, Department of Nuclear Medicine and PET, Aarhus University Hospital; C. Skjærbæk, Department of Nuclear Medicine and PET, Aarhus University Hospital; O.L. Munk, Department of Nuclear Medicine and PET, Aarhus University Hospital; K.V. Hansen, Department of Nuclear Medicine and PET, Aarhus University Hospital; H. Gottrup, Department of Neurology, Aarhus University Hospital; A.K. Hansen, Department of Nuclear Medicine and PET, Aalborg University Hospital; M.J. Grothe, Unidad de Trastornos del Movimiento, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Seville, Spain; P Borghammer, Department of Nuclear Medicine and PET, Aarhus University Hospital.

INTRODUCTION

[18F]fluoroetoxybenzovesamicol ([18F]FEOBV) is a positron emission topography (PET) tracer for the vesicular acetylcholine transporter (VAChT), a protein located in cholinergic nerve terminals. We used [18F]FEOBV PET to study the cholinergic topography of the healthy human brain.

MATERIALS AND METHODS

[18F]FEOBV PET brain images of healthy elderly humans were normalized to standard space. The spatial distribution of tracer was quantified using stereotactic atlases and compared with histological data as well as gene expression data. Eighteen participants (61% males) and a mean age of 73.7±6.0 years were recruited.

RESULTS

Highest tracer binding was present in the striatum, a few thalamic nuclei, and the basal forebrain. Intermediate binding was found in most nuclei of the brainstem, thalamus, and hypothalamus; the vermis and flocculonodular lobe; and key limbic structures such as the hippocampus and amygdala. Lowest binding was present in most areas of the cerebral cortex, and in the cerebellar nuclei and hemispheres. The spatial distribution of tracer correlated with immunohistochemical post-mortem data, as well as with regional expression levels of SLC18A3, the VAChT coding gene.

DISCUSSION

Our in vivo findings confirm the regional cholinergic distribution in specific brain structures as described post-mortem. A positive spatial correlation between tracer distribution and regional gene expression levels further corroborates [18F]FEOBV PET as a validated tool for in vivo cholinergic imaging. The study represents an advancement in the continued efforts to delineate the spatial topography of the human cholinergic system in vivo.

Keywords: Clinical neuroscience, Basic neuroscience, Psychiatry, psychology and mental health

ORAL SESSION 2

Large fiber-, small fiber- and autonomic neuropathy in adolescents with type 1 diabetes, relative risk factors, and diagnostic ability of bedside tests

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Aim

To estimate the prevalence of large fiber- (LFN), small fiber- (SFN), and autonomic neuropathy in adolescents with type 1 diabetes (T1D). In addition, to investigate possible risk factors and bedside methods used to assess neuropathy.

Methods

Sixty adolescents with a diabetes duration of T1D >5 years and 23 healthy adolescents were enrolled. Neurological examination and following diagnostic gold standard tests for LFN, SFN, and autonomic neuropathy were performed: nerve conduction studies (NCS), skin biopsies determining intraepidermal nerve fiber density (IENFD), quantitative sudomotor axon reflex test (QSART), cardiovascular reflex tests (CARTs), and tilt table test analyzing orthostatic parameters. In addition, bedside tests (biothesiometer, DPNCheck, Sudoscan, VAGUS) were performed and compared with gold standard tests with ROC analysis.

Results

The included adolescents with T1D had a mean diabetes duration of 9.8 years, and HbA1c of 61 mmol/mol [7.7%]. There were confirmed LFN or SFN in 14% and 2%, respectively. Abnormal sweat response was found in 20%, cardiovascular neuropathy in 8%, and orthostatic hypotension in 14%. A higher relative risk ratio for neuropathy was found in adolescents with higher insulin dose per weight per day, and changes in lipid profile. The included bedside tests had poor to acceptable concordance with the gold standard tests (all, AUC ≤ 0.75).

Conclusion

The high occurrence of neuropathy highlights the need for more focus on avoiding, screening, and monitoring neuropathy in adolescents with T1D in childhood. Identifying risk

factors for developing neuropathy and progression seems relevant to prevent accompanying symptoms later in life.

Keywords: Paediatrics, Clinical neuroscience, Molecular metabolism and endocrinolog

Supporting Self-Regulated-Learning in colonoscopy training - A comparison cohort trial.

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Aim: This study aimed to show that self-regulated learning can improve colonoscopy skills.

Background: Colonoscopy is the golden standard in detecting colorectal cancer and removing its precursors: polyps. Colonoscopy is difficult to learn and takes several hundred procedures to master. A well-known construct in education is the concept of self-regulated learning. It is the trainee's ability to understand and control her learning environment. Key abilities include self- and situation awareness, task analysis and strategic planning. Self-regulated learning has never been used in colonoscopy training before.

Methods: In a comparison cohort trial participants used the self-regulated-learning principles, video feedback and an online learning platform to train colonoscopy. In the control cohort participants performed patient-based colonoscopy as usual for their department. Improvement was monitored via three video based ratings (study start, end of study period, retention test) using the Gastrointestinal Endoscopy Competency Assessment Tool GiECAT. Outcomes were analysed using two-way ANOVA.

Results: 21 participants were recruited, 12 in the intervention and 9 in the control cohort. A total of 58 videos were rated. Scores ranged from 15 to 43 point, mean (SD) of 29.0 (8.4). Mean GRS scores increased in the intervention cohort during the study period from 17.7 (4.5) to 23.2 (5.0) as compared to 17.5 (4.7) and 18.1 (6.5) in the control cohort. Overall, this difference was not statistical significant (p=.235).

Conclusions: Self-regulated learning seemed to help trainees in improving their colonoscopy skills. More studies are necessary to show a clear effect.

Keywords: Health education and simulation-based training, Gastrointestinal surgery, Gastrointestinal surgery

Plasma potassium levels and eGFR poorly predict severe hyperkalemia following spironolactone introduction in patients with chronic kidney disease at high risk of hyperkalemia – A cohort study

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Background:

Mineralocorticoid receptor antagonists (MRAs) reduce blood pressure (BP), albuminuria and disease progression rate in patients with chronic kidney disease (CKD). However, hyperkalemia (HK) is a common side effect, and patients with high P-potassium and/or low eGFR are excluded from MRA studies and treatment guidelines due to the fear of HK-induced arrhythmias.

Aim:

To test the effect of the MRA spironolactone on P-potassium, eGFR and albuminuria in CKD patients at high risk of HK.

Methods:

58 patients with eGFR 25-60 ml/min and P-potassium > 4.5mmol/l on maximal tolerated RAS-blockade were included. Following counselling on a low-potassium diet, Spironolactone was introduced at 25mg and increased to 50mg daily if tolerated. Follow-up was 4 weeks. Paired t-test was used to compare pre and post-spironolactone means.

Results:

Baseline eGFR (mean 39ml/min) and albuminuria (median 1228mg/g) declined by 14% (11-18%) and 49% (44 – 54%) respectively. Mean BP did not change (p=0.6). Mean spironolactone dose was 45.7mg (43.2-48.2mg). P-potassium increased from 4.7 to 5.2mmol/l (Δ0.5mmol/l, 95% CI: 0.3-0.7mmol/l). 17 patients developed severe HK > 5.5 mmol/l; 2 were briefly admitted with P-potassium >6.3mmol/l without sequelae. Severe HK was neither predictable from baseline potassium levels (p=0.83) nor eGFR (p=0.13).

Discussion:

This study shows that given dietary counselling, MRAs can safely be introduced in most patients with CKD thought to be at high risk of HK. Importantly, neither baseline potassium

levels nor baseline eGFR predicted the risk of severe HK. Thus, excluding patients from MRA treatment based solely on eGFR and P-potassium levels may not be appropriate.

Keywords: Nephrology, Pharmacology, Multimorbidity

Improving team performance of severe postpartum haemorrhage using real-life video debriefing

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Introduction: Video debriefing of real-life emergencies offers an opportunity to review the care delivered in high-risk, and time-critical situations, supplementing the team members' memories. The objective of this study was to examine the effect of real-life video debriefing on the obstetric teams' management of severe postpartum haemorrhage.

Methods: The study was conducted at two Labour and Delivery Units, Horsens Regional Hospital and Aarhus University Hospital. Inclusion criteria was vaginal births with a blood loss >1000 mL within two hours after birth. All delivery rooms were equipped with an automatic recording system that enabled filming of teams managing severe postpartum haemorrhage. Video recording required informed consent from all participants. Videos were included as follows: 1) Video inclusion, before introducing real-life video debriefings of team performance; 2) During the start-up of the debriefings; 3) After real-life video debriefings had been introduced as standard procedure. Primary outcome is Clinical performance score (TeamOBS-PPH). Secondary outcomes are non-technical performance score (AOTP) and total blood loss (mL).

Results: 226 videos were included over 12 month (2020-2021) for baseline comparison. 206 videos were included over 12 months (2021-2022) during the intervention period. Of these, 93 videos were used in a subsequent video debriefing. Video analysis will be conducted within the next four months.

Conclusions: This project will contribute to novel knowledge on how to improve actual patient care during emergencies, and how communication and teamwork impacts on the emergency treatment we provide in the delivery room.

Keywords: Gynecology and obstetrics, Health education and simulation-based training, Other

Impacting the psycho-social work environment: how an organizational-level, workplace-adapted mindfulness-based intervention may affect the social capital and psychological safety. A qualitative content analysis

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Introduction: The program "Mindfulness-based stress reduction" (MBSR) has been found effective in enhancing individuals' mental health across study populations and settings, including workplaces. However, the knowledge of organizational effects of MBSR in the workplace is scarce. The purpose of this study was to investigate how social capital and psychological safety in the workplace may be impacted by an organizational-level MBI including a workplace-adapted MBSR program.

Methods: Four companies were included in this quasi-experimental study. The intervention followed three steps: 1. a two-hour introductory session, 2. voluntary participation in a 10-weeks workplace-adapted MBSR program, 3. an implementation workshop for selected company representatives. Data was collected via focus group interviews at baseline and post intervention and analyzed using deductive content analysis.

Results: Small positive changes to the bonding social capital (intradepartmental) and the linking social capital (between managers and employees) were seen. The greatest impact was on the bridging social capital (interdepartmental), characterized primarily by enhanced collaboration between departments. Improvements in the psychological safety among people at the same level of employment were seen post intervention. However, the psychological safety between managers and employees remained unchanged.

Discussion: This study offers insights into the potential beneficial impact of a workplace-MBI on social capital and psychological safety. Implications for workplaces and future research will be discussed, including a discussion of what characteristics of mindfulness that might contribute to this impact.

Keywords: Public health, Work environment and organisation, Qualitative research

ORAL SESSION 3

Understanding the mechanisms of interprofessional collaboration between care professions as the interplay between institutional work and temporal-oriented agency

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Introduction

We examined the underlying mechanisms of interprofessional collaboration between different care professions in the delivery of home care services in Danish municipalities by answering: 1. How do care professions through daily practices use their agency to secure the interprofessional collaboration? 2. How do they create, maintain and disrupt institutional arrangements in this process?

Methods

The case was the interprofessional collaboration between personal workers, nurses, and therapists in two Danish municipalities. Data consisted of 8 staff focus group interviews, 6 individual manager interviews, and 16 observation days. We performed thematic qualitative data analyses to answer the research questions

Results

Preliminary findings show that the care professionals secured the interprofessional collaboration through four identified categories of interplay between agency and institutional work: (1) maintaining by adopting new practices to account for inept institutional practices, (2) maintaining by enacting institutionalized practices, (3) disrupting by enacting habitual practices not aligned with new institutional practices, and (4) creating by inventing and establishing institutional mechanisms.

Discussion & Conclusion

Results show that different professional groups have different opportunities to perform institutional work if they are dissatisfied. The personal workers need to (3) disrupt institutional arrangements, whereas nurses and therapists can (4) create new institutional arrangements. Moreover, care professionals can switch between rationales to reason their practices when relevant, and do so in a smart and intelligent manner.

Keywords: Public health, Qualitative research, Other

Metabolic adaptations during heart regeneration in the axolotl salamander

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Aim: Illuminate the interplay of metabolism and heart regeneration by assaying metabolism during different time points of axolotl heart regeneration. The axolotl heart fully regenerates after infarction injury. Metabolism is proven to play a key role in regenerative processes, although the exact mechanisms involved are unclear.

Methods: We use a cryoinjury to model myocardial infarction and investigate the metabolic profile accompanying different stages of repair (4, 14, 30, 60 and 120 days post injury). We utilized echocardiography, respirometry, metabolite analysis in blood and cardiac tissue, histology and autoradiography.

Results: A systemic increase in oxygen consumption and altered plasma metabolites accompany the regenerative response, and a specific metabolic response is seen in cardiac tissue after injury. Glucose uptake in the myocardium is increased peaking 4 days after injury before returning to normal. Acetate uptake is upregulating peaking 30 days post injury, with uptake being especially high in the border zone surrounding the injury. Furthermore, metabolomics show that different time points after injury are associated with a specific metabolic profile with 4 days post injury showing the greatest number of altered metabolites.

Conclusion: cardiac regeneration in the axolotl is associated with alterations to both systemic and cardiac metabolism, with different pathways activated at different time points throughout the regenerative process. This poses important questions about the requirement for specific metabolic profiles to facilitate cardiac regeneration that may prove fundamental in devising cardiac regenerative therapies for humans in the future.

Keywords: Cardiovascular system, Animal models/disease models, Other

Validation of the Epilepsy Diagnosis and Identification of Drug Resistant Epilepsy in the Danish National Patient Registry

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Introduction: The main purposes of this study were to perform a validation of the epilepsy diagnosis in the Danish National Patient Registry (DNPR), and to identify drug resistant epilepsy (DRE) in the validated cohort, based on criteria set out by The International League Against Epilepsy (ILAE).

Methods: We identified all individuals who were registered with a first diagnosis of epilepsy or seizures in the Region of Central Jutland, Denmark from 2010-2019. We reviewed electronic records on a random sample of these patients and validated the epilepsy diagnosis according to ILAE criteria. In the validated cohort with confirmed incident epilepsy, we estimated the proportion that fulfilled ILAE's definition of DRE at the time of the latest hospital contact (at a mean of 5.3 years of follow-up).

Results: Of 20,723 patients with a first diagnosis of epilepsy or seizures in the Region of Central Jutland from 2010-2019, we reviewed the medical records of 1,589 patients (48% males, mean age = 39.3 years). Of these, 1,004 (64%) were registered with epilepsy in the DNPR. The epilepsy diagnosis was confirmed in 812 cases, providing a positive predictive value (PPV) of 81% (95% CI: 79-83%). The PPV of focal epilepsy was 84% (95% CI: 80-88%), and the PPV of generalized epilepsy was 67% (95% CI: 59-74%).

Of 812 patients with confirmed incident epilepsy, 119 (15%, 95% CI: 10-19%) fulfilled the definition of DRE.

Conclusion: In the Danish National Patient Registry, we found a high PPV of the epilepsy diagnosis. Among persons with confirmed epilepsy, 15% of fulfilled ILAE criteria of drug resistant epilepsy.

Keywords: Qualitative research, Clinical neuroscience, Other

A difference in α-synuclein protein trash in brains affected by Parkinson's disease and multiple system atrophy dictates disease phenotype

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Parkinson's disease (PD) and multiple system atrophy (MSA) are neurodegenerative diseases characterized by accumulation of α-synuclein (α-syn) aggregates. α-syn is a small pre-synaptic protein that unfortunately has a propensity to form toxic aggregates. α-syn aggregates are prion-like particles that can spread from cell to cell, leading to a progressive accumulation throughout the brain. While formation of α-syn inclusions is found in both PD and MSA, they present different symptoms and neuropathology. This difference in neuropathology is hypothesized to be due to conformational variations in the formed α-syn aggregates between diseases. To test this hypothesis, we set out to investigate α-syn aggregates derived from individual patients diagnosed with either PD or MSA.

From the cerebrospinal fluid of 4 PD and 4 MSA patients, we amplified α-syn aggregates using seed amplification assay and investigated aggregate structural variation between the groups. Aggregate functionality was tested in two different cell-type models of α-syn aggregation: α-syn overexpressing oligodendrocytes and induced pluripotent stem cell-derived neurons.

Our results show that PD-derived and MSA-derived aggregates consistently differ structurally and that the structural variation is conserved through amplification. In our two model systems, PD-derived and MSA-derived aggregates resulted in markedly different inclusion pathology and cellular impact.

We show that aggregates from PD and MSA are structurally and functionally different, implicating that conformational differences in aggregate structure are involved in the pathophysiology of α-syn aggregate-dependent neurodegenerative diseases.

Keywords: Basic neuroscience, Cell biology, Animal models/disease models

Nationwide register-based cohort study on school performance in children with incontinence compared with matched controls

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Introduction: Childhood incontinence affects the well-being of children, but not much is known on how it affects school performance.

Methods: We performed a nationwide matched cohort study of all children born in Denmark between 1997-2008 who after 5 years of age received an incontinence diagnose/treatment and had test results from the nationwide scholastic test in 2nd-8th grade. We matched at time of diagnose/treatment on birthdate and sex in a ratio of 1:10. This yielded 46.412 incontinence subjects and 464.120 matched controls. Incontinence subgroups were defined hierarchical according to assumed severity with fecal incontinence (FI) as the most severe, next group were daytime incontinence without FI (DUI), then nocturnal enuresis (without FI or DUI), and lastly unspecified incontinence diagnoses

Results: Mean age at diagnose/treatment onset was 7.5 for all subtypes. At treatment onset the prevalence of any psychiatric comorbidity was 3.7 % for subjects and 2.0% for controls, the highest prevalence was seen in FI with 12.0 %.

Testresults were statistically lower for children with incontinence compared to healthy controls in the crude analysis, although in the range of 1.4-3.8 % lower. FI was the subgroup that had the lowest testscores , which were in the range of 10-16.5 % lower than controls.

Conclusions: Children with incontinence scored a little lower than matched controls on the national school test throughout primary school. The subgroup scoring lowest was children with fecal incontinence. Some of the effect might be attributable to psychiatric comorbidity and sociodemographic factors, and adjusted analyses will be presented at Ph.D. day

Keywords: Paediatrics, Epidemiology and biostatistics, Psychiatry, psychology and mental health

ORAL SESSION 4

Chasing Biomarkers for Post-Concussion Syndrome: Baseline Data from a Randomized Controlled Trial

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INTRODUCTION: A concussion may entail debilitating long-term symptoms defined as post-concussion syndrome (PCS). The pathophysiology of PCS remains a mystery. Therefore, we aim to study its pathophysiology by measuring promising blood-based biomarkers.

METHODS: At baseline, we collected 86 blood samples from patients with PCS enrolled in an RCT (PMC6933237) and 120 samples from healthy controls. We measured kynurenine metabolites by developing a novel method using mass spectrometry. Neurofilament light (NFL) was measured with single molecule array technology; inflammatory markers, with a multiplex assay (Luminex). We used the two-sample t-test or the Mann–Whitney U test to compare the groups.

RESULTS: We found no group-level differences in NFL concentrations ($p= 0.22$). However, a subgroup of PCS patients (9%) had NFL concentrations above the clinical reference limit, which was the case in only 4% of the controls. PCS patients had 10-25% lower concentrations of all kynurenine metabolites ($p< 0.0001$), except for quinolinic acid ($p= 0.73$). The inflammatory markers monocyte chemoattractant protein-1 and eotaxin were 25-40% lower in PCS patients than in healthy controls ($p< 0.0001$). We saw a trend towards higher tumor necrosis factor alpha concentrations in PCS patients ($p= 0.08$).

DISCUSSION: Several biomarkers are changed in PCS patients compared with healthy controls. A subset of patients with PCS may have increased NFL concentrations which can indicate structural central nervous system damage. In conclusion, this study provides novel insights into possible pathophysiological mechanisms behind PCS. The next step is to analyze follow-up data using a linear mixed model.

Keywords: Clinical neuroscience, Laboratory science, Rehabilitation

Genetic variants associated with Childhood Daytime Urinary Incontinence – A genome wide association study

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Introduction: Daytime urinary incontinence (DUI) in children is bothersome, and may lead to low self-esteem, social withdrawal and loneliness. Literature suggests an increased risk of having DUI, if family members have been affected. We aimed to investigate the genetic architecture of DUI using Genome wide association study (GWAS).

Methods: DUI cases from a large Danish population-based cohort, the iPSYCH2015 cohort, originally established to investigate major mental diseases, were identified through DUI ICD-10 codes along with redeemed prescriptions of medication to treat DUI. Thorough quality control was performed. GCTA was used for heritability and correlation analysis. The online GWAS tool FUMAGWAS was used to annotation and gene mapping.

Results: The GWAS included 3,024 DUI cases. We identified two novel loci at chr6 and chr20 genome wide significantly associated with DUI. Lead variant on chr6: rs12210989, OR=1.240, p = 3.2x10-12. Lead variant on chr20: rs4809801, OR=1.178, p = 3.6x10-8. The liability scale SNP-heritability (h2SNP) was 12-18%. Candidate genes mapped with FUMA were, among others, PRDM13 on chr6, a gene crucial to development of a balanced

expression of inhibitory vs. excitatory neurons in the central nervous system. Furthermore, RIPOR3 on chr20, a gene with negative effect on Rho mediated cell signaling, was identified. Rho kinase inhibitors have earlier been suggested as treatment for OAB.

Conclusions: This study implicates that common variants contribute to the DUI phenotype, and we identify the first potential candidate risk variants/genes, that may be involved in DUI. Replication/meta-analysis data with an Icelandic cohort will be presented.

Keywords: Paediatrics, Nephrology, Urology

Effect of the GLP-1 analog Semaglutide on cognitive impairment and metabolic liver function in a rodent model of non-alcoholic steatohepatitis

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Background: Impaired cognition and increased risk of dementia are increasingly recognized as complications of non-alcoholic steatohepatitis (NASH). The GLP-1 analog, Semaglutide, is a promising therapeutic for NASH and for neurodegenerative disorders due to its neuroprotective effects. We previously demonstrated cognitive impairment in a rodent model of NASH accompanied by systemic inflammation, neuroinflammation and -degeneration. This study aimed to test the hypothesis that Semaglutide reverses such changes in NASH.

Methods: Eighty male Sprague Dawley rats were divided into 5 groups (n=16 per group): High-fat, high-cholesterol (HFHC) diet for 16 weeks and 10 weeks of treatment with either vehicle, Semaglutide, or Semaglutide for only 10 days; standard diet with vehicle or Semaglutide. The animals were studied for neurobehavioral changes, liver histology and biochemistry. Further analyses of neurobiology and liver function are planned.

Results: The HFHC diet induced NASH with extensive steatosis and mild fibrosis. Semaglutide efficiently suppressed food intake and decreased body weight as well as liver weight (% body weight) in HFHC animals indicating a reduction in hepatic fat accumulation. However, Semaglutide did not lead to histological resolution of steatosis or inflammation. ALT, AST, plasma triglycerides and ammonia were elevated in animals with NASH but reduced by Semaglutide treatment.

Conclusion: Our preliminary data affirm existing evidence that Semaglutide reduces liver fat accumulation and injury, but did not lead to NASH resolution after 10 weeks. Pending analyses will show if GLP-1 agonism improves the neurocognitive changes previously observed in this model.

Keywords: Gastroenterology and hepatology, Animal models/disease models, Basic neuroscience

A qualitative study exploring the patient perspective on web-based patient education in patients with rheumatoid arthritis.

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Introduction:

The effectiveness of web-based patient education (PE) in rheumatoid arthritis (RA) is currently tested in a randomized controlled trial, WebRA. However, the WebRA study does not provide in-depth insights into the patients' perspectives and likewise only a few studies have explored this area. Thus, the present study aims to explore patients' experiences of web-based PE, and whether this contributes to self-management of RA.

Methods:

We conducted 20 individual qualitative interviews based on the Interpretive Description methodology with patients from the WebRA study. Purposive sampling was used to achieve diversity and information power by inclusion of participants with different sex, age, and sociodemographic background. The analysis was inductive and revealed categories describing the experiences followed by interpretation and extraction of main messages.

Preliminary results:

Participants had positive experiences of the contents, presentation forms and usability, although minor technical difficulties were identified. Positive perceptions were driven by flexibility, the possibility for repetition and learning in familiar surroundings. Some emphasised that e-Learning should be combined with face-to-face (F2F) PE due to relational needs. The use of e-Learning is impelled by a need for clarity at time of diagnosis and less use seems to be associated with lower disease activity. The interaction between knowledge, disease experiences and a positive life approach creates synergy in self-management of RA.

Discussion:

These findings may prompt a discussion on combinations of web-based PE and F2F PE to accommodate both patients' informational needs and relational needs.

Keywords: Health education and simulation-based training, Rheumatology, Qualitative research

Does Cone Beam CT change the treatment plan for maxillary second and third molars?

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Aim: External root resorption (ERR) in the maxillary second molar (M2) caused by the maxillary third molar (M3) is more often observed in Cone Beam CT (CBCT) compared to 2D panoramic images (PAN). Presence of severe resorption may change the treatment plan undertaken. No evidence-based guidelines exist for when to perform a CBCT for maxillary M3. The aims of the study were 1) to evaluate whether additional information from CBCT changes the treatment plan for M3, originally based on PAN; 2) elucidate clinical and radiographic parameters with an impact on a change in the treatment plan.

Materials and methods: Two-hundred-and-sixty M3 with overprojection between M3 and M2 in 2D radiograph were included in this prospective study (170 patients; mean age 28 years, range 16-63). An initial treatment plan was established based on the clinical examination and PAN. Afterwards, the final treatment plan was based on the CBCT image. Logistic regression analyses were performed to evaluate the impact of clinical and radiographic parameters (independent variables) on a change in treatment plan (outcome variable).

Results: The treatment plan changed in 82 cases (31.54%). Change from no treatment to removal of M2 and/or M3 accounted for 55 cases, whereas 16 cases changed from removal of M3 to removal of M2. Gender and severe ERR in M2 seen in CBCT had a significant impact in the initial analyses. Multivariate logistic regression analyses showed that severe ERR in M2 seen in CBCT was significantly related to a change in treatment plan (p=0.000; CI 1.33-6.44).

Conclusion: CBCT revealing severe ERR in M2 can modify the original treatment plan, based on 2D images, resulting in removal of M2 ±M3.

Keywords: Dentistry, Other, Other

ORAL SESSION 5

Decision coaching preparing patients with kidney failure for making end-of-life decisions: a case study

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Introduction: Little is known about the usefulness of decision coaching for patients with kidney failure facing decisions about end-of-life care (EoLC).

Aim: To investigate experiences of patients with kidney failure who received decision coaching for end-of-life care decisions.

Methods: We conducted a prospective case study bound by time and location. The Ottawa Decision Support Framework guided it. Eligible participants were patients with kidney failure facing EoLC decisions. A nurse trained in decision coaching screened for unmet decisional needs with the SURE test and provided decision coaching using the Ottawa Personal Decision Guide. Post-coaching, the patient was re-screened and interviewed to explore their experience with decision coaching. Change in SURE test findings was analysed descriptively and systematic text condensation was used for analysis of interviews. Recorded sessions underwent content analysis using the DSAT-10 tool.

Results: Decision coaching was provided to four patients. Median pre-SURE test score was 2.5 (range 2 to 4) and post-test score was 3 (range 3 to 4), indicating a decrease in decisional needs. Patients described that decision coaching provided an overview of features of options to consider, identified remaining decisional needs for further discussion with relatives and health professionals, and clarified next steps. Median DSAT-10 score was 9 (range 8 to 9).

Discussion: Decision coaching supports the patients to participate in the decision making process, but still it is not shared decision making (SDM). Decision coaching might benefit from being performed in a way that supports the patients to engage more in a SDM process about EoLC.

Keywords: Nephrology, Health education and simulation-based training, Qualitative research

The impact of two decades of multidisciplinary efforts to reduce the risk of recurrence from non-metastatic colorectal cancer - a Danish population-wide registry-study

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Introduction: The last two decades have seen several initiatives aimed at reducing risk of recurrence in patients operated for non-metastatic CRC. The primary aim of this study was to determine up-to-date recurrence rates in CRC patients.

Material and methods: Patients undergoing first-time surgery for UICC TNM stage I-III CRC in the period 2004 to 2019 were included. All patients were identified using the population-wide clinical quality database DCCG, and hereafter linked with data from the Danish Cancer Registry, the Danish National Registry of Patients, and the Danish Pathology Registry. Recurrence status was determined using a validated algorithm. Cumulative risk of recurrence was reported by grouping the patients in calendar periods of 2004-2008, 2009-2013, and 2014-2019.

Results: Of 33,470 stage I-III patients, 7,002 developed recurrences within 5 years after primary surgery (incidence rate = 60.4 per 1,000 person years, 95% CI: 59-61.8). Rectal cancer patients had higher rates of recurrence compared to colon cancer patients (incidence rate ratio = 1.23, 95% CI: 1.17-1.29). The 5-year cumulative incidence of recurrence decreased for both colon cancers (2004-2009: 26% (95% CI: 25-27%); 2009-2013: 21% (95% CI: 20-22%); 2014-2019: 15% (95% CI: 14-16%)) and rectal cancers (2004-2009: 30% (95% CI: 29-32%); 2009-2013: 25% (95% CI: 24-27%); 2014-2019: 19% (95% CI: 18-20%)). The same pattern was found across stage I to III when stratifying by three calendar periods.

Conclusion: The last two decades have seen significant reductions in CRC recurrence risk for Danish stage I-III CRC patients.

Keywords: Oncology, Epidemiology and biostatistics, Public health

The Strengths and Difficulties Questionnaire Can Predict HbA1c Trajectories in Children and Adolescents with Type I Diabetes: A Population-based Study

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OBJECTIVE Using 11-year HbA1c trajectories in children and adolescents with type 1 diabetes, we seek to determine whether the Strengths and Difficulties Questionnaire (SDQ), sex, age at diabetes diagnosis, diabetes duration, family structure, and caregiver education level are associated with HbA1c trajectory membership.

RESEARCH DESIGN AND METHODS Design was longitudinal and population-based. HbA1c levels were obtained (2010-2020) from Danish paediatric and adult diabetic registries. HbA1c trajectories were identified with group-based trajectory modeling. SDQ scores were associated with group membership from 8-27 years.

RESULTS Four HbA1c groups were: 1) “on target, gradual decrease”, 2) “above target, mild increase then decrease”, 3) “above target, moderate increase then decrease”, and 4) “above target, large increase then decrease”. When adjusting for sex, diabetes-specific and socio-demographic variables, higher Total Difficulties scores were associated with likely group 3 (coeff.=0.83, SE=0.02, P =0.0001) and 4 (coeff.=0.769, SE=0.03, P < 0.0001) membership. Higher emotional symptoms and impact scores were associated with likely group 3 and 4 membership. Higher conduct problems or hyperactivity/inattention scores were associated with likely group 2, 3 and 4 membership. Peer relationship problems and prosocial behavior did not distinguish group membership.

CONCLUSIONS. Unfavorable SDQ total and/or subscale scores can identify children/adolescents with type 1 diabetes who have unfavorable HbA1c trajectories in adolescence and young adulthood. Future studies should investigate models of care where SDQ screening better guides interventions that improve HbA1c trajectories.

Keywords: Paediatrics, Psychiatry, psychology and mental health, Molecular metabolism and endocrinology

Impact of hemoglobin A1c level on the association between non-steroidal anti-inflammatory drugs and major adverse cardiovascular events in patients with type 2 diabetes mellitus: a population-based cohort study

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Background: Non-steroidal anti-inflammatory drugs (NSAIDs) should be used cautiously in patients with increased cardiovascular risk. It is unknown whether the cardiovascular risk associated with NSAID use depend on HbA1c level in patients with type 2 diabetes mellitus (T2DM).

Methods: We conducted a population-based cohort study of all adult Danes with first-time T2DM during 2010–2020. We used information on sex, age, comorbidity burden, and drug use to calculate time-varying inverse probability of treatment weights. Using these weights in a pooled logistic regression, we estimated hazard ratios (HRs) of the association between use of NSAIDs (ibuprofen, naproxen, or diclofenac) and a major adverse cardiovascular event (MACE; myocardial infarction, ischemic stroke, congestive heart failure, atrial fibrillation or flutter, or all-cause death). We stratified all analyses by HbA1c level (<53 or ≥53 mmol/mol).

Results: We followed 113,423 T2DM patients for 453,378 years. For ibuprofen use, the HR of MACE was 1.61 (95% confidence interval: 1.40–1.86) in patients with HbA1c<53 and 1.31 (1.06–1.61) in patients with HbA1c≥53 mmol/mol. For naproxen use, the HR was 0.60 (0.21–1.71) in patients with HbA1c<53 and 1.42 (0.53–3.76) in patients with HbA1c≥53 mmol/mol. For diclofenac use, it was 1.78 (1.09–2.89) in patients with HbA1c<53 and 3.13 (1.83–5.35) in patients with HbA1c≥53 mmol/mol.

Conclusion: In T2DM patients, the relative risk of MACE was increased for ibuprofen and diclofenac use both when HbA1c was <53 and ≥53 mmol/mol. Naproxen use was not associated with increased relative risk of MACE neither when HbA1c was <53 and ≥53 mmol/mol.

Keywords: Cardiovascular system, Pharmacology, Epidemiology and biostatistics

Interactive deep-learning for tumour segmentation in head and neck cancer radiotherapy

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With interactive deep-learning (iDL), manual corrections can update a sub-optimal neural network while delineating to minimise the input to achieve acceptable segmentations. We developed an iDL tool for tumour segmentation that took annotated slices as input and simulated its performance on a head and neck cancer (HNC) dataset. We aimed to achieve clinically acceptable segmentations with fewer annotated slices.

Multi-modal imaging data from 204 HNC patients with clinical tumour and lymph node delineations was used as the dataset. First, a convolutional neural network (CNN) was trained as a baseline. Subsequently, for fine-tuning, we simulated oncologist annotations on the test set by replacing a predicted tumour contour on selected slices with the ground truth. iDL performance was then evaluated with simulations on the independent test set using the optimised hyperparameters. Finally, a radiation oncologist performed real-time iDL on 3 cases.

For evaluation, dice similarity coefficient (DSC), mean surface distance (MSD), and 95% Hausdorff distance (HD95%) were assessed at baseline and after every iDL update. In iDL simulation, after 5 slices were annotated, segmentation accuracy on the independent test set improved from DSC=0.65 to 0.82, MSD=4.4mm to 1.4mm, HD95%=27.3mm to 8.9mm. In real-time iDL, the radiation oncologist annotated 16, 10, and 7 slices per patient in the first round. After the update, 3, 1, and 2 slices were annotated to achieve clinically acceptable segmentations.

In conclusion, in iDL simulation, annotating 5 slices substantially improved the segmentation. In real-time iDL, our tool was able to provide a satisfactory result after 2 rounds of annotation.

Keywords: Oncology, Other, Other

POSTER SESSIONS

POSTER SESSION 1

Effect of colchicine on cardiovascular target organ damage - A randomized placebo-controlled trial

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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.

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.

Keywords: Cardiovascular system, Inflammation, Pharmacology

Improved diagnostics of polymyalgia rheumatica using FDG-PET/CT

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Introduction

Polymyalgia rheumatic (PMR) is a clinical exclusion diagnosis that is extra challenging in patients started on prednisolone treatment which may mask their PMR symptoms. Therefore, 18F-fluorodeoxyglucose (FDG) positron emission tomography and computed tomography (PET/CT) have been suggested as a diagnostic tool to improve the diagnostic accuracy for diagnosing PMR. However, it is unknown whether PET/CT can be applied for diagnosing patient treated with prednisolone. The aim of this study was to investigate the diagnostic accuracy of PET/CT to diagnose patients with PMR before and after initiation of prednisolone.

Methods

Patients suspected of PMR were diagnosed clinically at baseline. In this study 69 patients were diagnosed with PMR and 26 with other diseases resembling PMR. A PET/CT was performed in all patients after the baseline visit. Patients diagnosed with PMR were started in prednisolone and received a second PET/CT at 8 weeks followed by a 2-week prednisolone taper and a third PET/CT at 10 weeks. The final clinical diagnoses were confirmed after one year.

Results

Preliminary results of the first PMR patients showed a classic FDG-uptake pattern around the hips and shoulders at baseline. Surprisingly, this uptake-pattern was still visible after 8 weeks of prednisolone treatment but with decreased intensity. The FDG-uptake was reintensified close to the baseline value after the 2-week prednisolone taper.

Conclusion

PET/CT may be a superior diagnostic tool in patients with PMR compared with initial clinical assessment. In particular, PET/CT may prove valuable for diagnosing patients started in prednisolone treatment prior to rheumatological assessment.

Keywords: Rheumatology, Inflammation, Medical technology and diagnostic techniques

Assessment of complement inhibitors for the treatment of Age-related Macular Degeneration

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Background: Age-related macular degeneration (AMD) is a common eye disease that affects the elderly, and it is one of the major causes of blindness. However, treatment options are limited for these patients. Many pathways have been associated with AMD pathogenesis, including an overactive complement system (CS). Our research group has designed a combinatorial gene therapeutic strategy in which a complement inhibitor may be an efficient component. The size of the inhibitor should be small to increase its diffusion in retinal cell layers, and thus a single-domain antibody derived from alpacas, called a Nanobody (Nb), is explored to inhibit the CS.

As the expression and functionality of four selected Nbs were confirmed in vitro, viral vectors were produced and subretinally injected in mice verifying Nb expression in their retinas. However, the subretinal injection is a surgically challenging technique, only a minor volume of vector can be injected, and they may vary extensively in quality. Thus, the GFP gene is included in the vectors as a marker of delivery and transduction. The in vivo Nb expression may then be related to the success of individual injections and the areas of transduction for a more precise evaluation of Nb expression. However, several viral vector preps produced seem efficient in vitro but lack efficiency in vivo. The production of viral vector preps is attempted optimized and they are subsequently injected subretinally in mice to validate their in vivo transduction efficiency represented by GFP expression on fundus pictures.

Keywords: Inflammation, Ophthalmology, Laboratory science

Leveraging serial intravital 2-photon microscopy to interrogate autoimmune processes in the spleen

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In autoimmune disease, B lymphocytes can break tolerance and produce autoantibodies that contribute to disease progression. Crosstalk between follicular T- and B lymphocytes is pivotal for B cell activation and selection. This takes place in so-called germinal centers, found in secondary lymphoid tissues such as the spleen or lymph nodes. However, the dynamic interplay of B and T cells in autoreactive germinal centers is poorly understood. Germinal centers in the spleen are of particular interest because splenomegaly and spontaneous splenic germinal center formation are hallmarks of autoimmunity.

Therefore, we are developing a method to study individual autoreactive germinal centers in the spleen longitudinally by making use of serial intravital 2-photon microscopy. Through an abdominal imaging chamber over the spleen, immunological processes in for example germinal centers can be observed over the course of several days and weeks in the same animal. We are combining this with unique transgenic reporters and intravital labeling strategies. To our knowledge, intravital microscopy of the spleen has not yet been performed serially, only in single imaging sessions, which have nevertheless brought important details of immunological processes to light already. Accordingly, we hypothesize that the expansion of intravital microscopy of the spleen to longitudinal studies will provide a unique and powerful tool to study cellular immunological processes such as the break of tolerance during autoimmunity. For proof-of-principle, we will benchmark our approach against selected observations made by Flow Cytometry analysis in cohort series.

Keywords: Inflammation, Animal models/disease models, Cell biology

Paragenetic inheritance of autoimmunity and 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 CNS.

Particularly infants of autoimmune pregnant women are at high risk, since maternal transfer of autoantibodies, combined with genetic predisposition, can negatively impact the development and health of the offspring. This may manifest as neurodevelopmental diseases such as autism spectrum disorders or even schizophrenia. Here, we used embryo transfers to examine the maternofoetal transfer of autoantibodies and autoimmune-induced activation of microglia 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.

A maternal transfer of both immunoglobulins and autoantibodies was measured using time-resolved immunofluorometric assays (TRIFMAs). We analysed germinal centers and plasma cells by flow cytometry, and microglia morphology and activation in the CNS of embryo transfer offspring were assessed using an immunohistochemical and immunofluorometric stain, respectively.

Keywords: Inflammation, Animal models/disease models, Paediatrics

Expression of macrophage phagocytosis checkpoints is modulated by cell-polarization

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Background

The phagocytosis checkpoint SIRPα is expressed by tumor-associated macrophages and, to escape phagocytosis, cancer cells can overexpress the ligand CD47. Antibody-based CD47-blockade immunotherapy can restore macrophage phagocytosis, but this effect can be blocked by alternative phagocytosis checkpoints such as LILRB1 or Siglec-10. In the present study we have investigated whether phagocytosis checkpoints are phenotype-dependent and if they are potentially regulated by the tumor microenvironment.

Methods

Human monocyte-derived macrophages from healthy blood donors were either polarized to commonly investigated macrophage phenotypes by treatment with IFN-γ+LPS (M1), IL-4+IL-13 (M2a), IL-10 (M2c), or treated with tumor-conditoned medium (TCM) from ovarian cancer cell lines (A2780 and COV318). Expression of SIRPα, LILRB1 and Siglec-10 was investigated by RT-qPCR and flow cytometry, and phagocytosis of A2780 cells following CD47-blockade was quantified by flow cytometry and visualized by fluorescense microscopy.

Results

Macrophage polarization modulated mRNA and protein levels of SIRPα, LILRB1 and Siglec-10. Notably, Siglec-10 membrane protein was only measurable following M1 or M2a polarization. Treatment with TCM from A2780 cells altered macrophage phenotype and increased the level of LILRB1 membrane protein. However, treatment with anti-CD47 antibody activated macrophage phagocytosis of A2780 cells in both control and TCM-treated macrophages.

Conclusion

Human macrophage expression of phagocytosis checkpoints is modulated by cell-polarization and TCM. Future treatment strategies may potentially benefit from targeting multiple checkpoints simultanously.

Keywords: Inflammation, Oncology, Laboratory science

Endothelial IRF3-activation links inflammation and phenotypic changes

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Research objective

Endothelial cells (ECs) play a crucial role in mediating inflammation in (patho)physiological situations. DNA-induced inflammation contributes to the development of a vast array of pathological conditions including cancer, infectious and autoimmune diseases. This study sought to investigate the metabolic and functional consequences of endothelial Interferon Regulatory Factor (IRF) 3 pathway activation.

Results

Activation of endothelial IRF3 increased expression of chemokines (CXCL10), pro-inflammatory cytokines (TNFa, IL6) and cell adhesion molecules (VCAM1 and ICAM) in vitro. Furthermore, actin rearrangement and decreased formation of lamellipodia were observed in activated ECs. That translated to decreased migrative and angiogenic ability of ECs. In vivo, activation of endothelial IRF3 decreases angiogenesis and vessel maturation.

We next evaluated, whether the phenotypic changes induced upon IRF3 activation were caused by metabolic rewiring of ECs. Targeted metabolomic analysis of IRF3-activated ECs show levels of glycolytic intermediates and amino acids. Metabolic flux of glucose and fatty acids was unaltered. However, several genes related to oxidative phosphorylation were increased upon IRF3 activation.

Conclusions

IRF3 activation alters junctional and cytoskeletal rearrangement of ECs, decreasing the EC capacity to migrate and form vascular sprouts. Mechanistically the alterations depend on IRF3 transcriptional regulation. IRF3 activation results in metabolic adaptations of the endothelium. The rewiring is crucial for induction of EC inflammatory responses but is not involved in mediating changes of EC morphology.

Keywords: Inflammation, Cell biology, Molecular metabolism and endocrinology

ILIT.NU – Documentation of efficacy for

3 intralymphatic allergen immunotherapy in a phase III

4 randomized, parallel group, double blind placebo-

5 controlled multisite field trial

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Background

Allergic rhinitis is a common disease in Western Europe with a prevalence of 23%. Allergen immunotherapy is the only disease-modifying therapy for these patients. Current treatments last 3 years and are demanding consequently adherence suffers.

Intralymphatic immunotherapy (ILIT) provides a shorter treatment of 3 ultrasound guided injections over 2 months. ILIT has only been investigated in small trials with mainly promising results. ILIT.NU is the first large randomized double-blind placebo-controlled trial testing ILIT safety and efficacy.

Method

We have recuited >500 patients suffering from grass pollen allergic rhinoconjunctivitis for ILIT treatment with moderate to severe disease (RTSS>8).

Three University hospitals; Linköping, Sweden, Zürich, Switzerland and Aarhus, Denmark and three ENT clinics in three Danish regions participate.

Recruited patients recorded a baseline in 2021. They evaluate their allergy symptoms in the pollen season by a combined Symptom Medication Score (cSMS) through REDCap.

We randomized patients 2:1 based on skin prick test (SPT) diameter and baseline cSMS to three ultrasound-guided injections of Alutard 225 (Phleum pratense, ALK) or POLVAC (Allergy Therapeutics) or saline into inguinal lymph nodes. The injections were given with >4 week intervals.

The primary effect parameter is cSMS evaluated in the summers of 2022 and 2023.

Results

Compliance was exceptional at 99.3%. Mild and self-limiting local and systemic side effects were recorded by 20% and 3% of patients. There were no SAEs.

Conclusion

ILIT improves compliance to allergen immunotherapy. It could also be more effective than other treatment options and have significant health economic

Keywords: Allergy, Public health, Respiratory system

A motivation-enhancing webapp to retain participants in a trial

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Background:

In the ILIT.NU trial during three grass pollen seasons, participants are asked daily to report medication use and to score symptoms in an online questionnaire. High attrition rates have been identifed in previous ILIT trials affecting generalizability, validity and reliability. To increase retention in the ILIT.NU trial, a motivation-enhancing intervention is developed.

Method:

To clarify that components as motivation and severity of allergy among other can interact and influence whether the intervention is successful, the framework for complex interventions is used as design. To understand how to motivate participants to retention and reporting, the Self Determination Theory is used. To ensure an intervention relevant for participants, patients are involved in the research process.

Results:

Results from two online workshops including ten patients and a subsequent evaluation suggested that an app configurable to personal preferences needs to be developed. Improvements included (a) only complete the entire questionnaire on days with symptoms, (b) integration of grass pollen counts and forecasts, (c) showing personal response rate, (d) access to own data via a graph, (e) advice against grass pollen allergy, (f) status of the study, g) individually choosing the time of response, (h) contact information.

Conclusion:

The webapp was tested in a feasibility study during grass pollen season 2022. If the test shows feasible results, it may be evaluated and tested as a Study Within a Trial during grass pollen season 2023. The participants will be randomised 1:1 across treatment groups to either the webapp or the standard reporting method.

Keywords: Allergy, Qualitative research, Other

Prevention of hypoparathyroidism following thyroid surgery by using intraoperative autofluorescence – Preliminary results

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Introduction: Damage to the parathyroid glands during thyroid surgery, and subsequent hypoparathyroidism (HPT) is a frequent and serious complication. This is in part due to difficulties in the intraoperative visualization of parathyroid glands. By using autofluorescence-based devices intraoperatively, parathyroid visualization becomes facilitated. We aim to investigate the impact of using intraoperative autofluorescence on the occurrence of postoperative HPT.

Methods: Prospective cohort study including 78 patients undergoing total thyreoidectomy at the ENT-departments in Goedstrup and Esbjerg. All surgeries will be performed with the autofluorescence-device Fluobeam LX. Transient HPT is defined as Alfacalcidol-requiring hypocalcemia that resolves within 1 year. Permanent HPT is considered, when Alfacalcidol is needed 1 year following surgery. The rate of HPT will be compared to a historic cohort of patients undergoing total thyroidtecomy.

Results: So far, 50 patients (64 %) have undergone autofluorescence-assisted surgery. Eight patients (16 %) were treated with Alfacalcidol postoperatively and 3 of these patients (6 %) are still on Alfacalcidol to date. Among the first 50 patients in the historic cohort, 17 patients (34 %) received Alfacalcidol postoperatively and 16 of them (32 %) were still on Alfacalcidol 1 year postoperatively. Mean s-PTH and s-ionized calcium on postoperative day 1 were 3,2 pM and 1,18 mM respectively. In the historic cohort, the corresponding values were 2,1 pM and 1,14 mM respectively.

Conclusions: The use of autofluorescence in thyroid surgery seems to contribute to a remarkable decrease in the rate of both transient and permanent HPT.

Keywords: Ear, nose and throat (ENT), Other, Other

Head and neck squamous cell carcinoma lymph node metastasis from an unknown primary: a phase-4 population-based cohort study from DAHANCA

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Background and purpose: Management of patients with squamous cell carcinoma metastasis in the head and neck of unknown primary (SCC-HNCUP) remains a challenge. In Denmark, the diagnostic work-up and treatment of SCC-HNCUP is standardized and follow national guidelines provided by the DAHANCA group.

Aim: The aim of the present study is to determine the oncologic outcome in patients with SCC-HNCUP subject to the current guideline (2013) and evaluate the significance of compliance to the DAHANCA guidelines.

Materials and methods: Prospectively registered data were extracted from the DAHANCA database. All patients treated for SCC-HNCUP in Denmark in the period 2014-2020 were included. The median follow-up was 35 months. A total of 286 patients were identified; 250 (88%) patients received curatively intended treatment. Of these 87% were treated according to guideline with surgery, radiotherapy (RT) and chemotherapy; either alone or in combination.

Results: The 3-year overall survival (OS) for the total population was 70%. For patients treated with a curative intent, the OS at 3 years was 77%. The three-year OS in patients

with p16 positive disease treated curatively was 90%. A primary tumour emerged in the head and neck region in 27 patients during the follow-up period.

Conclusion: Overall guideline compliance was good. Our data support that SCC-HNCUP is comparable to other head and neck cancers in terms of prognosis.

Keywords: Ear, nose and throat (ENT), Oncology, Medical technology and diagnostic techniques

POSTER SESSION 2

Refinement and Feasibility Testing of an Intervention Targeting Poor Mental Well-being in Patients with Chronic Disease in General Practice

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Background and aim:

Two out of ten of patients with type 2 diabetes (T2D) and/or chronic ischemic heart disease (IHD) suffer from poor mental well-being. It is pivotal that health care providers (HCP) handle psychological issues as an integrated part of chronic care in general practice.

Problem-solving therapy (PST) is a psychotherapeutic method that is effective in adults with depression and may be a valuable tool in the treatment of these patients.

This feasibility study investigated HCPs' and patients' perspectives on barriers and facilitators for implementation of PST delivered in general practice, especially focusing on acceptability and appropriateness regarding the intervention.

Methods:

Eight HCPs from three general practices participated in a two-day PST-course. Questionnaires regarding mental well-being were completed at the annual chronic care consultation for T2D or IHS and patients were offered PST if poor mental well-being was indicated. Semi-structured qualitative interviews and a focus group interview were conducted with HCPs and patients after delivery of the intervention.

Results:

Generally, both HCPs and patients regarded the intervention as highly acceptable and appropriate in the general practice setting and the intervention was found to be feasible. HCP's regarded time and workflow as the most important barriers for delivery of the intervention. Some patients were unaware that mental health issues can be addressed in general practice in line with somatic disease.

Conclusion:

Insights gained through this feasibility study informed the refinement of the intervention thus facilitating the delivery in a subsequent randomized controlled trial.

Keywords: Psychiatry, psychology and mental health, Cardiovascular system, Qualitative research

Identification of prodromal biomarkers of schizophrenia and bipolar disorder using magnetoencephalography

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Schizophrenia (SZ) and bipolar disorder (BD) are heritable severe mental disorders. Both disorders are associated with abnormal neurophysiological responses, including reduced auditory mismatch negativity (MMN) and 40-Hz steady-state responses (ASSR). These abnormalities reflect underlying cortical abnormalities and may serve as early markers of illness susceptibility, however longitudinal studies of at-risk individuals are lacking. As part of The Danish High-Risk and Resilience Study – VIA, we will investigate neurophysiological responses (MMN and ASSR) in 15 year old adolescents (n ≈ 175) born to parents diagnosed with either SZ, BD, or neither SZ or BD (population-based controls, PBC) using magnetoencephalography (MEG). We will apply dynamic causal modeling (DCM) to investigate whether familial high risk of SZ or BD is associated with changes in synaptic gain or effective connectivity. We will test competing hypotheses about the receptors and neuronal types involved, and investigate links with psychopathology, cognition, and genetics. Data collection is ongoing and expected to be completed in 2024. Altogether, the present study will represent one of the world's largest MEG datasets and will allow unprecedented insight into the the links between genetics, brain circuits, and psychopathology of SZ and BD, as well as prediction of long-term outcomes based on MEG-based biomarkers.

Keywords: Psychiatry, psychology and mental health, Clinical neuroscience, Basic neuroscience

Do children and adolescents with functional abdominal pain disorders show cognitive biases towards gastrointestinal related material?

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Background

Functional abdominal pain disorders (FAPD) are common in children and adolescents, cause functional disability and high health care use. Internet-based cognitive behavioural therapy (iCBT) focus on changing maladaptive symptom perceptions and behaviours and has shown to be clinical effective and cost-effective.

Cognitive biases are abnormalities in attention, interpretation and memory processes and have been shown to be involved in the onset, maintenance, and relapse of symptoms in a number of illnesses, including FAPD in adults. Currently cognitive biases in children and adolescents with FAPD are scarcely studied, despite their potential for being valuable targets in interventions such as CBT.

We aim to investigate if children and adolescents with FAPD show cognitive biases towards gastrointestinal related material, and if these potential biases change during iCBT.

Methods

Sixty children and adolescents undergoing iCBT for FAPD will be included. Cognitive biases in relation to gastrointestinal stimuli will be investigated using a novel experimental paradigm designed as a computerised online task. It comprises a word sorting task and a picture task. Each task consists of an encoding, recall, and recognition phase to assess both

biases in interpretation and memory which again allows us to examine the interplay between these biases. The paradigm will also be completed by 100 healthy controls.

Results and Perspectives

Results are expected to improve our knowledge about the role of cognitive biases in FAPD in youths, and how these may change during treatment with CBT. These insights could support us in making future psychological interventions even more effective.

Keywords: Psychiatry, psychology and mental health, Paediatrics, Gastroenterology and hepatology

Consensus draft of the native mouse podocyte-ome

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The podocyte is a key cell in maintaining renal filtration barrier integrity. Several recent studies have analyzed the genome and transcriptome in the podocyte at deep resolution. This avenue of "podocyte-ome" research was enabled by a variety of techniques, including 1) single-cell transcriptomics, 2) FACS with and without genetically encoded markers, and 3) deep proteomics. However, data across various omics techniques and studies are currently not well integrated with each other.

Here, we aim to establish a common, simplified knowledge base for the mouse podocyte-ome by integrating bulk RNA sequencing, bulk proteomics of FACS-sorted podocytes, and single-cell transcriptomics.

Three publicly available datasets of each omics technique from different laboratories were bioinformatically integrated and visualized.

We identified that high expression of glycan glycosylphosphatidylinositol anchor synthesis and turnover, as well as retinol metabolism, were relatively understudied features of podocytes. In addition, actin-binding molecules were organized in a podocyte-specific manner, as evidenced by differential expression in podocytes compared with other glomerular cells. We compiled a Web-based "PodIent" application that illustrates the features of the integrated dataset. This enables user-driven exploratory analysis by querying genes of interest for podocyte identity in absolute and relative quantification while also linking to functional annotation using keywords, Gene Ontology terms, and gene set enrichments.

Keywords: Nephrology, Molecular metabolism and endocrinology, Other

A preliminary study of transglutaminases profiling in a chronic kidney disease mouse model after transglutaminase 2 inhibition

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Chronic kidney disease (CKD) is characterized by progressive fibrosis which is not directly targeted by current treatment strategies. The transglutaminase (TG) family comprise 8 catalytically active enzymes: TG1-7 and coagulation factor XIII, of which TG2 is considered the most important. TG2 in its open conformation exerts transamidase activity, which can result in excessive extracellular matrix cross-linking and accumulation under pathological conditions (Prat-Duran et al, 2021). Inhibition of the enzyme may delay CKD progression. Furthermore, a recent study found a vasodilatory and blood pressure-lowering effect related to its closed conformation. The TG2 modulator LDN27219 has been shown to inhibit the transamidase activity by promoting the closed conformation of the enzyme (Pinilla et al, 2021). We studied the expression profile of different TGs in a CKD mouse model after treatment with LDN27219. Mice were subjected to sham or unilateral ureteral obstruction for 7 days and treated IP with vehicle or 15 mg/kg/12 hours of LDN27219. mRNA levels of TGs were determined using qPCR and western blot on the kidneys obtained immediately after sacrifice. Only TG2 and TG5 mRNA were upregulated in response to the obstruction. However, LDN27219 did not affect the relative distribution of TGs mRNA in the obstructed kidneys but was able to prevent TG2 upregulation at the protein level. Unexpectantly, TG5 at a protein level was downregulated in the obstructed kidneys, but treatment with LDN27219 had no effect. Our findings show that pharmacological inhibition of TG2 with LDN27219 does not alter the TGs expression profile in obstructed kidneys, suggesting a good specificity for TG2.

Keywords: Nephrology, Pharmacology, Cardiovascular system

The role of PCSK9 in kidney- and cardiovascular diseases

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Background and aim: Proprotein convertase subtilisin kexin/type 9 (PCSK9) is a key regulator of cholesterol metabolism and inhibition of PCSK9 is a main target in the treatment of hypercholesterolemia. Patients with chronic kidney disease (CKD) display elevated plasma cholesterol and lipid levels which are associated with worsened kidney disease progression. We aim to explore the potential dual cardioprotective and renoprotective effect of PCSK9 inhibition in rodent models of progressive proteinuric CKD and CVD with associated hypercholesterolemia.

Methods: The effect of PCSK9 inhibition on the cardio-renal axis is studied in both CKD (podocin KO) mice and proteinuric diabetic (ZSF1) rats. Furthermore, PCSK9 levels in patients with kidney disease (minimal change disease (MCD)) are investigated.

Results: In podocin KO mice, PCSK9 plasma levels were increased 5-fold compared with controls (1128 ±260 ng/ml vs. 300 ± 61 ng/ml, $p<0.0001$). One bolus with the PCSK9 inhibitor Alirocumab (50 mg/kg) showed a ~50% reduction in free plasma PCSK9 and enhanced hepatic LDLR protein ($p=0.0023$). In ZSF1 rats, plasma lipid parameters and urinary protein/creatinine levels raised with age. MCD patients displayed elevated plasma PCSK9 levels which were reduced by standard prednisolone treatment (492 ±24 ng/ml vs. 452 ±18 ng/ml).

Conclusion and perspectives: In conclusion, plasma PCSK9 levels were elevated in both rodents and humans with proteinuric kidney disease. Next, long-term PCSK9 inhibition studies in rodents are planned to investigate kidney disease progression.

Keywords: Nephrology, Cardiovascular system, Animal models/disease models

Causes and prevention of thromboembolic disease in nephrotic syndrome (CAPTAIN)

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Background: Thromboembolic events are a common complication of nephrotic syndrome (NS), and there is lack of studies exploring the optimal type of prophylactic anticoagulation. This study will identify abnormalities in the biochemical coagulation profile associated with NS and describe the effects of low molecular weight heparin (LMWH) and apixaban.

Methods: Substudy 1 compares 60 NS patients to 50 healthy controls and characterize the primary hemostasis by von Willebrand factor, thromboxane B2 and platelet aggregation; the coagulation system by thrombin generation; and fibrinolytic activity by a clot lysis test. Substudy 2 includes 50 NS patients and examine the effect of LMWH determined by thrombin generation and anti-factor Xa analysis. Substudy 3 compares 10 NS patients to 10 healthy controls examining the effect of apixaban determined by thrombin generation as well as plasma and urine drug concentrations.

Hypothesis: 1) Increased platelet activation and aggregation, increased thrombin generation and decreased fibrinolytic activity indicate a prothrombotic state in NS; 2) LMWH decreases thrombin generation relative to baseline in NS patients, thus indicating a reduced risk of thrombus formation; 3) Apixaban plasma and urine concentrations are comparable in NS patients and healthy controls, and apixaban decreases thrombin generation in both NS patients and healthy controls.

Perspectives: If apixaban has a favorable effect on the coagulation profile, it will support the use of apixaban in NS. Additional clinical trials will be initiated to establish apixaban's effect on preventing thromboembolic events in NS patients.

Keywords: Nephrology, Pharmacology, Other

Combined Effects of Potassium, Nitrate and Salt on Blood Pressure in atients with Hypertension (KANSA)

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Background

Components of the diet have shown to be important for the blood pressure. The role of sodium in hypertension is well known. However, patients respond differently to sodium restriction; some with a large decrease in blood pressure and some without. Studies have shown that a high intake of potassium and nitrate respectively leads to decreases in blood pressure. The effects on blood pressure of diet containing different combinations of high/low sodium, potassium and nitrate has never before been examined.

Hypotheses

- Low sodium intake leads to a reduction in blood pressure
- High intake of nitrate and potassium each decreases the blood pressure significantly and the combination therapy acts synergistically to decrease blood pressure even further
- The effects of nitrate and potassium on blood pressure are increased during high sodium intake

Methods

This is a randomized, controlled, double blind clinical trial including 120 patients with hypertension. Antihypertensive drugs are paused two weeks before baseline measurements, which include 24-hour blood pressure monitoring, plasma levels of vasoactive hormones and cytokines in the immune system as well as 24-hour urine collection separated into day and night time. Urine is analysed for levels of nitrite, nitrate, osmolality, Na, K, albumin and tubular sodium channels.

All participants are given the same diet with prepared meals from the hospital kitchen for one week and supplemented with tablets of 130 mmol sodium chloride or placebo, tablets of 40 mmol potassium chloride or placebo and beetroot juice containing 13 mmol nitrate or beetroot juice without nitrate. After one week the measurements are repeated.

Keywords: Nephrology, Cardiovascular system, Other

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:

Study completion is excepted in late 2022. Preliminary results will be presented if available.

Keywords: Nephrology, Cardiovascular system, Pharmacology

En Bloc Resection vs. Conventional Transurethral Resection of Non-Muscle Invasive Bladder Tumours – a Randomised Clinical Trial

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Aim: To compare the surgical method of En Bloc resection (EBR) to the conventional transurethral resection (TURB) of non-muscle invasive bladder cancer (NMIBC) in terms of complete removal of tumour, specimen quality, pathological certainty, and patient-reported outcome (PRO) of side effects.

Background: NMIBC is a common disease with a 5-year recurrence rate reported as high as 64%. The cornerstone in diagnosis and treatment of NMIBC is TURB where the tumour is dissected in pieces, removed from the bladder, and pathologically examined. As the tumour is fragmented before removal, the method violates basic oncological principles and compromises pathological examination. Hence, TURB is possibly part of the mechanism causing recurrences. A newer technique, EBR, where the tumour is removed in one piece, is supposed to overcome the flaws of conventional TURB, though large randomized trials are needed.

Methods: This project is a multicentre randomised clinical trial comparing EBR to conventional TURB. Patients with suspected NMIBC tumours with diameter ≥1cm and ≤6cm are randomised to either the intervention group, thus undergoing EBR, or the control group, undergoing conventional TURB. Sample size will be 220 patients in total, 110 in each group.

Results: As of October 31st 2022, 24 patients are included. Two sites have started inclusion, and three more are expected to start inclusion during fall 2022. Final results are expected in 2024.

Conclusion: Pending. If EBR can be shown to remove bladder tumours with better pathological quality and certainty, this could potentially spare patients from undergoing surgeries in the future, thereby reducing costs for both patients and society.

Keywords: Urology, Other, Other

Late effects impact on Quality of Life after treatment for bladder cancer (CONQUER)

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Aim: To investigate risk factors for impairment on QoL among patients with bladder cancer

Background:

Treatment of bladder cancer (BC) spans from conservative treatment with transurethral resection and instillation therapy to major surgery, radiotherapy, systemic oncological treatment and variations thereof. Each treatment has a risk of complications and impact on Quality of Life (QoL). This risk has been inconsistently described, and the impact on QoL has only been studied to a limited extend.

Methods:

This is a prospective follow-up questionnaire study. All patients referred for examination because of a suspicion of BC in the Central Denmark Region will be invited to participate. Invitations will be sent through "e-boks" along with the invitation for examination. The study group will fill out the questionnaire 6 times within a 5-year period. The questionnaires are validated and standardized QoL surveys as well as validated symptom-based questionnaires covering urological-, gastrointestinal-, and sexual function. Information about tumor, treatment and late effects will be obtained by accessing the patient's records.

Results:

The inclusion period is between 01/01/22 and 01/01/23. Per 15th of October approx. 2000 has been referred for examination. 1607 have met the inclusion criteria. 355 have responded, making the preliminary response rate 22.2 %. Among the first 1400 patients seen in the clinic, 14.2 % has been diagnosed with BC. Among the first 192 participants, 12.1 % has been diagnosed with BC. The groups are similar in gender distribution with 71.3 % males in the total cohort and 70.6 % males among participants. Additional results are pending.

Conclusion:

Pending.

Keywords: Urology, Other, Other

POSTER SESSION 3

Biomolecular signature of cannabidiol antidepressant effect

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Background: Major Depressive Disorder is a psychiatric disorder with complex interplay between genetic and environmental factors. Cannabidiol (CBD) has shown therapeutic potential as an antidepressant drug, but its mechanism of action is not completely understood. We investigated the effects of chronic treatment with CBD in Flinders Sensitive Line (FSL) rats and their control strain Flinders Resistant Line (FRL), which constitute a genetic model of depression.

Methods: FSL rats were treated with CBD (10 mg/kg; i.p.) or vehicle during 7 days. FRL were treated with vehicle. On the seventh day, animals were submitted to the Open Field Test (OFT) for 10 min and the Forced Swimming Test (FST) for 7 min. Medial prefrontal cortex (mPFC) were collected for Western Blotting (WB).

Results: FSL showed increased immobility time when compared with FRL in FST. FSL treated with vehicle or CBD were divided into different subsets: high immobility (HI) and low immobility (LI). FSL CBD LI showed a decreased immobility in FST when compared to FSL CBD HI and FSL Veh HI. No differences were observed in OFT. WB-Cytoplasmic Fraction: FSL CBD (HI+LI) showed an increased level of ERK2 and decreased level of mGluR5 when compared to FSL Veh. WB-Synaptosomes Fraction: FSL CBD (HI+LI) showed an increased level of Synaptophysin when compared with FSL Veh.

Conclusion: Results suggest that FSL rats present a variable response to CBD under chronic treatment related to different protein levels in mPFC. Further protein analysis and endocannabinoid levels are under investigation to understand the CBD effects in responders vs non-responders.

Keywords: Pharmacology, Basic neuroscience, Animal models/disease models

Effects of β-hydroxybutyrate on fatiguability and recovery in isolated skeletal muscle

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INTRODUCTION: Ketone bodies, namely β-hydroxybutyrate, are energy substrates that might improve performance by delaying skeletal muscle fatigue and aid recovery, partly by sparing muscle glycogen. However, ketone bodies also improve the function of heart muscle and neurons. The specific effects of ketone bodies on skeletal muscle fatigue and recovery are still unclear.

METHODS: Isolated rat soleus muscles were submerged in a physiological solution containing either sodium-β-hydroxybutyrate (10 mM) or no energy substrates. Muscles were electrically stimulated to contract and fatigued by a standardized, dynamic contraction protocol mimicking rodent locomotion. Following fatigue, muscles rested for 90 min and recovery was assessed every 30 min by peak force measurements during twitch, doublet, non-fused tetanus, and tetanic muscle activation. Glycogen content was determined following the recovery period.

RESULTS: The fatigue protocol resulted in ~50% decline in peak force with no significant difference between muscles submerged in BHB and no substrate fluid. During the first 30 min of recovery, muscles exposed to sodium-β-hydroxybutyrate partially recovered both twitch and tetanic force (by 10%), but did not recover further during the next 60 min. In contrast, in muscles with no energy substrates available force did not recover over 90 min of recovery. The frequency of activation used to asses fatigue had no effect on muscle fatigue or recovery. The results are preliminary, and we are currently awaiting glycogen measurements.

CONCLUSION: β-hydroxybutyrate significantly aids initial recovery of force following fatigue when no other energy substrate is available.

Keywords: Animal models/disease models, Pharmacology, Rheumatology

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, 4-10 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.

Keywords: Animal models/disease models, Basic neuroscience, Psychiatry, psychology and mental health

Dairy Proteins for Non-Alcoholic Fatty Liver Disease

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Background: Non-alcoholic fatty liver disease (NALFD) is a highly prevalent condition characterized by accumulation of intrahepatic fat and is in some cases accompanied by inflammation and fibrosis. Patients with NAFLD have an increased risk of developing type 2 diabetes and have an overall increased mortality, mainly driven by cardiovascular diseases.

The only treatment is weight loss and optimal lifestyle approaches are warranted. Clinical and animal studies show promising effects of high protein diets (HPD) in managing other aspects of the metabolic syndrome and observational studies showed that high intake of dairy products was inversely associated with NAFLD and insulin resistance (IR).

Aim: To investigate if a high protein diet supplemented with dairy proteins can ameliorate NAFLD and IR in overweight patients with NAFLD.

Method: This randomized, controlled trail is conducted at two centers. 54 patients with NALFD and BMI > 27.5 kg/m2 are randomized to a HPD with one of two dairy protein supplements or to a normal, control diet. For the first 4 weeks patients are instructed by to follow an eucaloric diet (HPD; 25% Protein, 25% Fat, 50% Carbohydrate. Control; 15% Protein, 25% Fat, 60% Carbohydrate). Hereafter they are instructed to follow a hypocaloric diet for 20 weeks or until achieving a weight loss of 5% (HPD; 35% protein, 35% Fat, 30% Carbohydrates. Control; 25% Protein, 35% Fat, 40% Carbohydrates).

At baseline, after 4 weeks and at the end of the study, patients undergo a MR-spectroscopy to measure the intrahepatic fat content. IR is assessed by a mixed-meal tolerance test and a hyperinsulinemic-euglycemic clamp with glucose, palmitate, and VLDL-tracers.

Keywords: Gastroenterology and hepatology, Molecular metabolism and endocrinology, Medical technology and diagnostic techniques

Module based laparoscopic training as a part of surgical education: a prospective study on surgical trainees

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AIM

The present study aims to investigate when and how many laparoscopic cholecystectomies (lap. chol) surgical residents performed during their first-year residency.

BACKGROUND

Tensions between receiving efficient workplace-based training in surgery and providing high-quality patientcare is often highlighted in educational literature.

Module-based training has been shown to improve and sustain surgical skills. Hence, this approach has gained recognition and 40 % of the surgical departments in our region is labelled as including module-based training. However, little is known about the status of module-based training among surgical residents.

METHODS

The study participants were residents in abdominal surgery employed in the Central Denmark Region in the period of 2015-2020 (n=59). Using a business intelligence portal, we collected the following data: date and number of lap. chol. performed by surgical residents, during their first year of residency, and the total number of lap. chol. performed in the department during the same period.

RESULTS

Of the included residents, 17 (28,8%) were identified with module based laparoscopic training. The median of performed lap. chol. by residents with module-based training were three times higher than the residents without, 36 (24-57) compared to 12 (0-36). At no time module-based trained residents performed more than 53% of the total number of the department´s lap. chol. per month.

CONCLUSION

Module-based training improves the residents' opportunities to perform and may therefore facilitate coherent leaner trajectories and enhance workplace-based training by ensuring the same structured training approach to all residents.

Keywords: Gastrointestinal surgery, Health education and simulation-based training, Work environment and organization

Aptamer biomarkers in non-alcoholic fatty liver disease

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Non-alcoholic fatty liver disease (NAFLD) is closely associated to the obesity epidemic. It is estimated that one third of the adult population is affected globally and the prevalence is increasing.

The current gold standard for assessment of NAFLD disease severity and fibrosis staging relies on liver biopsy; an invasive and costly procedure with potentially severe complications. In spite of vigorous research activity in the field of non-invasive assessment of NAFLD there is still an unmet need for reliable non-invasive biomarkers capable of diagnosis and monitoring of this heterogenous patient group.

In this PhD-project we will use APTA-SHAPE technology to solve this challenge.

APTA-SHAPE technology facilitates aptamer technology to discover biomarkers in a biological sample. Aptamers are short chemically stabilized RNA strands often termed “chemical antibodies”. The aptamers form defined 3D shapes capable of specific unbiased recognition of a biological target. Through consecutive trainings with plasma from patients with different disease severities of NAFLD we build a library specifically able to detect thousands of plasma molecules in NAFLD. In subsequent analysis, aptamers associated with the individual components of histological NAFLD are identified and the targets of these aptamers are identified by mass spectrometry.

Through this approach, we aim to discover novel biomarkers and develop biomarker panels that will aid in diagnosis and monitoring of patients with NAFLD.

Keywords: Gastroenterology and hepatology, Inflammation, Medical technology and diagnostic techniques

Platelet aggregation in colorectal cancer patients undergoing surgical treatment.

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INTRODUCTION

Surgical treatment of colorectal cancer carries a risk of venous thromboembolism, and minimally invasive surgery is considered low risk compared with open surgery. However, extended thromboprophylaxis is offered after both procedures.

The aim of the study was to compare perioperative changes in platelet aggregation in patients undergoing open cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) for peritoneal metastases compared with patients undergoing minimally invasive resection for localized rectal cancer.

METHODS

Blood samples were obtained after induction of anesthesia (baseline) and after wound closure for platelet count and platelet aggregation. Platelet aggregation was measured with Multiplate Analyzer using ADPtest, ASPItest, and TRAPtest agonists reported as area under the curve (AUC, AU*min).

PRELIMINARY RESULTS

We included 26 patients treated with CRS with HIPEC and 30 patients undergoing minimally invasive resection. Higher platelet count was found in patients undergoing minimally invasive resection than CRS with HIPEC (Difference in means (Δ), 95% confidence interval (CI): Δ 4.8 (-24:34). vs. -28 (-40:97). ADP, ASPI, and TRAP induced platelet aggregation was higher after minimally invasive resection than CRS with HIPEC ((ADP: Δ 269 (119:419) vs. 54 (-79:187), ASPI: Δ 187 (-20:395) vs. 94 (-94:283), TRAP: Δ 269 (57:364) vs. 200 (47:352))

CONCLUSION

In conclusion, both colorectal cancer surgery procedures caused increased platelet aggregation. Preliminary results indicate that minimally invasive resection induces higher platelet aggregation than CRS with HIPEC.

Keywords: Gastrointestinal surgery, Oncology, Cardiovascular system

Risk of venous thromboembolism in patients with inflammatory bowel disease: a nationwide population-based matched cohort study

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Background: Inflammatory bowel disease (IBD) is associated with venous thromboembolism (VTE). Previous studies have reported VTE relative risk to vary from 1.64 to 8.44 providing some uncertainty about the actual risk. In addition, existing evidence is outdated, does not reflect modern management of IBD, and does not consistently distinguish surgery-related and un-related VTE risk in IBD patients. We therefore aim to investigate risk of VTE in patients with IBD.

Methods: We are conducting a nationwide population-based cohort study in Denmark (1977-2018). We identified all patients with incident IBD and matched them with up to 10 general population comparators without IBD by sex, year of birth and region of residence. We categorized IBD according to subtype (Crohn's disease, ulcerative colitis, or both [IBD unspecified]). We calculated cumulative risk of VTE treating death as a competing risk.

Preliminary results: We identified 59,026 patients with an IBD diagnosis matched with 585,923 individuals from the general population. During the 42 years following an IBD diagnosis, 2180 IBD patients and 12,318 comparisons received a VTE diagnosis. The 40-year cumulative risk of VTE was higher in the IBD cohort than in the matched general population cohort overall: 8.8% vs. 5.5%, and in subtypes (Crohn's disease: 8.2% vs 5.5%; ulcerative colitis: 9.0% vs. 5.6%; IBD unspecified: 8.6% vs. 5.2%).

Further analyses: We will calculate adjusted hazard ratios comparing IBD patients with matched comparisons. We will do four subsequent analyses to evaluate the impact of surgery on the overall VTE risk.

Keywords: Gastroenterology and hepatology, Cardiovascular system, Epidemiology and biostatistics

Extended rat hepatectomy – Regeneration of fatal liver failure? An experimental animal study

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Background: After 90% partial hepactomy (PH) in rats, the animal is on the brink of fatal liver failure. So far, the model has been used only for investigating liver regeneration. Our aim was to assess post-hepatectomy liver failure (PHLF) in rats by identifying differences in liver morphology and molecular biology in order to identify which physiological processes are crucial for survival after extended hepatectomy.

Materials and method: Sixty-eight rats were randomized to 90% PH, sham operation or no surgery. We conducted further block randomization according to time of euthanization. General distress score was used to determine clinical liver failure. Liver-specific biochemistry and stereological methods were used to assess the functional and morphological liver response.

Results: All animals subjected to 90% PH experienced biochemical PHLF. For survivors, PHLF appeared to be reversed over time, indicated by regeneration increase and ALAT and ammonia decrease. Non-survivors seemed unable to restore the minimal level of functional liver capacity required to initiate regeneration and avoid fatal PHLF.

Conclusion: In conclusion, the 90% PH model seems to be suitable for investigating PHLF in rats. As expected, high mortality is associated with PHLF. The critical phase seems to be over after 48 hours, where survivors showed improvement in functional liver capacity and accelerated regeneration. Knowledge on the pathophysiology of PHLF may have important implications to improve outcome after extensive PH in clinical practise.

Keywords: Gastrointestinal surgery, Animal models/disease models, Cell biology

Perioperative Platelet Aggregation in Oesophageal Cancer Patients

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Thrombosis is the most common cause of death in cancer patients after the cancer itself. Cancer activates the coagulation, leading to an increased thromboembolic tendency. The risk of thrombosis is further exacerbated when patients undergo surgery.

We are performing a trial examining the coagulation activity in oesophageal cancer patients before, during and after they undergo intended curative surgery.

Here, we present interim data on the platelet aggregation of the 38 patients that had undergone surgery at the time of writing.

Blood samples were taken just before surgery, when surgery ended, and on the first postoperative day. Platelet aggregation was analysed by impedance aggregometry using three agonists: ADP, ASPI, and TRAP. Results are reported as area under the curve (AUC).

Median AUC for ADP was 830 (interquartile range: 619-1064), 986 (795-1174) for ASPI and 1281 (985-1431) for TRAP in the preoperative sample, which are all within reference range.

Median aggregation stayed within the reference ranges for all three agonists during surgery, though there was a statistically significant increase from the preoperative sample to the sample taken just after surgery for ADP ($p=0.001$) and TRAP ($p=0.002$). There was no significant difference between the preoperative sample and the day 1 postoperative sample.

In conclusion, most patients have a normal platelet aggregation before surgery. During surgery, the aggregation increases and then returns to baseline within 24 hours. A topic for future study, when the full cohort is included, will be to isolate those patients with an aggregation above reference range and examine whether they display an increased risk of thrombosis.

Keywords: Gastrointestinal surgery, Oncology, Cardiovascular system

Individualised perioperative blood pressure and fluid therapy in oesophagectomy

- a prospective, randomised controlled trial

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Background:

Oesophagectomy is the mainstay of curative treatment for oesophageal cancer, but it is associated with high risk of major complications.

Goal-directed fluid therapy and individualised blood pressure management may prevent infections and protect anastomosis after surgery. Extending goal directed fluid therapy after surgery and applying an individual blood pressure target may have substantial benefit in oesophagectomy.

This is a protocol for a clinical trial implementing a novel haemodynamic protocol from start of anaesthesia and until the next day with the patient's own night-time blood pressure as lower threshold

Methods:

Single-centre, single-blind, randomised, clinical trial. Oesophagectomy patients are randomised 1:1 to either perioperative haemodynamic management according to a goal-directed fluid therapy protocol with an individual target blood pressure or standard care.

Endpoints:

The primary endpoint is the total burden of morbidity and mortality assessed by the comprehensive complication index 30 days after surgery. Secondary endpoints are perioperative haemodynamic variables, complications and quality of life at 90 days after surgery

Conclusion:

The results from this trial provide an objective and easy to follow algorithm for fluid administration which may improve patient-centred outcomes in oesophagectomy patients

Funding: The trial is supported by Aarhus University (1 293 400 DKK) and the Novo

Nordisk Foundation (625 200 DKK)

Trial registration: EudraCT number: 2021-002816-30

Keywords: Gastrointestinal surgery, Oncology, Other

POSTER SESSION 4

Improved diagnosis of ovarian cancer

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Background: Preoperative differentiation between benign and malignant ovarian 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) may present a future diagnostic tool. The diagnostic work-up may 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 project is ongoing. The area under the ROC curves, sensitivities and specificities, positive and negative predictive values will be compared.

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.

Keywords: Gynecology and obstetrics, Medical technology and diagnostic techniques, Oncology

Specifically expressed markers in fetal membrane cells; potential biomarkers for Preterm Prelabor Rupture of Membranes

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BACKGROUND

Preterm Prelabor Rupture of the Fetal Membranes (PPROM) is preceded by a premature senescence of the amniochorionic cells causing “microfractures” of the fetal membranes. We hypothesize that this pathological process is associated with shedding of fetal membrane cells into the maternal circulation prior to the event, and that it can constitute as a biomarker for the risk of PPROM. The aims of the study were 1) on mRNA level, to identify gene markers differentially expressed in fetal membrane cells as compared to maternal white blood cells, and 2) on protein level, to evaluate their specificity for fetal membrane cells by immunohistochemical analyses.

METHODS

For RNA sequencing, we compared amnion and chorion cells from a term pregnancy (GA>37) to maternal white blood cells from a first trimester pregnancy.

For immunohistochemistry, we analyzed five fetal membrane and placental biopsies after normal vaginal delivery at term (GA>37), and one biopsy from the placental bed of the uterus (GA 38) obtained from the uterotomy of a placenta previa caesarean section.

RESULTS

RNA sequencing revealed 31 genes in the amnion and 42 genes in the chorion that were upregulated. AHNAK2, AQPEP, CNR1, DPYSL3, EMP1, FERMT2, FLT1, GPX8, KRT5, KRT17, MUC16, NPR3, PDLIM4, PRLR, PRTG, PVRL4, RXFP1, THY1, UCHL1 and UPK1B were evaluated by immunohistochemistry. All proteins but two were expressed in at least one type of fetal membrane cell, confirming a mutually high mRNA and protein expression.

CONCLUSION

These unique markers can contribute to the search for fetal membrane cells in maternal blood, which potentially can be used to diagnose high risk status in women for rupture of membranes.

Keywords: Gynecology and obstetrics, Cell biology, Laboratory science

Trans-placental transport of artificial sweeteners

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Obesity is increasing and evidence points towards it being rooted already in fetal life. Currently, overweight pregnant women are advised to substitute sugar-sweetened beverages with diet drinks containing artificial sweeteners. But recent evidence suggests that consumption of artificial sweeteners during pregnancy increases the risk of obesity in the child. The mechanism is unknown, but we hypothesized a transport of artificial sweeteners across the placenta into the fetal circulation and the amniotic fluid thus affecting the unborn child.

We included 19 pregnant women who were given an oral dose of acesulfame, cyclamate, saccharin and sucralose before planned caesarean section. Nine controls refrained from intake of artificial sweeteners 48 hours before the caesarean section. The concentrations of artificial sweeteners were then measured in maternal and fetal blood and amniotic fluid using mass spectrometry.

Fetal plasma concentrations of artificial sweeteners had a positive linear dependency on maternal plasma concentrations with adjusted coefficients of 0.49 ng/mL (95% CI: 0.28-0.70) for acesulfame, 0.72 ng/mL (95 %CI: 0.48-0.95) for cyclamate, 0.51 ng/mL (95% CI: 0.38-0.67) for saccharin and 0.44 ng/mL (95% CI: 0.33-0.55) for sucralose. There was no linear relationship between amniotic fluid and fetal plasma concentrations but there were positive ratios for all four sweeteners.

In conclusion, the four sweeteners investigated all crossed the placenta and were present in the fetal circulation and amniotic fluid.

Keywords: Gynecology and obstetrics, Paediatrics, Other

Risk and benefits of a national implementation of Sentinel lymph node mapping in women with low-intermediate risk endometrial cancer- the SENTIREC-endo study.

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Background: The surgical staging of endometrial cancer (EC) has changed dramatically during the past decade. It is crucial for these old and often comorbid women, to identify lymph node metastases with minimal surgical trauma. Sentinel lymph node (SLN) mapping represents a sensitive staging procedure with presumed limited surgical risk. The SENTIREC-endo study undertook a national adoption of SLN mapping for women with EC. There is limited knowledge of the risks and benefits of a broad adoption of SLN mapping for EC.

Methods: This national prospective study, included women with EC of low (LR) - and intermediate risk (IR) of lymph node metastases, from March 2017-Feb. 2022. All women underwent surgery with SLN mapping. This represented extended surgery for the majority of women (LR group) and less surgery for women with IR. All women completed validated patient reported outcome measures (PROM) prospectively. Lymphedema was evaluated using validated PROM sub-scales, and calculated as the mean difference score from baseline to three months postoperative. Intra- and postoperative complications were classified according to Clavien Dindo.

Results: 630 women were included in the analyses. Of these 459 were of LR and 171 of IR. The incidence of lymph node metastasis was 4.4% (20/459) in the LR- and 22.2 % (38/171) in the IR group. The mean difference score of lymphedema was 4.3/100 CI: (2.6-5.9), below the threshold for clinical importance. The incidence of intra-operative complications was 1.4% (9/630). The incidence of postoperative complications was 7.6% (50/630).

Conclusion: SLN mapping is a safe and accurate staging procedure to identify metastases in women with LR and IR EC.

Keywords: Gynecology and obstetrics, Oncology, Other

Twenty-two-year trends in revision due to periprosthetic joint infection after knee arthroplasty due to osteoarthritis: A Danish nationwide cohort study, 1997-2019

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Background: Knee arthroplasty (KA) is an effective treatment of disabling knee osteoarthritis. Periprosthetic joint infection (PJI) is a serious complication with great patient impairment, complex treatment, and great healthcare cost.

Aim: To describe the incidence and trend of PJI after KA due to osteoarthritis within the first year after surgery from 1997 to 2019 in Denmark.

Methods: In this nationwide population-based cohort study, we used Danish Knee Arthroplasty Register to identify patients who underwent primary KA surgery due to osteoarthritis from 1997 to 2019 (n=115,120). Our outcome was revision due to PJI, within the first 3 months (early) and 3-12 months (delayed) after KA. The PJI incidence was analyzed using the Kaplan-Meier method with 95% confidence intervals (CI) and calculated overall and by calendar periods. Cox regression analyses was used to estimate hazard ratios, crude and adjusted for early and delayed PJI in the calendar periods.

Results: The overall incidence of PJI within 0-1 year after KA was 0.7. We found an increase in the incidence of PJI within the first year from 0.5% in 1997 to 0.7% in 2019 corresponding to adjusted HR of 1.8 (CI: 1.2-2.6) in 2018-2019 relative to 1997-2001. The increase was driven by an increase from 0.1% to 0.5% in early PJIs, with the adjusted HR of 8.9 (CI: 3.6-22.0) in 2018-2019 relative to 1997-2001. We observed a decrease in the incidence of delayed PJIs from 0.4% to 0.2%.

Conclusion: The incidence of revision due to PJI after KA is low, but increasing, for early PJI. Further studies on risk factors are needed to identify patients at high risk, individualize patient information and initiate preventative initiatives.

Keywords: Orthopedic surgery, Epidemiology and biostatistics, Infection

Explanations for functional somatic symptoms across European treatment settings: a mixed methods study

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Engaging patients in treatment for functional somatic symptoms (FSS) relies on a shared understanding of the mechanisms underlying the complaints. Despite this, little is known about the explanatory models used in patient education in daily clinical practice. We examined the models typically used to explain FSS across European healthcare settings through an exploratory mixed methods study, combining sequential quantitative and qualitative analyses. 3 types of data were collected: a survey of Health-Care Professionals (HCPs) with special interest in FSS from 16 European countries (n=186), Patient Education Material collected systematically from survey respondents (n=72) and Semi-structured Interviews with HCPs (n=14). Findings were integrated through mixed-methods triangulation. Five main explanatory models for FSS that are used across treatment settings and diagnostic constructs were represented across data types. The 'Multisystem Stress' Approach explains FSS through physiological stress responses within a bio-psycho-social paradigm. 'Sensitized Alarm' and 'Malfunctioning software' are both approaches derived from the neurosciences. Within integrated psychosomatic therapies explanations related to 'Embodied Experience' are often used. In the person-centered 'Symptoms' approach, HCPs aim for co-constructed, individualized explanations. These approaches, which rely on different models of mind-brain-environment are complementary and are used flexibly by skilled HCPs. Taken together the explanatory models described might form the basis of a curriculum of medical explanation with the potential to equip clinicians to form more collaborative relationships with patients across healthcare.

Keywords: Qualitative research, Health education and simulation-based training, Other

Deconstructing the 'Leaky Pipeline'

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Background: At the Department of Clinical Medicine (DCM), Health, Aarhus University, only 23% of the professors were women in 2021, a number that has been almost stagnant since 2018. To gain insights into some of the barriers female researchers face at DCM, this project focus on epistemic injustice, that is injustices related to knowledge - a fitting first step toward creating a more just university since it is an institution based on the production and dissemination of knowledge.

Aims: The project addresses three research questions:

1) Do the researchers employed at DCM perceive DCM as a meritocratic institution?

2) How do hermeneutical injustices unfold at DCM?

3) How do testimonial injustices, related to gender bias, unfold at DCM?

Methods: The project is designed as ethnographic fieldwork which comprises of participant observation at three departments within DCM, semi-structured interviews with six male researchers and 15 female researchers, and two focused group interviews with five researchers in each.

Preliminary results: Data suggests that the meritocratic myth that pervades DCM has led to a hermeneutical ‘gap’ among the researchers who lack an adequate vocabulary to make sense of, and communicate, experiences of injustice and discrimination.

Conclusion and Perspective: Examining epistemic injustices at DCM will enable us to address previously underexamined causes of gender inequality. It will help us develop a vocabulary to talk about injustices within academia, thus reframing the conversation about gender inequality paving the way for dialogue and change.

Keywords: Qualitative research, Work environment and organisation, Other

'You are dealing with the bottom here...' A qualitative study about colorectal cancer screening among vulnerable men at shelters in Denmark

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BACKGROUND

Colorectal cancer (CRC) screening can reduce both incident and mortality. Even though men have a higher risk of developing CRC they are less likely to participate in the screening programme. Little is known about CRC screening behaviour among some of the most vulnerable men with social problems. In this study we explored the perceptions about CRC screening and perceived barriers and facilitators towards screening participation among vulnerable men at shelters in Denmark.

METHODS

Interview study with vulnerable men at a shelter in Denmark. The interviews were transcribed verbatim followed by an inductive content analysis.

RESULTS

Vulnerable men were concerned about their health and interesting in participating in CRC screening even though they were less concerned about cancer and had a misunderstanding of the concept of cancer screening. Furthermore, most had cognitive difficulties and needed social support and companionship in the health system. Suggested facilitators included face to face communication, awareness material and help to navigate the CRC screening process.

CONCLUSION

Despite interest in the CRC screening vulnerable men participate less often. Thus, there is an obvious opportunity to reduces social inequality in health by offering a targeted intervention to the most vulnerable.

Funding: Health Research Foundation of Central Denmark Region, the Danish Health Foundation, and the Danish Cancer Society

Keywords: Qualitative research, Public health, Socio-economic conditions

Perceptions and experiences with stigma among Danish women with gestational diabetes: a qualitative investigation

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Background & aim: Based on a recent literature review, gestational diabetes mellitus (GDM) has been suggested to be a stigmatised diagnosis; however, no studies have systematically investigated GDM-specific stigma using original data. Therefore, we aimed to explore the experiences of women with GDM, with a particular focus on the perception and experience of GDM-specific stigma. This abstract is based on preliminary findings, as the final analysis is not yet completed at the time of submission.

Method: Twenty pregnant women diagnosed with GDM were interviewed for this study. All interviews will be transcribed verbatim, coded using a data-driven approach and analysed using Andersen et al's conceptualisation of stigma.

Results: The women perceived GDM as a stigmatised diagnosis; feeling labelled and stereotyped negatively. They reported being content with healthcare personnel, however, the advice given could be perceived as presumptuous of their health behaviour. The stigma associated with GDM was perceived to stem from a general negative narrative about diabetes, especially type 2 diabetes. The women reported feeling guilty and blaming themselves. Further, some women did not want to disclose their diagnosis to people in general, as they were ashamed.

Conclusions: This is the first known study to investigate GDM-specific stigma on original data. The preliminary analysis finds that women with GDM perceived the diagnosis to be stigmatised. Not disclosing their diagnosis and feeling ashamed indicates that the women had internalised this stigma. This research provides important insights into future care optimisation and stigma alleviation among women with GDM in Denmark.

Keywords: Qualitative research, Public health, Psychiatry, psychology and mental health

First pill is the hardest to swallow: An evaluation study of how follow-up phone calls support screen-citizens' decision-making about preventive medicine for cardiovascular disease

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Background: We report the findings of an evaluation research. Cardiovascular disease (CVD) is the second leading cause of death globally. Screening of CVD and initiation of preventive measures are expected to reduce long-term consequences of CVD. However, the screening gain has been described as weakened by low medical adherence. To optimize future prevention efforts concerning CVD, there is a need for studies providing data on targeted individual-orientated intervention, combined with data on effectiveness of medical adherence.

Aims: The aim of this study was to explore whether follow-up phone calls supported screen-citizens in making an informed decision about preventive medicine for CVD.

Methods: We used Dahler-Larsen evaluation design. Hence, we developed a programme theory that described the intervention "follow-up phone calls" expected effect on how screen-citizens felt supported in making an informed decision about preventive medicine for CVD. We then tested the effect and identified how and why "follow-up phone calls" worked or did not work, for whom, and under what circumstances.

Results: Four main topics proved to be particularly decisive for whether citizens received support in making decisions about preventive medicine for CVD. These were: understanding the purpose of the medication, meaningfulness, a trusting relationship, and experience with medication.

Conclusion: To support citizens in making an informed choice about preventive medicine for CVD, it requires special communicative skills, where there is a greater focus on listening to and embracing the citizen's perspective on preventive medicine for CVD.

Keywords: Qualitative research, Cardiovascular system, Public health

The current nutritional- and mobilization care for patients with an exacerbation of chronic obstructive pulmonary disease at pulmonary wards: An observational study

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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. Pulmonary rehabilitation is the current non-pharmacological treatment to manage COPD but challenged with low participation. This project aims to develop and test a nurse-led intervention that promotes physical activity and nutritional status with a person-centered approach to patients with COPD and their relatives as a supplement to pulmonary rehabilitation. Identifying the current practices for nutritional- and mobilization care is essential to understand the context where an intervention will be implemented. This study is accomplished according to the medical research council framework for complex intervention.

Aim: To identify the current nutritional- and mobilization care for patients with an exacerbation of COPD at pulmonary wards.

Methods: Field observations with follow-up interviews with nurses and patients were conducted based on J. Spradley's participant's observational research cycle. The data were coded using NVivo 11. A thematic analysis will be conducted according to Braun and Clark's thematic analysis guide.

Preliminary results: The nutritional care primary consisted of serving the three main courses without further interaction during the meals. A systematic nutritional care plan is lacking; thus, the overview of nutritional care is missing. The patients and their relatives are motivated to change their behaviour to avoid readmission. Only patients with physical strength are encouraged to be active.

Keywords: Qualitative research, Rehabilitation, Respiratory system

POSTER SESSION 5

Patients' experiences of cognitive impairment following critical illness treated in an intensive care unit: A scoping review

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Background: Critical illness in the ICU affect many patients for several months or years as they suffer from cognitive impairments. Cognitive impairments are found with prevalence higher than 70% at discharge, 13%–79% at 3–6 months, 10%–79% at 1 year, 25%–47% at 2 years and approx. 25% at 6 years after discharge in intensive care survivors. Exploring their experiences on how and which cognitive impairments are affecting their everyday lives facilitates the planning of relevant research on interventions that may serve to alleviate the burden of post-ICU cognitive impairments.

Aim: To review the literature on patients' experiences of cognitive impairments following critical illness treated in an ICU.

Design: A scoping review using the Joanna Briggs Institute methodology and the PRISMA-ScR checklist.

Methods: A systematic search was conducted in PubMed, Cinahl, PsycInfo and Embase. Covidence was used by two independent researchers to select, compare and discuss relevant studies to include.

Results: The scoping review included 11 studies with qualitative and/or quantitative methods. Four themes emerged during the analysis reflecting patients' experiences of critical illness in the ICU: 'Experiencing poor memory', 'Managing everyday life', 'Unsupported by the healthcare system', and 'Strategies for support in recovery'. Patients made use of different strategies in recovery and rehabilitation to regain independence and not being a burden to others.

Conclusion: Patients experienced a variety of cognitive impairments following critical illness in the ICU affecting and challenging their quality of life and adaption to everyday life.

Keywords: Reviews and meta-analyses, Rehabilitation, Other

Task Shifting in Out-Of-Hours Primary Care – A Review of the Literature

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Background: An increased workload combined with workforce shortage among general practitioners (GPs) and other healthcare staff is challenging out-of-hours (OOH) general practice. Task shifting from the GP to other professionals could improve treatment capacity in face-to-face contacts. In daytime, task shifting has proven to be relevant and beneficial, but evidence is lacking in OOH general practice.

Aim: To evaluate the effect of task shifting from GPs to other healthcare professionals (e.g., nurses, physician assistants, and paramedics) in clinic consultations and home visits in OOH general practice.

Methods: We performed a systematic review, conducting an electronic search on 13th of December 2021 in PubMed/MEDLINE, EMBASE, Cochrane Library, and CINAHL. Two authors independently reviewed all abstracts and full-text articles. Data was extracted from the included articles and included the main outcomes: 1) content (patient groups, type of complaints) and 2) efficiency (consultation length, diagnostic tests, drug prescriptions and referrals). Included articles were quality appraised.

Results: The search identified 1,829 articles, resulting in inclusion of seven. These studies were heterogeneous; they used GPs as comparator in different ways and had different outcome measures. In general, other healthcare professionals saw younger patients with lower urgent health problems than GPs. The consultation length was longer for other healthcare professionals than for GPs. Overall, no differences were found for outcome measures on efficiency.

Conclusions: Other healthcare professionals can have a positive impact on OOH general practice, but more studies are needed.

Keywords: Reviews and meta-analyses, Public health, Work environment and organisation

Low-dose ketamine as an adjunct to opioid analgesics for acute pain management in the emergency department: A systematic review and meta-analysis

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Objective: To evaluate the effectiveness of low-dose ketamine (LDK) as an adjunct analgesic to opioids for acute pain in emergency department (ED) settings.

Design: Systematic review and meta-analysis.

Methods: A systematic search was performed in MEDLINE, Embase, Scopus and Web of Science through March 2022. Randomized controlled trials (RCTs) that investigated LDK as an adjunct to opioids in adult patients in ED settings were selected. Two reviewers screened studies, extracted data and assessed study quality. Data were pooled using random-effects models. The primary outcome was mean pain intensity score. Secondary outcomes included need for rescue analgesia, adverse events and patient satisfaction. Results were reported as mean differences and risk ratios. Statistical heterogeneity was calculated using the I2 statistic.

Results: Eight RCTs were included (n = 903). Studies were judged to be at moderate to high ROB. Mean pain intensity scores were significantly lower 60 minutes after study drug administration favoring adjuvant LDK (MD -0.76; 95% CI -1.19 to -0.33), compared to opioids alone. In a sensitivity analysis, mean pain intensity scores differed significantly favoring adjuvant LDK >15-30 (MD -1.09; 95% CI -1.78 to -0.39) and 60 minutes (MD -1.09; 95% CI -1.78 to -0.39), after study drug administration. Patients who received adjuvant LDK were less likely to require rescue analgesia, no more likely to experience serious side effects and had higher satisfaction scores.

Keywords: Reviews and meta-analyses, Other, Other

Seroprevalence of autoantibodies against type I interferons in patients with herpesvirus brain infections

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Brain infections with herpes simplex virus (HSV) or varicella-zoster virus (VZV), two alphaherpesviruses, are rare diseases that carry a high risk of permanent neurological sequelae or even death. In the past two decades, several genetic inborn errors of immunity

have been linked to heightened susceptibility to each virus, most of them related to the type I interferon (IFN-I) system. Errors in IFN-I pathways and autoantibodies directed against IFN-I have also been linked to critical or lethal COVID-19, and patients carrying these autoantibodies were at increased risk of herpesvirus reactivation from latency. We want to assess whether some cases of herpesvirus brain infections can be explained by the presence of autoantibodies against IFN-I, which would represent a novel predisposing factor for these diseases

Methods: We are collecting serum, plasma, and cerebrospinal fluid samples from patients with brain infections with HSV or VZV from two different biobanks: the Danish Study Group for Infections in the Brain (DASGIB) and clinical material stored at the Danish National Biobank at The State Serum Institute in Copenhagen. The presence of autoantibodies will be assessed with an ELISA and functionally validated for neutralizing capacity in an in vitro assay.

Project status: Collection of informed consent from patients and biological material is ongoing. Results are pending.

Keywords: Infection, Inflammation, Allergy

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) 330·106 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

Keywords: Infection, Animal models/disease models, Other

Phase 1 proteins in the airway epithelium

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NRF2 is a transcription factor that regulates the expression of antioxidant genes and inflammatory responses. We demonstrate that phase 1 proteins, a subset of NRF2 genes which are highly expressed in the airway epithelia, act antiviral towards Influenza A virus (IAV). Overexpression of the phase 1 proteins in Huh7 cells by CRISPR activation reduced IAV replication. Using human airway Air-liquid interface cell cultures, we investigated the expression of phase 1 genes through cellular maturation from basal cell stage to fully differentiated epithelium cells. This was done by qPCR and Western Blotting using samples harvested at different stages of cellular development. The expression of these genes increased vastly through differentiation on both RNA and protein level. p

We are trying to identify the antiviral mechanisms of these NRF2 subset genes and the mechanisms that control the increase in expression through differentiation.

Keywords: Infection, Respiratory system, Genetic engineering

Effects of light-guided nudges on healthcare workers' hand hygiene behavior

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Hospital-acquired infections continue to burden 7% of all patients in European countries but can be reduced by improving hand hygiene compliance (HHC) among healthcare workers´. We aimed to investigate the effect of nudging with sensor lights on healthcare workers´ HHC.

An 11-month, prospective, interventional study was conducted at four hospital wards at a Danish university hospital. An electronic monitoring system was used to collect the data. HHC was measured in patient rooms. Data were provided as HHC rates. We compared baseline HHC with periods of nudging with lights displayed on the hand sanitizers.

Intervention period 1: The four wards were randomly divided in two groups to start receiving either Reminder-nudges or Feedback-nudges

Intervention period 2: All four wards received both reminder- and feedback-nudges simultaneously

In total, 190.114 hygiene opportunities were collected from doctors (n=91), nurses (n=135) and cleaning assistants (n=15).

The Reminder-nudge-group increased their HHC from baseline to the first intervention period (21% vs 25%, P=0.0001) and stayed at this level when they subsequently received both reminder- and feedback-nudges simultaneously.

The Feedback-nudge-group increased their HHC from baseline to the first intervention period (19% vs 30%, P=0.0001) and increased further when they subsequently received both reminder- and feedback-nudges simultaneously (30% vs 34%, P=0.004).

Both groups increased HHC from baseline to the first intervention period receiving one nudge with light. In the second intervention period receiving both nudges, the Reminder-nudge-group remained at the higher level and the Feedback-nudge-group increased further.

Keywords: Infection, Medical technology and diagnostic techniques, Oncology

Frail old patients with Clostridioides difficile infection: improvement of quality in treatment and care – the CLODIFRAIL study: study protocol for a randomised controlled trial

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Introduction: Clostridioides difficile infection (CDI) is a complex disease with negative health outcomes among older patients, including a high mortality. Transition of care for patients with CDI is critical to reduce recurrence rates and improve health outcomes in these patients.

The main objective of this study is to investigate whether a multimodal geriatric assessment, treatment and follow-up of older patients with CDI can improve patient survival compared with standard care.

Methods: This is a parallel-group randomised controlled trial in which patients aged 70 years or more and diagnosed with CDI from the positive CD toxin test are randomised 1:1 to either 1) a geriatric tailored assessment and intervention or 2) standard care. We plan to recruit 216 patients, with randomisation at project manager level. The intervention consists of three main parts: (1) clinical geriatric assessment of the patient; (2) clinical evaluation of indication for faecal microbiota transplantation; (3) clinical follow-up weekly during 8 weeks. The study period is 3 months. The primary outcome is 90-day survival from date of positive PCR test for CDI. Secondary outcome measures include quality of life measured by the 5-level EQ-5D version (EQ-5D-5L) and by Overall Quality of Life Depression List (OQoL-DL) and functional status measured by the Functional Recovery Score (FRS).

Discussion: This study will provide new knowledge on the potential for clinical improvements after performing comprehensive geriatric assessment, including an early geriatric assessment of the indication for faecal microbiota transplantation.

Keywords: Infection, Multimorbidity, Gastroenterology and hepatology

Exploring the innate immune system; C-type lectins and their interactions with patterns of carbohydrate on bacteria

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The cell wall of microorganisms has complex patterns of carbohydrates. Germline encoded pattern recognition receptors (PRRs) of the innate immune system distinguish between intact self and foreign invaders via the recognition of these patterns. The C-type lectins (CTLs) are a superfamily of Ca2+-dependent PRRs, found as soluble as well as transmembrane proteins. CTLs have a carbohydrate recognition domain (CRD), which typically has a weak affinity for monosaccharides, but bind avidly to patterns of carbohydrates. We generated stable human HEK293 cell lines expressing CTLs and screened for binding to a range of bacteria using flow cytometry. We found that the CTL langerin, naturally occurring on the surface of Langerhans cells, recognizes the opportunistic pathogen Staphylococcus aureus. Which is one of the most frequent causes of bacterial infections in humans. S. aureus can evade the immune system, e.g., by forming a polysaccharide capsule. We find that the formation of such capsules by S. aureus shields the bacteria from recognition by langerin. In contrast, capsule formation does not inhibit the binding of the soluble CTL, mannose-binding lectin (MBL), which likewise recognizes S. aureus. In conclusion, we find that S. aureus avoid recognition by a membrane-bound CTL through the formation of capsules, whereas we do not see this for the soluble CTL.

Keywords: Infection, Inflammation, Laboratory science

Nrf2-addiction creates a niche for oncovirotherapy in lung cancer by suppressing antiviral innate immunity

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Nuclear factor erythroid 2-related factor 2 (Nrf2), a master regulator of redox homeostasis, is frequently activated in cancer cells giving rise to Nrf2 addiction in specific tumor subsets. Dysregulation of Nrf2 activity results in aggressive tumors and correlates with resistance to therapy. We have recently shown that Nrf2 plays an important role in regulating antiviral immunity. Using bioinformatic and biochemical analyses, we demonstrate that a panel of Nrf2-addicted lung cancer cells (A549 and NCI-H460) display high Nrf2-active levels which correlates with low antiviral protective immunity as compared to non Nrf2-addicted cell lines (Calu1 and NCI-H358). Interestingly, we show that Nrf2 addiction increases the susceptibility and virus-mediated killing by VSVd51M on cells otherwise resistant to conventional therapy such as carboplatin or teniposide. CRISPR/Cas9-mediated Nrf2 knockout or silencing of Nrf2 using a small interfering RNA significantly decreased the replicative and oncolytic capacities of VSVd51M in Nrf2-addicted cancer cells. Conversely, chemical activation of Nrf2 bolstered VSVd51M proliferation in otherwise refractory cell lines Calu1 and NCI-H358. Mechanistically, we show that Nrf2 poises cancer cells to be more sensitive to oncolytic virotherapy by dysregulating IFNAR signaling and elevating the basal levels of a subset of interferon-stimulated genes (ISGs). Altogether, our study indicates that Nrf2 addiction creates a niche for oncovirotherapy in these lung cancer cells by suppressing antiviral innate immunity. Ultimately, the knowledge acquired on the biology of these hard-to-treat cancer cells will open new therapeutic options for patients.

Keywords: Infection, Oncology, Cell biology

High-dose coenzyme Q10 therapy versus placebo in patients with post COVID-19 condition: a randomized, phase 2, crossover trial

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Background

Post COVID-19 condition (PCC) is defined as symptoms lasting more than 12 weeks after developing COVID-19. We hypothesized that PCC is caused by prolonged mitochondrial dysfunction. As Coenzyme Q10 (CoQ10) can improve mitochondrial function, we examined whether high-dose CoQ10 can reduce the number and/or severity of PCC-related symptoms.

Methods

In this placebo-controlled, double-blind, 2x2 crossover interventional trial, participants were recruited from Aarhus University Hospital and Gødstrup Hospital, Denmark. They were randomly assigned to receive either oral capsules of CoQ10 in a dose of 500 mg/day or placebo for six weeks, with crossover treatment after a four-week washout period. The ED-5Q and a PCC-symptom specific questionnaire were completed by the participants at 5 visits during the 20-week study period. The primary endpoint was change in the number and/or severity of PCC-related symptoms after the six-week intervention compared to placebo.

Findings

From May 25th to September 22nd, 2021, 121 participants underwent randomization, and 119 completed both dosing periods. At baseline, the mean PCC-related symptom score was 43·06 (95% CI: 40·18;45·94), and the mean EQ-5D health index was 0·66 (95% CI: 0·64;0·68). The difference between CoQ10 and placebo was not significant with respect to either the change in EQ-5D health index (with a mean difference of 0·01; 95% CI: -0·02;0·04; p=0·45) or the change in PCC-related symptom score (with a mean difference of -1·18; 95% CI: -3·54;1·17; p=0·32).

Interpretation

Based on self-reported data, CoQ10 treatment does not appear to significantly reduce the number or severity of PCC-related symptoms when compared to placebo.

Keywords: Infection, Molecular metabolism and endocrinology, Inflammation

POSTER SESSION 6

Improving immunotherapy outcome in solid tumor by combining with other established cancer treatments

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Introduction: There is a great focus on establishing combinational therapies in clinics, where radiotherapy or chemotherapy are administered prior to immunotherapy. This holds great importance for the clinical outcome of solid tumors, as majority of them are known to be less immunogenic. Our plan would be to investigate the combination of one such inhibitor (anti-CTLA-4; anti-cytotoxic T lymphocyte associated protein - 4) with treatments that have shown to have a bi-functional cell killing mechanisms. These include high dose proton radiation, and the vascular disrupting drug OXi4503, that not only have potential for tumor ablation, but also have shown to mediate tumor immunogenicity.

Materials & Methods: All experiments used C3H mammary carcinoma grown in the right rear foot of CDF1 mice. Treatments started when tumors were at specific sizes of 50, 100, 200, or 400 mm3. These included proton radiation (local tumor irradiation with 20 Gy on day 0), OXi4503 (50 mg/kg, injected i.p. on days 0, 3, 7, and 10), and anti-CTLA-4 (injected i.p. on days 1, 4, 8, and 11). The endpoint was tumor growth delay (time to grow to 1000 mm3).

Results: Our Tumor model is generally unresponsive to Anti-CTLA-4 as a single therapy agent, even though an effect could be observed in the smallest size tumors. An enhanced response was obtained only for smaller size tumors when it was combined with either proton radiation or OXi4503.

Conclusion: As primary tumor size at treatment increases, the benefit of combinational therapy becomes less apparent. Hence, the success of this combination is strongly dependent on the extend of prior damage caused by proton radiation/Oxi4503.

Keywords: Oncology, Animal models/disease models, Other

Automated quantification of the proliferation index in tumor tissue

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Background: The proliferation index is an important diagnostic and prognostic biomarker in many tumors. In this study we aim to develop a new method for automated quantification of the proliferation index using multiplex immunofluorescence (mIF) and digital image analysis (DIA) with artificial intelligence. We test the methods diagnostic performance in melanocytic lesions, breast carcinomas and neuroendocrine tumors (NET).

Methods: Tissue samples from 20 melanocytic lesions, 20 breast carcinomas and 13 NETs were retrieved from the archive at Department of Pathology. A tissue slide from each lesion was stained with mIF against Ki67 and a nuclear tumor marker, scanned digitally and then re-stained with Hematoxylin & Eosin (HE) and scanned. The two scans were aligned digitally, and DIA was performed using deep learning algorithms to identify all nuclei and quantify Ki67 positive tumor cells in different tumor regions. Ki67 indices of different tumor groups were compared.

Results: Mean Ki67 indexes were statically significantly different between breast Luminal A and Luminal B subtype (p: 0.0008) in breast cancers and between compound nevi and superficial spreading melanomas (p:0.0002) in melanocytic lesions. For NETs, no significant difference between mean Ki67 indexes of NET grade 1 and NET grade 2 was detected and the agreement between manual and automatically quantified Ki67 indices was poor.

Conclusion: Automated quantification of Ki67 indexes using artificial intelligence and mIF shows potential as a diagnostic aid in melanomas and breast cancers.

Keywords: Oncology, Medical technology and diagnostic techniques, Dermatology

Tissue-specific range uncertainty estimation in proton therapy

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Introduction

Proton therapy is sensitive to range uncertainties, which often are accounted for by range margins based on tissue-independent (TI) uncertainties (same uncertainty for all tissues). The aim of this study was to investigate the differences between range margins based on TI and tissue-specific (TS) range uncertainties.

Methods and materials

The range uncertainties were evaluated for lung, soft and bone tissues to quantify the TS range uncertainties. Proton plans were created for four cancer patients (1 brain, 1 lymphoma and 2 liver) to evaluate the range uncertainties in different tissue compositions. The proton plans were re-calculated after applying range uncertainties that were either TS or TI. The re-calculated proton plans were compared based on dose volume histogram (DVH) parameters. For each treatment site, the optimal TI range uncertainty was defined as the one resulting in the largest overlap between the TS and TI DVH values.

Results

The range uncertainties were found to be 8.0% of the proton range for lung, 1.0% for soft, and 2.3% for bone tissues. The optimal TI uncertainties were found to be 1.5% for the lymphoma cancer patient and 1.0% for the brain and liver cancer patients. When comparing the re-calculated proton plans, dose differences were mainly found in the vicinity of the target.

Conclusion

Different range uncertainties were found for lung, soft, and bone tissue, indicating that range margins based on TS range uncertainties may be more exact than the standard TI approach. However, a single TI range uncertainty might still be sufficient to capture the TS range uncertainties, with a value that will be dependent on the treatment site.

Keywords: Oncology, Medical technology and diagnostic techniques, Other

Energy calibrated images using Medipix3 for high resolution fresh frozen breast tumor imaging

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The main quality indicator of tumor surgery is the surgical resection margin, where tumor cells close to the surface of the specimen are an indication for poor local control. Currently, the surgical resection margin is determined post-operatively at the pathology department, days after the surgical procedure. This means that the patient needs re-operation in case of an involved margin. With the development of energy resolved photon counting detector (spectroscopic 2x2 Medipix3), there is an opportunity to acquire spectral microCT images with improved signal to noise, which provides better contrast between tumor and normal tissues enabling evaluation of the resection margin at µm level. To achieve this, pixel-wise energy calibration is performed by making use of x-ray fluoroscopy (XRF) imaging of multiple metal foils. After finding the relation between DAC setting and keV response per chip, we developed a correction method using the flat field images by fitting a second order polynomial. This fitting parameter is then used to correct the counts per pixel, resulting in a more homogeneous spectral image. To illustrate how the pixel-wise correction affects the image quality, we tested the method on a phantom made of different layers of ham and cheese and fresh frozen human breast tumor tissue, without the pixel-wise correction substantial ring-artifacts occur in the CT reconstruction. After correction, the CT reconstructed image has less noise with better contrast difference between the ham and cheese layers, and the effects of ring artefacts are limited substantially and thus, achieving precise keV CT images.

Keywords: Oncology, Medical technology and diagnostic techniques, Other

Incidence of colorectal cancer and advanced adenomas at surveillance colonoscopy in the Danish FIT-based screening program: A nationwide register-based cohort study

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Introduction:

Organised colorectal cancer screening has resulted in a great increase of surveillance colonoscopies due to adenoma findings in asymptomatic citizens. The evidence for these surveillance programs are mostly based on old colonoscopy data or screening that defers from the Danish program. Thus it is unclear what both patient and health care system gains from the current surveillance colonoscopy intervals.

In this study, we aim to evaluate the current Danish screening- and surveillance guidelines for citizens with screen-detected high risk(HR) or medium risk(MR) adenomas.

Does the detection rate of CRC and advanced precancerous lesions justify a 1- and 3-year surveillance interval for HR and MR adenomas?

Materials and methods:

In a retrospective register study, we follow MR and HR groups from initial colonoscopy between year 2014-2018 until surveillance colonoscopy (3.5 and 1.5 year) or interval CRC. Group stratification are based on data from both the national patient registry as well as the Danish pathology registry and will thus include all eligible participants.

Results:

Currently we have included approximately 9.500 participants in the HR and 12.000 participants in the MR group. The incidence of CRC and advanced adenomas at follow-up will be presented at the phd-day.

Conclusion:

If the risk of CRC or advanced adenomas are not equal in the two groups, one could argue that the intervals should be changed.

The results can help strengthening new surveillance guidelines so that participants will reduce their risk of CRC with as few colonoscopies as possible.

Keywords: Oncology, Epidemiology and biostatistics, Public health

Bayesian inference of spatio-temporal miRNA activity

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Throughout recent years, new methods within RNA sequencing have elucidated transcripts at the single cell level providing deeper insights into the heterogeneity of the human transcriptome. The increasing amount of publicly available single cell data sets and cell atlases represent a huge resource. However, most single cell RNA sequencing (scRNAseq) methods do not sequence small regulatory RNA molecules due to the use of poly-dT primers. Here, we attempt to develop a Bayesian framework to infer the spatio-temporal microRNA activity at the single cell level. The model is based on an expression-ranked sequence approach, where microRNA target-motif occurrence across ranked 3' untranslated regions (UTRs) are evaluated. Currently, we have applied a simple setup for individual microRNAs in a single cell, which we will expand to evaluate microRNA activity changes during cell differentiation and cancer progression. The model may provide further insight into the role of microRNAs in maintaining cell homeostasis.

Keywords: Oncology, Public health, Cell biology

Proteomic profiling identifies high-risk follicular lymphoma patients with subsequent histological transformation already at the time of diagnosis

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Histological transformation (HT) into an aggressive lymphoma remains the leading cause of follicular lymphoma (FL)-related mortality. Underlying mechanisms leading to HT remains unknown, and to date, no biomarkers have been able to mirror the risk of HT.

A mass spectrometry-based proteomics approach was performed to identify differentially expressed proteins in diagnostic tumor samples from 54 FL patients, of which 34 showed no sign of HT (non-transforming FL, nt-FL), while 20 patients subsequently experienced HT (subsequently transforming FL, st-FL). For the latter group, paired high-grade samples from the time of HT were also analyzed (transformed FL, tFL).

A total of 265 protein were identified as significantly differentially expressed between nt-FL and st-FL samples ($p<0.05$; fold changes 0.4-2.5). Based on this set of proteins, unsupervised clustering showed strong focusing of the respective patient groups, identifying a subset of high-risk patients. Pathway analyses revealed disturbances in RAC/RHO GTPase signaling, apoptosis, the cytoskeleton, and cell cycle. Within these pathways, specific proteins of interest attracted particular attention, encouraging further assessment of their clinical relevance. Between the paired st-FL samples and tFL samples, 813 proteins were identified as significantly differentially expressed, and as seen by completely distinct clustering and marked numbers of impaired pathways, this indicates that the tumors constitutes biologically distinct diseases.

This study provided an insight into a few of the many biological clues needed to fully elucidate HT of FL as well as future improvement of patient risk stratification.

Keywords: Oncology, Other, Laboratory science

The Impact of Type 2 Diabetes on Complications after Primary Breast Cancer Surgery: a Danish population-based cohort study

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Background Type 2 diabetes (T2D) is associated with comorbidities, increasing the risk of postoperative complications. We investigated the association of T2D and risk of complications after primary breast cancer (BC) surgery and evaluated the interaction contrast between T2D and comorbidities.

Methods We conducted a cohort study including all women diagnosed with early-stage operable BC from 1996-2018 registered in the Danish Breast Cancer Group clinical database. All patients underwent primary surgery—mastectomy or breast conserving surgery. From Danish registries, we defined prevalent T2D via diagnostic codes or ≥2 prescriptions for glucose-lowering drugs. We defined complications as hospital admissions for medical/surgical complications within 30 days of primary surgery. We calculated the 30-day cumulative incidence function (CIF) and used Cox regression to estimate hazard ratios (HR) and associated 95% confidence intervals (95%CI) of complications. We estimated the interaction contrast between T2D and comorbidities on the incidence rate of complications.

Results Among 84,491 women with BC, 4,669 (5.5%) had T2D at BC surgery. Overall, 800 (17.1%) and 8,621 (10.8%) BC patients with and without T2D developed complications yielding CIFs of 17% (95%CI= 16-18) and 11% (95%CI=10-11), respectively, and a HR=1.46 (95%CI=1.36-1.57). The most frequent were surgical and infection events. The incidence rate of complications explained by interaction in women with moderate and severe comorbidity was 21% and 41%, respectively.

Conclusion Women with BC and T2D have higher risk of postoperative complications after primary BC surgery compared with those without T2D.

Keywords: Oncology, Epidemiology and biostatistics, Other

Strategies for robust evaluation of proton therapy for high-risk prostate cancer patients in a randomized clinical trial

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Introduction: Inter-fractional anatomical changes in the pelvis may degrade treatment quality in radiotherapy of high-risk prostate cancer patients. Pre-treatment robust evaluation (PT-RE) of treatment plans takes into account isocenter shifts but not deformations or relative displacements. The aim of this study was to perform an offline during-treatment robust evaluation (DT-RE) using weekly control CT scans (cCTs), and compare this to the PT-RE.

Materials and methods: Treatment plans from the first three pilot patients in the randomized trial PROstate PROTON Trial 1 (NCT05350475) were used along with 7-8 cCTs per patient. The treatment plans were optimized following protocol guidelines with 78 Gy to the primary target (CTVp; prostate and involved seminal vesicles) and 56 Gy to the elective target (CTVe; pelvic lymph nodes) in 39 daily fractions. The treatment plans were recalculated on all the cCTs and subsequently, dose/volume measures corresponding to clinical constraints were checked to see if the DT-RE was within the predicted range from the PT-RE.

Results: Of the total 22 cCTs, 11 showed CTVp measures outside the range of the PT-RE. Similarly, this was the case for 10 of the cCTs when looking at the CTVe constraint. Further, the DT-RE constraint measures for the rectum, bladder and bowel were outside the range of the PT-RE in 0, 4 and 14 cCTs respectively.

Conclusion: All treatment plans were clinically assessed and accepted. The REs will be further investigated and the DT-RE will be used alongside manual clinical assessment of the online positioning cone beam CTs for evaluation of treatment robustness throughout the pilot phase of our randomized trial.

Keywords: Oncology, Urology, Other

Lipid nanoparticle-mediated delivery of CRISPR/Cas9 for precise depletion of subpopulations of tumor associated macrophages in ovarian cancer

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Ovarian cancer is a major contributor to cancer-related death in women, with many patients being diagnosed in late stages, with metastatic spread. High-grade serous ovarian cancer is the most common form, in which patients of have malignant ascites, omental and peritoneal metastasis, and prevalent recurrence of chemo-resistant disease. 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. Single-cell RNA sequencing has revealed remarkable heterogeneity of the TAM compartment, unveiling many subpopulations with heterogenous gene expression profiles. To discover which of these TAMs have protumoral functions, we have developed a method to specifically target them, by using surface proteins.

In order to specifically remove distinct TAM subpopulations, we have developed a lipid nanoparticle (LNP) based system to induce cell death. Using click-chemistry, we can attach any antibody to the surface of the LNPs, and the LNPs can encapsulate RNA of any kind, enabling delivery of siRNA, mRNA and the CRISPR/Cas9 system. In vitro and in vivo, we can deliver LNPs to cells expressing the surface target, with high specificity and sensitivity. By expanding this targeting, to dual targeting using 2 LNP formulations with separate antibody targets, we expect even higher specificity. Our results show that the antibody coated LNPs represent a powerful tool, which enables targeting any population found in the mouse.

Keywords: Oncology, Inflammation, Laboratory science

Association between tumor immune response and risk of recurrence in breast cancer patients treated with radiotherapy

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Background:

Radiotherapy (RT) reduces risk of loco-regional recurrence and improves overall survival (OS) in breast cancer (BC). High level of tumor infiltrating lymphocytes have been shown to be associated with an improved OS benefit after RT in BC patients. It is unclear, if the association is dependent on specific immune cells (IC). The aim of this PhD study is to investigate, if presence and/or composition of IC in treatment naïve tumor tissue is associated with risk of recurrence in BC patients treated with RT

Materials:

The study is planned as a case-control study (approximately 400 cases with recurrence: 1000 controls without recurrence) based on two Danish Breast Cancer Group cohorts of patients treated with various RT regimes. Tumor tissue from primary tumor and recurrences will be collected from all 1400 patients, and clinical outcome data will be obtained

Study 1:

Composition of specific IC in primary tumors of various subtypes will be characterized using multiplex immunohistochemistry and digital image analysis

Study 2:

In the 400 cases, differences in immune response and subtype in corresponding pairs of primary tumor and recurrences will be examined. In a subgroup of patients, gene-expression analysis of specific immunogenic pathways will be performed

Study 3:

Results from the histopathological analyses will be correlated with clinical outcome data for all patients to examine associations between the immune response in primary tumor and risk of recurrence

Perspectives:

If the immune response in treatment naïve tumor can predict clinical outcome in BC patients, it may lead to more individualized treatment and possible modification of treatment guidelines

Keywords: Oncology, Cell biology, Inflammation

POSTER SESSION 7

Temporal perspectives on inequitable medical care: a field study of the annual chronic care consultation in general practice

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Inequity and time have rarely been linked. Drawing on fieldwork in general practice, we explore how time may contribute to existing perspectives of social inequity in the medical encounter. We followed seven patients with multimorbidity and polypharmacy in and around their annual chronic care consultations. Data is derived from medical records, interviews, and observations. In the analysis, we found that the medical encounter was influenced by patients' alignment with the institutional and professional time, which is unfolded in three themes: timing, pacing, and sequencing. 1) Timing the consultation within patients' everyday lives to match the institutional rhythms was a prerequisite for receiving care. During consultations, patients needed to time their inputs to fit the health professionals' tacit agenda-setting which granted them the necessary opportunities to engage in the consultation. Yet, patients' social position influenced their flexibility in aligning with the institutional time and in engaging in the encounter. 2) In the consultation, the institutional rhythm caused some health professionals to increase the pace of the consultation. Opposing or coping with a high pace appeared to be easier for patients in higher social positions. 3) In preparing the consultation, patients and health professionals oftentimes needed to perform certain practices in a certain sequence. Yet, unclear and tacit organizational sequencing may be difficult to decode for patients with a low social position. In conclusion, patients' encounters with general practice had temporal references that linked to inequity in several ways; resulting from pre-existing inequities or causing new ones.

Keywords: Socio-economic conditions, Multimorbidity, Qualitative research

Testing Care and Morality: An ethnographic study of test practices during Covid-19 in Denmark

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Tests for COVID-19 have been a vital tool to counteract the spread of infection in Denmark. The public health authorities have revised the test strategy profoundly during the pandemic; from only providing testing to persons with symptoms and a doctor's referral; to providing free PCR and antigen testing to everyone, regardless of symptoms; and further, to introducing a national corona passport that regulated access to workplaces, educational institutions and public spaces. The public use of tests and the motivations to test in everyday life, however, are often quite differently situated than those of the public health authorities.

In order to explore everyday test practices in Denmark, we conducted an ethnographic fieldstudy and interviewed more than 40 people about Covid-19 test practices, between February 2021 and April 2022. The material was analysed using abductive, thematic analysis.

The study shows that while test practices shape social life, social life also shapes test practices. People are generally keen to follow guidelines from the health authorities about tests for Covid-19, and many adjust social practices on the basis of tests results. However, the decision to test is also shaped through social practices and moral dilemmas. Many people are not worried about being infected with the virus themselves, they are worried about infecting others, and the decision to test thus originates from an effort to show care and affection for others or conform to the new moral norms during the pandemic. These findings are important to understand and guide public test practices during pandemics now and in the future.

Keywords: Public health, Qualitative research, Other

Does a family-based health promoting intervention in the first year after birth impact the growth of infants exposed to gestational diabetes in pregnancy?

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Background:

Children exposed to gestational diabetes mellitus (GDM) in-utero are at high risk of developing obesity and dysmetabolic traits. Early life constitutes an opportunity for prevention, but the long-term effects of prenatal interventions in this high-risk group are discouraging. Breastfeeding and health behaviours in the family are associated with childhood growth, but the impact of family-based interventions after birth in this risk-group is yet to be explored. This study aims to investigate the effects of the Face-it intervention delivered to women with prior GDM and their families, focusing on health promotion relevant for preventing type 2 diabetes (breastfeeding, healthy eating, physical activity and family dynamics) on their infants' growth at age 12 months.

Methods:

This is a preliminary investigation of the baseline characteristics of children included in the post-hoc effect evaluation of the Face-it intervention, which is currently being tested in an RCT design with expected completion June 2023. The study population of this specific study is children exposed to GDM in-utero attending the 3 months postpartum baseline and 12 months follow-up visits in the Face-it RCT. We expect a final sample size of n=225. The primary outcome is the difference between the intervention and control group in BMI and skinfold thickness from age 3 to 12 months.

Perspectives:

This project will investigate if a postpartum intervention at the family level impacts growth in the first year of life among infants exposed to GDM in-utero. In a public health perspective, it can potentially identify new approaches to prevent early obesity in this target group.

Keywords: Public health, Epidemiology and biostatistics, Paediatrics

Acceptability of an intervention to increase participation in cervical and colorectal cancer screening among women attending breast cancer screening

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Background

Breast cancer (BC) screening has a higher uptake (83%) as compared to cervical cancer (61%) and colorectal cancer screening (61%). The aim of the present study was to offer women attending BC screening self-sampling kits for cervical and colorectal cancer screening if they were overdue. We present the first data related to acceptability of the intervention.

Methods

A cluster randomised trial was performed in five BC screening units in Central Denmark Region. On intervention days, one screening unit was selected for the intervention while the remaining four were control units.

A survey including five questions about satisfaction with BC screening was mailed to all women after attending BC screening on intervention days. The intervention group received additional questions related to their experience with the intervention.

Results

67% (3,719/5,571) in the intervention group and 63% (13,507/21,528) in the control group completed the survey.

We found no differences between intervention and control group regarding feeling welcome (RD=0.08, 95% CI: -1.7;1.9), professionalism (RD=0.94, 95% CI: -0.01;1.9), trust in the examination (RD=0.55, 95% CI: -0.50;1.60), if they intended to participate next time (RD=0.09, 95% CI: -0.12;0.30), or overall satisfaction (RD=1.14, 95% CI: 0.01;2.19).

In the intervention group, 88.8% (95% CI: 87.7;89.8) found the information about the intervention sufficient, 60.6% (95% CI: 58.9;62.2) found the offer very meaningful and 84.5% (95% CI: 83.3;85.7) would accept a similar offer another time.

Conclusion

The intervention was well received and did not affect the high satisfaction with BC screening negatively.

Keywords: Public health, Oncology, Other

Health literacy and related behaviour among pregnant women with obesity: a qualitative interpretive description study

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Background: Obesity in pregnant women is increasing worldwide, affecting the health of both mother and baby. Obesity may be associated with inadequate health literacy. This study explores women's health literacy by examining their knowledge, motivation, and skills to access, understand and evaluate health information and the related behaviour among a sample of pregnant women with a prepregnant body mass index (BMI) > 25 kg/m2.

Methods: An inductive, qualitative study using interpretive description methodology. Data was collected in ten semi-structured interviews with pregnant women with a prepregnancy BMI > 25 kg/m2 attending antenatal care at the midwifery clinic at Aarhus University Hospital in the Central Denmark Region.

Results: The women understand general health information provided by health professionals but translating this knowledge into specific healthy behaviours presents a challenge. Although difficulties navigating booking systems and available digital services contribute to this problem, apps can help facilitate navigation. However, successful navigation may depend on adequate e-health literacy. Conflicting information from health professionals, social media and families also present a challenge for pregnant women, requiring a broad skillset for critical evaluation and resolution.

Conclusions: Adequate health literacy is necessary for pregnant women receiving antenatal care to (i) translate general health information into personalised healthy behaviour, (ii) access and navigate complex and digitalised systems, and (iii) critically evaluate conflicting information. Person-centred differentiation in the organisation of antenatal care may benefit vulnerable pregnant women.

Keywords: Public health, Qualitative research, Other

Patient-Reported Diagnostic Pathways in Children with a CNS Tumor in Denmark

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Background and aims

Tumors of the central nervous system (CNS) are the second most common tumors among children with cancer. Diverse initial presenting symptoms complicate the diagnostic process, which might result in a diagnostic delay leading to higher mortality and a long-term morbidity.

Our aim is to map out the diagnostic intervals in Danish children and adolescents with CNS tumors to identify in which interval, the lag is present and where to aim interventions, thus accelerating diagnostics and enhance timely diagnosis.

Methods

We identified all Danish patients aged 0-17 years, who had survived a CNS tumor diagnosed from 2015–2019 through the Danish Cancer Registry and the Danish National Patient Register. The patients who had turned 18 at time of the study and custody-holding parent(s) for patients younger than 18 at time of the study, completed a web-based questionnaire, consisting of questions on time (date) of first registered symptoms, first contact to a physician and the date of diagnosis with a CNS tumor. Descriptive analysis will be performed based on the total study population analysing time intervals to measure delay in days (median; interquartile range (IQR)) categorized into a Total Interval (TI, time from symptom onset to diagnosis), a Patient Interval (PI, time from symptom onset to contact to a physician) and a Diagnostic Interval (DI, time from first contact to a physician to diagnosis).

Results and Conclusion

We have identified 346 patients and expect a participation rate of 50%.

Results are pending and will be presented at the PhD Day.

Keywords: Paediatrics, Oncology, Other

Associations between prenatal findings and pre- and postnatal outcomes in Danish children with Congenital Pulmonary Malformation

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BACKGROUND Congenital pulmonary malformations (CPMs) are a group of rare developmental abnormalities in the lungs. The diagnosis is now, because of the widespread use and increasing sensitivity of prenatal ultrasonography, often made prenatally. The prognosis of prenatally diagnosed CPM is often favorable with regression of the lesion before birth. However, in rare cases severe prenatal complications can occur, such as mediastinal shift, pulmonary hypoplasia and impairment of venous return leading to hydrops, cardiac failure and fetal death. Postnatally the prognosis is often favorable, but some children with CPM will have respiratory symptoms and need surgical removal of the lung lesion. Surgery is the standard care for symptomatic children with CPM, but the postnatal management of asymptomatic children with CPM remains controversial.

AIMS We aim to investigate the incidence of CPM in Denmark and evaluate associations between prenatal findings and pre- and postnatal outcomes.

METHODS National register-based prospective cohort study including pre- and postnatally diagnosed CPM from 2016 to 2022.

PERSPECTIVES The study will provide the first national data on patients with CPM including the first valid data on the incidence of CPM in Denmark. Furthermore, the study will help identify potential prenatal predictors of respiratory impact among newborns with CPM. This will allow for improved information and prenatal counseling to parents. The results of the study can contribute to the establishment of a national database for Danish children with CPM.

Keywords: Paediatrics, Respiratory system, Other

10 years follow-up after community-based lifestyle interventions for children with obesity - a retrospective cohort study

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Introduction: Childhood obesity is a major health concern and limited knowledge exist regarding long-term effects of lifestyle interventions. The aim of this retrospective cohort study was to investigate the effects of two community-based lifestyle interventions with a follow-up up to 10 years.

Methods: This study included 445 children from the Aarhus Protocol, 258 children from the Randers Protocol and 2237 children from a contemporary reference group. Data on anthropometrics were obtained by school nurses and all children were classified as obese. Data on socioeconomic parameters were obtained by Danish registers. Follow-up was described by mixed effect model.

Results: A total of 3040 children and 12980 observations were included in this study. A annual reduction in BMI z-score (mean (95% CI)) of -0.05 (-0.08;-0.02), $p<0.001$ was observed for the children in the Randers Protocol, while no overall change 0.01 (-0.01;0.04) for the Aarhus Protocol compared to the reference group. Interestingly, both interventions obtained a similar effect within the initial 6 months of the interventions.

For children in the interventions, low family income and being an immigrant (first or second generation) were both associated with attenuated weight reduction.

An annual increase in BMI z-score on 0.04 (0.00;0.08) was observed for children enrolled < 1 years comparing to children enrolled ≥ 1 year.

Conclusion: Similar short-term effect was observed for both interventions, but only the Randers Protocol obtained a sustainable weight reduction beyond the first year. Longer enrolment in the interventions (≥ 1 year) was associated with weight reduction.

Keywords: Paediatrics, Epidemiology and biostatistics, Public health

Fibroblasts in juvenile idiopathic arthritis - ready, set, explore!

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Local joint fibroblasts have recently been implicated in several disease traits in adult rheumatoid arthritis. In comparison, very few studies have investigated the potential role of local joint fibroblasts in juvenile idiopathic arthritis. We seek to change this by initiating a 10-year study into fibroblasts and inflammation in the pediatric stroma. A study aiming to achieve a similar depth and detail of molecular and cellular knowledge of the role of fibroblasts in juvenile idiopathic arthritis.

The scope of the project is based on our recently finished scoping review of the entire EMBASE, MEDLINE and Web of Science databases. The project was designed as a translational study in cooperation with the Department of Pediatrics at Aarhus University Hospital.

Our scoping review identified 18 original manuscripts investigating fibroblasts from patients with juvenile idiopathic arthritis. Included studies presented several fibroblast phenotypes and functions comparable to evidence from adult patients with rheumatoid arthritis. The review identified significant gaps in our knowledge of fibroblasts in juvenile idiopathic arthritis. Gaps that are easily amended by present day technology and through inspiration of studies conducted on pathological fibroblasts in different diseases and adults.

We plan to address these gaps by diving into 3 biological themes: Physical interactions between fibroblasts and immune cells, Inflammatory signalling, and Connective tissue homeostasis. The fourth theme is planned to connect the biological knowledge from the laboratory to disease- and treatment prognosis in the clinical setting.

Keywords: Paediatrics, Inflammation, Rheumatology

Psychiatric morbidity among children with juvenile idiopathic arthritis – a matched cohort study

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Background

Juvenile idiopathic arthritis (JIA) is a chronic condition causing joint destruction and pain. JIA has been shown to impact mental health and could be associated with an increased risk of psychiatric conditions.

We aim to explore differences in psychiatric morbidity between children with JIA and their peers in the Danish population. We further want to study if parental socioeconomic status (SES) influences the association between JIA and the risk of psychiatric morbidity.

Methods

We used a matched cohort design to estimate the association between JIA and psychiatric disease. Children with JIA born between 1995 and 2016 were identified in the National Hospital Register. Based on the Medical Birth register we randomly selected 100 children per index child matched on sex and age. Index date was date of fifth JIA diagnosis code or date of matching for reference children. End of follow-up was date of psychiatric diagnosis, death, emigration, or the 31st of December 2018 whatever came first. The data were analysed using a Cox proportional hazards model.

Results

We identified 2,086 children with JIA with a mean age at diagnosis of 8.1 years. Children with JIA had 17% higher instantaneous risk of a psychiatric diagnosis, adjusted HR=1.17 (95% CI 1.02;1.34) when compared with the reference group. Relevant associations were only found for depression and adjustment disorders. Stratifying our analysis for SES, showed no modifying effect of SES.

Conclusion

Children with JIA had higher risk of psychiatric diagnoses compared to their peers, especially for diagnosis of depression and adjustment disorders. The association between JIA and psychiatric disease did not depend on SES.

Keywords: Paediatrics, Epidemiology and biostatistics, Rheumatology

Lack of thoracentesis competencies and training in Danish Emergency Departments: A Danish Nationwide Study

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Background

Dyspnea caused by pleural effusion is a common reason for admission to the Emergency Department (ED). In such cases, thoracentesis performed in the ED may allow for swift symptom relief, diagnostics, and early patient discharge. However, the competence level of thoracentesis and training in Danish EDs are currently unclear. This study aimed to describe the current competences and training in thoracentesis in Danish ED.

Method

We performed a nationwide cross-sectional study in Denmark. A questionnaire was distributed to all EDs in March 2022 including questions on competencies and thoracentesis training methods. Descriptive statistics were used.

Results

In total, 21 EDs replied (response rate 100%) between March and May 2022. Overall, 50% of consultant and 77% of physicians in emergency medicine specialist training were unable to perform thoracentesis independently. Only 2 of 21 EDs (10%) had a formalized training program. In these 2 EDs, there were no requirements of maintaining these competences. Informal training was reported by 14 out 21 (66%) EDs and consisted of ad-hoc bedside procedural demonstration and/or guidance. Among the 19 EDs without formalized training, 9 (47%) had no intention of establishing a formalized training program.

Conclusion

We found a major lack of thoracentesis competencies in Danish EDs among both consultant and physicians in emergency medicine specialist training. Moreover, the vast majority of EDs had no formalized thoracentesis training program. We recommend a that each ED establish an evidence based formalized thoracentesis training program, that take a position on continuous education and required skill competency

Keywords: Health education and simulation-based training, Respiratory system, Other

Pulmonary function twelve months after hospitalization with SARS-CoV-2

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Title: Pulmonary function twelve months after hospitalization with SARS-CoV-2

Introduction: Persistent dyspnea after infection with SARS-CoV-2 is common. So far, contributing factors underlying pathogenesis and duration of persistent pulmonary symptoms remain to be clarified better. In this study, we aimed to investigate pulmonary function 12 months after hospitalization with SARS-CoV-2.

Methods: In an observational cohort study, 222 patients hospitalized with SARS-CoV-2 were recruited. Outcome measures were collected 3 and 12 months after hospitalization. At follow-up, pulmonary function test included forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and diffusion capacity for carbon monoxide (DLCO).

Based on disease severity, patients were categorized according to the WHO clinical progression scale: no oxygen therapy (NOT), low-flow oxygen therapy (LFO), high-flow oxygen therapy (HFO) or mechanical ventilation (IMV).

Results: Of 222 patients included, 179 (81%) completed 12-months follow-up. Here, 23 patients (13%) had FEV1 < 80% predicted and 26 patients (15%) had FEV1/FVC < 70%.

Moderate diffusion impairment (DLCO <80% predicted) was found in 61 (39%) patients and severe diffusion impairment (DLCO <60% predicted) in 17 (11%) patients. The lowest mean DLCO of 70.8% (95% 59.4, 82.2) was found in patients treated with IMV.

From 3-month follow-up to 12-month follow-up an overall increase in DLCO of 1.7% (95% CI 0.3, 3.1, p=0.02) was found. The largest improvement in DLCO of 6.2% (95% CI 1.5, 10.9) was found in patients treated with IMV.

Conclusion: Diffusion impairment is common 12 months after hospitalization with SARS-CoV-2.

Keywords: Respiratory system, Infection, Public health

POSTER SESSION 8

Automated, machine-learning derived software performs as well as a human investigator for determining the cardiac rest period in Cardiac Magnetic Resonance Angiography

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Cardiac Magnetic Resonance Angiography (CMRA) is a promising technique to diagnose coronary artery disease non-invasively and without ionising radiation. However, implementation is hindered by technical limitations that prevent accurate and consistent cardiac rest period identification, during which image acquisition occurs. The rest period is currently determined by either investigator visual analysis, which is subject to variability in interpretation, or a mathematical formula, which is limited to assess only diastolic imaging. A new algorithm developed using machine-learning can automatically identify the rest period. This required evaluation against the other methods.

20 individuals were scanned using all 3 methods. A 0.9 mm3 CMRA sequence was used. The scan order was randomised to avoid bias. Semi-quantitative analysis of vessel sharpness and vessel length were planned. Data was compared using a One-Way ANOVA with multiple comparisons.

There was no difference in pulse nor scan duration between each method. Average trigger delay was the same for the investigator-led and machine-learning methods, whilst the formula had a longer trigger delay (669 ± 131 vs 676 ± 150 vs 719 ± 82 msec, p = 0.047). Formal analysis of image quality was ongoing at the time of abstract submission. It is projected that the machine learning program will perform equal to the visual investigator approach, the most commonly used in clinical practice, as there is no difference in trigger delay or acquisition time. As such, this technique can likely be integrated into the CMRA workflow, improving consistency and accuracy of CMRA.

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Other

Non-invasive detection of coronary ischemia; Use myocardial perfusion imaging (PET) or estimated blood flow by computed tomography (CT-QFR)?

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Purpose

To assess the diagnostic performance of computed tomography-derived quantitative flow ratio (CT-QFR) compared to Rubidium-82 positron emission tomography (PET) in patients with suspected obstructive coronary artery disease (CAD) at coronary computed tomography (CTA) using invasive coronary angiography (ICA) with fractional flow reserve (FFR) as reference.

Background

In patients with suspected obstructive CAD on CTA, guidelines recommend non-invasive ischemia-verification. The ability of non-invasive CT-QFR and PET to detect ischemia by FFR in such patients is unknown.

Method

Patients referred with angina underwent routine CTA. Patients with ≥50% diameter stenosis on CTA were referred for PET and subsequent ICA. A CT-QFR ≤0.80 was abnormal. A core lab evaluated PET as abnormal/normal according to summed stress score, myocardial blood flows and ischemic dilation. Obstructive CAD was defined as ICA with FFR ≤0.80 or ≥90% diameter stenosis.

Results

In total 445/1732 patients had suspected obstructive CAD on CTA of whom 400/445 had PET and ICA. CT-QFR was analysed in 383/400 patients classifying 174/383 as having disease. By PET 130/383 had disease. Obstructive CAD by ICA was identified in 162/383 patients.

Area under the receiver-operating characteristic curves were similar for CT-QFR and PET; 0.84 (95%CI 0.80-0.89) vs. 0.81 (0.77-0.85), p=0.19). Sensitivity for CT-QFR was higher 78% (95%CI 71-84) than PET; 63% (55-70), p<0.01, while specificities were 78% (72-84) and 87% (82-91), p=0.01, respectively.

Conclusion

In patients with suspected obstructive CAD by CTA, CT-QFR demonstrated higher sensitivity while PET showed higher specificity, discriminatory ability was similar

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Other

Prognostic implications of residual left ventricular hypertrophy and systolic dysfunction in aortic stenosis following transcatheter aortic valve replacement.

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The impact of left ventricle (LV) hypertrophy (LVH) regression on the extent of residual cardiac dysfunction and prognostic implications after the initial remodeling process after transcatheter aortic valve replacement (TAVR) has not been investigated. We aimed to assess whether greater LV mass regression from pre-TAVR to 12-months after TAVR was associated with increased systolic function; and assess the prognostic value of residual LVH and systolic function 12-months after TAVR.

A total of 439 symptomatic patients were included and examined by echocardiography. LVH regression was assessed as percentage change in LV mass index (LVMi) from baseline to 12-months after TAVR. Primary outcome was all-cause mortality.

At 12-months after TAVR, multivariate analysis showed independent prognostic value of LVEF < 50% or GLS < 15% (HR 1.59, p = 0.049) for future all cause death.

LVH regression in AS after TAVR is associated with significant improvements of LV systolic function in contrast to patients without LV regression. Residual LVH and subsequent LV systolic dysfunction is substantial 12 months after TAVR and are associated with reduced survival. The combination of abnormal LVEF or GLS independently predicted all-cause mortality beyond 12 months after TAVR.

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Other

Cardiac CT Following Watchman FLX Implantation: Device Related Thrombus or Device Healing?

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Aims: Cardiac computed tomography (CT) is increasingly used for follow-up after left atrial appendage closure (LAAC). Hypoattenuated thickening (HAT) is a common finding and might represent either benign device healing or device-related thrombosis (DRT). The appearance and characteristics of HAT associated with the Watchman FLX have not been previously described. Therefore, we sought to investigate cardiac CT findings during follow-up after Watchman FLX implantation with a focus on HAT and DRT.

Methods and results: Retrospective single-center, observational study including all patients with successful Watchman FLX implantation and follow-up cardiac CT between March 2019 and September 2021 (n=244). Blinded analysis of CT images was performed describing the localization, extent, and morphology of HAT and correlated to imaging and histology findings in a canine model. Relevant clinical and preclinical ethical approvals were obtained.

Overall, HAT was present in 156 cases (64%) and could be classified as either subfabric hypoattenuation (n=59), flat sessile HAT (n=78), protruding sessile HAT (n=16) or pedunculated HAT (n=3). All cases of pedunculated HAT and five cases of protruding sessile HAT were considered as high-grade HAT (n=7). Subfabric hypoattenuation and flat sessile HAT correlated with device healing and endothelialization in histological analysis of explanted devices.

Conclusion: Subfabric hypoattenuation and flat sessile HAT are frequent CT findings for Watchman FLX, likely representing benign device healing and endothelialization. Pedunculated HAT and protruding HAT are infrequent CT findings that might represent DRT.

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Animal models/disease models

3-hydroxybutyrate improves cardiac and mitochondrial function during heart transplantation.

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Introduction: Donation after circulatory death (DCD) is increasingly used during cardiac transplantation. Subsequent normothermic regional perfusion (NRP) allows assessment of cardiac function and therapeutical interventions prior to organ preservation. Sodium-3-hydroxybutyrate (3-OHB) increases cardiac output in heart failure patients and diminishes ischemia reperfusion injury, presumably by improving mitochondrial energy metabolism. Methods: Donor pigs 80 kg underwent cardiac arrest followed by NRP. The reanimated hearts were weaned from bypass, put on static cold storage and transplanted to recipient pigs. During and after NRP and in the whole period following transplantation pigs were randomized to receive infusion with 3-OHB or Ringer Acetate. We measured hemodynamic function using pressure-volume catheters and mitochondrial function using high resolution respirometry. Results: Plasma levels of 3-OHB increased after infusion from 0.05±0.06 to 3.95±1.13mM. 3-OHB increased cardiac output compared to controls (11.2±0.4 vs. 6.0±2.2L*min-1, P<0.0001) driven by increased stroke volume (89.4±13 vs. 53.3±19mL, P=0.006) reduced arterial elastance (1.4±0.2 vs. 2.2±0.7mmHg*mL-1, P=0.02) and increased dP/dt max (1434±586 vs. 3641±1868mmHg*s-1, P=0.02). Following transplantation, 3-OHB caused mitochondrial respiratory capacity to improve compared to controls (121±25 vs. 62±25±molO2*s-1mg-1, P=0.009). Conclusions: 3-OHB had beneficial cardiac hemodynamic effects and restored mitochondrial respiratory capacity following cardiac transplantation. 3-OHB administration during and after NRP has a potential for optimizing cardiac function in DCD heart transplantation.

Keywords: Cardiovascular system, Animal models/disease models, Other

Molecular and physiological mechanisms behind anion-exchanger AE3-mediated regulation of the QT interval

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Short QT syndrome (SQTS) is a rare, genetically determined, severe cardiac disease with a high risk of syncope, ventricular fibrillation, and sudden cardiac death. We discovered that a loss-of-function variant in the SLC4A3 gene, which encodes the cardiac chloride-bicarbonate exchanger AE3, is associated with SQTS in patients. Previously, only six other genes, all encoding cation channels, have been known to be implicated in SQTS. Thus, the discovery of a SQTS-associated AE3 variant identifies a completely new disease mechanism for the development of SQTS.

In this study, we aim to create an optimized zebrafish model to facilitate in-depth functional characterizations of novel AE3 variants and investigate the molecular mechanism by which altered SLC4A3 function affects QT interval duration. Using CRISPR/Cas technology, we will generate novel knockout zebrafish lines and knockin zebrafish lines carrying selected AE3 variants. These zebrafish models will be used to explore the molecular and physiological mechanisms involved in AE3-mediated regulation of the QT interval. For this purpose, we will perform extensive molecular and physiological measurements on zebrafish hearts both in vivo and ex vivo, including ECG recordings and action potential, intracellular pH and calcium measurements in cardiomyocytes.

If successful, this project will provide valuable insights into the mechanisms behind AE3 involvement in the development of inherited heart disease and bring knowledge on the molecular and physiological role of AE3 in the regulation of QT interval and thereby potentially facilitate the development of brand-new treatment options for heart patients suffering from SQTS.

Keywords: Cardiovascular system, Animal models/disease models, Genetic engineering

Cross-species comparison of the smooth muscle cell lineage in atherosclerotic plaques

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Background: Recent studies in mice and humans have revealed that smooth muscle cells (SMCs) modulate from contractile into poorly characterized fibroblast-like phenotypes in atherosclerotic plaques. In the present study, we analyzed whether the subtypes of these SMC-derived cells differ between human atherosclerosis and experimental atherosclerosis in mice and pigs.

Methods: Single-cell RNA sequencing (scRNA-seq) was performed on aortic plaques from PCSK9-expressing mice that were fed a high-fat, high-cholesterol diet (HFD) for 20 weeks, and on 3 aortic plaques from PCSK9-D374Y transgenic minipigs fed HFD for 12 months. ScRNA-seq data of human carotid plaques was retrieved from a public data repository. Datasets were integrated and clustered using the Seurat package in R. Transcription factor (TF) activity was analyzed by the SCENIC workflow in R.

Results: We revealed that mouse, pig, and human SMCs shared subtypes with contractile, fibroblast-like, and pericyte properties. However, we found a mouse-specific SMC subtype with chondrogenic properties, particularly high Col2a1 expression. Using SCENIC we defined transcription factor-controlled regulons that include and can upregulate Col2a1 expression in mice: SOX9, REL, STAT3. Moreover, these regulons were not active in pig and human SMCs. Instead, their SMCs had higher expression of interferon response genes, which was supported by the finding of regulons controlled by STAT1 and IRFs.

Conclusions: SMC-derived cell subtypes are mostly concordant between pig and human atherosclerosis. Mouse plaque contains a population of Col2a1-expressing chondrocyte-like cells that are not present in the other species.

Keywords: Cardiovascular system, Animal models/disease models, Other

Myocardial Perfusion Imaging by 15O-H2O Positron Emission Tomography Predicts Clinical Revascularization Procedures in Symptomatic patients with previous CABG

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Aims

We wanted to assess if 15O-H2O myocardial perfusion imaging (MPI) in a clinical setting can predict referral to coronary artery catheterization (CAG), execution of percutaneous coronary intervention (PCI) and post-PCI angina relief for patients with angina and previous coronary artery bypass grafting (CABG).

Methods and results

We analyzed 172 symptomatic CABG patients referred for 15O-H2O positron emission tomography (PET) MPI at Aarhus University Hospital Department of Nuclear Medicine & PET. In total, 145 (87%) enrolled patients had an abnormal MPI. Of these, 86/145 (59%) underwent CAG within 3 months, however no PET parameters predicted referral to CAG. During the CAG, 25/89 (29%) patients were revascularized by PCI. Relative flow reserve (RFR) (0.49 vs. 0.54 p=0.03), vessel specific MBF (1.53 ml/g/min vs. 1.88 ml/g/min p<0.01) and vessel specific myocardial flow reserve (MFR) (1.73 v 2.13 p<0.01) were significantly lower in patients revascularized by PCI. ROC-analysis of the vessel specific parameters yielded optimal cut-offs of 1.36 ml/g/min (MBF) and 1.28 (MFR) to predict PCI. Angina relief was experienced by 18/25 (72%) of the patients who underwent PCI. MBF was an excellent predictor of angina relief both on a global and vessel specific level (AUC=0.87, p<0.01) with optimal cut-off levels of 1.99 ml/g/min (global) and 1.85 ml/g/min (vessel specific), respectively.

Conclusion

For CABG patients with angina, RFR, vessel specific MBF and vessel specific MFR measured by 15O-H2O PET MPI predict whether a subsequent CAG will result in a PCI procedure. In

addition, global and vessel specific MBF predicts whether CABG patients will experience post-PCI angina relief.

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Other

Right ventricular diastolic adaptation to pressure overload in different rat strains

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Background: Different rat strains are utilized in various animal models of pulmonary hypertension and right ventricular (RV) failure. However, until now no systematic assessment has been performed to test differences in RV response to pressure overload between rat strains. We compared RV adaptation to pulmonary trunk banding (PTB) in Wistar (W), Sprague Dawley (SD), and Fischer344 (F) rats by hemodynamic profiling focusing on diastolic function.

Methods: Age-matched male rat weanlings were randomized to sham operation (W-sham, n=6; SD-sham, n=4; F-sham, n=4) or PTB (W-PTB, n=9; SD-PTB, n=8; F-PTB, n=8). After five weeks RV function was evaluated by echocardiography, cardiac MRI, and invasive pressure-volume measurements.

Results: At evaluation, F-rats weighed 25% less than W- and SD-rats. PTB increased RV systolic pressures four-fold, and RV failure was evident by a decrease in cardiac index in all three PTB groups compared with sham. There was a 2.4-fold increase in RV end-systolic volume index in W-PTB and SD-PTB compared with sham, while F-PTB rats were less affected with only a 2.0-fold increase in RV end-systolic volume index compared with F-sham only reaching half the value of W-PTB. Diastolic and right atrial impairment were evident by increased end-diastolic pressure, end-diastolic elastance, and E/e' in the PTB rats compared with sham.

Conclusions: PTB caused RV failure in all rats subjected to the procedure including signs of diastolic dysfunction. F-PTB rats were less affected on volume parameters but equally effected on pressure parameters. All three rat strains are suitable for PTB and studies of RV failure.

Keywords: Cardiovascular system, Animal models/disease models, Laboratory science

Mitochondrial Function after Normothermic Regional Perfusion or Direct Procurement followed by Hypothermic Machine Perfusion in Heart Transplantation after Circulatory Death

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Aim

Heart transplantation (HTx) in donation after cardiac death (DCD) is based on cessation of circulatory and respiratory functions. Hence, warm ischemic injury is inevitable with DCD. Therefore, methods to recondition the heart and mitigate further ischemic damage is warranted.

In this study, we evaluated the effect of normothermic regional perfusion (NRP) and direct procurement (DP) on mitochondrial function.

Methods

In a porcine model, a DCD setting was simulated, followed by either NRP or DP. After oxygenated hypothermic machine perfusion (HMP; XVIVO Heart Box), HTx was performed. Mitochondrial function was evaluated with high-resolution respirometry (Oxygraph-2K; Oroboros Instruments) from myocardial biopsies taken at baseline, after HMP, and after reperfusion.

Results

Complex I-coupled respiration declined 39% (NRP) and 27% (DP) after HMP. After reperfusion, O2-flux was stable with NRP (43%) whereas a decline was seen with DP (58%) (NRP: p=0.18 DP: p=0.0003).

Maximally coupled respiration, complex I and II, followed the same trend: a 31% (NRP) and 28% (DP) flux-reduction was observed after HMP. After reperfusion, the decline reached 38% in the NRP- and 56% in the DP-group (NRP: p=0.084 DP: p=0.0008).

Looking at octanoylcarnitine (OC) oxidation, a 1% increase from baseline to reperfusion was seen in the NRP-group, whereas a 53% decline was observed in the DP-group (NRP: p=0.97 DP: p=0.0026).

Conclusion

Coupled respiration declined through the course of DCD HTx. NRP seemed to abrogate deterioration in respiration caused by reperfusion injury and preserved OC oxidation capacity. DP showed a significant decline in both coupled respiration and OC oxidation after reperfusion.

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Laboratory science

Guiding Catheter Extubation During Physiological Assessment of Coronary Stenosis: Effect on Pressure, Flow and Clinical Decision Making

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Background: Fractional flow reserve (FFR) is defined as the maximum achievable blood flow that can still be maintained to myocardium despite a coronary artery stenosis and is the golden standard in lesion significance assessment.

An observational study from 2016 found that FFR was significantly lower after extubation of the guiding catheter from the coronary ostium which changed the revascularization indication in 16% of all lesions. We hypothesized FFR to be lower and Coronary Flow Reserve (CFR) to be higher after guiding catheter extubation from the coronary ostium, potentially changing the indication for revascularization in borderline stenosis.

Methods: We included patients with stable angina referred to invasive coronary angiography based on suspected coronary artery disease following a cardiac computed tomography angiography. Physiological assessment was performed in all vessels with 30-90% diameter stenosis by visual estimate. FFR was measured during guiding-catheter intubation (FFRINT) and extubated (FFREXT during intravenous adenosine infusion using the thermodilution method.

Results: Preliminary results are as follows. N=15 patients and n=16 vessels were evaluated with physiological measurements. The median FFREXT was significantly lower compared to FFRINT (FFRINT-FFREXT: 0.02, IQR [0.01-0.04]. Consequently, in n=3 (20%) patients, the FFR value went from >0.80 to <0.80 when the guiding catheter was extubated.

Conclusion: FFR was lower with the guide catheter extubated versus intubated. This may have implications for patients with a borderline significant stenosis with FFR (0.75-0.85).

Keywords: Cardiovascular system, Other, Other

POSTER SESSION 9

Prescription use of Proton Pump Inhibitors and Colorectal Cancer recurrence and Mortality: a Danish Population-based Cohort Study

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Background

Proton pump inhibitors (PPIs) are widely prescribed drugs but may impede the effectiveness of cytotoxic drugs and disrupt the gut microbiome, thereby worsening the prognosis for colorectal cancer (CRC) survivors.

Methods

We investigated the associations of PPI prescription use (pre- and post-diagnostic) with CRC recurrence, all-cause, and CRC-specific mortality in a cohort of individuals diagnosed with stage I-III CRC between 2001 and 2011 using data from the Danish nationwide population-based and medical registries. We followed patients to date of recurrence, death, emigration, or 31st December 2012. We used multivariable Cox regression to compute hazards ratios (HR) and associated 95% confidence intervals (95%CIs).

Results

Among 21,152 CRC patients, 10,675 (50.5%) were PPI users. Overall, 53% of the study population were men, 3,024 (28.3%) PPI users developed recurrence and 4,298 (40.3%) died during follow up. The recurrence risk was not elevated when comparing pre- and post-diagnostic PPI user to PPI non-user (aHR=1.03 [95% CI: 0.95-1.12] and 1.06 [95%: 0.99-1.14], respectively). Pre-diagnostic PPI use were not associated with higher all-cause or CRC-specific mortality (aHR=1.09 [95%CI: 1.02–1.16] and 1.05 [95%CI: 0.95-1.15]) but an association was found for post-diagnostic PPI use (aHR=1.38 [95%CI: 1.31–1.43] and 1.38 [95%CI: 1.28–1.49]).

Conclusion

Pre-diagnostic PPI use was not associated with higher risk of recurrence, all-cause and cancer-specific mortality after CRC diagnosis. Post-diagnostic PPI use was associated with higher all-cause and cancer-specific mortality but not recurrence.

Keywords: Epidemiology and biostatistics, Oncology, Pharmacology

Improved survival after ST-segment elevation myocardial infarction during 15 years of primary percutaneous coronary intervention as a national strategy

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Introduction: In Denmark, primary percutaneous coronary intervention (pPCI) has served as the national reperfusion strategy in ST-segment elevation myocardial infarction (STEMI) since 2003. We investigated the temporal trends in one-year mortality and changes in presentation, PCI procedure, and post-discharge medication.

Methods: We included all first-time STEMI patients treated with pPCI in Western Denmark from 2003 to 2017. All patients were divided into four time-intervals based on the year of pPCI and followed for one year using the Danish national health registries. Main outcome was all-cause mortality. Groups were compared using adjusted hazard ratios (aHRs) by Cox regression with the first period as reference.

Results: A total of 18,538 STEMI patients were included. From 2003-2006 to 2015-2017, one-year mortality decreased gradually in STEMI patients from 10.8% in 2003-2006 to 7.8% in 2015-2017 (aHR 0.63, 95% CI 0.52-0.76). This benefit was primarily caused by improvements in the periprocedural phase with an absolute 2.3% reduction in 30-day mortality (aHR 0.55, 95% CI 0.43-0.71), and to a lesser extent by an absolute 0.9% reduction in 31-365 days mortality (aHR 0.74, 95% CI 0.55-0.99). These improvements coincided with changes in the prehospital organization with reduced prehospital delay and increased use of new guideline-initiated pharmacological and interventional treatments.

Conclusions: From 2003 to 2017, one-year mortality decreased by 37% among patients with STEMI undergoing pPCI. The largest reduction in mortality was observed in the periprocedural period from 0-30 days.

Keywords: Cardiovascular system, Epidemiology and biostatistics, Other

Performance of the race-free CKD-EPI creatinine-based estimated glomerular filtration rate (eGFR) equation in a Danish cohort with chromium-51-EDTA clearance measurements

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Background

A new eGFR equation based on serum creatinine, age, and sex without adjustment for race (eGFRCr(AS)), has recently been modeled and recommended for clinical use. However, the performance of the new equation has yet to be examined among patients with cancer and among potential living kidney donors.

Methods

We compared the performance of the eGFRCr(AS) equation with the performance of the original creatinine-based eGFR equation with the race-term defined as non-Black (eGFRCr(ASR-NB)) in patients with measured chromium-51-EDTA plasma clearance at Aarhus University Hospital during 2010-2018. We examined bias, accuracy, precision, and correct classification of CKD stage using the chromium-51-EDTA clearance as the reference standard. We assessed the performance in the total cohort (N=4,668) and in sub-cohorts of cancer patients and potential living kidney donors.

Results

Overall, we found that the eGFRCr(AS) equation performed slightly better than the eGFRCr(ASR-NB) equation, both when examining the total cohort and when examining sub-cohorts of cancer patients and potential living kidney donors. In the total cohort, the eGFRCr(AS) equation revealed lower median absolute bias (-0.2 vs. -4.4 ml/min/1.73 m2), higher accuracy (72.4% vs. 70.3%), but equal precision and correct classification of CKD

stages when compared with the eGFRCr(ASR-NB) equation. When we stratified by CKD stage, the eGFRCr(ASR-NB) equation performed slightly better than the eGFRCr(AS) equation at lower GFR.

Conclusion

Among patients with measured GFR, the eGFRCr(AS) equation performed slightly better than the eGFRCr(ASR-NB) equation. Our findings support the use of the eGFRCr(AS) equation.

Keywords: Epidemiology and biostatistics, Nephrology, Oncology

Prevalence of peripheral and cardiovascular autonomic neuropathy in Greenland based on national normative reference data

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Background and aims: Prevalence of diabetes is increasing in Greenland. However, studies on the prevalence of diabetic peripheral neuropathy (DPN) and cardiovascular autonomic neuropathy (CAN) are scarce. The aim was to determine the prevalence of DPN and CAN in Greenlanders with diabetes and prediabetes by applying national normative reference data.

Materials and methods: We evaluated DPN and CAN among Greenlanders with diabetes and prediabetes who participated in the nationwide Greenlandic Population Survey 2018. DPN was assessed by applying monofilament and vibration threshold (VPT). Cardiovascular autonomic reflex tests and heart rate variability were used to assess CAN. Normative reference data was used to determine the prevalence of DPN and CAN. Normal ranges for VPT and CAN in Greenlanders without diabetes were estimated by using quantile regression models at the 5th percentile.

Results: The study included 369 participants with diabetes (37.7%) or prediabetes (62.3%). Women comprised 54.2% and mean age was 60 years. DPN was diagnosed in 7.6% of participants with diabetes and in 3.9% with prediabetes. Prevalence of CAN and early CAN in participants with diabetes was 4.7% and 13%, respectively. CAN was diagnosed in 3.3% and early CAN in 13% with prediabetes.

Conclusion: We identified a relatively low prevalence of DPN and CAN in Greenlanders with diabetes and prediabetes. However, the use of likewise low normative thresholds for VPT and CAN may have resulted in an underestimated prevalence of DPN and CAN. This warrants studies on the pathophysiology of low nerve function and prevalence of neuropathy in Greenlanders with and without diabetes, respectively.

Keywords: Epidemiology and biostatistics, Cardiovascular system, Other

Pre-and post-diagnostic consumption of red and processed meat and risk of mortality after colorectal cancer diagnosis: a prospective observational study and meta-analysis

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Consumption of red and processed meat has been associated with risk of colorectal cancer (CRC) in several studies. However, less is known about the impact of red and processed meat consumption on prognosis outcomes after diagnosis of CRC. Therefore, this study aims to investigate associations between pre- and post-diagnostic consumption of red and processed meat and all-cause mortality in a prospective cohort study. Furthermore, we will include these results in a systematic review and meta-analysis of prospective studies to summarize the overall evidence on red and processed meat intakes pre- and post-diagnosis and mortality after CRC diagnosis (PROSPERO identifier: CRD42021241646). Using data from the Diet, Cancer and Health cohort, we will use Cox proportional hazard models to estimate hazard ratios and 95% confidence intervals for associations between high (>500 g/week) vs. low (≤500 g/week) intakes of pre- and post-diagnostic red and processed meat consumption and mortality in CRC patients. We have conducted systematic literature searches in PubMed and Embase through December and January 2021-2022 including citation searches of eligible studies and will assess the risk of bias of the included studies using the Risk of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool. We will use random-effect models to compare the highest with the lowest consumption category of pre- and post-diagnostic red and processed meat in meta-analyses. The result of this study contributes to a better understanding of the role of red and processed meat consumption on mortality after CRC diagnosis.

Keywords: Epidemiology and biostatistics, Oncology, Reviews and meta-analyses

Psychometric testing in Danish general practice – Variation and association with patient treatment

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Background:Most patients with mental disorders are diagnosed and treated in general practice. Psychometric tests (PTs) are instruments that aid the general practitioner (GP) during the diagnostic process and monitoring of treatment outcomes.

Aim:We aimed to assess the use of PTs in general practice and whether variation in propensity for PT-use between GPs was associated with patient related outcomes.

Methods:In a nationwide explorative cohort study from 2007 through 2018, all PTs performed in Danish general practices was identified. Predictors for use were investigated. We estimated the standardized PT-rates between general GPs and assessed whether treatment variation modified the patients' risk of being referred to different treatment regimens.

Results:The frequency of PT-use in general practices increased over time. A great variation in PT-use among GPs was observed. A positive association between a GP's propensity for PT-use and talk therapy sessions was observed. Patients listed with a GP with a low propensity for use of PTs had an increased rate of redemptions of anxiolytics medication and those with a high propensity had an increased rate of anti-dementia drugs. No association was found between PT-use and other treatment outcomes. Being woman, having low income, low educational level, and presence of comorbid disorders increased the PT-rate.

Conclusion:PTs are a common tool in general practice. They are most used among women, those with a low socio-economic status and comorbid diseases. The use of PTs depends on GP-listing and is associated with use of talk therapy, redemptions for anxiolytics and anti-dementia drugs but not related with other treatment outcomes.

Keywords: Epidemiology and biostatistics, Public health, Psychiatry, psychology and mental health

Fracture Risk in Patients with Anorexia Nervosa:

A 40-year-cohort-study

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Objective:

Anorexia nervosa (AN) is associated with low bone mass density which may contribute to increased fracture risk.

We aimed to estimate the long-term overall and site-specific fracture risk in Danish patients diagnosed with AN in a 40-year cohort follow-up study.

Methods:

A nationwide population-based cohort study including all 14774 patients diagnosed with AN from 1977 to 2018 and 147740 matched general population comparisons.

We calculated Odds Ratio (OR) for 1-2 fractures and 3+ fractures.
We used Cox proportional hazards analysis to compute hazard ratio (HR) for fractures stratified by age and sex, and adjusted for time period of diagnosis, psychiatric comorbidity, and Charlson comorbidity index.

Results:

We found an Odds Ratio for 1-2 fractures: 1.3 [95% CI 1.25-1.37] and 3+ fractures: 2.7 [95% CI 2.35-3.19] in the AN cohort compared to the comparison cohort.

We found a significantly increased fracture incidence in the AN cohort from the time of diagnosis and up to 40 years after 1,29 [95% CI 1.23-1.35]

The HR for any fracture was 1.42 [95% CI 1.32-1.52] and higher at typical fragility fracture sites;

Spine: 2.16 [95% CI 1.56-3.0], femur 3.6 [95% CI 2.8-4.62], and shoulder/upper arm 2.40 [95% CI 1.99-2.28]

Conclusion:

We found an increased fracture risk in AN patients compared to the general population from 0-40 years after diagnosis. Furthermore, we found that fracture risk measured as adjusted HR was increased at all fracture sites, particularly at typical fragility fracture sites, causing an increased risk of prolonged immobilization and chronic pain for the patients.

Keywords: Epidemiology and biostatistics, Molecular metabolism and endocrinology, Psychiatry, psychology and mental health

Comorbid diseases as prognostic factors for infection after surgery for hip fracture: a population-based cohort study among 87,593 patients

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Background

Comorbidity as measured by the Charlson comorbidity index (CCI) is associated with risk of infection up to one year after hip fracture surgery. However, the impact of the individual CCI diseases on prediction of infection among patients with hip fracture is poorly understood.

Method

Utilizing Danish medical registries, we obtained data on 87,593 patients undergoing hip fracture surgery between 2004-2017. Information on CCI diseases was obtained 5 years prior to surgery. Outcome was any hospital-treated infection within the first postoperative year. Cumulative incidence of infection was calculated, overall and by the CCI diseases. For each CCI disease odds ratio (OR) of infection was estimated using logistic regression. Scores were assigned to each disease by multiplying the beta coefficient from adjusted analysis by ten and rounding to the nearest integer.

Results

Most common comorbidities were cerebrovascular disease (14%) and chronic obstructive pulmonary disease (COPD) (10%). The cumulative incidences of infection were highest among patients with AIDS (53%), renal disease (43%), COPD (43%), and leukaemia (42%). Among those with record of infection (N=24,558) 0.04% had AIDS whereas 17% had cerebrovascular disease and 16% had COPD history. Crude OR varied between 1.05 for

dementia, 1.98 for renal disease, 2.07 for COPD, and 2.89 for AIDS. In multivariate analysis, 17 of the 19 new weighted score-point varied from the original.

Conclusion

Setting-specific scores varied from the original CCI scores. Most of the CCI diseases were strong prognostic factors for infection among hip fracture patients. Particularly COPD and renal disease may be of clinical relevance.

Keywords: Epidemiology and biostatistics, Orthopedic surgery, Infection

Developmental course of Functional Somatic Symptoms (FSS) from pre- to late adolescence and associated internalizing psychopathology

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BACKGROUND: Functional somatic symptoms (FSS), i.e. symptoms without well-defined somatic pathology, are associated with adverse long-term consequences in psychological functioning. Severe FSS might persist across different life stages, e.g. from adolescence to midlife adulthood. Yet, knowledge about developmental courses of FSS and co-occurring psychological functioning at younger ages is scarce. The current study aims to investigate 1) symptom continuity of pre-adolescent FSS (age 11/12; T0) to late adolescence (age 16/17; T1) and 2) the effect of pre-adolescent FSS on internalizing psychopathology at late adolescence. METHOD: Data from the general population Copenhagen Child Cohort (CCC2000) on assessment waves at age 11/12 (n = 1890) and 16/17 (n = 2542) will be utilized. We will include data on self-reported FSS (Children's Somatization Inventory; Bodily distress syndrome checklist), internalizing psychopathology (The Strengths and Difficulties Questionnaire; Spence Children's Anxiety Scale; The Mood and Feelings Questionnaire; Whiteley Index), and register-based data on sex, parental education and chronic medical conditions. The developmental courses of FSS will be categorized as: persistence (high FSS at T0 & T1), remission (FSS only at T0), incidence (FSS only at T1) or no FSS at either time point (no FSS at T0 & T1). We will conduct multiple linear regressions with stepwise adjustment. EXPECTED RESULTS: We will describe the developmental course of FSS and the effect of pre-adolescent FSS on internalizing psychopathology in late adolescence. DISCUSSION: Findings on the progression of FSS and their potential importance for prevention and treatment will be discussed.

Keywords: Epidemiology and biostatistics, Psychiatry, psychology and mental health, Other

Hyperinsulinemic type 2 diabetes and polyneuropathy in a Danish cohort

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Background: Hyperinsulinemia and low insulin sensitivity are associated with diabetic polyneuropathy (DPN). We investigated the association of DPN within subgroups of hyperinsulinemic, classical, and insulinopenic type 2 diabetes mellitus (T2DM).

Methods: We estimated insulin sensitivity and beta-cell function in patients with newly diagnosed T2DM enrolled throughout Denmark (n=3,397). Patients were classified into hyperinsulinemic (low insulin sensitivity, high beta-cell function), classical (low insulin sensitivity, low beta-cell function), and insulinopenic (high insulin sensitivity, low beta-cell function) T2DM. DPN was defined as a score ≥4 on the Michigan Neuropathy Screening Instrument questionnaire. We applied Poisson and spline regressions to calculate adjusted prevalence ratios (aPRs).

Results: The prevalence of DPN was 23% among hyperinsulinemic, 16% among classical, and 14% among insulinopenic patients. After adjustment for age, sex, diabetes duration and therapy, and lifestyle, the aPR of DPN was 1.42 (95% CI 1.21-1.65) for hyperinsulinemic patients, compared with the classical subgroup. DPN prevalence remained elevated (1.35 [95% CI 1.15-1.57]) after further adjustment for central obesity, hypertriglyceridemia,

hypertension, and HbA1c. No difference in aPR was observed for insulinopenic patients. Gradually increasing beta-cell function was associated with higher DPN occurrence, independent of insulin sensitivity.

Conclusion: The prevalence of DPN is increased in patients with hyperinsulinemic T2DM. Our findings indicate that hyperinsulinemia has a dose-response relation with DPN, independent of insulin resistance.

Keywords: Epidemiology and biostatistics, Molecular metabolism and endocrinology, Epidemiology and biostatistics

Endometriosis: Consequences of delayed diagnosis

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Background: Endometriosis is a benign gynecological disease that can cause severe pelvic pain and infertility. The condition is underdiagnosed and associated with a diagnostic delay that has been reported as long as 10 years from onset of symptoms until diagnosis. Therefore, the aim of this study was to investigate the utilization of both primary and secondary health care in the 10 years preceding endometriosis diagnosis as indicators of consequences of the diagnostic delay.

Methods: This study was conducted as a register-based case-control study in Denmark. Cases were women who received a hospital-based diagnosis of endometriosis. Each case was matched to five controls, defined as women without diagnosed endometriosis. Using negative binomial regression analysis, we estimated the yearly mean number of contacts with the general practitioner (GP) and hospital contacts for cases and controls and estimated incidence rate ratios in the 10 years preceding the index date.

Preliminary results: We included 129,696 women in our study. Cases had a significantly higher use of healthcare compared to controls for all 10 years before index. This was especially profound in the two years leading up to index, where the incidence rate ratio for any GP-contact was 1.54 (1.52;1.56); for hospital contacts this was 3.44 (3.39;3.50) in the year before index.

Conclusion: Women with diagnosed endometriosis had a higher overall utilization of health care in both primary and secondary health care in the 10 years leading up to diagnosis. This was especially profound in the last few years before diagnosis. Additional conclusions for this study will be based on further statistical analysis.

Keywords: Epidemiology and biostatistics, Gynecology and obstetrics, Public health

POSTER SESSION 10

The role of single-chain SorCS2 in cerebellar development and connectivity: implications for motor and cognitive function

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Emerging research has indicated that the cerebellum is involved in higher-order cognitive functioning including spatial learning, attention, and memory, through extensive interconnections between the deep cerebellar nuclei and several limbic structures. Furthermore, aberrant cerebellar functionality is implicated in several neurodevelopmental diseases (NDDs) such as autism spectrum disorder as well as neuropsychiatric diseases. We focus on SorCS2, a member of the sortilin receptor family, known for its involvement in sorting and signaling, which is abundantly expressed during cerebellar development as well as in the adult Purkinje neurons, the main inhibitory output from the cerebellar cortex. Additionally, SorCS2 is involved in various types of memory and a risk factor for several NDDs, including autism. The receptor undergoes proteolytic cleavage resulting in a single-chain receptor which can be further processed into a double-chain isoform, each with distinct expression patterns and biological functions. Whilst both isoforms are highly expressed at early cerebellar postnatal stages, the expression shifts to predominantly the double-chain form from postnatal day 3 and onwards. By utilizing a transgenic mouse model which solely expresses the single-chain isoform, we have found that single-chain SorCS2 impairs cellular morphology, dendritic spine density and synaptic composition of Purkinje neurons. We hypothesize that correct expression of the different isoforms in a spatiotemporal manner is critical for proper Purkinje cell morphogenesis and synaptogenesis. And that ablation of SorCS2 contributes to cognitive and motor impairments as well as memory deficits.

Keywords: Basic neuroscience, Cell biology, Animal models/disease models

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

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The use of monoclonal antibodies (mAbs) and other Biotherapeutics for treating brain disorders is to a large extend challenged by a limited drug exposure in the brain as only 0.1 % of administered antibodies crosses the blood-brain barrier (BBB). One of the natural routes for large biomolecules to cross the BBB is known as receptor-mediated transcytosis (RMT), which facilitates transport via cellular uptake and sorting through the endosomes. Several attempts have been made to target this pathway and determine the mechanisms impacting the fate of the antibodies, however the biological mechanism leading to successful RMT remains unclear. One major challenge to succeed with RMT for drugs, is to find a receptor with enriched expression on brain endothelial cells (BECs) that also have the capacity to be transcytosed efficiently. We will use the Basigin receptor as a novel target for transcytosis across the BBB and determine whether antibody affinity or valency impacts the sorting process.

Keywords: Cell biology, Laboratory science, Basic neuroscience

Locus coeruleus: the master switch for brain health?

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The Locus Coeruleus (LC) is located in the brainstem and produces about half of brain noradrenaline (NA). Although the LC consists of mere thousands of neurons, it projects to the entire brain and is the only supply of NA to the brain cortex and hippocampus. Much is known about the many roles of the LC and the action of NA in the brain. Centrally, the LC is known to impacts not only facets of behavior such as anxiety, fear, and motivation but also processes of basic physiological importance such as sleep, brain blood flow, and capillary permeability. However, the details of the short and long-term consequences of LC dysfunction remain unclear. Recent evidence suggests LC is the first-affected brain structure in patients suffering from neurodegenerative diseases, potentially hinting that LC dysfunction may play a central role in disease development and progression. Animal models with modified or disrupted LC function are essential to further our understanding of LC function in the normal brain, the consequences of LC dysfunction, and its role in disease development. Therefore, there is a need for well characterized animal models of LC dysfunction to investigate the role of LC under controlled conditions. One often used method is LC ablation using the selective neurotoxin N-(2-chloroethyl)-N-ethyl-Bromo-benzylamine (DSP-4). Here we present work to more firmly establish the optimal dose of DSP-4 and the effect of LC ablation on brain structure and vasculature.

Keywords: Basic neuroscience, Animal models/disease models, Medical technology and diagnostic techniques

Non-classical GABAergic cortical neurons and neurovascular coupling in healthy and Alzheimer's Disease model mice

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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 GCamp8f. We will also evaluate capillary hemodynamics during activation of INs combining single-cell two-photon optogenetic stimulation and single capillary scans in awake transgenic mice. Last, we will examine changes in tissue oxygenation during the activation of NDNF cells and correlate them to cell activity and capillary hemodynamic changes. Our preliminary results show that optical stimulation of NDNF-INs at physiological theta frequency (4 Hz) evokes transient changes in capillary flows consistent with a vasodilator effect. Our study supports the role of INs during neurovascular coupling and suggests that during NVC, NDNF cells might be implicated in the post-stimulus undershoot observed in the blood-oxygen-level-dependent imaging (BOLD) used in functional magnetic resonance imaging.

Keywords: Basic neuroscience, Clinical neuroscience, Animal models/disease models

Structural and functional aspects of the transmembrane protein, slitrk5, role in developing OCD-similar behavior

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Obsessive-compulsive disorder (OCD) is a neuropsychiatric condition, where our understanding is limited, and today's treatment is only partially effective. The occurrence of OCD has several hypotheses, we hypothesize that a rare genetic mutation in the slitrk5 protein causes an imbalance in the excitatory and inhibitory signaling leading to a dysfunctional Cortico-Striatal Circuit (CSC). The aim is a thorough structural and functional study building upon current knowledge of this slitrk5 protein and its association with OCD. This research is based on the OCD mouse model, Slitrk5-/-, a transgenic knockout mouse. This particular mouse model has demonstrated OCD similar phenotypes, such as overgrooming behavior and increased anxiety. Previous research has detected structural changes in the orbitofrontal Cortex (OFC) and striatum, namely overactivity in OFC and reduced striatal volume. Through ultrastructural analysis and 3D reconstruction of cellular objects in the striatum, we expect to identify dissimilarities within the cortico-striatal circuit and cellular and subcellular objects between the OCD mouse model and wild-type mouse.

With comprehensive techniques incorporated, such as Serial-Block Face Scanning Electron Microscopy and tissue clearing combined with immunohistochemistry and light-sheet microscopy, we expect to detect structural alterations leading to a malfunctioning cortico-striatal circuit. We believe that this study can provide new information about the occurrence of OCD, which can be crucial in explaining molecular and neural structural deficits underlying OCD.

Keywords: Basic neuroscience, Psychiatry, psychology and mental health, Animal models/disease models

Brain mechanisms underlying recognition of simple and complex musical sequences

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Auditory recognition is a complex cognitive processes that relies on the organization of single elements that evolve in time, such as phonemes or musical notes. However, unlike visual recognition, little is known about the spatiotemporal dynamics underlying recognition of auditory stimuli. Recently, we investigated the brain mechanisms of music recognition in 71 participants using magnetoencephalography (MEG) and magnetic resonance imaging (MRI). Participants were asked to learn and recognize simple tonal musical sequences and matched complex atonal sequences while their brain activity was recorded using MEG. We then reconstructed the source of the activity from MRI scans. Results revealed changes in neural activity that were dependent on stimulus complexity: recognition of tonal sequences engaged hippocampal and cingulate areas, whereas recognition of atonal sequences mainly activated the auditory processing network. Our findings reveal the involvement of a cortico-subcortical brain network for auditory recognition and support the idea that stimulus complexity qualitatively alters the neural pathways of recognition memory. In future studies, we aim to explore whether stimulus complexity also affects the brain mechanisms underlying the encoding of musical sequences.

Keywords: Basic neuroscience, Psychiatry, psychology and mental health, Other

Uptake Capacity of a Putative Bacterial Serotonin Transporter

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Enterochromaffin cells of the gut produce upwards of 90 percent of the body's serotonin content and in the enteric nervous system (ENS), serotonin acts as an important neurotransmitter. Certain bacteria of the microbiome might be able to sense signaling molecules from the ENS and utilize this to colonize specific sites.

A putative serotonin transporter was identified in Turicibacter sanguinis. T. sanguinis are part of the microbiome and are enriched if the intestinal lumen serotonin content is increased.

The data indicating transport through the putative T. sanguinis serotonin transporter (TuriSERT) was unconvincing. In this project, we attempt to show time-dependent uptake of tritium-labeled serotonin in Escherichia coli expressing TuriSERT. Additionally, we attempt to show that uptake is Na+-dependent, as transport through other members of the neurotransmitter-sodium-symporter family is Na+-dependent. Finally, we attempt to show uptake of tritium-labeled serotonin in human embryonic kidney (HEK)-293 cells transfected with TuriSERT in a human expression vector.

Time-dependent uptake of tritium-labeled serotonin could not be detected in E. coli. However, the radioactive signal was greater in TuriSERT expressing cells compared to controls, indicating serotonin binding rather than uptake. This binding appeared to be Na+-dependent. In transfected HEK-293 cells, TuriSERT expressing cells showed the same radioactive signal as mock-transfected controls, while hSERT-expressing cells showed expected uptake levels. These results suggest that TuriSERT is not a serotonin transporter but may be able to utilize the transporter-like scaffold to act as a serotonin receptor.

Keywords: Basic neuroscience, Cell biology, Pharmacology

elucidating phosphorylation-related regulatory mechanisms that govern retromer-dependent trafficking of sorla

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Aim

SORL1 (Sortilin Related Receptor 1) encodes an endosomal trafficking receptor and is currently the gene most frequently affected in patients with Alzheimer's Disease (AD). Acting as an adaptor molecule of the retromer trafficking complex, SORLA is not only linked to AD through recycling Amyloid precursor protein out of endosomes, but also through neuronal endosomal recycling of several transmembrane receptors back to the cell surface. Despite this important role, it is poorly understood how SORLA-retromer interaction is regulated. In this study, we aim to elucidate the phosphorylation-related regulatory mechanisms that govern retromer-dependent trafficking of SORLA.

Methods and results

An in Vitro Kinase assay (KinaseFinder, ProQinase) was performed and Glycogen synthase kinase3 (GSK3) was identified as a hit. GSK3 is involved in AD pathology and has a phosphorylation motif, which is present in SORLA cytoplasmic tail and is predicted to be phosphorylated by NetPhos3.1 Phospho-site prediction. This potential phosphorylation modifies Serine-2175 in the center of 2172FANSHY sorting motif. SORLA binds to retromer via this motif and this binding is prerequisite for its maturation and shedding. We hypothesized that Serine-2175 phosphorylation weakens SORLA-retromer interaction, leading to its decreased shedding. To test this hypothesis, we developed a construct to sensitively measure SORLA shedding by fusing the reporter Gaussia Luciferase to SORLA (eGluc-SORLA), and we are designing an experiment to co-transfect eGluc-SORLA with GSK3 in HEK cells and detect possible changes in SORLA shedding.

Conclusion

SORLA-Retromer interaction is regulated by GSK3 phosphorylation of the cytoplasmic tail.

Keywords: Basic neuroscience, Genetic engineering, Laboratory science

Quantitative gait analysis as motor assessment in translational porcine models of neurological disorders

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The increasing use of minipigs in neuroscience has resulted in various translational models of neurologic diseases implicating the motor system. While motor deterioration can be assessed by neurological examination, such may be investigator-dependent and bias-susceptible. Quantitative methods constitute useful alternatives to detect motor deterioration, e.g., in chronic models of Parkinson's disease (PD).

We used a pressure-sensitive gait mat (GAIT4Dog®/GAITFour®, CIR Systems Inc., NJ, US) to characterize normal quadruped gait parameters of 7 healthy, female minipigs (7-10 months; 19.2-26.5 kg). Then, we induced a unilateral lesion in the right medial forebrain bundle using stereotaxic microinjections of 6-hydroxydopamine resulting in a hemi-parkinsonian phenotype (n=5). We compared with saline controls (n=2) and repeated the gait analysis to assess pathological gait dynamics.

We determined a symmetric gait pattern in step length, stride length, stance time, and stance % across the four extremities, but found a frontally placed center of gravity. Gait parameters varied across healthy animals. Post-lesion gait dynamics were characterized by a mean velocity decrease from 102.4 cm/sec to 90.42 cm/sec (P = 0.0275), an ipsilateral step length decrease from 26.21 cm to 25.53 cm (P = 0.008), and bilaterally increased stance times in the PD animals, whereas no changes were found in the controls. Although not clinically evident, even subtle motor deterioration was detected in the gait analysis. Our findings suggest that pressure-sensitive gait mat analysis is a sensitive, useful, and reliable tool to monitor motor deterioration in porcine models of neurological disorders.

Keywords: Basic neuroscience, Animal models/disease models, Other

Satellite glial cell heterogeneity

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Satellite glial cells (SGCs) ensheath neuron somata in dorsal root ganglia (DRG). In normal conditions, they are believed to control neuronal homeostasis, but evidence suggest that they contribute to the development of chronic pain after peripheral nerve injury.

Recent advances in single-cell RNA sequencing (scRNA-seq) have revealed the presence of SGC subtypes, yet validation and characterization of the findings remain largely unexplored. To explore the characteristics of different SGC subtypes, we used scRNA-seq of dissociated mouse DRG and identified 5 clusters. Gene expression analysis revealed subtype specific markers, which we then used for investigating the protein expression by immunohistochemistry.

Especially a Scn7a expressing subtype stood out and could be identified using IHC, although constituting only a small portion of total SGCs (~3.5%). Co-staining with neuronal subtype markers revealed that this subtype does not ensheath large diameter neurons, and among the small diameter neurons, predominantly ensheaths non-peptidergic neurons.

Our clusters demonstrate high conservation when comparing similarities in gene expression with clusters identified in scRNA-seq data sets from other groups. The most prominent and reproducible clusters include one which express markers that have previously been used to identify and characterize SGCs, one which express high levels of Scn7a with concomitant low levels of classical SGC markers and one which express immune response-related genes.

The continuation of the project will involve a characterization of the immune response related subtype and validation in human DRG.

Keywords: Basic neuroscience, Animal models/disease models, Laboratory science

POSTER SESSION 11

Glucocorticoids and circadian rhythms from bedside to bench

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BACKGROUND: Circadian rhythms generated by clock proteins underpin all biological systems. Glucocorticoid hormones (GC) may disrupt circadian rhythmicity.

AIM: Utilizing three human data sets, we study acute and chronic effects of GC exposure and withdrawal on biological readouts linked to disruption of clock gene expression.

METHODS: Circadian energy metabolism, blood pressure, spontaneous physical activity and sleep patterns are recorded in the acute study (n=10). Body composition, muscle strength, glucose homeostasis and lipid profiles are recorded in the chronic (n=66) and withdrawal study (n=30). Clock gene expression (mRNA) in fat and muscle tissue and immune cells are assessed with RTqPCR and Fluorescence-Activated Cell Sorting.

PERSPECTIVES: We combine translational research with multidisciplinary and international collaboration to elucidate the pathophysiology of GC excess, which is of profound clinical relevance considering 3 % of the population receive GC treatment.

Keywords: Molecular metabolism and endocrinology, Laboratory science, Pharmacology

Highly efficient and selection-free CRISPR gene editing in human primary endothelial cells with ribonucleoprotein complex

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Primary endothelial cells (ECs), especially human umbilical vein endothelial cells (HUVECs), are broadly used in vascular biology. Gene editing of primary endothelial cells is known to be challenging, due to the low DNA transfection efficiency and limited proliferation capacity of ECs. We report the establishment of a highly efficient and selection-free CRISPR gene editing approach for primary endothelial cells (HUVECs) with ribonucleoprotein (RNP) complex. We first optimized an efficient and cost-effective protocol for messenger RNA (mRNA) delivery into primary HUVECs by nucleofection. Nearly 100% transfection efficiency of HUVECs was achieved with EGFP mRNA. Using this optimized DNA-free approach, we tested RNP-mediated CRISPR gene editing of primary HUVECs with three different gRNAs targeting the HIF1A gene. We achieved highly efficient (98%) HIF1A knockout in HUVECs without selection. The effects of HIF1A knockout on ECs' response to hypoxia and on angiogenic characteristics were validated by functional assays. Our work provides a simple method for highly efficient gene editing of primary endothelial cells (HUVECs) and study of ECs functions.

Keywords: Molecular metabolism and endocrinology, Genetic engineering, Cardiovascular system

The effect of alginate encapsulated supplements on recovery, performance and health

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Background: Carbohydrate (CHO) ingestion during exercise has been demonstrated to improve exercise performance. Current guidelines suggest high CHO availability to promote optimal performance during competition. During ultra-endurance exercise (>2.5-3 hrs) an intake of CHO of up to 80-90 g/hr is recommended. Although these high rates benefit performance, they may also potentiate gastrointestinal (GI) distress. Purpose: The purpose of the current study is to investigate the effect of an alginate encapsulation technology, where we encapsulate CHOs. Our primary end-point is cycling performance. Secondary end-points include substrate utilization and gastrointestinal distress symptoms. Method: Healthy men, 18-50 years old and accustomed to cycling training (e.g. cyclists, triathletes) are recruited to complete 3 experimental trials consisting of a 2-hr pre-load cycling bout at different intensities followed by a Time-To-Exhaustion performance test and a 2-hour recovery. In a cross-over design, the participants will consume three different energy supplements in a randomized order. The supplements consists of: A) encapsulated CHO and amino acids, B) encapsulated CHO-only and C) CHO-only (not encapsulated). During each experimental trial blood-, urine- and saliva samples are measured. In addition, questionnaires and Visual Analogue Scales are administered to assess perceptual GI symptoms (e.g. nausea, abdominal pain, fullness). Perspectives: Understanding how prolonging the release rates of carbohydrates affects the substrate utilization and GI symptoms may result in new nutritional solution for endurance athletes and potentially for Type 2 Diabetics.

Keywords: Molecular metabolism and endocrinology, Pharmacology, Other

Understanding Muscular Deficits of Diabetic Myopathy

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Background: Diabetic myopathy encompasses functional and structural changes of skeletal muscles in diabetes. Diabetic neuropathy (DPN) leads to progressive loss of muscle volume and strength. However, deterioration of intrinsic muscle function is expected to commence even prior to the presence of DPN, as patients with diabetes are shown to experience a higher risk of falling and a lower walking capacity, irrespective to the presence of DPN. Patients with diabetes are consequently less likely to commence in physical activity, aggravating muscle deterioration. A vicious cycle increasing the risk of complications, morbidity and mortality. Yet, the parameters needed to identify diabetic myopathy in individuals with diabetes remain unestablished.

Aim: We aim to identify muscular deficits of diabetic myopathy, unrelated to diabetic neuropathy, and to assess how functional muscle changes relate to hyperglycemia and obesity in individuals with type 1 and 2 diabetes.

Methods: This is an ongoing project (enrollment started Nov 23) to assess the effects of obesity and prolonged hyperglycemia on muscle function in two follow-up studies: 1) non-obese participants with dysregulated type 1 and 2 diabetes are examined prior to and 6 months following glycemic improvement. 2) Obese participants with and without type 2 diabetes are examined prior to and 12 months following bariatric surgery. Primary measures of muscle performance include assessment of muscle contractile function, fatigue, and sarcopenia on a BioDex dynamometer.

Implications: We aim to help define diabetic myopathy and to identify parameters needed to diagnose diabetic myopathy in the clinic.

Keywords: Molecular metabolism and endocrinology, Medical technology and diagnostic techniques, Other

Mechanisms of growth hormone-induced fibrosis in human adipose tissue

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Background: Adipose tissue fibrosis denotes excessive, pathological accumulation of extracellular matrix (ECM) in adipose tissue and is a marker of tissue dysfunction with potential metabolic implications. Understanding the underlying mechanisms adipose tissue fibrosis may unravel new targets for treatment of obesity-associated disorders. Growth hormone (GH) activates adipose tissue lipolysis and stimulates collagen synthesis in lean tissues. Intriguingly, we have novel pilot data to suggest that GH excess (acromegaly) also induces reversible fibrosis in vivo and potently activates the expression of fibroblast activation protein alpha (FAPα).

We hypothesize that GH-induced adipose tissue fibrosis is mediated by increased FAPα expression together with proliferation and fibrogenic differentiation of fibro-adipogenic progenitor cells (FAPs).

Methods: We will use a reverse translation approach using single-cell technologies, fluorescence-activated cell sorting (FACS), single-nuclei sequencing as well as RNA sequencing, and cell culture studies, combined with in vivo assessment of adipose tissue turnover and metabolism.

Perspectives: Understanding fibrosis formation in human models may identify new targets for treatment of obesity-associated disorders.

Keywords: Molecular metabolism and endocrinology, Cell biology, Inflammation

Diffusional kurtosis MRI as a possible predictor if outcome in spinal cord injury

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BACKGROUND

Magnetic resonance imaging (MRI) lacks predictive value in spinal cord injury (SCI) Diffusional kurtosis imaging (DKI), type of MRI which has been hypothesized to be able to estimate microstructural changes in neuronal tissue. This cohort study is the first prospective study on DKI as a possible predictor for acute traumatic SCI. We aimed to explore whether in a pilot cohort, a correlation of DKI metrics, and long-term neurological outcome in traumatic SCI was present

METHODS

Eight acute traumatic SCI patient with incomplete AIS-D (American Spinal Cord Injury Association Impairment Scale) were included. A fast, mean kurtosis DKI protocol was implemented in the acute trauma scan of SCI patients. Mean kurtosis values at the injury site were normalized to the mean kurtosis values of a non-injured site. Outcome was evaluated using The Spinal Cord Independence Measure-III (SCIM-III) and AIS-score at discharge from the highly specialized rehabilitation center. The DKI metrics and outcome were correlated using Spearman's Ranks Correlation.

RESULTS

A significant correlation between decreasing mean kurtosis values at the injury site of the spinal cord and a detrimental outome measured by the SCIM-III ($p = 0.002$). A significant negative correlation between motor score and mean kurtosis was observed (= -0.87, p-value = 0.003) and as a significant correlation with pin prick score was observed (= -0.76, p-value = 0.03) as well.

CONCLUSION

DKI metrics were found to correlate with functional neurological outcome in this small eight patient cohort. All patients were AIS grade D. The study is limited by the low number of patients, and the fact, that patients were alle AIS grade D.

Keywords: Medical technology and diagnostic techniques, Clinical neuroscience, Other

Hyperpolarized 13C NMR for metabolic fingerprinting of leukemia cancer as a potential marker in diagnostics and treatment evaluation

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A deranged metabolic phenotype (Warburg effect) is often seen in cancer cells, leukemic cells included, and is increasingly a target for improved diagnosis and treatment. The treatment response of leukemia is directly coupled to the leukemic subtype, and therefore knowledge of the metabolic profile before and after treatment is of importance, as a wrongly treated leukemia could be a fatal disease. In this work, we sought to use hyperpolarized carbon-13 (13C) Nuclear Magnetic Resonance (NMR) spectroscopy to get a better basic understanding of metabolic differences between leukemic subtypes. Hyperpolarized 13C NMR spectroscopy allows tracking of 13C labelled bio-probes such as pyruvate as the cells convert it to metabolites such as lactate and bicarbonate. Metabolic signatures of the various leukemia subtypes can be extracted through the real-time monitoring of the labelled bio-probe conversions. Six different leukemia cell lines (representing 3 of the 4 major leukemic subtypes), namely ML-1, CCRF-CEM, THP-1, MOLT-4, HL60 and K562, were all cultured and analyzed with hyperpolarized 13C NMR spectroscopy using [1-13C]pyruvate as bio-probe. Lactate production was seen for all cell lines, and pyruvate-to-lactate conversion rates extracted from the data showed a span of values for the various cell lines with THP-1 on the lower end and K562 on the higher end. Additionally, bicarbonate production was observed for some of the cell lines (primarily THP-1, CCRF-CEM and K562). Further experiments are planned using alanine as a bio-probe, to further characterize the metabolic signatures of the various cell lines for possible future diagnostic and treatment evaluation purposes.

Keywords: Medical technology and diagnostic techniques, Molecular metabolism and endocrinology, Cell biology

Cross-dataset cancer detection from cfDNA fragment coverage correlations with DNase 1 Hypersensitivity sites across 248 cell & tissue types

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Fragmentation patterns in whole-genome sequenced cell-free DNA (cfDNA) has been shown useful in detection and subtyping of cancers within single datasets. We apply cross-dataset-validation to a novel cancer detection method and show generalization of the method across multiple datasets and their differing cancer types. The method correlates GC-corrected fragment coverage within 10bp bins across the genome with the presence of DNase Hypersensitivity sites for 248 different cell & tissue types and feeds the coefficients to a set of machine learning algorithms. We compare our cross-dataset results with those of existing cfDNA fragmentation frameworks.

Keywords: Medical technology and diagnostic techniques, Epidemiology and biostatistics, Cell biology

Genetic therapy of GATA2 deficiency based on allele-specific genome editing

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GATA2 deficiency is a disease caused by haploinsufficiency of the transcription factor GATA2. The main symptoms seen in GATA2 deficiency patients are immunodeficiency with increased risk of viral and mycobacterial infections, and a high risk of leukemia, both of which are caused by reduced survival and renewal capacity of the hematopoietic stem cells (HSC). The only current treatment option for patients with GATA2 deficiency is allogeneic hematopoietic stem cell transplantation (HSCT), which has a high morbidity and mortality due to graft vs. host disease. A safer treatment option would be autologous HSCT of HSCs, in which the disease-causing variant has been corrected. In this study, we focus on correcting a gene variant causing GATA2 deficiency identified in a family at Aarhus University Hospital. In cell line models and patient-derived PBMCs, we show efficient and allele-specific correction of the GATA2 gene variant by ex vivo delivery of Cas9/sgRNA ribonucleoprotein (RNP) complexes and rAAV6-mediated DNA donor delivery. We find that the locus where the variant is located is highly susceptible to editing in HSCs, resulting in 92% homology directed repair (HDR) efficiency in HSCs. Furthermore, we use RNA-sequencing to identify novel GATA2-regulated mRNA transcripts and investigate their expression level upon GATA2 editing. We also investigate the colony forming unit potential of HSCs upon correction of the GATA2 gene. To investigate potential Cas9 off-targets, we study the use of DISCOVER-Seq to screen the genome for double-strand breaks. Collectively, we present the first evidence of a gene editing-based therapy for GATA2 deficiency.

Keywords: Genetic engineering, Cell biology, Other

Chimeric antigen receptor (CAR) T-cells targeting FLT3-positive acute myeloid leukemia (AML)

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Background: FLT3 is a promising drug-target in acute myeloid leukemia (AML). We utilize the promising immunotherapy chimeric antigen receptor (CAR) T-cells wherein T-cells are genetically reprogrammed to target a receptor on AML cells, FLT3. To enable use of donor-derived T-cells we use CRISPR/Cas-mediated targeted integration of the CAR gene into a T cell receptor gene.

Methods: Four different CAR constructs were developed: two targeting FLT3 and two control constructs targeting CD19. These were generated as CRISPR/Cas9 repair templates into Adeno-Associated Virus (AAV) vectors, serotype 6. The constructs were designed for targeted integration into the safe harbor locus AAVS1 (with a strong heterologous EF1α promoter), or into the TRAC locus (T-cell receptor α chain constant) to enable TCR knockout while facilitating CAR expression by the endogenous TRAC promoter. A truncated nerve growth factor receptor gene is co-expressed with the CAR gene to enable detection of gene integration into T-cells by flow cytometry.

Results: Optimization of CRISPR-mediated targeted gene insertion into the TRAC locus of primary T-cells led to 72% of T-cells expressing the anti-FLT3 CAR, comparable to 70% for the anti-CD19 CAR. Integration into the AAVS1 locus led to 26% of T-cells expressing the anti-FLT3 CAR and 23% of cells expressing the anti-CD19 CAR. We tested the potential of CAR T-cells to kill AML target cells. The anti-FLT3 CAR T-cells (TRAC) showed killing of 54% of target cells and the anti-CD19 CAR T-cells (TRAC) showed killing of 55% of target cells.

Conclusion: Efficient anti-FLT3 CAR T-cells can be generated using CRISPR/Cas9.

Keywords: Genetic engineering, Oncology, Other

POSTER SESSION 12

Cancer risk in ectodermal dysplasia and isolated congenital tooth anomalies

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Introduction

Congenital tooth anomalies can present isolated or as part of a syndrome, and may be due to one or more genetic mutations in cellular signaling pathways important for tooth formation. Some of these pathways also play a role in cancer development. In the Wnt-pathway, germline mutations in the AXIN2 or APC genes are associated with tooth agenesis and supernumerary teeth, respectively, but also an increased risk of cancer, especially colorectal tumors. Germline mutations in the EDA pathway can cause ectodermal dysplasia (ED) with various anomalies of ectoderm-derived appendages such as teeth, hair and skin. The EDA pathway is also a known modulator of cancer cell proliferation, but cancer risks in ED remain uninvestigated.

Methods

We included all singleton births in the years 1977-2018 from the Danish Medical Birth Registry. Information on tooth agenesis was obtained from the Central Odontologic Registry, that contains national data from the municipal children's dental care since 1972. Information on other tooth anomalies and ED was obtained from the Danish National Patient Registry, and information on cancer diagnoses from the Cancer Registry. Associations between teeth anomalies and early cancer (before 40 years of age) are evaluated by Cox proportional hazards models. As early exposure to chemotherapy can cause anomalies of the permanent dentition, cases with cancers prior to diagnosis of tooth anomalies are excluded. Results are presented as hazard ratios with 95% confidence intervals

Results

Preliminary results will be presented. We expect cancer risk to be increased in individuals with congenital tooth anomalies, with or without ED.

Keywords: Oncology, Epidemiology and biostatistics, Dentistry

Does data curation matter in deep learning segmentation? Clinical vs edited GTVs in glioblastoma.

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To automatically segment the gross tumor volume (GTV) in glioblastoma patients, deep learning (DL) models can be developed using clinical GTVs. However, clinical GTVs suffer from interobserver variation, which may impact DL-model performance. The aim of this study was to compare performance of a DL-model based on clinical GTVs to a DL-model based on edited GTVs.

259 patients were included. For each patient, the clinical GTV was edited by a single independent radiation oncologist. The cases were randomly split into train and test set (80:20), stratified on surgery type. We used nnU-net to train a model on clinical GTVs and similarly on edited GTVs, with contrast enhanced T1w-MRI as input. For evaluation surface Dice with a 2mm tolerance (sDSC) were reported using both models and delineation-sets. For statistical comparison a paired Wilcoxon signed-rank test was used.

Clin:Clin

Median (range) sDSC was 0.91 (0.35-0.996)

Clin:Edit

0.94 (0.66-0.993)

Edit:Edit

0.98 (0.79-0.9999)

Edit:Clin

0.90 (0.37-0.995)

The Edit model evaluated on the Edit test set (Edit:Edit), outperformed all other model test combinations ($p<.001$). Interestingly, the sDSC results significantly improved when the clinical model was evaluated on the edited test set instead of the clinical (Clin:Clin vs Clin:Edit $p<.001$). Altogether showing that both the clinical and edited model predictions better resembled the edited GTVs in the test set.

Data curation had a significant impact on model performance and on the evaluation of model performance. The model based on curated data had a much higher precision and accuracy than the model based on clinical data. Our results emphasize the importance of data curation in DL.

Keywords: Oncology, Other, Other

How does natural genomic structural variation influence colorectal cancer if it develops?

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Motivation

Colorectal cancer (CRC) is a molecularly heterogeneous disease, and outcomes differ between patients with similar tumors for mostly unknown reasons. Interestingly, we have preliminary evidence that the biology and aggressiveness of CRC tumor subtypes are influenced differently by natural structural variants (SVs) in our inherited genome. This suggests that characterization of natural SVs in our genome may help explain differences in CRC outcomes between patients. The full repertoire of SVs in the population is, however, not yet identified, and their expected impact on disease is therefore undescribed.

Aim

Our overall aim is to identify the full repertoire of natural SVs in the inherited genomes of CRC patients and describe how they associate with tumor molecular biology, tumor subtypes, and patient disease outcomes.

Approach and initial results

Using long-read WGS (Oxford Nanopore), we have identified ~20.000 unique SVs per patient and ~60.000 unique SVs in total in 16 CRC patients. Next, we will use short-read WGS (Illumina) to genotype the identified SVs in > 300 CRC patients with molecularly well-characterized tumors and good clinical annotation. We will evaluate the genome-wide impact of SVs on gene RNA expression, DNA methylation, tumor subtypes, and relapse-free and overall survival.

Perspectives

Our project will contribute to a new perspective on cancer where the combination of inherited genomic variation and alterations occurring only in the tumor together may explain CRC biology and outcome. This may highlight a potential of SVs as novel biomarkers for individualized patient treatment based on integrated analysis of both their inherited genome and tumor.

Keywords: Oncology, Medical technology and diagnostic techniques, Other

A method to explore dose and LET for normal tissue response studies in large proton therapy cohorts

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Purpose / Objective

Normal tissue complication probability (NTCP) calculations in proton therapy (PT) are usually performed using models derived from photon-based radiotherapy, with the assumption of a constant relative biological effectiveness (RBE) of 1.1. However, RBE has been shown to vary with a the so called dose weighted linear energy transfer (LETd), which is often not considered by NTCP models.

We seek to explore a method of analyzing dose and LETd distributions with respect to morbidity, based on dose and LETd thresholds, for prostate cancer patients treated with PT.

Materials / methods

For the organ of interest we iteratively selected a dose threshold and from the sub-region of the organ with a dose higher than this threshold, we selected an LETd threshold. For each combination we then graphed the dose threshold vs. the LETd threshold for each patient.

The method was explored on rectal morbidity data from a cohort (n=111) of PT prostate cancer patients. We calculated LETd using Monte Carlo simulations in FLUKA.

Results

The calculated distributions visualized the extent of variation in different areas of the dose and LETd volume space, and thus where potential differences between patients with vs. without morbidity can be observed.

There were no observed differences between with patients with vs. patient without grade 2 rectal morbidity.

Conclusion

We developed a method to explore the potential impact of LETd for a selected LETd threshold within a dose threshold, applied on rectal morbidity data for prostate cancer patients. In the present analysis of our cohort, we did not see any separation in the data for patients with vs. without rectal morbidity.

Keywords: Oncology, Medical technology and diagnostic techniques, Other

Quality of life by patient-reported outcomes in patients with locally advanced rectal cancer receiving modern neoadjuvant radiotherapy

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Introduction: Patient-reported outcome measures (PROM) are valuable for patient-centred information and evidence-based recommendations. This study reports quality of life (QoL) and symptoms measured by PROM after modern radiotherapy (RT) for locally advanced rectal cancer (LARC).

Materials and methods: Patients with LARC were included in a prospective study from 2017-2021. IMRT/VMAT was delivered as short (SCRT; 25Gy/5F) or long (LCRT; 50.4Gy/28F) course RT ± concomitant capecitabine. PROMs were collected prior to RT (PT), at end of RT (EOT), preoperatively (PO) and at one-year follow-up (1Y) using validated questionnaires (EORTC QLQ-C30 and -CR29). PROMs were assessed according to EORTC guidelines and raw symptoms reported as frequencies of scores 3-4 (quite a bit-very much).

Results: Of 110 included patients, 91 received LCRT; 19, SCRT. Completion of PROMs ranged from 84.5% at PT, 73.6% at EOT, 71.8% at PO to 71.8% at 1Y. Global Health Status/QoL mean scores were 64.9 at PT and significantly declined at EOT, 57.4. Scores improved at PO, 66.7, with a trend towards further increase at 1Y, 69.1. The same pattern applied for the functional scales: physical, role, and social functioning and symptom items pain and fatigue. The most frequently reported raw gastrointestinal scores at PT were buttocks/rectal/anal pain (27%), blood in stool (30%), and diarrhoea (26%) which significantly improved at 1Y. Of patients completing questionaries at 1Y, 80% had stoma with the highest reported item being embarrassment of stoma (16%).

Conclusion: Global Health Status/QoL and functional scales deteriorated at EOT and were restored already at PO with a trend towards further improvement at 1Y.

Keywords: Oncology, Other, Other

Cell-free chromatin immunoprecipitation can determine tumor gene expression in lung cancer patients

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Cell-free DNA (cfDNA) in blood plasma can be bound to nucleosomes that contain post-translational modifications representing the epigenetic profile of the cell of origin. This includes histone H3 lysine 36 trimethylation (H3K36me3) which is a marker of active transcription. We hypothesized that cell-free chromatin immunoprecipitation (cfChIP) of H3K36me3 modified nucleosomes present in blood plasma can delineate tumor gene expression levels. First, H3K36me3 ChIP followed by targeted next-generation sequencing (NGS) and RNA-seq was performed on lung cancer cell lines. Furthermore, H3K36me3 cfChIP followed by targeted NGS (cfChIP-seq) was performed on blood plasma samples from non-small cell lung cancer patients (NSCLC, n = 8), small cell lung cancer patients (SCLC, n = 4) and healthy controls (n = 4). We found a correlation between H3K36me3 ChIP enrichment and mRNA levels in lung cancer cell lines. H3K36me3 cfChIP-seq demonstrated increased enrichment of mutated alleles compared to normal alleles in plasma from patients with known somatic cancer mutations. Additionally, genes identified to be differentially expressed in SCLC and NSCLC tumors have concordant H3K36me3 cfChIP enrichment profiles in NSCLC blood plasma (sensitivity = 0.80) and SCLC blood plasma (sensitivity = 0.86). This study describes how cfChIP-seq in liquid biopsies can be used to determine mRNA expression in the tumor. This will expand the utility of cfDNA in liquid biopsies in order to characterize tumor biology related to gene expression changes such as treatment resistance and disease progression.

Keywords: Oncology, Respiratory system, Other

Monitoring of circulating tumor DNA from EGFR-mutated advanced non-small cell lung cancer patients treated with first-line osimertinib

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Background: Despite advancements in the treatment of lung cancer, it remains one of the leading cancers worldwide, both in terms of incidence and mortality. Patients with the subtype non-small cell lung cancer (NSCLC) with mutated EGFR can be treated with the EGFR-TKI osimertinib. The aim of the study is to evaluate the efficacy of first-line osimertinib and to identify predictive biomarkers for response using circulating tumor DNA (ctDNA).

Materials and methods: Blood samples were collected from 100 EGFR-mutated advanced NSCLC patients before the start of osimertinib treatment and after two weeks of treatment. Cell-free DNA was isolated from blood samples and analyzed with targeted next-generation sequencing using a 197-gene panel. The analysis resulted in successful sequencing of ctDNA from 96 patients.

Preliminary results: Mutations in ctDNA could be detected in 83/96 patients (86.5%) at baseline with a median of 2 mutations. 73/96 patients (76.0%) had a detectable EGFR mutation in baseline ctDNA. After two weeks of treatment 57/96 patients (59.4%) had detectable ctDNA mutations with a median of 1 mutation, and only 36/96 patients (37.5%) had a detectable EGFR mutation.

Conclusion: Sequencing of ctDNA from osimertinib-treated EGFR-mutated advanced NSCLC patients can be used to detect and monitor EGFR mutations. Future analyses will investigate if the observed clearing of ctDNA and EGFR mutations in ctDNA is predictive of response to osimertinib. The results will elucidate the potential of using ctDNA as a monitoring tool and as a biomarker for response and survival.

Keywords: Oncology, Other, Other

Proof-of-concept: Novel CBCT-based adaptive robust optimization in sinonasal cancer proton therapy

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Objectives: Proton therapy is highly sensitive to changes in the beam path. Variations in nasal cavity fillings can potentially deteriorate treatment quality for sinonasal cancer patients. In this study, we investigated novel strategies combining adaptation and anatomical robust planning by using anatomical variations from daily CBCTs.

Material & Methods: A retrospective study on five sinonasal cancer patients was performed. Plans for four robustness schemes were generated:

1. conventional plans (cRO)

2. adaptation after the first week with anatomical robust plans using the first five fractions' synCTs (afRO)

3. weekly adaptation with anatomical robust plans including the previous five fractions' synCTs (wafRO)

Results were evaluated by comparison of target coverage for fraction doses recalculated on the daily images and accumulated dose by deformable mapping of fraction doses to the planning CT.

Results: All approaches showed sufficient robustness in accumulated target coverage. Adaptive approaches using daily images showed comparable or better robustness than conventional plans and recovered two cases of underdosage for single fractions. Largest improvements in accumulated and daily target coverage were obtained for weekly adaptation.

Conclusion: Using prior daily images as uncertainty scenarios for plan adaptation with anatomical robust plans improved target coverage with superiority for weekly adaptation.

As conventional plans for this patient group were already quite robust with respect to target coverage, doses to OAR may take priority. However, adaptive CBCT-based robust optimization could be considered for cases with severe anatomical changes.

Keywords: Oncology, Other, Other

Rationale for combining stereotactic radiation and hyperthermia

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Priyanshu Sinha

Introduction: Indirect cell killing by Stereotactic radiation treatments (SRT) sensitizes cells to heat treatment. Thus combining heat with SRT should have greater anti-tumor effects.

Objectives: To investigate the potential of combining various SRT schedules with hyperthermia in our C3H mammary carcinoma, which response to both high radiation doses and heat treatment.

Materials & methods: A C3H mammary carcinoma grown in the right rear foot of CDF1 mice was used when at 200 mm3. SRT (X-rays), involves 1-5 fractions of 5-25 Gy administered in a one-week period. Hyperthermia entails immersing the tumor-bearing leg in a water bath and heating at 40.5-42.5OC for 60 minutes starting 30-240 minutes after the final irradiation. Endpoints include tumor growth delay (time to 5x treatment volume; TGT5) or local tumor control at 90 days; 3-days after the final radiation a clamped top-up dose was given to produce a dose-response curve from which the TCD50 value (radiation dose controlling 50% of tumors) was determined. Statistical analysis involved a Student's T-test ($p<0.05$ for both).

Results: The mean (+ 1 S.E.) TGT5 for control tumors was 5 days (+ 0.2) and this significantly increased to 22 days (+ 0.7) with 20 Gy treatment. Preliminary studies with a SRT treatment of 3 x 15 Gy resulted in a TCD50 value (+ 95% CI) of 30 Gy (+ 8). Heating tumors at 41.5OC 4-hours after the last irradiation significantly decreased this value to 10 Gy.

Conclusions: Findings are consistent with some degree of vascular damage and applying heat after SRT significantly enhanced local tumor control. Studies are ongoing to determine the optimal SRT schedule and heat treatment for the greater therapeutic benefits

Keywords: Oncology, Other, Other

Sequence dependencies and mutation rates of localized mutational processes in cancer

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Background:

Mutations accumulate across the cancer genome due to DNA damage and erroneous repair. Both damage and repair show an affinity for certain types of genomic segments in terms of nucleotide contexts and regionality. Yet, understanding the extent of variation in mutation rates across the genome continues to pose challenges, hindering accurate modeling of the genome.

Results:

We here describe how subsets of mutations occur in well-defined nucleotide contexts within genomic regions, enriching mutation rates up to 3,603-fold compared to the whole genome average. In addition, we observe localized behavior of mutational processes linked to POLE, UV, lymphomas, and signature 17b with unknown etiology, and report these findings in an extensive catalog of localized mutational processes in cancer.

Conclusion:

This catalog may provide a basis for future mutation rate modeling, cancer driver detection, and clinical tools for early cancer detection.

Keywords: Oncology, Other, Other

POSTER SESSION 13

Prevalence and Burden of Painful Temporomandibular Disorders in the Danish National Birth Cohort

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Background: Painful temporomandibular disorders (TMD-P) are one of the most common forms of chronic pain, but its prevalence and the psychological and physical comorbidities associated with it are unknown in Denmark. Aims: To assess the prevalence of TMD-P in the Danish National Birth Cohort (DNBC), and to examine its psychological and physical comorbidities as well as the extent of current disability. Methods: A subgroup of 33412 young adults (18 to 23 years old) of the DNBC were invited to participate in a pain survey that included the TMD pain screener to identify TMD-P cases, the patient health questionnaire-4 (PHQ4) to assess psychological distress, the patient health questionnaire-15 (PHQ15) to assess physical symptoms, and the graded chronic pain scale (GCPS) to assess pain intensity and related disability. The survey included questions about headache frequency, and previously diagnosed migraine and/or tension- type headache (TTH). Results: Out of 12383 respondents, 3269 (26.4%) screened positive for TMD-P (TMD-P+). TMD-P+ individuals had 2.01 and 2.15 times the prevalence of moderate and severe PHQ4 and PHQ15 scores compared to people who screened negative for TMD-P (TMD-P-). The prevalence of headaches (>15 days/month) was 3.5 more prevalent in TMD-P+ individuals. Diagnosis of both TTH and migraine was 1.27 more prevalent for the TMD-P+ individuals. High-impact GCPS scores were found in 22.7% of the TMD-P+ individuals, and there was a 2.65-fold greater prevalence in TMD-P+ comorbid with headaches, compared to only TMD-P+ or headache alone. Conclusion: The prevalence and burden of TMD-P is high for the age group.

Keywords: Dentistry, Epidemiology and biostatistics, Other

Semi-automated planimetric quantification of dental plaque using an intraoral fluorescence camera

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Dental plaque accumulation is quantified using clinical indices or else, the planimetric plaque index (PPI), which measures the relative area of a tooth that is covered by plaque deposits. Compared to clinical indices, the PPI has a higher discriminatory power, but traditional planimetry is a time-consuming analysis, as plaque-covered and clean tooth areas have to be determined manually for each image using an image-processing software.

Here, we present a method for semi-automated planimetric quantification of dental plaque allowing for rapid processing of up to 1000 images simultaneously. The method exploits the enhanced contrast between disclosed plaque, sound tooth surfaces and soft tissues in fluorescence images acquired with an intraoral camera. Careful execution of the clinical procedures and accurate image acquisition are crucial for a successful semi-automated identification of the plaque-covered areas. The method is suitable for planimetry on sound facial and oral tooth surfaces, on most composite resin restorations and on teeth with orthodontic brackets, but not on metallic and ceramic restorations. Compared to traditional PPI recordings, semi-automated planimetry considerably reduces the amount of time spent on the analysis, as well as the subjective human input, which increases the reproducibility of planimetric measurements.

Keywords: Dentistry, Other, Other

Effect of Dyslipidemia on Periodontitis: Findings from NHANES III

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Background: Periodontitis is a progressive inflammatory condition characterized by the destruction of tissues anchoring the teeth and has been associated with dyslipidemia. Thus, this study aimed to explore the pathways between dyslipidemia and periodontitis among adults sample during the third National Health and Nutrition Examination Survey (NHANES III).

Methods: The sample included 11817 US individuals aged >20 years. The structural equation modelling (SEM) approach included direct and mediated pathways (via dyslipidemia) considering age, sex, HbA1c, smoking, and alcohol consumption, plus two latent variables for socioeconomic status (poverty index and education) and for obesity (body mass index and waist-to-hip ratio). Dyslipidemia was defined according to the National Cholesterol Education Program (NCEP-ATP III). Periodontitis was clinically measured and set as a latent variable reflecting the shared variance of the number of surfaces with periodontal pocket depth [PPD]=4mm, PPD=5mm, PPD≥6mm, clinical attachment level [CAL]=4mm, CAL=5mm, CAL≥6mm, and furcation involvement.

Results: Dyslipidemia was directly associated with periodontitis, as well as obesity, smoking, age, socioeconomic status, and sex ($p<0.01$). High levels of HbA1c and obesity revealed a significant indirect effect on periodontitis via dyslipidemia ($\beta=0.002$; SE 0.010; $p=0.02$ and $\beta=0.036$; SE 0.012; $p<0.01$, respectively), and resulted in a total effect on periodontitis.

Conclusion: Dyslipidemia influenced periodontal conditions through a direct pathway and indirectly through HbA1c and obesity in the US population sampled during the NHANES III.

Keywords: Dentistry, Epidemiology and biostatistics, Inflammation

Workplace intervention among pregnant hospital employees - a protocol of a cluster randomized trial

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Background

Sick leave during pregnancy is frequent and reported by 36-75% of pregnant employees. This intervention applies preventive sessions with the pregnant employee, her manager and a midwife in addition to usual practice (standard pregnancy policy management) at Aarhus University Hospital, Denmark. It is hypothesised that pregnant employees who participate in preventive sessions with their manager and midwife in addition to AUH´s standard pregnancy policy management will have less sick leave and report better wellbeing compared to the reference group.

Methods

All departments at Aarhus University Hospital were cluster randomized. A total of 25 and 24 departments are allocated to the intervention and reference group, respectively. The intervention is protocolled with preventive sessions in addition to usual practice. The reference group receives usual practice. The primary outcome is mean number of days on sick leave during pregnancy measured at gestational week 30. Secondary outcomes are wellbeing measured as physical and mental health, general work ability, work-life balance, manager support, and completed work adjustments during pregnancy. Data on sick leave will be collected from the hospital payment system and survey data will be collected at inclusion and follow-up.

Discussion

This study is ongoing and will contribute to limited experimental research aimed to reduce sickness leave during pregnancy. The overall strength is the study design with easy access to study participants within a large hospital. Health care professionals are considered a risk population in relation to sick leave during pregnancy due to high work load, long working days, night work or shifts.

Keywords: Work environment and organisation, Public health, Other

Exposure levels of dust, endotoxin, and microorganisms in the Danish recycling industry

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BACKGROUND

The amount and recycling of domestic waste and subsequent numbers of employees in the recycling industry is expected to increase. This study aims to quantify current exposure levels of dust, endotoxin, and microorganisms and to identify determinants of exposure among recycling workers.

METHODS

This study investigates employees in the Danish recycling industry, who pre-treat or recycle domestic waste. We collected inhalable dust with personal samplers and analysed the samples for endotoxin (n = 172) and microorganisms (n = 102). Exposure levels of dust, endotoxin, and microorganisms and determinants of exposure were explored by mixed-effects models.

RESULTS

The overall geometric mean exposure level among workers pre-treating or recycling domestic waste was 0.6 mg/m3 for inhalable dust, 10.7 EU/m3 for endotoxin, 1.6×104 CFU/m³ for bacteria, 4.4×104 CFU/m³ for fungi (25 °C), and 1.0×103 CFU/m³ for fungi (37 °C). Workers handling metal, plastic, paper/cardboard, or mixed fractions were higher exposed than workers handling electronics and hazardous waste. For inhalable dust and

endotoxin, exposure levels for outdoor work were low compared to indoor work. Indoor ventilation decreased fungi exposure (up to 3.5 times).

CONCLUSION

Exposure levels of inhalable dust and endotoxin among recycling workers in Denmark are generally low; however, 8 - 58% of individual measurements are above established or suggested occupational exposure limit. Waste fraction and to a less degree, also location and ventilation were determinants of inhalable dust, endotoxin, and microorganism exposures, and thus an implication of this study is for the companies to use ventilation when working indoors.

Keywords: Work environment and organisation, Epidemiology and biostatistics, Public health

Use of video in telephone contacts at out-of-hour general practice - a register-based study

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Background

Out-of-hours general practice (OOH-GP) services are suffering from high workload, shortage of workforce, and long travel - and waiting time for patients, leading to political attention, debate, and reorganizations. Under the COVID-19 pandemic, video consultations was introduced as an alternative to face-to-face contact in Danish OOH-GP.

Aim

The aim of this study was to investigate the use of video in telephone contacts at OOH-GP, by studying user rate, patient characteristics related to the use of video, and effect on patient flows (i.e., triage outcome, follow-up contacts, hospital admissions).

Methods

We conducted a register-based study of video use in OOH-GP, including all Danish residents contacting OOH-GP services in the Regions of Central Denmark, Southern Denmark, Northern Denmark, and Zealand. The study population was followed from birth, immigration, or the 13th of March 2020 (whatever came last), until death, emigration, or the 1st of December 2021 (whatever come first). We used data from the OOH-GP electronic registration systems linked to national registers. We conducted descriptive analyses, calculating the proportion of video use in all telephone contacts during the study period. Regression models were used to measure the association between video use and triage outcome, follow up contacts, and the association between video use and patient characteristics.

Results

Data analyses are under conduction and will be presented at the PhD Day.

Keywords: Work environment and organisation, Epidemiology and biostatistics, Medical technology and diagnostic techniques

How Do Music Tempo and Dance Experience Affect Leading and Following in Salsa Dancing?

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Dance is a field rich in potential for studying many aspects of interpersonal communication and social interaction, such as social entrainment, interpersonal synchronisation, coordination, and synergy, in a naturalistic setting. However, to date very little research has been done in these fields using dance. In my PhD, I am using both behavioural and neuroscientific measures to probe some of them.

I will use a tapping task to explore how dance training and musical training affect the ability to extract metrical information from complex, yet naturalistic, rhythms. This will build on research previously carried out on musicians.

Furthermore, I will use motion capture to investigate how dance experience, and music tempo, affect interpersonal coordination, including synchronisation, leading, and following, in a naturalistic dance setting.

Lastly, I will use a two-person foot tapping task with concurrent EEG hyperscanning to determine how music tempo, amount of rhythmic information, and dance experience, affect leading and following behaviour. I will also analyse the neural correlates of the foot tapping movement and the leader/follower roles.

These studies will allow me to explore various aspects of interpersonal interaction, especially leading and following in joint action, and the effect of dance experience and music tempo on this.

Keywords: Other, Other, Other

Effect of a Point-Of-Care Ultrasound-Driven vs Standard Diagnostic Pathway on 24-Hour Hospital Stay in Emergency Department Patients with Dyspnea (POCUS PATHWAY) — Study Protocol for a Randomized Controlled Trial

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Introduction

Point-of-care ultrasound (POCUS) poses as a potential valuable test in the diagnostic work-up of emergency department (ED) patients with dyspnea. The clinical performance of focused lung and cardiac ultrasound is well-founded to equalize or outperform other diagnostic tests currently used for the spectrum of disorders causing dyspnea, but the clinical benefit remains unclear.

To our knowledge, no studies have found evidence that a diagnostic pathway guided by POCUS results in better patient outcomes. However, recent studies have found promising results for a simplification of the healthcare process, i.e., shorter hospital admission. Therefore, in ED patients with dyspnea, we aim to determine the effect of a point-of-care ultrasound-driven diagnostic pathway on 24-hour hospital stay when compared to the standard diagnostic pathway.

Methods

In this randomized, controlled, multicenter trial, we will include adult ED patients with dyspnea as chief complaint. Eligible patients will be randomly allocated in a 1:1 ratio to either a POCUS-driven diagnostic pathway (intervention) or a standard diagnostic pathway (control). The primary outcome measure will be the proportion of patients with a hospital length-of-stay shorter than 24 hours. Secondary outcomes include hospital length of stay, image resources, 72-hour revisits, 30-day hospital-free days, time to treatment, and patients' experiences.

Discussion

This trial will investigate the clinical benefit of a POCUS-driven diagnostic pathway where treating ED physicians apply POCUS and integrate findings into clinical practice. We hypothesize that such a POCUS intervention will lead to a more efficient healthcare process.

Keywords: Other, Respiratory system, Cardiovascular system

Constructing a pipeline for calling SNPs from deep, targeted cfDNA-seq data

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Detection of circulating tumor DNA in blood increasingly attracts attention as a cancer biomarker. For instance, early and reliable detection of cancer mutations in blood may enable early detection of relapse and adjustment of treatment based on the tumor mutational landscape. Yet accurate detection of tumor mutations in deep, targeted sequencing of cell-free DNA remains challenging as the low frequency of mutations in blood makes them hard to discriminate from background signals such as artifacts generated from the sequencing process. To identify variants present in deep, targeted cfDNA-seq data, we are developing a pipeline for tumor/normal paired datasets to call low-frequency somatic variants with high sensitivity and specificity, especially for UMI-seq data. The pipeline constitutes of three main steps: alignment, UMI consensus creation, and variant calling. We compared different UMI consensus strategies and five variant calling algorithms. This work could improve the quality of deep, targeted cfDNA-seq analysis and enables its widespread adoption in the clinic.

Keywords: Other, Other, Other

Progressive slowing of clonic phase predicts postictal generalized EEG suppression.

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Postictal generalized EEG suppression (PGES) has been reported as surrogate marker of sudden unexpected death in epilepsy (SUDEP). It is though still unclear which ictal phenomena lead to prolonged PGES and increased SUDEP risk. Semiology features of convulsive seizures (GCS type 1: bilateral, symmetric tonic and clonic phase) have been reported as PGES predictor. Progressive slowing of clonic phase (PSCP) has been observed in GCSs, with gradually increasing inhibitory periods interrupting the tonic contractions. We hypothesized that PSCP is associated with prolonged PGES.

We analyzed 90 bilateral convulsive seizures in 50 consecutive patients recruited to video-EEG. Five raters independently assessed the presence of PSCP, blinded to all other data. PGES and seizure semiology were evaluated independently. We determined inter-rater agreement for the presence of PSCP, and we evaluated its association, as well as that of other ictal features, with the occurrence of PGES, prolonged PGES (≥20s) and very prolonged PGES (≥50s) using logistic regression analysis.

We found substantial IRA for the presence of PSCP (Gwet´s AC1=0.655). PSCP was independent predictor of PGES and prolonged PGES ($p<0.001$). All seizures with very prolonged PGES had PSCP. GCS type 1 was an independent predictor of PGES ($p=0.02$) and prolonged PGES ($p=0.03$), but not of very prolonged PGES. Only half of the seizures with very prolonged PGES were GCS type 1.

PSCP predicts prolonged PGES, emphasizing the importance of gradually increasing inhibitory phenomena at seizure termination. These phenomena may provide basis for algorithms implemented into wearable devices, for identifying GCS with increased SUDEP risk.

Keywords: Other, Other, Other

POSTER SESSION 14

Proteomes of the Tg-SwDI Murine Model of Alzheimer's Disease

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Aging is an unavoidable risk-factor for dementia, and with the elderly population growing worldwide, dementia is a growing health problem already of considerable size. Alzheimer's disease (AD) is by far the most common type of dementia. Despite being first described more than a century ago, and having been the subject of intense research, finding a treatment for the disease has been elusive and an astonishing number of phase 3 clinical trials have failed to produce a positive outcome for patients. The etiology of the disease, initially thought to be relatively simple, has become controversial and now appears more complicated. To complicate things further, despite 2/3 of AD patients being female, scientific in vivo research has traditionally, as in many fields, focused solely on male subjects.

A step back to further investigate the molecular basis of the disease is required and studying gender variability is necessary to elucidate the reason for females being more prone to developing the disease, which may contribute to an overall better understanding of the disease.

We have undertaken deep discovery proteomics analysis of blood plasma, cerebral cortex and hippocampus from male and female mice, comparing wild-type mice with Tg-SwDI mice - an established AD murine model. In our preliminary analysis, we have found the proteomes of female mice to be more severely dysregulated than those of the males and we have identified general and gender/tissue specific phenotypes of dysregulated pathways, which we hope will contribute to shedding further light on the molecular basis of this detrimental disease of the mind.

Keywords: Clinical neuroscience, Animal models/disease models, Molecular metabolism and endocrinology

Biomarkers of disease activity in Chronic Inflammatory Demyelinating Neuropathy

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Background: Biomarkers for predicting and monitoring disease activity in patients with Chronic Inflammatory Demyelinating Neuropathy (CIDP) are lacking. In other autoimmune diseases, lower sex hormone levels, higher leptin levels and high levels of free light chains have correlated with disease activity.

Hypothesis: For CIDP patients in steady state treatment with immunoglobulin, we hypothesis that high levels of testosterone and estradiol and low levels of light free chains and leptin can predict who can be tapered off treatment without clinical deterioration. Further, we hypothesize that CIDP patients will have lower sex hormone levels and higher leptin and free light chains levels than healthy controls.

Methods: Plasma were collected from 55 CIDP patients in a previous study where patients stable on immunoglobulin treatment were tapered off immunoglobulin and followed with functional testing. Clinical information and plasma evaluations from the first and the last visit are used. Additional plasma from 55 healthy age (+/-2 years) and sex matched controls are currently being collected. Plasma from CIDP patients and healthy controls will be analysed at Department of Clinical Biochemistry, AUH, using standard analysis, for levels of: Testosterone, dehydroepiandrostreonsulfate (DHEAS), estradiol, estron, LH, FSH, albumin, SHBG, leptin and free light chains.

Analysis: Biomarker levels will be compared between CIDP patients who deteriorate and those who do not, and between CIDP patients and healthy controls.

Time frame: The study is expected to be completed in March 2023.

Keywords: Clinical neuroscience, Inflammation, Molecular metabolism and endocrinology

Rhythm perception and experience of groove in cochlear implant users

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Despite the success of cochlear implants (CIs) when it comes to regaining speech perception, they remain poor in conveying music. However, CI users typically perform on par with normal hearing (NH) controls in simple rhythmic tasks. Yet, being able to perceive more complex real-world musical rhythms is important for the experience of groove, i.e., the pleasurable urge to move to music. NH listeners show higher groove ratings for medium rhythmic complexity compared to high and low complexity, implying that there is a "sweet spot" at which a maximum pleasurable sensation of wanting to move is experienced. In CI users, the sensation of groove remains unexplored.

In this online study, we will investigate CI users' rhythm perception and experience of groove, as compared to NH controls.

100 CI users and 100 NH controls will be recruited for this study. Stimuli consist of drum patterns varying in rhythmic complexity, based on degree of syncopation (low, medium, high) and number of instruments (one, two, three; different combinations of snare drum, kick drum and hi hat). Participants are asked to rate "wanting to move" and "experienced pleasure" for each drum pattern. This allows us to investigate whether CI users show a different "sweet spot" of complexity and whether this depends on the number of instruments.

This is work in progress. Preliminary findings of rhythm perception and experience of groove in CI users will be presented at the event.

As the sensation of groove has yet to be investigated in CI users, this online study is an original contribution to the research area of music perception in CI users.

Keywords: Clinical neuroscience, Ear, nose and throat (ENT), Psychiatry, psychology and mental health

Mortality after discharge from post-acute comprehensive inpatient rehabilitation following moderate to severe acquired brain injury – an overall prognosis study

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Introduction:

Optimised treatment has increased survival rates in acute care for patients with an acquired brain injury. Severely affected patients displaying recovery potential are typically referred to comprehensive neurological inpatient rehabilitation. Rehabilitation aims to assist patients in regaining maximum functioning and achieving a meaningful life post-injury. Hereto, rehabilitation appears effective for most patients. Yet, some patients may have a poor prognosis post-discharge (i.e. increased mortality). Investigating the overall prognosis may provide an insight into the current care and referral system.

Objectives:

To describe the overall prognosis for all-cause mortality after discharge.

Methods:

A retrospective cohort of patients admitted to Hammel Neurorehabilitation Centre (HNC) between March 2011 and February 2022 was created. Personal health-data, including date of death, were extracted from the electronic health records. Inclusion criteria were: first ever admission, distinct rehabilitation course and complete diagnostic information. Mortality rates were estimated for the first five-years post-discharge.

Results:

A total of 5,872 patients were included. Patients were mostly male (62%), older than 41 years (83%) and suffered a stroke (61%). Fifteen percent of patients (n=915) died during follow-up; hereof 310 patients (34%) deceased within the first year post-discharge. Mortality rates were highest in the first year post-discharge.

Conclusion:

A considerable 5-year mortality post-discharge from comprehensive rehabilitation was observed in the present cohort of patients with moderate-severe ABI. This observation should be considered and investigated further.

Keywords: Clinical neuroscience, Rehabilitation, Epidemiology and biostatistics

Neuropathic pain in diabetic polyneuropathy

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Background: Diabetic polyneuropathy (DPN) is a common complication of type 2 diabetes (T2D). Up to 50 % of patients with DPN suffer from neuropathic pain (P-DPN). The relationship between severity in sensory symptoms, signs and the development of pain in DPN is relatively unstudied. Neuroinflammation is thought to contribute to the development of DPN and P-DPN. There is a lack of prospective studies on DPN and P-DPN.

Aim: To study the development of DPN and pain in patients with T2D over time, identify risk factors and describe the natural history of nerve changes that occur during the course of the disease.

Methods: Originally, 389 patients with newly diagnosed T2D and a likelihood of polyneuropathy as assessed by questionnaire and 97 healthy controls were recruited to establish the diagnosis of DPN. All participants from the baseline study will be invited for a 5 year follow up examination

Results: As of November 1st 2022 304 participants have been invited and 148 participants (follow-up rate: 49 %) have agreed to a follow-up visit. Of these, 115 participants (88 diabetes patients + 17 controls) have completed the examinations. Mean follow-up time was 4.2 (SD 0.6) years and mean diabetes duration was 6.2 (SD 2.7) years and 10.8 (SE 2.7) years at baseline and follow-up, respectively. Data on symptoms and diagnostic changes are currently being processed and the study is ongoing

Perspectives: With the lack of prospective studies in DPN, this study will provide a unique insight into the natural history of DPN and P-DPN.

Keywords: Clinical neuroscience, Basic neuroscience, Molecular metabolism and endocrinology

Cholinergic alterations in the pedunculopontine nucleus of patients with Parkinson's disease treated with spinal cord stimulation for gait problems.

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Introduction: Among the symptoms of Parkinson's disease (PD) that cannot fully be relieved by dopaminergic medications are the debilitating gait problems of PD. These include tripping steps and freezing of gait. Spinal cord stimulation (SCS) has been suggested as a new treatment. Evidence implicates a cholinergic involvement due to degeneration of the pedunculopontine nucleus (PPN). The PET tracer 18F-FEOBV targets the vesicular acetylcholine transporter and can provide information on the cholinergic integrity of the brain.

It is the aim of this study to investigate the possible cholinergic changes after 6 months of treatment with SCS in patients with PD and gait problems.

Methods: 13 patients with idiopathic PD will have a brain 18F-FEOBV PET and MRI. Hereafter, they will all have a SCS devise implanted at thoracic level. 7 patients will receive active microburst stimulation while 6 patients will serve as controls with no stimulation. After six months all participants will repeat the 18F-FEOBV PET scan.

The individual PET-images will be co-registered to their corresponding MRI which is transferred from native space to the Montreal Neurological Institute common space in PMOD as well as in the Computational Anatomy Toolbox in Statistical Parametric Mapping, running on MATLAB. Analyses of the standardised uptake values will be conducted on volume of interests, including the PPN and thalamus, derived from the Brainstem Navigator atlas as well a modified Hammers N30R83 atlas.

Perspectives: This study will provide knowledge on changes induced by SCS and could also identify levels of abnormal cholinergic neurotransmission that could predict the outcome following SCS therapy.

Keywords: Clinical neuroscience, Other, Other

Treatment of chronic cluster headache with burst and tonic occipital nerve stimulation; a case series

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Background: Chronic cluster headache (CCH) is a rare but severely debilitating primary headache. Growing evidence suggests that occipital nerve stimulation (ONS) can offer effective treatment in patients with severe CCH for whom conventional medical therapy does not have sufficient effect. The paraesthesias evoked by conventional (tonic) stimulation can be bothersome and may thus limit therapy. Burst ONS produces paraesthesia-free stimulation, but the amount of evidence on the efficacy of burst ONS is scarce.

Materials and methods: Fifteen patients with CCH were treated with ONS, nine of whom received burst stimulation either as primary treatment or as a supplement to tonic stimulation. Results were assessed in terms of frequency of headache attacks per week and their intensity on the numeric rating scale as well as the patients' global impression of change (PGIC) with ONS treatment.

Results: At a median follow-up of 38 months, 12 out of 15 (80%) patients reported a reduction in attack frequency of at least 50% ($P < 0.001$). Seven of these patients were treated with burst ONS. A significant reduction was also seen in maximum pain intensity. Ten patients stated a clinically important improvement in their headache condition, rated on the PGIC scale.

Conclusion: ONS significantly reduced the frequency and intensity of headache attacks. As burst stimulation is imperceptible and was well tolerated, burst ONS seems to function well alone or as a supplement to conventional tonic ONS as treatment for CCH. However, larger prospective studies are needed to determine whether the effect can be confirmed and whether the efficacy of the two stimulation paradigms are even.

Keywords: Clinical neuroscience, Other, Other

Development of an implementation strategy in collaboration with physiotherapists and chiropractors - A user involvement study

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Introduction: Low back pain (LBP) is the leading cause of disability worldwide. Providing evidence-based practice (EBP) for patients with LBP is more cost-effective compared with non-EBP. To help health care professionals provide EBP, several clinical practice guidelines have been published. However, a relatively poor uptake of the guidelines has been identified in a Danish context among physiotherapist and chiropractors.

Objectives: The aim of phase 2 of the PhD project is to develop a contextually designed active implementation strategy in collaboration with the health professionals.

Design and methods: The PhD project is an implementation-science study using a mixed methods explorative sequential design, including three phases. In Phase 1 the barriers and facilitators by using the guidelines in clinical practice was explored in a qualitative study.

In Phase 2 the implementation strategy is developed. The strategy is contextually designed as it is developed in collaboration with stakeholders, and addresses the identified barriers and facilitators found in phase 1. In Phase 3 the implementation strategy will be evaluated in an implementation process evaluation study.

Development (phase 2): By conducting four workshops with health professionals and practice consultants, a two-track stepwise strategy has been developed. Track 1 addresses the health professionals' lack of knowledge and skills by webinars and e-learning videos. Track 2 addresses a change of culture in the clinics by supervisions and audits. The change of behaviour will be supported by reminders, goalsetting and visits by an implementation consultant.

Keywords: Rehabilitation, Health education and simulation-based training, Other

Feasibility testing Robotic technology (ROBERT®) as an intervention to enhance muscle strength in very weak muscles in inpatient rehabilitation after spinal cord injury

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Introduction: There is a lack of knowledge about how to rebuild voluntary muscle strength in very week muscles in subacute inpatient rehabilitation following a spinal cord injury (SCI). The rehabilitation robot ROBERT® (Life science Robotics, Denmark) enables the patient to perform movements with gravity eliminated and as they regain strength to add resistance to the movement.

The objective of this preliminary study is to test and explore the feasibility of a proposed intervention focusing on muscle training to enhance strength in hip flexion subacute after SCI by using ROBERT®. This to explore if it is feasible to conduct a pilot randomised controlled trial.

Methods: An explorative feasibility study using a mixed-method design was conducted in November 2021 until June 2022 at an inpatient specialised neurorehabilitation center in Denmark. The following parameters were evaluated:

1. Recruitment capability
2. Data collection procedures and outcome measures
3. Procedures and conduction of the intervention
4. Time and resources
5. Patient perspectives of acceptability and suitability of the intervention and measurements

Results: 4 participants completed a training protocol for hip flexion strength training using ROBERT® 3 times a week for 4 weeks. The analysis is ongoing and the results will be presented at the PhD day in January 2023.

Keywords: Rehabilitation, Clinical neuroscience, Other

The consolidating effect of multiple sclerosis and advanced age diminishes neuromuscular function in older people with multiple sclerosis

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Background: The prevalence of older (>60 years) people with multiple sclerosis (pwMS) is increasing. This introduces several challenges as both MS and aging separately affect neuromuscular function negatively.

Aim: Using a cross sectional study design, we investigated the neuromuscular function in pwMS and healthy controls (HC) in three age subgroups (young, middle-aged, and old).

Methods: Maximal muscle strength (Fmax) and rate of force development (RFD) of the knee extensors (KE) and plantar flexors (PF) were assessed using a dynamometer. In addition, voluntary activation (VA) and resting twitch (RT) was measured using the interpolated twitch technique in both muscle groups.

Results: Fmax, RFD, and VA of KE and PF was reduced in pwMS (n=53) compared to HC (n=48) and reduced with age in KE for both groups (except for VA) and only in PF for pwMS. This reduction with increasing age differed in trajectory between pwMS and HC. As pwMS showed reductions from young to middle-aged and HC from middle-aged to old in KE. VA and RT did to some extend follow the same patterns of reduction as neuromuscular function.

Conclusion: The negative effects of MS and aging consolidated in neuromuscular function of the PF but to a small degree in the KE. RFD showed especially large deficits (upwards of ~70% deficits) for pwMS compared to HC across age groups. Findings could partly be explained by reduction in VA and RT; however, further investigations of neural regulation are needed to explain the large RFD deficits.

Keywords: Rehabilitation, Clinical neuroscience, Public health

Flash Talk Sessions

Flash Talk session 1

Mind the gap! Incorporation of the social determinants of health in home care nursing - a quest for health equity and social justice.

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Background: Nurse's play an important role in ensuring health equity and social justice. Current changes in healthcare shift the focus of care and treatment from hospitals to homes. Home care nursing has attributes that make it an ideal practice to work towards health equity. One way to do so which has been widely advocated is by addressing the social determinants of health (SDoH).

Aim: To investigate and describe how home care nurses incorporate the social determinants of health in the planning and delivering of care for their patients. And by that extract clinical wisdom and expertise from home care nurses and let practice inform theory. The overall aim is to facilitate the incorporation of SDoH in home care nursing practice and thereby contribute towards more health equity and social justice for patients.

Method: The project has an interpretive qualitative design as described by Benner. Participant observation and small group interviews will be used for data collection. Twelve nurses from two districts will participate. A scoping review on social justice and nursing will be conducted at the onset and will assist in framing the project in a social justice perspective. In the scoping review the five-stage approach proposed by Arksey and O'Malley is employed. The JBI Manual for Evidence Synthesis and the PRISMA extension for Scoping Reviews checklist are additionally used for guidance and support. CINAHL Complete, Medline (PubMed), Embase, Web of Science, Scopus, APA PsychInfo and Academic Search Premier were searched in June 2022 using the search terms "social justice" (title/abstract) and "nurse" or "nursing" (all fields) identifying a total of 1559 different sources.

Keywords: Public health, Qualitative research, Reviews and meta-analyses

Implementing telehealth at a national scale in Denmark

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Background:

Telehealth solutions are viewed as a central part of the future provision of healthcare and may reduce healthcare costs while also improving patient-relevant outcomes and quality of care. However, positive results are not robust across studies and scale-up and implementation remain a challenge. Yet, large-scale implementation of telehealth remains understudied and more knowledge is needed about the key mechanisms of telehealth and what facilitates and hinders implementation.

In 2016, it was decided that a home-monitoring telehealth intervention for patients with COPD 'TeleCOPD' should be implemented in Denmark. This presents a unique chance to study how telehealth solutions are implemented in practice within a national scale framework, and thereby provide knowledge for future large-scale implementations.

Design and methods:

This project aims to investigate the national implementation process of TeleCOPD. The PhD employs a two-phased mixed methods design to investigate the process on multiple levels. The first phase consists of two qualitative studies. It provides an in-depth understanding of how the wider context as well as the role of healthcare professionals influence the implementation process. Study one investigates the process on a political-administrative level seeking to understand the process from a top-down system-wide perspective. Study two investigates the process from a frontline perspective that seeks to understand how TeleCOPD is implemented and translated into daily practice by healthcare professionals. Knowledge from these two studies will then be used in study three to systematically examine what impacts implementation using a survey design.

Keywords: Public health, Qualitative research, Medical technology and diagnostic techniques

Working life exposome, lung function, and obstructive lung disease among men and women

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COPD (chronic obstructive pulmonary disease) and asthma are the two most prevalent contributors to the global respiratory disease burden. Occupational exposures contribute to the development and se-verity of COPD and asthma.

Knowledge on the association between occupational and non-occupational exposures and develop-ment of COPD and asthma mainly originates from data analysed with a 'one exposure, one disease' approach. Most individuals are exposed to both potentially hazardous and beneficial exposures, hence assessing the total burden of exposure is crucial. The exposome concept allows us to investigate com-bined exposures and disentangle the importance of specific exposures.

The overall aim of this study is to investigate how long-term working-life exposome affects lung health. We will examine the association between working life exposome and change in lung function, and risk of COPD and asthma.

The study population (n = approx. 5000) consist of two existing population-based cohorts, the Europe-an Community Respiratory Health Survey (ECRHS)) and the French Constances cohort. Clinical infor-mation on lung function, COPD and asthma is available at multiple time points together with abundant information on occupational and non-occupational exposures. A European Job exposure matrix (EU-ROJEM) will be applied to assess multiple individual occupational exposures from job titles.

The analyses will follow an exposome approach. Correlations between the independent variables will be assessed followed by a data driven variable selection. The retaining variables will be analysed using e.g., Bayesian Kernel Machine Regression, Weighted Quantile sum Regression and/or Lasso.

Keywords: Public health, Epidemiology and biostatistics, Respiratory system

Patient-perceived treatment burden and associated factors in the Danish adult population

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This PhD project aims to conduct a population-based investigation of patient-perceived treatment burden and how this relates to multimorbidity patterns, healthcare utilisation and mortality.

Worldwide, healthcare systems struggle to deliver coherent healthcare of high quality to patients with multimorbidity and to overcome the social inequality in the distribution and consequences of multimorbidity. The overall challenge is that healthcare systems are not structured to manage multimorbidity – neither organisationally nor professionally. At a patient level, navigating complex healthcare systems and treatment regimens often create complex and fragmented care pathways with a considerable workload resulting in patient-perceived treatment burden. This may lead to poor compliance and poor health-related quality of life which is ineffective and costly. A population-based investigation of treatment burden will provide essential information to guide future patient-centred interventions and reorganisations to improve healthcare and reduce treatment burden for patients with complex multimorbidity.

The project consists of four population-based link-studies of national health surveys and longitudinal register data to: 1) identify and characterise patient groups with multimorbidity patterns (disease combinations), 2) investigate the association between multimorbidity patterns and treatment burden, 3) investigate the association between treatment burden and healthcare utilisation, 4) investigate the association between treatment burden and mortality. Combined, this will help identify high-risk patient groups with complex multimorbidity that may be in special need of integrated care.

Keywords: Multimorbidity, Public health, Epidemiology and biostatistics

Inequality in prenatal care participation in Denmark

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Aim

It is unknown what characterises those who have inadequate participation in the universally provided prenatal care program in Denmark. Therefore, the aim of this study is to explore potential social differences in attending the Danish prenatal care program.

Methods

In this nationwide register-based study, the study population will consist of the families of all children born in Denmark in the period 2000-2022, with approximately 60,000 births per year. The exposures will be maternal age, geography (region/municipality), ethnicity, education, marital status, and maternal and paternal psychiatric and chronic illnesses. The dependent variable will be the use of prenatal care measured as any use, frequency of use, and early prenatal care, i.e., attendance to the routine first trimester hospital visit. Data will be collected from the National Patient Register (NPR), the DREAM database, and the national registers within Statistics Denmark. Odds Ratios will be estimated using Binary and Ordinal Logistic Regression Analysis. The regression models will be designed as random coefficient models to account for multiple births by the same mother. In addition, a Latent Class Analysis will be performed to identify latent non-user subgroups.

Perspectives

The PhD-project is a part of the larger 'One Stop' project on inequality in prenatal care focusing on future differentiated prenatal care. Thus, the results from this particular study will lay the foundation of tailoring recruitment strategies and interventions to reach the mothers that are least likely to use prenatal care. Further, it will inform decision-makers and health professionals within prenatal care.

Keywords: Socio-economic conditions, Public health, Other

Dietary quality in adolescents as a risk factor for painful temporomandibular disorder in young adult members of the Danish National Birth Cohort

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Background:

Painful temporomandibular disorder (TMD-P) is the most common non-odontogenic-related chronic orofacial pain. It is associated with various degrees of disability due to jaw pain and dysfunction and seems to be a risk factor for headache development. The most well-established risk factors for TMD-P are gender, age, psychosocial factors, and pain sensitivity phenotype. Although there is some evidence that the presence of TMD-P affects dietary choice and nutritional intake, the way that nutritional factors may influence the development of TMD-P has not been explored. One proposed reason for the relationship between TMD-P and diet is that proinflammatory markers increased in chronic pain and obesity situations.

Identifying risk factors for TMD-P is critical, as it could eventually be a target for either prevention or early intervention. Based on this, we aim to investigate adolescent diet as a potential risk factor for TMD-P and headaches.

Study design:

A total of 33412 young adults from the Danish National Birth Cohort (DNBC) who contributed with diet data when they were 14 years old (Healthy Eating Index at age 14 (HEI-14)) were invited to answer a questionnaire including TMD symptoms and headaches when they were 18 to 23 years old. The response rate was 37%. Based on their replies, they will be categorized into two groups regarding TMD-P status (TMD-P positive and TMD-P negative) and similarly two groups regarding headache status.

Data analyses:

Existing data on the adolescent diet will be evaluated as risk factors for TMD-P and headache case status through multiple logistic regression modeling adjusted for known confounders.

Keywords: Dentistry, Epidemiology and biostatistics, Public health

Time-trends in cholangiocarcinoma incidence – a Danish nationwide cohort study

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Background and Aims: Cholangiocarcinoma (CCA) is a usually fatal primary liver cancer originating from the biliary epithelium. Up-to-date data on incidence are crucial for our understanding of the disease and, therefore, we set out to examine incidence of CCA in a nationwide Danish cohort.

Methods: We included all Danish patients, N=2600, with an ICD-10 diagnosis code of CCA (intrahepatic [iCCA]: C221; extrahepatic [eCCA]: C240) in the Danish Cancer Registry, between 1999-2019. We computed the standardized annual incidence rates of CCA and standardized to the Danish population in 1999. We estimated annual change using a Poisson regression model.

Results: The standardized incidence rate (SIR) for iCCA increased from 0.41 (95% confidence interval [CI] 0.26-0.63) in 1999 to 1.90 (95% CI 1.55-2.31) in 2019 (Incidence rate ratio [IRR]: 4.59 [95% CI 2.89-7.28]). The SIR for eCCA decreased from 1.75 (95% CI 1.41-2.14) in 1999 to 0.85 (95% CI 0.62-1.13) in 2019 (IRR: 0.48 [95% CI 0.34-0.69]). For total CCA, the IRR was 1.29 (95% CI 1.01-1.64) and the annual increase was 2.51% (95% CI 1.81-3.22).

Conclusion: The incidence of CCA has increased since 1999, driven by a 4-fold increase in incidence of iCCA while incidence of eCCA has decreased by half. The reasons for this pattern are unclear but are likely due to changing environmental exposures over time.

Keywords: Gastroenterology and hepatology, Epidemiology and biostatistics, Gastrointestinal surgery

Obsidian in anastomotic healing after rectal cancer resection:

Preliminary results of a prospective clinical feasibility study

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Anastomotic leakage following rectal cancer resection is a serious complication with a high incidence, despite previous attempts to eliminate it. One recent method that has shown great promise is the use of Obsidian, an autologous fibrin matrix in combination with thrombocytes, derived from the patient's blood, used to promote healing. Its feasibility and practicality in the context of rectal anastomosis, however, requires further research. The aim of this study is to assess the feasibility of Obsidian use as a supplement in rectal anastomosis creation during minimally invasive rectal cancer resection.

This feasibility study will include 50 patients undergoing rectal cancer resection with anastomosis with minimally invasive surgery at the Department of Surgery, Aarhus University Hospital. Use and application of Obsidian is categorized as 'Complete', 'Almost Complete' and 'Incomplete', using our own predefined rating assessment scale. To deem the use of Obsidian feasible, we require the application be rated 'Complete' or 'Almost complete' in at least 90% of patients.

Patient inclusion began in December 2021. We have included 27 patients thus far and hope to have included all 50 by February 2023. In total, 10 of the applications can be categorized as 'Complete', 17 as 'Almost Complete' and 0 as 'Incomplete'. The application of Obsidian has thus been feasible in 27 of 27 patients.

We expect the application of Obsidian to be feasible in over 90% of the patients. If this holds true, we will participate in a large, international, randomized multi-centre study investigating the effect of Obsidian use on the rate of anastomotic leakage within 30 days after rectal cancer resection.

Keywords: Gastrointestinal surgery, Oncology, Other

To coordinate or not to coordiante: Social bias effects on musical communication.

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The modern world relies more than ever on globalized interactions and communications between cultures. To generalize across the global cultural variability, distinctions such as 'collectivistic' and 'individualistic' cultures have been made. One such 'collectivistic' culture is the Chinese, where the ideal is to meet the duties and obligations of one's social role to maintain group harmony. On the other hand, danish culture is considered 'individualistic', appertaining to the cultural ideal of expressing one's uniqueness and to be agree agent that acts according to one's own volition. Additionally, cultures generalized under these terms further distinguish themselves in inter-individual relations. Such 'social biases' has been a social marker to understand how people from around the world interact and communicate. In my PhD project I hope to study the effect of social biases on music interaction between participants from China and Denmark when interacting in a signaling game. Using metrics such as coordination, asymmetry, and convergence speed as proxies for a musical communication success, I hypothesize that the in-culture bias is stronger for collectivistic cultures and thus constitutes a dyad constellation (Chinese-Chinese) that marks the greatest foundation for a successful musical interaction. Alternatively, cross-cultural dyads (Chinese-Danish) will coordinate the least. Using first a behavioral paradigm to assess the metrics that elucidates cross-cultural differences, I wish to follow up with an exploratory neural imaging study using MEG to address the neural correlates of the effects of social biases on coordination between cultures.

Keywords: Other, Other, Socio-economic conditions

Improving guidance for researchers to engage patient partners in the research process

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Background:

Engaging patients as partners in the research process can strengthen the quality of health service research by incorporating the perspective of those ultimately affected by the research. However, how researchers can best engage patient partners, and with what impact, is still not clear. The aim is to develop an intervention to improve the partnership between researchers and patient partners.

Methods:

The Complex Intervention framework is used to guide three studies each answering a 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 its impact on research outputs.

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

Study 3. How can guidance for researchers be improved in order to engage 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 using interpretive descriptions. Patient partners and researchers will be engaged in a steering committee during the PhD project.

Perspectives:

This project will contribute with new knowledge to improve the partnership between researchers and patient partners. The results are expected to be generalizable for research within different patient groups and can form the basis for nationwide strategies.

Keywords: Public health, Qualitative research, Other

Do we have time for End-of-Life care, in Danish Intensive Care Units (ICUs)?

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Abstract

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Title:

Do we have time for End-of-Life care, in Danish Intensive Care Units (ICUs)?

Background:

ICU staff must accurately combine information about clinical signs, the patient's medical history and the acute illness, to be capable of diagnosing the dying patient in time to deliver EOL care interventions

Aim:

The study aims to characterise the dying ICU patients in ICUs on all hospitals in Denmark and examine the level of intensive therapy up until death.

Methods:

A register-constructed population of 1360 patients ≥18 years of age, with a minimum ICU-stay of four days, who died during an ICU admission or within seven days from discharge from an ICU in Denmark from January to December 2020.

Relevant data on age, gender, comorbidity, use of intensive care therapy and time from initiation and termination of intensive care therapy to death will be extracted from the Danish Intensive Care database (DID).

Conclusion:

Together with characteristics of dying patients at Danish ICUs, our study shows that there is a window of opportunity to perform End-of-Life care. Hence further research is needed to determine the use and focus on EOL care interventions in Danish ICUs.

Keywords: Other, Other, Other

Associations between General Practitioner factors and video use in out-of-hours General Practice – A register-based study

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Keywords: After hour care. Remote consultation. Primary care physicians.

Background: At out-of-hours general practice (OOH-GP) services in Denmark, video was implemented in telephone contacts at the start of the Covid-19 pandemic. Use of video has the potential to reduce patient waiting time, increase patient satisfaction, reduce GP workload, and reduce the cost of primary care. The decision to use video or not lies with each general practitioner (GP) at the telephone triage center, as they can send the patient a text message with a link to activate the camera in their smartphone. There are major variations in the use of video among the GPs. Several GP-related factors may be related to this variation, and more knowledge in this area is important to ensure successful and optimal use of video within the OOH-GP.

Aim: To explore associations between variation in OOH-GP video use and GP factors (e.g. age, sex, seniority, activity level).

Methods: Data from the OOH-GP registration system, Authorization registries, Statistics Denmark, and the Danish National Health Service Register is used. The data include GP factors (e.g. age, sex, seniority, activity level), video use in OOH-GP telephone contacts, and patient factors (e.g., age, sex, civil status, occupation, comorbidity). Descriptive analysis will be conducted to calculate the proportion of video consultations per 100 telephone contacts. Linear regression analysis will be used to investigate associations between GP video user rate and GP factors. We adjust for case mix, using patient factors such as age, sex, and comorbidity.

Results and Conclusion: The study is currently under conduction.

Keywords: Public health, Other, Other

Identification and development of a rehabilitation intervention to ensure adherence to life-long follow-up for patients with Myotonic dystrophy type 1 (DM1).

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Background: Myotonic dystrophy type 1 (DM1) is a multisystemic neuromuscular disease causing progressive physical and cognitive impairment. Patients are often involved in several lifelong follow-ups in the health system, which puts them at risk of missing important check-ups. To optimize patients with DM1s follow-up in the health system, the projects overall aim is to investigate different experiences of and perspectives on living with DM1 and challenges related to adhering to life-long follow-ups, understanding, and navigating within health systems.

Methods: A scoping review guided by the PRISMA Extension for Scoping Reviews, will identify the existing literature on problems and challenges related to living with DM1. Three qualitative studies will investigate experiences and perspectives related to adherence to life-long follow-ups, understanding and navigation within health systems from the perspectives of patients, their caregivers, and healthcare professionals. The methods used are semi-structured interviews and observations. The research methodology used is Interpretive Description, and health literacy will be applied as the analytical lens guiding the data analysis. The project is planned from September 2022 – August 2025.

Perspectives: The project will generate new knowledge supporting the development of a model for a complex rehabilitation intervention for patients with DM1. Examining the different perspectives on challenges related to lifelong follow-ups is essential knowledge to optimize the follow-up and develop a rehabilitation intervention that contributes to active participation and ensure patients the follow-up they are entitled and need.

Keywords: Rehabilitation, Qualitative research, Other

FLASH TALK SESSION 2

Method for regular calibration of small point detector in brachytherapy

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In vivo dosimetry (IVD) is a standard part of brachytherapy treatments at AUH. The IVD is performed using a small detector (1x0.5x0.5mm3) based on a scintillating crystal. During BT, the probe is placed inside the tumorous organ through BT catheters. The response of the detector varies from treatment to treatment due to re-attachment of the probe. This gives rise to the need of recalibrating the detector before each use. A simple method, which takes <10 min and can be performed as part of the pre-treatment QA, has been developed.

The calibration is performed using a plastic phantom with two straight and parallel needles; one for the probe and one for the radioactive source. A measurement is performed with 15 dwell positions, spaced 5 mm apart, each with a fixed dwell time of 10 s. A function of the dose rate is fitted to the data. This procedure was performed on data from 48 different calibrations, using 4 different probes between March 2019 and December 2020.

Large fluctuations (up to 46% (1SD)) are seen in the calibration factors (from voltage to dose) for each probe. This is expected to stem from the re-attachment of the probe. Furthermore, the calibration factor for probe 1 and 2 increased over time, which indicates degradation of the probe sensitivity.

We have presented a method to calibrate small point detectors, which is easily implementable and can be performed in less than 10 minutes. The calibration factors vary both on the long and short term, based on both degradation of the material and coupling of the probe. This variation can be as large as a factor of three and confirms the need for regular recalibration.

Keywords: Medical technology and diagnostic techniques, Oncology, Other

Study protocol: Hyperpolarized 129Xe Magnetic Resonance Imaging in Diagnosing Progressive Pulmonary Fibrosis

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Background: Progressive Pulmonary Fibrosis (PPF) is a heterogeneous group of diseases characterized by formation of fibrous tissue in the lung resulting in deteriorating ventilation and gas diffusion capacity. Specific diagnosis is currently made in a multidisciplinary setting based on history, clinical findings and high-resolution CT (HRCT) findings, and sometimes invasive diagnostic tests. Currently, progression is defined as at least two of following three criteria occurring within the last year: Worsening of symptoms, decline in specified pulmonary function parameters and/or radiographic findings on HRCT of the lungs.

Hypothesis: Using Hyperpolarized (HP) 129Xe gas as inhaled Magnetic Resonance (MR) contrast, a specific PPF diagnosis can be made, and the risk of disease progression can be estimated.

Materials and Methods: Hyperpolarized (HP) 129Xe gas as inhaled MR contrast agent offers complementary information about regional ventilation, function, and microstructure as the MR signal shifts when the gas enters different compartments. At time of PPF diagnosis, patients (N=30) will undergo HP 129Xe MR imaging and spectroscopy of ventilation, alveolar microstructure, and diffusion barrier. Characteristics differentiating PPF are identified comparing to multidisciplinary decision and additionally patterns detecting progression are identified compared to clinical follow-up at 6 and 12 months.

Perspective: Hyperpolarized 129Xe MR imaging and spectroscopy as a new tool for diagnosing PPF will minimize the need for invasive tests and identify risk characteristics associated with progression of PPF.

Keywords: Medical technology and diagnostic techniques, Respiratory system, Other

ACTIVE study – use of active fluid exchange to treat intraventricular hemorrhage

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The severity of communicating hydrocephalus appears to be related to IVH volume and the duration of exposure of cerebrospinal fluid (CSF) to blood products. This current phase 2 safety/feasibility study evaluates the IRRAflow system, which is designed for active intracranial CSF lavage.

The ACTIVE study is a prospective, multi center, 1:1 randomized phase 2 trial evaluating the safety and efficacy of active intracranial CSF irrigation vs. passive external ventricular drainage (EVD) in the treatment of IVH. The trial will enroll 58 patients with primary or secondary IVH or subarachnoid hemorrhage with intraventricular breakthrough. The primary endpoint is catheter occlusion rate. Secondary endpoints include clearance of ventricular blood as measured by head CT scan, rates of catheter related infections and shunt dependency, functional Status – Extended Glascow Outcome Scale (eGOS) and modified Rankin Scale (mRS) at inclusion, discharge to rehabilitation and 90 days and mortality rates at 30 days and 90 days.

Currently, 5 patients have been enrolled and 3 treated with IRRAflow. We observed no catheter occlusions or catheter related infections during treatment and none of the patients required permanent a ventricular-peritoneal shunt (VP-shunt). Only 2 patients have been enrolled in the EVD control group at the moment. In comparison to our results using the IRRAflow device occlusion rates of passive EVDs are found to be 41% with a replacement rate of 19%. Shunt dependency is seen in 24% of the cases and intraventricular infections are seen in 19% of patients treated with standard passive EVD.

Keywords: Medical technology and diagnostic techniques, Other, Basic neuroscience

From Training to Clinic: Future Performance of Thoracentesis

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Introduction:

Despite years of medical education, residents are challenged when facing the transition to the clinical setting. Performing a thoracentesis involves aspiration of fluid between the visceral and parietal pleura by inserting a catheter. While the procedure is common, it may lead to a range of complications. Simulation-based training creates a safe learning space and has been shown to reduce the risk of complications and improve patient safety. Despite the benefits of simulation, it cannot fully replicate the complexity and diversity of the clinical environment. Developing training modules that foster adaptability is therefore a necessity in order to increase transfer from the simulated setting to the clinic.

Objectives:

This study aims to develop a simulation-based training module and assessment of thoracentesis performance, which will enable learners to transfer skills from the simulated setting to the clinic.

Methods:

Residents with limited thoracentesis experience will be invited to participate in the study. Participants will engage in a training module designed to increase transfer of skills gained during simulation to the clinic. Two weeks after training, all participants will complete a simulation-based thoracentesis assessment. Kane's validation framework will be used to collect validity evidence for this assessment.

Outcomes:

This Research Year Project will develop a simulation-based module for thoracentesis training. An assessment of the ability to transfer skills learned during the simulation-based thoracentesis training module to the clinical setting will be developed.

Conclusion:

Pending.

Keywords: Health education and simulation-based training, Respiratory system, Other

Improving patient care for Hemifacial microsomia patients.

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Introduction: Hemifacial microsomia (HFM) is a congenital anomaly causing unilateral facial deformity. Approximately 1:7000 children are diagnosed with HFM making it the second most common congenital craniofacial anomaly after cleft-lip-palate.

HFM causes a spectrum of underdevelopment of the ear, orbit, mandible, facial soft tissue, and facial nerve, with considerable variation in expression. The resultant conditions of HFM are orofacial dysfunction and sleep-related breathing with severe impact on social life and health-related quality of life. Management of HFM is a challenge for healthcare providers.

Aims: This research ultimately aims to propose an evidence-based strategy for managing HFM-related dentofacial deformity using a specific non-surgical orthopaedic, dental appliance. The general aim is to improve the lives of children with this devastating craniofacial anomaly and equalise the offer for treatment with other anomaly groups.

Study design: 1) A Delphi study is planned to develop consensus-based guidelines for the radiological evaluation of HFM-related dentofacial deformities.

2) Analysis of retrospective data comparing orthopaedic treatment outcome with the outcome of an untreated control group.

Data analysis:

1) Validity and reliability tests for the outcome measures done on 3D CBCT scans.

2) Intra- and Inter-group differences of relevant outcome variables will be analysed in treated and control groups.

3) We will evaluate intra-and inter-group differences using parametric and nonparametric statistics.

Goal: An evidence-based protocol will not only benefit patients; it may also reduce societal costs associated with the management of HFM within the Danish healthcare system.

Keywords: Dentistry, Medical technology and diagnostic techniques, Orthopedic surgery

Automated use of 3D data in forensic odontology identification

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In the case of catastrophes, such as disasters or terror attacks, hundreds of casualties need to be identified quickly and unambiguously. For such identification purposes crucial identification methods such as forensic odontology identification using 2D data is used. The shift from 2D to 3D data in the dental clinics causes classic forensic odontology identification to become still harder to practice.

To be compatible with the dental records of tomorrow, forensic odontology identification methods relying on 3D data instead of 2D data must be developed. In addition, 3D data have a greater level of detail compared to 2D data, aiding the identification process when only partial remains are available. This could prove particularly important in disasters where the remains are few.

We have identified three parameters of great importance when creating a robust 3D data-based dental identification method:

1) The presence of partial dentitions.

2) The impact of the time span between ante mortem 3D data collection and post mortem data collection.

3) Dentitions exposed to trauma such as thermal stress.

To our knowledge, these three parameters have not been sufficiently reported on in the scientific literature, for which reason this study aims at exploring their impact on the outcome of 3D data-based forensic odontology identification.

Keywords: Dentistry, Medical technology and diagnostic techniques, Epidemiology and biostatistics

MAGNETIC RESONANCE IMAGING IN THE DIAGNOSIS OF PERIAPICAL AND PERIODONTAL DISEASE: SYSTEMATIC REVIEW

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Aim: Early preclinical inflammatory changes in periodontal and/or periapical lesions are problematic to diagnose using ionizing-radiation-based imaging modalities. Magnetic resonance imaging (MRI) provides relevant additional diagnostic information of inflammatory processes in soft and hard tissues. The aim of the present study was to undertake a systematic review of the literature on MRI in the diagnosis of periapical and/or periodontal disease.

Materials and methods: The PubMed/MEDLINE and Scopus bibliographic databases were searched (2000-2021) using

the search string: ("MRI" or "magnetic resonance imaging") and ("periodontitis" or "periodontal" or "apical pathology" or

“endodontic pathology” or "periapical" or "furcation" or "intrabony"), limited to studies published in English. The studies were assessed independently by three reviewers, focusing on the MRI sequences, imaging modalities (radiographs, cone beam CT – CBCT, and MRI), disease definition, assessed parameters, and outcome measurements.

Results: The search strategy yielded 34 studies, from which 13 were included. The studies showed that MRI provided diagnostic information of the hard and soft tissue components affected by periapical and/or periodontal disease with a fairly high sensitivity and specificity. However, the assessed parameters (e.g., MRI acquisition protocols, and disease definition) differed substantially.

Conclusion: The use of MRI in the diagnosis of periapical and/or periodontal disease is feasible and promising. More studies are needed to define the accuracy of this diagnostic modality, in the assessment of periapical and/or periodontal lesions.

Keywords: Dentistry, Medical technology and diagnostic techniques, Reviews and meta-analyses

Gastrointestinal stimulation as a treatment of paralytic ileus following extensive surgery for peritoneal metastases (STIMULATE) - A prospective blinded randomized controlled clinical trial

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Introduction:

Postoperative paralytic ileus (POI) is a frequent complication following abdominal surgery. It causes nausea, vomiting, stomach cramps and general discomfort for the patient. Currently, no efficient treatment exists. Pre-clinical studies have shown a beneficial effect on POI by electrical stimulation of the bowel. The aim of this clinical trial is to investigate electrical stimulation of the gastrointestinal (GI) tract as a potential treatment of POI.

Materials & Methods:

The study is a blinded randomized controlled single center clinical trial including 100 patients (1:1). Patients undergoing cytoreductive surgery and heated intraperitoneal chemotherapy for peritoneal metastasis (PM) are eligible for participation.

Two hours before surgery the patients will ingest a wireless motility capsule (SmartPill). Before closing the abdomen, two pace leads will be mounted on the surface of the stomach, and exteriorized trough the abdominal wall. The pace wires will be connected to an external pacemaker. In the intervention group the pacemaker will be turned on. In the control group, the pacemaker is turned off.

In the postoperative period patients are asked to fill out a patient diary on GI symptoms. GI transit times are wirelessly monitored by the SmartPill. When normal GI function is restored the pace leads will be removed by simple traction (like a surgical drain).

Results:

Patient enrolment is planned to begin in spring 2023.

Conclusion:

This study will aid in clarifying if GI stimulation is a new treatment for POI following surgery for PM. If the study is positive, it will have a great impact on faster patient recovery, leading to fewer complication.

Keywords: Gastrointestinal surgery, Medical technology and diagnostic techniques, Rehabilitation

Study Protocol: Predicting Small Hepatocellular Carcinoma Lesions Non-Invasively with Hyperpolarized MRI

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Background: Hepatocellular carcinoma (HCC) is the most common primary liver tumor and is one of the most common causes of cancer-related deaths worldwide. Patients with liver cirrhosis have a 30 percent lifetime risk of developing HCC, and the risk increases by the severity of the disease. The diagnosis is based on characteristic radiological findings of tumors ≥ 10 mm, and these findings are often absent in tumors smaller than 10 mm. Using Hyperpolarized [1-13C]pyruvate as a MR contrast agent, metabolic conversion to lactate, alanine and bicarbonate can be quantified due to the chemical shift effect.

Hypothesis: Hyperpolarized magnetic resonance imaging (MRI) can quantify metabolism in HCC suspected tumors and thus distinguish benign lesions from HCC.

Materials and Methods: The clinical study will consist of healthy volunteers (n=6), patients with large HCC tumors >10 mm (n=8) and patients with HCC suspected liver tumors <10 mm (n=16). All patients and volunteers will undergo hyperpolarized [1-13C]pyruvate MRI. Patients with small tumors will be followed with conventional MRI scans every three months for up to two years until the lesions is finally characterized as benign or HCC. Metabolic characteristics from the Hyperpolarized MRI scans will then be compared to HCC and benign lesions.

Perspective: Hyperpolarized MRI is a new tool for diagnosing small HCC liver tumors in a non-invasive manor. The method could aid in better treatment options for those patients and therefore overall survival for patients at risk.

Keywords: Medical technology and diagnostic techniques, Gastrointestinal surgery, Gastroenterology and hepatology

Laser Speckle Contrast Imaging for perioperative quantification of intestinal microcirculation

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Aim To evaluate Laser Speckle Contrast Imaging (LSCI) for perioperative quantification of intestinal microcirculation.

Background Anastomotic leakage (AL) is among the most severe and feared postoperative complications of colorectal surgery, as it is directly associated with an increase in mortality and morbidity. The blood supply to the anastomotic site is considered one of the most important risk factors for AL. The assessment of the blood supply for the anastomosis is currently based on a subjective clinical assessment by the surgeons. However, these assessments lack objectivity, quantitatively, and predictive accuracy.

Methods We will investigate the microcirculation in the intestine during surgery and by inotropic agents, by two animal experiments and a clinical trial.

Result We expect to have results ready for presentation at PhD day for Study 1.

Conclusion The studies aim to identify factors that influence the microcirculation of the colon, and thus the risk of anastomotic leakage. The study is considered important and the acquired knowledge may have an impact on clinical practice.

Keywords: Gastrointestinal surgery, Animal models/disease models, Medical technology and diagnostic techniques

Dorsal genital nerve stimulation for the treatment of faecal incontinence and overactive bladder

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Background

Patients with the diseases faecal incontinence (FI) and overactive bladder (OAB) often lives a restricted life with social isolation and their quality of life is often reduced. Electrical stimulation is an effectively treatment for reducing symptoms of FI and OAB. Currently a pacemaker that can stimulate nerve fibers at the sacral plexus, Sacral Nerve Modulation, are today implanted in the gluteal region. SNM is an invasive and expensive treatment. Dorsal genital nerve (DGN) innervates the clitoris/penis, and therefore can be targeted by applying electrical stimulation at the genitals. "Innocon Medical" developed a new device, UCon, that with new electrode technology, can stimulate the DGN through the skin a using patch electrode or percutaneously using a bar electrode.

Methods

Study A:

Single arm prospective, multicenter study in Denmark at three different departments of surgery.

Primary purpose is to investigate the safety and evaluate this new UCon device performance using both the patch electrode and the bar electrode with DGN stimulation. Furthermore, to document the efficacy on FI.

Hypothesize that UCon is safe, subjects do not experience an unacceptable number of device- or procedure related serious adverse events or adverse events and is effective for the treatment of FI in a home setting. Further, subjects using UCon experiences an improvement in the disease specific quality of life.

Results

Patient enrollment ongoing. (Spring 2022)

Conclusion

If the UCon device is able to reduce FI symptoms this will bring an affordable, minimally invasive treatment to the market helping patients suffering from FI and OAB, and thereby having a great socio-economic impact.

Keywords: Gastrointestinal surgery, Medical technology and diagnostic techniques, Socio-economic conditions

Optimizing communication with older patients at ward rounds: A scoping review

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Objectives: Ward rounds are essential to patient care; however, little is known about how communication with older patients and their relatives can be optimized. Hence, this scoping review aims to provide an overview of quality-enhancing elements of physicians' ward round communication with older patients. Such an overview would provide a point of departure for developing future post-graduate medical education in ward round communication training.

Method: A scoping review was performed by searching CINAHL, Embase, Medline, and Pubmed databases. The search strategy included terms synonymous with “ward rounds” and “older patients”. We included studies regarding communication with patients above 65 years during ward rounds. Thematic analysis was applied.

Results: Seven of the 2,322 identified papers were included in the present review. Neither of the papers referenced patients' level of frailty, however, most studies included patients with some level of frailty. Thematic analysis revealed three overall themes: Communication strategy, patient participation and frailty, and organizational and age norm challenges. However, the papers focused mainly on what the optimal ward round communication should include rather than how it should be performed.

Conclusion: Characteristics of frail patients and organizational barriers challenge effective and safe ward round communication. Little is known about how ward round communication with older patients can be optimized to improve patient care.

Keywords: Health education and simulation-based training, Other, Reviews and meta-analyses

Assessing the quality of donor kidneys during normothermic machine perfusion using nanoparticle-based vitality sensors

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Background: The use of suboptimal kidney grafts has increased availability of kidneys, but also exposed a vital need for better organ assessment in kidney transplantation. For now, there is no objective method, resulting in possibly poor kidney transplants or potential grafts being discarded. To utilize available kidneys, we aimed to develop a method to objectively quantify kidney quality through the combination of normothermic machine perfusion (NMP), nanoparticle-based biosensors, and near-infrared-fluorescence (NIRF) kidney imaging.

NMP creates an opportunity for kidney assessment prior to transplantation. Nanoparticles (NPs) are vehicles that can facilitate cell-uptake via the active process of endocytosis. We investigated the option to assess kidney vitality through NPs loaded with a self-quenching NIRF dye, that will emit fluorescence upon release in the cytoplasm. Hypothesized that viable cells are more metabolically active, they will have superior nanoparticle uptake. Thus, fluorescence could function as a readout for kidney vitality.

Methods: Nephrectomy was performed on pigs to acquire kidneys, which were preserved at hypothermic machine perfusion before transferred to NMP. Warm ischemia was used to induce damage. NMP was performed with a red-blood-cell-based perfusate containing a mixture to meet metabolic requirements. NMP was performed at sinusoidal pressure of 100/60 mmHg using a centrifugal pump at 60 bpm. Real time whole kidney imaging was performed using a laser and camera connected to the NMP setup.

Results: First data have proven nanoparticle uptake and detection of fluorescence by real-time kidney imaging, but final results are yet to come.

Keywords: Nephrology, Urology, Medical technology and diagnostic techniques

FLASH TALK SESSION 3

"Nursing interventions for paediatric oncology patients and their families: A scoping review protocol".

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Objective: The objective of this scoping review is to identify and map existing nursing interventions for paediatric patients with cancer and their families. We aim to develop a comprehensive overview of the available evidence and identify research gaps to guide future intervention development and research.

Introduction: Clinical nursing care activities and interventions is an essential part of paediatric oncology. In paediatric oncology nursing research, a shift from explorative to intervention studies is recommended and the body of nursing intervention research is growing. However, no overview of existing nursing interventions in paediatric oncology is currently available.

Inclusion criteria: For articles to be included, they must meet the following inclusion criteria: refer to paediatric patients diagnosed with cancer and their family, nurse-led non-pharmacological and non-procedural interventions, provided by a paediatric oncology unit, peer-reviewed studies published from year 2000 and written in English, Danish, Norwegian or Swedish.

Methods: This scoping review will follow the JBI guidelines for scoping reviews as described in the JBI Reviewer's Manual. A three-step search strategy, using the mmeonic PCC (Population, Content, Context) will be conducted. The following databases will be searched: SCOPUS, MEDLINE (PubMed), ProQuest (Dissertations and Thesis), Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Psychology Information (PsycINFO). The identified studies will be managed using the Covidence platform and screened by title and abstract by two independent reviewers. A summary of the results will be presented in a descriptive manner, supported by tables.

Keywords: Paediatrics, Oncology, Qualitative research

Function and dysfunction of the autonomic nervous system in Neuronal Ceroid Lipofuscinosis type 3

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Background: Neuronal Ceroid Lipofuscinosis type 3 (NCL3) is a neurodegenerative disorder that starts at age 4-6 years. Clinical presentation includes blindness, epilepsy, dementia, parkinsonian movements, cardiac involvement, and premature death. Previous research has shown an age-dependent alteration of the Heart Rate Variability (HRV) in patients with NCL3. HRV is a biomarker of the function of the autonomic nervous system. Seizure attack resembling Paroxysmal Sympathetic Hyperactivity (PSH), are observed in adolescents with NCL3. The seizures consist of episodes of increased motor activity, tachycardia, tachypnoea, hyperthermia, sweating and hypertension.

Aim and hypothesis: We want to investigate the likelihood of the presence of PSH in NCL3 by measuring the HRV and thereby evaluate the function of the autonomic nervous system in relation to the seizures.

Methods: This study is an observational study of patients with NCL3. We perform out-patient measurements of the HRV with a Polar H10 chest belt and a standard Holter during a 7-days period. Concurrent video documentation and relevant data of the non-epileptic attacks are registered.

Results: We are currently collecting and analysing data. Preliminary results indicate that the level of the parasympathetic nervous system decreases before the seizures and regain function immediately after. Furthermore, reported symptoms, heart rate data and the video recordings seem compatible with the clinical presentation of PSH mostly seen following severe traumatic brain injury.

Conclusion: Paroxysmal Sympathetic Hyperactivity seems to explain the episodic non-epileptic seizures occurring during the late course of the NCL3 disease.

Keywords: Paediatrics, Clinical neuroscience, Cardiovascular system

Bifidobacterium Infantis to newborns: Effects of modulating the gut microbial composition on infections and inflammatory conditions

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Background and aim:

Growing evidence suggests that the gut microbiome plays an important role in the early development of the human immune system and the increasing number of autoimmune and inflammatory diseases. Modifying the gut microbiota early in life by introducing probiotics, e.g. bifidobacteria, may have beneficial effects on disease prevention.

This study aims to explore effects of introducing Bifidobacterium longum subsp. infantis (B. infantis) to newborns. B. Infantis is of special interest as a supplement to newborns, due to its superior capacity for utilization of human milk oligosaccharides, a silencing effect on Th2 and Th17 responses, and is associated with diminished enteric inflammation and reduced abundance of antibiotic resistance genes in stool.

Material and methods:

1000 newborn children will be included at regional hospitals in Midtjylland, Denmark, in a randomised controlled intervention trial to receive B. infantis or placebo for 21 days.

Primary outcome: Incidence of bacterial infections measured as prescriptions of antibiotics.

Secondary outcomes: Bowel function, infantile colic, and antibiotic resistance genes in stool.

Outcome parameters will be measured using questionnaires, information from Danish registries and from stool samples.

Perspectives:

This study will evaluate potential effects of B. infantis to healthy term newborns. We aim to create a large cohort of children to be followed in many years. Additional studies will analyse explorative and later outcomes as development of autoimmune and inflammatory diseases.

Keywords: Paediatrics, Molecular metabolism and endocrinology, Inflammation

Perinatal asphyxia and long-term neurodevelopmental outcome

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Background: 'Asphyxia' is often used to describe a newborn thought to be exposed to hypoxia at birth. Asphyxia is defined as low Apgar score. However, Apgar score is a clinical assessment of the state of the newborn and may be affected by other exposures than hypoxia. Biochemical measures (umbilical cord blood pH) are needed to evaluate if the newborn has been exposed to hypoxia. Low Apgar score or low cord blood pH alone has been associated with adverse outcomes. However, affected Apgar score in combination with cord blood pH and the risk of long-term neurodevelopmental outcome is sparsely investigated.

Aim: We aim to investigate the association between combinations of Apgar score and umbilical cord blood pH and neurodevelopmental outcomes in a register based nationwide cohort study.

Methods: The cohort will consist of all Danish children born between 2004-2014. Their Apgar score and cord blood pH will be retrieved from the Danish Medical Birth Register. Outcomes of neurodevelopment will be school performance, diagnoses of autism, ADHD, epilepsy, and cerebral palsy retrieved from Danish national registries. We will compare the risk of neurodevelopmental impairments in newborns with affected Apgar score and cord blood pH to healthy peers using Cox regressions. Child- and parent covariates will be retrieved from national Danish health registers and Statistics Denmark. Results will be validated in a Norwegian cohort.

Perspective: The study will provide new insight to the state of newborns, previously described as 'asphyxia', which can be used for future prognostication and clinical decision making on which children may require special attention and additional treatment.

Keywords: Paediatrics, Gynecology and obstetrics, Epidemiology and biostatistics

A Mixed Methods Study of a Nurse Led Intervention based on couplet care to Support Zero Separation In A Neonatal Intensive Care Unit

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Background: Families experiences a spontaneous separation after childbirth if both mother and infant have a treatment requiring condition. This is due to a current and historical division of medical specialties into neonatal care and maternal care. The separation has adverse impact on maternal, infant, and family health.

Objective: The objective of the study is to implement and evaluate a nurse-led intervention based on couplet care by comparing it with usual care and examine implementation, context, and mechanism af impact.

Design: The study will apply a prospective mixed-methods design comprising a quasi-experimental trial, a field study and two qualitative studies.

Intervention: The intervention is two-folded and involves a competence development program and an organizational change in practice, with the implementation of couplet care. Couplet care is defined as one nurse delivering neonatal intensive care and maternal care in the same unit. The competence program consists of education in family nursing, postpartum treatment and care, and supervision.

Methods: The effect of the intervention will be examined in a quasi-experimental trial with two groups (N = 620). The control group will receive usual care. The process evaluation consists of field observation of practice and four focus group interviews with healthcare professionals (n=32). Further, it consists of phenomenological dyadic interviews with admitted families (n = 10).

Implications for practice: The study can help bridge the gap between current practices and the establishment of a new model of care where mother-infant dyads are admitted together.

Keywords: Paediatrics, Public health, Qualitative research

Detection of mosaicism using optical genome mapping

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Objective:

Sometimes a chromosomal anomaly is not present in all cells (mosaicism), causing diagnostic uncertainty and delay in fetal diagnostics. New analyses may reduce this uncertainty. We evaluate placental mosaicism using two different methods; array comparative genomic hybridization (aCGH) and optical genome mapping (OGM).

Methods:

Post-termination placental biopsies from two pregnancies with mosaicism on aCGH were analysed with OGM and compared to the results of aCGH.

Results:

In case A a translocation between chromosome 6p and Xp was found in a mosaic form. This was confirmed post-termination in placental biopsies examined by OGM.

In case B a complex aberration on chromosome 18 (a full deletion on 18p11.32p11.22, a mosaic amplification on 18p11.22p11.21, a full duplication on 18p11.21 and a mosaic duplication of 18q) was found on aCGH. OGM on post-termination samples corroborated these finding, except the duplication of 18q in low-grade mosaic form which was not called by the OGM algorithm, but could be visually identified.

Conclusion:

Optical genome mapping can supplement aCGH, however the current algorithm does not always call the aberration even though it can be visually seen.

As the biopsies were taken at different timepoint (for CVS and after termination) we hypothesize that the differences between aCGH results and OGM results more likely due to a biological difference or change, which we have seen in previous studies, rather than a disagreement between the two methods. Further studies into this biological phenomenon as well as direct comparison of aCGH and OGM on mosaic samples are needed for better diagnostic procedures and counselling prior to termination.

Keywords: Medical technology and diagnostic techniques, Gynecology and obstetrics, Cell biology

Next-generation effects of vitamin D supplementation in pregnancy

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Background

Vitamin D deficiency is common among Danish pregnant women, although most women adhere to official guidelines suggesting a supplement of 10 µg/day vitamin D throughout pregnancy. Vitamin D deficiency increases the risk of pregnancy complications e.g., gestational diabetes, preeclampsia and fetal growth retardation. Fetal vitamin D supply is dependent on maternal levels. Vitamin D is essential for the immune system, bone development and glucose metabolism, and several studies indicate, that maternal vitamin D deficiency has adverse effects on offspring health, including increased risks of obesity, asthma and multiple sclerosis.

This study aims to investigate if a daily vitamin D supplement of 90 vs 10 µg to pregnant women affects the growth and development of offspring at birth and at the age of 12 months.

Method

Within an ongoing randomized controlled trial (90 vs 10 µg daily vitamin D3), a cohort of participants will be invited to a follow-up study. The immune reactivity of PBMC samples from umbilical cord blood and at 12 months will be investigated and post-natal development and colic will be evaluated based on questionnaires. Clinical 12-month examination will be performed including measurements of weight, height, head circumference, size of the anterior fontanel and growth rate.

Results

The results are pending as the study is ongoing.

Conclusion

With this study we will gain insight on the effects of intra-uterine vitamin D exposure on growth, immune system and colic during the first year of life. This insight can help guide health authorities when evaluating the need for new guidelines on vitamin D intake in pregnancy.

Keywords: Paediatrics, Gynecology and obstetrics, Cell biology

Late pulmonary adverse effects and pulmonary function in children and adolescent survivors of acute lymphoblastic leukemia (ALL-STAR Lungs)

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INTRODUCTION

The most common childhood cancer, acute lymphoblastic leukemia (ALL), affects approximately 35 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. Hematopoietic stem cell transplantation decreases forced vital capacity and diffusion capacity compared with chemotherapy treatment only. Previous studies fall short because they study only irradiation, now obsolete and known to cause PFD, other older treatment regimens, and because they lack controls and have register-based data as their sole reference. Forgoing these shortcomings, we aim to uncover late pulmonary adverse effects (LPAE) and PFD in childhood NOPHO ALL-2008 survivors.

METHODS

This national observational cohort study includes examination of a childhood ALL survivor cohort treated according to the NOPHO ALL-2008 protocol during 2008-2018 (N=303) and matched controls including physical examination, lung function testing, and questionnaires. The primary outcomes are incidence of LPAE and PFD in ALL survivors compared with matched controls.

PERSPECTIVES

The study will provide national results regarding the burden of LPAE and PFD 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.

Keywords: Paediatrics, Respiratory system, Oncology

Simulation training of emergency situations in pediatrics: A controlled intervention project

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Introduction:

Treating critically ill newborn and children is challenging, because emergency situations are rare, and consequences often severe. When a healthcare team faces a pediatric emergency, skills related to teamwork are critical determinants of survival. By applying simulation-based team training, it is possible to improve skills, including teamwork, leadership, and communication. Simulation training allows the healthcare team to rehearse specific emergency situations, by mimicking authentic real-life scenarios in the clinical setting. The optimal frequency and method of simulation remains undetermined, and only few studies report effects related to patient safety or survival.

Objectives

This PhD-project aims to investigate the impact of a simulation-based team training intervention across two Danish regions.

Methods

During a one-year period (April 2023 to April 2024), a controlled simulation-based training intervention will be implemented in all pediatric departments in the Central Denmark Region. Every three months 598 healthcare professionals located at pediatric departments, will perform two-hour sessions (a total of eight hours). Simultaneously, 613 healthcare professionals from the Region of Southern Denmark will be included as a control group, with no intervention.

Outcomes

This PhD project will compare three main outcomes in both regions before and after the simulation intervention: 1) quality of treatment of critically ill newborns, 2) patient safety culture within pediatric departments, and 3) rate of sick leave.

Conclusion

Pending.

Keywords: Health education and simulation-based training, Paediatrics, Work environment and organisation

The trajectory of stress from adolescence to young adulthood

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Background: Stress is an increasing problem and can potentially have major consequences for both the individual and the society. Long-term stress has negative influence on quality of life and work ability and may potentially lead to diseases such as depression and cardiovascular disease. This PhD project investigates risk factors and predictors of stress in adolescence and early adulthood.

Aims:

To examine the development in perceived stress levels among 15/16-year-old adolescents over time in relation to social position (SP) and geographical neighbourhood.

To examine the trajectory of perceived stress from adolescence into early adulthood in relation to SP.

To develop and validate a prediction model to identify adolescents with a risk of high stress levels in early adulthood.

Method: Primary outcome is perceived stress measured by the Perceived Stress Scale. Data originates from two youth cohorts of 15/16-year-old adolescents (VestLiv (VL) (2004,2007,2010,2017,2021) and FOCA (2017)) and from Statistics Denmark. Study 1 includes VL's first wave and FOCA to compare stress levels from 2004 to 2017. Study 2 includes data from all waves of VL and register information on both own and parental SP. Study 3 includes VL's first and last three waves. Possible predictors are characteristics from 2004 and register information from childhood.

Perspectives: This project will contribute the current discussion about increasing stress levels among young people and contribute with new knowledge on the significance of SP in stress development. Furthermore, we aim to provide a practical applicable tool for use in school health care settings in order to target preventive efforts against stress.

Keywords: Public health, Psychiatry, psychology and mental health, Socio-economic conditions

My Avatar – Equal mobility in education for children and adolescents with neuromuscular diseases in Scandinavia using telepresence robots

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Background: Children and adolescents with neuromuscular diseases (NMD) are expected to live well into adulthood which makes it essential to ensure mobility of education. A weak affiliation with educational institutions can have social as well as economic consequences for the individual and the society. The projects aim is to examine whether the use of telepresence robots by children, adolescents, and teachers in Scandinavia can support children and adolescents with NMD's adherence to and participation in education by offering flexibility during periods where symptoms of their chronic disease prevent them from beings physically present in the classroom.

Methods: The project period is from 2022-2026. A comparative policy analysis will examine the legislation on education in relation to school absence due to illness in Scandinavia. Furthermore, two qualitative studies will evaluate the use of telepresence robots in Scandinavia for children and adolescents with NMD from a child and teacher perspective. The evaluation will focus on flexibility, facilitations, and barriers in the use of telepresence robots in the education institutions. The methods used are document analysis and semi-structured interviews. The methodology used is Interpretive Description seeking to improve and qualify practice through qualitative method.

Perspectives: The knowledge from the project may help ensure that more children and adolescents with NMD in Scandinavia and other countries get better opportunities to complete primary through upper secondary education. Keeping children and adolescents in the educational system will increase their chances of entering the labor market and doing well in life.

Keywords: Public health, Qualitative research, Socio-economic conditions

Informational needs concerning family planning and pregnancy in patients with atopic dermatitis and specific worries regarding pregnancy

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Atopic dermatitis (AD) is an inflammatory skin disease affecting approximately 20% of children and 5-10% of adults in affluent countries. AD can persist into adulthood, entailing many adult patients to deal with their disease during family planning and pregnancy (FPP). Informational needs and worries in patients with AD of reproductive age in relation to FPP have not previously been investigated. The aim of this study is to examine the extent of information regarding FPP which patients with AD receive from their dermatologist while being treated. Furthermore, to investigate specific worries that patients with AD may have concerning FPP.

The study is conducted as an anonymized questionnaire-based cross-sectional study. Patients of both genders will be recruited from the Department of Dermatology at Aarhus University Hospital, Bispebjerg Hospital as well as two private dermatology clinics. The goal is to collect 200 questionaries from patient with AD. Patients must be between 18 and 45 years of age and receive topical or systemic treatment for AD. The questionnaire is designed in REDCap and divided into four sections with questions regarding socio-demographics, disease specific characteristics, family situation, and information received from healthcare professionals concerning FPP.

This study addresses potential informational needs patients with AD have regarding FPP. This gives the possibility to change the standard practice of FPP information physicians at hospitals as well as in private clinics inform patients. By exploring worries concerning FPP, specific worries can be addressed, and thereby hopefully eased, which will lead to less emotional stress in a period of FPP.

Keywords: Dermatology, Inflammation, Other

Linear Energy Transfer Distributions for Pencil Beam Scanning of Pediatric Brain Tumors

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Purpose:

In radiotherapy of pediatric central nervous system (CNS) tumors with protons, preclinical data shows that the relative biological effect (RBE) increases near the end of the beam. This effect is of concern in particular in patients where the tumor is close to critical organs such as the brainstem. Therefore, we surveyed the distribution of Linear Energy Transfer (LET, which correlates with RBE) in the brainstem of pediatric CNS patients.

Methods:

A cohort of 15 patients was selected from the 47 pediatric CNS patients we have treated with state-of-the-art pencil beam scanning (PBS) proton therapy at the Danish Center for Particle Therapy. None had experienced clinical brainstem toxicity. We selected patients that had focal brain irradiation only and where the maximum dose to the brainstem was at least 50 GyRBE. All treatment plans used a minimum of 3 fields spaced by at least 30 degrees to avoid high LET. We estimated the LET in the brainstem using Monte Carlo simulations of the treatment plans.

Results:

The 0.3cc of the brainstem with the highest LET, receiving at least 95% of prescribed dose, varied from 2.6keV/µm to 4.4keV/µm (median 3.5keV/µm). In many cases, the brainstem LET was relatively higher than the rest of the target volume. The five patients with the highest brainstem LET were younger than the median age.

Conclusion:

Even when field configurations are chosen to mitigate high LET, some patients have regions in the brainstem with relatively high LET and dose. Further clinical data is still needed to link increased LET to brainstem toxicity. New strategies for reducing LET in the brainstem and other high-risk organs for PBS should be investigated.

Keywords: Oncology, Paediatrics, Medical technology and diagnostic techniques

FLASH TALK SESSION 4

Anticoagulant treatment and thromboembolic events prior to renal cell carcinoma: Impact on stage at diagnosis and postoperative prognosis

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Introduction

Surgical resection of localized renal cell carcinoma (RCC) can be curative. RCC increases the risk of developing venous thromboembolisms (VTE), like surgery itself does. Anticoagulants are indicated as treatment and prophylaxis for VTEs, but are also indicated in other conditions like atrial fibrillation, mechanic heart valve etc . For patients diagnosed with RCC, the median age is around 64, and the prevalence of e.g. atrial fibrillation increases with age. A considerable number of patients with RCC may therefore receive anticoagulant treatment at time of diagnosis. But whether use of anticoagulants prior to diagnosis as well as previous VTEs effect staging or prognosis of RCC remains unclear.

Aim

We wish to investigate whether a history of VTE and/or use of anticoagulant treatment at time of RCC diagnosis, affect the stage distribution and prognosis for patients undergoing nephrectomy compared with patients without a thromboembolic event and those who are not in anticoagulant treatment.

Methods

The study is conducted as a nationwide population-based cohort study, where we expect to include around 8800 patients diagnosed with RCC in the period 2009-2020.

Results

Our analyses are currently in progress. If available, we will present our provisional results.

Perspectives

By comparing these groups, we will be able to evaluate whether some patients are diagnosed at a more advanced disease stage, have a higher risk of post-operative complications, or suffers higher mortality rates. Our findings could lead to an increased attention or special consideration towards certain patients in terms of treatment or follow-up protocol, and thereby potentially improve their prognosis.

Keywords: Urology, Epidemiology and biostatistics, Pharmacology

Utility of DNA methylation for risk-stratification of women aged ≥45 referred for colposcopy

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The performance of colposcopy is often impaired in older women due to age-dependent changes. We recently showed that biopsies missed more than 50% of CIN2+lesions in older women without a fully visible transformation zone (TZ). To reduce the risk of overtreatment without increasing risk of underdiagnosis, there is a need to explore the use of biomarkers for risk-stratification such as DNA methylation. Thus, in this study we aimed to evaluate the clinical utility of host-cell DNA-methylation markers for risk-stratification of older women at colposcopy.

We conducted a cross-sectional study during 2019-2021. Eligible women were ≥45, referred for colposcopy due to an abnormal screening result, and did not have a fully visible TZ. At colposcopy, we collected a cervical cytology sample and multiple biopsies, and all had a loop electrosurgical excision procedure (LEEP) performed. Cervical samples were analysed using a new panel of methylation markers. We calculated sensitivity and specificity of the methylation markers for CIN2+ detection using the LEEP result as reference standard.

A total of 96 women were included for analysis. Median age was 67.9 years (IQR: 62.8-70.3), and 80.3% were referred based on HPV-screening. Thirty-one (32.2%) had CIN2+, and 61 (63.5%) women tested methylation positive. Sensitivity for the new methylation markers was 83.9% (95% CI: 66.4-94.5%) and specificity was 46.2% (95% CI: 33.7-59.0%).

The two new DNA-methylation markers showed promising results for risk-stratification of women aged ≥45 with abnormal cervical cytology. However, there was a significant risk of overtreatment. Further research into validated markers is needed.

Keywords: Gynecology and obstetrics, Medical technology and diagnostic techniques, Public health

Comprehensive Geriatric Assessment for perioperative optimization in cystectomy – A national randomized study (COMPETENCE)

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Introduction: Patients with muscle-invasive bladder cancer are often older and multimorbid, thus in an increased risk of perioperative mortality and morbidity in relation to radical cystectomy (RC). The aim of the study is to investigate the effect of perioperative Comprehensive Geriatric Assessment (CGA) and tailored intervention in older, frail patients with bladder cancer undergoing RC.

Methods: The study will be a national randomized trial (Aarhus, Odense, Aalborg, and Herlev). In total 140 patients ≥65 years will be included. Preoperative frailty will be assessed by the G8 screening tool.

Patients will be randomized 1:1 and allocated into either control or intervention study arm. The control group will receive perioperative "care as usual" according to exciting principles and guidelines. The intervention will comprise a preoperative, thorough geriatric, multidisciplinary assessment, focused on optimizing health issues of expected importance in further course of surgery. Furthermore, postoperative ward rounds by a geriatric team will be conducted. Thus, the course of treatment for each patient will be a close interdisciplinary collaboration.

Outcomes: Primary outcome is DAOH 90-d postoperative, a valid marker for cumulative morbidity after RC. Secondary outcomes will be complications 30- and 90 days, mortality, hospital readmissions, length of stay (LOS), and Quality of Life (QoL)

Results: Expected in 2025.

Perspective: We expect an increase in DAOH, as a combined measurement of the reduction in postoperative complications including perioperative mortality, LOS, and any potential readmissions, in combination with improved QoL, for older patients with bladder cancer.

Keywords: Urology, Multimorbidity, Other

iMproving thE Dlagnostics And Treatment Of ceRvical precancer - the MEDIATOR study

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Background: In Denmark, cervical cancer incidence has remained stable in the past decade. Colposcopy is performed in women with abnormal cervical screening tests.

Objectives: To explore whether the implementation of a systematic colposcopic scoring system, the Swede score, can improve diagnostic accuracy of cervical lesions. Furthermore, to evaluate whether the Swede score can be used to assess when random biopsies can be safely omitted. Since optimizing diagnostic procedures is only effective with adequate treatment, we also aim to evaluate the performance of excisional treatment for cervical lesions.

Design: Non-randomized intervention study and a national register study.

Setting and population: All public colposcopy clinics in Central Denmark Region and two private colposcopy clinics will enrol patients. Also, data will be collected by using the Danish national registers.

Perspectives: We hope to improve the diagnostics and treatment of women with cervical precancer and cancer.

Keywords: Gynecology and obstetrics, Oncology, Infection

Ultrasound measurements in pregnancies complicated by T2DM - Can we optimize the prediction of children at risk?

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Aims:

Firstly, to assess the timing of fetal growth spurt in pregnancies complicated by maternal type 2 diabetes mellitus (T2DM) and investigate the impact of glycemic control on fetal growth and birth weight.

Secondly, to assess the accuracy of the Estimated Fetal Weight (EFW) of small-(SGA), appropriate-(AGA) and large-for-gestational-age(LGA) infants and the optimal timing of ultrasound examinations in T2DM pregnancies.

Methods:

Approximately 1300 singleton pregnancies complicated by maternal T2DM followed at Danish University Hospitals were studied prospectively between January 2004 and November 2019. Pregnancies were excluded in the case of fetal congenital malformation or no recorded visits. Pregnancies were analyzed individually if the woman had >1 pregnancy. Ultrasound measurements included: biparietal diameter, occipitofrontal diameter, head circumference, transverse abdominal diameter, anterior-posterior abdominal diameter, abdominal circumference and femur length. Z-scores were made using gestational age specific means. EFW was calculated based on visits up to 14 days from birth, only including the visit closest to birth. Secondary outcomes included HbA1c, urine ACR and diabetes treatment regime.

Results:

The collection of data is still in progress.

Conclusion:

The prevalence of T2DM among young adults, including women in the reproductive age, is rising due to increasingly unhealthy lifestyle. LGA-infants is a well-known complication to diabetic pregnancies. With this study, we aim to optimize the use of ultrasound examinations specifically in pregnancies complicated by T2DM with the hope of increasing the chance of identifying the women in risk of LGA-infants.

Keywords: Gynecology and obstetrics, Other, Other

Risk of anogenital human papillomavirus-related precancer and cancer in women undergoing active surveillance of cervical intraepithelial neoplasia grade 2

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Background

Incidence rates of several non-cervical human papillomavirus (HPV)-related cancers, for example vulvar and anal cancer, have been increasing in the last decades. Thus, there is a great need to understand the underlying reasons. Women who have undergone surgical treatment for cervical intraepithelial neoplasia (CIN) are at increased risk of developing other HPV-related precancers and cancers. Given that HPV can establish latency in the cervical mucosa, we hypothesize that women undergoing active surveillance of CIN grade 2 (CIN2) have an even higher risk of developing HPV-related precancer and cancer later in life compared to women treated surgically, as neither the precancerous lesion nor the underlying HPV infection is removed.

Methods

Using data from nationwide Danish registries, we will perform a cohort study including all women with incident CIN2 from 1998-2020. Women will be classified as undergoing either active surveillance, i.e., control visits, or cone biopsy. Using cox proportional hazards-regression, we will calculate risks of vaginal, vulvar, and anal precancer and cancer, comparing women undergoing active surveillance with women undergoing cone biopsy. Women will contribute time at risk from date of first CIN2 diagnosis until time of death, emigration, or on December 31, 2020.

Perspectives

Our results will provide important knowledge on risks associated with active surveillance of CIN2, which will improve clinical counselling of women diagnosed with CIN2, thereby strengthening shared decision-making regarding treatment.

Keywords: Gynecology and obstetrics, Oncology, Epidemiology and biostatistics

Multicenter Study for Evaluation and Development of New Liquid Biomarkers for Early Detection of Prostate Cancer

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Prostate cancer (PC) is the second leading cause of cancer-associated mortality among men in Denmark. While early-stage asymptomatic PC can be cured by surgery and radiotherapy, advanced PC is incurable. Magnetic resonance imaging (MRI) has recently been implemented to guide biopsies of suspect lesions, improving diagnosis accuracy but it remains an expensive procedure with limited capacity at the Danish hospitals. Hence, there is an urgent need for a biomarker test capable of pre-selecting patients in need of a prostate MRI.

We will recruit 2.500 men with suspicion of PC, who are referred to a prostate MRI scan at Aarhus University Hospital (AUH), Herlev & Gentofte Hospital (HGH), or Odense University Hospital (OUH), and having a subsequent targeted biopsy of any suspicious lesions. Prior to MRI results, blood and urine will be collected, and the expression levels of a panel (uCaP) of previously identified microRNAs, found in urine, quantified. Furthermore, we wish to explore the T-cell receptor (TCR) repertoire in the PC patients through DNA-based TCR sequencing.

Pilot study results in a cohort of 34 men undergoing MRI demonstrated uCaP's ability to outcompete prostate specific antigen (PSA) in detecting aggressive PCs with an AUC of 0.76 versus the AUC of 0.51 for PSA, resulting in a reduction of false positives by 47 %. Meanwhile the same number of aggressive PCs were detected.

While preliminary results have indicated strong potential for the uCaP panel to have a clinical impact, further validation is needed. Furthermore, identification of novel liquid biomarkers may improve PC diagnosis accuracy and subsequent well-being of patients.

Keywords: Oncology, Urology, Laboratory science

Symptoms, side effects and immediate functional outcome following transurethral surgery of bladder tumours

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Background

The standard procedure for diagnosis and treatment of tumour tissue in the urinary bladder is transurethral resection of bladder tumour (TURBT). Despite that, research into patient-reported outcome (PRO) following this surgery is limited. Assessment of the impact of TUBRT on patients' lives will be useful when evaluating and comparing newer treatment options such as En Bloc resection (EBR) or laser ablation (LA) with the conventional method.

Objective

To elucidate the immediate symptom burden, functional outcome, and quality of life (QoL) for patients undergoing TURBT.

To compare the PRO after conventional TURBT, EBR and LA among patients with non-muscle invasive bladder cancer (NMIBC).

Materials and methods

Patients undergoing TURBT at Aarhus University Hospital will be asked to complete a validated symptom-based questionnaire (ICIQ-M/F-LUTS), a QoL-questionnaire (EQ-5D-3L) and a newly created post-transurethral operation questionnaire (PROTO) at day 1 and day 14 post-operation.

The questionnaires will also be used to compare PRO between the following 4 groups: patients with NMIBC undergoing EBR (1) or conventional TURBT (2), patients with recurrent NMIBC undergoing LA (3) and patients undergoing control cystoscopy without finding of tumour tissue (4).

Results

Final results are expected in August 2023.

Perspectives

The study will provide knowledge to ensure better patient information regarding the course of bladder surgery and help guide clinicians to better patient-centred care. Furthermore, it will provide insight in to whether newer techniques (EBR, LA) have better PRO compared to TURBT, hence help shape recommendations for NMIBC treatment.

Keywords: Urology, Other, Other

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:

We will perform a prospective cohort study analysing data from 14 days of continuous glucose monitoring from 100 women with GDM, 50 women with GDM expecting a large fetus and 50 women with GDM expecting an average to low weight fetus. 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.

Keywords: Gynecology and obstetrics, Molecular metabolism and endocrinology, Other

Vaginal laser therapy for genitourinary syndrome in breast cancer survivors

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Background: Between 50-75 % of breast cancer survivors experience one or more symptoms as part of the genitourinary syndrome of menopause (GSM), which results in impairment of their quality of life.

Vaginal laser induces a wound-healing cascade with formation of elastin-, and collagen-fibres and thereby activates tissue remodelling in the vaginal wall, which is supposed to reduce symptoms from the vagina.

Methods: This project contains threes studies which will be performed from January 2023 to June 2025.

Study I: A dose-response study to explore the number of laser treatments needed to achieve an effect on GSM symptoms in breast cancer survivors. 30 participants will receive five vaginal laser treatments with 4-6 weeks intervals.

Study II: A randomized, single blinded placebo-controlled study comparing vaginal laser therapy with placebo laser therapy in 60 breast cancer survivors. Number of treatments is identified in study I.

Study III: A 1-year follow up of the participants in study II.

Patient-reported outcomes will be collected by online questionnaires (VAS, UDI-6, ICIQ-FLUTSsex, FSFI, SCS-W). Moreover, tissue effects will be evaluated by collection of vaginal fluid pH values, vaginal and urine microbiome and punch biopsies.

Results: Patient inclusions starts January 2023.

Conclusion: The short and long-term effect of vaginal laser therapy in breast cancer survivors with GSM symptoms will be investigated for the first time in Denmark. If we can demonstrate that vaginal laser treatment is an effective and patient friendly treatment which can increase the quality of life among breast cancer survivors, it could immediately be implemented in daily clinical use.

Keywords: Gynecology and obstetrics, Rehabilitation, Oncology

MoveMOM: Are mothers less physically active than their childless peers? A register-based cross-sectional study in Denmark

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Introduction: Physical inactivity is a risk factor for poor health. Nevertheless, a large proportion of Danish citizens remain inactive. Specifically, mothers are at increased risk of being inactive because childcare is a barrier to be physically active. However, no previous studies have compared physical activity (PA) among Danish women, who have and have never given birth.

Aim: The primary aim is to investigate whether PA measured as weekly hours of moderate to vigorous physical activity (MVPA) differ in Danish women aged 16-64 years, who have and have never given birth. Secondary, to compare PA in mothers at different time points after their latest childbirth.

Methodology: This study is a registry-based cross-sectional study. Data on PA from the Danish population-based survey "Hvordan Har Du Det?" (HHDD survey) will be linked to national registers through the unique personal identification number (CPR-number). The population is women aged 16-64 years who completed the HHDD survey in 2017 and 2021. The primary outcome is PA measured as weekly hours of MVPA. In 2022, we applied Denmark's Statistics for covariates and the Danish Health Data Authority for data on childbirths from The Danish Medical Birth Register. The CPR-number of the mother is linked to the CPR-number of the child, thus enabling us to distinguish women with previous childbirth from women with no previous childbirth.

Perspectives: This will be the first register-based study to examine PA in Danish mothers and their childless peers. Findings may help future research in health promoting primary care interventions targeted PA among mothers. Hereby assisting to combat physical inactivity in Denmark.

Keywords: Public health, Gynecology and obstetrics, Other

Intraoperative clonidine for postoperative pain management in patients undergoing surgical treatment for endometriosis: a prospective, double- blind, randomised controlled trial

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Background: Postoperative pain is a major and common concern for the large number of patients who undergo surgery each year. Unrelieved pain can result in decreased patient satisfaction, increased morbidity, prolonged hospital length-of-stay and increased risk of persistent pain. Therefore, adequate and effective treatment of acute postoperative pain should be prioritized. Opioid analgesics remain the mainstay treatment for postoperative pain. However, there are several potential harms associated with opioid use. It is, therefore, important to investigate whether adjuvant analgesics may reduce the postoperative pain and the use of opioids. This is why the drug clonidine is relevant since it has analgesic properties.

Aim: To investigate the effect of a single dose of intraoperatively administered intravenous clonidine on postoperative opioid consumption, pain intensity and opioid-related side effects after surgical treatment for endometriosis.

Methods: This is a prospective, randomised, double-blind, placebo-controlled trial with two arms. Patients (n=120) scheduled for surgical laparoscopic treatment of endometriosis at Aarhus University Hospital are randomised into two arms. An intervention arm with a single-dose intravenous clonidine (150 microgram) immediately after intubation, and a control arm with a single-dose intravenous isotonic saline (placebo) immediately after intubation.

Perspectives: The results of the study are expected to provide valuable information on safe and effective postoperative pain treatment, with a reduction in the postoperative consumption of opioids.

Keywords: Gynecology and obstetrics, Other, Other

FLASH TALK SESSION 5

The neuroanatomy and connectivity of the Göttingen minipig ventral capsule/ventral striatum

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It is estimated that around 25% of the Danish population will experience depressive episodes during their lifetime. As one of the most common psychiatric diseases, depression is a serious and costly disorder not only for the patient and their relatives but also to public health. Although many can be treated effectively with anti-depressant medication, electroconvulsive therapy, and psychotherapy, those with major depressive disorder are not seldomly treatment resistant.

Recent advances in neuropsychiatric research suggest deep brain stimulation (DBS) in the ventral capsule/ventral striatum (VC/VS), a brain area associated with motivation and reward, as a novel treatment option for treatment-resistant depression. DBS utilizes the neuromodulatory effects of electric current to alter the neural circuitry in the brain, thus potentially altering the neural activities associated with depressive thinking and behavior.

The aim of this study is to describe the anatomy and connectivity of the VC/VS in the Göttingen minipig (GM) to develop a novel large animal model for DBS treatment of major depression.

To describe the connectivity, antero- and retrograde neuronal tracers will be injected into the VC/VS of 4 female GM. Other, already obtained GM brains will be used to describe the neuroanatomy using Nissl staining and several immunohistochemical labellings.

The findings will be compared to the corresponding rodent and human VC/VS areas to evaluate the GM as a suitable translational large animal model for DBS treatment of major depression.

This study is expected to lay the groundwork for the future development of neurosurgical treatment options for treatment-resistant depression.

Keywords: Basic neuroscience, Animal models/disease models, Laboratory science

The role of SorCS1 in neuronal activity, learning, and memory

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Memory defines our personality, behavior, and skills. When memory fails, we might lose our identity. Hippocampus is involved in the formation, organization, and long-term storage of new memories. The hippocampal circuitry comprises of the trisynatic loop where the entorhinal cortex (EC) projects to the principal cells of the dentate gyrus (DG), the granule cells (GCs), GCs project to the dendrites of CA3 pyramidal cells which, in turn, project to CA1pyramidal cells. To form and retrieve a specific memory, neurons form a functional unit called engram. Engram cells thus become activated upon an experience. Engram cells located in the hippocampal dentate gyrus (DG) are represented by specific ensembles of activated GCs that express the immediate-early gene Arc2. Recently, the transmembrane receptor SorCS1 was identified as one of the most upregulated genes in engram GCs. The SorCS1 receptor, a member of the VPS10p receptor family, is involved in post-synaptic sorting and trafficking of synaptic receptors that are essential for synaptic function (Neurexin, AMPAR). Also, its expression has been shown to be regulated by neuronal activity.

Keywords: Basic neuroscience, Cell biology, Other

Predicting drop in post stroke physical activity

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Background and aims

Physical activity (PA) reduces the risk of stroke and improves functional outcome. However, sedentary behaviour after stroke is prevalent. We aimed to study pre- and post-stroke PA levels and to predict drop in PA after stroke.

Methods

We used the Physical Activity Scale for the Elderly questionnaire (PASE) to quantify PA. Demographic and clinical data were collected at inclusion. We created a predictive model of drop in PA using a generalised, regularised logistic regression model (elastic net).

Results

A total of 522 patients, participating in The Efficacy of Citalopram Treatment in Acute Ischemic Stroke (TALOS) trial, completed PASE on both prestroke and six months poststroke PA. Median [IQR] age was 68 [59, 76], 180 (34%) were males and median [IQR] National Institute of Health Stroke Scale (NIHSS) score was 3 [2, 5]. We included 391 (75%) patients in constructing a predictive model. In total, 77 patients (19.7%) had a drop in post-stroke PA. Factors associated with predicting drop in PA were increasing age, living alone, daily or occasionally smoking, hypertension, previous myocardial infarction and stroke severity. Sensitivity of the model was 0.862, specificity 0.290 and AUROC was 0.607.

Conclusions

We found that 19.7 % of patients with PA above the first quartile before stroke had a drop in PA after stroke. Our prediction model only achieved modest performance, highlighting that PA after stroke is highly modifiable and encouraging increased intervention.

Keywords: Clinical neuroscience, Rehabilitation, Other

Neurophysiological biomarkers for early diagnosis of ALS

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Background: Transcranial magnetic stimulation (TMS) is a widely used non-invasive tool for investigating the physiology of the cortico-motor system. It has not yet been adopted widely as a clinical biomarker in neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS) due to limitations such as a lack of convenient software.

Methods: Advanced TMS protocols which includes a new suite of automated recording and analysis programs will be used to improve understanding of the pathophysiology of ALS and other neurodegenerative disorders. In the first part of the study, we expect to include 40 carriers to familial ALS patients to examine the sensitivity of TMS. In the second part of the study, we expect to include 80 patients (20 with sporadic ALS, 20 with Alzheimers disease, 20 with Parkinson disease and 20 with Frontotemporal dementia to examine the specificity of TMS. Data will be compared with 40 age- and sex-matched healthy controls. All patients will be examined again after 6 months. In ALS patients, the biochemical biomarkers neurofilament light chains (NFL) and the most recent biochemical biomarker glial fibrillary acid protein (GFAP) will be measured in serum and compared with TMS data.

Conclusion: We expect that these advanced TMS methods may help to provide as diagnostic biomarkers applicable to sporadic ALS enabling earlier diagnosis of ALS. Furthermore, we expect that TMS can help monitor disease progression in sporadic ALS. The pathophysiological insights gained into ALS, improved assessment of early diagnosis and monitoring of disease progression will hopefully aid future treatment trials.

Keywords: Clinical neuroscience, Medical technology and diagnostic techniques, Basic neuroscience

Mechanisms behind cognitive symptoms in schizophrenia

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Schizophrenia is a disorder with several underlying causes and patients suffer from a variety of symptoms that affect their daily life, their families, and society. It is possible to treat some of their symptoms, but there is no available treatment for their cognitive symptoms. Their cognitive symptoms affect their close relationships, their work, and their life quality. Brodmann area 46 is a brain area that regulates some cognitive functions. In schizophrenia, this brain area is abnormally activated and layer III in this area has dendritic spine deficits.

The aim of this project is to study the mechanisms behind cognitive symptoms using human Brodmann area 46 layer III biopsies from controls and schizophrenic patients. To explain some of the underlying mechanisms, quantitative immunofluorescence, western blot, autoradiography, RNA-Seq, and Nanostring will be used to look at changes in protein and gene expression between the two groups. Genetic data from schizophrenic patients will be correlated with multimodal magnetic resonance imaging data to look at changes in functional networks in Brodmann area 46 layer III and changes in genetic networks from Brodmann area 46 layer III to other brain areas. Aside from obtaining knowledge about schizophrenia as a disorder, results will open a field for potential biomarkers of schizophrenia and novel drug targets to treat cognitive symptoms in schizophrenia.

Keywords: Clinical neuroscience, Pharmacology, Psychiatry, psychology and mental health

Autonomic neuropathy in type 2 diabetes patients with and without diabetic polyneuropathy

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BACKGROUND AND AIMS: Cardiovascular autonomic neuropathy (CAN) in patients with diabetes has been associated with poor prognosis. We aimed to assess the prevalence of CAN and autonomic symptoms among type 2 diabetes patients with and without diabetic polyneuropathy (DPN and noDPN), painful DPN (PDPN) and healthy controls (HC).

METHODS: We included patients from the Danish Centre for Strategic Research in Type 2 Diabetes (DD2) cohort. DPN was defined according to the Toronto classification. Subjects were examined with the Vagus device for the diagnosis of CAN where one abnormal test of heart rate variability indicates possible CAN, and two or more abnormal tests indicate definite CAN. To assess autonomic symptoms, subjects filled out the COMPASS 31 questionnaire.

RESULTS: Of 277 subjects with diabetes, 90 had PDPN, 124 had DPN, and 63 had noDPN. There were 97 HC. We found definite CAN in 19% of patients with PDPN, 25% with DPN, 7% with noDPN and 3% of HC with a higher proportion in DPN compared with noDPN. Global autonomic severity scores were higher in patients with PDPN compared to DPN (29.5 vs 12.4, $p<0.0001$), while patients with DPN without pain tended to report more autonomic symptoms than noDPN (12.4 vs 8.3, $p = 0.2$). Subjects with definite CAN reported more autonomic symptoms than subjects with possible CAN (21.6 vs 8.0, $p = 0.001$) and no CAN (21.6 vs 7.4, $p = 0.0002$).

CONCLUSION: CAN was more common among patients with DPN and PDPN than in those with noDPN and HC. Autonomic symptoms were more common in patients with PDPN than DPN, despite similar CAN proportions.

Keywords: Clinical neuroscience, Molecular metabolism and endocrinology, Other

Prevalence of dizziness and vestibular dysfunction in patients with persistent post-concussion symptoms: a cross sectional study

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BACKGROUND: Concussion is an important public health concern. About 20 % of patients experience persistent post-concussion symptoms (PCS) longer than 3 months post-injury. Dizziness is a frequently reported symptom which can be extremely disabling for the individual patient, affecting both workability and quality of life. We know little about the prevalence of dizziness in patients with persistent PCS and how frequently it is related to vestibular dysfunction.

AIM: We aim to investigate the prevalence of dizziness in patients with PCS. In addition, we aim to investigate whether these patients have vestibular dysfunction.

METHODS: A cross-sectional study is conducted on 100 patients (18-60 years) with persistent PCS 2-4 months after injury. Patients is consecutively recruited from general practitioners or emergency departments in Central Region of Demark as a part of an intervention study (ClinicalTrials.gov ID: NCT04798885). Inclusion of patients is current from May to November 2022. The patients' dizziness symptoms are measured and an otoneurological examination of balance and vestibular function is conducted.

RESULTS: In October 2022 we have included 95 patients in the study. Prevalence of self-reported dizziness, and descriptive results from the otoneurological examination of balance and vestibular function will be presented.

PERSPECTIVES: This study will provide knowledge about the prevalence of dizziness in patients with persistent PCS. Furthermore, the study will contribute with knowledge about whether dizziness in PCS may be related to injury to the vestibular organ. Knowledge about the etiology of post-concussion dizziness is important in developing future treatment.

Keywords: Clinical neuroscience, Ear, nose and throat (ENT), Rehabilitation

Can new fast-acting drugs solve the puzzle of the involvement of serotonin in the mechanism of action of antidepressants?

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Currently available antidepressants show a delayed response and a relatively low efficacy. The development of drugs that address these limitations is critical to improving public health. Cannabidiol (CBD), a non-psychotomimetic component of Cannabis sativa, is a promising compound, since it shows large-spectrum therapeutic potential in preclinical models and in humans. We recently showed that CBD induces rapid antidepressant-like effects in rodents, similarly to ketamine. Although the effects of both drugs seem to involve the modulation of the serotonergic neurotransmission, it is not clear how they differ from conventional drugs (i.e., selective serotonin reuptake inhibitors, SSRIs). Therefore, this study aims at investigating: i) how CBD and ketamine (in comparison to an SSRI, citalopram) regulate the activation of the dorsal raphe nuclei (DRN), the main source of serotonergic neurons to the forebrain in the Flinders Sensitive/Resistant Line animals (FSL/FRL), a genetic model of depression; and ii) whether manipulation of the serotonergic pathways arising from the DRN can interfere with the behavioural and neuroplastic effects induced by CBD and ketamine. First, immunofluorescence will be used to investigate the neurocircuitry activated in the DRN of FSL/FRL rats in response to stress and treatment. Next, a pharmacogenetic approach (DREADD) will be used to manipulate serotonergic pathways to depict their involvement in CBD/ketamine effects. This investigation can potentially contribute to the advancement of our understanding of the molecular and behavioural effects induced by CBD, especially as a promising new fast-acting antidepressant drug.

Keywords: Basic neuroscience, Pharmacology, Psychiatry, psychology and mental health

The effect of aging on hippocampal hemodynamics

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The vascular network in the brain is responsible for delivering oxygen and nutrients to cells to maintain normal brain function. Cerebral blood flow is regulated by pericytes, vascular mural cells embedded in the walls of capillaries, and damage to these cells may lead to increased capillary transit time heterogeneity (CTH) and insufficient oxygen availability to areas of high metabolic demand. Age-related vascular abnormalities and dysfunction are associated with disturbances of capillary flow dynamics and often precede cognitive impairments. This study aims to investigate capillary flow dynamics in the hippocampus of the aging brain to understand how cerebral blood flow is regulated to reduce CTH and maintain oxygen availability in young and aged mice. Using two-photon microscopy to perform awake-restrained imaging, we will acquire measures of oxygen tension, estimate capillary flow dynamics, and determine the severity of blood-brain barrier disruption in young and aged female mice. Hippocampal hemodynamics will be investigated during steady state and vasoreactivity to assess the regulatory ability of aging capillaries. These vascular changes will be coupled to behavioral changes using a behavioral assay to evaluate cognitive impairment and spatial- and learning memory. Histology will provide pericyte quantification and allow comparison of capillary morphology between young and aged mice. Knowledge of vascular, molecular, and behavioral changes will be applied to later studies investigating changes associated with Alzheimer's disease.

Keywords: Animal models/disease models, Basic neuroscience, Medical technology and diagnostic techniques

Intravenous Thrombolysis and Risk of Post-Stroke Dementia. A Nationwide Propensity Score Matched Cohort Study.

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Background: Dementia is a common consequence of a stroke. Intravenous thrombolysis (IVT) is an effective treatment of acute ischemic stroke, however, it is still not known if IVT affects the risk of post-stroke dementia.

Methods: When IVT was introduced in Denmark from 2004-2006, not all eligible patients were treated due to restricted treatment access. We conducted a nationwide register-based cohort study comparing acute ischemic stroke patients eligible for IVT, but not treated, to acute ischemic stroke patients treated with IVT. Patients treated with IVT were matched with non-treated patients by propensity score. Cox proportional hazards regression was used to estimate the hazard ratio for post-stroke dementia defined as a diagnosis of vascular dementia or unspecified dementia within 5 years after acute ischemic stroke.

Results: Before matching 8158 patients were eligible for the study. Median(SD) age was 69 (13.1), 57.7% were male, and median(IQR) Scandinavian stroke scale score was 47(34-54). Non-treated patients were older, more often female, and had lower stroke severity. A propensity score based on baseline covariates was computed, and 2353 IVT-treated were matched with 2353 non-treated with a similar propensity score. After matching, baseline characteristics were balanced between groups. Rate of post-stroke dementia among the IVT-treated was 4.8/1000 person years compared to 7.5/1000 person years among the non-treated. The hazard ratio for post-stroke dementia was 0.64 (0.44-0.93, p = 0.019) for the IVT-treated compared to the non-treated.

Conclusions: Intravenous thrombolysis in acute ischemic stroke was associated with lower risk of post-stroke dementia.

Keywords: Clinical neuroscience, Epidemiology and biostatistics, Other

Regional changes in retinal blood flow during increased blood pressure

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Background: Disturbances in the regulation of retinal blood flow are involved in the pathogenesis of the most frequent vision threatening retinal diseases, including age-related macular degeneration, diabetic retinopathy and retinal vein thrombosis. These diseases are accompanied by a characteristic regional pattern of lesions with hyperperfusion in the central retinal area and capillary occlusion leading to ischemia and hypoxia in the retinal periphery.

Materials and methods: Thirty normal persons aged 20-33 years were examined with Doppler OCT to assess the retinal blood flow at rest and during isometric exercise. The blood flow was measured on the upper temporal arteriole and venule close to the optic disc and on the first larger branch from these vessels towards respectively the macular area and the retinal periphery.

Results: The increase in blood pressure caused by isometric exercise resulted in a significant increase in the blood flow in the peripapillary arteriole (p=0.008) and venule (p=0.01) and the peripheral arteriole (p=0.04) and venule (p=0.04), but not in the macular arteriole (p=0.11) and venule (p=0.06).

Conclusion: An increase in blood pressure in young healthy adults will increase the blood flow in the peripapillary vessels and in vessels supplying the retinal periphery. However, it will not increase the blood flow of the vessels supplying the macular area. This finding may help improve our understanding of retinal rheology in health and elucidate the regional pattern of lesions observed in retinal vascular diseases.

Keywords: Ophthalmology, Medical technology and diagnostic techniques, Other

The neural mechanisms underlying affective responses to sound

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How emotions are formed from auditory input is still open for debate. This Ph.D. project concerns itself with the difference between the perception and production of different acoustic stimuli and their interaction on core affect (i.e., valence and arousal) and thus on the emotional state. The first study concerned itself with acoustic feedback manipulations (i.e., sad, happy, or neutral) in a novel functional magnetic resonance imaging (fMRI) emotion elicitation paradigm to understand how our own vocal expressions may interact with our emotional state. Behavioral analyses showed that participants self-reported valence ratings followed the emotional intentions of the acoustic manipulation. Preliminary fMRI analyses on direct comparisons between conditions suggest an increase in functional activity in brain areas related to emotion. The second part of this Ph.D. project will focus on uncovering the differences between covertly manipulated self-administered vocal feedback and perceiving auditory rhythmic stimuli. Following up on this we introduce the aspect of participation in the production of the rhythms heard and how this differs on the level of pleasure and wanting to move from solely perceiving rhythms.

Keywords: Basic neuroscience, Clinical neuroscience, Other

Investigating alpha-synuclein pathology using novel antibodies against oligomeric alpha-synuclein

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Background: Synucleinopathies are neurodegenerative diseases characterized by the misfolding of the protein alpha-synuclein (a-syn) in different cell populations in the CNS. They include Parkinson's disease, multiple system atrophy (MSA), and dementia with Lewy body (DLB). Although aggregated a-syn is common across these diseases, the type of cell affected, and the neuronal death observed differs across diseases. It is believed that different a-syn strains, i.e. subtypes of aggregates, may contribute to these disparities. However, available tools for distinguishing a-syn pathology are limited, and current tools show overlapping pathology among the diseases.

Hypothesis/Aim: Our aim is to generate antibodies (Ab) that can specifically recognize different pathological a-syn species/aggregates across brain regions in PD and other synucleinopathies.

Methods: We generated several a-syn-specific monoclonal Ab with high preferential affinity for oligomeric (pathologic) a-syn. We tested these by immunohistochemistry of brains from rodent PD models and in post-mortem human brain tissue from patients with different synucleinopathies. Commercial antibodies were used for comparison and co-stainings.

Results and conclusion: Our data show that all Abs recognize human a-syn albeit to a different extent. Co-immunofluorescence showed that our Abs detected pathology that did not fully overlap with that found by commercial Abs. Moreover, the Abs were able to find pathology in post-mortem human brain tissue from both PD, DLB, and MSA patients.

Keywords: Basic neuroscience, Medical technology and diagnostic techniques, Laboratory science

FLASH TALK SESSION 6

N-terminal Pro-Brain Natriuretic Peptide as a Predictor for Detection of Carcinoid Heart Disease in Patients with Neuroendocrine Tumors

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Background: Carcinoid heart disease (CHD) is a serious complication for patients with neuroendocrine tumors (NETs), and early detection is crucial. We aimed to investigate if N-terminal pro-brain natriuretic peptide (NT-proBNP) and 5-hydroxyindoleacetic acid (5-HIAA) could be used as a screening tool for detection of CHD.

Methods: We prospectively included patients with disseminated SI-NETs and performed trans-thoracic echocardiography (TTE), a questionnaire, and biochemical assessment of NT-proBNP and 5-HIAA. The presence and severity of CHD was assessed using a scoring system based on echocardiographic characteristics.

Results: Ninety-three patients were included in the final cohort. Fifteen (16%) of them were diagnosed with CHD. The median NT-proBNP was significantly higher in patients with CHD (219 ng/l vs. 124 ng/l, p = 0.05) and NT-proBNP positively correlated with the severity of CHD (rho = 0.41, p <0.001). At a 300 ng/l cut-off level of NT-proBNP, the area under receiver operator curve for the prediction of CHD was 0.67 with sensitivity 38% and specificity 87%; and positive predictive value of 36% and negative predictive value of 88%. No significant differences in levels of 5-HIAA was found between CHD and non-CHD patients.

Conclusion: Despite a correlation between NT-proBNP and CHD, NT-proBNP lacks the accuracy to be used as a screening tool for CHD in patients with disseminated SI-NETs.

Keywords: Other, Gastroenterology and hepatology, Oncology

Defining and measuring knowledge in cancer screening – is there a need for new information materials?

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Aim: The aim of this PhD project is to examine the concept and measurement of knowledge in cancer screening, as a key element of making informed choices about (non)participation.

Methods: A systematic review evaluating the psychometric properties of the existing scales for the measurement of knowledge about cancer screening will form the basis of this project. Focus group interviews with international scientific experts and around 50 Danish residents eligible for breast, colorectal and/or cervical cancer screening will be used to determine what constitutes relevant knowledge of cancer screening. The results from the interviews will be used to develop a scale for the measurement of knowledge about cancer screening, and the psychometric properties of the scale will be evaluated. The scale will be used in a cross-sectional study to investigate the level of knowledge of cancer screening among Danish residents.

Results: It is expected that the project will contribute to international consensus on what constitutes relevant knowledge of cancer screening and how it is measured. The scale will contribute to an evaluation of Danish residents' level of knowledge of cancer screening based on the current information materials.

Discussion: Consensus on what constitutes relevant knowledge in cancer screening and the development of a scale for measurement of knowledge will enable comparison of residents´ knowledge of cancer screening across countries and between studies. Further, it will contribute with insight of whether current information materials sufficiently support citizens in making an informed choice about (non)participation in population-based cancer screening.

Keywords: Public health, Reviews and meta-analyses, Qualitative research

Ectodermal Dysplasias in Denmark: Identification and characterization of a nationwide cohort

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Purpose: Ectodermal dysplasia (ED) is a large group of rare genetic disorders of the skin and skin appendages. Common features of ED include hypohidrosis, hypotrichosis, and hypodontia. The epidemiology of ED is poorly investigated and large population-based studies of this group of disorders are needed. Therefore, we aimed to identify a large nationwide cohort of patients with ED allowing population-based investigations of the disease epidemiology.

Methods: The Danish National Patient Registry was searched for hospitalizations and out-patient contacts registered with International Classification of Diseases (ICD)-10 diagnoses indicative of ED from 1995-2021. The search was extended using the Danish Central Dentistry Registry (1995-2021), Danish Database of Rare Diseases (2007-2021), and Danish Database of Genodermatoses (2018-2021). Medical records of all identified patients are then reviewed for validation and for detailed patient characterization.

Results: A detailed three-level algorithm of various ICD-10 codes has been developed for the identification of the ED patient cohort. The first level includes available ICD-10 codes for specific ED disorders, whereas level two and three are based on ICD-10 codes for cardinal and minor phenotypical features of ED disorders. We are currently performing data collection from medical records.

Conclusions: Nationwide health registries are a valuable resource in the identification of a large population-based cohort of ED. However, validation from patient medical records is important when studying rare disorders as ED.

Keywords: Dermatology, Epidemiology and biostatistics, Other

Screening of psoriasis patients for psoriatic arthritis

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Up to 30% of patients with psoriasis develop psoriatic arthritis (PsA), which is a chronic disease that can have debilitating consequences without treatment. Patients often suffer from joint symptoms for a prolonged period before being diagnosed with PsA. National Danish guidelines recommend screening patients with psoriasis for PsA; however, there is no consensus on which method is best suited for this purpose. Several screening questionnaires have been developed abroad; thus, the main objective of this study is to validate and compare three PsA screening questionnaires (PEST, PURE-4 and EARP) in a Danish setting. Furthermore, we aim to test whether a simple dermatological assessment of joint swelling, dactylitis, and inflammatory back pain can predict which patients are diagnosed with PsA.

The project is a non-interventional cross-sectional study. Patients with dermatologically verified psoriasis are recruited from the Department of Dermatology at Aarhus University Hospital and a private dermatology clinic. Patients must be ≥ 18 years of age, be able to read and understand Danish and have no prior PsA diagnosis. We aim to include 150 patients in the project. The patients will answer the screening questionnaires and participate in the simple dermatological joint assessment. All patients are subsequently seen by a rheumatologist who rules out or verifies the diagnosis of PsA.

It is our expectation that this study will support and optimize the guidelines for screening patients with psoriasis for PsA in Denmark. As a result, it will be possible to secure a more focused referral of patients with psoriasis to rheumatologists leading to earlier detection and treatment of PsA.

Keywords: Dermatology, Rheumatology, Other

Pilot Study on High-Plex Spatial RNA Profiling to Reveal Cell Type-Specific Biomarker Expression at Initial Diagnosis in Patients with Advanced Stage Mycosis Fungoides

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The biomarkers of early Mycosis Fungoides (MF) evolution and their origin within the malignant CD4+ T-cell clone and its microenvironment, are poorly defined. To address this, we used spatial transcript profiling that maintain the morphological tumor context to measure the expression of > 1000 RNA's in situ in patient-derived formalin-fixed paraffin-embedded tissue sections at time of diagnosis in MF. We are waiting for data.

Keywords: Dermatology, Oncology, Cell biology

Visualization of carbohydrate components of the dental biofilm matrix by fluorescence lectin-binding analysis (FLBA)

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Extracellular polysaccharides and glycoconjugates are matrix carbohydrate components that play an important role in the stability and virulence of dental biofilms. Glucose-based polysaccharides have been investigated extensively, mainly in the matrix of Streptococcus mutans biofilms, but little is known about the role of other matrix carbohydrates in complex multispecies biofilms. This study used fluorescence lectin binding analysis (FLBA) to visualize glycoconjugates/polysaccharides in in situ biofilms from ten healthy volunteers, grown for 48 h with exposure to 4% sucrose (8x2 min/day) or physiological saline. After growth, biofilms were fixed and stained with the FITC-labelled lectins Aleuria aurantia lectin (AAL), Allium sativum agglutinin (ASA) and Morniga agglutinin G (MNA-G), which bind specifically to fucose, mannose and galactose, respectively. Microbial cells were counterstained with SYTO 60. The spatial distribution and biovolumes of each lectin were analyzed by confocal scanning microscopy. All lectins visualized high biovolumes relatively to the microbial biovolume (MNA-G: 170.1%±117.2SD; AAL: 133.6%±127.9SD; ASA: 114.2%±64.9SD). AAL and ASA bound both to areas of low and high cell density, while MNA-G predominantly visualized carbohydrate components in cell-free areas of the biofilm matrix. AAL and ASA, but not MNA-G, showed an increased binding in biofilms grown with sucrose exposure, which may suggest that they visualize sucrose-induced matrix components. FLBA with lectins of different specificities may be a powerful tool to investigate the complex architecture and metabolism of dental biofilms.

Keywords: Dentistry, Other, Other

Communication on obesity-related health and illness in primary care: An applied anthropological approach to strengthen respectful and person-centered weight communication.

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Background

Today, more than 18 % of the Danish population lives with obesity, making obesity one of the biggest health care challenges. Primary care providers (PCPs) carry out an important role in the early prevention and management of obesity-related diseases. However, conversations on obesity in primary care rarely happen which has been linked to the sensitive and awkward nature of weight discussions. Stigma and bias around obesity are well-known and documented challenges in health care settings and being met with negative attitudes, judgments and avoidance prevent people with obesity (PwO) from reaching out to their PCPs.

Objective

This project aims to explore communication on obesity-related health and illness in primary care consultations. Based on in-depth empirical data, we aim to promote respectful, person-centered and anti-stigmatizing communication by co-creating new communication tools in close collaboration with PwO and PCPs.

Methods

The project is twofold and consists of an opening ethnographic study comprising observations of primary care visits and interviews with PCPs and PwO. Inspired by action research, a process of development then follows where PCPs, PwO and researchers will be involved in dialogue and co-creation aiming to develop new communication tools.

Perspectives

- Provide in-depth empirical knowledge on the difficulties and possibilities of obesity-related communication in the interaction between PCPs and PwO.
- Create tangible communication tools to support and educate PCPs to address obesity-related health and illness in well-informed, respectful, and constructive ways.

Keywords: Qualitative research, Public health, Other

The death clock: Biomarkers and models of time since death in humans from metabolomics data

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Determination of the post-mortem interval (PMI) is an important task in forensic investigations of homicides or un-witnessed deaths, not only to establish time of death, but also to distinguish ante-mortem pathology from post-mortem artifacts. Traditional methods in PMI determination involves observation of rigor mortis, livor mortis, algor mortis and the decomposition due to bacteria and bugs. However, as PMI elapse, these observations are no longer applicable, and precision and accuracy are lost. Following death, irreversible changes take place in the metabolome of the corpse. The metabolome is the complete set of small molecules, metabolites, within the body that functions as nutrients, messengers etc. Untargeted metabolomics encompasses simultaneous and unbiased detection of thousands of individual metabolites within a sample. Thus, it provides a detailed snapshot of the metabolite composition at a given time point. Untargeted metabolomics may reveal potential metabolites that exhibit robust and time dependent degradation patterns to be used for PMI estimation. Previous studies have revealed potential markers for PMI using untargeted LC-MS/MS. However, their potential for PMI estimation have only been sparsely investigated through machine learning methods and even less PMI estimation methods have been tested in the forensic practice. Therefore, this project aims to identify markers of PMI using LC-MS based untargeted metabolomics and test this method in forensic practice. This includes testing of different tissue/matrix types to explore which matrix provides PMI markers most suitable for accurate and precise PMI estimation using machine learning methods.

Keywords: Laboratory science, Medical technology and diagnostic techniques, Public health

Comparative and temporal analysis of epigenetics and transcriptomics in patients with sex chromosome aneuploidies

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Background: The most prevalent sex chromosome aneuploidies (SCAs) are Klinefelter syndrome (KS) and Turner syndrome (TS), together with the karyotypes 47,XXX and 47,XYY. Most SCAs suffer from various diseases including congenital malformations, metabolic disease, hypogonadism, infertility, autoimmune disease and psychiatric disease. However, the genetic mechanisms causing these phenotypes are largely unexplained. The phenotypes are suggested to arise from alterations in DNA methylation and RNA-expression

Aim: We aim to increase our understanding of the link between phenotype and genotype in patients with SCAs.

Methods: Blood, Muscle, skin, fat, buccal and urothel tissue will be sampled from 160 patients with SCAs and matched controls. Participants will be scanned using whole-body DEXA-scan, fibro-scan of the liver and Ultrasound of the testis. Other clinical tests include calorimetric analysis, activity and diet tracking. Blood samples will be analyzed for coagulation, metabolism, pituitary and liver function, as well as immunological features. Twenty blood samples from TS patients will be analysed using flow cytometry to describe immunological components. Gene expression analysis, mi-RNA and DNA methylation will be analysed on all tissue samples. Genotype-phenotype association analyses with weighted correlation network analysis (WGCNA) will uncover the patterns in which genes behave and associate with the phenotype.

Perspectives: Understanding genotype-phenotype associations in patients with SCAs would be of great significance to these patients; furthermore, it could lead to a larger understanding of similar diseases in patients without SCAs.

Keywords: Other, Other, Other

A study in healthy volunteers to improve methods for detection of GHB in drug rape victims

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In forensic toxicology, γ-hydroxybutyrate (GHB) presents a challenge, as it is eliminated rapidly from the organism and is difficult to distinguish from endogenous GBH. Apart from medicinal use to treat narcolepsy, GHB is used recreationally, and it is presumed to be used increasingly to incapacitate victims of crime, such as rape, due to its sedative and amnestic effects.

Recently, the Department of Forensic Medicine, Aarhus University, has used metabolomics analysis to identify potential biomarkers for GHB from a large database of blood samples from persons driving under the influence of drugs (DUID).

To validate the findings from the DUID-database, a randomized, double-blinded, placebo-controlled clinical trial involving 30 healthy volunteers, will be performed. The trial subject will be followed for 4 weeks after ingestion of the trial medication and samples of blood, urine, oral fluid, dental calculus, hair, and sweat will be collected. The aim is to identify biomarkers of GHB that can be detected longer or more reliably than GHB itself.

The samples of blood, urine and oral fluid will be analyzed using an explorative, untargeted UPLC-TOF metabolomics analysis, and a quantitative analysis of the concentration of potential biomarkers over time will be performed. A similar analysis of blood proteins prone to GHB-adduction will be carried out, to delineate if these constitute a better alternative to the circulating metabolites.

The samples of dental calculus, hair and sweat will be prepared and analyzed with LC-MS/MS.

Furthermore, it will be evaluated whether the participants' physical appearance and memory is affected by the trial medication.

Keywords: Pharmacology, Other, Laboratory science

Cervical Range of Motion and Pericranial Total Tenderness Score in Post-Concussion Syndrome

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BACKGROUND: Post-concussion syndrome (PCS) following mild traumatic brain injury (mTBI) is an increasing public health issue associated with prolonged disability and reduced quality of life. Due to similarities in clinical presentations, it is considered if PCS shares etiology with Chronic Whiplash-Associated Disorder (WAD). In previous studies a reduced cervical range of motion (CROM) and an increased pericranial total tenderness score (pTTS) have been found common in WAD. However, research on changes in CROM and pTTS in PCS is sparse.

AIM: We aim to examine CROM and pTTS in patients with PCS. Secondly, we aim to investigate the association between the level of PCS symptoms (measured by the Rivermead Post-Concussion Symptom Questionnaire (RPQ)), CROM, and pTTS in patients with PCS.

METHODS: A cross-sectional study is conducted on patients (19-30 years) with PCS and an RPQ-score ≥ 20 2-6 months after mTBI. CROM is assessed using a gravity-referenced inclinometer system and pTTS is stratified by the verbal and visual reaction provoked by manual palpation of eight pericranial trigger points. Values on CROM and pTTS are compared to reference values in existing literature.

RESULTS: A total of 108 patients are included in the study. Mean values of CROM and pTTS in patients with PCS will be presented. Further, I will present an estimate of the association between CROM, pTTS, and the RPQ score.

DISCUSSION: This study will provide important information on CROM and pTTS in patients with PCS, which will contribute to the etiological understanding of PCS. Etiological similarities between PCS and WAD will accentuate the benefits of developing a shared treatment strategy.

Keywords: Rehabilitation, Clinical neuroscience, Medical technology and diagnostic techniques

Developing tumor agnostic approaches to define tumor biology from ctDNA at diagnosis, during treatment and surveillance

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Circulating tumor DNA (ctDNA) has recently become a promising cheap and non-invasive biomarker for detection of cancer throughout all stages of the disease. Currently, most methods focus on tumor-informed approaches for detection of minimal-residual-disease (MRD), where prior genomic analysis of the tumor is required in order to guide the selection of patient-specific panels. This limits the application of ctDNA to the adjuvant and metastatic setting and does not allow for detection of new resistant mutations during treatment. With this study, we aim to investigate ctDNA in a tumor-agnostic setting without a tissue sample, to characterize tumor biology at diagnosis, during treatment and surveillance.

We will analyze whole genome sequencing (WGS) data of circulating free DNA (cfDNA) with paired primary tumor samples from 1.132 patients of different cancer types. With paired genomic data, we will investigate the utility of ctDNA to inform about tumor burden, cancer type and potentially cancer subtype, as well as individual somatic mutations and genomic alterations. More specifically, we will apply current ctDNA calling methods to detect SNVs and CNAs and comparatively analyze these between primary tumor and paired cfDNA profiles. This is done to investigate the utility of plasma WGS to detect SNVs and CNAs present in the tumor. Additional analysis of clonal and subclonal mutations found in cfDNA might inform about intratumor heterogeneity. Furthermore, we will analyze data from serial plasma samples every 3-4 months to investigate the ability to characterize the mutational landscape during treatment, for early identification of treatment resistant subclones.

Keywords: Other, Other, Other

FLASH TALK SESSION 7

Group-based trajectories of endocrine therapy adherence and risk of recurrence among premenopausal breast cancer patients

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Background:

Adjuvant endocrine therapy (AET) halves recurrence risk among the two-thirds of premenopausal breast cancer patients whose tumors overexpress the estrogen receptor (ER+), but many women discontinue AET prematurely. Describing longitudinal patterns of AET adherence is an important step towards identifying patients at highest risk of nonadherence who may benefit from adherence-enhancing interventions.

Methods:

We identified 4,100 premenopausal breast cancer patients in the Danish Breast Cancer Group (DBCG) database treated with AET (2002-2011). At semi-annual follow-up visits, women were registered as having received (or not) a six-month supply of AET. We used group-based trajectory modeling to define patterns in AET adherence for the first 4.5 years following treatment initiation. We fit Cox regression models, adjusted for age and clinical factors, to estimate the association between adherence trajectory groups and recurrence.

Results:

Trajectory modeling identified three groups: women with high adherence (83%), slow decline (9.5%), and quick decline (7.7%). Compared with high adherence women, the estimated rate of breast cancer recurrence was higher among those with slow decline (HR=1.33, 95%CI=1.18–1.50) and those with quick decline (HR=1.41, 95%CI=1.22–1.62).

Conclusions:

Group-trajectory modeling facilitated empirical description of AET adherence patterns in a premenopausal breast cancer cohort. Women who more rapidly became AET-nonadherent were at increased risk of breast cancer recurrence compared with those who remained adherent. These patterns may inform the design of interventions to improve adherence and reduce recurrence risk in breast cancer patients.

Keywords: Epidemiology and biostatistics, Oncology, Pharmacology

Establishment of a regional cohort of 768,083 individuals with a first time Vitamin D blood result between 2000 and 2020

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Background: Vitamin D (vitD) is well-known for its critical role in bone calcium homeostasis. How-ever, it also plays an immunoregulatory role, and vitD deficiency has been linked to serious diseases such as cancer and autoimmune disorders. The objective of this study was to establish a cohort of individuals within the Danish Central Region who has a vitD result in the local laboratory databases.

Materials & Methods: VitD results produced at clinical biochemical departments in the Danish Cen-tral Region in the period from January 2000 to September 2020 were extracted from local laboratory databases.

Results: A cohort of 768,083 individuals (305,942 men and 462,141 women, age range: 0-105 years) with at least one vitD result from 2000 to 2020 was established. The number of vitD results per year increased markedly from 2000 to 2019 (7,496 to 47,845). The concentration of first time vitD measurements increased abruptly from 2002 to 2003 (median 31 nmol/l to 53 nmol/l) but re-mained at this level until 2019 (median 60 nmol/l). Seasonal fluctuations were observed with lowest concentrations in the winter/early spring and highest concentrations in the summer (median 19 nmol/l vs 81 nmol/l). Based on age, lowest concentrations of vitD were observed for teenagers (13-19 years, median 47 nmol/l) and elderly (>90 years, median 49 nmol/l) (all, median 55 nmol/l). VitD concentrations were higher among women than men (median 59 nmol/l vs 50 nmol/l).

Conclusion: We have established a cohort of individuals with their earliest known vitD status which can be used to investigate relations between vitD status and later disease. VitD supplementation among certain age groups need further attention.

Keywords: Epidemiology and biostatistics, Public health, Other

The patterns of health care utilisation and cross sectional care fragmentation in patients with type 2 diabetes

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INTRODUCTION

Type 2 diabetes (T2D) is one of the most common chronic diseases and the incidence is increasing. Patients with T2D often have comorbidities resulting in many contacts to the primary and secondary healthcare sectors. Previous studies have reported some aspects of the health care utilisation of patients with T2D, but we have found no studies covering cross sectional care fragmentation. Additionally, it is of clinical relevance to identify patient in high risk of cross-sectional care fragmentation.

AIM

Firstly, we aim to describe the contacts to the primary sector and the secondary sector respectively, and explore the degree of cross-sectional care fragmentation in patients with T2D.

Secondly, we aim to explore how patient characteristics are associated with i) the use of the health care system in patients with T2D and ii) the degree of cross-sectional care fragmentation.

METHOD

Design: A nationwide register-based cohort study

Population: Patients diagnosed with type T2D in Denmark the 1st of January 2017.

Main covariates: Morbidity status, demographic and socioeconomic variables.

Outcome measures: Contacts to the primary and secondary healthcare system and continuity of care indices.

PERSPECTIVES

The results can be used to get an overview of the health care use of patients with T2D, which has health economic relevance. Based on the patient risk factors related to a high degree of cross sectional care fragmentation, it is possible to identify patients who could benefit from interventions consisting of collaboration between the primary and secondary sector.

Keywords: Multimorbidity, Epidemiology and biostatistics, Public health

How effective is mammography screening on the reduction of breast cancer mortality among breast cancer survivors?

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Background: The project will analyse how much mammography screening reduces breast cancer mortality rates among breast cancer survivors. The results will help with evaluating and improving the ongoing follow-up programme for breast cancer survivors.

Methods: In Denmark, mammography screening was started at different times in different counties. The Funen county implemented a mammography screening program in 1994, while most other Danish counties implemented a screening program in 2008. This variation in timing created an opportunity to compare two similar groups of breast cancer survivors invited and not invited to screening. The study populations will consist of all Danish breast cancer survivors born 1924-1957. Breast cancer survivors will be identified from the national Cancer registry, the national patient registry and the national registry for Pathology. We will identify breast cancer survivors invited to the Funen mammography screening, from the Funen Mammography database. The study population will be followed from the (pseudo) invitation date. Women born before 1938 will never have been invited to the national mammography screening program, wherefore these women can be followed until end 2020. The remaining of the study group will be followed until end 2007. We will compare breast cancer mortality rates among invited and not-invited breast cancer survivors.

Discussion: It is essential that breast cancer survivors get the best available follow-up after their breast cancer diagnosis.

Keywords: Epidemiology and biostatistics, Oncology, Public health

Neonatal invasive Group-B Streptococcus disease and long-term risk of epilepsy – a population-based cohort study.

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Abstract

Objective: To examine the impact of neonatal iGBS (sepsis or meningitis) on the long-term risk of epilepsy, stratified by gender, prematurity, and maternal socioeconomic position (SEP).

Design, setting, and participants: Population-based matched cohort study of children born in Denmark between 1997-2017, followed until 2018, with hospital-diagnosed iGBS in the first 89 days of life. A comparison cohort was computed and matched 10:1 on gender, child´s year and month of birth, and gestational age. SEP was defined by maternal income and education.

Outcome and measures: Epilepsy was defined by ICD-10 codes and prescription codes for anti-epileptic medication. Cumulative risk (%) (CR) of epilepsy was calculated treating death as competing event. Cox proportional hazards regression computed hazard ratios (HRs) including 95% confidence intervals (CIs). Effect modification was calculated on an additive scale for gender, prematurity, and maternal SEP.

Results: 1432 children were identified with iGBS, 1264 had sepsis and 168 meningitis. The overall (0-22 years) CR of epilepsy in iGBS children was 3·6% compared to 2·3% in the comparison cohort. The overall CR for iGBS meningitis was 15.1% (95% CI 8.9 - 22.8), and 2.2% (95% CI 1.4 - 3.4) for iGBS sepsis. Adjusted HR for iGBS children was 2·04 (95% CI 1·46-2·85). Being a boy, born premature or belonging to a low SEP-group added to the risk.

Conclusion: Invasive Group-B Streptococcus disease, especially meningitis, was associated with an increased risk of epilepsy in later childhood. Premature birth, gender, and low SEP were attributable risk factors to develop epilepsy after infant iGBS.

Keywords: Epidemiology and biostatistics, Paediatrics, Infection

Low-dose aspirin prescriptions and breast cancer recurrence: a Danish nationwide cohort study with up to 23 years of follow-up

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Background: Low-dose aspirin inhibits platelet aggregation through inhibition of the cyclooxygenase enzymes. Platelets are thought to play a role in tumorigenesis. As such, aspirin may have a beneficial effect on breast cancer (BC) prognosis.

Objectives: To evaluate the association between aspirin use and BC recurrence.

Methods: We included all women diagnosed with an early BC during 1996-2004 registered in the Danish Breast Cancer Group database. We obtained information on aspirin prescriptions (>= 2) from the Danish National Prescription Registry. We modelled aspirin as a time-varying variable lagged by 1 year. Follow-up started at BC diagnosis and ended at the first of recurrence, death, second cancer, or end of 2018. We conducted landmark analyses starting at years 5, 10 and 15 after diagnosis. We fit Cox regression to compute crude and adjusted hazard ratios (aHRs) with 95% confidence intervals (CI).

Results: Among 21,684 BC patients and 245,309 person-years of follow-up, 4,939 experienced recurrence. Aspirin users had a slightly reduced risk of recurrence (5-year aHR=0.92 (0.76-1.12); 10-year aHR=0.91 (0.78-1.06); 15-year aHR=0.86 (0.76-0.98); 20-year aHR=0.84 (0.75-0.95). Landmark analyses showed a reduced hazard of recurrence at the 5-, 10-, and 15-year landmarks (5-year landmark aHR=0.85 (0.72-1.00); 10-year landmark aHR=0.88 (0.74-1.04), 15-year landmark aHR=0.92 (0.67-1.27). Aspirin users had lower cumulative incidence of recurrence, but higher incidence of death.

Conclusions: Our observed reduced risk of BC recurrence associated with aspirin use is likely due to competing risks given the higher cumulative incidence of mortality in aspirin users.

Keywords: Epidemiology and biostatistics, Oncology, Other

Legume consumption for hepatobiliary and cardiometabolic health

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Background: In January 2021 the new climate-friendly Danish dietary guidelines were launched. A marked change from the old guidelines was the inclusion of 100g/d precooked legumes (edible beans, lentils, chickpeas, etc.) as a substitute for animal protein foods. The current average Danish intake of legumes is 2 g. While cohort studies have found that a higher intake of legumes was related to lower risk of cardiovascular disease, less is known about hepatobiliary health. Research in mice has shown a higher risk of gallbladder disease and a lower risk of non-alcoholic fatty liver disease with a high compared to low consumption of legumes.

Methods: With data from the UK Biobank cohort (N~176,000), I will investigate the association between legume consumption and risk of developing diseases of the liver and gallbladder and putative mechanisms related hereto. Further, I will investigate characteristics associated with consumption of legumes in the Danish Diet, Cancer and Health – Next Generations cohort (N~45,000). Lastly, I will investigate changes in barriers and drivers of legume consumption over time among Danes in two population surveys.

Results: This project will provide knowledge on potential population-level ramifications of full adoption of the new guideline for incidence of hepatobiliary diseases and shed light on which population groups that may easily adopt the new guideline, and which may not, as well as reasons why not and how these reasons change over time.

Conclusion: This knowledge is necessary for the Danish Health Authority to evaluate the benefits and risks of a high legume consumption to direct the green transition of Danish dietary habits.

Keywords: Epidemiology and biostatistics, Public health, Gastroenterology and hepatology

The role of social relationships in the association between mental disorders and mortality – a population-sampled cohort study

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Background: Mental disorders represent one of the greatest global public health challenges due to its prevalence, consequent disability and excess mortality. In the last decade, research has also identified social relationships, measured with indicators such as loneliness, social isolation and poor social support, as key determinants of mortality. However, it remains unclear to what extent loneliness, social isolation and poor social support are also predictors of increased mortality among individuals with mental disorders.

Methods: The study population will be composed of appr. 160,000 individuals aged 16+ years who participated in the Danish National Health Survey ("How are you?") in 2013 or 2017. A cohort design will be applied in which individuals will be followed up from the date of survey participation until death, emigration or end of data availability (currently 31st December 2021), whichever came first. Information on mental disorders in 18 years prior to the survey will be obtained from the Danish Psychiatric Central Research Register.

Results: As the main analysis, we will report age-adjusted, sex-specific mortality rate differences (MRDs) and mortality rate ratios (MRRs). Additionally, MRRs will also be estimated with added adjustment for i) country of origin, education and income and ii) severity of the prior mental disorder.

Conclusion: Importantly, this study may lead to identification of relevant target groups for preventive interventions. Furthermore, the results will provide knowledge on the potential role of social relationships in the excess mortality among individuals with a mental disorder and thus provide indications on the underlying causal mechanisms.

Keywords: Epidemiology and biostatistics, Psychiatry, psychology and mental health, Public health

Thiamine against chronic rheumatoid arthritis fatigue

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Background: Up to 98% of patients with rheumatoid arthritis experience fatigue. Up to 40% experience it daily. The fatigue is overwhelming and uncontrollable. Even though some decrease in fatigue can be achieved by medical treatment and a biopsychosocial approach there is still a lack of opportunities for treatment of fatigue in patients with rheumatoid arthritis. A randomised controlled trial with patients with quiescent inflammatory bowel disease and chronic fatigue have shown that a 28-day high-dose oral thiamine treatment reduced the patients' fatigue.

Objective: To investigate the efficacy of 4 weeks of high-dose oral thiamine (600-1800 mg/day) as treatment for chronic fatigue in patients with rheumatoid arthritis.

Methods: This is a randomised, double-blinded, placebo-controlled, cross-over trial. We expect to include 40 patients with rheumatoid arthritis in remission/low disease activity (based on DAS28-score) and chronic fatigue with no other explanation for the fatigue. Patients will be allocated 1:1 to either A) high-dose oral thiamine for 4 weeks, 4 weeks wash-out period, and 4 weeks of oral placebo or B) 4 weeks of oral placebo, 4 weeks wash-out period, and 4 weeks of high-dose oral thiamine. Fatigue will be measured using the Bristol Rheumatoid Arthritis Fatigue Multi-Dimensional Questionnaire (BRAF-MDQ). The Primary outcome is a reduction (7,43 points) of the chronic fatigue after 4 weeks of thiamine treatment.

Results and conclusion: The study is not complete; results and conclusion are expected in spring/summer 2023.

Keywords: Rheumatology, Other, Other

Underuse of oral anticoagulant treatment among patients with atrial fibrillation and variation between Danish general practices: a register-based cohort study

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Background

Oral anticoagulant treatment (OAT) reduces the five-fold higher risk of ischaemic stroke in patients with atrial fibrillation (AF). In Denmark, approximately 130,000 patients live with AF, and register studies suggest that at least one third do not receive OAT. For most patients with AF, the treatment responsibility rests with the general practitioner (GP), but little is known about determinants of OAT initiation and persistence in general practice.

Aim

We aim to map the extent of potential OAT underuse among patients with AF in general practice and identify patient characteristics associated with increased risk of OAT underuse. Further, we will investigate the extend of GP-related variation in OAT.

Methods

The study is a register-based cohort study using data from the Danish nationwide registers from 2000-18. The population and OAT underuse will be identified based on diagnoses and prescriptions using the STOPP/START criteria adapted to a Danish register context. The overall frequency of OAT underuse and its association with patient-level factors will be estimated using multivariate Poisson models to produce forest plots. Variation in potential OAT underuse among GPs will be quantified in terms of ratios between observed and expected frequencies in the GPs' patient populations. Expected frequencies will be based on patient characteristics, including multimorbidity status using the Danish Multimorbidity Index. To account for random variation, a sampled reference population will be constructed for each GP.

Results

Preliminary findings suggest that OAT underuse is associated with male gender, middle age, and the presence of multi-morbidity. Further analyses are needed.

Keywords: Epidemiology and biostatistics, Cardiovascular system, Public health

Myocardial infarction incidence rates among night workers in the Danish health care sector: exposure-response relations

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Objectives

To examine the exposure-response relation between number of monthly night shifts, other quantitative night work characteristics and myocardial infarction.

Design

National cohort study.

Setting

All public hospital employees with night shift work in Denmark, 2007-15.

Participants

100 784 nurses, physicians and other health care workers working night shifts (80% women) with day-by-day work hour information from a national payroll register.

Main outcome measures

First time hospital admission rates for myocardial infarction by number of monthly night shifts and other quantitative night work characteristics since study entry.

Results

During follow-up, 397 night workers (56% women) were diagnosed with first time myocardial infarction. For female night shift workers, we observed exposure-response relations for number of monthly night shifts, cumulative night shifts, and consecutive night shifts, but not for years with rotating night shifts or years with any night shifts. For male night shift workers, we observed no exposure-response relations.

Conclusion

Increasing extent of monthly night shifts was among women night workers related to an increasing risk of myocardial infarction. No such patterns were observed among men. This may indicate a sex specific effect of night shift work, but this was not an a priori hypothesis

Keywords: Epidemiology and biostatistics, Cardiovascular system, Other

Contacts in general practice during the COVID-19 pandemic: a register-based study

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Background: The COVID-19 pandemic has altered the provision of health care and expanded tele health consultations.

Aim: To study the effect of the COVID-19 pandemic on contact patterns in general practice, and to identify patient groups at risk of losing care.

Design and setting: Register-based study of Danish general practice, including daytime and out-of-hours (OOH) services.

Method: All individuals residing in Denmark from 1 January 2017 to 31 October 2020 were included. The incidence rate for six contact types in general practice and adjusted incidence rate ratio were calculated by comparing the incidence rate in the pandemic period with the adjusted expected incidence rate based on the incidence rate in the pre-pandemic period.

Results: The number of face-to-face in-clinic consultations declined during the lockdown

in March 2020. A subsequent increase in the number of clinic consultations was observed, rising to a level above that of the pre-pandemic period. The number of daytime email consultations increased, whereas the number of daytime home visits decreased. Likewise, the number of OOH telephone consultations increased, whereas the number of OOH home visits and clinic consultations decreased. Consultation rates of patients who are vulnerable, that is, those with low education, old age, and comorbidity, were most adversely affected by the pandemic. The most adverse impact in OOH clinic consultations was seen for children aged 0–9 years.

Conclusion: New methods are called for to ensure access to general practice for patients who are vulnerable during a pandemic. The potential of tele health consultations should be further investigated.

Keywords: Epidemiology and biostatistics, Public health, Other

FLASH TALK SESSION 8

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

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Historically, treatment of mRCC patients has been challenging due to no response to chemo- and radiotherapy, and thus, immune therapy with IL-2 and IFN- was introduced as standard of care, despite a high degree of adverse events, and poor response rates. Recently, the introduction of Immune Checkpoint Inhibitors (ICIs) as a therapeutic option has markedly improved the outcome for these patients. However, ~40% of patients still do not respond to treatment.

In mRCC, interaction between tumor-associated macrophages (TAMs), tumor infiltrating lymphocytes (TILs), and cancer cells is not fully understood. However, TAMs play key roles in promotion of tumor cell proliferation and survival, angiogenesis, matrix remodeling, immune suppression, and facilitation of metastasis. These changes in tumor immune microenvironment (TIME) skew TILs towards an exhausted phenotype with decreased proliferation and effector functions, which at least in part is mediated by increased expression of immune checkpoint molecules e.g., Programmed cell Death protein 1 (PD-1).

The aim of this study is to prospectively validate promising biomarker candidates (sCD163, sCD206, and PD-1) as part of the NORDIC-SUN clinical trial, which will hopefully aid in identifying non-responders to traditional ICIs, whom may benefit from alternative therapeutic strategies. Further, we hypothesize that re-programming of TAMs towards a pro-inflammatory state could potentially improve treatment options for the ~40% of non-responders to ICI treatment. In the future, macrophage targeted lipid nanoparticles (LNPs) containing small molecule drugs may unleash effective anti-tumor immunity from resident TILs.

Keywords: Oncology, Inflammation, Urology

Dosimetric consequences of intra-fractional motion for stereotactic treatment of central lung lesions

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Purpose:

In the STRICT-lung trial (NCT05354596), central lung lesions are treated with stereotactic radiotherapy, using an inhomogeneous dose distribution to the target, always favoring rigorous constraints to organs at risk (OAR). The proximity to the OAR results in a steep dose gradient, very sensitive to intra-fractional shifts. This study presents the dosimetric consequences of intra-fractional motion observed for STRICT-lung patients (pts).

Material and Methods:

Eighteen pts have been treated in/ad modum the STRICT-lung trial. The pts 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 D(GTVmean) and dose D(0.5cc) to the OAR closest to 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 D(GTVmean) was 0.44Gy [-14.11, 5.61], meaning that some of the pts received far less target dose than planned due to intra-fractional target shifts. For most of the pts, the OAR in the closest proximity to the lesion was shifted towards the high-dose region resulting in an increased dose.

Conclusion:

Intra-fractional movements of the target and OAR may result in a risk of increased toxicity and for some pts under-dosage of the target. To ensure the safe delivery of SRT to centrally located lung lesions, it is necessary to monitor and correct for the intra-fractional target shift of the treated pts.

Keywords: Oncology, Medical technology and diagnostic techniques, Other

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. Patients with MM develop an immunosuppressive and cancer-promoting tumor immune microenvironment (TIME) in their bone marrow. This likely, at least in part, explains the fact that some MM patients respond poorly to conventional therapies and that the disease remains incurable to date.

Macrophages displaying an anti-inflammatory (M2-like) polarization state play major roles in establishing a cancer-promoting microenvironment in MM and other cancers. They are therefore regarded as attractive targets for novel immunotherapy that may unleash anti-tumor immunity via activation of T cells. However, knowledge on macrophage and T cell subset activation state/transcriptome in MM, and the implications for treatment response and outcome, is limited.

The aim of this project is to characterize the TIME within the bone marrow of MM patients – on the single cell level – with focus on macrophages and T cell subsets. Thereby, we aim to identify de-regulated signaling pathways responsible for inducing the immunosuppressive and cancer-promoting TIME. Furthermore, we aim to develop macrophage-targeted lipid nanoparticles (LNPs) containing small-molecule drugs or siRNA that can alter these de-regulated pathways and hereby re-program macrophages towards a pro-inflammatory (M1-like) state. We hypothesize that such re-programming of macrophages by targeted LNP-based immunotherapy may activate T cells to kill MM cancer cells. 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.

Keywords: Oncology, Inflammation, Other

Exploring the biomarker potential of the T cell receptor repertoire in bladder cancer patients

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The need for reliable biomarkers to facilitate for early cancer diagnosis, detection of relapse, and prediction of treatment response is urgent. We hypothesize that characterization of the T cell receptor (TCR) repertoire can provide an attractive solution to this need. Cancer specific T cells recognize cancer neoantigens and target malignant cells for destruction and expansion of these is thought to be an early response to malignant transformation. Multiple studies have examined the TCR repertoire and found association with cancer.

Cellular characteristics and diversity of the TCR repertoire has been measured in treatment naive tumor samples and longitudinal blood samples in two bladder cancer (BC) cohorts (cohort 1 and 2) using ultra-deep amplicon sequencing of the TCR-beta. Cohort 1 includes 30 non-muscle invasive BC patients treated with Bacillus Calmette-Guérin immunotherapy and cohort 2 includes 33 muscle invasive BC (MIBC) patients that received neoadjuvant chemotherapy before cystectomy. Detailed follow up data is available for all patients.

Initial analysis shows that MIBC patients that relapse have lower TCR diversity of the peripheral repertoire at diagnosis. The low diversity is often dominated by few large T-cell clones that are consistent throughout the disease. This shows potential for the TCR repertoire as a prognostic biomarker for patients with MIBC but further analysis is needed to evaluate its ability as a diagnostic and predictive biomarker.

Furthermore, T cell subtypes will be determined using bulk RNA sequencing, single cell sequencing and spatial transcriptomics to inspect the T cell status of the samples.

Keywords: Oncology, Other, Other

OxaNeuro - Prevention of oxaliplatin-induced peripheral neuropathy – a randomized controlled trial.

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Background: Chemotherapy-induced peripheral neuropathy (CIPN) is a chronic late effect due to neurotoxic chemotherapeutic agents e.g. oxaliplatin. Neuroinflammation has shown to be a relevant mechanism in CIPN pathogenesis and for development of neuropathic pain.

Polyunsaturated fatty acids (PUFA) are precursors to many active mediators of immune homeostasis. In the inflammatory process, the equilibrium of n-6 PUFA derived pro inflammatory mediators (prostaglandins, leukotrienes etc.) and n-3 PUFA derived specialized proresolving mediators (SPM) (resolvins, protecins etc.) are shifted. With a dietary fish oil supplement concentrations of SPMs increase in peripheral blood and mediate translational changes in the immune cells towards inflammatory resolution.

Aim: To examine if a high dosage of n-3 PUFA reduces the incidence and severity of CIPN 8 months after adjuvant oxaliplatin following surgery for high-risk colorectal cancer. We want to explore Inflammatory mechanisms and biomarkers of CIPN in skin biopsies and in blood (SPM, IL6, IL1, NfL, etc). Furthermore, we want to investigate whether n-3 PUFAs influence nutritional status, cognition and mental health.

Methods: A multicenter investigator-initiated, randomized, double blinded clinical trial including 120 patients operated for colorectal cancer and candidates to receive adjuvant chemotherapy (oxaliplatin and capecitabin) for 3 months. The intervention group will receive capsules of fish oil in an anti-inflammatory dosage (3.0 g/d of DHA + EPA). The control group will receive corn oil in identical capsules daily for 8 months. Patient enrollment has started June 1st, 2022 and will run for approx. 1 year.

Keywords: Oncology, Clinical neuroscience, Inflammation

Identifying signatures of k-mers in indels with non-negative matrix factorization

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It is important to understand the underlying mechanisms, which contribute to the creation of pathogenic mutations, whether it be genetic diseases or carcinogenesis

The sequence around a mutation has been shown to influence the mutation rate. Grouping mutations together into k-mers by their extended sequence context we can use their similarities to construct models, for unpacking the mutational landscape, and extract biological interpretable signals

Traditionally only mutational signatures of point mutations have been investigated and have contributed greatly to identifying carcinogenesis processes. Models, which analyze the breakpoint of insertions and deletions are lacking.

Indels emerge at a much lower rate than point mutations. To identify signals and negate the sparse counts for larger and more unique k-mers we partition the observed k-mers patterns. The partitioning of kmerpapa uses the IUPAC standard, which groups one or more nucleotides together by their chemical similarities

Mutations with a low frequency can be used as a proxy for de novo mutations. Statistically decomposing the rates and spectra of indels using non-negative matrix factorization can extract signatures of mutations from complex biological data sets. Deciphering mutational signatures can unravel underlying biological mechanisms acting on the genome. This same line of thought can be applied to reveal underlying processes in the creation of cancer genomes when dissecting the spectra of indels

Keywords: Oncology, Epidemiology and biostatistics, Other

Detection of cancer with fragment breakpoint motifs

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Introduction: Detecting aberrant cell free dna in the blood have shown potential to be a viable alternative method of detecting cancer when the standard imaging approaches have failed. Cell free DNA from cancerous origin(ctDNA) seems to deviate from that of healthy origin, for example by the pattern of how the DNA is fragmented (fragmentomics).

But fragmentomic signals are influenced by bias effects, which might make it hard to apply the results from one cohort to another, which confounds the use in clinical practice where one wants the test to apply to all settings, centers, hospitals etc.. How well fragmentomics can be used to detect cancer is thus still uncertain, especially with the requirement of cohort-generalization.

Problem: In this project, we tested the fragmentomic feature "fragment breakpoint motifs" to see how well it diagnoses cancer and how well the method generalizes across cohorts.

Material: 9 cohorts were included, totaling shallow WGS cfDNA samples from 1108 healthy and 967 cancer subjects, with all cohorts being sequenced by either department of molecular medicine, Denmark, or by Delfi-diagnostics, USA.

Method: We extracted the breakpoint motifs for all subjects, and applied logistic regression with l1 regularization to predict cancer/healthy given the motif distribution. To test cohort generalization we used a "cohort cross-validation", i.e. trained the method on all cohorts but one, and tested on the excluded cohort, then rotate.

Results: The auc for each tested cohort was delfi1: .82, delfi2: .69, Lucas: .69, cruk-swgs: .65 and c2i-part 2: .69., resulting in a cross-cohort average of .71 (std 5.8). The remaining 4 cohorts were either all healthy or cancer subject

Keywords: Medical technology and diagnostic techniques, Oncology, Other

Gene Therapy for Core-Binding Factor Acute Myeloid Leukemia with t(8;21)(q22;q22.1) – A PhD Study

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BACKGROUND Acute myeloid leukemia (AML) is a malignant disease that originates in the hematopoietic stem cell, impairing differentiation that leads to bone marrow failure and death. Despite new emerging therapies, the prognosis remains poor. Recurrent genetic abnormality t(8;21)(q22;q22.1) defines one of the core-binding factor (CBF) AMLs. The resulting fusion oncogene RUNX1-RUNX1T1 drives the leukemogenesis. Gene editing technology CRISPR-Cas9 allows for induction of specific dsDNA breaks inducing premature stop codons or major DNA damage, resulting in a functional knock-out of the target. Previous research has established that disruption of the RUNX1-RUNX1T1 inhibits leukemic cell growth and proliferation. This PhD study will explore the efficacy and safety of gene therapy for treatment of CBF AML. METHODS Molecular analysis of patient cells from patients diagnosed with CBF AML with RUNX1-RUNX1T1 will be correlated to clinical data from the Danish National Leukemia Registry. Longitudinal samples will be analyzed in order to determine potential clonal events predicting relapse following first line treatment. CRISPR-Cas9 delivered in a lipid nanoparticle (LNP) vector will be tested in vitro and in vivo. The human AML cell line Kasumi-1 and primary AML cells carrying RUNX1-RUNX1T1 will be used in both the in vitro and in vivo testing of treatment efficacy. Healthy tissues will be evaluated to uncover potential off-target effects. RESULTS AND CONCLUSION The data generated will provide data on patients at high risk of relapse who could benefit from targeted therapy and preclinical data on efficacy and safety of LNP-CRISPR-Cas9 as a potential future treatment of AML.

Keywords: Oncology, Cell biology, Medical technology and diagnostic techniques

Overall survival amongst patients with neurofibromatosis type 1 and malignant peripheral nerve sheath tumor

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Background: Patients with neurofibromatosis type 1 (NF1) have a lifetime risk of 8-13% of developing an aggressive sarcoma called malignant peripheral nerve sheath tumor (MPNST). The prognosis is generally poor, with high mortality and poor treatment outcomes.

Aim and hypothesis: This descriptive study will provide new knowledge on the survival of NF1-associated MPNST and compare it to sporadic MPNST within Denmark.

Methods: The study is based on two cohorts: 1) Patients with NF1 from the two Danish National Centers of Expertise for NF1, and 2) All patients diagnosed with MPNST from the national Danish sarcoma database. Dead and alive patients will be included. Data collected are demographics, NF1 characteristics and MPNST characteristics, including treatment and survival. The primary endpoint is overall survival.

Results: 150 patients are included in the study. Out of those, 30 patients were identified with NF1 and MPNST. In the NF1-MPNST subgroup, 10 (33.3%) are still alive, median age at death was 44.9 (15.5-59.1), and median age at diagnosis of MPNST was 35.6 (12.8-67.5). In the sporadic MPNST subgroup, 56 (47.5%) are still alive, median age at death was 62.4 (13.7-92.3), and median age at MPNST diagnosis 52.2 (3.4-92.7).

Conclusion: Further data on NF1-associated MPNST compared to sporadic MPNST will be presented. Results from the study will highlight differences in overall survival between the two subgroups.

Keywords: Oncology, Paediatrics, Other

Outpatient laser ablation of large recurrent non-muscle invasive bladder cancer- OPTIMA

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Background: Non-muscle invasive bladder cancer (NMIBC) is associated with a high yearly recurrence rate up to 61%. These tumours are most frequently treated with TURBT. Patients with NMIBC are generally elderly, multi-morbid, and as a result, they often show a poor tolerability of general anaesthetics. Thus, the need for non-surgical treatment modalities than current TURBT is imminent.

The aim of this study is to investigate the feasibility and tolerability of the Olympus Soltive Thulium fibre laser in treatment of large recurrent low-grade Ta bladder tumours in an outpatient setting.

Methods: Patients will be included from, Spain, France, Czech Republic and Denmark. Included patients must have a recurrent tumour larger than 1 cm and have a history of low-grade Ta tumours. Prior to commencement of the laser ablation procedure, local anaesthesia will be instilled in the bladder. The tumour number, size of the largest tumour and the localization of the tumours will be registered. Non-complete procedures will be registered. Primary endpoint is the fraction of completed procedures without the need for TURBT. On day one and day fourteen following the procedure, patients will be contacted to assess satisfaction with the procedure and to register any adverse events.

Result: For feasibility, we expect a minimum of 80% completed procedures. A total of 145 patients are expected to be enrolled. Inclusion is ongoing.

Conclusion: Outpatient laser ablation of large tumour recurrences has the potential to reduce the number of TURBTs per patient, thus easing the life of patients with NMIBC, with fewer surgical procedures as well as reducing the overall treatment related costs for society.

Keywords: Oncology, Medical technology and diagnostic techniques, Urology

Boron as a Radiosensitizer in Proton Therapy: In-vitro Cell Irradiation and Monte Carlo Simulations

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The recently proposed proton boron capture and proton boron neutron capture therapy both assert that adding a certain amount of high-LET secondary particles may lead to an increased RBE in proton beams. Here, we take a closer look at the magnitudes and cross sections involved, and also attempt to reproduce some of the findings in vitro.

Cultures of the V79 cell line were irradiated in a water tank with a 9x9 cm² uniform field, with the SOBP ranging from 6-9 cm. Cell survival curves were produced at 6 dose points ranging from 1-10 Gy. Each dose point consisted of 3 biological replicates, either with or without sodium borocaptate (BSH) enriched (0.17 µg/ml) medium. From simulations (with TOPAS and SHIELD-HIT12A) we calculated the yield of different boron nuclear reactions and how they change depending on the setup geometry.

No statistical significance between the regular and BSH exposed cells was observed. However, an apparent BSH toxicity affected the colony growth and plating efficiency. A photon (6 MV linac) reference experiment further indicated BSH toxicity, but no radiosensitization. Simulations show the n+10B capture reaction produces a factor of 177 +/-24 more high-LET particles than the p+11B reaction. The fluence of low energy neutrons can increase/decrease up to two orders of magnitude depending on phantom and field size.

No enhanced RBE was observed for natural BSH exposed V79 cells when irradiated with protons. However, should nuclear reactions be the main mechanism of the previously postulated increase in RBE, then the n+10B would be the main contributor to production of high-LET particles.

Keywords: Oncology, Cell biology, Other

FLASH TALK SESSION 9

The requirements for a self-reactive B cell clone to initiate autoimmune disease

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Autoimmunity has been an increasing problem in first world countries for decades. However, it is still uncertain how exactly any polygenic autoimmune disease is initiated. Autoimmunity progresses as it breaks the tolerance of an increasing number of proto-autoreactive or anergic lymphocytes. B cells, acting as professional antigen presenting cells, have been discovered to play an essential part in this process. Here, we investigate what mechanisms B cells employ and what they require to initiate and propagate autoimmunity. By using a transgenic bone marrow chimera model that spontaneously develops autoimmunity, we try to elucidate whether or not the first autoimmune B cell clone must participate in germinal centers to break tolerance of wild-type B cells. To this end, we combined an Aicda-Cre driver line with a Bcl6flx/flx line to preclude germinal center participation. Data, obtained by using time-resolved fluorometric assay and flow cytometry, showed that the total level of anti DNA antibodies and the total level of plasma cells, was not dependent on the first autoimmune B cell clone participating in germinal centers. Histological data furthermore showed that germinal center seeding was equally frequent in both groups and the presence of extrafollicular plasma cells in both groups. Understanding the basis of the autoimmune initiation is key to developing future therapies that target the early stages of autoimmunity.

Keywords: Animal models/disease models, Other, Cell biology

Sustaining fibrotic injury in animal models of idiopathic pulmonary fibrosis

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A.G. Petersen, H.H. Hansen, Gubra

Idiopathic pulmonary fibrosis (IPF) is an interstitial fibrotic lung disease with a high mortality. No curative treatments exist for the disease and the few therapeutic agents available only slow down the imminent decline in lung function. New anti-fibrotic agents are therefore highly sought after, but the drug development is hampered by drug responses in current preclinical IPF models, not being sufficiently predictive for therapeutic benefit in clinical trials.

The murine bleomycin instillation model is the best-characterized rodent model of IPF in preclinical drug discovery, although lung histopathology is not entirely consistent as fibrosis resolves over time. This contrast with histopathological hallmarks in IPF patients, where the fibrotic injury is a chronic and progressive condition. The underlying mechanism of IPF is thought to involve repeated injuries to the alveoli, and the disease has intrinsic risk factors, which display a higher incidence correlating positively with age, male sex, and genetics.

To make more efficacious treatments possible to discover, this PhD project aims to develop and validate an optimized disease model of IPF that fully recapitulate the hallmarks of the disease.

Keywords: Animal models/disease models, Ear, nose and throat (ENT), Allergy

Automatized image segmentation of forensic, biomedical, and biological cases.

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Medical imaging such as x-ray computed tomography (CT) and magnetic resonance imaging (MRI) is a fundamental part of clinical practises and imaging is becoming a more and more integrated research-tool in pre-clinical and basic research disciplines. While the radiologist performs qualitative interpretation, imaging quantification is needed for e.g., measurement of organ size (as obtained during autopsy). However, quantification is a labour-intensive process known as "segmentation", where anatomic structures are 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.

Biomedisa (Lösel et al., 2020) is a novel open access software specifically developed for image segmentation of biomedical and biological data, which are more variable compared to medical imaging. Additionally, the Biomedisa online platform offers an easy-to-use artificial intelligence (AI) function for constructing a neural network (NN) for completely automatic "hands-off" segmentations of large volumetric images.

This Ph.D.-project will use a novel approach. Because AI-imaging analysis is often a "black box" when it comes to understanding how input-parameters translates into the obtained result, the AI-segmentation-development in this project will be performed on carefully selected biological model specimens with optimal body-compositions for a given problem. These species lend themselves to controlled studies, compared to using conventional human or forensic imaging-data repositories, which would be more like "looking for a needle in a haystack".

Keywords: Other, Animal models/disease models, Other

Adaptation and function of liver sinusoidal endothelial cells in obesity

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Liver sinusoidal endothelial cells (LSECs) are highly specialized endothelial cells in the mammalian body. LSECs display unique characteristics and are comprised of fenestrations, display high endocytic capacity, and play a prominent role in maintaining overall liver functions. Healthy LSECs maintain liver homeostasis, while LSEC dysfunction is a key event in multiple liver disorders, including obesity or non-alcoholic fatty liver disease (NAFLD). However, still little is known about the adaptation and metabolic changes of LSECs during progression of obesity.

The LSEC phenotype was evaluated at late (15-20 weeks) stages of obesity in male ob/ob C57Bl/6 mice. Using an untargeted approach, we performed proteomics analysis of isolated LSECs and could validate the obtained results using immunohistochemistry, mRNA gene expression (qRT-PCR), and metabolic flux analysis with radioactive tracers. NAFLD was featured by a prominent activation of pro-inflammatory LSEC phenotype (ISG15, ICAM-2, Galectin-9 expression), decrease in junctional protein expression (VE-cadherin), and altered LSEC bioenergetics. Interestingly LSECs displayed an increased protein expression of enzymes engaged in fatty acid metabolism and oxidative phosphorylation. Furthermore, the endocytic capacity of LSEC from ob/ob mice was significantly altered. Compared to control cells, ob/ob LSECs upregulated scavenger receptors and proteins linked with lysosome formation and endocytosis. These results demonstrate a capacity of LSEC adaptations that might contribute to overall liver disfunction and disease progression.

Keywords: Animal models/disease models, Molecular metabolism and endocrinology, Cell biology

Expanding the CRISPR interference toolbox for targeted transcriptional regulation and in vitro transcribed mRNA delivery

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The CRISPR activation and interference (CRISPRa/CRISPRi) systems allow for targeted transient transcriptional regulation of a specific gene. These systems utilize a nuclease-deficient Cas protein fused to transcriptional recruitment or effector domains allowing for transient transcriptional modulation. While a variety of effective CRISPRa systems have been developed using Cas variants from multiple organisms and various effector domains, limited expansion of the CRISPRi system has occurred. With this project we aim to characterize and expand the CRISPRi toolbox to Cas variants from the bacterial species S. pyogenes, S. aureus, and Acidaminococcus sp., and one from DPANN-type archea, and combine these variants with three known transcriptional repressor domains, KRAB, KRAB-MeCP2, and ZIM3. Finally, we wanted to adapt these systems for in vitro transcription of mRNA and synthetically modified gRNAs for potent RNA delivery to primary blood cells. dCasMINI is an artificially modified variant of Cas12f from archea that is drastically smaller than Cas9 and Cas12a variants, which could make it a great alternative to CRISPR/Cas9 based gene editing and gene regulation as size is often a limiting factor for CRISPR/Cas delivery and gene editing. While dCasMINI was previously developed for CRISPRa, no reports have been made for CRISPRi, nor for RNA delivery of the system. To enable mRNA and gRNA delivery of dCasMINI we are testing two truncated Cas12f gRNA scaffolds for dCasMINI activity in HEK293T, K562, and Jurkat cell lines, as well as variations of 2-O-Methyl and phosphorothioate modified bases to improve stability of the sgRNAs.

Keywords: Genetic engineering, Cell biology, Other

A novel cancer therapy using genetically modified plasmacytoid dendritic cells

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Background: Plasmacytoid dendritic cells (pDCs) are rare, unique immune cells that only make up 0.1% of human peripheral blood mononuclear cells (PBMCs). The cells have several immunological functions that place them as a bridge between the innate and adaptive immune system. This makes pDCs an attractive candidate as novel cell-based immunotherapy against cancer. However, due to their low numbers combined with a low proliferation potential and resistance toward genetic manipulations, pDCs have not yet been explored as a relevant therapeutic cell product.

Aim: By in vitro generation of pDCs from hematopoietic stem and progenitor cells (HSPCs), I aim to gain a better understanding of different effector mechanisms of pDCs which might also be targeted for genetic manipulation. I will work in both human and murine settings and explore the natural properties of pDCs that are linked to anti-tumor activity.

Method: HSPC-pDCs will be generated in vitro via a proprietary differentiation protocol. Using CRISPR knock-out, different effector mechanisms of pDCs will be investigated in vitro using co-culture studies with cancer cell lines. Furthermore, development and investigation of murine pDCs in an in vivo setting will be performed. Genetic modification, based on findings in these studies, will be achieved by either lentiviral gene integration or CRISPR-based genetic engineering.u

Perspectives: Cell-based immunotherapy, including CAR T-cell therapy, is an established cancer treatment, though it still has several complications and limitations to overcome. This project has the potential to overcome these limitations and contribute to a greater understanding of cancer immunology

Keywords: Genetic engineering, Animal models/disease models, Cell biology

Spatial proximity based induced chromosomal rearrangements in the human genome using CRISPR/Cas9

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Copy number variations (CNVs) and chromosome rearrangements contribute to genetic diversity and evolution and are as such important for human health. The frequency with which deletions and inversions occur in the human genome is believed to be inversely correlated with the linear distance in base pairs between the breakpoints. Here, we nuance this assumption by showing that deletions and inversions occur more frequently and faster when we use CRISPR to target loci that often interact in the 3D space - the borders of topologically associated domains (TADs) – as compared to loci that rarely interact – inter-TAD loci.

Our results suggest that spatial proximity is an important, yet undescribed, variable for large-scale deletion- and inversion frequency. This may have implications for understanding the aetiologies of genetic diseases that arise from such structural variations.

Keywords: Genetic engineering, Cell biology, Other

Autophagy as an underlying mechanism for Cannabidiol effects on human microglia

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Cannabidiol (CBD) is the major non-euphoric component of Cannabis sativa. Microglia activation is a major factor in depression pathophysiology. In the last years, marked CBD anti-inflammatory effects have been described. Since autophagy was demonstrated as an important mechanism for microglia anti-inflammatory polarization [4], this study aimed to investigate the role of (macro)-autophagy in CBD anti-inflammatory effects in activated microglia. The human microglia (CRL-3304-ATCC) were exposed to lipopolysaccharide (LPS, 0.1 µg/mL) and 24 hours later, they were treated with CBD (1,10 and 100 µM) for 24 hours. Hydroxychloroquine (HCQ)10 µM and starvation (STV, 2h) were used as autophagy inhibitor and inducer respectively. Nitrite, cytokines (TNFα, IL-1β and IL-4) and arginase activity were determined in supernatants. LC3BI conversion to LC3BII isoform was determined by western blot. The formation of acidic vesicles (AVOS) was determined through acridine-orange flow cytometry. Based on MTT assay, we chose 10 µM as the non-cytotoxic concentration for our subsequent assays. CBD rescued LPS-induced increase in nitrite, TNFα and IL-1β in microglia ($P<0.001$). CBD also increased IL-4 and arginase activity ($P<0.05$) compared to LPS. HCQ pre-treatment diminished CBD effect on nitrite and TNFα ($P<0.05$), and blocked CBD-induced rise in IL-4 and arginase activity ($P<0.01$). CBD increased the % of AVOS compared to LPS ($P<0.05$), which was blocked by HCQ ($P<0.05$). Also, CBD showed a non-significant tendency to increase the LC3BII compared to LPS ($P=0.11$). Therefore, this study demonstrates the participation of autophagy for CBD anti-inflammatory action in human microglia.

Keywords: Pharmacology, Basic neuroscience, Inflammation

Water tank phantom for proton in vitro studies: A proof of concept.

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We designed a large water phantom with the possibility of controlling the precise position of medium filled cell flasks for use in radiobiological in vitro research for proton radiation. This is needed to conduct studies on LET impact in radiobiological in vitro systems. As proof of concept for the water phantom workflow, cell survival curves in different positions of the proton beam were produced.

V79 Chinese hamster lung fibroblasts were seeded in flasks in numbers dependent on expected survival. Flasks were filled with medium and placed in upright position in the water phantom. All cells were fixed 6 days after irradiation. Colonies were then stained using toluidine blue staining agent. Colonies were counted manually with a cutoff-value of 50 cells pr. colony. For all doses, positions and modalities experiments were performed in biological triplicates.

The samples were irradiated cell side first, with either LINAC 6MeV photons or 85-111MeV Protons. For proton irradiations cells were placed at entrance, middle SOBP and semi-late SOBP. For photons 6,4 Gy/min were delivered at the patient's clinic at Aarhus University Hospital. Protons were delivered in DCPT experimental facilities. Samples received the prescribed dose with a total dose certainty of +/- 2%.

Experiments yielded expected dose/survival curves for three tested radiation modalities. The survival curves were used to calculate RBE between protons and LINAC at 10% survival and revealed an RBE for this cell line of 1.0 in both entrance position, middle SOBP and semi-late SOBP.

The setup for the in vitro work was validated through cell survival curves. The water phantom can be used for a variety of proton studies.

Keywords: Cell biology, Medical technology and diagnostic techniques, Animal models/disease models

The novel role of the phosphatidylinositol 3-kinase complex I for autophagy in Saccharomyces cerevisiae

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Macroautophagy, hereafter autophagy, is a self-degradative process conserved among eukaryotes. It is involved in multiple physiological functions to maintain cellular homeostasis. The hallmark of autophagy is the formation of autophagogomes. PhosphatidylInositol-3-phosphate (PtdIns3P) , the product of phosphatidylinositol 3-kinase (PI3K) complex I, plays a vital role for this process. However, it is still unknown how PI3K complex I is recruited at the site of formation of autophagosomes and whether this complex plays other roles in autophagy than producing PtdIns3P. PI3K complex I is composed of five subunits including a lipid kinase Vps34/VPS34 to produce PtdIns3P, a protein kinase Vps15/VPS15 that activates Vps34/VPS34, Vps30/VPS30, a protein with unknown function and two specific proteins: Atg14/ATG14 and Atg38/ATG38, which distinguish PI3K complex I from II. In this project, we use Saccharomyces cerevisiae as a model organism to unveil the recruitment mechanism of PI3K complex I and its extra functionalities. It is interesting that the recruitment of Vps34 and Vps15 to the Pre-Autophagosomal Site (PAS) is upstream of Atg14, Vps30 and Atg38. Moreover, their kinase activities are not necessary to recruiting Atg14. Meanwhile, we also prove that Atg14 has insignificant effect on producing PtdIns3P at the PAS, which indicates it might have other unknown functionalities in autophagy. All these results and the ongoing experiments will increase our knowledge of the autophagy mechanism and may provide insights into the design of therapeutic approaches to prevent or cure autophagy-related diseases.

Keywords: Cell biology, Cell biology, Cell biology

Mapping niche dynamics at single-cell resolution to boost the regenerative potential of aged skeletal muscle

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Aging is characterized by a decline in skeletal muscle mass, strength and regenerative capacity, also known as sarcopenia. Sarcopenia, which leads to loss of mobility and quality of life in the elderly population, is a major public health issue that has now been recognized as a disease by the World Health Organization. On this basis, there is a need for new strategies to boost the regenerative capacity of skeletal muscle in aging. Skeletal muscle stem cells (MuSCs) are required for skeletal muscle regeneration throughout life. There is strong evidence that sarcopenia is accompanied by loss of MuSC function. 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. Research has shown that during aging the immune system shifts from a lymphoid to a myeloid bias, which could potentially drive MuSC dysfunction. Thus, the project hypothesis is that immune system dysregulation with aging impairs muscle regenerative capacity by disrupting the communication between MuSCs and immune cells. To address this question at the single-cell level, the project will capitalize on two technologies, Cytometry by Time of Flight (CyTOF) and imaging mass cytometry to (i) resolve the cellular dynamics of immune cells during muscle regeneration and aging; (ii) investigate if immune dysregulation in aging disrupts the signaling between MuSCs and immune cells; (iii) determine whether defective signaling impairs MuSC function and muscle regeneration in aging. This research will help us develop strategies to modulate the immune system to boost muscle tissue repair in the elderly.

Keywords: Cell biology, Inflammation, Public health

FLASH TALK SESSION 10

Real-time dose reconstruction in radiation therapy accounting for independent 6DoF motion of prostate and lymph node targets

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Purpose: High-risk prostate cancer patients require radiotherapy of both prostate and pelvic lymph nodes (LN) which undergo independent six degrees of freedom (6DoF) motion. This study develops a method for real-time 6DoF motion-including dose reconstruction for two independently moving targets and applies it to prostate patients.

Methods: The study includes 5 patients treated with radiotherapy in 39 fractions with 78/56 Gy to prostate/LN Clinical Target Volume (CTV). The prostate and LN motion was estimated at ten fractions based on x-ray imaging of implanted prostate markers and a post-treatment cone-beam CT scan (CBCT).

Real-time motion-including dose reconstruction was performed post-treatment by in-house developed software. The motion-induced change in minimum dose to 95% of the prostate/LN CTV (ΔD95%) was calculated for each fraction and for all fractions averaged.

Results: The largest observed 6DoF target position error (averaged over one treatment field) was 4.3 mm (left-right, LR), -6.7 mm (cranio-caudal, CC), -18.2 mm (anterior-posterior, AP) and -20.6° (LR), -2.7° (CC), -3.8° (AP) for prostate and 4.8 mm (LR), 10.9 mm (CC), 11.2 mm (AP) and 2.9° (LR), 2.1° (CC), 0.7° (AP) for LN.

For a single fraction the CTV ΔD95% range was [+0.3;-6.5]% for prostate and [+0.3;-12.4]% for LN. It decreased to [+0.1;-2.1]% for prostate and [+0.3;-1.8]% for LN after averaging over all fractions.

Conclusion: X-ray images and post-treatment CBCTs were successfully used to estimate the independent 6DoF prostate/LN motion. Motion-including dose reconstruction revealed large dose distortions for both targets at individual fractions which tended to smear out after more fractions.

Keywords: Oncology, Urology, Other

Cancer recurrence in general practice: diagnostic interval and one-year mortality

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Background: Cancer recurrence (CR) is frequently detected between planned routine follow-up visits (42-60% depending on cancer type). General practice is part of the majority of these CR trajectories. Although treatment options for CR have improved, evidence regarding effects of early diagnosis on survival is sparse. We aim to examine if the diagnostic interval (the time from first symptom presentation to diagnosis) is associated with one-year survival for patients diagnosed with recurrence of seven common cancer types.

Methodology: We will conduct a retrospective, national cohort study based on questionnaire data linked to register data at the individual level. Patients diagnosed with cancer recurrence of malignant melanoma, lung, breast, colorectal, bladder, ovarian and endometrial cancer between November 2021 and April 2024 will be included. Patients are identified consecutively using previously validated, register-based algorithms. Supported by the patient journal, the GP will report if the detection of the CR started in general practice and the date of first symptom presentation. Danish national registers provide information on date of CR diagnosis, comorbidity, education, income, vital status, sex and age. Logistic regression analyses will be used to estimate one-year survival odds ratios as a function of length of the diagnostic.

Results: We plan to include 1100 CR patients and to report the results during 2024. Preliminary results will be presented.

Conclusion: Findings will provide important new knowledge to inform the organisation of cancer survivorship care in Denmark and allocate resources to maximise the benefit for the patients.

Keywords: Oncology, Public health, Other

Intrafractional dose coverage of the internal mammary nodes in high-risk breast cancer patients

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Introduction: Internal mammary node (IMN) irradiation in high-risk breast cancer patients improves overall survival. The Danish Breast Cancer Group (DBCG) guidelines for adjuvant breast cancer radiotherapy recommend ≥98% of the IMN CTV receives 90% of the prescribed dose (V90_CTVn_IMN). This study examines the delivered IMN dose coverage at treatment using continuous portal images (CINE MV).

Methods: A prospective single-center quality assurance study was conducted in a consecutive cohort of left-sided node-positive breast cancer patients treated during 2021 using a wide tangential field technique. During treatment delivery, CINE MV images were recorded. On the final frame of each CINE MV recording the chest wall was matched with the Digital Reconstructed Radiograph (DRR) from the planning CT scan. The geometrical errors were rounded to integer millimeters and binned. For each 1 mm bin a new treatment plan was recalculated. This allowed for a weighted plan sum recalculation of the delivered V90_CTVn_IMN. The primary outcome was the difference between delivered and planned V90_CTVn_IMN.

Results: In total, 39 breast cancer patients were included for analysis. The mean number of CINE MV observations per patient was 36 (range 26-55). Most patients (67%) had on average a lowered chest wall position on CINE MV images compared to the plan. This translated into a statistically significant reduction of the delivered mean V90_CTVn_IMN of 1.54 % (95% CI, 0.59-2.48; p=0.002). The V90_CTVn_IMN reduction was >3 % in six patients and >9 % in three patients.

Conclusion: Using CINE MV images, we found that the delivered V90_CTVn_IMN was significantly lower than planned.

Keywords: Oncology, Other, Medical technology and diagnostic techniques

STING modulation & radio-immunotherapy treatment of malignancies

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Background: Radiotherapy (RT) is known to induce a local inflammatory response, that triggers multiple parts of the immune system. However, it is not yet established how to fully exploit the immunostimulatory effect of RT in cancer treatment. Stimulator of Interferon Genes (STING) is an endogenously expressed protein involved in innate immune activation by sensing cytosolic DNA. Cytosolic DNA has been shown to be present in tumor tissue after RT, however, it is not fully understood how and to what extent cGAS-STING mediated DNA detection and subsequent immune activation is essential for a proper anti-tumoral response.

Methods: STING wildtype (WT) and knock-out (KO) murine cancer cell lines will be used to investigate the effect of STING expression on the response to photon and proton irradiation in vitro. Furthermore, WT or STING KO mice strains will be challenged with either WT or KO murine cancer cells and receive RT in various doses and treatment schedules. The dependency of RT-induced tumor clearance and immune cell infiltration linked to host or cancer cell STING expression will be evaluated by measuring tumor growth and by a multiple-parameter immunophenotyping flow panel.

Perspectives: Immunotherapy has shown impressive results with the clearance of otherwise incurable cancers. However, there are still patients who do not respond to conventional immunotherapy, thus there is an increasing need for synergistic treatment regimens to overcome this resistance. Knowledge of the immune-activating effects of RT and possible synergistic effects with immunotherapy could potentially lead the way to new and better treatment regimens for this group of patients.

Keywords: Oncology, Inflammation, Laboratory science

Validation of data in the Danish Lung Cancer Registry

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Background:

The Danish Lung Cancer Registry (DLCR) prospectively includes information on all Danish patient newly diagnosed with lung cancer from the Danish registries as well as from the treating clinicians. The clinical information in the DLCR has never been systematically validated. We aimed to asses the data validity of the DLCR.

Method:

The validity of the DLCR was assessed by crosschecking with information from medical records. Information from the DLCR was granted from The Danish Clinical Quality Program, National Clinical Registries (RKKP) and a random sample of 1000 patients diagnosed with lung cancer between 2014 and 2016 was evaluated. Data was collected from all 5 regions and stored in REDCap. STATA was used to calculated positive predictive values of selected clinically relevant variables.

Results:

Preliminary results are expected to be presented at the PhD-day.

Conclusion:

We expect our findings to show that the DLCR holds valid information on Danish lung cancer patients and is can be used for research in lung cancer.

Keywords: Respiratory system, Oncology, Epidemiology and biostatistics

Characterizing the impact of the T-cell repertoire on the clinical outcome of bladder cancer

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Expansion of cancer specific T-cell clones is thought to be an early response to malignant transformation, where T-cells recognize cancer specific neoantigens and target the malignant cells for destruction. Due to this expansion, we hypothesize that characterization of the T-cell receptor (TCR) repertoire based on minimally-invasive liquid biopsies could serve as an biomarker for cancer, possibly allowing for early detection.

We have characterized the TCR repertoire for two bladder cancer cohorts, using ultra-deep amplicon-based sequencing of the TCR-beta chain. Treatment naïve tumor samples as well as longitudinal liquid biopsy samples taken before and after treatment were characterized for each patient.

Initial analysis shows that high TCR diversity at baseline and high blood T-cell fraction is associated with better outcome in muscle invasive bladder cancer (MIBC). Additionally, longitudinal analysis revealed that patients with worse clinical outcomes showed reduced variation in their TCR repertoire. In these patients, large clones often dominated the T-cell landscape with little variation observed over time. We show that these large T-cell clones are not associated with clonal hematopoiesis, but further analysis is required to fully characterize the nature of this subset of T-cells.

Further analysis aims to identify tumor specific T-cells by matching liquid biopsy TCR sequences with sequences obtained from TCR sequencing of tumor tissue. In time, detection of tumor associated T-cells in liquid biopsies could potentially be used to distinguish cancer from non-cancer patients, allowing the TCR repertoire to be used for cancer detection.

Keywords: Oncology, Other, Other

A reference-free strategy for detecting circulating tumor DNA

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Cancer recurrence after tumor resection surgery decreases the survival rate of patients. Therefore, it is crucial that recurrence is detected early, so treatment could be offered promptly. Several approaches have been proposed that use circulating tumor DNA (ctDNA) in patients' blood plasma samples as a biomarker for cancer detection. In most cases, few somatic point mutations known to be present in the cancer genome are used to detect ctDNA. However, these point mutations become less reliable when ctDNA fraction is low and sequencing is carried out with low coverage.

The aim of this project was to develop a strategy that identifies tumor specific somatic variation from cell-free DNA (cfDNA) and estimates ctDNA fractions to detect recurrence. The method uses somatic variation across the genome and is not limited to point mutations.

The developed approach creates a set of k-mers (DNA sequences of length k) which are expected to be unique to the cancer genome by removing k-mers observed in germline samples and setting constraints on the k-mer counts. Subsequently, unique tumor k-mers are searched for in the cfDNA and a fixed ctDNA fraction threshold is used to find the relapse time point.

We tested the method on 96 stage III colorectal cancer patients. Relapse was detected correctly for 12 out of 18 patients and falsely for 8 patients out of 78. The low sensitivity can be explained by germline k-mers that are not removed from the tumor specific k-mer set and additional germline k-mer filtering is needed to improve results.

In conclusion, the developed method is a novel solution to detect ctDNA, but the sensitivity of the method needs further improvement.

Keywords: Oncology, Other, Other

FLASH radiotherapy - the effect of dose rate in pre-clinical experiments

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FLASH radiation, a promising new radiotherapy modality, has received massive interest, and several studies have shown an increased therapeutic window by normal tissue sparing and unaltered tumour response. A step on the path to clinical translation would be to better understand the underlying mechanisms of dose rate. This study aims to provide preclinical knowledge on the radiobiological effect of radiation FLASH beams by increasing comparability between electron FLASH (eFLASH) and proton FLASH (pFLASH), to enable comparisons of the difference in time structure of the dose rate.

The study will use the experimental setup of previous pFLASH experiments. The right hindleg of CDF1 mice will be irradiated with a single fraction using either conventional electron beams (eCONV) within ranges of 25-60 Gy or eFLASH beams within dose ranges of 35-75 Gy. Alanine dosimetry will be used for in vivo dose validation.

Dose modification factor from acute skin score and ratio of fibrotic mice will be compared between eCONV and eFLASH treatment. The achieved dose responses are then compared to previous pFLASH studies. With the identical experimental setting, the difference in tissue damage between eFLASH and pFLASH can be primarily ascribed to the difference in the time structure of the dose delivery with a similar mean dose rate but differing pulse duration and instantaneous dose rate.

Data has yet to be collected, but we expect to see a generally reduced normal tissue damage with eFLASH relative to eCONV and to be able to assess a conversion factor between electron and proton beam FLASH.

Keywords: Oncology, Animal models/disease models, Other

Genetic reprogramming of cancer cells to induce anti-tumoral responses

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Recent evidence indicates that the tumor microenvironment often induces a dysfunctional local immune response, preceding tumor evasion and tumor survival. In some cancers the mechanism behind this evasion strategy can in large part be linked to epigenetic regulation of selective genetic pathways. One of these is the cGAS-STING pathway, in which the protein STING is downregulated. STING is central in the cGAS-STING pathway - an evolutionary conserved innate immune pathway, which senses foreign and self-DNA accumulating in the cell cytoplasm. As cancer cells often have increased DNA instability, the downregulation of STING leads to a reduced response and thus the activation of the innate immune system is impaired.

In our project, we rewire the epigenetic silencing of STING in cancer cells by using CRISPR-Cas9 activation technology. So far, our data demonstrate that STING suppression can be overcome, leading to a significant increase in STING expression, activation, and downstream expression of interferons and inflammatory cytokines. This project seeks to elucidate the basic cellular and immunological effects observed when epigenetic regulation is overcome in tumor cells. . Our main model is triple-negative breast cancer, using the murine 4T1 cancer cell line. We aim to generate a proof-of-concept for reprogramming the tumor microenvironment in vivo and to show anti-tumoral responses leading to tumor regression.

By unraveling the molecular mechanisms resulting from CRISPR-Cas9 activation of STING and other targets, this project will take the next step towards offering highly effective and specifically targeted cancer treatment.

Keywords: Oncology, Genetic engineering, Cell biology

Infection and risk of late breast cancer recurrence: A Danish population-based cohort study

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Background:

About 17% of Danish breast cancer patients who survive at least 10 years after primary diagnosis develop breast cancer recurrence. Yet, risk factors for such "late" recurrence are not fully understood. Dysregulation of the immune system has been associated with regrowth of tumor cells in several cancer types. Lab studies suggest that antibiotic-induced disturbances of the gut microbiota disrupt immunologic signaling, reduce chemotherapy effectiveness, and stimulate neoplastic progression. Thus, the objective of this study is to evaluate the association of antibiotic use and hospitalization due to infection—as markers of immune dysregulation—on the risk of late breast cancer recurrence.

Methods:

In a population-based cohort study we will cross-link data from Danish registries on breast cancer diagnosis and recurrences, antibiotic prescriptions and hospitalizations. The study population includes Danish women diagnosed with non-metastatic breast cancer during 1987-2004, who were alive and without recurrent disease 10 years after primary diagnosis. We will classify women as exposed if they redeemed ≥2 antibiotic prescriptions and/or had ≥1 hospitalization for infection between primary diagnosis and end of follow up. Follow up will begin 10 years after primary diagnosis and end on the date of late recurrence, second cancer, emigration, death, or 31st December 2020. We will use Cox regression to calculate hazard ratios associating hospitalization due to infection or antibiotic use with late recurrence.

Results:

Under preparation.

Conclusion:

Our findings will contribute to knowledge on late breast cancer recurrence and could potentially identify women at increased risk.

Keywords: Oncology, Epidemiology and biostatistics, Infection

Cancer Patients with Pre-existing Severe Mental Disorders (CASEMED)

- 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 / severe depression, bipolar disorders and schizophrenia, are known to have reduced life expectancy. Collaborative care models show promising results of improving cancer care among these patients.

The aim of this new PhD-study is to develop a Danish collaborative care model for patients with cancer and pre-existing SMD.

METHODS

The intervention will be developed with directions from the Medical Research Council guidelines focusing on development, feasibility, piloting, and evaluation. Through systematic literature search and a yet not published anthropological study barriers at patient-level, provider-level and system-level has been identified.

With inspiration from the Bridge Model (led by assistant professor Kelly Irwin) and in context of the COM-B-MODEL the research group are developing a possible collaborative care model. The meaningfulness, feasibility and implementation of the proposed care model will be discussed at a workshop with participating health care professionals from the oncology, psychiatry, and primary care sector. After modelling the intervention, a small-scale feasibility test will be performed and evaluated by patients and participating health care professionals.

Subsequently, a pilot test among all SMD-patients with head- and neck, breast, or lung-cancer at AUH for approximately one year will be included and evaluated.

CONCLUSION

This study has a high potential to optimize treatment for cancer patients with SMD and hopefully we will be able to show, in the future, that the cancer care model can enhance the quality of health care, patient satisfaction and outcome.

Keywords: Oncology, Psychiatry, psychology and mental health, Qualitative research

FLASH TALK SESSION 11

Mind the Heart - Lived experiences of parents to children with congenital heart disease and mental health issues

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Objective

Congenital heart disease (CHD) affects nearly 1% of live births. Diagnosis and subsequent treatment procedures can cause significant parental psychological distress, which might affect parenting behaviours. Further, children with CHD face an increased risk of mental health issues, such as depression, ADHD and autism. The aim of this qualitative study is to explore the lived experiences of parents caring for a child with both CHD and mental health issues.

Methods

Seven parents were recruited through social media and the children's outpatient cardiology ward at Aarhus University Hospital using purposive sampling, aiming for variation in child sex, age, CHD and mental health issues. Parents were interviewed online using a semi-structured interview guide with open-end questions, focusing on how they understood their child's CHD and mental health issues. As mental disorders are often overlooked in young patients with chronic somatic diseases, the interviews also focused on the parent's perspectives on whether the CHD affected how the child's mental health issues were recognized and supported within the family, school and health care system. The interviews will be analysed using interpretative phenomenological analysis (IPA).

Results and conclusion

The results will be ready during spring 2023. We expect they can increase clinical awareness on the mental health in children with CHD and inform communication in clinical encounters.

Keywords: Psychiatry, psychology and mental health, Qualitative research, Cardiovascular system

Mental Health Status of People Living with HIV in Rwanda

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Christian Kraef, Department of Infectious Diseases, Rigshospitalet, and Danish NCD Alliance (co-supervisor)

Addressing mental disorders in people living with HIV (PLWH) is the next big challenge ahead in fighting HIV in order to ensure an optimal treatment response to antiretroviral therapy (ART). However, only few studies have investigated mental disorders in PLWH in Sub-Saharan Africa. Thus, more epidemiological evidence in this area could improve management of mental health among these individuals.

The objectives of this cross-sectional study are to assess and compare the prevalence of depression, anxiety and post-traumatic stress disorder (PTSD); their risk factors; and their effect on ART adherence and viral suppression in a cohort of Rwandan PLWH.

To estimate the prevalence of these mental health disorders, the validated Mini International Neuropsychiatric Interview (MINI) will be used. Data on viral load and ART adherence will be collected at the time of the MINI. The participants are enrolled from an ongoing prospective cohort study on PLWH and non-communicable diseases in Rwanda. We aim at including 480 PLWH stratified by age, gender and time since HIV diagnosis from hospitals within each province of Rwanda.

The results of this study will contribute to the integration of mental health care services with existing HIV treatment programmes with implications globally by complying with the goals of the United Nation's declaration "Ending Inequalities and Getting on Track to End AIDS by 2030" which commits to making mental health care accessible to 90% of PLWH by 2025. This is an important step towards solving the challenge of health inequality which we are still facing with the HIV epidemic.

Keywords: Psychiatry, psychology and mental health, Infection, Public health

Mental health of generation Z female athletes

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In the context of elite sport, mental health is a concern. One might expect that because athletes are physically healthy and strong and can perform at a high sporting level, they must also be mentally healthy. This, however is not the case. Some skilled elite athletes do also experience mental ill-health (Rice et al., 2019; Gouttebarge et al., 2019). Up until now, the literature within mental health in elite sport mainly focused on adult elite athletes, yet little is known about mental health in the context of young athletes who is a part of the talent development system (Schinke et al., 2018). When we look at the general population, an increasing number of young people in Denmark are not thriving. Teenagers and young adolescents report that they experience mental health problems (Danskernes Sundhed, 2018). This project will contribute to our understand of mental health in elite sport, especially in the context of talent development. The project is designed as a short-term ethnographic study using go-along interview and observation. The first author will follow 12 female athletes that are a part of the national youth team in their respective sport and a part of a dual career program. Each girl will be followed for 14 days (in total six month of fieldwork) and the first author will be together with the athlete individually, during school, training and competitions. The project will attempt to answer the following questions: How do young female athletes' experience flourishing and languishing in their sporting life? How can we understand mental health in an elite sport context? And how does support staff and family influences their mental health state?

Keywords: Qualitative research, Psychiatry, psychology and mental health, Other

The impact of workload on burnout in Danish general practitioners – a combined survey and register-based study

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Burnout is a common issue among general practitioners (GPs). The aim of this study was to assess the risk of burnout among Danish GPs in relation to workload, assessed by register and self-reported data.

Burnout was measured using the Maslach Burnout Inventory (MBI). A composite score of quartile points was calculated for the three subscales of the MBI. The questionnaire provided data on working hours. Register data provided information on number of consultations and patient list size. Data were analysed with binomial regression adjusting for age, gender, and liability from socially vulnerable patients.

The survey was sent to 3381 Danish GPs. 1866 GPs (55.5%) responded, 392 were included. Regarding working hours per day, GPs belonging to the second and third quartile both in the unadjusted (RR = 2.26, 95% CI [1.35—3.79] and RR = 1.90, 95% CI [1.11—3.23]) and adjusted analyses (RR = 2.86, 95% CI [1.78—4.61] and RR = 2.19, 95% CI [1.28—3.74]), had higher risk of a high burnout score.

We found a correlation between burnout and long daily working hours in practice. Interestingly, the same relationship did not apply to weekly working hours. This means that GPs, who accumulates their work in practice onto fewer days, resulting in longer hours per day, are more prone to burnout. There are several possible explanations for this. Firstly, GPs with fewer workdays in practice may have other obligations on their days off, resulting in a high workload that we were unable to measure. Secondly, GPs experiencing stress may choose to reduce the number of days they spend in practice as a coping mechanism. Meanwhile, if the workload is not likewise reduced, this strategy may backfire.

Keywords: Work environment and organisation, Psychiatry, psychology and mental health, Other

Specific contamination symptoms are associated with experiencing a limited response of cognitive-behavioral therapy in pediatric patients with OCD

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A recent study identified three distinct OCD treatment-response trajectories during and after treatment in a large pediatric sample, where higher levels of contamination symptoms predicted being a limited responder to cognitive-behavioral therapy (CBT). This study is an extension of this, examining what characterizes a group of limited responders to CBT regarding contamination symptoms from baseline to 3-year follow-up. The study sample comprised 269 patients with OCD, aged 7-17 years, from Denmark, Sweden, and Norway. All participants received stepped-care treatment with 14 weekly sessions of manualized CBT. Differences in the sum of contamination symptoms and differences in single item-reporting between the three groups was examined using linear mixed-effect modeling. Limited responders were characterized by a higher symptom load across all OCD symptom categories at 3-year follow-up, dominated by contamination symptoms. A significantly smaller reduction of the sum of contamination items from baseline to 3-year follow-up between the limited responders and the other groups was found. In the limited responder group, five contamination items showed persistence from baseline to 3-year follow-up. The results indicate that specific contamination symptoms may play an important role for a certain group of young patients with OCD and their response to CBT.

Keywords: Psychiatry, psychology and mental health, Other, Other

Social inequality in depressive symptoms among Danish 15-year-olds in two longitudinal cohort studies.

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Background

In Denmark, medication use, psychiatric diagnosis, and self-reported poor mental health in adolescence have increased the last decade. A social gradient in mental health is well-known among adults, but little is known about whether social inequality is associated with the negative development in adolescents' mental health.

Method

In two cohorts, VestLiv in 2004 (n=3,004) and FOCA in 2017 (n=11,206), self-reported depressive symptoms were measured with the 4-item version of the CES-DC scale. Subjective social status (SSS) was measured with the MacArthur Scale–youth version.

The prevalence of depressive symptoms among females and males was stratified on objective SES (mother's educational level and equalized household income 5 years prior to the survey) and SSS (in society and school) in the two surveys.

Results

The prevalence of depressive symptoms in 15-year-olds increased from 2004 to 2017 in females (39% to 62%) and males (30% to 44%). The only associations between objective SES and depressive symptoms found was in females of mothers with low educational level (OR=1.36) compared to medium educational level and females from families with high household incomes (OR=0.59) compared with average household incomes. The prevalence of depressive symptoms was highest among adolescents with low SSS and lowest among adolescents with high SSS. The association between SSS and depressive symptoms was stronger in 2017 than in 2004.

Conclusion

The prevalence of depressive symptoms increased from 2004 to 2017, especially among females. No association between objective SES and depressive symptoms was found, while a strong association between SSS and depressive symptoms was found.

Keywords: Psychiatry, psychology and mental health, Socio-economic conditions, Public health

The role of socioeconomic status on the association between mental disorders and mortality: a systematic review

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Aim

This review aims to identify, appraise, and synthesize the evidence for whether and how the association between mental disorders and mortality is modified by socioeconomic status (SES).

Methods

Studies were included if they were observational studies (e.g., cohort studies, case-control studies) that reported the estimates of mortality associated with mental disorders stratified on SES. Four databases (MEDLINE, EMBASE, PsycINFO and Web of Science) were searched from 1980 to June 23, 2022. A snowball search for reference and citation lists was also applied. Titles, abstracts, and full text of included studies were screened by independent reviewers. We primarily extracted data from eligible studies on study characteristics, SES measures and effects, and study quality (the Newcastle-Ottawa Scale). Narrative synthesis will be conducted.

Results

Of 21,077 articles screened, 63 were included. In preliminary results, we observed that most studies were conducted in high-income countries and China. In addition, 44 (69.8%) were patient-only studies; 5 (7.9%) studies on the interplay of individual and area-level SES. Great heterogeneity in SES measures and effects was found between studies. We will report the summary of both absolute and relative mortality estimates for males and

females separately and both sexes combined. All estimates will be stratified by SES indicators, type of mental disorders and causes of death.

Conclusion

This study helps understand the existence, strength, and direction of SES's impact on the association between mental disorders and mortality. Knowledge of this association may help identify high-risk subgroups.

PROSPERO registration number: CRD42022340438

Keywords: Psychiatry, psychology and mental health, Socio-economic conditions, Reviews and meta-analyses

A new experimental approach to examine cognitive biases for gastrointestinal related stimuli – A first test on healthy children and adolescents

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Background: Cognitive biases refer to abnormalities in attention, interpretation and memory of specific stimuli. The interplay of such biases for disorder-specific stimuli are suggested to be crucial in the development and maintenance of functional disorders in adults. However, the influence of cognitive biases in children and adolescents with functional disorders is sparsely examined. Among children and adolescents, functional gastrointestinal disorders (FGID) are very common. Therefore, we developed a new method for examining cognitive biases for general bodily symptoms and symptoms specific for the stomach. This study was a first test on healthy children and adolescents to explore possible sex- and age-related differences regarding cognitive reactions to such stimuli. Further, we aimed to produce a comparison material for examining potential cognitive biases in youth with FGID.

Methods: Participants were aged 8 to 17 years and recruited through school intranets, social media and word of mouth. The participants completed an online survey, which included two experimental tasks; a picture task and a word task. Each task had three phases: encoding, free recall and recognition to ensure that the interplay between biases could be assessed. Participants were presented with pictures and words with relation to general bodily symptoms and symptoms specifically related to the stomach.

Results and discussion: The data collection is not yet complete. Results will be presented and discussed at the PhD-day.

Perspectives: A greater knowledge of cognitive biases in functional disorders could help support the development and implementation of effective treatment for affected individuals.

Keywords: Psychiatry, psychology and mental health, Paediatrics, Other

Mobile app-assisted behavioural treatment (MA-BT) in Children and Adolescents with an impairing tic disorder.

-Study protocol for a randomized, controlled, superiority trial.

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Background:

Chronic tic disorders affect about 1% of children and adolescents. Tics may be extremely distressing, and may result in impairment that affects social and physical well-being and academic achievements, but the severity is very variable.

There is good experience with manualized behavioral treatments, but it can be challenging for families to attend the frequent sessions at the hospital. Furthermore, manualized treatment is offered only by a limited number of clinics, and often psychoeducation is the only available treatment. The main objective of this project is to investigate the efficacy of app-assisted behavioral treatment of tics.

Methods:

A randomized clinical superiority study comparing the efficacy of app-assisted tic training versus app-assisted tic learning. Eligible participants are children and adolescents, aged 9–17 years with tic disorders, referred to the Department of Child and Adolescent Psychiatry, AUH.

After randomization to either the learning group or training group both have access to a newly developed app in which they are taught about tics. The training group, also learn how to handle tics through app sessions released at each treatment session. The content of the app is comparable to the information and training as defined by the well-established manual "Niks to Tics". Both groups can chat with a therapist.

Perspectives:

This project contributes to increased knowledge about tics and tic treatment, and leads the way towards a more stepped care approach in the treatment of tics. It allows for earlier intervention, which could prevent or reduce severe episodes of tics and secondary reactions, and may prevent social inequalities in treatment.

Keywords: Psychiatry, psychology and mental health, Clinical neuroscience, Other

Using machine learning in early detection of cancer among patients with mental illness

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The life expectancy of people suffering from severe mental illness is approximately 10-25 years shorter than that of the general public. Cancer is one of the main contributors to the excess mortality, with late detection being a key challenge. Detection of early signs of cancer in patients with mental illnesses is a complicated matter, as the underlying effects are complex and interdependent. Success in identifying early warning signs, thus, requires sophisticated techniques capable of identifying subtle latent factors in large quantities of data. This project proposes to develop and apply deep learning techniques from the field of Natural Language Processing combined with recent advances in information theory to identify early indicators of cancer among individuals with mental disorders. This will be done using transformer-based language models to detect subtle indicators and complex patterns in clinical notes in Electronic Health Records. Deep learning models have shown impressive performance across many fields, but the increase in performance typically comes at the cost of explainability. Explainability is, however, critical for building algorithms to inform clinical practice. This project circumvents this by implementing increased explainability of the model predictions using information theoretic measures to detect and describe changes in the latent representations of the EHRs. The project can contribute to a monitoring system that helps clinicians continuously monitor early warning signs of cancer based on patterns that are otherwise too complex to detect and, thereby, identify at-risk patients. This would enable initiation of treatment in time and improve prognosis

Keywords: Psychiatry, psychology and mental health, Oncology, Medical technology and diagnostic techniques

Problem-solving therapy for patients with coronary heart disease and poor mental well-being in general practice

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Background: Coronary heart disease (CHD) is associated with poor mental health, including psychological distress, depression and anxiety. Mental health problems often remain unrecognised and insufficiently treated in patients with CHD and may lead to poor compliance with medical treatment, unhealthy behaviours and reduced physical wellbeing. Most patients with CHD are managed in general practice. Problem-solving therapy (PST) is a method helping and engaging patients in solving mental health problems by focusing on improving the patient's problem-solving skills through empowerment and behavioural activation. PST has proven effective and has been used in different settings.

Aim: We aim to investigate the effect of providing PST in general practice to patients with CHD and poor mental well-being. We hypothesize that PST will enhance the patients' mental and clinical health, including CHD risk profile.

Methods: Twelve general practices are recruited for a stepped wedge cluster-randomised controlled trial with a one-year follow-up. General practices consecutively undergo PST training in clusters of six. From Nov 2022, 200 patients are enrolled at their annual CHD consultation. Patients with poor mental well-being are offered a maximum of seven PST consultations when exposed to the intervention. Patients in the control group are treated as usual. Patients are asked to complete questionaries regarding their mental health at baseline and after six and 12 months. Clinical outcomes include medication adherence, lipid profile, blood pressure and smoking status.

Perspectives: Findings may demonstrate that PST is feasible and effective in helping patients CHD and poor mental well-being.

Keywords: Psychiatry, psychology and mental health, Cardiovascular system, Other

FLASH TALK SESSION 12

Ventilation Strategies During General Anaesthesia for Non-Cardiac Surgery: A Systematic Review and Meta-Analysis

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Background

This systematic review investigated the relationship between ventilation targets (e.g., positive end expiratory pressure, tidal volume, recruitment manoeuvres) and postoperative outcomes.

Methods

PubMed and Embase were searched on March 8, 2021 for randomized trials investigating the effect of different ventilation targets in adults undergoing non-cardiac surgery. Two investigators reviewed trials for relevance, extracted data, and assessed risk of bias. Meta-

analyses were performed for relevant outcomes, and subgroup analyses were conducted. The certainty of evidence was evaluated using GRADE.

Results

This review included 63 trials. Lung protective ventilation (i.e., low tidal volume with positive end expiratory pressure) reduced the risk of combined pulmonary complications (odds ratio [OR]: 0.37; 95%CI: 0.28, 0.49; 9 trials), atelectasis (OR: 0.39; 95%CI: 0.25, 0.60; 8 trials), and need for post-operative mechanical ventilation (OR: 0.36; 95%CI: 0.13, 1.00; 5 trials). Recruitment manoeuvres reduced the risk of atelectasis (OR: 0.44; 95%CI: 0.21, 0.92; 5 trials). For all comparisons across targets, no effect was found on mortality or hospital length of stay. For all outcomes, the results should be evaluated with caution as the certainty of evidence was rated as very low to moderate.

Conclusions

Although lung protective ventilation results in a decrease in pulmonary complications, there is limited evidence from randomized clinical trials to guide specific ventilation strategies during general anaesthesia for adults undergoing non-cardiac surgery.

Keywords: Reviews and meta-analyses, Respiratory system, Other

Biochemical regulation of NF-κB-signaling in human vascular smooth muscle cells

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With their high plasticity, vascular smooth muscle cells (SMCs) play an important role in atherosclerosis. Changes in the vascular microenvironment results in phenotypic modulation of the SMCs giving rise to many alternative phenotypes contributing to the development of atherosclerosis. Since atherosclerosis is an inflammatory disease, a better understanding of the phenotypic modulation of SMCs into inflammatory SMCs is essential.

To investigate this, we aim to do a CRISPR-Cas9 screening of human aortic SMCs to perform large-scale gene knockouts. The nuclear factor-κB (NF-κB) is a master regulator of inflammation and is associated with atherosclerosis. We have a fluorescent NF-κB reporter system where NF-κB response elements control the expression of d2eGFP and using this for the CRISPR-Cas9 screening will allow us to identify NF-κB-regulating genes.

Atheroprone sites are found at curvatures and branches in the vascular tree characterized by changes in the mechanical forces experienced by the blood vessel wall. To investigate the effect of mechanical forces, we have an in vitro setup where SMCs can be exposed to stretch. Preliminary results of RNA-sequencing indicate that stretch regulates inflammatory signaling in SMCs. Performing the CRISPR-Cas9 screening on NF-κB-d2eGFP-SMCs exposed to stretch, may identify mechano-sensors regulating SMC inflammation.

The cytokine, TNFα, promotes atherosclerosis and activates NF-κB. Preliminary tests treating NF-κB-d2eGFP-SMCs with TNFα indicate successful activation of the NF-κB reporter. By performing the CRISPR-Cas9 screening on NF-κB-d2eGFP-SMCs treated with TNFα we can potentially identify novel regulators of inflammation in SMCs.

Keywords: Cardiovascular system, Genetic engineering, Inflammation

Assessing cerebral blood flow following ischemia-reperfusion in a rodent model of acute ischemic stroke

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BACKGROUND: Acute ischemic stroke is a leading cause of death and disability. Early neurological deterioration is a feared complication of acute ischemic stroke, and abnormal changes in cerebral blood flow may play an important role.

Pulsatility of cerebral blood flow in humans can be estimated with transcranial doppler ultrasound (TCD), and with TCD and laser speckle contrast imaging in rodents. Based on estimates of blood flow velocities, the pulsatility index (PI) can be calculated. PI obtained from both brain hemispheres following acute ischemic stroke in one hemisphere has previously been used to evaluate inter-hemispheric cerebrovascular resistance. However, this approach assumes that cerebral hemodynamic parameters remain unchanged in the stroke-free hemisphere following acute ischemic stroke. We hypothesize that PI obtained from non-affected hemisphere is also affected by stroke, but differently than the stroke-affected hemisphere.

METHOD: Wild-type C57BL/6 mice will undergo acute ischemic stroke by transient mechanical occlusion of the middle cerebral artery for one hour. Cerebral blood flow in both hemispheres will then be assessed by TCD and laser speckle contrast imaging at baseline, during occlusion, immediately and 24 hours after reperfusion.

Mice will be implanted with cranial windows, i.e., a part of the dorsal cranium will be replaced with cover glass, prior to arterial occlusion, which will improve the imaging quality of laser speckle contrast imaging. The mice will then rehabilitate for 2 weeks prior to stroke intervention.

RESULTS: The protocol is currently under development. The research will be presented at the PhD Day if ready.

Keywords: Cardiovascular system, Basic neuroscience, Animal models/disease models

Improvement of risk stratification by incorporation of cardiovascular genomics and proteomics into existing pre-test probability models

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Object: Improve pre-test probability (PTP) estimation in the assessment of risk of chronic obstructive coronary artery disease (CAD) by combining proteomics and genetics with existing clinical prediction models.

Background: The model currently in place for PTP estimation of chronic CAD has recently been improved by the addition of cardiovascular risk factors. Despite this, further optimisation of the model is needed to reduce the amount of anatomical testing of healthy individuals, and to assure testing of patients with obstructive CAD that - according to existing models - would have been deferred from investigation due to a benign risk profile.

Methods: The project is a genetic and proteomic expansion of the prospective, multi-centre, cross-sectional cohort-study of 4,400 patients included in the Danish study of non-invasive testing in coronary artery disease trials.

Patients with de novo symptoms suggestive of chronic CAD were referred for evaluation by coronary computed tomography angiography.

Based on blood samples we will investigate the patients' genomic and proteomic profiles. The genomic data will be used to construct polygenic risk scores for chronic CAD, and machine learning will be used to identify which of 3,072 Olink-measured circulating plasma proteins are involved in CAD development.

Also, we will measure concentrations of lipoprotein(a) in all patients – a lipoprotein with established atherosclerotic properties.

Based on these biomarkers, a new PTP model combining the existing model with the new data will be developed and validated. We will then compare the predictive power of our new model with the existing one in regards to obstructive CAD.

Results: Pending.

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Other

Treatment effects of Bisoprolol and Verapamil in symptomatic patients with non-obstructive hypertrophic cardiomyopathy

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Background: Hypertrophic cardiomyopathy (HCM) is the most common genetic heart disease affecting up to 10.000 Danes. It is characterized by hypertrophy and cell dysfunction resulting in decreased cardiac output. Patients can be asymptomatic or develop symptoms of heart failure. They are at risk of arrhythmia and sudden cardiac death which may precede heart failure symptoms. The survival is usually good, but management of symptoms and risk factors are important clinical aims.

Aim: To compare the treatment effects of Bisoprolol and Verapamil in 140 patients with non-obstructive HCM. The overall clinical aim is to reduce the symptomatic burden and arrhythmic complications in HCM patients.

Method: The study is designed as a multicenter double-blinded randomized placebo-controlled cross-over trial. Patients are randomized into three 35-day treatment periods of Bisoprolol, Verapamil and Placebo. Each treatment period consists of 7-day up-titration period, 21-day target dose period and 7-day down-titration period. Endpoints will be evaluated by echocardiography, cardiopulmonary exercise test, 7-day Holter monitoring, biomarkers, and Kansas City Cardiomyopathy Questionnaire at day 21. A subgroup of patients will be evaluated by cardiac MRI.

Results/Perspectives: Results are not available as the study is still recruiting. The study will be the so far largest randomized trial on the effects of beta blockers and calcium channel blockers in patients with HCM and the only study making a head-to-head comparison between the two guideline recommended treatments of HCM.

Conclusion: The study has the potential to form the basis of the future recommended treatment of non-obstructive HCM.

Keywords: Cardiovascular system, Pharmacology, Other

Oximetry guided versus traditional rapid deflation technique for achieving hemostasis after radial procedures - A randomised study

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Christian Juhl Terkelsen

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 individualised. 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.

Keywords: Cardiovascular system, Other, Other

Use of nonsteroidal anti-inflammatory drugs and cardiovascular risk in patients with documented coronary artery disease

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Background: Non-aspirin non-steroidal anti-inflammatory drugs (NSAID) use increases the risk of major adverse cardiovascular event (acute myocardial infarction, ischemic stroke, congestive heart failure, atrial fibrillation or flutter, or cardiovascular death). Since 2002, use of NSAIDs has declined in patients with cardiovascular disease, but use remains common at 10–15% within one year after the cardiovascular event. There are few studies on the cardiovascular risks of NSAID use in patients with imaging and angiography confirmed coronary artery disease. Also, no studies have examined the cardiovascular risks of NSAID use in patients undergoing coronary artery bypass graft in Denmark, despite the high demand for pain relief after surgery in these patients.

Aim: The aim of this PhD project is to examine NSAID-associated cardiovascular risks according to both severity (graded by cardiac computerized tomography, myocardial scintigraphy, and coronary angiography), type of treatment (percutaneous coronary intervention or coronary artery bypass graft), and comorbidities.

Methods: The PhD project is designed as a series of population-based cohort studies using Danish health registries (2008–2022). We will follow the patients until the first major adverse cardiovascular event, emigration, death, or October 2022. We will use Cox proportional-hazards regression to compute hazard ratios with 95% confidence intervals for the study outcomes stratified by the degree of coronary obstruction and the Agatston calcium score (continuous and categorical). Dose-response and sensitivity analyses to further address confounding and misclassification will be included.

Keywords: Cardiovascular system, Epidemiology and biostatistics, Pharmacology

Prognostic impact of COVID-19 infection and vaccination on myocardial infarction survival

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Introduction: Coronavirus disease 2019 (COVID-19) is associated with an increased risk of myocardial infarction (MI) within the first 12 months following infection. Small studies suggest that MI may also have a worse prognosis in recently COVID-19 infected patients. Whether previous vaccination modifies any impact of COVID-19 infection on MI prognosis needs to be investigated.

Aim: To compare the prognosis of MI in individuals with versus without a recent COVID-19 infection, and to examine whether this association is modified by vaccination status.

Methods: Using Danish health registries, we will conduct a population-based cohort study comprising all adults (≥18 years) with a first-time MI between 26 May 2020 and 9 March 2022. Comparing the patients with and without recent COVID-19 before their MI, we will calculate adjusted relative risks of death within 30 days and 1 year after MI as well as MI recurrence, heart failure, ischemic stroke, and cause-specific death. Furthermore, we will stratify the analyses according to vaccination status. Additionally, we will perform subgroup analyses stratified according to age, sex, type of MI, comorbidity burden, COVID-19 variant, and COVID-19 admission.

Results: Our analyses are currently in progress. If available, we will present preliminary results.

Conclusions: As very little is known on the outcomes of MI after COVID-19 infection and vaccination, this study may provide important knowledge of major clinical and public health relevance. Additionally, the results may be of great value in relation to assessment of vaccine safety.

Keywords: Cardiovascular system, Epidemiology and biostatistics, Infection

Coronary Atherosclerotic High-Risk Plaque and Stenosis Detection using Magnetic Resonance Imaging

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Background:

The term high-risk plaque (HRP) specifies coronary atherosclerosis with increased risk of acute coronary syndrome. Intraplaque haemorrhage (IPH) is one HRP trait, and it occurs within the lipid or necrotic core of the plaque, but its role in risk assessments in coronary artery disease (CAD) is not well understood. Coronary Magnetic Resonance Angiography (CMRA) with technical innovations such as advanced motion correction is a promising non-invasive method for visualization of the coronary arteries. A novel state-of-the-art T1-weighted CMRA scanning has the potential to do vessel wall and plaque imaging of the coronary arteries, but also to detect IPH due to the short T1-value of methaemoglobin.

Objectives:

This study aims to investigate the incidence of coronary IPH detected by T1-weighted CMRA in patients with stable CAD, and to evaluate the possible association between IPH and accelerated plaque expansion.

Methods:

Patients (n=120) with at least one proximal coronary high-risk low-attenuation plaque can be recruited. T1-weighted CMRA, coronary CT angiography (CCTA) and blood samples will be performed at inclusion, and after 12 months all examinations will be repeated. The primary endpoint is plaque progression in plaques with IPH versus non-IPH plaques at follow-up which will be evaluated using a semi-automated software for CCTA images including analysis of plaque volume and plaque composition. Data collection is ongoing.

Perspectives:

CMRA is a future alternative for diagnosing CAD without exposure of ionising radiation or contrast agents, and it can contribute to improved patient risk assessments if IPH is proven associated with a more severe CAD phenotype.

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Inflammation

Risk of errors in pacemakers and ICDs during out-of-field proton beam therapy in an in vitro setting

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Background: Cancer patients with a cardiac implantable electronic device (CIED) who undergo radiotherapy, present a complex challenge because CIEDs are sensitive to ionizing radiation. CIEDs may be harmed even outside the radiation field due to scattered secondary neutrons. Proton beam therapy for cancer patients have recently been enabled for cancer treatment, but risk of CIED malfunctioning is unknown. This experimental in vitro study investigated risk of CIED errors during out-of-field proton therapy.

Methods: We used 62 explanted CIEDs from four manufacturers; 49 CIEDs underwent a patient-like clinical protocol with daily irradiations at three different lateral distances from the radiation field. All devices underwent a total of 36 radiation fractions of 2 Gy. Additionally, 13 devices were monitored live during consecutive irradiations. Dose of scattered secondary neutrons was estimated with Monte Carlo Simulations.

Results: We observed 61 reset errors in 1,728 fractions and all except one CIED was reprogrammed to normal function. Secondary neutron dose was found to significantly increase the odds of CIED resets by 55% per millisievert. Battery depletion was observed in five devices. We observed no noise, over-sense, pace-inhibition or inappropriate shock therapy during 362 fractions of live-monitoring.

Conclusion: During out-of-field pencil beam proton therapy, the risk of resetting to backup mode is non-negligible and dependent on secondary neutron scatter. The benefits of proton therapy are expected to outweigh the risk of CIED malfunctioning in most clinical cases. Following this study, we have now treated the first four patients with CIEDs with proton therapy.

Keywords: Cardiovascular system, Oncology, Other

Why do patients develop in-hospital cardiac arrest?

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Background

Annually, 2,000 patients suffer an in-hospital cardiac arrest (IHCA) in Denmark and only 25-30% survive to hospital discharge. The aetiology of IHCA, and therefore our ability to tailor peri-arrest treatment and prevent future IHCA's, is uncertain.

Methods

In a prospective, single-center, observational cohort study, we wish to establish the causes of IHCA in adult patients at Aarhus University Hospital. All patients surviving IHCA will be examined by laboratory values, computed tomography, and echocardiography. Non-survivors will undergo virtopsy in the form of post-mortem whole-body magnetic resonance imaging. An appointed expert panel will classify IHCA aetiologies based on this information as well as the clinical history. The degree of discrepancy between the presumed cause of arrest as determined by the cardiac arrest team and the actual cause as determined by the expert panel will be evaluated.

Results

Results are pending as patient inclusion is expected from the first quarter of 2023.

Perspectives

The research group believes the results will shed new light on the aetiology of IHCA. This will be valuable information from a future preventive perspective as well as in tailoring peri-arrest treatment accordingly.

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Other

FLASH TALK SESSION 13

Influence of Intensive Lipid lowering with statin and ezetimbe prescription on Computed Tomography Derived Fractional Flow Reserve in Patients With Stable Chest Pain. The FLOW-PROMOTE study

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Coronary CT angiography (CTA) has emerged as a guideline-directed first-line test in patients with stable chest pain. FFR analysis can be performed non-invasively on CTA scans (FFRCT) using specialized softwares and has demonstrated high diagnostic performance against invasive FFR. Coronary CTA is also accurate for detection and quantification of adverse plaque characteristics (APC) such as low-density plaque (LDP). LDP determined by coronary CTA is a high-risk phenotype. Recent studies have shown that LDP volume, even in patients with non-obstructive coronary artery disease (CAD), is associated to the severity of ischemia determined by either FFRCT or FFR.

Statin therapy is associated with plaque stabilization through favorable changes in plaque morphology including reduction in non-calcified plaque volume, specifically LDP. In a meta-analysis with serial plaque assessment by coronary CTA, regression of non-calcified plaques was more pronounced with potent than with regular statins.

This study aims to investigate, whether two lipid-lowering strategies in stable CAD patients with FFRCT ≤0.80 are associated with regression of coronary APC and FFRCT recovery.

A total of 105 patients with stable CAD (≥1 CTA detected stenosis ≥50% and FFRCT ≤0.80 in non-proximal coronary segments) and baseline LDL >2.0 mM are randomized to either usual care with atorvastatin 40 mg or intensive care with rosuvastatin 40 mg and ezetimibe 10 mg per day. At 9 months, an interview, biochemistry sampling (lipids) and two CTA scans are performed (second scan is for plaque and FFRCT reproducibility analysis). Final interview, biochemistry and CTA assessment are conducted after 18 months.

Keywords: Cardiovascular system, Other, Medical technology and diagnostic techniques

PERFORM-CCS (PERfusion estimation For Optimal Revascularisation and Medical therapy in Chronic Coronary Syndrome – protocol for a randomised trial)

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Simon Winther, Department of Clinical Medicine; Morten Bøttcher, Department of Clinical Medicine,

Background:

It is unclear whether an initial invasive strategy, in addition to optimal medical therapy in patients with chronic coronary syndrome (CCS) and inducible ischemia by non-invasive testing, improves outcomes.

Objectives:

The primary objective is to compare the additional benefit of early invasive coronary angiography (ICA) versus guideline-directed medical therapy (GDMT) on symptomatic relief defined as Seattle Angina Questionnaire-7 (SAQ-7) angina frequency score = 100 after 3 months following a positive [15O]H2O cardiac PET/CT in patients with symptomatic CCS.

Secondary objectives include estimation of associations between [15O]H2O cardiac PET/CT results and symptom burden.

Methods:

Patients with symptomatic CCS clinically referred for [15O]H2O cardiac PET/CT at Gødstrup Hospital are included in a prospective cohort followed with repeated SAQ-7 and Rose Dyspnea Scale (RDS) questionnaires.

Patients with [15O]H2O cardiac PET/CT results below ischemic thresholds undergoes coronary CT angiography, SAQ-7, RDS, and six-minute walking test (6MWT) at baseline. Then, patients are randomised 1:1 to either immediate referral for ICA or three months delayed referral for ICA. Both groups undergo optimisation of GDMT. Repeat [15O]H2O cardiac PET/CT, SAQ-7, RDS, and 6MWT will be assessed 3 and 6 months after randomisation.

Two hundred patients are planned for inclusion in the randomised trial. It is estimated that 570 patients are included in the prospective cohort.

Conclusion:

The results of the study are expected to improve selection of patients for different treatment strategies after [15O]H2O cardiac PET/CT in symptomatic CCS. The study protocol awaits regulatory approval.

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Pharmacology

Coronary stent edge segments as determinant of clinical outcomes. An OCTOBER trial substudy

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Atherosclerotic coronary artery disease can reduce blood flow to the myocardium. Percutaneous coronary intervention (PCI) is the implantation of stents guided by angiography. It is used for improving blood flow. Stent edge segments are defined as the 5 mm vessel adjacent to each end of the implanted stent. Small lumen dimensions and high plaque burden in stent edge segments are known to increase risk of edge restenosis and need for re-treatment.

Optical coherence tomography (OCT) is an intravascular imaging modality providing high resolution histology-like images of the vessel wall and implanted stents. It stands as a supplement to angiography during the procedure. For OCT, stent edge cutoff values for acceptable edge results remain unknown. This study aims to investigate the relation between edge results and subsequent cardiac events.

The study is a predefined sub analysis of 600 patients enrolled in the OCTOBER trial on OCT guided bifurcation PCI. Inclusion criteria for this sub analysis are analyzable post-PCI OCT including at least one stent edge segment. Exclusion criteria are scans without analyzable stent edges. Main endpoints are the following potential predictors of cardiac events: residual edge stenosis, extent of lipid and calcium in the edge segment, and edge dissections. Analysis is performed with frame intervals of 0,5 mm. Lumen diameters and plaque composition, arcs and subtypes, are analyzed using a dedicated software. Data are analyzed by multi-level cox regression analysis to identify independent predictors of clinical events.

The results may advise physicians on the clinical importance of edge results after stent implantation.

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Other

Safety and effectiveness of direct oral anticoagulants following percutaneous coronary intervention in patients with atrial fibrillation

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Introduction: Following percutaneous coronary intervention (PCI) in patients with atrial fibrillation (AF), guidelines recommend dual therapy with a direct oral anticoagulant (DOAC) and a platelet inhibitor for up to 1 year. However, no recommendation is given as to which DOAC should be favoured. The current study compared the three most commonly used DOACs in Western Denmark.

Methods: All patients with AF undergoing PCI between 2003 and 2017 in Western Denmark were included. The study compared 1) rivaroxaban vs apixaban, 2) rivaroxaban vs dabigatran, and 3) apixaban vs dabigatran. The endpoints were major adverse cardiac events (MACE) and hospitalization for bleeding. MACE was a composite of myocardial infarction, ischemic stroke, and all-cause death. Crude and inverse probability of treatment weighted hazard ratios (HRw) were calculated using Cox regression.

Results: The study included 800 patients. Generally, apixaban treated patients had a higher baseline risk than their counterparts. Rivaroxaban use was associated with a higher risk of hospitalization for bleeding compared to apixaban (HRw 0.48 (0.27 – 0.85)) and dabigatran (HRw 0.56 (0.32 – 0.99)). Dabigatran and apixaban had a comparable risk of bleeding. For MACE, apixaban (HRw 1.19 (0.67 – 2.09)) and in particular dabigatran (HRw 1.76 (0.99 – 3.13)) were associated with numerically higher risks than rivaroxaban although not reaching statistical significance.

Conclusion: In AF patients undergoing PCI, rivaroxaban was associated with a substantial higher risk of hospitalization for bleeding than apixaban and dabigatran. These major differences highlight a need for a randomized trial in this setting.

Keywords: Cardiovascular system, Epidemiology and biostatistics, Other

Influence of cholesterol levels on the cardiovascular risks associated with use of NSAIDs after myocardial infarction

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Background: The importance of cholesterol levels on the association between non-aspirin nonsteroidal anti-inflammatory drug (NSAID) use and cardiovascular events remains to be investigated.

Aim: To examine whether low density lipoprotein cholesterol (LDL-C) level influences the association between NSAID use and cardiovascular events in patients with first-time myocardial infarction (MI).

Methods: We conducted a population-based cohort study of all adult (≥ 18 years) first-time MI patients from 2010 through 2020. We used Cox proportional-hazards regression to compute hazard ratios of the association between use of ibuprofen, naproxen, or diclofenac and a composite outcome of all-cause death, recurrent MI, ischemic stroke, or heart failure. In the primary analysis, we stratified by baseline LDL-C and followed all first-time MI patients for one year. In a secondary analysis, we stratified by one-year LDL-C and followed one-year MI survivors for additional five years.

Results: Analyses are currently in progress. Preliminary results will be presented if available.

Conclusion: Knowledge on the impact of cholesterol level on the association between use of NSAIDs and cardiovascular events would add to the understanding of the adverse effects of NSAIDs and thereby improve clinical guidance when it comes to who should and who should not receive NSAID treatment.

Acknowledgements: The project is supported by the Novo Nordisk Foundation (grant NNF19OC0054908). The authors declare no conflict of interests.

Keywords: Pharmacology, Cardiovascular system, Epidemiology and biostatistics

Fibrinolysis in sepsis patients in the intensive care unit: new biomarkers

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Background: Abnormalities in the fibrinolytic system are frequent in critically ill sepsis patients and are associated with organ dysfunction and mortality. However, laboratory assays for the evaluation of fibrinolysis are lacking in clinical practice. Thus, a quick and sensitive assay could hold the potential to improve the early diagnosis and management of this condition. We aim to assess fibrinolysis with a newly developed modified rotational thromboelastometry (ROTEM®) assay in sepsis patients in the intensive care unit (ICU) and to investigate the association between fibrinolytic capacity and disease severity.

Methods: This single-center prospective cohort study will include adult sepsis patients and non-sepsis controls from the ICU at Aarhus University Hospital. Blood samples will be obtained the morning after admission (day 1) and on days 2 and 3 and analyzed with ROTEM® modified with tissue plasminogen activator (tPA) to assess fibrinolysis. Clinical information regarding organ failure, sepsis-related coagulopathy, and 30-day mortality will be collected prospectively. The primary outcome is the difference in lysis time between sepsis patients and non-sepsis patients on day 1 of ICU admission.

Results: This research year project commenced on 1st September 2022. Inclusion is ongoing. We plan to include at least 23 sepsis patients and 23 non-sepsis patients over six months.

Perspectives: Our study will be the first to assess fibrinolysis in sepsis patients using ROTEM®-tPA with an ICU control group. The perspective is better diagnosis and management of disturbed fibrinolysis in sepsis and thus, ultimately, improved survival for these patients.

Keywords: Laboratory science, Cardiovascular system, Infection

Low pH inhibits K+-induced vasorelaxation in coronary but not cerebral arteries

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Introduction

Regulation of artery tone in response to accumulating metabolites plays critical physiological and pathophysiological roles by matching local blood flow to the metabolic demand. Increased cellular activity or disturbed perfusion elevates the extracellular K+ concentration and moderate increases in extracellular K+ cause potent vasorelaxation in certain vascular beds. However, increased metabolism or ischemia not only elevates the K+ concentration, it also reduces pH and the acidic environment modulates arterial tone. In the current study, we evaluated the functional interplay between hyperkalemia and acidification.

Methods and results

Rat coronary and cerebral arteries mounted in wire myographs relax to baseline when exposed to moderate increases in extracellular K+ concentrations. Whereas acidosis inhibits K+-induced relaxation of coronary arteries, relaxation of cerebral arteries remains unaffected. Simultaneous measurements of isometric force and intracellular Ca2+ reveal that K+-induced decreases in vascular smooth muscle cell (VSMC) Ca2+ concentrations are inhibited under acidic conditions in coronary but not cerebral arteries. There is no major difference in the magnitude of VSMC acidification during extracellular acidosis.

Conclusions

Extracellular acidification inhibits K+-induced vasorelaxations and associated decreases in VSMC Ca2+ concentrations in coronary but not cerebral arteries. These differences occur despite equal reductions in VSMC intracellular pH. Our findings provide new mechanistic insights on how alterations in pH regulate blood flow both directly and indirectly through effects on vascular responses to metabolites.

Keywords: Cardiovascular system, Animal models/disease models, Laboratory science

Bicarbonate sensing improves cardiac perfusion and protects against ischemia and inflammation

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BACKGROUND: Ischemic heart disease and its frequent complications - heart failure and arrhythmia - remain the leading causes of cardiovascular death and morbidity in Denmark. Ischemia is mainly a result of imbalance between local perfusion and metabolic demand. Upon this imbalance metabolites such as H+ and HCO3– accumulate. Receptor protein tyrosine phosphatase type gamma (RPTPγ) has been identified as a potential sensor of extracellular HCO3–. In humans, predicted loss of function mutations of RPTPγ are associated with severely elevated risk of ischemic heart disease.

AIM AND METHODS: This study explores HCO3– signaling and RPTPγ in the context of physical exercise capacity and development of ischemic heart disease. This is examined by Langendorff set-up of excised heart along with forced and voluntary exercise evaluation. Both types of experimental set-ups are performed with or without excess HCO3– in wildtype and global RPTPγ knockout mice.

PERSPECTIVES: RPTPγ is expressed in pathophysiologically relevant cell types of ischemic heart disease development particularly cardiomyocytes, immune, and endothelial cells. This makes RPTPγ a potential target for prevention and/or therapeutic treatment. of ischemic heart disease. The discovery of a potential drug target would broaden the field of cardiovascular medicine to focus not only on treatment after an incident has already occurred but also on prevention before potential incidences.

Keywords: Cardiovascular system, Animal models/disease models, Pharmacology

The influence of neuropeptides on tone regulation of porcine retinal arterioles in vitro

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Background: Disturbances in retinal blood flow is a common cause of retinal diseases leading to blindness. A key to prevention and treatment is clarifying the regulation of blood flow. Previous studies indicate that neuropeptides affect tone regulation of retinal arterioles, but it is unknown to which extent they act on the isolated arteriole or depend on the perivascular retinal tissue. This study measured the tone of porcine retinal arterioles with perivascular retinal tissue and isolated arterioles after addition of the following: neuropeptide Y (NPY), vasoactive intestinal polypeptide (VIP), calcitonin gene related peptide (CGRP), substance P (SP) and insulin.

Materials and methods: Porcine retinal arterioles with perivascular retinal tissue were mounted in a wire myograph and the tone was recorded after addition of either NPY, VIP, CGRP, SP or insulin in increasing concentrations. The perivascular tissue was removed, and the experiments were repeated on the isolated arteriole.

Results: NPY induced contraction, and VIP and CGRP induced relaxation of the retinal arteriole with perivascular retinal tissue. These results were concentration dependent and significant. NPY, VIP and CGRP had no effect on the isolated arteriole. SP had no effect on the arteriole with perivascular retinal tissue or the isolated arteriole. Insulin induced a significant concentration dependent relaxation of both the arteriole with perivascular retinal tissue and the isolated arteriole.

Conclusion: NPY, VIP and CGRP influence on tone regulation of porcine retinal arterioles depend on the perivascular retinal tissue, while insulin acts on the arteriole. SP has no influence on tone regulation.

Keywords: Ophthalmology, Laboratory science, Pharmacology

Determining residual risk conferred by non-HDL and remnant cholesterol in patients with statin-treated coronary heart disease

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Background: Patients with coronary heart disease (CHD) continue to experience new atherosclerotic events despite having secondary preventive medical therapy. Statins are known to reduce cardiovascular risk attributed to LDL, however the risk conferred by other atherogenic lipoproteins is not properly addressed.

Aim: To determine residual risk conferred by non-HDL and remnant cholesterol in a general cohort of statin-treated CHD patients and specifically diabetics.

Methods: The study cohort includes all adult patients (age 18 years or older) with an incident coronary angiography (CAG) and coronary artery disease since 2011. Baseline characteristics are obtained from the Western Denmark Heart Registry. From the Danish Laboratory Information System, we will collect measurements of cholesterol fractions (total cholesterol, LDL-C, HDL-C, and triglyceride) from both before and after CAG. Based on these lipid parameters, we will calculate non-HDL and remnant cholesterol. Patients are followed until death, emigration, or end of study in the year 2021 whichever comes first. The outcomes of interest are diagnosis of myocardial infarction and ischemic stroke as recorded in the Danish National Patient Registry. The association among non-HDL, remnant cholesterol, LDL-C and myocardial infarction or ischemic stroke will be estimated by Cox proportional Hazards regression model.

Conclusion: We hypothesize that high non-HDL and high remnant cholesterol are associated with elevated residual risk of myocardial infarction and ischemic stroke in statin-treated patients with CHD.

Keywords: Cardiovascular system, Rehabilitation, Epidemiology and biostatistics

Will SGLT2-inhibition improve vascular function in patients with type 2 diabetes and chronic kidney disease? A double-blinded, randomized, placebo-controlled crossover trial

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Background

Type 2 diabetes mellitus (DM2), chronic kidney disease (CKD), and the combination of both diseases are associated with endothelial cell dysfunction. The antidiabetic drug class, Sodium Glucose Cotransporter 2 inhibitors (SGLT2i), is found to have significant improvements in cardiovascular endpoints in DM2 as well as in non-diabetic CKD, reducing the risk of cardiovascular death and end stage kidney disease up to 30 % in both patient populations.

The vascular benefits from SGLT2i are suggested to be found partly in an improvement of endothelial cell function. This association is sparsely examined in patients with DM2 and has never been examined in patients with CKD.

We aim to investigate if SGLT2-inhibition improves vascular function in patients with DM2, CKD, or both.

Methods

The study is conducted as a double-blinded, randomized, placebo-controlled crossover trial. The participants are divided into three groups, either DM2, CKD, or DM2 and CKD respectively, with 15 participants in each group. The participants are randomized to 4 weeks of SGLT2i-treatment (empagliflozin 10 mg) or matching placebo, followed by crossover. After each period of treatment, we evaluate vascular function by classic venous occlusion plethysmography. Absolute and relative forearm blood flows are measured during intra-arterial infusion of acetylcholine and sodium nitroprusside, assessing endothelium-dependent and non-dependent vasodilation, respectively.

Results

Data collection is currently in progress and is planned to be completed by the end of 2022. Preliminary results will be presented.

Keywords: Cardiovascular system, Nephrology, Pharmacology

FLASH TALK SESSION 14

Damage-limiting immune mechanisms in HSV brain infections

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Inflammation is a highly efficient mechanism of acute defense against pathogens and is initiated upon detection of pathogen-associated molecular patterns by respective pattern recognition receptors (PRR). However, PRR-driven mechanisms tend to act disruptive within sensitive tissues, like the brain, which does not tolerate extensive inflammation. Those tissues are dependent on stringent regulation of inflammatory signaling. Inborn errors of immunity confer susceptibility to viral infections, including herpes simplex virus 2 meningitis, mainly by impaired control of virus replication and interferon signaling. However, we hypothesize that an underestimated part of the patient phenotype originates from compromised damage limitation and excessive spread of inflammation due to mutations in immunoregulatory genes and pathways of cell stress response and cell death.

We use whole exome sequencing of patients suffering from severe/recurrent viral infections of the central nervous system to identify candidate gene variants/mutations. The impact of those variants on viral defense and inflammatory signaling will be analyzed by infecting patient-derived periphery blood mononuclear cells, monocyte-derived macrophages, as well as neuronal cell lines mimicking the genetic variants. The interplay of antiviral defense and inflammation will finally be modelled in brain organoids developed from induced pluripotent stem cells from relevant patients.

A new concept of damage-limiting immune mechanisms will spawn new druggable targets in inflammatory and infectious diseases.

Keywords: Inflammation, Infection, Genetic engineering

Lipid-Nanoparticle delivery of human mRNAs encoding anti-viral genes for protection of host airway epithelial during Influenza A and Sars-CoV2 infections

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The development of effective mRNA vaccines 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 passive cellular uptake with subsequent protein expression in vivo. Today, the development of mRNA vaccines is based on LNP-encapsulated mRNAs that encode viral antigens. Our approach aims to exploit this novel LNP technology in a conceptionally different manner where LNP-encapsulated mRNAs from anti-viral host genes are utilized for the prevention or treatment of infections directly in the airway epithelium. We have produced mRNA-LNPs and confirmed their ability to deliver full-length mRNA to human airway epithelial cells in-vitro and ex-vivo. Further research will determine if LNP-based delivery of mRNAs encoding human anti-viral genes can elicit anti-viral control at physiologically relevant epithelial surfaces during infection with Influenza A virus and SARS-CoV2. This new approach could offer a significant breakthrough in anti-viral therapy, thus a leap forward in protection against epidemics and pandemics.

Keywords: Infection, Respiratory system, Other

Change in pulmonary infections 12 months 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 pathogens colonize the lungs and cause infection. 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 pulmonary pathogens before and 12 months after ETI initiation.

Methods

The study includes Danish cystic fibrosis patients ≥12 years 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 S. aureus, H. influenzae, P. aeruginosa, Achromobacter, Burkholderia, and Aspergillus. 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. 283 patients with minimum 12 months follow up were included. Median age was 26 years [IQR 18;35], and 52 % were female. 74% were homozygous and 26% heterozygous for the F508del mutation. Mean ppFEV1 was 75% (SD± 25.3) and mean BMI was 21.4 (SD± 3.6). Pulmonary pathogen infection declined significantly after ETI initiation.

Keywords: Infection, Respiratory system, Pharmacology

Developing a bispecific Knob-in-Hole recombinant protein for efficient HIV killing

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Cytotoxic T lymphocytes (CTL) are important for elimination of virus-infected cells. In most HIV-1-infected individuals, HIV-1-specific CTLs are exhausted resulting in limited capacity to control or eliminate HIV-1 replication. Therefore, we seek to develop a novel immunotherapy concept in which potent vaccine-induced effector CTLs can be redirected to target and eliminate HIV-1-infected cells.

Specifically, we aim to develop a bispecific molecule (RoVER: Redirector of Vaccine-induced Effector Responses) comprising two functionally distinct domains: 1) a single-chain variable fragment (scFv) domain from specific broadly anti-HIV-1 neutralizing antibodies targeting the HIV-1 envelope (Env), and 2) a Human Leukocyte Antigen class I (HLA-I) molecule carrying a yellow fever (YF) vaccine epitope facilitating binding and activation of YF-specific CTL.

Our data on Peripheral Blood Mononuclear Cells (PBMCs) isolated from healthy volunteers following YF-17D vaccination (Stamaril ®, Novartis) shows that the vaccine induced strong epitope-specific CTL responses in all study participants. We we have established a proof-of-concept that in vivo generated YF-specific effector CTLs can be redirected to kill target cells by the introduction of RoVER. In contrast, no target killing was observed using autologous CTLs obtained prior to YF-17D vaccination or without exposure to RoVER demonstrating that target cell killing is dependent on the presence of RoVER as well as YF-specific CD8+ T cells.

This novel technology is highly specific and easily adaptable to any target of interest, thus holding a great potential for various diseases.

Keywords: Infection, Other, Other

Vaccination of immunocompromised patients against COVID-19

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Background: Immunocompromised patients are at high risk of severe illness and mortality due to SARS-CoV-2. Furthermore, these patients are known to have reduced response to vaccines in general.

The underlying biology and causes of vaccine hypo-responsiveness are unclear. In other studies, specific gene expression and cytokine induction have been used to predict the antibody response.

Aims: To investigate the serological response of SARS-CoV-2 vaccines, compare T cell SARS-CoV-2 specific immune responses as well as identifying plasma biomarkers and biological pathways associated with humoral and cellular vaccine responses in immunocompromised patients.

Material and methods: This project is a sub-study to the national SARS-CoV-2 vaccine study ENFORCE. We include participants with immunocompromising conditions and in immunosuppressive treatment prior to their first vaccination against Covid-19, with a two-year follow-up period. We describe the serological response to the vaccines by measuring the levels of antibodies against SARS-Cov-2 spike epitopes as well as the neutralizing potential. The cellular immune response is examined by characterizing T cell immunity. Furthermore, we analyze cryopreserved blood samples to identify plasma biomarkers and differences in gene expression and innate immunity associated with sub-optimal vaccine response.

Perspectives: Characterization of patient groups in risk of hypo-responsiveness of vaccines and identification of immunological predictors for suboptimal vaccine response could contribute to the development of optimized vaccines and vaccination regimens that are tailored specifically to these high-risk populations.

Keywords: Infection, Other, Other

The role of cross-talk in functional amyloid formation

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Bacterial biofilms in biofilm-associated infections (BAI) cause severe problems in modern healthcare environments, owing to their high resistance to mechanical interference, host defenses, and antibiotic treatment. Staphylococcus aureus is a prominent cause of BAI where the PSM peptide family serve as key virulence factors in the pathogenesis. In the soluble monomeric form, PSMs hinder host immune response by recruiting, activating and lysing human neutrophils while also promoting biofilm dissociation. Interestingly, PSMs also self-associate to form functional amyloid fibrils that fortify the biofilm matrix to resist disassembly by mechanical stress and matrix degrading enzymes. Previous studies have revealed the formidable structural plasticity of PSM peptide functional amyloids, resulting in an understanding of the structures and the intrinsic aggregation mechanisms in the fibril formation of individual PSM peptides. However, very little is known about cross-talk between the PSM peptides during the biofilm formation.

The current project will focus on characterization of the PSM peptide composition changes of aggregates structure, and visualization of the morphology in the aggregation process which will result in a detailed understanding of the cross-talk mechanism between the PSM peptides. The relationship between the structure of PSM aggregates and the mechanical properties will also be uncovered to better explain the resistance to mechanical stress in the biofilm. This study will provide insight to the structural and mechanistic models in functional amyloids and the treatment strategies such as design of inhibitors to better combat BAI.

Keywords: Infection, Inflammation, Other

Treating primary immunodeficiencies by prime editing in human CD34+ hematopoietic stem cells

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Ex vivo gene editing of autologous human hematopoietic stem cells is currently being developed as a treatment for primary immunodeficiencies (PIDs), but the current genome editing platform relying on Cas9 and the use of AAV6 as a donor for homology-directed repair are challenged by indel formation, off-target editing and high toxicity in hematopoietic stem and progenitor cells (HSPCs). Therefore, alternative genome editing platforms are needed of which the novel 'prime editing' system holds great promise. Prime editing does not rely on formation of DNA double-stranded breaks (DSBs), and the procedure is associated with very little cellular toxicity and no indel formation or off-target editing. In this PhD project, I aim to develop a mRNA-based delivery platform of prime editors to human CD34+ hematopoietic stem cells. My goal is to adapt and optimize the prime editing system to correct specific disease-causing genetic variants derived directly from patients in Denmark suffering from PIDs - including chronic granulomatous disease, hyper-IgM syndrome and GATA2 deficiency. I propose that by avoiding the generation of DSBs and use of AAV, a prime editing-based gene editing approach will offer less indel formation, less off-target editing and less toxicity than conventional HDR-based gene editing strategies, which ultimately reflects in a superior engraftment of prime-edited HSPCs in NOG-f mice.

Keywords: Genetic engineering, Cell biology, Infection

Small intact HIV-1 proviral DNA reservoir and potent HIV-specific CD8 T cell responses (the SAPPER study) – a recipe for post-treatment control?

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Background: Despite effective antiretroviral therapy, HIV persists as a latent infection. Therefore, individuals infected with HIV necessitate therapy throughout life.

Hypothesis: Small intact HIV-1 proviral DNA reservoir and potent HIV specific CD8 T cell responses are the key to controlling viral burden post treatment making it possible to achieve a functional cure in chronically HIV-infected individuals.

Methods: Three studies within the European collaboration The EU2Cure Consortium: Two studies examining HIV-1 reservoir size and HIV-1 specific immunity and one clinical study of HIV-infected individuals with small intact proviral HIV-1 reservoir and/or high levels of IFN- response who participate in an analytical treatment interruption of 12 weeks.

Perspectives: A functional cure will lead to a dramatic reduction of costs related to HIV treatment and management and will improve patient's quality of life.

Keywords: Infection, Other, Other

A universal CRISPR/Cas9 gene editing approach as a definitive cure for DOCK8 immunodeficiency syndrome

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Introduction: Defects in the DOCK8 gene primarily causes combined immunodeficiency. This devastating genetic disorder usually debuts in the first decade of life and leads to recurrent viral and bacterial infections, atopic diseases, and malignancy resulting in high morbidity and mortality. Early allogeneic hematopoietic stem cell transplantation is recommended, but due to a lack of HLA-matched donors, this is only an option for a subset of patients and is associated with severe adverse effects such as graft versus host disease.

Methods: This research project will employ CRISPR/Cas9-mediated gene correction to develop a cure for this fatal immune defect. The ideal therapy for this disease would be to correct the disease-causing mutation in the patient's own hematopoietic stem cells (HSCs), thereby establishing a restored immune system from the corrected cells. Here, we will apply these tools to the DOCK8 gene in human and mouse HSCs.

To accommodate the profound diversity in mutations causing DOCK8 deficiency, we have devised two gene correction strategies, which either is a) applicable to all patient mutations downstream of exon 25 or b) one that is applicable to almost all known DOCK8 mutations.

Results: Tailored CRISPR/Cas9 reagents and preliminary proof of concept for DOCK8 gene editing is established, providing initial validation of our ability to successfully deliver the reagents and modulate the DOCK8 gene by inducing site-specific integration of new sequence encoding a GFP reporter gene both in vitro and in vivo.

Conclusion: These preliminary experiments support the possibility of phenotypic disease correction in a mouse model and in human cells.

Keywords: Genetic engineering, Medical technology and diagnostic techniques, Laboratory science

Nontuberculous mycobacteria in immigrants in Denmark through 31 years

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Background: Evidence about nontuberculous mycobacterial (NTM) infection and disease in the immigrant population is sparse. Consequently, we aimed to investigate NTM epidemiology among immigrants in Denmark.

Methods: Nationwide historical cohort study of all positive NTM cultures from immigrants in Denmark from 1991 through 2021, stratified by patient demographics, country of origin, and clinical significance.

Findings: 1126 positive NTM cultures from 707 immigrants were identified. The overall incidence rate (IR) of positive NTM cultures among immigrants was 6.0/100,000 (95%CI 5.6-6.4). Although the number of immigrants more than tripled in Denmark during the study period, there was no trend in the IR of positive NTM cultures (Quasi-Poisson regression, p=0.259). When stratified according to disease categories, the IR of definite NTM disease was 1.0/100,000 (95%CI 0.8-1.2), possible NTM disease 1.1/100,000 (95%CI 0.9-1.3) and NTM colonization 4.0/100,000 (95%CI 3.6-4.3). Immigrants had higher IRs of possible NTM disease (incidence rate ratio (IRR)=1.7, 95%CI 1.4-2.1, p<0.000) and NTM colonization (IRR=4.7, 95CI 4.2-5.2, p<0.000) compared to Danish-born. For definite NTM disease, IRs were lower for immigrants compared to Danish-born (IRR=0.8, 95%CI 0.6-0.9, p=0.007).

Summary: We found a higher incidence of NTM among immigrants compared to Danish-born but a slightly lower incidence of definite NTM disease. Whether these findings reflect differences in true disease or in diagnostic sampling remains unknown.

Keywords: Infection, Epidemiology and biostatistics, Respiratory system

Single-cell transcriptome reveals key regulator in mouse brain stem in the defence against HSV1 infection

Xiangning Ding, Department of Biomedicine

Unpublished

Herpes Simplex Virus 1(HSV-1) is one of the most common viruses worldwide and their host might suffer from serious disease and lifelong latent infection. The viral infection can trigger immune response to fight this virus. The innate immune system, adaptive immune system and the complementary system are involved in the defense against HSV-1. The innate immune responding quickly and playing important role in HSV-1 infection is the first line of protection and defense against HSV-1 and the conductor of subsequent immune response. The uncertain outcome of battle between virus and host cells may lead to completely different impact on health of the host. Nuclear replicative viruses HSV-1 is a neurotropic herpesvirus that establishes latency within neurons. The reactivate of virus lytic cycle genes and the control of HSV-1 latency in host genome is one key of the host/virus interaction. The resistance to lethal disease in mice infected with HSV-1 is mouse strain dependent. So, the various mouse strains are the precious resource to study the process of immune response upon HSV-1 invasion. Virus is specially restricted to the brainstem of C57BL/6 mice in the central neuron system (CNS).

We constructed a transcriptomic profile for HSV-1 infected brain stem at single-cell resolution in virus restricted strain C57BL/6. Through exploring the newly migrating cells upon viral infection and subsequent transcriptomic changes in the host cells, we found pivotal responsive role of certain activated cell type. We deciphered the mechanism in the defence process by identifying the significantly up-regulated and down-regulated genes and the regulated antiviral cell-to-cell communication pairs.

Keywords: Infection, Cell biology, Other

FLASH TALK SESSION 15

Estrogen replacement therapy in women with Turner syndrome

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BACKGROUND: Nearly all females with Turner syndrome (TS) suffer from gonadal dysfunction causing hypergonadotropic hypogonadism and estrogen deficiency. Estrogen has a wide range of beneficial effects throughout the female body, where estrogen receptors are localized in most tissues. Consequently, estrogen deficiency causes cardiovascular, endocrine and physiological changes, impairing TS patients' health profile.

Patients with TS are subject to hormone replacement therapy (HRT) from puberty to menopause, as either oral or transdermal treatment. HRT is a well-implemented treatment; however, evidence concerning the optimal route, dose and monitoring of estrogen therapy is greatly lacking.

AIM: We aim to compare the long-term effects of transdermal versus oral estrogen replacement therapy in women with TS.

METHODS: A 14-month, randomized, crossover study including 50 females with TS (aged 18 to 50 years) and 50 healthy, age-matched female controls. Patients are randomized to receive 6 months of oral and 6 months of transdermal estrogen therapy. Treatment doses of estrogen are individualized to normalize levels of gonadotropins. Effects on cardiovascular, coagulation, pharmacological, endocrine and physiological endpoints are studied.

PERSPECTIVES: The outcomes of this project will be crucial for optimizing estrogen replacement therapy in TS patients. In addition, our results can likely be extended to a wider population of females with premature ovarian failure. Our goal with the present study is to provide basis for new and improved national and international recommendations for HRT in TS patients.

Keywords: Molecular metabolism and endocrinology, Cardiovascular system, Other

Effects of extensive Weight loss on Insulin resistance and Lipid-kinetics in people with obesity, fatty liver disease and type 2 Diabetes - The WILD study

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Background:

Obesity drives the development of type 2 diabetes mellitus (T2DM), non-alcoholic fatty liver disease (NAFLD) and dyslipidemia. A central pathophysiologic feature of diabetic dyslipidemia (DD) is proposed to be increased serum concentrations of very-low-density lipoprotein triglycerides (VLDL-TG).

We wish to study the VLDL-TG kinetics in obese patients with T2DM and NAFLD before, during and after a weight loss intervention induced by either Roux-en-Y Gastric Bypass (RYGB) or high dose Semaglutide treatment.

Methods:

24 female patients with T2DM and NAFLD referred to bariatric surgery will be recruited from our out-patient clinic at Steno Diabetes Centre Aarhus. The patients will get to choose either RYGB or Semaglutide treatment, until the groups consist of 12 patients each.

Anthropometrics, blood samples, insulin resistance, stool samples, hepatic fat content, metabolic liver function and VLDL-TG-, palmitate, and glucose kinetics will be registered at 3 time points:

1) Baseline, before treatment initiation, 2) After a weight loss of 10 % of baseline weight,

3) 8 months after treatment initiation.

Primary end point:

Changes in VLDL-TG kinetics during weight loss and after 8 months of treatment initiation.

1. Differences between the two groups

2. Changes in relation to the degree of weight loss

Significance of the project:

The WILD study is a combined basic research study of the VLDL-TG kinetics during weight loss and a comparable study of the effects of RYGB or Semaglutide treatment. We hope to elucidate some of the mechanisms of the resolution of insulin resistance, DD, changes in hepatic secretion of VLDL-TG particles and improvement in NAFLD during weight loss.

Keywords: Molecular metabolism and endocrinology, Gastroenterology and hepatology, Cardiovascular system

Dissecting the Genetics of Non-Obstructive Azoospermia – A Study of Male Factor Infertility

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Non-obstructive azoospermia (NOA) belongs to the most severe category of male infertility, affecting ~0.6% of all males. This condition arises from endocrinological or testicular dysfunction, leading to decreased sperm cell production. With numerous underlying causes, NOA has a highly variable presentation in respect of endocrinology and testicular genetics and histology. However, the interplay between these components, leading to a testicular crisis, is poorly understood. This understanding will be essential to gain a better molecular disease understanding and hence improve diagnostics and treatment.

With this study, our primary aim is to characterize cellular interaction patterns in NOA through single-cell RNA sequencing (scRNAseq); secondly, these patterns will be placed in an anatomical context by linking them to histology through spatial transcriptomics; and, thirdly, we will relate these findings to circulating hormone levels.

Our cohort will include males diagnosed with NOA undergoing testicular sperm extraction as part of fertility treatment. Controls will include males subjected to vasectomies. At the current stage, we have generated a scRNAseq reference atlas, integrating +100,000 testicular cells from publicly available data of relevant cases and controls. These data will be used to define research questions and serve as a validation cohort.

Integration of the different data types described above will increase our disease understanding at multiple levels, resulting in a more holistic understanding of NOA. This will pave the way for improved and more personalized treatment options, and hence make a substantial contribution to the field of male factor infertility.

Keywords: Molecular metabolism and endocrinology, Other, Other

Impact of glucocorticoid exposure on skeletal muscle function: experimental study in human subjects

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J. Farup, Department of Biomedicine

N. Jessen, Department of Clinical Medicine – SDCA Steno Diabetes Center Aarhus, Denmark

Background: 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.

Hypothesis: Muscle stem cells and FAPs mediate the GC-induced myopathy.

Aim: Utilizing a human data set, we study the effects of GC exposure on skeletal muscle structure and function in healthy older subjects.

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.

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.

Keywords: Molecular metabolism and endocrinology, Pharmacology, Laboratory science

The Role of Sortilin in Diabetic Retinal Neurodegeneration

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The multifunctional receptor sortilin was studied in the diabetic retina. The localization of sortilin and co-localization with the p75 neurotrophin receptor (p75NTR) and Müller cell (MC) markers were determined using immunofluorescence on retinal sections from human diabetic patients and streptozotocin-induced diabetic C57BL/6J male mice. In the diabetic mice, levels were further quantified using Western blot and qPCR. Therapeutic studies were performed on diabetic mice using intravitreally injected anti-sortilin antibodies. Neuroprotection was evaluated in vivo by optical coherence tomography and by quantification of retinal ganglion cells (RGCs) in flat mounts.

Increased levels of sortilin were observed in human and murine diabetic retinas compared with non-diabetic controls. Sortilin was highly localized to retinal MCs and, notably, co-localization with p75NTR was only seen in diabetic retinas. A remarkable 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 10.0% [-14.2,-5.9] (p=0.0008; n=8) in the control group compared with the anti-sortilin injected group. Similarly, the count of RGCs was reduced by 20.5% [-32.2,-8.8] (p=0.021) in the control group.

In conclusion, sortilin is upregulated in the diabetic retina, and activation of the p75NTR/sortilin complex is essential to the loss of retinal neurons in experimental diabetes. Thus, sortilin emerges as a potential target in diabetic retinal neurodegeneration – an important early event in the pathogenesis of diabetic retinopathy.

Keywords: Ophthalmology, Animal models/disease models, Laboratory science

Changes in peripheral volumetric bone mineral density and microarchitecture in patients with established Rheumatoid Arthritis

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Objective: High-resolution peripheral quantitative computed tomography (HR-pQCT) is a non-invasive 3-dimensional imaging modality capable of providing volumetric estimates of bone mineral density (BMD) and bone microarchitecture. Patients with Rheumatoid Arthritis (RA) have an increased risk of low systemic and juxta-articular BMD due to chronic inflammation. Furthermore, low juxta-articular BMD is associated with erosive disease activity and could potentially be an adjunct to evaluating RA disease progression. Thus, the aim of this study is to assess HR-pQCT as a candidate for disease monitoring of RA.

Methods: In this longitudinal, one-year observational study, 363 patients with established RA were imaged at the distal radius by HR-pQCT at baseline and at one-year follow-up from March 2018 to November 2021. Furthermore, all patients underwent clinical examination with a focus on their joints, and blood samples were collected to determine biomarkers related to systemic inflammation and bone turnover. From the HR-pQCT scans, which are analysed from October 2022 to February 2023, information about the one-year change in volumetric BMD and bone microstructure is assessed, and the association between changes in BMD, disease activity and medical treatment during follow-up is investigated.

Perspectives: HR-pQCT is a promising imaging tool for treatment guidance and prognostication. Accurate assessment of BMD, bone microarchitecture and the association with disease activity could result in a more precise evaluation of the progression of RA, thereby improving the possibilities for individualised treatment and optimising patient prognosis.

Keywords: Rheumatology, Inflammation, Medical technology and diagnostic techniques

Subtyping patients with chronic inflammatory diseases: the importance of tissue remodeling and identification of treatment responders

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Purpose:

Inflammation is a key aspect of tissue repair after injury, in which the extracellular matrix is remodeled to form new tissue. Non-resolving chronic inflammation eventually results in the development of fibrotic disease, however. Fibrotic tissue remodeling is a feature of a variety of chronic inflammatory diseases. Growth factor- and inflammatory cytokine activated signaling networks intersect during chronic tissue damage to influence the expression of profibrotic/proinflammatory genes, which dictate tissue remodeling. The purpose of this work is to investigate the pro- and anti-fibrotic remodeling induced by inflammatory cytokines in the 'scar-in-a-jar' model, a high-throughput preclinical model for fibrosis.

Methods:

Healthy human primary dermal fibroblasts are cultured to passage 6-9. Cells are cultured in 48-well plates at 30.000 cells per well in DMEM-F12 + GlutaMAX supplemented with 1% P/S and 0.4% FBS. Culture extends for 12 days. Pro-fibrotic treatments or pro-inflammatory treatments are added to the cell culture every four days. Pro-fibrotic treatments include TGF-β1 and PDGF. Pro-inflammatory cytokines to be investigated alone or in combination with TGF-β1 or PDGF include OSM, TNF, IL-36, IL-4, IL-13, IL-15, IL-17A, IL-23, IL-6 and IL-31. Conditioned media is stored upon media change. Fibrosis biomarkers developed by Nordic Bioscience are measured in the conditioned media. The ELISAs PRO-C1, PRO-C3 and PRO-C6 measure the formation of type I, III and VI collagens, respectively. The FBN-C ELISA measures the remodeling of fibronectin. The assays are specific for protein fragments generated after proteolytic processing of the respective proteins.

Keywords: Animal models/disease models, Inflammation, Dermatology

Insulin Resistance and Statin Treatment in Renal Transplant Recipients and Patients with Chronic Kidney Disease

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Background: Disorders of glucose metabolism such as insulin resistance, type 2- and post-transplant diabetes are highly prevalent in populations of patients with chronic kidney disease (CKD), including renal transplant recipients (RTRs). Cardiovascular disease (CVD) risk is significantly increased in these populations and augmented by disorders of glucose metabolism. Statins are cholesterol lowering drugs used in CVD prophylaxis; evidence indicates adverse effects of statins on glucose metabolism, with increased insulin resistance and risk of diabetes, albeit with significant differences across statin types and doses. Pravastatin has different chemical properties than other statins and seems to have neutral or beneficial effects on glucose metabolism.

Methods: Two double-blinded, placebo-controlled, cross-over studies are conducted in 10-15 non-diabetic RTRs and 10-15 non-diabetic CKD patients. Two sequence-randomized treatment phases of 12 weeks Pravastatin 40 mg daily or placebo are separated by a 4-week wash-out phase, utilizing the patients as their own control. The primary outcome is insulin sensitivity measured with a Botnia Clamp at the end of each treatment phase. Secondary outcomes include insulin secretion, surrogate markers of glucose metabolism, muscle and adipose tissue biopsy analyses for insulin signalling-related gene and protein expression, and faecal microbiotic composition.

Aims & perspectives: We aim to test if Pravastatin improves insulin sensitivity compared to placebo in non-diabetic RTRs and CKD-patients, respectively. Improving glucose metabolism and CVD prophylaxis is of vital importance in these high-risk patients with impaired renal function.

Keywords: Nephrology, Molecular metabolism and endocrinology, Other

Isotope-guided metabolomics for the analysis of kidney arginine metabolism

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Background-Aim: L-arginine metabolism contributes to the organism detoxification via the ammonia turnover to urea and could participate in the development of kidney disease. This study aims to detect the arginine uptake and its metabolic fate in kidney ex-vivo models by metabolic flux analysis. Method: Isolated glomeruli, cortical tubules and micro-dissected nephron segments from healthy mice were incubated with 13C6-labeled arginine. Generated metabolites were extracted and analyzed with UHPLC/QQQ-based mass spectrometry targeting metabolites of the urea cycle (arginine, citrulline, ornithine, urea), the polyamines pathway (agmatine), and the nitric oxide (NO) synthesis (13C6-Citrulline). Results: In the cortex, arginine was ubiquitously taken up except for into the proximal straight tubule. It was mainly consumed in the urea cycle for ornithine accumulation, excluding the thin ascending limb of the Henle's loop. Urea was only detected in the distal convoluted tubule. It also contributed to the polyamines' synthesis and NO pathway in the proximal convoluted tubule and the collecting duct. In the glomeruli, the polyamines synthesis was primarily observed. Conclusion: This proof-of-concept study allowed for detection of the basic arginine's metabolites in the renal compartments and offers the potential to explore a detailed isotope-based arginine metabolic flux. The role and in vivo fate of arginine in kidney disease models will be determined next.

Keywords: Nephrology, Animal models/disease models, Other

Temporal changes in incidence of acute kidney injury among children

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Background

Acute kidney injury (AKI) is defined by a sudden decrease in renal function and is associated with increased morbidity and mortality. The reported incidence of AKI among hospitalized children is approximately 30% but varies widely depending on population characteristics and method used to define AKI. Little is known about the temporal changes in AKI incidence in a pediatric population including both community- and hospital-acquired AKI.

Objective

To examine temporal changes in the incidence of AKI among children and associated changes in potential etiologies mainly focusing on perinatal factors.

Methods

In this descriptive study, we will include children aged 0-17 years from 1 January 2007 to 31 December 2018. We will use measurements of plasma creatinine from the Danish laboratory databases to define all AKIs within the study period. We will estimate the AKI incidence as: New AKI cases in the area coved by the laboratory database each year divided by the number of children residing in this area in the same year. Unadjusted incidences as well as sex- and age standardized incidences will be reported. We will obtain data on perinatal factors such as birth weight and gestational age from the Danish Medical Birth register.

Results

No results yet.

Perspectives

This study will contribute with fundamental knowledge on the AKI epidemiology among children, which is pivotal for further analytic studies of pediatric AKI.

Keywords: Nephrology, Paediatrics, Epidemiology and biostatistics

Ex-vivo TNFα inhibition of Donor Kidneys during Normothermic Machine Perfusion

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BACKGROUND: End stage kidney disease is increasing and transplantation is the only curative option meanwhile demand exceeds the organ supply. To combat this organ shortage, the use of expanded criteria donors has been proposed. However, these kidneys are often of lower quality and more susceptible to ischemia/reperfusion injuries (IRI). It has become evident that TNFα is a key player in the pathogenesis of renal IRI. However, systemic anti TNFα therapies comes with high risk of adverse effects. Our aim is to neutralize TNFα ex-vivo during normothermic machine perfusion (NMP) and hereby circumvent adverse effects and diminish renal IRI.

APPROACH: Using a porcine kidney model both kidneys are exposed to 75 minutes of warm ischemia to introduce kidney damage. The ischemic kidneys are perfused ex-vivo with an oxygenated red blood cell based perfusate during 6 hours of NMP. NMP is used to deliver TNFα neutralizing therapeutics such as Etanercept to the kidney. In order to generate post-transplant TNFα neutralization we also explore the use of a tissue binding inhibitor of TNFα. Biodistribution and tissue binding is measured by fluorescent pre-labeling of the administered therapeutics combined by whole kidney bioimaging.

RESULTS: We demonstrated that administration of therapeutics during kidney NMP is possible. We could track the therapeutics in urine, perfusate and kidney tissue and found that our modified tissue binding molecule binds to the kidney and stays bound even after a thorough flush with saline.

CONCLUSION: Kidney NMP can be used to deliver TNFα inhibiting therapeutics to donor kidneys and thereby circumvent severe systemic adverse affects of anti TNFα therapy.

Keywords: Inflammation, Nephrology, Pharmacology

FLASH TALK SESSION 16

Should we use corticosteroid in Percutaneous Needle Fasciotomy for Dupuytren's Contracture? – A protocol for a multicenter randomized controlled trial

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INTRODUCTION:

Dupuytren's contracture causes flexion contracture of one or more fingers. Percutaneous Needle Fasciotomy (PNF) is a minimal invasive surgical procedure performed under local anesthesia using a fine syringe needle to release the Dupuytren chord until the finger can be extended.

Variations in PNF techniques across orthopedic departments include use of corticosteroid injection during the procedure.

PURPOSE:

The purpose of this trial is to investigate if add-on corticosteroid improves the short/long-term effect of PNF, such as a lower recurrence rate, and whether it entails a higher complication rate compared with PNF alone.

METHOD:

This is a clinician-initiated, multicenter, two-armed, randomized controlled trial (RCT) on PNF +/- corticosteroid injection for Dupuytren's contracture.

Based on a sample size calculation, a total of 400 patients will be included. Patients scheduled for PNF at one of the participating study sites will be screened for enrolment and included if eligible. All patients will receive PNF. Following PNF, patients will be randomized to either corticosteroid injection (intervention) or saline injection (placebo) (1:1). Both procedures are performed in one session. Patients will be blinded for the intervention, and followed at 90 days, 1-year, and 2-year postoperative by an independent research member who is also blinded for the intervention.

RESULTS:

Final results are expected in 2026.

Keywords: Orthopedic surgery, Other, Other

Time trends in the use of opioids for elderly patients undergoing hip fracture surgery in 1997-2018: a population-based cohort study

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Background: Hip fractures are a major public health concern with around 7000 elderly patients hospitalized yearly in Denmark. Opioids are a mainstay in the perioperative pain management of hip fracture patients but have severe side effects. Of the hip fracture patients who did not use opioids prior to their fracture, 17% became chronic opioid users after hip fracture surgery. Increasing awareness of the risks pertaining to opioid use has led to a general decline in opioid prescription in Denmark in recent years. However, little is known about the tendency in acute pain management and opioid use after hip fracture surgery.

Objective: To examine time trends in opioid use for elderly patients undergoing hip fracture surgery during a 22-year period from 1997 to 2018.

Methods: The Danish National Patient Registry will be used to identify patients undergoing surgery for first hip fracture during 1997-2018. Patients redeeming an opioid (identified in The Danish National Prescription Registry) during the 6 months before surgery will be excluded. Prevalence rates of opioid use will be calculated for the four quarters after the surgery by two-year calendar periods. Prevalence rate ratios will be calculated using Poisson regression with 1997-1998 as reference and adjusted for age, sex, and comorbidity. The trend in the use of the most common types of opioids will also be investigated.

Results: The analysis is currently in progress.

Perspectives: Knowledge of opioid use for hip fracture patients undergoing surgery will aid the improvement of future treatment strategies, especially regarding pain management and opioid dependency, and help optimize care for this fragile patient group.

Keywords: Orthopedic surgery, Pharmacology, Epidemiology and biostatistics

Prevalence Of Dehiscence Of The Internal Carotid Artery In Patients With Eustachian Tube Dysfunction

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T. Ovesen, Department of Clinical Medicine

Background: The Eustachian tube (ET) connects the middle ear and nasopharynx and has a variety of functions. Among these is ventilation of the middle ear cavity. Eustachian tube dysfunction (DER) is a common disease, causing impaired hearing, ear fullness and earache. Balloon Eustachian Tuboplasty (BET) is a procedure where a catheter is introduced in ET and a balloon is inflated. BET is offered to patients with chronic DER. The internal carotid artery (ICA) is located adjacent to ET in the temporal bone, separated only by a thin layer of bone. In some, this bone is missing which is called dehiscent ICA (dICA). In these cases, the catheter can potentially damage the artery during BET. Therefore, pre-operative CT-scan is performed to exclude dICA. The aim of the study is to investigate the prevalence of dICA in patients with DER.

Method: Subjects were recruited from the Ear, Nose and Throat Department, Regional Hospital West from 2019 to 2021. All patients were scanned with a CT-scanner with a slice thickness of 0.625 mm.

Results: 23 patients (30 symptomatic ears) were scanned. In 13 patients (56.6 %) ICA had a bone cover. Three patients (13 %) had dICA on a symptomatic ear, two (8.7 %) had dICA on a non-symptomatic ear and five patients (21.7 %) had bilateral dICA. Three (13 %) of these patients had bilateral symptoms, 1 (4.3 %) had symptoms on the left ear and one (4.3 %) had symptoms on the right ear.

Conclusion: Compered to other studies, the prevalence of dICA in our study is significantly higher. This is likely due to restrictions in CT scans, whereby a thin bone-cover is not visual. We suggest scanning these patients with a higher resolution scanner.

Keywords: Ear, nose and throat (ENT), Medical technology and diagnostic techniques, Other

Impact of socioeconomic status and its interaction with sex, age and comorbidities on the opioid use after total hip arthroplasty for osteoarthritis

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Aim

We examined the association between socioeconomic status (SES) and opioid use after total hip arthroplasty (THA), and whether age, sex and comorbidity modified the association.

Methods

We used Danish medical databases to create a population-based cohort of patients undergoing primary THA during 2001-2018 (n=88,962). We calculated prevalence rates (PRs) and prevalence rate ratios (PRRs) (with 95% confidence interval) of immediate opioid use (0-1 month) after THA and continued opioid use (1-12 months) among immediate opioid users. Exposure: SES status (education, cohabitation and wealth). Effect modifiers: age, sex and comorbidity.

Results

PRs of immediate opioid use was approximately 40% and 60% in preoperative non-users and users, respectively, with little to no variation between SES markers.

Among preoperative non-users (no opioid prescription 0-6 months before THA) , PRs for continued opioid use were 21% for low education vs 27% for high (PRR=1.29 (1.21-1.38)), 23% for cohabiting vs 27% for living alone (PRR=1.11 (1.06-1.17)), and 20% for high wealth vs. 30% for low (PRR=1.43 (1.35-1.51)).

Among preoperative users, the PRs for continued opioid use were 55% for low education vs 67% for high (PRR=1.22 (1.18-1.27)), 60% for cohabiting vs 68% for living alone (PRR=1.10 (1.08-1.13)), and 54% for high wealth vs. 73% for low (PRR= 1.32 (1.28-1.35)). Stronger associations between SES and opioid use were found in younger patients, and no association was observed in patients with high comorbidity.

Conclusion

Low SES was associated with an increased risk of continued opioid use after THA. Age and comorbidities slightly modified the effect of SES on opioid use.

Keywords: Socio-economic conditions, Pharmacology, Orthopedic surgery

Effect of an exercise intervention targeting hip strengthening in patients undergoing revision total hip replacement - Study protocol for a multicenter, randomized controlled trial (The Strong Hip Trial)

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Background:

Total hip replacement (THR) is effective at reducing pain and improving function, however, the implant may at some time fail, resulting in need for revision THR. There is evidence that revision THR improves pain and function, nevertheless, the effectiveness of rehabilitation after revision THR is debated. Further, clinical outcomes on hip pain and function are poorer for revision THR compared to primary THR. This calls for research exploring different rehabilitation approaches for patients after revision THR.

Purpose:

The primary purpose of this trial is, in a community setting, to investigate the effectiveness of a partly tele-delivered exercise intervention targeting hip strengthening (STRENGTH) with the standard community-based rehabilitation (CONTROL) in patients undergoing revision THR.

Material and Methods:

This randomized controlled trial will be a multicenter trial involving six hospitals and their collaborating municipal rehabilitation centres across Denmark. A total of 84 patients undergoing revision THR will be recruited and randomized to either STRENGTH or CONTROL. Outcomes, including functional performance, leg extensor muscle power, self-reported physical function, pain and quality of life, will be measured at baseline, after the initial 16 weeks of intervention, and at 12-month follow-up.

Results:

Results will be submitted for publication by May 2025.

Conclusion:

If the STRENGTH intervention is superior to the CONTROL intervention in improving clinically important outcomes, patients undergoing revision THR may be offered a moreeffective rehabilitation that may lead to improved functional performance, physical function and quality of life.

Keywords: Rehabilitation, Orthopedic surgery, Other

Is vitamin B12 malabsorption a late side effect in patients undergoing surgery for colorectal cancer?

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Introduction: Colorectal cancer can be treated with hemicolectomy and pelvic exenteration among others. Both surgeries involve resection of terminal ileum, where vitamin B12 is absorbed. Vitamin B12 deficiency may cause megaloblastic anemia, neuropathy and impaired cognitive function.

The purpose of this study is to investigate the vitamin B12 absorption using the vitamin B12 absorption test in colorectal cancer patients who receives either a right hemicolectomy or a pelvic exenteration with construction of a Bricker bladder using terminal ileum. Furthermore, we want to investigate whether these patients develop vitamin B12 deficiency within months after surgery, assessed using biomarkers.

Methods: The study will be performed as a prospective observational study. The study will include 40 patients admitted for surgery with either right hemicolectomy or pelvic exenteration and reconstruction with a Bricker bladder. The patients are examined using the vitamin B12 absorption test and blood samples (total cobalamin, MMA, homocysteine, creatinine, hemoglobin, MCV, folate and ferritin) before surgery and three months after surgery.

Results: Patient enrolment started in fall 2022.

Conclusion: The study is expected to contribute to a) a more precise diagnosis and better organization of treatment of vitamin B12 deficiency after colorectal cancer surgery and b) new knowledge about the association between reduced vitamin B12 absorption and changes in the circulating vitamin B12 biomarkers.

Keywords: Gastrointestinal surgery, Oncology, Rehabilitation

Reduction of emotional and physical harm after surgery cancellation – Development, feasibility testing and evaluation of a complex intervention.

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Background: Cancellation of planned surgery is a huge challenge to the healthcare system with negative impacts on patients, healthcare staff and costs. In Denmark, the COVID-19 pandemic and lack of healthcare personnel has further increased the number of surgery cancellations.

This project concerns the issue of harm in relation to surgery cancellation by investigating the frequency and severity of negative consequences. Furthermore, to explore how the health system can enhance the management and care for patients experiencing surgery cancellation.

Aim: To reduce emotional and possible physical harm in patients who experience cancellation of surgery by developing a Surgery Cancellation Care Program (SCaP), feasibility test and evaluate the effect.

Methods: An intervention study conducted in accordance with the Medical Research Council framework of complex interventions.

Results: The project consists of three studies which are expected to be published in three papers.

In study one, a detailed intervention (SCaP) will be developed based on a published review, examination of current practice and contribution of patients and healthcare professionals. In study two, the intervention is feasibility tested on optimal content, acceptability and capacity of providers to deliver the intervention. In study three, the effect of the intervention will be evaluated in a pilot RCT study.

Keywords: Other, Other, Other

Prehabilitation in prostate cancer patients undergoing nerve sparring robot assisted radical prostatectomy – The TelePrehabTrial

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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. Previous literature shows the benefit of interventions prior to surgery to enhance treatment success, known as prehabilitation (PREHAB). To enhance compliance to PREHAB, home-based exercise using Telehealth to support implementation can potentially be used.

Aim:

To examine whether a four-week PREHAB intervention program is feasible, prior to nerve sparring RP.

A secondary purpose is to collect preliminary data on changes in patient-reported outcome.

Design:

A randomized clinical feasibility trial.

Methods:

A total of 40 patients referred to RP, will be randomized to the intervention group or the control group. The control group will receive standard intervention. The intervention group will receive physical exercise, pelvic floor exercise, a diet intervention and stress management.

Outcome:

The primary outcome is to determine adherence to the intervention, recruitment, randomization, safety and suitability of the exercise and adverse events.

Statistical analysis:

Descriptive statistics will be used to describe the sample. Preliminary measures in outcome efficacy will be measured.

Based on the potential differences, the main outcome will be identified, and a power calculation of a final RCT will be performed.

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.

Keywords: Other, Urology, Oncology

Outcome and complications in external ventriculostomy drainage in intraventricular hemorrhage patients, what we need to know

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Background and aim: External ventricular drainage (EVD) has been shown as an effective treatment to lower the case fatality rate in intraventricular hemorrhage (IVH) patients. However, EVD treatment of IVH is associated with significant challenges, i.e., obstructions and infections, presumably contributing to mortality and morbidity. Although EVD is widely used, patient outcomes and complication rates of using EVD for IVH treatment are not fully elucidated. This study aims to describe the outcomes and complication rates of EVD in patients suffering from IVH.

Methods: This study is a historical, descriptive, multi-center cohort registry study, covering two Danish Regions. All patients with primary or secondary IVH treated with at least one EVD from 2016 to 2021 at Aarhus- and Odense University Hospitals are included. Patients are identified through the Danish National Patient Register by combining treatment code for EVD with relevant IVH diagnoses. Data will be recorded by reviewing individual medical records and stored in a REDCap database. Analysis will be performed, the outcome is measured in Glasgow Outcome Scale Extended, and complication rates are defined in frequency, incidence, incidence rate per 1000 catheter days, and rate per EVD.

Results will be presented if ready.

Keywords: Other, Other, Other

Reduction of musculoskeletal pain among abdominopelvic surgeons

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Background

Within colorectal, gynecological, and urological surgery (abdominopelvic) 93% of Danish surgeons have musculoskeletal pain (MSP), and 77% have multi-site pain that affects work and leisure time. Awkward and prolonged working positions are possible causes. The literature suggests improved ergonomics in the operating room (OR). However, surgeons focus on the patient, and they de-emphasize potential ergonomic solutions, thus OR ergonomics might not be sufficient. The training concept of Intelligent Physical Exercise Training (IPET) accounts for one's work exposure and individual health profile may add on the effect of improved ergonomics. IPET has demonstrated its effects among other professions with a high prevalence of MSP by reducing the relative workload. The overall aim of this PhD project is to alleviate MSP among surgeons. The hypothesis is that in addition to up-to-date OR ergonomics, IPET will significantly reduce MSP among surgeons.

Methods

1) A systematic literature review with the aim to elucidate the effects of applied OR ergonomic interventions on surgeon musculoskeletal health within abdominopelvic surgery. Up-to-date ergonomic recommendations will, based on the findings of the review along with surgeons' input on priority and practical issues, be recommended. The recommendations will act as usual care in study 2) a 20-weeks, two-arm RCT. The aim is to assess the effect of IPET on surgeon MSP. In addition to usual care, the intervention will consist of IPET.

Results

Results will emerge the next 2-3 years in peer-reviewed journals.

Conclusion

IPET is expected to be effective in reducing surgeons' MSP in addition to up-to-date OR ergonomics.

Keywords: Rehabilitation, Work environment and organisation, Gynecology and obstetrics

Faecal microbiota transplantation for first or second Clostridioides difficile infection (EarlyFMT): a randomised, double-blind, placebo-controlled trial

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Introduction: Clostridioides difficile infection (CDI) is an urgent antibiotic-associated health threat with few treatment options. Faecal microbiota transplantation (FMT) is an effective treatment for patients with multiple, recurrent CDI. We investigated FMT compared with placebo after vancomycin for the first or second CDI.

Methods: We conducted an investigator-initiated, double-blinded, placebo-controlled, randomized clinical trial. Patients were randomly assigned (1:1) to FMT or placebo administered day 1 and day 3-7 after they had received standard-care oral vancomycin 125 mg four times daily for 10 days. The primary endpoint was cure of Clostridioides difficile-associated diarrhoea (CDAD) 8 weeks after treatment. We followed patients for 8 weeks or until recurrence. We planned to enrol 84 patients with a prespecified interim analysis after 42 patients.

Results: The trial was stopped at the interim analysis because of unethical high effect differences between the two groups. Among 42 patients randomized patients, 19/21 patients (90.5%, 95%-CI 70–99%) in the FMT group, and 7/21 patients (33.3%, CI 15–57%) in the placebo group had CDAD cure at week 8 (P=0.0003). Adverse events (204 total) occurred equally frequent in both groups. No deaths or colectomies occurred during primary follow-up.

Perspectives: In patients with first or second CDI, first-line FMT is highly effective and superior to the standard-care vancomycin alone in achieving sustained resolution from CDI. To validate the results, we currently treat patients with first or second CDI with early FMT in a prospective cohort.

Article pubslished in Lancet Gastroenterology and Hepatology September 2022

Keywords: Gastroenterology and hepatology, Infection, Other

CO-CHAIRS' ABSTRACTS

Patients' Care Transition in Cardiac Rehabilitation – A Scoping Review on Facilitators and Challenges Related to Referral and Enrolment

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Background

Cardiac rehabilitation (CR) is a class 1A recommendation and is an integrated part of standard treatment for patients with coronary heart disease. CR can reduce rehospitalisation, activity related symptoms and improve function. In many countries CR is an outpatient programme conducted partly in community healthcare services (CHS) however, despite high evidence for benefits from CR, it remains underutilised.

Aim

To identify and synthesise facilitators and challenges in patients' care transition between hospitals and CHS, and how they influence referral and enrolment to CR.

Method

A systematic literature search was conducted in six databases using search terms in accordance with PICo. Exclusion criteria were reviews, meta-analysis, patients aged ≤ 18 years and studies solely measuring effect of CR. Reference lists in included studies were screened through same process. Thematic analysis was used for analysis.

Results

The analysis is ongoing and a total of 26 studies were included. Two main themes emerged; (1) Setting independent facilitators and challenges and (2) Setting dependent facilitators and challenges. Setting independent facilitators and challenges refer to factors that can occur along the entire patient care transition. Setting dependent facilitators and challenges are however setting and/or time specific and influence separate parts of the

patients' care transition. Even though it appears as there is a lack of connection between setting dependent facilitators and challenges each may influence the entire transition.

Conclusion

The analysis is ongoing and the results and conclusion will be presented at PhD day 2023.

Keywords: Cardiovascular system, Rehabilitation, Qualitative research

Increased relative biological effectiveness (RBE) at the distal edge of the proton beam track in an in vivo model of early normal tissue damage

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In radiotherapy, protons display a favorable dose-depth distribution that spare the surrounding normal tissues and a different biological response compared to conventional radiation with photons. To account for the biological difference, an RBE of 1.1 is used in the clinic. This translates into a 10% lower dose of protons compared to photons. However, the RBE varies. In vitro studies show that more cells are killed towards the end of the particle track with an abrupt increase at the distal edge of the Spread-out Bragg peak (SOBP), showing an increased RBE. In vivo data is much needed to quantify this. We aimed to do this in a model of early normal tissue damage between protons and photons.

The right hindlimb of C3H mice were irradiated with a single dose of protons, or as reference, clinical 6MV photons. For proton radiation, the legs were placed in the SOBP center or at the distal edge SOBP. The endpoint was acute skin damage within 30 days post irradiation.

The ED50 (dose producing skin damage in 50% of mice, with 95% CI) was 33.2Gy (31.9- 34.4Gy) (distal edge SOBP), 35.8Gy (34.8-36.8Gy) (center SOBP) and 37.5Gy (36.2- 38.9Gy) (photons). The distal edge protons calculated an RBE of 1.13 (1.07-1.19) and the center an RBE of 1.05 (1.0-01.10). An enhancement ratio of 1.08 between center versus distal edge SOBP was observed as well.

The biological effect was enhanced at the distal edge of the proton SOBP, and the study thus demonstrates an increase in RBE toward the distal edge for early reacting normal tissue for high single doses. This study shines bright light on the variable RBE disputing the standard of care constant RBE value of 1.1.

Keywords: Oncology, Animal models/disease models, Laboratory science

Genetic Rewiring of Cancer Cells Activates Inflammatory and Anti-tumoral Responses

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The cGAS-STING pathway is a crucial innate immune pathway responsible for detecting accumulating cytosolic DNA fragments derived from unfavorable events such as a virus infection or a state of chromosomal instability seen in cancer cells.

In many cancers, the functionality of the cGAS-STING pathway has been obstructed by epigenetic rearrangements of STING leading to suppressed gene expression. This enables cancer cells to escape killing by the immune system despite the presence of cytosolic DNA.

During my PhD, I established a non-toxic and highly specific epigenetic method that counteracts the epigenetic downregulation of STING expression. Using this method, we found that upregulation of STING expression in vitro rendered cancer cells immunologically active in terms of producing a broad range of interferon-stimulated genes. This activation was further boosted when increasing the level of cytosolic DNA by either transfecting cells with dsDNA or treating cells with the chemotherapeutic drug, doxorubicin. We are now investigating if epigenetic rewiring of the STING pathway in cancer cells can revitalize sensitivity to the host anti-tumoral response in murine models.

The perspective of our method can be pivotal and decisive for future cancer therapy. Triggering a transient activation of the patients' own immune system to kill cancer cells can be a personalized, pan-cancer treatment strategy. Furthermore, the potential for combining this treatment approach with already existing treatments like chemotherapy, radiation etc. can potentiate the effects of those and in the end lead to a far better prognosis for cancer patients.

Keywords: Oncology, Inflammation, Cell biology

Is result on first-trimester combined screening associated with the phenotype of Down syndrome? A population-based cohort study

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Background: First-trimester combined screening (FTS) identifies Down syndrome pregnancies, but can FTS predict the Down syndrome phenotype? We aimed to investigate the association between FTS result and phenotype severity in Down syndrome.

Method: A register-based cohort study including all cases of trisomy 21 in Denmark diagnosed during 2005-2018. We compared screen negative (odds <1:300) and screen positive (odds ≥1:300) cases as well as screen result subgroups with respect to anthropometry, congenital malformations and childhood hospitalization.

Results: Of 2,167 trisomy 21 cases, 1,672 (77.2%) were screen positive and 242 (11.2%) screen negative. Absolute measures of fetal and birth anthropometry were comparable between groups. A fetal malformation diagnosis was more prevalent in screen positive than screen negative cases (congenital heart disease (CHD) 36.6% (95% confidence interval (CI) 27.7, 46.2) vs. 12.9% (95% CI 8.6, 24.2)). Data suggested that this could reflect a detection bias. A FTS result of 1:2-1:10 was associated with a higher probability of a fetal malformation diagnosis and postnatal severe CHD compared with a result of 1:11-1:300.
Similar proportions of screen positive (24.7% (95% CI 15.8, 35.5)) and screen negative (20.6% (95% CI 14.8, 27.3)) cases had a postnatal diagnosis of severe CHD. In contrast, screen positive cases more often had non-severe CHD but less often a non-heart malformation. Data on hospitalizations showed inconsistent results.

Conclusion: The 1:300 FTS threshold had limited or no value in predicting Down syndrome phenotype severity. In contrast, cases with a screen result between 1:2-1:10 may represent a more severe phenotype.

Keywords: Paediatrics, Gynecology and obstetrics, Epidemiology and biostatistics

10-year nationwide trends in incidence, treatment patterns, and mortality of patients with myelodysplastic syndromes in Denmark

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Temporal data on incidence, treatment patterns, and prognosis for patients with myelodysplastic syndromes (MDS) are lacking. This study examined 10-year trends in incidence, treatment patterns, and all-cause mortality in a population-based cohort of 2309 MDS patients using Danish nationwide registries (2010-2019).

We computed annual incidence rates overall and according to sex and age-groups. We examined temporal changes in the cumulative incidence of MDS specific treatments initiated within one year from diagnosis and temporal changes in the absolute risk of death and five-year adjusted hazard ratios (aHRs) for death, adjusting for age, sex and comorbidity.

The age-standardized incidence rate of MDS per 100,000 person-years increased slightly from 5.3 in 2010 to 6.4 in 2019. Between 2010-2012 to 2016-2017, the use of azacitidine increased overall (8% to 22%), in patients with intermediate risk MDS (12% to 34%), and in patients with high-risk MDS (22% to 50%), while it remained stable (around 5%) for patients with low-risk MDS. The five-year aHR for death in the most recent calendar period compared to the earliest calendar period remained unchanged in patients with low-risk MDS, aHR = 0.90 (95% CI, 0.72-1.12) and in patients with high-risk MDS, aHR = 1.19 (95% CI, 0.89-1.61), while survival improved over time among patients with intermediate risk MDS, aHR = 0.67 (95% CI, 0.48-0.92).

In conclusion, the incidence of MDS slightly increased during a 10-year period. The use of azacitidine increased markedly but five-year overall survival remained unchanged.

Keywords: Oncology, Epidemiology and biostatistics, Other

Inclusion of metabolic tumor volume in prognostic models of bone and soft tissue sarcoma increases the prognostic value

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Introduction: Sarcomas are a rare group of heterogenic tumors with a high mortality rate. With accurate prognostic prediction, patients at low risk of disease recurrence can be spared toxicity of further treatment, whereas patients at high risk can be considered for adjuvant therapy. It is warranted to improve the current prognostic classification, preferably using readily available parameters. The aim of this study was to examine the prognostic value of several scoring systems in combination with PET parameters.

Materials and Methods: We included patients with newly diagnosed sarcoma, treated and scanned at Aarhus University Hospital, Denmark, from January 2016 to December 2019.
Metabolic tumor volume (MTV) was calculated with threshold SUV 2.5. The Akaike information criterion and Harrell's concordance index were used to evaluate whether MTV added prognostic information to existing prognostic models. Backward stepwise selection was used to create a new prognostic model combining circulating biomarkers and PET parameters.

Results: A total of 148 patients were included. The existing prognostic models were combined with MTV and the prognostic value improved in all models. A new model, SBSpib, was created. It included albumin, lactate dehydrogenase, alanine aminotransferase and two PET parameters. It has scores from 0 to 4 and increasing hazard ratios; HR=2.59 (1.00-6.75) for group 1, HR=5.66 (2.31-13.86) for group 2, HR=10.96 (4.43-
27.09) for group 3 and HR=650.50 (93.99-4504.92) for group 4.

Conclusion: Implementing MTV in existing prognostic models clearly improves the prognostic value. SBSpib is a new prognostic model including circulating biomarkers and PET parameters.

Keywords: Oncology, Orthopedic surgery, Other

Periacetabular Osteotomy to treat hip dysplasia; a systematic review of harms and benefits

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Introduction: Periacetabular osteotomy (PAO) is often performed in patients with hip dysplasia. The aim of this systematic review and meta-analysis was to evaluate the harms and benefits of PAO in patients with hip dysplasia in studies reporting both adverse events and patient-reported hip pain and function.

Materials and Method: A systematic search combing PAO and patient-reported outcomes was performed in the databases MEDLINE, CINAHL, EMBASE, Sports Discuss and PsychINFO. Studies including both harms and benefits defined as adverse events and patient-reported hip pain and function were included. Risk of bias was assessed using The Cochrane Risk of Bias In Non-Randomized Studies – of Interventions.

Results: Twenty-nine cohort studies were included, of which six studies included a comparison group. The majority of studies had serious risk of bias and the certainty of evidence was very low. The proportion of adverse events was 4.3 (95% CI: 3.7;4.9) for major adverse events and 14.0 (95% CI: 13.0;15.1) for minor adverse events. Peroneal nerve dysfunction was the most frequent adverse event among the major adverse events, followed by acetabular necrosis and delayed union or non-union. All patient-reported hip pain and function scores improved and exceeded the minimal clinically important differences after PAO. After five years, scores were still higher than the preoperative scores.

Conclusion: PAO surgery has a 4% risk of major, and 14% risk of minor adverse events and a positive effect on patient-reported hip pain and function among patients with hip dysplasia.

Keywords: Orthopedic surgery, Rehabilitation, Reviews and meta-analyses

'Look- your baby is talking to you' A family focused, relationship based and optimized postpartum stay at the obstetric department and transition to primary healthcare sector for vulnerable families

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Maternal vulnerability challenges parenthood and poses an essential task to health professionals working in postnatal care. Being born by a vulnerable mother may have wide-ranging effects on child development and carry a risk of impairment in cognitive, behavioral, and mental problems. Healthcare professionals in the obstetric department are in a unique position to initiate early intervention to improve outcomes for both mother and infant.

By working family focused and relationship based with the families the complex intervention 'Look-your baby is talking to you' has been carried out at Copenhagen University Hospital Hvidovre. The intervention combines components from the methods Family Focused Nursing (FFN) and Newborn behavioral observations (NBO), as well as a systematized transition to the primary healthcare sector. The intervention hypotheses that when providing the mother with optimal support, understanding of their infants' cues and empowering family resource's chance is to lower maternal depressive symptoms 3-month post-partum.

The target group of the intervention is mothers with current or past depression and/or anxiety. The intervention consisted of a five-day standardized stay at the obstetric department including 3 NBO sessions and 3 family conversations. In total 49 mothers received intervention and 51 were included in the comparison group. Baseline data were collected 24-48 hours post-partum and 3-month post-partum.

This short-term intervention will contribute with a new perspective on the potential of the postpartum stay at the obstetric department and provide knowledge about the application of both NBO and FFN at the obstetric department.

Keywords: Gynecology and obstetrics, Public health, Psychiatry, psychology and mental health

Targeted Stem Cell Therapy to Inhibit Renal Fibrosis

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Chronic kidney disease (CKD) is a major health concern and current treatment strategies are ineffective. Thus, the identification of novel therapeutic strategies targeting renal fibrosis, is of utmost importance. The aim of this study is to establish targeted stem cell therapy to minimize the progression of renal fibrosis in CKD.

To establish targeted stem cell therapy we have transiently transfected adipose derived mesenchymal stem cells (AD-MSCs) with constructs carrying our genes of interest VEGF and BMP-7. The hypothesis is that MSCs secreting tissue-repair factors can be utilized as a therapeutic modality to inhibit the progression of renal fibrosis in CKD.

Protein secretion of the tissue repair factors in conditioned media (CM) was verified and followed for 7 days with ELISA. Here, we saw secretion of the factors which peaked around 48-72 hours and thereafter declined steadily. To test the antifibrotic efficacy of the stem cells, conditioned media from TNF-α and INF-γ MSCs was concentrated and added to
TGF-β stimulated human renal fibroblasts. These data showed us that CM from INF-γ stimulated AD-MSCs reduced the increase in Collagen-1a1 induced by TGF-β stimulation.

Two models will verify this; 1) Preconditioned MSCs, co-incubated with precision put kidney slices stimulated with TGF-β 2) Preconditioned MSCs will be grown on dishes coated with a temperature responsive polymer allowing for the release of MSCs as a sheet. This sheet will be transplanted onto the kidney of UUO mice.

We will thereby establish a therapeutic modality providing transient local secretion of specific tissue-repair factors, providing local effects with limited systemic exposure.

Keywords: Nephrology, Animal models/disease models, Cell biology

Reduced synaptic SV2A density in a porcine model of Parkinson's disease and its modulation by deep brain stimulation of the subthalamic nucleus

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Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an effective non-pharmacologic treatment for Parkinson's disease (PD). It acts in part by suppressing STN hyperactivation, however, the synaptic density modulation it promotes remains uncertain. [11C]UCB-J binds to synaptic vesicle glycoprotein 2A (SV2A), expressed in all synapses, and can be used for positron emission tomography (PET). Here we test the hypothesis that 6-OHDA-injected minipigs present with reduced synaptic SV2A density, and that this deficit is reversible by DBS-STN. Female Göttingen minipigs were unilaterally injected into the median forebrain bundle with 6-OHDA(n=5) or saline(n=2). [18F]FDOPA PET and behavioral assessments were used to confirm the lesion. Minipigs then received ipsilateral STN-DBS implants under sterile surgical conditions. [11C]UCB-J PET scans were acquired prior to and 2 hours after DBS onset. We observed a 46% ($p<0.01$) reduction in ipsilateral striatal [18F]FDOPA uptake, 14%($p<0.01$) reduced gait velocity, and increased ipsilateral rotations in 6-OHDA-injected minipigs, while no changes were observed in the saline- injected minipigs. Significantly lower [11C]UCB-J binding in ipsilateral substantia nigra 24% ($p<0.02$) and caudate 23% ($p<0.01$) was observed in 6-OHDA-injected minipigs. After two hours of acute DBS, we observed a bilateral increase in nigral and striatal [11C]UCB-J binding in a small subset of minipigs consisting of both 6-OHDA and saline-injected minipigs. 6-OHDA-injected minipigs have reduced ipsilateral nigral and striatal synaptic SV2A density. Acute DBS-STN may have the capacity to enhance synaptic density in healthy minipigs and in a parkinsonian model.

Keywords: Animal models/disease models, Basic neuroscience, Laboratory science

Prediction of MACE and death among kidney transplant candidates using clinical risk factors, CACS and coronary CTA

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Objective: To evaluate the prognostic ability of clinical risk factors, Coronary Artery Calcium Score (CACS) and coronary Computed Tomography Angiography (CTA) in a real-life setting of kidney transplant candidates.

Background: Kidney transplant candidates have increased risk of cardiovascular disease, which causes both graft loss and death. Screening for cardiovascular disease is recommended in guidelines, but the optimal method remains to be determined.

Method: Retrospectively, data from kidney transplant candidates were obtained. Patients were systematically referred to CACS and coronary CTA prior to approval for transplantation. End-points were Major Adverse Cardiovascular Events (MACE) and all- cause mortality. Time to event analyses were performed using cox regression.

Results: 529 kidney transplant candidates were included in the KTX-CTA cohort. CACS and coronary CTA were performed in 437 and 411 candidates, respectively. Three or more risk factors predicted MACE (HR 2.09 (95% CI 1.35-3.23)) in the total cohort. CACS > 0 and < 400, CACS ≥ 400, 2-vessel and 3-vessel/left main artery disease in coronary CTA further differentiated patients with elevated risk (e.g., 3-vessel/left main: HR 4.90 (95% CI 2.40- 10.01), p < 0.001). Risk factors ≥ 3, CACS ≥ 400, 2-vessel and 3-vessel/left main artery disease predicted increased risk of all-cause mortality.

Conclusion: Overall, ≥ 3 risk factors predict increased risk of both MACE and all-cause mortality among kidney transplant candidates in a real-life setting. CACS and coronary CTA further distinguish patients at different levels of risk, which may aid risk stratification prior to kidney transplantation.

Keywords: Nephrology, Cardiovascular system, Other

A novel method to screen amphetamines for their ability to release monoaminergic neurotransmitter

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Amphetamines are among the most prevalent drugs of abuse. They elicit increased wakefulness and self-confidence; however, long-term effects include depression, anxiety and paranoia. On the illicit drug market, new amphetamine-based designer drugs are constantly synthesized that evade law enforcement. The effects of designer drugs is unknown and unpredictable – neither can they be controlled, nor do we know how to treat abuse or overdose effectively.

Amphetamines act on monoamine transporters (MATs), which facilitate, among others, the uptake of the neurotransmitter serotonin (5-HT) from the synaptic cleft and hereby terminate 5-HT neurotransmission. The ability of amphetamines to force MATs like the serotonin transporter (SERT) to run in reverse and release neurotransmitters is the main pharmacological action of these drugs.

So far, existing assays to characterize this releasing effect suffer from methodological problems as well as low throughput. To overcome these problems, we developed a fluorescence-based plate-reader assay capable of not only measuring 5-HT uptake, but also 5-HT release via the SERT. Our assay utilizes a novel fluorescent 5-HT sensor protein and obtains inhibitory potencies of known SERT inhibitors comparable to those obtained with the radiotracer uptake assay. Furthermore, our assay is capable of measuring 5-HT release induced by MDMA – obtained EC50 values are comparable to the literature. Hereby, we are able to study the molecular effect of monoamine releasers on the SERT and in a next step will utilize the assay to screen amphetamine-based designer drugs for their ability to force the SERT to run in reverse and release 5-HT.

Keywords: Basic neuroscience, Cell biology, Pharmacology

Reducing events in coronary bifurcations - Is it possible? Rational and design of the OCTOBER Trial

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Background: Treatment of coronary bifurcation lesions by percutaneous coronary intervention constitutes a technical challenge. Lesions with significant disease in the main - and the side branch often require treatment by complex stenting with an elevated risk of suboptimal stent implantation result and poor clinical outcome. Intravascular optical coherence tomography (OCT) is a light-based imaging modality which can detect correctable factors not visible by standard angiography, improve procedural control and optimize stent implantation. The aim of the OCTOBER Trial is to compare median two-year clinical outcome after OCT guided vs. standard angiography guided revascularization of patients requiring complex bifurcation treatment.

Method: The OCTOBER Trial is a randomized, investigator-initiated, multicenter, superiority trial with inclusion of 1200 patients from 37 centers in Europe. Patients are randomized 1:1 to either OCT guided - or standard guided revascularization. Inclusion criteria are stable - or unstable angina pectoris, or clinically stable non-STEMI, and indication for revascularization of a complex coronary bifurcation. Treatment of patients randomized for OCT guiding treatment follows a systematic OCT protocol with specified time - and checkpoint for OCT during procedure. The primary outcome measure is a 2-year composite endpoint of cardiac death, target lesion myocardial infarction and ischemia- driven target lesion revascularization.

Conclusion: A positive outcome of the OCTOBER trial may establish OCT as a routine tool for optimization of complex PCI. Last patient was enrolled in March this year. Estimated reporting of primary endpoint in spring 2023.

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Other

Societal costs of out-of-hospital cardiac arrest survivors

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Introduction:

Survival rates in out-of-hospital cardiac arrest (OHCA) increase worldwide, leaving more people to live a life as a cardiac patient with associated altered health behaviour. Health behaviour of OHCA survivors often results in frequent hospital contact and sheltered accommodation with increased societal costs to follow. Furthermore, lost productivity and sick leave may have significant socioeconomic consequences.

Aim:

To evaluate the costs of OHCA survivors compared to a matched non-cardiac arrest control group of myocardial infarction (MI) and to a matched non-cardiac disease control group.

Methods:

This study is a nationwide register-based cost-of-illness study on OHCA survivors with matched controls. Using data from the Danish registries each case will randomly be assigned one control with non-cardiac arrest MI and one control with no cardiac disease. Data will be retrieved from Danish registers through Statistics Denmark and will include both demographic data, medical data, costs of health care use and costs of lost productivity. Costs will be estimated and reported for each year, including the year before event to end of study period or no registration (e.g. due to death). Student's unpaired t-test will be used to determine differences in costs between OHCA survivors and matched controls.

Results:

Results are expected to be available primo 2023.

Conclusion:

Conclusions will be drawn upon results. Knowledge of the economic burden of OHCA survivors is important when prioritizing and allocating available health resources in order to improve daily living in OHCA survivors through rehabilitation.

Keywords: Rehabilitation, Cardiovascular system, Other

Development of the Cirrhotic Ascites Severity model that describes the whole spectrum of cirrhotic ascites and predicts one-year mortality

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Background: Ascites formation is a sign of cirrhosis decompensation. The traditional classification into diuretic-responsive and refractory ascites has limited prognostic information and does not describe the dynamic course of cirrhotic ascites. We developed the Cirrhotic Ascites Severity (CIRAS) model that relies on ascites-related variables, describes the whole spectrum of ascites, and predicts 1-year mortality.

Methods: The CIRAS model was developed using baseline data of 465 patients randomized to placebo treatment in the satavaptan trials with complete 1-year follow-up of survival. We used multivariable logistic regression based on these ascites-related variables: 1) patient-reported ascites discomfort score (≤50 or >50), 2) plasma sodium (≥140, 133–139, 125–132, or <125 mmol/L), and 3) a composite of ascites accumulation and diuretic treatment. The CIRAS model was validated in the 697 patients who received satavaptan treatment.

Results: The 1-year all-cause mortality was 20%. The CIRAS model had a better ability to discriminate between patients that were dead or alive after one year than the classification into diuretic-responsive and refractory ascites in both the development cohort (AUC 0.68 [95% CI: 0.62-0.75] vs 0.62 [95% CI: 0.57-0.68] and the validation cohort
(AUC 0.68 [95% CI: 0.64-0.72] vs 0.55 [95% CI: 0.51-0.60].

Conclusion: The CIRAS model combines only ascites-related variables to describe the ascites severity and predict 1-year all-cause mortality for patients with all grades of cirrhotic ascites. It outperforms the traditional binary ascites classification and may be a promising clinical tool for the management of patients with cirrhotic ascites.

Keywords: Gastroenterology and hepatology, Gastroenterology and hepatology, Epidemiology and biostatistics

Biomarker Identification for Non-alcoholic Fatty Liver Disease by Manifold Learning-based Transcriptomics

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Background: Non-alcoholic Fatty Liver Disease (NAFLD) has been recognized as a clinical challenge for decades. Detection of gene expression alteration in NAFLD, with traditional bulk RNA sequencing (RNA-seq), could be associated with the changes in cell abundance and/or expression transcription levels. Single-cell RNA sequencing (scRNA-seq) has developed from RNA-seq as one of the most promising technologies to reveal the composition and evolution of cells during the progression of NAFLD.

Methods: ScRNA-seq and RNA-seq data from NAFLD patients and healthy controls were collected from the public NGS data depository GEO. ScRNA-seq data of 104,094 liver cells from 9 healthy and 8 NAFLD patients were included in this analysis. RNA-seq data were derived from 625 liver samples of 83 healthy and 542 NAFLD patients.

Results: CD163 and VCAN were specifically expressed in monocytes. Sub-clustering of monocytes showed that CD163 is mainly expressed by macrophages, whereas VCAN is mainly expressed in tissue-monocytes. At single cell levels, expression of both CD163 and VCAN was decreased in NAFLD compared to healthy controls. However, bulk RNA-seq from liver biopsies showed no difference in CD163 expression between healthy and NAFLD groups, while the expression of VCAN was higher in NAFLD. This collectively suggests the accumulation of CD163+ macrophages and VCAN+ tissue-monocytes in the NAFLD liver.

Conclusion: Our integrative analysis showed that monocyte recruitment, rather than activation of CD163 and VCAN expression is associated with NAFLD. The monocyte recruitment may help maintain a stable CD163 level in liver tissue between the healthy and NAFLD.

Keywords: Genetic engineering, Gastroenterology and hepatology, Cell biology

The potential causal effect of maternal vitamin D levels in early pregnancy on pubertal timing in children and markers of male fecundity in young men

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Maternal vitamin D levels in pregnancy may be important for later reproductive health in the children. However, potential confounding may hamper the validity of observational studies investigating the effect of maternal vitamin D in pregnancy.

We therefore aimed to investigate the association between maternal vitamin D levels and pubertal timing in children and male fecundity in young men using season of early pregnancy as an instrumental variable for maternal vitamin D levels.

We conducted a follow-up study of 15,819 children and of 827 young men from the Danish National Birth Cohort including the Puberty Cohort and the Fetal Programming of Semen Quality (FEPOS) cohort. Season of gestational week 8 was used as an instrumental variable to predict maternal vitamin D levels, which was analysed according to age at attaining numerous pubertal markers, including a combined estimate for overall pubertal timing, and markers of male fecundity, including semen characteristics, testes volume, and reproductive hormone levels.

We found that girls and boys had earlier pubertal timing, when their mothers had lower predicted vitamin D levels in early pregnancy of -1.3 months (95% CI: -2.1 to -0.4) and -1.0 months (95% CI: -1.8 to -0.2) per SD (22 nmol/L) decrease in 25(OH)D3 respectively. Young men had -13% (-30 to 9) lower sperm count, -5% (-11 to 1) lower testes volume and 12% (2 to 24) higher follicle-stimulating hormone per SD lower predicted 25(OH)D3 in early pregnancy.

Low vitamin D levels during pregnancy was associated with earlier pubertal timing in the children and poorer markers of male fecundity and may therefore be a modifiable risk factor for poor reproductive health.

Keywords: Epidemiology and biostatistics, Public health, Gynecology and obstetrics

The coverage of influenza vaccination and predictors of not receiving influenza vaccination in Danish cancer patients

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Introduction

Influenza vaccination is free-of-charge for Danish citizens aged ≥65 years and for, among others, persons with acquired immune defects, which can be caused by some cancer types or treatments. We aimed to estimate the influenza vaccination coverage and to identify predictors of non-influenza vaccination in Danish cancer patients.

Methods

In this register-based cohort study, patients ≥18 years with a diagnosis of incident cancer from 1/10-2002 to 1/10-2017 were followed for up to five years. We obtained influenza vaccination status at the end of each influenza season (2007/2008–2017/2018) and data on health, treatment, and demographic and socioeconomic factors. We applied a Poisson model to estimate adjusted prevalence ratios (aPR) and 95% confidence intervals (95%CI) of non-influenza vaccination separately for patients aged <65 and ≥65 years.

Results

We included 269,836 patients. Overall, 87% of patients <65 years and 49% of patients ≥65 years were unvaccinated. Non-influenza vaccination in the previous season was associated with non-vaccination in the current season (aPR [95%CI]:
<65: 2.75[2.71-2.80];
≥65: 5.15[5.10-5.21]). Receipt of chemotherapy compared with non-receipt was associated with lower prevalence of non-vaccination in solid tumor patients <65 years (0.90 [0.89-0.90]) and with higher prevalence in hematological cancer patients ≥65 years (1.18 [1.15-1.21]).

Conclusion

Non-vaccination in the previous season was the strongest predictor of not receiving influenza vaccination in the current season. Chemotherapy was associated with higher vaccination prevalence in solid tumor patients <65 years and lower prevalence in hematological cancer patients ≥65 years.

Keywords: Epidemiology and biostatistics, Oncology, Pharmacology

the Functions of RNA sensors in Herpes Simplex Encephalitis

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not published

Herpes simplex encephalitis (HSE) is the most common form of acute viral encephalitis in industrialized countries, which is mainly caused by HSV-1 infection. TLR3 and RIG-I/MDA5 are both RNA sensors, but located in endosomes and the cytoplasm, respectively. The receptors recognize double-stranded RNA (dsRNA) intermediates or by-products generated during HSV-1 infection, triggering the production of inflammatory cytokines, including type I interferon (IFN), for the control of HSV-1 replication. In the case of TLR3, this is dependent on the adaptor protein TRIF, and in the case of RIG-I/MDA5, it depends on MAVS. One central unresolved question in innate immunology is whether and how pattern recognition receptors cross-talk, and how this impacts on host defense.

In my project, I will establish murine ocular HSV-1 infection model to mimic the natural way of HSV-1 invasion on TLR3-/- and MAVS-/- mice for studying the roles and mode of action of TLR3 and RIG-I/MDA5 in pathogenesis of HSE. Our aim is to decipher the function of RNA sensors in vivo in HSV-1 infection, and to pave the way for improved HSE treatment.

Keywords: Animal models/disease models, Infection, Cell biology

Scintillation imaging for time-resolved 2D monitoring of ultra-high dose rate proton beam scanning

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Introduction: Ultra-high dose rate (UHDR) or FLASH radiotherapy could increase the therapeutic window of radiation therapy by preferential sparing of normal tissue. Dosimetry is essential for FLASH studies. For proton pencil beam scanning (PBS) it requires monitoring each individual spot delivery. Here we propose the use of scintillation imaging for monitoring the dose and dose rate distribution during beam delivery.

Methods: A transparent scintillator sheet was imaged at 1kHz rate using a fast camera. A UHDR PBS field was delivered using a high beam energy. After image processing and calibration against an ionization chamber, the single spot and total field profiles were found. The results were compared to radiochromic film measurements and a commercial scintillation-based beam profiler.

Results: All individual beam spots were temporally resolved with 0.6mm spatial resolution and their signal intensity fluctuated by 3%. The measured Gaussian width of individual spots was 0.6mm smaller than the film width, while it matched better the commercial beam profiler width. The measured spot positions matched the planned positions within
0.3 and 0.1mm in x and y direction, respectively. The field size at 50% isodose showed an average size difference of 1.5mm between the scintillator and the film.

Conclusion: Scintillation imaging using a transparent scintillator sheet offers a unique dosimetry method. It will allow direct 2D monitoring of the instantaneous dose rate in vivo, with direct spatial correlation to the target's external anatomy, when placed downstream the target in transmission beams. Further work will include characterizing the scintillator sheet response.

Keywords: Oncology, Other, Other

Muscle fiber type-specific hypertrophy and stem cell responses to low.load blood flow-restricted resistance training in older individuals

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Low-load blood flow-restricted resistance exercise (BFRRE) potentially constitute a mechanically gentle, yet effective means to counteract the phenotypical and functional deficits exhibited by aging skeletal muscle. This study investigated the effect of BFRRE on muscle functional capacity as well as muscle fiber morphology, cumulative myofibrillar protein synthesis, muscle stem cells (MuSCs) and myonuclear abundance. To this end, from a cohort of healthy older individuals (65 6 years), 23 individuals were randomized to either 6 weeks of supervised BFRRE (3 sessions x week) or non-exercise intervention. Deuterium oxide was orally administered throughout the intervention period, enabling tracing of cumulative myofibrillar protein synthesis rate (MPS). Biopsies were collected from v. lateralis before and after the intervention period. Immunofluorescent microscopy was utilized to assess muscle fiber type-specific cross-sectional area (CSA) as well as MuSC and myonuclear content. We report that six weeks of BFRRE effectively increased muscle contractile function while promoted robust 20% increase in muscle fiber CSA, that was equally consistent in type I as in type II fibers ($p<0.05$). This occurred without concomitant expansion of the MuSC pool ($p>0.05$), and without apparent myonuclear addition to support increased transcriptional demands ($p>0.05$). Surprisingly, the observed muscle fiber hypertrophy was not mirrored by increases in MPS. In conclusion, BFRRE was highly effective in stimulating skeletal muscle growth and increases in muscle function. These results advocate for the application of BFRRE as a countermeasure of age-related deterioration of muscle mass and strength.

Keywords: Health education and simulation-based training, Public health, Cell biology

Investigating neuromodulators release from Locus Coeruleus terminals in the hippocampus during novelty exploration: Dopamine and Noradrenaline story

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Daily experiences are easily forgotten, but when we witness something new, we tend to vividly recall the events that happened close in time from that novel incident.

Novelty has been shown to improve memory retention and learning in animals and humans. The hypothesis of my project suggests that dopamine (DA) is the responsible neuromodulator for the memory boost. Previous research showed that the source of dopamine in the hippocampus (HPC) might surprisingly be the noradrenergic center of the brain, the Locus Coeruleus (LC) (Kempadoo et al., 2016; Takeuchi et al., 2016). When novelty occurs, it stimulates LC neurons to co-release DA with noradrenaline (NA) in the HPC.

In my project, I am investigating how novelty improves memory retention in HPC via DA release from LC neurons. The main aims are 1) Detecting the co-release of DA and NA during novelty exposure in freely moving rats, 2) Checking the co-release of DA and NA from LC in HPC using optogenetic stimulation. In the in-vivo study, I detected an increase of NA signal in the HPC during novelty exposure by using its biosensor and fiber- photometry recording. Next, I detected the release of DA and NA in HPC during optogenetic stimulation of LC. To check possible dynamics of DA and NA release in HPC from LC axons, I expressed red-shifted opsin in LC terminals and used mouse acute hippocampal slices expressing NA sensor. I detected an increase in NA signal during optogenetic stimulation using 2-photon microscopy. These results suggest that DA and NA might be co-released in HPC due to LC activation. Further analysis is needed to clarify the releasing dynamics of DA and NA from LC neurons in HPC using ex-vivo study.

Keywords: Basic neuroscience, Other, Other

What determines time to decannulation in tracheostomy patients following severe traumatic brain injury. A Danish registry-based cohort study

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Introduction

Prolonged tracheal tube placement after severe traumatic brain injury (TBI) can cause severe complications. Safe removal requires adequate functional ability to self-maintain breathing and ensure airway protection. Thus, identifying important factors for time to removal of the tracheal tube (decannulation) is key to efficient weaning for early post- tracheostomy rehabilitation.

Aim

The aim of the study is to identify significant factors for time to decannulation in a Danish population of patients with tracheostomy after TBI.

Method

Retrospective cohort database study. Patients with severe TBI and a tracheal tube were selected from the Danish Head Trauma Database (DHD) between 2011 and 2021.

Time to decannulation was calculated as time from injury to decannulation to account for the heterogeneity for the timing of tracheostomies. Selected explanatory variables on demographic and clinical characteristics, e.g. GCS, cause of injury, Functional Oral Intake Scale (FOIS), total Early Functional Abilities (EFA) score, EFA facio-oral function subscale, complications and adverse events, were extracted.

Results

Potential independent explanatory variables for time to decannulation will be identified by univariate analysis. Variables associated with shorter time by comparison are included for multivariable analysis to identify independent predictors of time to decannulation.
Preliminary results of the present ongoing study will be presented.

Discussion

Identifying factors that could potentially explain differences in time to decannulation are important for patient outcomes, especially if these factors are modifiable and could be targeted through rehabilitation.

Keywords: Rehabilitation, Clinical neuroscience, Respiratory system

Pre-meal consumption of whey in gestational diabetes mellitus

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Background:

Pre-meals of whey protein isolate (WPI) lowers postprandial glucose trajectories in healthy and type 2 diabetes patients. Whether this translates into patients with gestational diabetes mellitus (GDM) is unknown, but pre-meal WPI servings may potentially improve glucose homeostasis and reduce GDM complications such as macrosomia.

Objective:

To investigate the metabolic effects of WPI in women at risk of and with GDM.

Methods:

Trial A) Twenty-four women at risk of GDM (n=12) or with GDM (n=12) will undergo a randomized crossover study receiving placebo and WPI prior to an oral glucose tolerance test. For five days between visits, they will consume either placebo or WPI in various doses prior to breakfast at home and wear continuous glucose monitors (CGM).

Trial B) Sixty-two women will undergo a randomized parallel study and have either placebo or whey protein prior to breakfast from GDM diagnosis until delivery. They will visit the laboratory twice and wear CGM at home in the four following days. At delivery, cord blood and breast milk will be sampled.

Results:

Preliminary results of trial A shows that WPI lowers peak blood glucose levels by 1.8 mM
following an OGTT in women at risk of or with GDM

(n=19). Conclusion:

The trials are ongoing and no conclusions can yet be drawn.

Keywords: Gynecology and obstetrics, Reviews and meta-analyses, Other

Improved sensitivity and specificity of 3T laminar fMRI with GE-BOLD using NORDIC and phase regression

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Introduction: Submillimeter-spatial-resolution fMRI enables measurements of activation across cortical layers in humans. To reduce problems of low signal stability associated with small voxels as well as spatial specificity degradation due to large veins, laminar fMRI studies almost exclusively employed ultra-high field strength scanners (≥7T). However, such systems are relatively rare, and only a subset of those are clinically approved.
Therefore, we examined if NORDIC denoising and phase regression could improve 3T- laminar-fMRI feasibility. Methods: 5 healthy subjects were scanned on a Siemens MAGNETOM Prisma 3T scanner. Subjects were scanned in 3-8 sessions on 3-4 consecutive days to assess across-session reliability. A 3D-gradient-echo EPI (GE-EPI) sequence was used for BOLD acquisitions (voxel size = 0.82 mm isotopic, TR = 2.2 s) using a block design finger tapping paradigm. NORDIC denoising was applied to magnitude and phase time series to overcome limitations in temporal signal-to-noise ratio (tSNR). Phase regression was subsequently applied to correct for large vein contamination using the denoised phase timeseries. Results and conclusion: NORDIC denoising resulted in tSNR values comparable to or higher than commonly observed at 7T. Layer-dependent activation profiles could thus be extracted robustly from regions of interest located in the hand knob of the primary motor cortex (M1), both within and across sessions. Phase regression led to substantially reduced superficial bias in obtained layer profiles although residual macrovascular contribution remained.
Accordingly, we believe NORDIC and phase regression improved 3T-laminar-fMRI feasibility.

Keywords: Basic neuroscience, Clinical neuroscience, Medical technology and diagnostic techniques

Discovery and Study of Hotspots for Proteome Advanced Glycation

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Introduction: Diabetes mellitus type 1 and 2 (T1DM and T2DM) are major metabolic diseases and leading causes for several late stage complications. The standard therapy is glycaemia control; however, this does not prevent disease progression. Increasing evidence from human association studies and animal studies have demonstrated that methylglyoxal (MG), a toxic glycolytic byproduct, and its protein advanced glycation end- products (AGEs) are common factors in the development and progression of e.g. T2DM. Despite these well-established connections, the molecular details usually remain elusive.

The objective is to identify proteins very reactive towards MG (hotspots). The hypothesis being that hotspots most likely are relevant in relation to e.g. T2DM. With this knowledge, we ultimately aim at elucidating mechanistic links between protein alterations and physiological consequences.

Methods: Using chemoproteomics, targets of MG have been identified in HEK293 cells. Selected hotspots have undergone further investigations like activity assays, and bioinformatics studying e.g. the protein structure surrounding the modification site.

Results: We have succeeded in elucidating potential hotspots for MG glycation. Folding assisting proteins were found to be prone to being modified. This suggest that not only can MG affect the structure of targeted proteins, but MG may also impair protein folding enzymes leading to partially folded or misfolded proteins in general; a state named proteotoxic stress. This may consequently affect the proteostasis; a condition that have been linked to e.g. T2DM.

Conclusion: We have demonstrated that proteins show different reactivity towards MG.

Keywords: Molecular metabolism and endocrinology, Other, Other

Dose response of cuvette-sized versus bulk silicone-based radiochromic dosimeters

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Aim:

Silicone-based radiochromic dosimeters allow for 3D dose verification with high spatial resolution. Key dosimetric properties are often characterized using cuvette-sized dosimeters, since 3D experiments are time consuming and costly. However, dosimetric properties for larger samples must also be validated. The aim of this study was therefore to assess the dose response obtained from cuvette-sized dosimeters read out using a spectrophotometer versus larger cylindrical dosimeters read out using an optical 3D CT scanner.

Material and Methods:

Cuvette-sized and bulky cylindrical dosimeters were fabricated from silicone elastomer, curing agent, chloroform and leucomalachite green and irradiated with a 6 MV photon beam to dose levels ranging from 2 to 20 Gy. Cuvettes were read out using a spectrophotometer at 625 nm while cylinders were read out using a 3D optical CT scanner at 635 nm.

Results:

Linear dose responses were found in the investigated dose ranges for both cuvettes and cylindrical dosimeters. The dose response for the cuvettes was (0.0222 ± 0.0003) 1/(Gy · cm) while it for the cylindrical dosimeters was (0.019 ± 0.002) 1/(Gy · cm).

Conclusion:

The dose response for cuvettes reported by spectrophotometry at 625 nm and for larger samples measured using an optical CT scanner operating at 635 nm were comparable. The discrepancy is attributed to difference in read-out wavelength, read-out modality, volume and irradiation conditions. This study showed that the dose response of small samples with good approximation can be translated into larger ones, however, the volume effect is yet to be investigated and fully understood to relate these two distinct types of experiments.

Keywords: Oncology, Other, Other

Vitamin D in Pregnancy (GRAVITD) – Identifying Associations and Mechanisms Linking Maternal Vitamin D Deficiency to Placental Dysfunction and Adverse Pregnancy Outcomes

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Background

The prevalence of vitamin D deficiency is high among Danish pregnant women despite high adherence (90 %) to the official recommendations (10 µg/day). Vitamin D deficiency in pregnancy is associated with increased risk of adverse pregnancy outcomes especially complications related to placental dysfunction and insulin resistance.

The object of this study is to investigate if a higher dose of vitamin D in pregnancy reduces the prevalence of vitamin D deficiency and prevents adverse pregnancy outcome like preeclampsia, fetal growth restriction and gestational diabetes. Further, the object is to explore the placental effects of a high dose of vitamin D to improve our understanding of underlying risks and disease pathology.

Methods

GRAVITD is a double-blinded randomised trial. A total of 2000 pregnant women seeking prenatal care at Randers Regional Hospital will be included. Participants are randomised into two groups: 1) control (10 µg vitamin D), 2) intervention (90 µg vitamin D). Maternal blood samples and questionnaires describing life-style habits are collected upon enrolment. For half of the participants this is repeated in their 3rd trimester. Upon delivery placental tissue and umbilical cord blood are collected and information on maternal and fetal outcomes are extracted from medical records.

Results

The study is ongoing. Since June 2020, we have included 1679 women and collected 648
placentas.

Conclusion

We expect to provide new knowledge about vitamin D' effect on pregnancy- and perinatal health. We will provide scientific evidence which will help decision makers to make a new and more accurate recommendation concerning the ideal dose of vitamin D in pregnancy.

Keywords: Gynecology and obstetrics, Molecular metabolism and endocrinology, Laboratory science

Does revascularization therapies reduce the risk of post-stroke epilepsy?

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Purpose: Acute ischemic stroke is treated with revascularization therapies, thrombolysis and thrombectomi, which have improved survival and functional outcome after stroke. Stroke is the most important cause of epilepsy in the elderly; however, research on how revascularization therapies affect the risk of post-stroke epilepsy is sparse.

Methods: We all identified patients with a primary ischemic stroke in the Danish Stroke Registry between January 1 2011 and December 16 2018. The registry collect information on all acute strokes treated at Danish hospitals. We followed the patients until December 31 2018, first diagnosis of epilepsy, death, or emigration whether came first. Epilepsy was identified using the National Danish Patients Registry. The effect of revascularization therapy was estimated using Cox-regression models.

Results: We identified 54,430 patients epilepsy free persons who had a prior stroke, of these 7,250 were treated with thrombolysis, 640 with thrombectomi, and 1,130 with both thrombolysis and thrombectomi. Adjusted for stroke severity, sex, age, and cortical symptoms the risk of epilepsy were 29 % lower for patients treated with thorombectomi and thrombolysis (aHR: 0.71; 95% CI: 0.56-0.90), 26 % lower for patients treated with thrombolysis (aHR: 0.74; 95% CI: 0.64-0.85), and 11 % lower for patients treated with thrombectomi (aHR: 0.89; 95% CI: 0.65-1.23) compared to patients who had no revascularization therapy.

Conclusion: Revascularization therapies reduce the risk of epilepsy after stroke. We found no difference between thrombolysis and thrombectomi.

Keywords: Clinical neuroscience, Epidemiology and biostatistics, Basic neuroscience

Optical coherence tomography in coronary bifurcatons

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Background: Percutaneous coronary intervention (PCI) of bifurcation lesions is challenging with high risk of acute and long-term complications. Visual limitations of coronary angiography for stent implantation constitute important difficulties that increases risk of clinical complications. Optical coherence tomography (OCT) is a high definition, intravascular imaging modality that can guide physicians in optimizing treatment results and potentially improve clinical outcomes. We aim to compare the clinical outcome after OCT-guided vs. standard angiography-guided PCI of patients with coronary bifurcation stenosis.

Methods: The study is randomized, prospective, superiority trial randomizing 1200 patients with coronary bifurcation stenosis 1:1 to either standard angiography-guided PCI or OCT- guided PCI. Major inclusion criteria are; stable or unstable angina pectoris, clinically stable non-STEMI, main vessel reference diameter ≥2.75 mm and side branch reference diameter
≥2.5 mm. Major exclusion criteria are; STEMI within 72 hours, renal failure and severe tortuosity of involved vessels. The primary endpoint is two-year major adverse cardiovascular events, a composite of cardiac death, target lesion myocardial infarction and ischemic driven target lesion revascularization.

Results & conclusion: Inclusion of 1201 patients has completed in March 2022 at 37 sites around Europe. Patient follow-up and data analysis is currently ongoing and will conclude in early 2023.

Perspectives: Intravascular imaging modalities are used in selected, complex cases. This trial will illuminate if a routine use of OCT in patients with bifurcation stenosis could emerge as gold standard in complex PCI.

Keywords: Cardiovascular system, Medical technology and diagnostic techniques, Other

A repeated cohort study of root-filled teeth in two parallel Danish cohorts

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Aim: To compare the frequency of root-filled (RF) teeth and quality of root-fillings (RFs) in two parallel, Danish cohorts each examined over 10-years and to evaluate factors associated with apical periodontitis (AP) and extraction. Methodology: Two randomly selected cohorts (C1, C2) from Aarhus County (age: 20-64 years) were followed over 10- years, with a full-mouth radiographic survey at 5-year intervals (C1: 19988–2003–2008; C2: 2009–2014–2019). Frequency of RF teeth, quality of RFs and coronal restorations, AP and extraction were registered. Logistic regression analyses compared C1 with C2 and assessed parameters associated with AP and extraction at follow-up. Results: C1 had 330 and C2 had 170 individuals who attended all three examinations over 10-years. The relative frequency of RF teeth was significantly lower in C2 than C1 (C1: 4.7%, C2: 3.6%; $p<0.001$). The relative frequency of new RFs was significantly lower in C2 than in C1 ($p<0.02$). No significant difference between the cohorts was observed in the quality of new RFs, risk of extraction ($p=0.93$) and risk of AP ($p=0.37$) at 10-years follow-up. RF teeth with AP at baseline had increased risk of AP ($p<0.001$) and extraction ($p<0.001$) at follow-up. RF premolars ($p=0.01$) and molars ($p=0.01$) had higher risk of extraction; risk of AP was higher for RF molars ($p<0.001$). Inadequate quality of RFs and coronal restorations increased risk of AP ($p=0.02$, $p=0.04$) but did not affect extraction at follow-up. Conclusion: The frequency of RFs and new RFs decreased with no significant change in new RFs' quality, AP, or extraction over time (1997–2019). RF molars and AP at baseline had increased risk of AP and extraction.

Keywords: Dentistry, Epidemiology and biostatistics, Medical technology and diagnostic techniques

An update on type 2 diabetes in pregnancy

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Aim: This study aimed to provide an updated characterisation of pregnancies in women with type 2 diabetes (T2DM) from a national cohort in order to identify future challenges in the management of women with T2DM of reproductive age.

Material and methods: A retrospective national cohort study was conducted including all pregnancies in women with pregestational T2DM (P-T2DM) or manifest T2DM (M-T2DM) giving birth to a live infant after 24 weeks of gestation at a University Hospital in Denmark from 2004 until 2019. Variables on maternal characteristics and morbidity, treatment of diabetes and the glycaemic control during pregnancy and pregnancy outcomes were analysed between groups using univariate analyses.

Results: The final cohort consisted of 1207 pregnancies in women with P-T2DM and 90 pregnancies in women with M-T2DM. Preliminary results showed that the majority of women in both groups had a prepregnancy BMI ≥30.0 (P-T2DM 62.5% vs. M-T2DM 71.3%), but women with P-T2DM had a significantly higher weight gain during pregnancy (P-T2DM 12.1 [SD 7.3] vs. M-T2DM 8.3 [SD 7.5] kg at gestational age 36+0-42+6). Data from P-T2DM showed that all BMI groups exceeded the recommended weight gain during pregnancy. Pregestational HbA1c were <53 mmol/mol in 58.3% of women with P-T2DM, whereas the rest had a higher HbA1c resulting in an increased risk of fetal malformations.

Conclusion: In this large national cohort, preliminary results show that there are still target areas such as weight and glucose control that could be improved before and during pregnancy in women with T2DM. Specifically, optimizing the preconception care might help lower the risk of adverse pregnancy outcomes.

Keywords: Gynecology and obstetrics, Molecular metabolism and endocrinology, Epidemiology and biostatistics

Post-translational modifications derived from acetoacetyl-CoA

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Background:

Ketone bodies are mainly produced in the liver and used as an alternative energy source when glucose is limited in the body. In recent years, ketone bodies have shown a beneficial effect on aging. In monkeys with elevated levels of ketone bodies, the onset of age-related diseases is delayed and the overall longevity is prolonged. Acetoacetate, one of the ketone bodies, is metabolized to acetoacetyl-CoA (AcAcSCoA) that consists of a thioester, which chemically can undergo several types of reactions.

Aim:

The aim of this study is to elucidate the importance of AcAcSCoA in the biological system by identifying post-translational modifications (PTMs) derived from AcAcSCoA. Our hypothesis is that the thioester on AcAcSCoA is able to react with proteins.

Methods:

Proteins susceptible to react with AcAcSCoA are identified by applying proteomics. These studies are performed on liver tissue collected from control, fasted and ketogenic mice.
Furthermore, reactivity-based studies have been performed on model peptides to verify the modifications.

Results:

AcAcSCoA-derived modifications on proteins were detected and identified mainly on serine, cysteine, lysine and threonine residues. Data analysis is still on going. Furthermore, the modifications have also been verified on synthetized model peptides indicating that serine modification is driven by a cysteine residue close to the modification site.

Future perspective:

Based on the results obtained so far, we will do follow-up studies looking into how these identified modifications affect the function of a protein by performing functional studies. Furthermore, the modifications will be verified on model peptides.

Keywords: Molecular metabolism and endocrinology, Other, Other

Influence of second-generation oral contraceptive use on muscle recovery following repeated bouts of resistance exercise in trained women

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Background: Oral contraceptives (OCs) are the preferred type of contraception used by female athletes. How OCs influence skeletal muscle is still uncertain. In untrained women, the use of OCs is associated with delayed strength recovery after muscle-damaging exercise when compared to non-users of OCs in a few, but not all studies. Consequently, there is a need for a well-controlled study comparing muscle recovery in trained OC-users and non-users of OCs before any conclusions can be drawn. The aim of the present study was to investigate if OC use affects muscle recovery following repeated bouts of resistance exercise in trained women.

Methods: 20 trained OC-users and 20 non-users of OCs were recruited to perform three strenuous resistance exercise bouts within a 24-hour period. Before, and 3, 24, and 48 hours after the resistance exercise sessions, blood samples were collected and the participants completed measurements of maximal voluntary isometric (MVIC) and dynamic contraction (MVDC), vertical jump height, Wingate power performance, Leg press performance test, and the Yo-Yo intermittent recovery test. All participants were provided with an energy-macronutrient-balanced diet during the experimental period.

Results: MVIC, MVDC, jump height, and Wingate peak and average power were reduced,
and markers of muscle damage increased following resistance exercise ($p < 0.05$). However, in OC-users a significantly greater reduction in MVDC was observed 3, 24, and 48 hours after the last exercise session compared to non-users of OCs (interaction: $p < 0.05$). No other significant interactions were observed.

Conclusion: OC-users experienced a greater deterioration of maximal dynamic strength compared

Keywords: Public health, Other, Other

Prevalence of hepatitis C among Danish patients on oral substitution treatment: A cross-sectional study.

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BACKGROUND: People on oral substitution treatment (OST) are at high risk of infection with hepatitis C virus (HCV). However, the prevalence of both HCV antibodies (HCVab, exposure to infection) and HCV-RNA (chronic infection) vary considerably between studies. In recent years, encouraged by the advent of new, effective HCV treatment, WHO have set ambitious goals to eliminate HCV. Fundamental to achieving this, are studies on HCV prevalence, in order to monitor elimination progress, inform ressource allocation and identify gaps in the care of HCV among people on OST. Thus, the aim of this study is to estimate HCV prevalence and associated risk factors among patients attending OST.

METHODS: Cross-sectional study with consecutive enrolment from 2018-22 of adult patients receiving OST at drug treatment centers in Region Midtjylland (RM). We estimate prevalence of HCVab and HCV-RNA through universal testing and collect data on risk factors for HCV exposure through a standardized questionnaire and linkage to national registers.

RESULTS: Currently 329 patients have been included: females 29.2%, mean age 45.2 years
(SD 12.9), lifetime injection of drugs 49.8% (95% CI: 44.2; 55.4), lifetime sharing of needles
23.9% (19.1; 29.4). Overall, HCVab prevalence is 46.5% (41.0; 52.1) and HCV-RNA 12.2%
(8.8; 16.2). HCV-RNA prevalence among HCVab positive patients is 32.8% (24.6; 41.9).

CONCLUSION: The prevalence of HCVab among patients attending OST in RM, is comparable to similar populations studied in other Danish regions. However, the prevalence of HCV-RNA among HCVab positive patients is lower than in past studies, most likely reflecting increased cure rates from the new HCV treatment.

Keywords: Epidemiology and biostatistics, Infection, Public health

Longitudinal Serum Neurofilament Light Chain Levels in Diabetes and Diabetic Polyneuropathy

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Background and aims: Diabetic polyneuropathy (DPN) is one of the most common complications of diabetes, routinely diagnosed by means of clinical signs and symptoms indicative of neuropathy. As DPN often is diagnosed late, an objective tool facilitating early detection and follow-up is needed. We have shown that the axonal cytoskeletal protein neurofilament light chain (NfL) is a promising biomarker for DPN in type 2 diabetes as it is associated with both the presence and severity of DPN. Nevertheless, it appears that NfL probably is most suitable for individual follow-up over time instead of cross-sectional DPN diagnosis. Hence, we will study longitudinal NfL levels and their associations to DPN to further investigate the potential of NfL as a biomarker for DPN. Additionally, the relationship between changes in NfL levels and changes in risk factors for DPN will be studied.

Methods: We will perform a longitudinal analysis of data from the 5- and 10-year follow- ups of 200 participants of the ADDITION-Denmark cohort of people with screen-detected type 2 diabetes. Biobank serum samples from both time points are analysed for NfL using the Single molecule array platform. Clinically confirmed DPN at the 10-year follow-up is defined as presence of symptoms and/or signs of DPN together with abnormal nerve conduction studies. Diagnoses of confounding neurological disease are obtained from Danish national registers.

Results: No results yet.

Conclusion: With this study, we expect further clarification of the potential of NfL as a biomarker for DPN.

Keywords: Clinical neuroscience, Molecular metabolism and endocrinology, Other

An analysis of the associations between degrees of psychosocial stress and blood sugar (HbA1c) levels in a younger Danish population

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Background:

Psychological stress has been proposed in the etiology of type 2 diabetes (T2D), and how people respond to psychosocial stress depends, amongst others, on resilience. Early onset T2D (<45 years) is a more aggressive sort of T2D with poorer medication outcomes and severe complications. However, little is known about the association between stress and T2D for adults less than forty years old. The aim of this study is to explore the associations between degrees of psychosocial stress and blood sugar (HbA1c) levels, a marker of T2D risk if heightened, and if the association is mediated by personal resilience.

Methods:

In a subsample (n=365) from the Danish cohort VestLiv, a regional cohort following people born in 1983 and 1989, we obtained information about the participants T2D status in 2022 (age 32/38) via a blood sample measuring the HbA1c level. In 2021 they participated in a survey and reported perceived stress levels (PSS) and personal resilience. Data will be analyzed using multiple linear regressions with HbA1c as the dependent variable as a continuous variable and PSS categorized in low, moderate, and high stress, as the independent variable; and adjusted for relevant covariates. The mediating and moderating role of resilience on the associations will be examined by mediation analyses and stratification.

Findings:

Data analysis has not yet been completed. Results are expected to be available at the time of the presentation.

Perspectives:

The study may deepen the knowledge on associations between psychosocial stress, resilience, and elevated blood sugars in a young population where T2D is still rare however, the consequences for those with T2D are very severe.

Keywords: Public health, Psychiatry, psychology and mental health, Molecular metabolism and endocrinology

Optimizing Multi-Targeting Gene Therapy in Neovascular Age-Related Macular Degeneration

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Background

Patients with neovascular age-related macular degeneration (nAMD) receives repeated intravitreal injections with vascular endothelial growth factor (VEGF) inhibitors. A substantial fraction of these patients can be regarded partial or non-responders to current VEGF inhibitors. There is a need for new, sustainable treatment modalities with the potential to target multiple pathways. This can be obtained with gene therapy.

We designed multigenic vectors with intron-embedded double Dicer-independent short hairpin RNAs (agshRNAs) targeting VEGF with a downstream gene. However, analysis has revealed an interplay between splicing of the agshRNA unit/downstream protein expression and agshRNA efficacy. Accordingly, we aimed to determine the optimal balance between agshRNA-mediated VEGF knockdown and downstream protein expression.

Methods

Based on splice site prediction, we designed new agshRNA-constructs predicted to eliminate different combinations of problematic splice sites. For easy assessment of downstream protein expression, green fluorescent protein (GFP) was inserted downstream. Fluorescent microscopy and flow cytometry were used to investigate GFP expression.
Knockdown of VEGF was tested with a dual luciferase reporter

assay. Results

An optimal level of VEGF knockdown and downstream protein expression (GFP) was found among tested constructs.

Conclusion

We determined predicted problematic splice sites key to ensuring optimal splicing for high downstream protein expression while maintaining a potent level of VEGF knockdown. This has paved the way for a multigenic vector containing a VEGF-targeting agshRNA-casette combined with an antiangiogenic protein.

Keywords: Ophthalmology, Laboratory science, Animal models/disease models

PERFORMANCE OF A PHENOTYPIC AND TWO GENOTYPIC ALGORITMS FOR BNAB SENSITIVY PREDICTION

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The use of broadly neutralizing antibodies (bNAbs) in HIV-1 cure-related clinical trials has greatly increased in recent years. Even though bNAbs are broadly neutralizing, not all HIV- 1 variants are sensitive to a given bNAb due to tremendous viral diversity and development of escape mutations. Screening of participants for bNAb sensitivity before or after inclusion in a clinical trial is therefore crucial to obtain valid antibody efficacy data.
Different assays are currently being used to screen bNAb sensitivity. Here we compare one phenotypic ("PhenoSense") and two genotypic bNAb prediction methods ("HIV screening analysis" and "bNAb-ReP") for the two bNAbs: 10-1074 and 3BNC117. The PhenoSense assay is a pseudovirus neutralization assay and the prediction pipelines use HIV-1 envelope from single genome amplification. Fifty-nine clinical samples from ART-naïve participants in the eCLEAR trial (NCT03041012) were evaluated.

Concordant classification across all three methods were obtained for 85% and 56% of the participants for 10-1074 and 3BNC117, respectively. Longer time with HIV infection without treatment was not associated with a higher risk of harboring resistant virus, regardless of the method used. For 10-1074 we found that all participants with subtype CRF01 harbored resistant virus.

We observed good agreement in bNAb sensitivity prediction between the phenotypic assay and both genotypic prediction algorithms for the V3-loop binding bNAb 10-1074. The agreement between the methods was lower for the CD4-binding site bNAb 3BNC117, which may pose greater challenges when screening participants for clinical studies and comparing results across different trials.

Keywords: Infection, Other, Other

Sortilin in Excitatory and Inhibitory Neurons

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Memory formation can be encoded by changes in connectivity between neurons. These changes are generally described by activity-dependent synaptic plasticity and the concepts of long-term potentiation (LTP) and long-term depression (LTD). The receptor protein sortilin is highly expressed in neurons and is critical for neuronal viability and function. Sortilin is involved in several neuronal mechanisms including intracellular sorting, secretion and/or signaling of several ligands, which have been shown to be involved in neuronal plasticity, learning, and memory. Moreover, sortilin is implicated in several diseases characterized by memory impairment or distorted cognitive function, such as Alzheimer's disease, schizophrenia, and prion disease.

The aim of this study is to elucidate the implication of sortilin in memory formation in different neuronal populations. We hypothesize that sortilin contributes to the regulation of connectivity between neurons. When receptor function fails it will result in perturbed plasticity, memory impairment, and behavioral deficits. To investigate this, we have generated transgenic mice with conditional sortilin knockout in excitatory or inhibitory neurons, respectively. By performing behavioral tests, we observe altered learning in mice lacking sortilin in excitatory neurons and reduced contextual fear memory in mice lacking sortilin in inhibitory neurons. Our results suggest that sortilin has consequences in memory formation in different neuronal populations. Our next step is to elucidate the molecular mechanisms and analyze the neuronal circuit by electrophysiology and calcium imaging.

Keywords: Basic neuroscience, Cell biology, Animal models/disease models

High-resolution RNA isoform variation analysis by combining the advantages of single-cell RNA and nanopore sequencing

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Compared with the importance of pigs in the human disease model, xenotransplantation and agricultural science, pig transcriptome annotation is far from satisfaction. The overlap of annotated transcripts between the two widely used databases is only 8052. In the current study, we combined the advantages of single-cell mRNA barcoding with 10X Genomics technology with nanopore long reads sequence to identify the novel isoforms in pigs and then investigated the isoform usage preference in different cell types across different tissue types. Briefly, single cells were isolated from 9 porcine-wide type tissues (Spleen, Liver, Retina, PBMC, Lung, Brain, Visceral adipose, Subcutaneous adipose, and Intestine) and subjected to single-cell RNA library construction. Part of the amplified cDNA was converted to a nanopore library and sequenced at the full-length level. Firstly, after QC, we integrated long reads from all tissues into a whole one for novel isoform identification. Then the pseudo-bulk analysis on tissue and cell type levels is effective in high-accuracy cell barcode assignment. Data mining focus on different transcript usage (DTU) related to protein-coding genes detection and isoform-level clustering. For example, the MHC gene (SLA-3) isoform preferences of endothelial cells in the heterogeneity analysis. According to the isoform analysis on both tissue and cell type levels, we identified the novel isoforms which are dominant in specific groups. And pig retina has a significant DTU of the housekeeping gene ENSSSCG00000038062 compared to the other tissue. This study provided a valuable resource in the field of pig transcriptome.

Keywords: Qualitative research, Cell biology, Animal models/disease models

Novel enrichment strategy for the selection of CRISPR/Cas-mediated transgene integrations

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Site-specific integration of transgenes into the genome using CRISPR/Cas editing has a wide range of applications within gene- and cellular therapies. However, the primary cells required for these therapies often suffer from low gene editing efficiencies thereby impeding such therapies. As a solution, various strategies have been developed to enrich for cells with successful transgene integrations. The best strategies rely on inclusion of a surface reporter gene subsequently used for selection of gene edited cells. However, permanent expression of a reporter gene may perturb cell homeostasis and lead to unwanted effects. Instead, we develop a broadly applicable and versatile strategy for enriching cells carrying a transgene by harnessing the capability of CRISPR activation (CRISPRa) to transiently induce expression of a therapeutically relevant reporter gene that can be used for immunomagnetic enrichment and assessed by flow cytometry. We demonstrate that this strategy is readily adaptable to primary cells, including primary human T cells and CD34+ hematopoietic stem and progenitor cells (HSPCs). We achieve both stable transgene expression and inducible reporter expression, thereby achieving enrichment up to 3.7-fold and 4.2-fold in primary human T cells and CD34+ HSPCs, respectively. Furthermore, we demonstrate that T cells expressing a chimeric antigen receptor (CAR) can be enriched 2.5-fold to >80% CAR+ T cells, which consequently demonstrated improved killing of target cells. This novel enrichment strategy expands the possibility to enrich for transgene integrations in therapeutically relevant settings and may further improve gene- and cellular therapies.

Keywords: Genetic engineering, Oncology, Other

Genetic and structural insights into PTPRF guides psychiatric drug discovery

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Psychiatric drug discovery and development has been driven largely by serendipitous discoveries of molecules altering mood and/or diminishing psychotic symptoms but the lack of effective curative treatments attests to the need for novel intervention strategies.

The heritability of neuropsychiatric disorders is well established and recent genome sequencing techniques have revealed that the underlying genetic risk loci converge on the synapse as the key neuronal structure underlying neuropsychiatric pathobiology.

The PTPRF gene, encoding the presynaptic adhesion receptor LAR, is a top risk gene in ADHD and schizophrenia. To investigate potential disease-associated alterations in protein function, we used whole exome sequencing data from psychiatric patients and healthy controls to extract rare missense variants and map them onto the LAR protein crystal structure.

Domain-wise analysis of missense burden showed that disease-associated variants clustered on the FN1-2 domains of LAR, a region crucial for its interaction with the postsynaptic partner NGL-3 and thus their synaptogenic effects. Experimental evaluation of these variants revealed altered LAR stability and cellular processing, suggesting that disease associated variants are coupled to loss of protein function.

Combining these bioinformatic, structural and functional information from LAR missense variants has guided a virtual screening campaign to identify molecules that target and modulate LAR biology via its FN1-2 domain. Subsequent experimental optimization and refinement will elucidate the potential of such molecules to target synaptic homeostasis as a drug intervention in psychiatric disease.

Keywords: Cell biology, Psychiatry, psychology and mental health, Basic neuroscience

Testing implementation of a shared decision-making medication model in a social psychiatric residence institution. An acceptability study

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Background

Shared decision making (SDM) involving general practitioner (GP), psychiatrist, pharmacist and residents in social psychiatric residence institutions (SPRI) can reduce use of antipsychotics and thereby its side-effects (e.g. diabetes, hypertension) without affecting residents' quality of life (QoL) negatively. Although essential, SDM in SPRI is rare in Denmark. Participants' degree of acceptability of SDM affects implementation. The aim of this study was to assess acceptability of a new developed SDM model in a SPRI.

Methods

Guided by the MRC framework for complex interventions and using a co-production approach we first investigated barriers and facilitators of SDM in SPRI and second we used the results to develop a new SDM model. Finally, from June to September 2022, we feasibility tested the SDM model by performing ten SDM consultations in a Danish SPRI. Physically present were six residents, ten employees, two GP's, four psychiatrists and one pharmacist. A seven item questionnaire inspired by the Theoretical Framework of Acceptability was used to measure the acceptability before, under and after the implementation. Included were professionals' associated with the residents´ as well as all employees in the SPRI.

Results

A total of 53 completed the questionnaire before (March) and 49 under (June) the implementation of the new SDM model. Measurements is scheduled in November (after). Additional data collection and analysis is in progress.

Conclusion

The new SDM model and knowledge of acceptability can be a guide to implementation of SDM in medication treatment of residents in SPRI and potentially lead to reduction of antipsychotics without affecting QoL negatively.

Keywords: Qualitative research, Psychiatry, psychology and mental health, Public health

HIV-RESISTANT CAR T CELLS BY CRISPR/CAS-MEDIATED CAR INTEGRATION INTO THE CCR5 LOCUS

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HIV is a chronic infection that, despite effective antiretroviral therapy, cannot be cured due to latently infected cells. Current efforts to cure HIV has not yet led to profound reductions in the size of the viral reservoir. There is therefore an urgent need for novel approaches to eliminate latently infected cells. Chimeric Antigen Receptor (CAR) T cells have revolutionized treatment of hematological malignancies by enhancing the patient's own immune system to kill diseased cells. The CAR consists of an extracellular antigen-binding domain fused to intracellular signaling domains. This enables the CAR T cell to MHC-independently kill target cells. Because of the autologous origin, the T cells can engraft and persist in the patient lifelong. This project utilizes single-chain variable fragments from clinically potent broadly neutralizing antibodies against HIV envelope to effectively target the CAR T cells towards latently infected cells. Furthermore, we have used the CRISPR/Cas9 system to integrate the expression cassette into the CCR5 locus, a co- receptor necessary for viral entry into cells. This leads to concurrent knock-out of CCR5 making the engineered CAR T cells resistant to infection. The anti-HIV CAR T cells effectively kill HIV-infected primary human T cells ex vivo. Ultimately, the goal is to develop HIV-resistant anti-HIV CAR T cells that can effectively target HIV-infected cells and persist in patients lifelong. This will remove the need for antiretroviral therapy leading to a functional cure.

Keywords: Infection, Genetic engineering, Cell biology

Investigating the molecular genetic basis of hereditary spastic paraplegia due to a large chromosomal insertion in the SOX3 topologically associating domain

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Hereditary spastic paraplegias (HSP) are monogenic neuromuscular disorders that may be caused by pathogenic variants in many different genes. Massive parallel sequencing techniques to study genome architecture, such as high-throughput chromosomal conformation capture (Hi-C), have led to the discovery that Mendelian disorders are sometimes caused by disruption of topologically associating domains. We are investigating the molecular basis of a rare form of HSP linked to a 149 kilobase duplication from chromosome 4 inserted in a non-coding region of the X-chromosome. The insertion is located within a topological associating domain that includes the transcription factor gene SOX3 at a distance of 50 kilobases. We use induced pluripotent stem cells (iPSC) as disease models to investigate how the disease-causing insertion affects genome architecture and gene regulation. Using the CRISPR/Cas9 system, we have deleted the large insertion and use these corrected iPSCs as an isogenic control. RNA sequencing demonstrates that the insertion alters the regulation of SOX3, which is strongly downregulatated in patient iPSC compared to control iPSC. To elucidate the molecular mechanism behind the altered regulation and to investigate our hypothesis of a CTCF- mediated effect, we have performed Hi-C indicating reduced interactions between SOX3 and an upstream potential regulatory region on the X-chromosme in patient cells. To better understand the mechanism behind the alterations in genome architecture and SOX3 regulation, we are now generating additional CRISPR-edited iPSC with deletions of smaller parts of the insertion to identify the causative sequence elements.

Keywords: Genetic engineering, Cell biology, Basic neuroscience

Severe VZV CNS Infection – A Role for Autophagy?

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Invasion of the central nervous system (CNS) by the common pathogen Varicella Zoster Virus (VZV) is a rare, yet severe complication of infection. We hypothesize the susceptibility to viral CNS infections can, at least partly, be explained by host genetics.

Exome analysis of affected patients has revealed several possibly damaging gene variations in genes involved in autophagy. Autophagy is a highly conserved, cellular degradation pathway which has previously been described to play a role in viral infections, both in pro- and antiviral manner. Importantly, inhibition of autophagy has been suggested to be required for neurovirulence in the closely related Herpes Simplex Virus 1.

Earlier, our group was able to connect severe infection with both Herpes Simplex Virus 2 and poliovirus with a defect in autophagy. We hypothesize that autophagy plays an important role in the antiviral response to VZV infection as well, possibly particularly prominent in neuronal cells. We show that VZV infection does in fact lead to upregulated autophagy in-vitro. Now, we aim to elucidate whether autophagy in the context of VZV infection is rather pro- or antiviral. Therefore we want to confirm functional impairment of the identified gene variants and connect this to impaired ability to control VZV. Following, we aspire to uncover the specific interactions of VZV and autophagy in different, physiologically relevant cell types.

This project is part of our efforts to increase knowledge about the pathogenesis and complications of VZV infection, which will be valuable in the future development of improved patient diagnosis, prophylaxis, and treatment.

Keywords: Infection, Inflammation, Cell biology

Single nucleus and spatially resolved intra-tumor subtype heterogeneity in bladder cancer

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Transcriptomic subtyping of bladder cancer using bulk gene expression profiling has been in focus for two decades. However, current transcriptomic classification systems for bladder cancer do not consider the level of intra-tumor subtype heterogeneity.

Single cell technologies provide a new opportunity to study tumor ecosystems and tumor heterogeneity at single cell resolution. Here we present an investigation of the extent and possible clinical impact of intra-tumor heterogeneity across early and more advanced disease stages of bladder cancer. We performed single nucleus RNA-sequencing of 59,052 nuclei from 48 bladder tumors and four tumors were additionally analyzed using spatial transcriptomics. By analyzing frozen biobanked samples, we had detailed clinical follow-up of the patients and were able to compare our results to previously generated total RNA-sequencing (RNA-seq) and multiplex immunofluorescence staining for 44 and 13 of the tumors, respectively.

We demonstrated that tumors from both early and more advanced disease stages display large intra-tumor subtype heterogeneity and that the level of subtype heterogeneity could be estimated from both single nucleus and bulk RNA-seq data with a high concordance between the two. Notably, we show that a high class 2a weight estimated from bulk RNA- seq data is associated with worse outcome in patients with molecular high-risk class 2a tumors. Our results indicate that discrete subtype assignments from bulk RNA-seq data may lack biological granularity and continuous subtype scores may have the potential to further refine the biological characterization of tumors and clinical risk stratification of patients.

Keywords: Oncology, Urology, Cell biology

Intraoperative Methadone in Children Undergoing Surgery:

METACEBO - a single-center, investigator-initiated, double-blinded randomized placebo-controlled phase III trial.

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Treatment of postoperative pain is a challenge in younger children undergoing outpatient surgery. After discharge, it is up to the parents to assess the pain and to administer the analgesics as needed. Several studies have shown that parents find this difficult and often hesitate to administer analgesics. This results in unrelieved pain that negatively affects the family and the child's experience with healthcare.

In this respect, methadone is of great interest. Methadone is an opioid with a half-time of 19,2+/-13, hours. A single shot may provide stable analgesia throughout the early postoperative period, this has been suggested in adults. However, its use for postoperative pain in the youngest children undergoing surgery has not been investigated.

We decided to investigate whether children would benefit from receiving this long-acting analgesic and

aim to investigate whether a single dose of intravenous methadone improves postoperative pain in children undergoing minor open urological surgery.

Methods: Ninety-six children, 0-4 years of age, scheduled to undergo minor open urological surgery at Aarhus University Hospital, DK.

Patients are randomized to receive either methadone(0,1mg/kg) or placebo(saline) during anesthesia.

Outcomes include: Postoperative analgesic consumption and pain intensity, events in the PACU and quality of sleep the first night following surgery. Follow-up period is four days.

Conclusion: This will provide important information about the use of methadone in same- day urological operations on children.

Keywords: Other, Paediatrics, Urology

Visual Function following ultrathin Descemet's stripping automated endothelial keratoplasty (UT-DSAEK) and Descemet's membrane endothelial keratoplasty (DMEK): A randomized controlled trial.

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Introduction:

Corneal endothelial failure results in edematous corneas and hence reduced visual function as seen in Fuchs' endothelial dystrophy. Endothelial keratoplasty, where the diseased corneal endothelium of a patient is replaced by that of a donor, is the treatment of choice for such conditions. This restores the endothelial function and thereby corneal deturgescence and transparency. Endothelial keratoplasty can be performed as UT- DSAEK or DMEK. UT-DSAEK and DMEK grafts are characterized by a thickness of about 80 and 15 µm, respectively.

Purpose:

The aim of the study is to compare the visual function by means of visual acuity and contrast sensitivity following UT-DSAEK and DMEK combined with cataract surgery for the treatment of Fuchs' endothelial keratoplasty.

Methods:

The study uses a randomized, controlled design. Patients suffering from Fuchs' endothelial dystrophy and cataract are invited to participate. Included subjects are randomized (1:1) to either UT-DSAEK or DMEK. Evaluation of visual function is undertaken preoperatively and intermittently through the first 12 postoperative months.

Results:

The primary study outcome is visual acuity 12 months postoperatively. The follow-up of patients is still ongoing. On the PhD Day, study results on visual acuity and contrast sensitivity will be presented.

Discussion:

The study results will provide knowledge on visual function following UT-DSAEK and DMEK. However, in the overall evaluation of the techniques, future investigations on refractive outcomes and adverse events must be taken into consideration.

Keywords: Ophthalmology, Inflammation, Other

Intrinsic energy dependent response of scintillation detectors for low-energy dosimetry,

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Introduction: Small volume dosimetry in low-energy radiation is challenging due to large variation in dose-to-signal conversion efficiency for energies below 1 MeV in many common detectors. Some inorganic scintillation detectors have indicated resistance to this variation but have not been fully characterised.

Methods: 3 point-like detectors made from individual fibre-coupled cuboid scintillators (ZnSe:O ~1 mm3) were calibrated in terms of air-kerma free in air, in 13 x-ray beam qualities, (from 25 to 300 kVp) and in terms of dose-to-water in a Co60 beam at the National Metrology Laboratory in Sweden. For each quality, the photon spectrum was obtained with the SpekPy software and laboratory filtration data. The corresponding absorbed dose, D_det, relative to K_air, were obtained with the Monte Carlo (MC) code Topas (Geant4). The kerma- and dose-to-signal conversion was calculated and normalised to Co60.

Results: Above 30 keV effective energy, the detectors dose-to-signal conversion efficiency showed negligible variation (within 5%). Below 30 keV the detectors showed noticeable varying results, likely due to differences in detector material and geometry not captured by the simulations using nominal dimensions.

Conclusion: The detectors have shown promise for dosimetry applications in beam qualities where the photon spectrum contribution is small below 30 keV, above which the dose-to-signal conversion efficiency is nearly constant. The detectors could thus be calibrated in any quality from 30 keV and above, and transferred to another quality with energy dependent correction factors approximated purely by absorbed-dose energy dependence from MC.

Keywords: Oncology, Other, Other

A qualitative study exploring the patient perspective on web-based patient education in patients with rheumatoid arthritis.

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Introduction:

The effectiveness of web-based patient education (PE) in rheumatoid arthritis (RA) is currently tested in a randomized controlled trial, WebRA. However, the WebRA study does not provide in-depth insights into the patients' perspectives and likewise only a few studies have explored this area. Thus, the present study aims to explore patients' experiences of web-based PE, and whether this contributes to self-management of RA.

Methods:

We conducted 20 individual qualitative interviews based on the Interpretive Description methodology with patients from the WebRA study. Purposive sampling was used to achieve diversity and information power by inclusion of participants with different sex, age, and sociodemographic background. The analysis was inductive and revealed categories describing the experiences followed by interpretation and extraction of main messages.

Preliminary results:

Participants had positive experiences of the contents, presentation forms and usability, although minor technical difficulties were identified. Positive perceptions were driven by flexibility, the possibility for repetition and learning in familiar surroundings. Some emphasised that e-Learning should be combined with face-to-face (F2F) PE due to relational needs. The use of e-Learning is impelled by a need for clarity at time of diagnosis and less use seems to be associated with lower disease activity. The interaction between knowledge, disease experiences and a positive life approach creates synergy in self-management of RA.

Discussion:

These findings may prompt a discussion on combinations of web-based PE and F2F PE to accommodate both patients' informational needs and relational needs.

Keywords: Health education and simulation-based training, Rheumatology, Qualitative research

A handsewn pericardial valved pulmonary conduit: pulsatile flow loop in vitro and acute porcine in vivo evaluation

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Objective: Right ventricle to pulmonary artery anatomic discontinuity is common in complex congenital heart malformations. Handsewn conduits are a practiced method of repair. We performed pulmonary valve replacement with a handsewn pericardial valved pulmonary conduit in vitro and in vivo.

Methods: A pulsatile flow-loop model (in vitro) and an acute 60-kilogram porcine model (in vivo) were used. With echocardiography and invasive pressure measurements, baseline geometry and hydro-/hemodynamics were measured. The pulmonary valve was replaced with a handsewn glutaraldehyde treated pericardial valved pulmonary conduit corresponding to a 21-mm prosthetic valve. Geometry and hydro-/hemodynamics were then reassessed.

Results: In vitro, 15 trunks at 4 L/min and 13 trunks at 7 L/min, and, in vivo, 11 animals were investigated. The valved pulmonary conduit was easy to produce and to perform pulmonary valve replacement. Geometric orifice area in the conduit measured 2.9 cm2 (SD: 0.5) at 4 L/min and 2.9 cm2 (SD: 0.4) at 7 L/min. All valves were sufficient in vitro and in vivo. In vivo, conduit transvalvular pressure gradient was 6 mmHg (SD: 3). Diastolic pulmonary artery sinus circumference in vitro was 7.0 cm (SD: 0.5) and in vivo 7.2 cm (SD: 0.7).

Conclusions: Acute in vitro and in vivo investigations demonstrated an easy pericardial valved pulmonary conduit with no clinically significant regurgitation and stenosis. Further studies should be performed to evaluate the performance long-term.

Keywords: Cardiovascular system, Animal models/disease models, Paediatrics

PHD DAY HEALTH

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THE LAKESIDE LECTURE THEATRES