PHD DAY
HEALTH

PROGRAMME & ABSTRACTS
24 JANUARY 2020

AARHUS UNIVERSITY

INNOVATE AND INITIATE
– from academia to business

PHD DAY 2020 PROGRAMME

24 JANUARY 2020, THE PER KIRKEBY AUDITORIUM, THE LAKESIDE LECTURE THEATRES

8.15   **Welcome by the Head of the Graduate School**
Helene Nørrelund, Head of the Graduate School of Health, Aarhus University

8.25   **Welcome and presentation of the programme by the chair of the PhD Association**
Cecilie Siggaard Jørgensen, PhD student, Chair of the PhD Association at Health, Aarhus University

8.45   **"Innovate and Initiate – *from Academia to Business!*", keynote lecture**
Keynote speaker Paul J. Zak, PhD, scientist, entrepreneur and public speaker
Introduced by Michael Winterdahl, Associate professor, Dept. of Clinical Medicin, Aarhus University

9.45   **Presentation of the "innovation network-session"**
By Anette Poulsen Miltoft, Division Manager, AU Research Support and External Relations - Technology Transfer Office, Aarhus University

9.55   **Networking with coffee/tea and fruit**

10.15   **Poster and flash talk presentations**
Poster: *The Lakeside Lecture Theatres and the Bartholin Building (build. 1241)*
Flash talk: *The Lakeside Lecture Theatres, the Bartholin Building (build. 1241) and Samfundsmedicinsk Auditorium (build. 1262/101)*

11.45   **Networking with lunch and poster viewing**
The Lakeside Lecture Theatres and the Bartholin Building (build. 1241)

12.30   **Oral presentations and flash talk presentations**
Oral: *The Lakeside Lecture Theatres and the Bartholin Building (build. 1241)*
Flash talk: *The Bartholin Building (build. 1241)*

14.00   **Networking with coffee/tea and cake**

14.15   **"Innovate and Initiate – *from Academia to Business!*", keynote lecture**
Keynote speaker John Haurum, MD, PhD, board member and advisor
Introduced by Claus Olesen, Senior researcher, Dept. of Biomedicine, Aarhus University

15.15   **Networking**

15.30   **Fogh-Nielsen Competition**
Chaired by Søren K. Moestrup, Professor, Chairman of the Fogh-Nielsen board and Signe Mosegaard, PhD student, Dept. of Clinical Medicine, Aarhus University

16.15   **Awards: Poster-, oral- and flash talk presentations**
Professor Ebbe Bødtkjer and PhD student Jacob Thyrsted Jensen, Chair and Co-chair of the Organizing Committee, PhD Day 2020

16.25   **Closing remarks**
Helene Nørrelund, Head of the Graduate School of Health, Aarhus University

16.30   **The programme for the day ends**

18.30   **Dinner and award ceremonies**
Centralværkstedet, Aarhus C.
Festive speech: *Lars Østergaard, Professor and Consultant, Dept. of Clinical Medicine, Aarhus University*

AARHUS UNIVERSITY

Aarhus University
Graduate School of Health

PHD DAY
24 JANUARY 2020

Innovate and Initiate – from Academia to Business!

On behalf of the PhD Association, the Graduate School of Health, Aarhus University and this year's Organizing Committee, we welcome all students, faculty members and distinguished guests to the PhD Day 2020.

This year's theme will show you the way from academia to business by encouraging you to innovate your research project and ideas into a startup or business collaboration. To help us do this, we have invited two outstanding scientists and entrepreneurs, Paul Zak and John Haurum who will give inspiring keynotes lectures.

Paul J. Zak has degrees in mathematics and economics from San Diego State University, a PhD in economics from University of Pennsylvania, and post-doctoral training in neuroimaging from Harvard. He was one of the first scientists to integrate neuroscience and economics into neuroeconomics. Furthermore, his work has influenced our understanding of interpersonal trust, economic growth, oxytocin, empathy, and virtuous behaviors.
John Haurum has an MD from Aarhus University and a PhD from University of Oxford. He is an experienced biotech leader, with expertise in biological discovery, development, and manufacturing. He is the co-founder of Symphogen, former managing director of the British biotechnology company F-star as well as board member and advisor for biotech companies and investors.

During our networking sessions, you will get the chance to innovate your project, exchange ideas or develop a business idea with investors and company representatives from among others Novo Holdings and the Lundbeck Foundation.

In the sessions of oral-, poster- and flash talk presentations by your fellow students and the Fogh Nielsen competition, we encourage you to grasp the chance to think about how these projects can be innovated.

A warm thank you to everybody who has participated and helped create a highly scientific, inspiring and exciting programme for the PhD Day 2020.

Ebbe Bødtkjer, Professor
Chairman of the Organizing Committee
Health, Aarhus University

Helene Nørrelund
Head of Graduate School
Health, Aarhus University

Jacob Thyrsted Jensen, PhD student
Co-chairman of the Organizing Committee
Health, Aarhus University

Cecilie Siggaard Jørgensen, PhD student
Chairman of the PhD Association
Health, Aarhus University

Practical information

- Posters can be hung up between 16:30 and 19:00 on 23 January or between 7:30 and 8:00 on 24 January. Posters can be removed from 12:30 on 24 January 2019. Posters that have not been removed at 15:15 will be placed near the reception desk in the Lakeside Lecture Theatres and can be collected after the conclusion of the scientific programme of the PhD day

- Oral presenters for sessions O1-O5 must meet in the auditorium concerned between 7:30 and 8:00 on 24 January to save their presentations onto the auditorium hard disk

- Lunch is served at the Lakeside Lecture Theatres and at the poster viewing areas in the Bartholin building

- 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

Organizing committee PhD Day 2020

- *Ebbe Bødtkjer, Professor, Department of Biomedicine, Chair*
- *Jacob Thyrsted Jensen, PhD student, Department of Biomedicine, Co-chair*
- *Alice Knudsen, PhD student, Department of Biomedicine*
- *Angela Herengt, PhD student, Department of Biomedicine*
- *Bente Pedersen, PhD administrator, the Graduate School of Health*
- *Ellen Lund Schaldemose, PhD student, Department of Clinical Medicine*
- *Fabio Renato Manzolli Leite, Associate professor, Department of Dentistry and Oral Health*
- *Henning Grønbæk, Clinical professor, Department of Clinical Medicine*
- *Julia Blay Cadanet, PhD student, Department of Biomedicine*
- *Karin Lykke-Hartmann, Associate professor, Department of Biomedicine*
- *Laura Øllegaard Johnsen, PhD student, Department of Biomedicine*
- *Lene Krarup Monrad, PhD administrator, Graduate School of Health*
- *Malene Blond Ipsen, PhD student, Department of Clinical Medicine*
- *Maria Louise Gamborg, PhD student, Centre for Health Sciences Education*
- *Michael Winterdahl, Associate professor, Department of Clinical Medicine*
- *Pernille Louise Kjeldsen, PhD student, Department of Clinical Medicine*
- *Pernille Aaen Sloth, PhD student, Department of Biomedicine*
- *Rasmus Bysted Møller, Assistant professor, Department of Public Health*
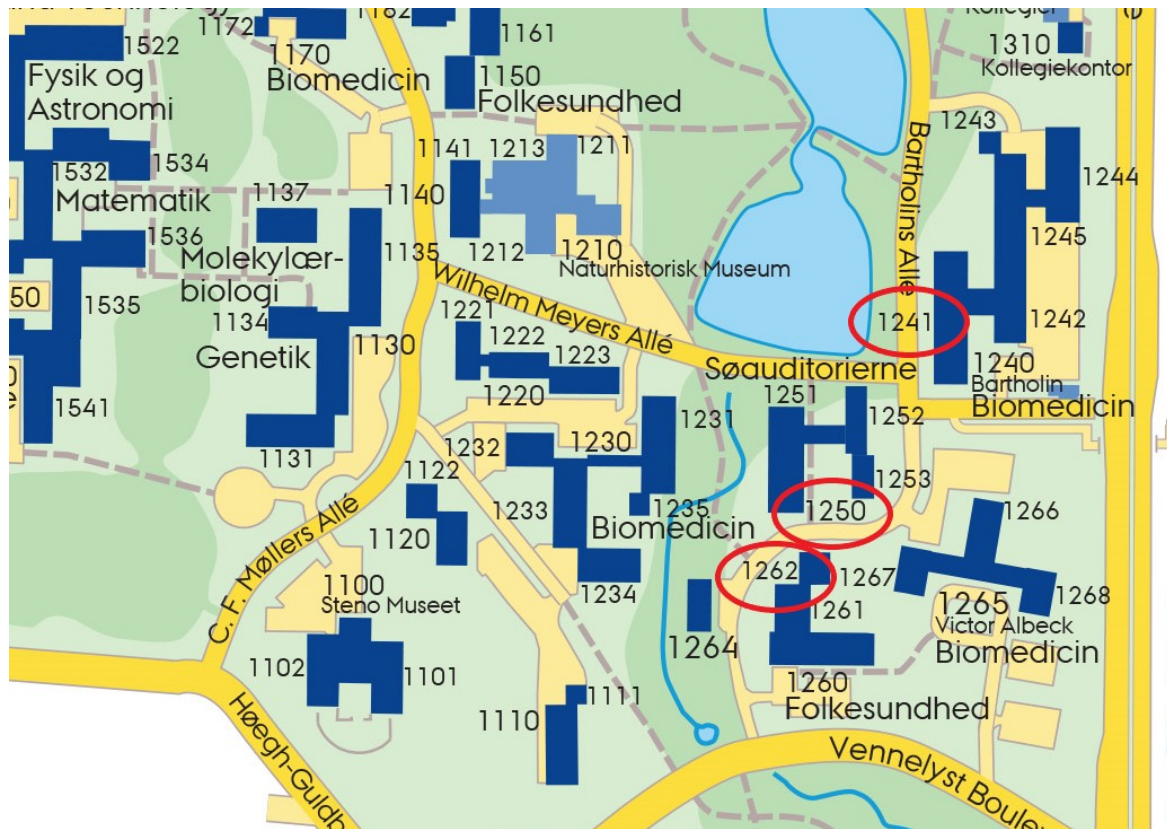- *Signe Mosegaard, PhD student, Department of Clinical Medicine*

Social Media: Facebook: PhD Association Health

Session overview

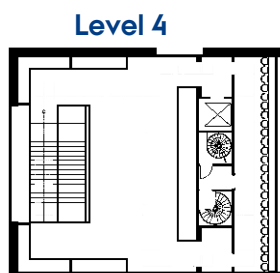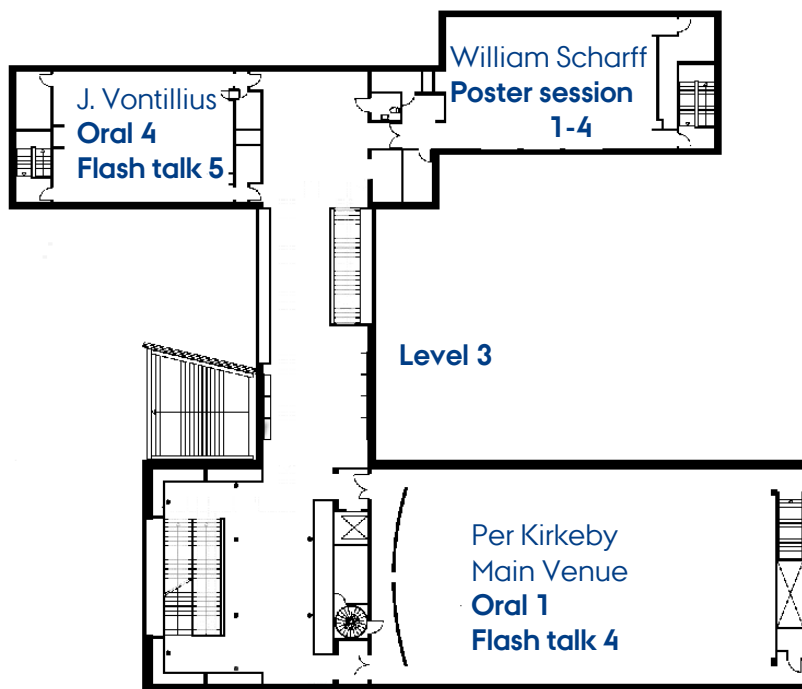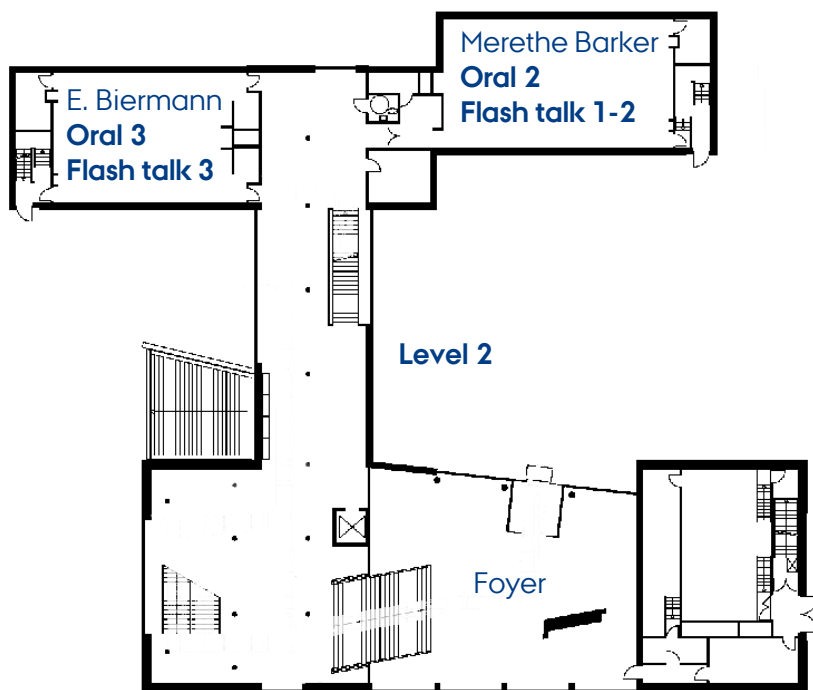|	
Oral session 1:	Lakeside Lecture Theatres, **Per Kirkeby Auditorium**
Oral session 2:	Lakeside Lecture Theatres, **Merete Barker Auditorium**
Oral session 3:	Lakeside Lecture Theatres, **Eduard Biermann Auditorium**
Oral session 4:	Lakeside Lecture Theatres, **Jeppe Vontilius Auditorium**
Oral session 5:	Bartholin building (1241/135), **Auditorium 1**
Poster session 1-4:	Lakeside Lecture Theatres, **William Scharff Auditorium**
Poster session 5-8:	Bartholin building (1241/211), **Studyroom,** (1st Floor)
Poster session 9:	Bartholin building (1241/231), **Gardenroom** (1st floor)
Poster session 10-12:	Bartholin building (1241/125+129), **Auditorium 2**
Flash talk session 1-2:	Lakeside Lecture Theatres, **Merete Barker Auditorium**
Flash talk session 3:	Lakeside Lecture Theatres, **Eduard Biermann Auditorium**
Flash talk session 4:	Lakeside Lecture Theatres, **Per Kirkeby Auditorium**
Flash talk session 5:	Lakeside Lecture Theatres, **Jeppe Vontilius Auditorium**
Flash talk session 6:	Bartholin building (1241/135), **Auditorium 1**
Flash talk session 7-8:	Building 1262/101, **Samfundsmedicinsk Auditorium**
Flash talk session 9-10:	Bartholin building (1241/119), **Auditorium 3**
Flash talk session 11-12:	Bartholin building (1241/114), **Auditorium 4**
Flash talk session 13-14:	Bartholin building (1241/119), **Auditorium 3**
Flash talk session 15-16:	Bartholin building (1241/114), **Auditorium 4**

Flash talk schedule

Sessions no.	Room	Time
1	Merete Barker Auditorium	10:15-10:55
2	Merete Barker Auditorium	11:00-11:40
3	Eduard Biermann Auditorium	10:15-11:00
4	Per Kirkeby Auditorium	10:15-11:00
5	Jeppe Vontilius Auditorium	10:15-11:00
6	Auditorium 1 (1241/135)	10:15-11:00
7	Samfundmedicinsk Auditorium (1262/101)	10:15-10:50
8	Samfundmedicinsk Auditorium (1262/101)	10:55-11:30
9	Auditorium 3 (1241/119)	10:15-10:50
10	Auditorium 3 (1241/119)	10:55-11:30
11	Auditorium 4 (1241/114)	10:15-10:55
12	Auditorium 4 (1241/114)	11:00-11:45
13	Auditorium 3 (1241/119)	12:30-13:10
14	Auditorium 3 (1241/119)	13:15-13:55
15	Auditorium 4 (1241/114)	12:30-13:05
16	Auditorium 4 (1241/114)	13:10-13:50

Lakeside Lecture Theatres

Merethe Barker
Oral 2
Flash talk 1-2

E. Biermann
Oral 3
Flash talk 3

Level 2

Foyer

William Scharff
Poster session 1-4

J. Vontillius
Oral 4
Flash talk 5

Level 3

Per Kirkeby
Main Venue
Oral 1
Flash talk 4

Level 4

Bartholin Building (building: 1240/1241)
- Oral session no. 5
- Poster session 5-12
- Flash talk 6 and 9-16

Samfundsmedicinsk Auditorium (1262/101)
- Flash talk 7-8

PhD Day 2020

Innovate and Initiate – from Academia to Business!

Your research and research ideas could provide new solutions for major societal health challenges. We invite you to participate and share your research at the PhD Day 2020 to recognize and develop your innovative potential!

The PhD Day is an annual event organised by the PhD Association Health in collaboration with the Graduate School of Health, Aarhus University. The theme of the PhD Day 2020 is "Innovate and Initiate – *from Academia to Business*!"

In a fast-paced globalized society, innovation drives development of new health solutions. Funding and investments from private sources increase steadily; and to be competitive, it is important to identify and advance novel and innovative aspects of your research. Innovative academic research that addresses current or imminent health challenges can initiate business development and collaboration with industry partners.

We have invited experts in innovation and entrepreneurship from major Danish investment funds and legal representatives from the Technology Transfer Office (TTO) at Aarhus University. During the networking sessions, we urge you to discuss possible commercialization strategies for your projects with the invited experts.

The PhD Day 2020 focuses on high-quality research and how to integrate innovation and drive development of new health solutions. Keynote speakers skilled in innovation and entrepreneurship will share their experiences from diverse medical ventures. The programme also provides PhD students, Research Year students and Research honours programme students the opportunity to present their own research in flash talks, oral or poster presentations, or act as co-chairs at scientific sessions.

We look forward to welcoming you at the PhD Day 2020!

The Organizing Committee 2020
Graduate School of Health, Aarhus University

Keynote speaker

Paul J. Zak, PhD, scientist, entrepreneur and public speaker
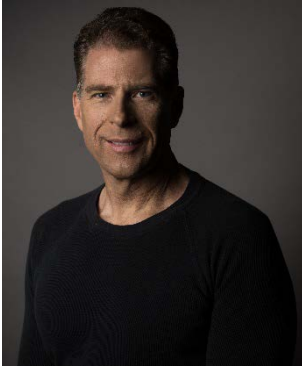
Paul J. Zak's two decades of research have taken him from the Pentagon to Fortune 50 boardrooms and to the rain forest of Papua New Guinea. His ideas have been used by the World Bank to stimulate prosperity in developing countries and by businesses to enhance economic performance.
Paul J. Zak delivered a TED Talk titled "Trust, Morality—and Oxytocin?" in 2011 that has been viewed more than 1.4 million times.

Paul J. Zak discovered the neurologic mechanisms that enable cooperation and trust and was one of the first scientists to integrate neuroscience and economics into a new discipline: neuroeconomics. His research has identified the brain processes that support such virtuous behaviors as trustworthiness, generosity, and sacrifice, as well as those whose absence leads to evil, immorality, and conflict.

He is the founding Director of the Center for Neuroeconomics Studies and Professor of Economics, Psychology and Management at Claremont Graduate University, Claremont, USA. He has degrees in mathematics and economics from San Diego State University, a PhD in economics from University of Pennsylvania, and post-doctoral training in neuroimaging from Harvard.

He also serves as a senior advisor to Finsbury, a global leader in strategic communications, that advises many of the world's most successful companies.

Paul J. Zak's work has made substantial impact on our understanding of interpersonal trust, economic growth, oxytocin, empathy, and virtuous behaviors. His works have been cited over 14,000 times.

Keynote speaker

John Haurum, MD, PhD, board member and advisor

John Haurum is one of the most successful Danish biotech leaders with rich experience from leading international companies particularly within immuno-oncology. He is currently Executive Chairman of the Board at Synklino, Chairman of the Board of Agomab, and on the Board of Directors at NeoPhore, Synact Pharma ApS, and STORM Therapeutics.

John Haurum has an MD from Aarhus University and a PhD in immunology from University of Oxford. He has expertise in biological discovery, development, and manufacturing as well as innovative R&D leadership.

John Haurum was previously Chief Executive Officer of F-star, a clinical-stage biopharmaceutical company pioneering the development of novel bispecific antibodies that target the immune system to fight cancer. Under his leadership, F-star successfully expanded and raised €200 million in equity and non-dilutive funding.

Prior to that, John Haurum was Vice President of Research at ImClone Systems and co-founder and Chief Scientific Officer at Symphogen.

Hey, you!

Do <u>you</u> want to help improve the PhD education at AU Health?

Then join the PhD Association!

Come and hang out with us after work at Studenterhus Aarhus, Aarhus University on February 6th, 2020 at 4 pM –we will make sure that there is cake and beer!

All are welcome!

See more and follow us at 'PhD Association Health' on facebook
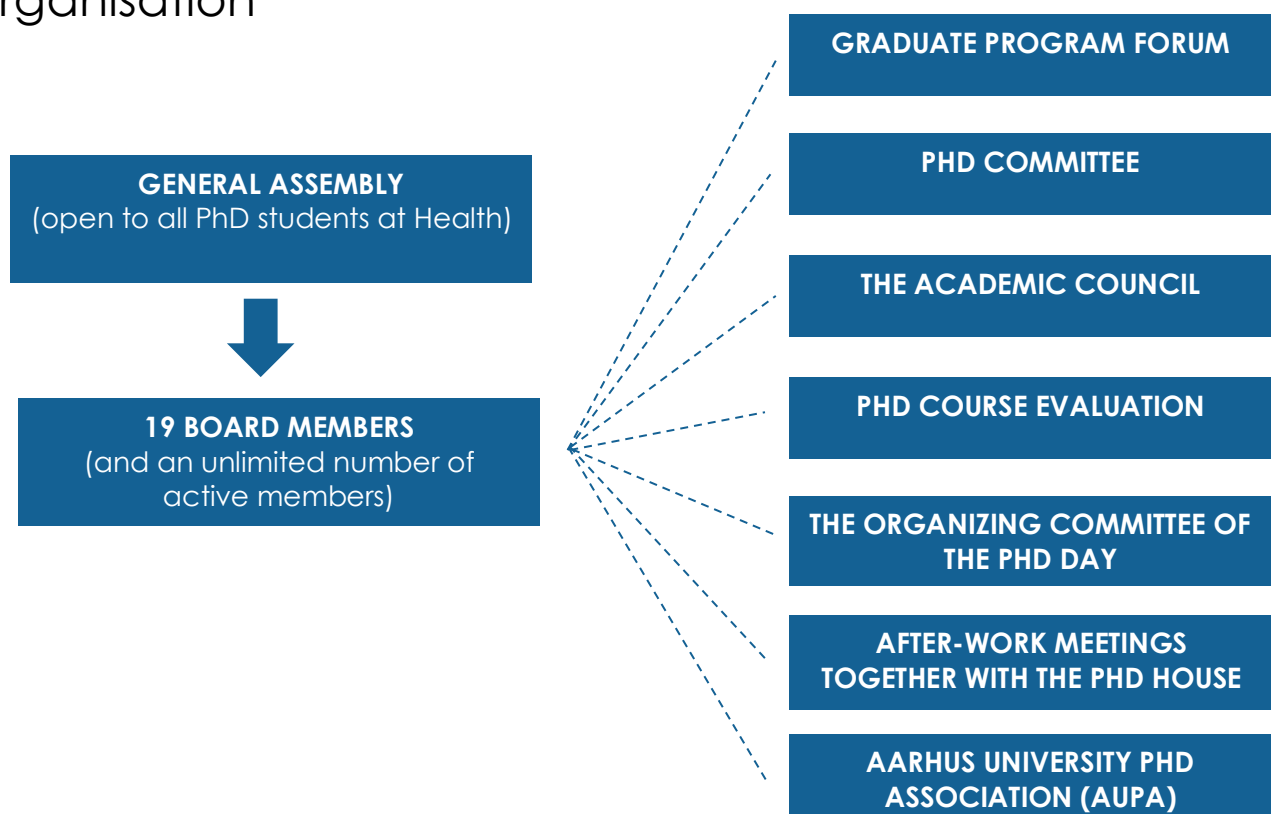
PhD Association
Health, Aarhus University

- 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!

Technology Transfer Office

Aarhus University Technology Transfer Office (TTO) is the department at AU helping you with commercialisation of inventions.

Aarhus University, has experience with over 1000 inventions filed by employees. We cover technologies within a variety of fields, such as biotech and healthcare, food and agriculture, ICT and software, physics and engineering.

Aarhus University TTO offers a designated commercial contact person for your inventions. The commercial contact person manages the commercialisation process from initial meetings with industry contacts through to potential final contract negotiations

If you have any questions concerning commercialisation activities, please contact one of our TTO business development managers. We are ready to help and support further dialogue.

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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
- PURE, BFI, Journal Impact Factor, ORCID, and H-index
- 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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BIBLIOTEK
Royal Danish Library

Danish Diabetes Academy: Education, networking and recruitment - Want to join?

Danish Diabetes Academy (DDA) is a national platform for diabetes researchers. Our mission is to train and educate the next generation of researchers in the field of diabetes.

Thus, we are constantly working on enhancing the opportunities for PhD students and postdocs to carry out research on diabetes in collaboration with academia, hospitals and the life science industry.

Some of the activities in 2020 in the Danish Diabetes Academy are:

PhD & Postdoc Course in R Programming – beginner and advanced level
PhD & Postdoc Course on Brain, Gut, Stem Cells & Exercise
PhD & Postdoc Course on Big Data & Artificial Intelligence
PhD & Postdoc Course on Presenting Powerfully

PhD Couse: DDA Summer School on Diabetes & Metabolism
PhD Course on Basal Metabolism & Molecular Mechanisms in Diabetes
PhD Course on Meeting the reproducibility challenges in research - Importance of quality assessment in the laboratory

Postdoc Course on Project Management in Research
Postdoc Course: Winter School in Malaga

Workshop on Psychosocial Support Needs & Appropriate Support Initiatives in People Diagnosed with Type 1 Diabetes in Adulthood
Workshop on How to Improve Assessment of Nerve Fibre Damage in Diabetes

Grants for PhD scholarships, deadline 6 February 2020 and 20 August 2020
Grants for Postdoc Fellowships deadline 6 February 2020 and 20 August 2020
Grants for Visiting Professorships deadline 6 February 2020 and 20 August 2020

The DDA is always pleased to invite new members into our community. At our website, https://www.danishdiabetesacademy.dk/, you can join the DDA, sign up for the activities, submit your application for grants or just browse around.
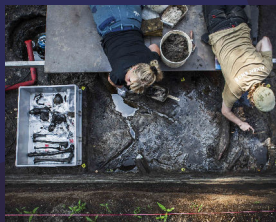
You can also follow us on Twitter, Facebook, LinkedIn and Instagram, where you can stay up-to-date with all the latest news and get to know us better.

Hope to see you around in 2020.

Kind regards,
Tore Christiansen
Managing Director
Danish Diabetes Academy

AU Career PhD & JR

Career services for PhDs and junior researchers

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

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

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

Are you aware of your many opportunities?

Our services

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

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

Jane Midtgaard Madsen
Ph.D. Career Consultant
Phone: +45 5122 6880
Email: jamm@au.dk

www talent.au.dk/career

f /AUCareerPhDandJR

AU **CAREER** PHD & JR

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

INTERNATIONAL **ACADEMIC STAFF SERVICES** (IAS)

DO YOU NEED HELP FOR YOUR RESEARCH STAY ABROAD?

We provide advice and information about the practicalities of a research stay abroad:

- Country specific guides
- Checklists for remembering all the small details
- Advice and information about visas, insurances and much more

Read more at www.ias.au.dk/goingabroad
Read more about IAS services at www.ias.au.dk

PHD & POSTDOC **ACTIVITY GROUP**

ARE YOU LOOKING FOR A VIBRANT COMMUNITY OF INTERNATIONAL PEERS?

PhD & Postdoc Activity Group offers junior researchers:
- A relaxed and fun setting
- A place to unwind from long working days
- An informal setting to meet your peers from across academic disciplines and cultural backgrounds

Keep updated about current activities at www.facebook.com/phdpostdocactivityau

OFFICE OF INTERNATIONAL RELATIONS

From going abroad to international recruitment, the Office of International Relations at Health assists and advise on the many available international opportunities.

The core activities of the Office of International Relations include:

- Establishing and maintaining partner agreements with universities abroad
- Travel grants, scholarships and international stipend programs
- Advising of students and faculty about exchange opportunities
- International Semester for medical students
- Summer University
- Mentor programs
- PhD degree collaborations
- International recruitment
- Guest PhD students and visiting researchers
- Delegations from partner universities abroad

In addition, the Office of International Relations performs tasks within:

- Support to management in international affairs
- Development and project tasks in internationalization
- International partnerships
- Internationalization strategy

All students, staff and faculty members are welcome to contact us for information and assistance.

Rikke Korgaard Præstegaard
International Coordinator
HE Studies
Phone: +4593508396
E-mail: rkp@au.dk

Tanja Hansen
International Advisor
Dean's Office
Phone: +4593508108
E-mail: tanja.hansen@au.dk

INNO X
HEALTHCARE

" The PhD course has had immense impact on my way of approaching research activities. It has helped me create the greatest value and impact with my work, to a better success rate with funding applications and furthermore improved my presentation skills.

Anders Rosendal Korshøj, Ph.D. MD.

Improve your research project

- with entrepreneurial methods

Ph.D. course offered by Graduate School of Health, Aarhus University

Whether your future holds research or innovative projects you will need the skills to achieve funding, attract collaborators, and carry out projects in a successful manner to solve the needs of healthcare and adjoining sectors.

The rationale for this course is that researchers need to be better at identifying the value and applicability of their research, both basic research and applied science. In the course we use methodologies inspired from the start-up environment as a way to leverage results and increase value for patients, peers and society in general.

This course will help you:

- Leverage your oral communication skills and prepare you for your PhD defence
- Build a stronger researchdesign - from start or by involving relevant partners continuously
- Prepare for large grand applications through a better communication of your project
- Use business model components to strenghten the scope of your study design
- Identify and validate the applicable value of your project
- Reach out to other proficiencies and build an interdisciplinary network
- Master combining a quantiative approach with interview techniques and qualitative research
- Gain knowledge about why entrepreneurship and innovation is in demand and usefull in your future work

This course is usefull both when you are designing a future research as well as during ongoing research.

ECTS: 5,5
Course dates: 27.2, 13.3, 3.4 and 30.4 2019 (Application deadline: January 30. 2019)
Head of course: Anne-Mette Sonne Andersen & Martin Vesterby, INNO X Healthcare, HEALTH, AU

If you have questions please contact us at info@innox.au.dk

Application via: http://phd.health.au.dk/doingaphd/phdcourses/

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If help is needed

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.

For details consult the homepage:

http://phd.health.au.dk/aboutus/phdstudentcounselling

All discussions are confidential, and you are guaranteed anonymity.

How innovative are you?

Find out at Medical Innovation Day 2020

8 October 2020, Aarhus University.
Pre-event for the Challenge Track on 7 October 2020.

———

Here's your chance to make a great career-move while testing your skills in innovative thinking. Medical Innovation Day brings together students, researchers and business representatives to exchange ideas and think up solutions for the health challenges of the future.

Two tracks

The event offers two tracks: the **Challenge Track** (7 and 8 Oct.) and the **Innovative Ideas Track** (8 Oct.). The Challenge Track lets you take on a case assignment from an established company in the health care sector, while the Innovative ideas Track gives you the opportunity to pitch your ideas or results to potential investors or future collaborators who can help you move forward.

What's in it for you?

Participation is completely free and includes full board for the entire day. PhD students are even eligible for ECTS points for participating.

More info

Registration opens in spring 2020.
Keep yourself updated at http://phd.health.au.dk/aboutus/mid/

MEDICAL
INNOVATION DAY

AARHUS
UNIVERSITY
HEALTH

HELP US REACH YOU!

Do not miss important information regarding **your PhD programme**.

Sign up for our monthly letter to get it directly in **your inbox**!

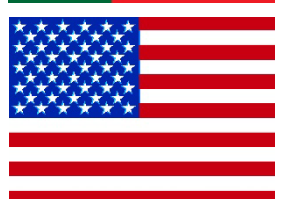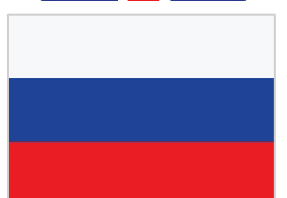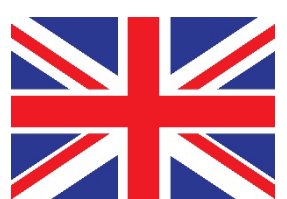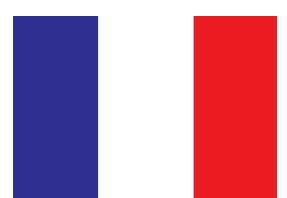GRADUATE SCHOOL
OF HEALTH

AARHUS
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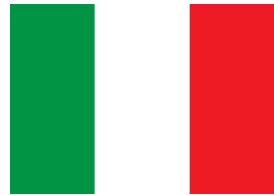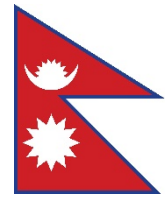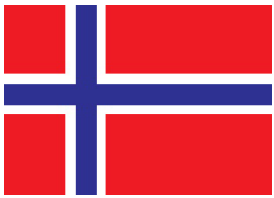http://phd.health.au.dk/aboutus/monthlyletter/

NorDoc

is going to launch its

4th Nordic Summit for Doctoral Students

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PhD Day 2020

PHD DAY 2020

Abstracts and sessions overview

Session chairs

Fogh-Nielsen Competition	Søren Kragh Moestrup (Chair) and Signe Mosegaard (PhD student)
O1	Ulf Simonsen, Vladimir Matchkov and Gro Grunnet Pløen (PhD student)
O2	Thea Lillethorup, Michael R. Horsman and Kia Busch (PhD student)
O3	Alisa D. Kjærgaard, Jens Leipziger and Millicent Addai Boateng (PhD student)
O4	Hans Jürgen Hoffmann, Gregers Wegener and Rune Nguyen Rasmussen (PhD student)
O5	Bent Deleuran, Mette Nørgaard and Francesco Maria Iena (PhD student)
P1	Arne Møller, Qichao Zhang (PhD student) and Maimaitili Muyesier (PhD student)
P2	Nelson Ferreira, Ole Søndergaard Schwartz (PhD student) and Tingting Gu (PhD student)
P3	Jakob Christensen, Janne Tidselbak Larsen (PhD student) and Nanja Holland Hansen (PhD student)
P4	Else Marie Damsgaard, Sif Sund Blandfort (PhD student) and Mette Bisgaard Andersen (PhD student)
P5	Johan Palmfeldt and Kata Wolff Pedersen (PhD student)
P6	Stinne Ravn Greisen, Nick Yin Larsen (PhD student) and Xiaowen Niu (PhD student)
P7	Niels Uldbjerg, Maria Keilow (PhD student) and Cathrine Hjorth Hansen (PhD student)
P8	Rikke Damkjær Maimburg, Sidsel Boie (PhD student) and Bodil Karen Bæksted Jørgensen (PhD student)
P9	Erling Bjerregaard Pedersen and Haiyun Qi (PhD student)
P10	Simon Eskildsen, Karen Baden Alstrup (PhD student) and Mads Valdemar Anderson (PhD student)
P11	Mette Madsen, Lene Wulff Krogsgaard (PhD student) and Liv Marie Duus (PhD student)
P12	Therese Juul, Mette Eline Brunbjerg (PhD student) and Maja Bendtsen Sharma (PhD student)
F1	Tina Birgitte Wisbech Carstensen, Julie Jacoby Petersen (PhD student) and Helle Elisabeth Andersen (PhD student)
F2	Tue Kragstrup, Morten Aagaard Nielsen (PhD student) and Cecilie Blenstrup Patsche (PhD student)

F3	Morten Nielsen, Sara Raquel Almeida Ferreira (PhD student) and Martin Kinnerup (PhD student)
F4	Samia Joca, Rasmus H. Olesen (PhD student) and Pauline Cantou (PhD student)
F5	Ellen M. Mikkelsen, Simon Bang Kristensen (PhD student) and Mette Jørgine Kirkeby (PhD student)
F6	Annette Haagerup, Louise Lindholdt (PhD student) and Martin Rune Hassan Hansen (PhD student)
F7	Rune Dall Jensen, Lotte Levison (PhD student) and Andreas Halgreen Eiset (PhD student)
F8	Agnete Larsen and Mette Kaasgaard (PhD student)
F9	Michael Mulvany, Birgit Refsgaard Iversen (PhD student) and Jakob Hansen (PhD student)
F10	Simon Tilma Vistisen and Morten Riemenschneider (PhD student)
F11	Esben Søndergaard, Ana C. G. Ebsen (PhD student) and Eva Forsom (PhD student)
F12	Peter Jepsen and Stine Karlsen (PhD student)
F13	Jesper Grau Eriksen, Helle Kristensen (PhD student) and Anders Schwartz Vittrup (PhD student)
F14	Brita Singers Sørensen, Thomas Buus (PhD student) and Marianne Ørum (PhD student)
F15	Kristian Stødkilde, Samuel Joseph Windross (PhD student) and Anne Mette Fløe Hvass (PhD student)
F16	Konstantinos Kamperis, Berit Bargum Booth (PhD student) and Marlene Louise Nielsen (PhD student)

Session overview

Fogh-Nielsen Competition

Chairs: Søren Kragh Moestrup and Signe Mosegaard (PhD student)

Pankaj Taneja. MULTISENSORY INTEGRATION OF OROFACIAL STIMULI WITH POSSIBLE IMPLICATIONS IN OROFACIAL PAIN

Sidsel Støy. LOW INTERLEUKIN-22 BINDING PROTEIN IS ASSOCIATED WITH HIGH MORTALITY IN ALCOHOLIC HEPATITIS

Julie Jacobsen. PATIENT-REPORTED OUTCOME AND MUSCLE-TENDON PAIN AFTER PERIACETABULAR OSTEOTOMY ARE RELATED: 1-YEAR FOLLOW-UP IN 82 PATIENTS WITH HIP DYSPLASIA

Oral session 1

Chairs: Ulf Simonsen, Vladimir Matchkov and Gro Grunnet Pløen (PhD student)

O01.01   Martin Mæng Bjørklund. SMOOTH MUSCLE CELL SPECIFIC DELETION OF SOX9 INCREASES NECROTIC CORE FORMATION IN ATHEROSCLEROSIS

O01.02   Johanne Hovgaard Egedal. HYALURONIC ACID IS A NEGATIVE REGULATOR OF FIBROBLAST-MEDIATED ENHANCEMENT OF HIV INFECTION

O01.03   Estefano Pinilla. MODULATION OF TRANSGLUTAMINASE 2 CONFORMATION TO COUNTERACT VASCULAR DYSFUNCTION IN DIABETES AND AGING

O01.04   Khoa Manh Dinh. THE ASSOCIATION BETWEEN STAPHYLOCOCCUS AUREUS NASAL CARRIAGE, CCR5 Δ32 DELETION AND THE RISK OF INFECTIONS IN HEALTHY INDIVIDUALS: RESULTS FROM THE DANISH BLOOD DONOR STUDY

O01.05   Marie Vognstoft Hjortbak. INTERACTIONS BETWEEN INHERENT AEROBIC CAPACITY, MYOCARDIAL ISCHEMIA REPERFUSION AND CARDIOPROTECTION

O01.06   Mads Dam Lyhne. COMBINATION OF RIGHT VENTRICULAR FUNCTION AND PULMONARY PRESSURE IMPROVES PREDICTION OF ADVERSE OUTCOME IN ACUTE PULMONARY EMBOLISM

Oral session 2

Chairs: Thea Lillethorup, Michael R. Horsman and Kia Busch (PhD student)

O02.01   Line Stensig Lynggaard. ASPARAGINASE ENCAPSULATED IN ERYTHROCYTES - A PROMISING ALTERNATIVE TO PEG-ASPARAGINASE IN CASE OF HYPERSENSITIVITY IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA.

O02.02   Sofia Spampinato. RISK FACTORS FOR URINARY INCONTINENCE AFTER RADIOTHERAPY IN LOCALLY ADVANCED CERVIX CANCER: AN EMBRACE ANALYSIS

O02.03   Mads Ryø Jochumsen. CAN TUMOR BLOOD FLOW ESTIMATE PROSTATE CANCER AGGRESSIVENESS?

O02.04   Michael Brun Andersen. IMPACT OF SPECTRAL IMAGING IN PATIENTS SUSPECTED FOR OCCULT CANCER: A STUDY OF 93 PATIENTS

O02.05   Jakob Haldrup Jensen. FRMD6 IS A NOVEL TUMOR SUPPRESSOR GENE IN PROSTATE CANCER

Oral session 3

Chairs: Alisa D. Kjærgaard, Jens Leipziger and Millicent Addai Boateng (PhD student)

O03.01   Benedicte Marie Winther Johannsen. SOMATIC MORBIDITY AND MORTALITY IN WOMEN WITH POSTPARTUM PSYCHIATRIC DISORDERS

O03.02   Sara Koed Badre-Esfahani. NEARLY ONE THIRD OF WOMAN WITH NON-NATIVE BACKGROUND, NEITHER ATTEND HPV-VACCINATION NOR CERVICAL CANCER SCREENING - A NATIONWIDE DANISH REGISTER-BASED COHORT STUDY

O03.03   Maria Daniella Bergholt. DO PATIENTS RECEIVE MORE APPROPRIATE HEALTHCARE IN ACCREDITED HOSPITALS?

O03.04   Malene Thygesen. THE ASSOCIATION BETWEEN RESIDENTIAL GREEN SPACE IN CHILDHOOD AND DEVELOPMENT OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A POPULATION-BASED COHORT STUDY

O03.05   Signe Hjuler Boudigaard. OCCUPATIONAL EXPOSURE TO RESPIRABLE QUARTZ AND RISK OF SYSTEMIC SCLEROSIS: A COHORT STUDY OF THE DANISH WORKING POPULATION 1977-2015

O03.06   Daniel Borch Ibsen. REPLACING RED MEAT WITH ALTERNATIVE FOOD SOURCES OF PROTEIN ON THE RISK OF DEVELOPING TYPE 2 DIABETES - MODELLING DIETARY CHANGES IN A CAUSAL FRAMEWORK

Oral session 4

Chairs: Hans Jürgen Hoffmann, Gregers Wegener and Rune Nguyen Rasmussen (PhD student)

O04.01   Jose Manuel Cerdan de Las Heras. TELE-REHABILITATION PROGRAM IN IDIOPATHIC PULMONARY FIBROSIS

O04.02   Søren Helbo Skaarup. INTRA LYMPHATIC ALLERGEN IMMUNE THERAPY.

O04.03   Gabriela Silote. CANNABIDIOL AND S-KETAMINE ANTIDEPRESSANT EFFECTS ARE ASSOCIATED WITH GENE EXPRESSION CHANGES IN THE BRAIN OF THE FLINDERS SENSITIVE LINE RAT

O04.04   Emil Gregersen. PRION-LIKE SPREADING OF PARKINSON'S DISEASE - THE ROLE OF USP19 IN EXCRETION AND CYTOTOXICITY OF ALPHA-SYNUCLEIN

O04.05   Asbjørn Petersen. KNOCKOUT AND PHARMACOLOGICAL INHIBITION OF KCA3.1 CHANNELS COUNTERACT HYPOXAEMIA IN A VENTILATOR-INDUCED LUNG INJURY MODEL

O04.06   Agnes Hauschultz Witt. A NOVEL NEUROPHYSIOLOGICAL METHOD MSCANFIT MUNE DETECTS LOSS OF MOTOR UNITS AND SIGNS OF REINNERVATION IN CHRONIC SPINAL CORD INJURED PATIENTS

Oral session 5

Chairs: Bent Deleuran, Mette Nørgaard and Francesco Maria Iena (PhD student)

O05.01   Andreas Engel Krag. ANATOMICAL STUDY OF THE DEPRESSOR ANGULI ORIS MUSCLE AND IMPLICATIONS FOR FACIAL PARALYSIS

O05.02   Samuel Levi Svinth C. Svendsen. SECRETIN ACTIVATES CFTR AND PENDRIN-DEPENDENT HCO_3^- SECRETION IN β-INTERCALATED CELLS

O05.03   Anders Gyldenkerne. THE OBJECTIVE QUALITY OF VISION FOR NEARSIGHTED
CANCELLED PATIENTS FOLLOWING CORNEAL REFRACTIVE SURGERY

O05.04   Wenqian Gu. STEVIOL GLUCURONIDE, A METABOLITE OF STEVIOL GLYCOSIDES, POTENTLY STIMULATES INSULIN SECRETION FROM ISOLATED MOUSE ISLETS: STUDIES IN VITRO

O05.05   Leonardo Bonetti. SPATIOTEMPORAL BRAIN DYNAMICS OF ACOUSTIC PATTERNS RECOGNITION

O05.06   Mads Bisgaard Bengtsen. METABOLIC AND HORMONAL RESPONSES TO HYPOGLYCEMIA: A HUMAN RANDOMIZED CROSSOVER TRIAL INVESTIGATING TYPE 1 DIABETES MELLITUS PATIENTS AND HEALTHY CONTROLS

Poster session 1

Chairs: Arne Møller, Qichao Zhang (PhD student) and Maimaitili Muyesier (PhD student)

P01.01   Søren Krogh Jensen. CAN MAGNETIC BRAIN STIMULATION IMPROVE RECOVERY AFTER SPINAL CORD INJURY?

P01.02   Laura Øllegaard Johnsen. THE ROLE OF NCBE IN CEREBROSPINAL FLUID PRODUCTION

P01.03   Rolf Blauenfeldt. DO CHANGES IN RED BLOOD CELL DEFORMABILITY AND FUNCTION CAUSE SECONDARY ISCHEMIC INJURY IN ACUTE ISCHEMIC STROKE? - RATIONALE AND METHODOLOGY

P01.04   Simone Schandorf Elstrøm Nielsen. TRACKING THE TRANSFERRIN RECEPTOR IN THE BLOOD-BRAIN BARRIER

P01.05   Meet Sanjaykumar Jariwala. THE GABA-ERGIC ENGRAM IN CENTRAL AMYGDALA FOR AVERSIVE LEARNING.

P01.06   Kristian Stær. CORRELATION BETWEEN CORTICAL CHOLINERGIC DYSFUNCTION AND MICROGLIAL ACTIVATION IN THE SUBSTANTIA INNOMINATA IN REM SLEEP BEHAVIOUR DISORDER

P01.07   Victor Manuel Pando Naude. MUSICAL RHYTHM AND PLEASURE IN PARKINSON'S DISEASE

P01.08   Pernille Louise Kjeldsen. DETECTING PRECLINICAL ALZHEIMER'S DISEASE WITH AMYLOID PET IMAGING TO ESTIMATE THE PREVALENCE OF INFLAMMATION AND TAU IN RELATION TO COGNITIVE DECLINE

P01.09   James Isaac Lubell. NATURAL IMAGERY THROUGH THE RETINA: DOES THE RETINA ENCODE LOW-LEVEL STIMULUS FEATURES?

P01.10   Jeppe Lund Schaldemose. NEUROIMAGING BIOMARKERS OF COGNITIVE DECLINE IN ALZHEIMER'S DISEASE - A LONGITUDINAL PET-STUDY

Poster session 2

Chairs: Nelson Ferreira, Ole Søndergaard Schwartz (PhD student) and Tingting Gu (PhD student)

P02.01   Cagla Cömert. A RECURRENT *DE NOVOHSPD1* VARIANT IS ASSOCIATED WITH HYPOMYELINATING LEUKODYSTROPHY

P02.02   Michael Nørregaard Vinkel. SENSORY DISTURBANCES AND PAIN IN YOUTH WITH CEREBRAL PALSY

P02.03   Julie Schjødtz Hansen. THE EFFECT OF MEDICAL CANNABIS ON NEUROPATHIC PAIN AND SPASTICITY IN PATIENTS WITH MULTIPLE SCLEROSIS AND SPINAL CORD INJURY: A NATIONAL MULTICENTRE DOUBLE-BLINDED PLACEBO-CONTROLLED STUDY IN DENMARK.

P02.04   Malene Overby. DISCOVERY OF NEURONAL VESICLE TRAFFICKING-ASSOCIATED PROTEIN 1 (NSG1) AS AN INTERACTING PROTEIN OF THE SORTILIN RECEPTOR - INSIGHTS INTO THE COMPLEXITY OF PROTEIN INTERACTIONS CONTROLLING NEUROLOGICAL AND PSYCHIATRIC DISORDERS

P02.05   Linda Karin M. Sundvall Germeys. MULTIPLE SCLEROSIS ALTERS WHITE MATTER MICROVASCULAR PERFUSIN

P02.06   Katrine Tang Stenz. EXTRACELLULAR VESICLES RELEASED BY REMOTE ISCHEMIC CONDITIONING AND BLOOD FLOW RESTRICTED EXERCISE IN STROKE INCREASE ISCHEMIC TOLERANCE OF BRAIN MICROVASCULAR ENDOTHELIAL CELLS

P02.07   Christine Ahrends. DYNAMIC NETWORK CHANGES OF AUDITORILY BIASED DECISION-MAKING

P02.08   Weine Dai. THE DYSFUNCTION OF INHIBITORY CONTROL IN HEROIN ADDICTION AND PROBLEM GAMBLING

P02.09   Hannah Brogård Andersen. EFFECT OF ADRENALINE ON SURVIVAL AND NEUROLOGICAL OUTCOME IN A NEWBORN PIGLET MODEL OF HYPOXIC CARDIAC ARREST

Poster session 3

Chairs: Jakob Christensen, Janne Tidselbak Larsen (PhD student) and Nanja Holland Hansen (PhD student)

P03.01   Astrid Høeg Tuborgh. THE ASSOCIATION BETWEEN ATTACHMENT INSECURITY AND POST-CONCUSSION SYMPTOMS IN YOUNG ADULTS.

P03.02   Benjamin Mac Donald. PATTERNS OF TREATMENT IN SEVERE ANOREXIA NERVOSA.

P03.03   Bardia Varastehmoradi. OPIOID SYSTEM HAS AN IMPACT ON HPA AXIS, COGNITIVE PROCESSES AND DEPRESSION

P03.04   Line Elmerdahl Frederiksen. HOSPITAL CONTACTS FOR MENTAL DISORDERS IN CHILDHOOD CANCER PATIENTS AND SURVIVORS IN A LONG-TERM PERSPECTIVE: A NATIONWIDE REGISTER-BASED COHORT STUDY

P03.05   Davide Ligato. A COMPARISON BETWEEN CLASSICAL SINGERS, RHYTHMIC SINGERS, AND NON-SINGERS INVESTIGATING MUSICAL AND PHYSICAL TRAINING. CAN THESE AFFECT HUMAN SENSORY PERCEPTION?

P03.06   Katrine Ingeman Beck. DEVELOPMENT OF THE HEALTH ANXIETY BY PROXY SCALE: A NEW MEASURE FOR EXCESSIVE PARENTAL WORRIES FOR CHILDREN'S HEALTH.

P03.07   Nanna Weye. ALTERNATIVE METRICS TO QUANTIFY PREMATURE MORTALITY IN MENTAL DISORDERS. A POPULATION-BASED COHORT STUDY

P03.08   Cecilie Marie Nielsen. HOW CAN WE IMPLEMENT MEASUREMENT-BASED CARE OF SCHIZOPHRENIA? CLINICAL VALIDATION OF PANSS-6, A BRIEF RATING SCALE TO MEASURE SYMPTOM SEVERITY

P03.09   Maria Christensen. THE ECONOMIC BURDEN OF MENTAL DISORDERS: A SYSTEMATIC REVIEW

P03.10   Sanne Toft Kristiansen. INSOMNIA IN DEPRESSION AND THE EFFICACY AND APPROPRIATENESS OF BALL BLANKETS: AN INDUSTRIAL PHD

Poster session 4

Chairs: Else Marie Damsgaard, Sif Sund Blandfort (PhD student) and Mette Bisgaard Andersen (PhD student)

P04.01   Troels Græsholt-Knudsen. SIGNS OF DANGER - A SYSTEMATIC REVIEW OF THE RISK OF CHILD ABUSE

P04.02   Nina Mckinnon Edwards. THE IMPACT OF SOCIOECONOMIC STATUS ON THE INCIDENCE OF TOTAL HIP ARTHROPLASTY DURING 1995-2018

P04.03   Jon Hagen Herskind. TESTING DYNAMIC MUSCLE FUNCTION USING ELECTRICAL STIMULATION IN HUMANS.

P04.04   ~~CANCELLED~~ Karin Rosenkilde Laursen. INVESTIGATING POTENTIAL HEALTH EFFECTS OF EXPOSURE TO PASSIVE VAPE FROM E-CIGARETTES - A RANDOMIZED CONTROLLED CHAMBER STUDY

P04.05   Jakob Schöllhammer Knudsen. THE CHANGING FACE OF EARLY TYPE 2 DIABETES: HBA1C AND LIPID MANAGEMENT TRENDS, 2000-2017 A DANISH POPULATION-BASED STUDY

P04.06   Susanne Fogh Jørgensen. TIMELY FOLLOW-UP AND ADHERENCE TO FOLLOW-UP GUIDELINES AFTER CERVICAL SCREENING ABNORMALITIES: A NATIONWIDE REGISTER-BASED COHORT STUDY.

P04.07   Susanne Boel Graversen. RISK FACTORS FOR REHOSPITALIZATION AND PREMATURE MORTALITY IN ELDERLY AFTER AN ADMISSION FOR PNEUMONIA - A POPULATION-BASED COHORT STUDY

P04.08   Rikke Nørgaard Pedersen. THE LONG TERM RISK OF BREAST CANCER RECURRENCE IN DENMARK 1987-2018

P04.09   Tina Lützen. PRELIMENARY RESULTS: GP ATTENDANCE IN PROXIMITY TO HPV VACCINATION

P04.10   Gitte Hoff Valentin. SOCIO-ECONOMIC INEQUALITIES IN FRAGILITY FRACTURE OUTCOMES: A SYSTEMATIC REVIEW AND META-ANALYSIS OF PROGNOSTIC OBSERVATIONAL STUDIES

Poster session 5

Chairs: Johan Palmfeldt and Kata Wolff Pedersen (PhD student)

P05.01   Andreas Ladefoged Ebbehøj. ADRENAL TUMORS AND INCIDENTALOMAS IN A
          POPULATION-BASED STUDY: THE GOOD, THE BAD, AND THE ZEBRA

P05.02   Signe Mosegaard. NOVEL GENETIC DISCOVERIES DETECTED USING WHOLE EXOME
          SEQUENCING AND RNA TRANSCRIPTOMICS IN 14 PATIENTS DIAGNOSED WITH
          MULTIPLE ACYL-COA DEHYDROGENATION DEFICIENCY (MADD)

P05.03   Marc Daniel Opfermann. ACETOACETATE DERIVED METABOLIC CHANGES AND
          PROTEIN MODIFICATIONS

P05.04   Mette Gude. THE "STANNIOCALCIN-2 - PAPP-A - IGFBP-4 - IGF-I AXIS" IN
          ATHEROSCLEROSIS

P05.05   Rasmus Espersen. EFFECT OF CALCIUM CITRATE VS CALCIUM CARBONATE ON
          ELEVATED PARATHYROID HORMONE AFTER ROUX-EN-Y GASTRIC BYPASS. A DOUBLE-
          BLINDED, RANDOMIZED TRIAL.

P05.06   Katrine Brodersen. EFFECTS OF ROUX-EN-Y GASTRIC BYPASS SURGERY OR GASTRIC
          SLEEVE SURGERY ON INSULIN SENSITIVITY, INSULIN SECRETION AND WHOLE BODY
          GLUCOSE TURNOVER IN MORBIDLY OBESE SUBJECTS WITH TYPE 2 DIABETES

P05.07   Katrine Meyer Lauritsen. KETONE BODY INFUSION INCREASES CIRCULATING
          ERYTHROPOIETIN AND BONE MARROW GLUCOSE UPTAKE

P05.08   Esben Stistrup Lauritzen. MELATONIN INHIBITS GIP SECRETION DURING AN ORAL
          GLUCOSE TOLERANCE TEST IN HEALTHY YOUNG MEN

P05.09   Jeyanthini Risikesan. LIPID METABOLISM IN INDIVIDUALS WITH NAFL/NASH

P05.10   Katrine Bilde. EFFECT OF OVERWEIGHT AND AGE ON THE BLOOD-BRAIN-BARRIER

Poster session 6

Chairs: Stinne Ravn Greisen, Nick Yin Larsen (PhD student) and Xiaowen Niu (PhD student)

P06.01   Mathilde Frost Kristensen. A CUSTOM ADJUSTABLE 3D PRINTED MICROFLUIDIC FLOW-
          CELL FOR MICROSCOPY ANALYSIS OF IN SITU-GROWN BIOFILMS

P06.02   Andreas Steenholt Niklassen. DANISH VALIDATION OF SNIFFIN' STICKS OLFACTORY
          TEST FOR THRESHOLD, DISCRIMINATION, AND IDENTIFICATION

P06.03   Kevin Kris Warnakula Olesen. TEN YEAR RISK OF MYOCARDIAL INFARCTION DIABETES
          PATIENTS WITHOUT ANGIOGRAPHIC CORONARY ARTERY DISEASE

P06.04   Thorsten Rasmussen. CARDIOVASCULAR ADRENERGIC NEUROPATHY IN TYPE 2
          DIABETES MELLITUS

P06.05   Olesya Svystun. SEVERE IMAGE-STITCHING ARTEFACTS AND DISTORTION IN CCD-
          BASED CEPHALOGRAMS AND THEIR ASSOCIATION WITH SENSOR TYPE AND HEAD
          MOVEMENT. AN EX-VIVO STUDY

P06.06   Johan Fridolf Hermansen. NOVEL ULTRASOUND TECHNIQUES FOR PREDICTION OF
          ACUTE KIDNEY INJURY

P06.07   Ane Bull Iversen. KNOWLEDGE OF STROKE CORE SYMPTOMS, HELP-SEEKING
          BEHAVIOR AND PRE-HOSPITAL DELAY IN ACUTE STROKE

P06.08 Jelmer Sybren Westra. DIAGNOSTIC PERFORMANCE OF QUANTITATIVE FLOW RATIO FOR FUNCTIONAL ASSESSMENT OF CORONARY ARTERY DISEASE IN PROSPECTIVELY ENROLLED PATIENTS: AN INDIVIDUAL PATIENT-DATA META-ANALYSIS

P06.09 Christian Stæhr. UPREGULATION OF ENDOTHELIAL $KIR_{2.1}$ CHANNELS LEADS TO DISTURBANCE IN NEUROVASCULAR COUPLING IN FAMILIAL MIGRAINE

P06.10 Martin Faurholdt Gude. PREHOSPITAL IDENTIFICATION OF LARGE VESSEL OCCLUSION BY PRESS (PREHOSPITAL STROKE SCORE) - A NEW COMBINED SYMPTOM SCORE

Poster session 7

Chairs: Niels Uldbjerg, Maria Keilow (PhD student) and Cathrine Hjorth Hansen (PhD student)

P07.01 Michal Frumer. NEW CONFIGURATIONS OF CANCER CONCERN. WHO CARES FOR WHAT?

P07.02 Birgith Engelst Grove. A CONTENT AND FACE VALIDITY STUDY OF A NEPHROLOGY PRO QUESTIONNAIRE USED AS DECISION AID IN CLINICAL PRACTICE

P07.03 ~~CANCELLED~~ Kristoffer Brix Olesen. FROM HIGHER EDUCATION TO WORK: DO DANISH UNIVERSITIES IGNORE IMPORTANT EMPLOYABILITY SKILLS IN CURRICULUM?

P07.04 Mathilde Stærk. ARE BASIC LIFE SUPPORT INSTRUCTORS COMPETENT?

P07.05 Mie Østergaard. INNOVATION - THE POLITICAL HEALTHCARE AGENDA IS ALL ABOUT IT, BUT WHAT IS THE ACTUAL UNDERSTANDING OF THE PHENOMENON? PRELIMINARY RESULTS FROM A QUALITATIVE EXPLORATION OF INNOVATION IN THE DANISH HEALTHCARE SECTOR

P07.06 Maria Louise Gamborg. CLINICAL DECISION-MAKING IN GERIATRIC EMERGENCY MEDICINE: A SYSTEMATIC REVIEW

P07.07 Simon Meyer Lauritsen. ACCURATE AND EXPLAINABLE ARTIFICIAL INTELLIGENCE FOR THE EARLY PREDICTION OF ACUTE CRITICAL ILLNESS

P07.08 Louise Sofia Madsen. COMMUNITY-BASED REHABILITATION IN OUTDOOR SETTINGS: A SYSTEMATIC REVIEW OF QUALITATIVE ARTICLES ON PEOPLE WITH DISABILITIES AND PROFESSIONALS' EXPERIENCES AND PERCEPTIONS

P07.09 ~~CANCELLED~~ Sigurd Beier Sloth. SELF-REGULATED VS. INSTRUCTOR-REGULATED TRAINING IN LAPAROSCOPY

P07.10 Camilla Lundquist. FROM RESEARCH TO CLINICAL PRACTICE. BARRIERS AND FACILITATORS FOR IMPLEMENTATION OF UPPER LIMB PREDICTION ALGORITHMS FOR PATIENTS WITH STROKE

Poster session 8

Chairs: Rikke Damkjær Maimburg, Sidsel Boie (PhD student) and Bodil Karen Bæksted Jørgensen (PhD student)

P08.01 Peter Bo Jørgensen. HIGHER EARLY PROXIMAL MIGRATION OF HEMISPHERICAL CUPS WITH ELECTROCHEMICALLY APPLIED HYDROXYAPATITE (BONEMASTER) ON A POROUS SURFACE COMPARED WITH POROUS SURFACE ALONE: A RANDOMIZED RSA STUDY WITH 53 PATIENTS

P08.02   Lea Lykke Harrits Lunddorf. MATERNAL THYROID DISEASES AND PUBERTAL
              DEVELOPMENT IN DAUGHTERS AND SONS

P08.03   Thor Haahr. ABNORMAL VAGINAL MICROBIOTA IS SIGNIFICANTLY ASSOCIATED WITH
              POOR CHANCE OF PREGNANCY IN PATIENTS UNDERGOING *IN VITRO* FERTILIZATION
              TREATMENT

P08.04   Pelle Emil Hanberg. PHARMACOKINETICS OF DOUBLE-DOSE CEFUROXIME IN PORCINE
              INTERVERTEBRAL DISC AND VERTEBRAL CANCELLOUS BONE - A RANDOMIZED
              MICRODIALYSIS STUDY

P08.05   Sara Bønløkke Simonsen. HPV IN THE BLOOD OF CERVICAL CANCER PATIENTS -
              CLINICAL IMPLICATIONS

P08.06   Line Winther Gustafson. "SEE AND TREAT" IN AN OUTPATIENT SETTING IN WOMEN
              AGED 45 YEARS AND OLDER WITH CERVICAL DYSPLASIA

P08.07   Helle Østergaard. IS A ROTATOR CUFF TEAR A PROGNOSTIC FACTOR OF PHYSICAL
              FUNCTION AND QUALITY OF LIFE IN PATIENTS WITH A PROXIMAL HUMERUS
              FRACTURE? PRELIMINARY SUB-ANALYSIS FROM A NORDIC MULTICENTER STUDY
              (NITEP)

P08.08   Louise Lilleøre Kjeldsen. PELVIMETRY MEASURED BY MRI; IS PELVIC CAPACITY
              DEPENDENT ON PHYSICAL POSITION IN PREGNANT WOMEN?

P08.09   Kris Chadwick Hede. CARGEL BIOSCAFFOLD IMPROVES CARTILAGE REPAIR AFTER
              BONE MARROW STIMULATION IN A MINIPIG MODEL

P08.10   Christine Rohr Thomsen. NEW METHOD FOR EVALUATING THE STIFFNESS OF THE
              HUMAN UTERINE CERVIX BASED ON ELASTOGRAPHY AND A FORCE-MEASURING
              DEVICE

Poster session 9

Chairs: Erling Bjerregaard Pedersen and Haiyun Qi (PhD student)

P09.01   Jordan Nicolas Alves. MOTION-RELATED ACTIVITY IN THE HUMAN RETINA ELICITED BY
              MOVING GRATINGS

P09.02   Charlotte Ernst. INTRAVASCULAR ADENOSINE TRIPHOSPHATE (ATP)-INDUCED
              CONTRACTION IS MEDIATED BY P2-PURINERGIC RECEPTORS AND THE A3-ADENOSINE
              RECEPTOR IN PORCINE RETINAL ARTERIOLES EX VIVO

P09.03   Søren Viborg Vestergaard. INCIDENCE, PREVALENCE AND MORTALITY OF NEPHROTIC
              SYNDROME IN ADULTS

P09.04   Christina Voss Ernstsen. ACUTE PYELONEPHRITIS: THE EFFECT ON RENAL WATER
              CHANNELS

P09.05   Stine Julie Hyldal Tingskov. THE EFFECT OF TAMOXIFEN ON GENDER DIFFERENCES IN
              UNILATERAL URETERAL OBSTRUCTED RATS AND HUMAN KIDNEY SLICES

P09.06   Monica Dahlstrup Sietam. THE ROLE OF SYNDECAN 2 IN VISUAL BEHAVIOUR

P09.07   Silja Hansen. A NOVEL PORCINE MODEL FOR EXPERIMENTAL CNV

P09.08   Ann Mai Hindkjær Østergaard. THE EFFECT OF 0.9% NACL COMPARED WITH PLASMA-
              LYTE ON BIOMARKERS OF KIDNEY DAMAGE IN PATIENTS UNDERGOING PRIMARY
              UNCEMENTED HIP REPLACEMENT

P09.09   Linea Sandfeld Blichert-Refsgaard. TREATMENT OF NON-MUSCLE INVASIVE BLADDER CANCER: DO WE DESTROY THE BLADDER FUNCTION?

P09.10   Sofie Schmøkel. DISSECTION OF THE TUMOR ECOSYSMTEN IN BLADDER CANCER

P09.11   Signe Krejberg Jeppesen. THE RETINAL OXYGEN SATURATION MEASURED BY DUAL WAVELENGTH OXIMETRY IN LARGER RETINAL VESSELS IS INFLUENCED BY THE LINEAR VELOCITY OF THE BLOOD

Poster session 10

Chairs: Simon Eskildsen, Karen Baden Alstrup (PhD student) and Mads Valdemar Anderson (PhD student)

P10.01   Katrine Andersen. THE RELATIONSHIP BETWEEN SYNAPTIC DENSITY AND COGNITIVE DECLINE IN PARKINSON'S DISEASE (PD) AND EARLY DEMENTIA WITH LEWY BODIES (DLB)

P10.02   Peter Uhrbrand. PROLONGED OPIOID-USE AFTER PLANNED BACK SURGERY: A PROSPECTIVE STUDY

P10.03   Anna Holm. UMBRELLA REVIEW OF THE EVIDENCE: NURSES' COMMUNICATION WITH MECHANICALLY VENTILATED PATIENTS IN THE INTENSIVE CARE UNIT

P10.04   Jeppe Foged Vigh-Larsen. MUSCLE METABOLISM AND FATIGUE DURING INTENSE INTERMITTENT EXERCISE IN ELITE MALE ICE HOCKEY PLAYERS

P10.05   Jacob Horsager. PARKINSON'S DISEASE STARTS IN THE GUT OR THE BRAIN - A MULTI-MODALITY IMAGING STUDY

P10.06   Tatyana D Fedorova. DECREASED PARASYMPATHETIC INNERVATION OF THE GUT IN VAGOTOMISED PATIENTS: AN IN-VIVO PET STUDY

P10.07   Mustafa Aykut Kural. LARGE SYNCHRONIZED BILATERAL CORTICAL NETWORKS GENERATING TRIPHASIC WAVES IN ENCEPHALOPHATIC EEG RECORDING

P10.08   Sebastian Skejø. PREDICTING THROWING SPEED USING ACCELOMETERS: A FIRST STEP TOWARDS MONITORING THROWING LOAD IN HANDBALL

P10.09   Simon Kjeldsen. MEASURING DAYTIME RESTING PERIODS IN PATIENTS WITH SEVERE ACQUIRED BRAIN INJURY

P10.10   Troels Kjærskov Hansen. FRAILTY ASSESSMENT IN OLDER PATIENTS USING A RECORD-BASED MULTIDIMENSIONAL PROGNOSTIC INDEX IS RELIABLE

Poster session 11

Chairs: Mette Madsen, Lene Wulff Krogsgaard (PhD student) and Liv Marie Duus (PhD student)

P11.01   Jesper Emil Jakobsgaard. SKELETAL MUSCLES FROM RATS SELECTIVELY BRED FOR DIVERSE RUNNING CAPACITY DISPLAY DIFFERENTIAL STRESS- AND METABOLIC-RELATED SIGNALLING IN RESPONSE TO FATIGUING ELECTROSTIMULATION

P11.02   Ensieh Farahani. FUNCTIONAL ANALYSIS OF GENOME-WIDE RNA-SEQ DATA AFTER HSV1 INFECTION   REVEALS NOVEL INFLAMMATORY RESPONSE PATHWAYS

P11.03   Josephine P Geertsen Keller. TOPOISOMERASES AS A REGULATOR OF PROMOTERS IN HUMAN PROTO-ONCOGENES THROUGH STABILIZATION OF G-QUADRUPLEXES

P11.04   Bertram Dalskov Kjerulff. USING ROUTINE WHITE BLOOD CELL COUNTS TO PREDICT INFECTIONS IN BLOOD DONORS

P11.05   Lixiang Jiang. REGULATION OF α-SYNUCLEIN TRANSCRIPTION BY THE PLK-2/GSK-3B SIGNALLING PATHWAY - A POTENTIAL MODULATOR OF PARKINSON'S DISEASE RISK

P11.06   Christina Valbirk Konrad. USING HIV-SPECIFIC SINGLE-CHAIN VARIABLE FRAGMENTS TO TARGET THE PERSISTENT HIV RESERVOIR

P11.07   Anne Borup. THE POWER OF PARASITES: EXPLORING THE IMMUNOMODULATORY PROPERTIES OF HELMINTH-DERIVED EVS

P11.08   Michelle Mølgaard Thomsen. IDENTIFICATION OF NOVEL INNATE IMMUNODEFICIENCIES IN PATIENTS WITH SEVERE VARICELLA ZOSTER ENCEPHALITIS.

P11.09   Signe Schöllhammer Knudsen. RHEUMATOID ARTHRITIS IN PREGNANCY AND OFFSPRING SCHOOL PERFORMANCE. A DANISH NATIONWIDE REGISTER-BASED STUDY

P11.10   Fanghui Ren. MECHANISM OF ACTIVATION OF AUTOPHAGY IN NEURONS BY HERPES SIMPLEX VIRUS

Poster session 12

Chairs: Therese Juul, Mette Eline Brunbjerg (PhD student) and Maja Bendtsen Sharma (PhD student)

P12.01   Erik Buch Jørgensen. ACCURACY OF IN VIVO DOSIMETRY BASED SOURCE-TRACKING IN HDR PROSTATE BRACHYTHERAPY

P12.02   Simon Grund Sørensen. DO DEFECTS IN DNA DAMAGE RESPONSE GENES LEAD TO PATTERNS OF MUTATIONS ACROSS THE WHOLE CANCER GENOME?

P12.03   Signe Neldeborg. TURNING COLD TUMORS HOT

P12.04   Pernille Aaen Sloth. IN VIVO MOUSE MODEL OF HER2/ERBB2-INDUCED METASTATIC BREAST CANCER AND CHARACTERIZATION OF LUNG METASTASES

P12.05   Karen Schow Jensen. PRIMARY HEALTH CARE UTILIZATION AMONG SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA: A MATCHED COHORT STUDY

P12.06   Rasmus Blechingberg Friis. SYMPTOM DEVELOPMENT FROM INITIAL TREATMENT TO PROGRESSIVE DISEASE IN PATIENTS WITH ADVANCED LUNG CANCER

P12.07   Marie Louise Milo. RADIOTHERAPY ASSOCIATED CORONARY ARTERY STENOSIS IN 87,550 PATIENTS WITH EARLY BREAST CANCER

P12.08   Andreas Gravgaard Andersen. VALIDATION OF AN A PRIORI CONE-BEAM SCATTER CORRECTION APPLICATION FOR ONLINE PROTON THERAPY RANGE VERIFICATION

P12.09   Nadia Øgaard. BLOOD-BASED DETECTION OF COLORECTAL CANCER USING DNA METHYLATION BIOMARKERS - CLINICAL APPLICATIONS FOR EARLY DETECTION AND PREDICTION OF POSTSURGICAL RELAPSE

P12.10   Laura Patricia Kaplan. A NEW TOOL TO ASSIST IN CLINICAL COMPARISON OF RADIOTHERAPY TREATMENT PLANS

P12.11   Casper Gammelmark Muurholm. EXPERIMENTAL VALIDATION OF REAL-TIME ROTATION-INCLUDING DOSE RECONSTRUCTION DURING TUMOR TRACKING

Flash talk session 1

Chairs: Tina Birgitte Wisbech Carstensen, Julie Jacoby Petersen (PhD student) and Helle Elisabeth Andersen (PhD student)

F01.01   Emina Gültekin. CONSTRUCTIONS OF ETHNIC MINORITY PATIENTS: A CONSTRUCTIVIST GROUNDED THEORY APPROACH

F01.02   Kathrine Carstensen. QUALITY IMPROVEMENT COLLABORATIVES IN THE IMPLEMENTATION OF THE DANISH HEALTHCARE QUALITY PROGRAMME

F01.03   Anne Timm. A PROCESS EVALUATION OF THE FAMILY LEVEL IN A COMPLEX HEALTH PROMOTION INTERVENTION

F01.04   Marie Ernst Christensen. FOOD AND EATING CHALLENGES AMONG ADOLESCENTS AND YOUNG ADULTS WITH CANCER UNDERGOING CHEMOTHERAPY

F01.05   Anders Schmidt Vinther. PREVENTING ANABOLIC STEROID USE IN GYMS - WHAT WORKS?

F01.06   Lene Klem Olesen. A COMPLEX INTERVENTION STUDY ON A PALLIATIVE REHABILITATION BLENDED LEARNING PROGRAM TO SUPPORT RELATIVES AND HEALTH CARE PROVIDERS OF PEOPLE WITH ALS AND FTD IN COPING WITH CHALLENGES

F01.07   Anna Louise Skovgaard. THE WORK OF BEING A PATIENT

F01.08   Mia Hansen Mandau. NURSES' PRACTICES OF COORDINATING CARE BETWEEN EMERGENCY AND SPECIALIST HOSPITAL DEPARTMENTS - A MULTIPLE-CASE STUDY

Flash talk session 2

Chairs: Tue Kragstrup, Morten Aagaard Nielsen (PhD student) and Cecilie Blenstrup Patsche (PhD student)

F02.01   Signe Risbøl Vils. THROMBOEMBOLIC RISK IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

F02.02   Cecilie Rud Budtz. SERIOUS PATHOLOGY IN PRIMARY CARE PHYSIOTHERAPY

F02.03   Angela Anna Paula Victoria Herengt. NRF2 CONTROL A NOVEL ANTI-VIRAL PROGRAM

F02.04   Diana Salomi Ponraj. SLOW GROWING GRAM-POSITIVE ANAEROBIC BACTERIA IN ORTHOPAEDIC IMPLANT ASSOCIATED INFECTIONS

F02.05   Philip Therkildsen. POSITIVE PREDICTIVE VALUE OF THE GIANT CELL ARTERITIS DIAGNOSIS IN THE DANISH NATIONAL PATIENT REGISTRY: A VALIDATION STUDY

F02.06   Susanne Gundersborg Sandbøl. THE EFFECT OF A NEWLY BUILT HOSPITAL ON INFECTION CONTROL

F02.07   Frederik Holm Rothemejer. UTILIZING CRISPR/CAS9 TO PRODUCE ANTI-HIV CAR T CELLS

F02.08   Janne Møller. TRANSLATION AND INITIAL VALIDATION OF KING'S SARCOIDOSIS QUESTIONNAIRE

Flash talk session 3

Chairs: Morten Nielsen, Sara Raquel Almeida Ferreira (PhD student) and Martin Kinnerup (PhD student)

F03.01   Katarzyna Grycel. FUNCTIONAL AND STRUCTURAL ANALYSIS OF CRMP2 KNOCKOUT MOUSE MODEL

F03.02   Sine Mette Øgendahl Buus. SOCIOECONOMIC DISPARITIES IN REVASCULARIZATION THERAPY FOR ISCHEMIC STROKE

F03.03   Cecilie Siggaard Jørgensen. GENOME-WIDE ASSOCIATION STUDY OF NOCTURNAL ENURESIS IDENTIFIES RISK-LOCI ON CHROMOSOME 6 AND 13

F03.04   Kirsten Nordbye-Nielsen. RELIABILITY OF THE DANISH CHALLENGE: AN ADVANCED MOTOR SKILLS TEST FOR CHILDREN WITH CEREBRAL PALSY

F03.05   Tobias Glaston Stærmose. UNDERSTANDING ALS THROUGH MAGNETISM - A PRELIMINARY LOOK AT THE PLANS FOR THIS MEG BASED PHD-STUDY

F03.06   Alana Miranda Pinheiro. INJURY- RESPONSE OF SATELLITE GLIAL CELLS AND THEIR POTENTION AS TARGETS IN NEUROPATHIC PAIN TREATMENT

F03.07   Kathrine Abildskov Friis. IN VITRO INVESTIGATION OF THE ROLE OF NCBE IN INFLAMMATION INDUCED CEREBROSPINAL FLUID HYPERSECRETION OF THE CHOROID PLEXUS

F03.08   Helene Honoré. CRITERION VALIDITY OF AN ACCELEROMETER-BASED METHOD TO
~~CANCELLED~~   MONITOR PHYSICAL ACTIVITY IN DAILY LIFE ACTIVITIES AFTER ACQUIRED BRAIN INJURY

F03.09   Anette Bach Jønsson. EFFECTS OF BLOOD FLOW RESTRICTED EXERCISE ON QUALITY OF LIFE, PHYSICAL FUNCTION AND NEUROMUSCULAR RECOVERY IN INDIVIDUALS WITH SPINAL CORD INJURY - A RANDOMIZED CONTROLLED TRIAL

F03.10   Frederik Junge Egersgård. THE VASOACTIVE EFFECTS OF SEMAGLUTIDE ON PORCINE RETINAL RESISTANCE VESSELS EX VIVO

Flash talk session 4

Chairs: Samia Joca, Rasmus H. Olesen (PhD student) and Pauline Cantou (PhD student)

F04.01   Rasmus Eich Hammer. THE EFFECT OF RECOMBINANT BOTULINUM NEUROTOXIN A ON NEUROPATHIC PAIN IN SPARED NERVE INJURY MOUSE MODEL

F04.02   Hamed Zaer. A NEW PORCINE MODEL FOR NEUROMODULATORY BRAIN RADIOSURGERY

F04.03   Anna Krogh Andreassen. A DEVELOPMENTAL PERSPECTIVE OF WORKING MEMORY IN CHILDREN AT FAMILIAL HIGH RISK OF SCHIZOPHRENIA OR BIPOLAR DISORDER - THE DANISH HIGH RISK AND RESILIENCE STUDY

F04.04   Nadia Flensted Høgholt. MUSIC AS A TREATMENT FOR PREGNANCY-RELATED INSOMNIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

F04.05   Kamilla My Thanh Lê Truong. CRYONEUROLYSIS' OUTCOME ON PAIN EXPERIENCE - A RANDOMIZED CONTROLLED BLINDED TRIAL

F04.06   Caroline Juhl Arnbjerg-Nielsen. PSYCHOEDUCATION FOR PATIENTS WITH BIPOLAR DISORDER IN RWANDA

F04.07	Maiken Krogsbæk Mikkelsen. THE EFFECT OF OLANZAPINE TREATMENT ON THE FEEDING REGULATING REGIONS OF HYPOTHALAMUS
F04.08	Maja Fuhlendorff Jensen. GUT-FIRST AND BRAIN-FIRST PARKINSON'S DISEASE - STUDIES IN ANIMAL MODELS AND PRODROMAL HUMAN TISSUE SAMPLES
F04.09	André Dias. DYNAMIC WHOLE BODY FDG PET/CT - NEXT GENERATION FUNCTIONAL IMAGING
F04.10	Casper Skjærbæk. DOES PARKINSON'S DISEASE START IN THE GUT - AN ESOPHAGEAL TRANSIT AND INTESTINAL DYSFUNCTION STUDY

Flash talk session 5

Chairs: Ellen M. Mikkelsen, Simon Bang Kristensen (PhD student) and Mette Jørgine Kirkeby (PhD student)

F05.01	Anne Østergaard Nannsen. THE EFFECT OF LOW INTAKE OF NON-STARCHY VEGETABLES ON RISK OF COLORECTAL CANCER
F05.02	Frederik Pagh Kristensen. STATIN THERAPY AND RISK OF NEUROPATHY IN DIABETES: A POPULATION-BASED COHORT STUDY
F05.03	Katrin Debes Kristensen. DESCRIPTION OF SPORTS INJURY RATE OVER TIME: IS IT APPROPRIATE TO EXCLUDE SUBSEQUENT EVENTS?
F05.04	Katrine Hjuler Lund. A PROSPECTIVE COHORT STUDY OF PERCEIVED STRESS AND SEMEN QUALITY
F05.05	Buket Öztürk. PRENATAL EXPOSURE TO ANTIDEPRESSANTS AND THE RISK OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDHOOD: FINDINGS FROM A NATIONWIDE COHORT STUDY
F05.06	Philip Munch. IS THE RISK OF CARDIOVASCULAR DISEASE INCREASED AFTER LIVING KIDNEY DONATION?
F05.07	Lisa Fønss Rasmussen. EFFECTS OF TRANSITIONAL INTERVENTIONS BETWEEN HOSPITAL AND HOME ON READMISSIONS AMONG OLDER PATIENTS DISCHARGED FROM A MEDICAL WARD: A SYSTEMATIC REVIEW
F05.08	Line Thams. EFFECTS OF MILK PROTEIN AND VITAMIN D ON MUSCLE STRENGTH IN DANISH 6-8-YEAR-OLD CHILDREN: STUDY PROTOCOL
F05.09	Anders Emil Ejskjær Gravholt. THE EFFECT OF ELECTRICALLY EVOKED ECCENTRIC CONTRACTIONS ON MUSCLE HEALTH
F05.10	Nanna Husted Jensen. IMPLEMENTATION OF A DIABETES PREVENTIVE PROGRAMME FOR WOMEN WITH PRIOR GESTATIONAL DIABETES AND THEIR FAMILIES: THE FACE-IT PROGRAMME

Flash talk session 6

Chairs: Annette Haagerup, Louise Lindholdt (PhD student) and Martin Rune Hassan Hansen (PhD student)

F06.01	Pia Johansson Heinsvig. DOPING AGENTS IN DENMARK - AN ANALYTICAL EXAMINATION OF THE DANISH DOPING MARKET

F06.02 Jeppe Damgren Vesterager. HOSPITAL VARIATION IN POST-OPERATIVE INFECTIONS AMONG HIP FRACTURE PATIENTS

F06.03 Mette Lauge Kristensen. THE INFLUENCE OF CERVICAL DYSPLASIA ON FEMALE FERTILITY

F06.04 Christine Leonhard Birk Sørensen. MENTAL HEALTH THROUGH ADOLESCENCE AND EARLY ADULTHOOD

F06.05 Søren Mose. TRAJECTORIES OF HEALTH CARE SERVICE UTILISATION IN PEOPLE WITH MUSCULOSKELETAL PAIN

F06.06 Birgitte Laier Bitsch. EFFECTIVENESS OF CARDIAC REHABILITATION FOLLOWING ACUTE CORONARY SYNDROME FOR PATIENTS WITH AND WITHOUT CONCURRENT DIABETES (A SYSTEMATIC REVIEW AND META-ANALYSIS

F06.07 Kasper K Friedrichsen. REPEATED TRAUMATIC BRAIN INJURY AND RISK OF EPILEPSY

F06.08 Louise Ruby Høj Illum. REGIONAL DIFFERENCES IN ENDOMETRIOSIS IN DENMARK: WHO GETS THE DIAGNOSIS?

F06.09 Nils Skajaa. STROKE IN YOUNG ADULTS - INCIDENCE AND PROGNOSIS: DANISH POPULATION-BASED COHORT STUDIES

F06.10 Jie Zhang. DOES GRANDPARENTAL BODY COMPOSITION INFLUENCE THAT OF THE GRANDCHILDREN?-A FAMILY LINKAGE STUDY ACROSS THREE GENERATIONS

Flash talk session 7

Chairs: Rune Dall Jensen, Lotte Levison (PhD student) and Andreas Halgreen Eiset (PhD student)

F07.01 Lotte Sørensen. MEASUREMENT PROPERTIES OF HAND-HELD DYNAMOMETRY FOR ASSESSMENT OF SHOULDER MUSCLE STRENGTH: A SYSTEMATIC REVIEW

F07.02 Louise Binow Kjær. THE PATIENT, THE STUDENT AND THE EDUCATIONAL ENVIRONMENT: A MULTI-METHOD STUDY OF LEARNING IN STUDENT-RUN CLINCS

F07.03 Sivaranjani Madhan. SYSTEMATIC ASSESSMENT OF ORAL FUNCTION, QUALITY OF LIFE AND CRANIOFACIAL MORPHOLOGY CHANGES IN ORTHOGNATHIC SURGICAL PATIENTS

F07.04 Cathrine Bell. INTEGRATING MEDICAL SPECIALTIES AND OUTPATIENT APPOINTMENTS - A NOVEL PATHWAY FOR MULTIMORBID PATIENTS ENCOUNTERING SEVERAL OUTPATIENT CLINICS

F07.05 Mikkel Bo Brent. PTH AND THE ACTIVIN TYPE IIA DECOY RECEPTOR IN PREVENTION OF IMMOBILIZATION-INDUCED BONE AND MUSCLE LOSS

F07.06 Louise Hermann Poulsen. DOES 3D IMAGING CHANGE THE TREATMENT DECISION FOR WISDOM TEETH IN THE UPPER JAW?

F07.07 Tora Hauh. DEVELOPMENT AND VALIDATION OF A MONITORING ASSESSMENT TOOL FOR A NEW OPERATION TECHNIQUE, LAPAROSCOPIC COMPLETE MESOCOLIC EXCISION

Flash talk session 8

Chairs: Agnete Larsen and Mette Kaasgaard (PhD student)

F08.01   Thomas Johannesson Hjelholt. ASSOCIATION OF CHA_2DS_2-VASC SCORE WITH STROKE, THROMBOEMBOLISM AND DEATH IN HIP FRACTURE PATIENTS WITH OR WITHOUT ATRIAL FIBRILLATION: A NATIONWIDE COHORT STUDY

F08.02   Niels Moeslund. IMPACT OF OXYGENATION DURING NORMOTHERMIC REGIONAL PERFUSION IN A DONOR AFTER CIRCULATORY DEATH IN A PORCINE MODEL

F08.03   Malene Enevoldsen. PERFORMANCE EVALUATION OF TEMPORARY EPICARDIAL PACE WIRE WITH INTEGRATED SENSOR FOR PACING, SENSING, AND CONTINUOUS POSTOPERATIVE MONITORING OF MYOCARDIAL FUNCTION AFTER OPEN HEART SURGERY

F08.04   Martin Sejr-Hansen. CLINICAL VALIDATION OF QUANTITATIVE FLOW RATIO IN EVALUATION OF CORONARY ARTERY STENOSIS -THE FAVOR III TRIAL

F08.05   Salma Karim. EVALUATION OF CORONARY PRESSURE, FLOW AND RESISTANCE IN CHRONIC TOTAL OCCLUSIONS (CTO) - A SUB-STUDY OF THE NORDIC-SPANISH RANDOMIZED TRIAL ON THE PROGNOSTIC EFFECT OF REVASCULARIZATION OR OPTIMAL MEDICAL THERAPY OF CHRONIC TOTAL CORONARY OCCLUSIONS (ISCHEMIA-CTO) NCT03563417

F08.06   Anne Mette Dybro. THE EFFECT OF METOPROLOL ON MYOCARDIAL FUNCTION, PERFUSION AND HEMODYNAMICS IN SYMPTOMATIC PATIENTS WITH HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY

F08.07   Kristian Hylleberg Christensen. HEMODYNAMIC EFFECTS OF ORAL KETONE SUPPLEMENTS IN PATIENTS WITH CHRONIC HEART FAILURE AND REDUCED EJECTION FRACTION

Flash talk session 9

Chairs: Michael Mulvany, Birgit Refsgaard Iversen (PhD student) and Jakob Hansen (PhD student)

F09.01   Lauge Vammen. DEVELOPING A CLINICALLY RELEVANT CARDIAC ARREST MODEL IN PIGS

F09.02   Sivagowry Rasalingam Mørk. OUT-OF-HOSPITAL CARDIAC ARREST, CENTRAL DENMARK REGION: TEMPORAL USE OF MECHANICAL CIRCULATORY SUPPORT AND ASSOCIATED OUTCOME

F09.03 *CANCELLED* Marte Holmen. THROMBOEMBOLIC RISK AMONG PATIENTS WITH ELEVATED HOMOCYSTEINE LEVELS

F09.04 *CANCELLED* Katrine Berg. CARDIAC MITOCHONDRIAL STRUCTURE AND FUNCTION FOLLOWING HEART TRANSPLANTATION - ENERGY HTX

F09.05   Steen Hylgaard Jørgensen. METABOLIC ALTERATIONS IN THE FAILING HUMAN HEART

F09.06   Simone Juel Dragsbæk. LONG-TERM CARDIOPULMONARY RESPONSES TO PULMONARY EMBOLISM IN AN IN VIVO ANIMAL MODEL

F09.07   Andreas Lind Johannessen. LYMPHATIC FUNCTION AND MORPHOLOGY IN THE ARMS OF BREAST CANCER TREATED WOMEN - A FOLLOW-UP STUDY

Flash talk session 10

Chairs: Simon Tilma Vistisen and Morten Riemenschneider (PhD student)

F10.01   Omeed Neghabat. OPTICAL COHERENCE TOMOGRAPHY OPTIMIZED BIFURCATION EVENT REDUCTION - THE OCTOBER TRIAL

F10.02   Jakob Tobias Nyvad. THE IMPACT OF AORTIC CALCIFICATION ON CENTRAL BLOOD PRESSURE AND MARKERS OF HYPERTENSION MEDIATED ORGAN DAMAGE IN CHRONIC KIDNEY DISEASE

F10.03   Rajkumar Rajanathan. MICE WITH MIGRAINE ASSOCIATED MUTATION IN THE NA^+,K^+-ATPASE $\alpha2$ ISOFORM DEVELOP CARDIOMYOPATHY-LIKE CHANGES

F10.04   Mia Klinkvort Kempel. THE IMPACT OF SOCIAL INEQUALITY AND INSECURITY ON THE RISK OF EARLY SIGNS OF CARDIOVASCULAR AND METABOLIC DISEASE

F10.05   Johannes Enevoldsen. CARDIO-PULMONARY INTERACTION IN OPEN-CHEST CONDITIONS - PREDICTING THE RESPONSE TO FLUID ADMINISTRATION

F10.06   Daniel Julius Lauritzen. LONG-TERM EFFECTS OF ANESTHETIC DRUGS ON NEURODEVELOPMENT IN ADULTS OPERATED FOR ASD OR VSD

F10.07   Cecilie Budolfsen. NT-PROBNP MEASUREMENTS TO RULE-OUT HEART FAILURE AMONG ATRIAL FIBRILLATION PATIENTS: A PROSPECTIVE CLINICAL STUDY

Flash talk session 11

Chairs: Esben Søndergaard, Ana C.G. Ebsen (PhD student) and Eva Forsom (PhD student)

F11.01   Søren Gullaksen. EFFECT OF EMPAGLIFLOZIN AND SEMAGLUTIDE ON CARDIO-RENAL TARGET ORGAN DAMAGE IN PATIENTS WITH TYPE 2 DIABETES - A RANDOMIZED TRIAL

F11.02   Gry Høst Dørflinger. DIABETIC NEPHROPATHY - AUTOATTACK AND IMPAIRED REGULATION OF COMPLEMENT

F11.03   Zheer Husain. THE EFFECTS OF IMPROVED INSULIN SENSITIVITY ON BONE MARKERS AND BONE BIOMECHANICAL PROPERTIES IN INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS

F11.04   Christine Bodelund Christiansen. ARONIA IN THE TYPE 2 DIABETES TREATMENT REGIMEN

F11.05   Julie Nielsen. NOVEL PHARMACOLOGICAL APPROACH FOR ACTIVATION OF DORMANT FOLLICLES

F11.06   Tue Duy Nguyen. ATHE MECHANISTIC LINK BETWEEN THE NA,K-ATPASE ABUNDANCE AND BLOOD GLUCOSE HOMEOSTASIS

F11.07   Fredrik Brustad Mellbye. EFFECTS OF CAFESTOL, A POTENTIAL ANTIDIABETIC SUBSTANCE IN COFFEE, IN SUBJECTS AT RISK OF TYPE 2 DIABETES

F11.08   Johanne Blanner Jul. SEX-SPECIFIC ALTERATIONS IN HEPATIC GLYCEROL METABOLISM IN MICE FED A HIGH-FAT DIET

Flash talk session 12

Chairs: Peter Jepsen and Stine Karlsen (PhD student)

F12.01   Morten Daniel Jensen. AUTOIMMUNE HEPATITIS AND CANCER RISK

F12.02   Mira Mekhael. COMPARISON OF TRANSANAL IRRIGATION AND GLYCEROL
SUPPOSITORIES IN TREATMENT OF LOW ANTERIOR RESECTION SYNDROME: A
MULTICENTRE RANDOMISED CONTROLLED TRIAL

F12.03   Astrid Højmark Andersen. PROTON PUMP INHIBITORS INCREASE RISK OF ORAL
CANCER AMONG PATIENTS WITH ALCOHOLIC CIRRHOSIS

F12.04   Ditte Emilie Munk. EFFICACY OF ZINC ON HUMAN GUT COPPER UPTAKE DEPENDING
ON ZINC TYPE AND DOSE REGIMEN QUANTIFIED WITH^{64}CUCL$_2$PET/CT-SCAN

F12.05   Frederik Kraglund. DECREASING INCIDENCE OF ALCOHOLIC LIVER DISEASE IN
DENMARK: A NATIONWIDE STUDY

F12.06   Frederik Heiberg Brix. FIBRINOGEN LIKE-PROTEIN 1 AND LYMPHOCYTE ACTIVATING-
~~CANCELLED~~ GENE 3 IN ALCOHOLIC HEPATITIS

F12.07   Kristoffer Kjærgaard. COGNITIVE DYSFUNCTION IN NON-ALCOHOLIC FATTY LIVER
DISEASE: A MECHANISTIC RAT STUDY

F12.08   Frederikke Schønfeldt Troelsen. RISK AND PROGNOSIS OF POST-COLONOSCOPY
COLORECTAL CANCERS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A
DANISH POPULATION-BASED COHORT STUDY

F12.09   Lotte Lindgreen Eriksen. INHIBITORY SKEWING OF T-LYMPHOCYTE PHENOTYPE IN
ALCOHOLIC HEPATITIS

F12.10   Charlotte Rud. ARE OUTPATIENTS WITH AN ILEOSTOMY SUB-CLINICALLY
DEHYDRATED?

Flash talk session 13

Chairs: Jesper Grau Eriksen, Helle Kristensen (PhD student) and Anders Schwartz Vittrup (PhD student)

F13.01   Søren Reinhold Jakobsen. PULMONARY MORPHOLOGY IN THE DECEASED - FORENSIC
PULMONARY IMAGING

F13.02   Nicolai Toft. FUNCTIONAL REGULATION OF NA$^+$,HCO$_3^-$-COTRANSPORT IN HUMAN
~~CANCELLED~~ BREAST CANCER: ASSOCIATION WITH HISTOLOGY, EXPRESSION OF HORMONE AND
GROWTH FACTOR RECEPTORS, AND PROLIFERATIVE ACTIVITY

F13.03   Cathrine Overgaard. PRECLINICAL RELATIVE BIOLOGICAL EFFECTIVENESS (RBE) FOR
NORMAL TISSUE DAMAGE IN ANIMAL MODELS

F13.04   Tenna Vesterman Henriksen. THE EFFECT OF SURGICAL TRAUMA ON CIRCULATING
FREE DNA LEVELS IN CANCER PATIENTS - IMPLICATIONS FOR STUDIES OF
CIRCULATING TUMOR DNA

F13.05   Mette Tiedemann Skipper. THE ACUTE LYMPHOBLASTIC LEUKEMIA SURVIVOR
TOXICITY AND REHABILITATION (ALL-STAR) STUDY

F13.06   Jintao Ren. DEEP LEARNING FOR IMPROVED TUMOUR DELINEATION IN RADIOTHERAPY
OF HEAD AND NECK CANCER

F13.07   Arththy Antony. NA$^+$,HCO$_3^-$-COTRANSPORTERS AS ANTI-CANCER THERAPEUTIC TARGETS

F13.08   Stine Høvring Godsk. IMPROVING THE PROSPECTS OF IMMUNOTHERAPY IN SARCOMA THROUGH INVESTIGATION OF SARCOMA-SPECIFIC IMMUNE-EVADING MECHANISMS

Flash talk session 14

Chairs: Brita Singers Sørensen, Thomas Buus (PhD student) and Marianne Ørum (PhD student)

F14.01   Mads Sandahl. EARLY DETECTION OF CLINICALLY SIGNIFICANT PROSTATE CANCER

F14.02   Ninna Hinchely Ebdrup. NITRATE AND ARSENIC IN DRINKING WATER AND ADVERSE REPRODUCTIVE OUTCOMES IN MEN AND WOMEN

F14.03   Jacob Damgaard Eriksen. RISK FACTORS FOR ANASTOMOTIC LEAK IN PATIENTS UNDERGOING RECTAL RESECTION FOR CANCER. A RETROSPECTIVE, POPULATION-BASED STUDY

F14.04   Anna Louise Christ Vestergaard. VITAMIN D DEFICIENCY IN PREGNANCY - IS INCREASED SUPPLEMENTATION NEEDED?

F14.05   Rosa Marie Østergaard Kiil. PREGNANCY-RELATED MRI FINDINGS AT THE SACROILIAC JOINTS IN FEMALES REFERRED WITH LOW BACK PAIN - A 4-YEAR MRI FOLLOW-UP STUDY

F14.06   Anne Sophie Fischer. COGNITIVE LATE EFFECTS IN CHILDHOOD BRAIN TUMOR SURVIVORS

F14.07   Marie Tvilum Chadwick Hede. OPTIMAL INDIVIDUAL TREATMENT STRATEGY FOR EVERY LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER PATIENT

F14.08   Camilla Ejlertsen. LOOK - YOUR BABY IS TALKING TO YOU

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Chairs: Kristian Stødkilde, Samuel Joseph Windross (PhD student) and Anne Mette Fløe Hvass (PhD student)

F15.01   Kristian Wiborg Antonsen. IS THE SOLUBLE PD-1 VARIANT (SPD-1) EXPRESSED BY HUMAN MACROPHAGES?

F15.02   Alexey Ferapontov. MOLECULAR REQUIREMENTS FOR B CELL RECEPTOR ENGAGEMENT, B CELL ACTIVATION AND RECEPTOR-MEDIATED ENDOCYTOSIS OF ANTIGEN

F15.03   Jacob Thyrsted Jensen. LACTATE INHIBITS TYPE I IFNS TO PROMOTE INFLUENZA A VIRUS REPLICATION IN HUMAN AIRWAY EPITHELIUM

F15.04   *CANCELLED*   Mastaneh Afshar. INVESTIGATION ABOUT SLOW-GROWING BACTERIA AS CAUSATIVE AGENTS OF IMPLANT-ASSOCIATED INFECTIONS: HOW TO DETECT A WOLF IN SHEEP'S CLOTHING

F15.05   Thomas Emmanuel. THE EFFECT OF DEAD SEA CLIMATOTHERAPY ON PSORIASIS SKIN

F15.06   Kamilla Vandsø Petersen. DEVELOPMENT OF A LOW-TECHNOLOGICAL, FAST AND QUANTITATIVE DIAGNOSTIC METHOD FOR DETECTION OF TUBERCULOSIS IN SALIVA SPECIMENS

F15.07   Anne Sophie Schou. USING EXTRACELLULAR VESICLES AS A TEMPLATE FOR
              AUTOIMMUNE DIAGNOSTIC SCREENING

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Chairs: Konstantinos Kamperis, Berit Bargum Booth (PhD student) and Marlene Louise Nielsen (PhD student)

F16.01   Thomas Karmark Dreyer. SURVEILLANCE OF HIGH GRADE NON-MUSCLE INVASIVE
              BLADDER CANCER USING XPERT®BLADDER CANCER MONITOR - SEALS XPERT

F16.02   Amanda Frydendahl Boll Johansen. THE ROLE OF CIRCULATING TUMOR DNA
              ANALYSIS IN THE POST-OPERATIVE MANAGEMENT OF COLORECTAL CANCER
              PATIENTS

F16.03   Simone Weiss. GENOME-WIDE EXPLORATION OF LNCRNAS DRIVING PROSTATE
              CANCER PROGRESSION AND THEIR POTENTIAL AS NOVEL PROGNOSTIC BIOMARKERS

F16.04   Lise Skovgaard Svingel. ACUTE PYELONEPHRITIS: INCIDENCE AND MICROBIOLOGY

F16.05   Maria Bisgaard Bengtsen. ACUTE URINARY RETENTION IN MEN: TRENDS IN INCIDENCE
              AND MORTALITY, 1997-2018

F16.06   Anna Cecilie Lefèvre. CIRCULATING FREE DNA IN ANAL CANCER: RELATION TO RISK
              FACTORS AND RECURRENCE

F16.07   Peder Berg. THE CYSTIC FIBROSIS URINE TEST

F16.08   Josephine Hyldgaard. INFLUENCE OF HORMONE TREATMENT IN BLADDER CANCER -
              INCIDENCE, PROGNOSIS AND FUNCTIONAL OUTCOME

PhD student chairs

CH.01   Gro Grunnet Pløen. SMC PHENOTYPIC MODULATION - A TARGET FOR ALLOGRAFT VASCULOPATHY

CH.02   Kia Busch. BENCHMARKING PROTON THERAPY WATER EQUIVALENT PATH LENGTH CALCULATIONS AGAINST TPS ALGORITHMS

CH.03   Millicent Addai Boateng. ABSTRACT TITLE: CULTURAL ADAPTATION AND PSYCHOMETRIC PROPERTIES OF THE HEALTH LITERACY QUESTIONAIRE (HLQ) IN A GHANAIAN LANGUAGE (AKAN-TWI)

CH.04   Rune Nguyen Rasmussen. A SEGREGATED CORTICAL STREAM FOR RETINAL DIRECTION SELECTIVITY

CH.05   Francesco Maria Iena. THE IMPACT OF HIGH FAT DIET ON GLYCEROL METABOLISM IN ADIPOSE TISSUE IS INFLUENCED BY SEX AND LIRAGLUTIDE TREATMENT.

CH.06   Qichao Zhang. THE MITOCHONDRIAL-PROCESSING PEPTIDASE SUBUNIT BETA INTERACTS WITH AMYLOID BETA AND EXACERBATE THE ALZHEIMER'S DISEASE

CH.07   Maimaitili Muyesier. DIRECT CONVERSION OF FLOOR PLATE CELLS INTO MESDA NEURONS

CH.08   Tingting Gu. EVALUATING THE ROLE OF CONDITIONED EXTRACELLULAR VESICLES IN A TRANSIENT MURINE STROKE MODEL

CH.09   Ole Søndergaard Schwartz. THE CELLS OF THE SUPERIOR COLLICULUS

CH.10   Nanja Holland Hansen. COMPASSION CULTIVATION TRAINING (CCT) FOR INFORMAL CAREGIVERS OF PEOPLE WHO SUFFER FROM A MENTAL ILLNESS.

CH.11   Janne Tidselbak Larsen. ANOREXIA NERVOSA AND INFLAMMATORY BOWEL DISEASES

CH.12   Sif Sund Blandfort. ANALGESIC AND PSYCHOACTIVE MEDICATIONS AND THE RISK OF FALLS IN RELATION TO DELIRIUM IN SINGLE-BED ROOMS COMPARED TO MULTIPLE-BED ROOMS IN GERIATRIC INPATIENTS.

CH.13   Mette Bisgaard Andersen. CYCLING REDUCES BLOOD GLUCOSE EXCURSIONS AFTER AN ORAL GLUCOSE TOLERANCE TEST IN PREGNANT WOMEN: A RANDOMIZED CROSSOVER TRIAL

CH.14   Kata Wolff Pedersen. INVESTIGATING PORCINE CYP PROTEINS IN PLM BY TARGETED PROTEOMICS

CH.15   Nick Yin Larsen. CHARACTERISATION OF MINICOLOUMNARITY AND VOLUME TENSORS OF NEURONS IN BRODMANN AREA 46 IN NORMAL, SCHIZOPHRENIC AND DEPRESSIVE HUMAN AUTOPSY BRAINS

CH.16   Xiaowen Niu. NOVEL THREE-DIMENSIONAL METHODS TO ANALYSE THE MORPHOLOGY OF NASAL CAVITY AND UPPER AIRWAY

CH.17   Maria Keilow. THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE AND STANDARDIZED ACADEMIC TESTS: RELIABILITY ACROSS RESPONDENT TYPE AND AGE

CH.18   Cathrine Hjorth Hansen. EXPLORING DEMENTIA CARE IN A PRIVATE NURSING HOME FOR PEOPLE LIVING WITH DEMENTIA. AN ETHNOGRAPHIC STUDY

CH.19   Sidsel Boie. THE CHILDBIRTH EXPERIENCE QUESTIONNAIRE (CEQ) - VALIDATION OF ITS
CANCELLED   USE IN A DANISH-SPEAKING POPULATION OF NEW MOTHERS STIMULATED WITH OXYTOCIN DURING LABOUR

CH.20   Bodil Karen Bæksted Jørgensen. EARLY TELEREHABILITATION OF GERIATRIC PATIENTS AFTER DISCHARGE FROM ACUTE CARE

CH.21   Haiyun Qi. ASSESSING THE SEX DIFFERENCES OF RENAL FUNCTION AND METABOLISM BY USING HYPERPOLARIZED [1-^{13}C] PYRUVATE

CH.22   Karen Baden Alstrup. CHARACTERISTICS OF PATIENTS TREATED BY THE DANISH HELICOPTER EMERGENCY MEDICAL SERVICE FROM 2014-2018: A NATIONWIDE POPULATION-BASED STUDY

CH.23   Mads Valdemar Anderson. GENOME EDITING BY TRACELESS CRISPR-CAS9 DELIVERY USING LENTIVIRUS-DERIVED NANOPARTICLES

CH.24   *CANCELLED* Liv Marie Duus. COMPARISON OF WHOLE BLOOD AND PLASMA FOR DETECTION OF CYTOMEGALOVIRUS DNA IN TRANSPLANT PATIENTS

CH.25   Lene Wulff Krogsgaard. ARE UNEXPLAINED HEALTH EVENTS FOLLOWING HPV VACCINATION ASSOCIATED WITH PRIOR EBV INFECTION? -A DANISH REGISTERBASED CASE CONTROL STUDY

CH.26   Maja Bendtsen Sharma. SUBSTANTIAL LONG-TERM DOSE-DEPENDENT MORBIDITY AFTER RADIOTHERAPY FOR SINONASAL CANCER. A CROSS SECTIONAL STUDY

CH.27   Mette Eline Brunbjerg. IMMEDIATE IMPLANT-BASED BREAST RECONSTRUCTION. COMPARISON OF TWO SURGICAL METHODS

CH.28   Julie Jacoby Petersen. NAVIGATING THE COMPLEXITY: NURSES' EXPERIENCES WITH CROSS-SECTORIAL COLLABORATION AND PATIENT INVOLVEMENT

CH.29   Helle Elisabeth Andersen. CARING RESPONSIBILITY FROM THE PERSPECTIVES OF OLDER PERSONS WHOSE ADULT CHILDREN ARE THEIR CARERS - A PHENOMENOLOGICAL-HERMENEUTIC STUDY

CH.30   Morten Aagaard Nielsen. CHITINHEPTOSE - A NOVEL ANTIGENIC GLYCAN LINKED TO DIAGNOSIS AND DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS

CH.31   Cecilie Blenstrup Patsche. MID-UPPER ARM CIRCUMFERENCE IS A PREDICTOR OF TUBERCULOSIS WASTING

CH.32   Sara Raquel Almeida Ferreira. INVOLVEMENT OF THE CD163 RECEPTOR IN THE ALPHA-SYNUCLEIN INDUCED NEURODEGENERATION IN PARKINSON'S DISEASE

CH.33   Martin Kinnerup. COGNITIVE IMPAIRMENT IN PARKINSON'S DISEASE

CH.34   Pauline Cantou. NEGATIVE CUES MODULATE CONFLICT PROCESSING: AN FMRI STUDY IN EARLY-ADOLESCENTS

CH.35   Rasmus H. Olesen. OBESITY INCREASE MRNA EXPRESSION OF INFLAMMATORY GENES IN HEALTHY HUMAN BRAINS

CH.36   Simon Bang Kristensen. BIVARIATE LOGISTIC MIXED EFFECT REGRESSION MODELS BASED ON LATENT VARIABLES

CH.37   Mette Jørgine Kirkeby. ANALYSING THE ROLE OF CHILDHOOD NEGATIVE LIFE EVENTS AND DIVERGENSES FROM NORMAL BIOGRAPHY ON LABOUR MARKET TRAJECTORIES OVER THE LIFE-COURSE

CH.38   Martin Rune Hassan Hansen. EXPOSURE TO ORGANOPHOSPHATE INSECTICIDES IS ASSOCIATED WITH DECREASED LUNG FUNCTION: A SHORT-TERM FOLLOW-UP STUDY IN UGANDA

Abstracts

Pankaj Taneja

MULTISENSORY INTEGRATION OF OROFACIAL STIMULI WITH POSSIBLE IMPLICATIONS IN OROFACIAL PAIN

P. Taneja[1, 2], H. Olausson[3], M. Trulsson[2, 4], L. Vase[5], P. Svensson[1, 2, 6], L. Baad-Hansen[1, 2]

[1]Department of Dentistry and Oral Health, Section of Orofacial Pain and Jaw Function, Aarhus University, [2]Scandinavian Centre for Orofacial Neurosciences (SCON), [3]Department of Clinical and Experimental Medicine, Linköping University, Sweden, [4]Department of Dental Medicine, Karolinska Institute, Sweden, [5]Department of Psychology and Behavioural Sciences, Aarhus University, [6]Department of Orofacial Pain and Jaw Function, Faculty of Odontology, Malmö University, Malmö, Sweden

AIMS: To investigate 1.The modulatory effects of painful, pleasant and unpleasant somatosensory stimuli on experimental facial pain. 2.If modulation could be changed by blocking the peripheral nerves via application of a local anaesthetic: EMLA, or by blocking endogenous opioid receptors via naltrexone. 3.Any correlation between pain ratings and psychometrics.

METHODS: 38 healthy women were received either burning facial pain (0.1% capsaicin) or jaw myalgia (hypertonic saline) for 4 randomised sessions. The painful region was stimulated with mechanical and thermal painful, pleasant, unpleasant and control stimuli, with ratings recorded prior to and during stimulation. The sessions differed in pre-treatment: EMLA, naltrexone, placebo tablet/cream.

RESULTS: A significant main effect of thermal and mechanical stimuli was found in both pain models ($P<0.017$). No significant effects of session was identified ($P>0.102$).

Myalgia

Painful cold resulted in greater stimulus-evoked pain reduction than unpleasant cold, pleasant cold, control and pleasant warmth ($P<0.004$). Pain relief from painful, unpleasant and pleasant mechanical stimuli was greater than control ($P<0.002$).

Skin burning pain

Painful cold resulted in greater pain reduction than all but one of the other thermal stimuli ($P<0.033$). The pleasant mechanical stimulus reduced pain more than all other mechanical stimuli ($P\leq0.003$).

CONCLUSION: Painful, unpleasant and pleasant thermal and mechanical stimuli significantly but differentially modulated experimental facial pain ($P<0.017$). EMLA or naltrexone did not significantly affect the modulation and no significant correlations between pain and psychometrics were detected.

Sidsel Støy

LOW INTERLEUKIN-22 BINDING PROTEIN IS ASSOCIATED WITH HIGH MORTALITY IN ALCOHOLIC HEPATITIS

S. Støy[1], T.L. Laursen[1], E. Glavind[1], P.L. Eriksen[1], E. Terczynska-Dyla[2], N.E. Magnusson[3], S. Hamilton-Dutoit[4], F.V. Mortensen[5], S.S. Veidal[6], K. Rigbolt[6], O. Riggio[7], B. Deleuran[8], H. Vilstrup[1], T.D. Sandahl[1]

[1]Department of Hepatology and Gastroenterology, Aarhus University Hospital, [2]Department of Molecular Biology and Genetics, Aarhus University, [3]Diabetes and Hormone Diseases-Medical Research Laboratory, Aarhus University, [4]Department of Pathology, Aarhus University Hospital, [5]Department of Surgical Gastroenterology, Aarhus University Hospital, [6]Gubra, Hørsholm, Denmark, [7]Department of Clinical Medicine, Sapienza University of Rome, [8]Department of Biomedicine, Aarhus University,

Objectives: In alcoholic hepatitis (AH), high IL-22 production is associated with disease improvement, purportedly through enhanced infection resistance and liver regeneration. IL-22 binding protein (BP) binds and controls IL-22 bioactivity, but data on IL-22BP in liver disease suggest more complex interactions. Despite the scarcity of human data, IL-22 is currently in clinical trial as treatment for AH. We, therefore, in AH patients, described the status of the IL-22 system with a focus on IL-22BP and associations with disease course, and mechanistically pursued the human associations in vitro.

Methods: We studied 41 patients with AH at diagnosis, days 7 and 90 and followed them for up to one year. We measured IL-22 pathway proteins in liver biopsies and blood and investigated IL-22BP effects on IL-22 in hepatocyte cultures.

Results: In AH, plasma IL-22BP was reduced to 50% of control. Low plasma IL-22BP was closely associated with high 1-year mortality whereas IL-22 was not. Liver IL-22R protein was elevated together with plasma IL-22 and the IL-22/IL-22BP ratio. Consequently, IL-22 inducible genes were upregulated in AH livers. In hepatocytes, IL-22BP reverted the IL-22 induced lowering of IL-22R. When mimicking AH by stressing hepatocytes and repeating IL-22 stimulation, hepatocytes accordingly maintained higher IL-22R expression and production of antimicrobial genes when IL-22BP was present.

Conclusions: Low plasma IL-22BP is associated with an adverse disease course, possibly because its absence reduces IL-22 signalling. This suggests the interleukin-binding protein interplay to be central in AH pathogenesis and future treatment trials.

Julie Jacobsen

PATIENT-REPORTED OUTCOME AND MUSCLE-TENDON PAIN AFTER PERIACETABULAR OSTEOTOMY ARE RELATED: 1-YEAR FOLLOW-UP IN 82 PATIENTS WITH HIP DYSPLASIA

J.S. Jacobsen[1], K. Søballe[2,3], K. Thorborg[4], L. Bolvig[5], S.S. Jakobsen[2], P. Hölmich[4], I. Mechlenburg[2,3,6]

[1]Department of Physiotherapy and Research Centre in Health and Welfare technology, VIA University College, [2]Department of Orthopaedic Surgery, Aarhus University Hospital, [3]Department of Clinical Medicine, Aarhus University, [4]Sports Orthopaedic Research Center-Copenhagen (SORC-C), Department of Orthopaedic Surgery, Copenhagen University Hospital, Amager-Hvidovre, [5]Department of Radiology, Aarhus University Hospital, [6]Department of Public Health, Aarhus University

Background and purpose

Larger prospective studies investigating periacetabular osteotomy (PAO) with patient-reported outcome measures are lacking, while role of extra-articular structures in relation to the development of pain in hip dysplasia has not been documented. We investigated changes in patient-reported outcome (PRO), changes in muscle-tendon pain, and any associations between them from before to 1 year after PAO.

Patients and methods

Outcome after PAO was investigated in 82 patients. PRO was investigated with the Copenhagen Hip and Groin Outcome Score (HAGOS). Muscle-tendon pain in the hip and groin region was identified with standardized clinical tests, and any associations between them were analyzed with multivariable linear regressions.

Results

HAGOS subscales improved statistically significantly from before to 1 year after PAO with effect sizes ranging from medium to very large (0.66-1.37). Muscle-tendon pain in the hip and groin region showed a large decrease in prevalence from 74% (95% CI 64 to 83) before PAO to 35% (95% CI 25 to 47) 1 year after PAO. Statistically significant associations were observed between changes in HAGOS and change in the sum of muscle-tendon pain, ranging from -4.7 (95% CI -8.4 to -1.0) to -8.2 (95% CI -13 to -3.3) HAGOS points per extra painful entity across all subscales from before to 1 year after PAO.

Interpretation

PAO results in medium to very large improvements in PRO 1 year after PAO, associated with decreased muscle-tendon pain. The understanding of hip dysplasia as solely a joint disease should be reconsidered since muscle-tendon pain seem to play an important role in relation to the outcome after PAO.

O01.01 Martin Mœng SMOOTH MUSCLE CELL SPECIFIC DELETION OF SOX9 INCREASES
        Bjørklund   NECROTIC CORE FORMATION IN ATHEROSCLEROSIS

M.M. Bjørklund[1, 2], D. Morales[2], C.B. Sørensen[1], L. Carramolino[2], J.F. Bentzon[1, 2]

[1]Department of Clinical Medicine, Heart diseases, Aarhus University, Denmark, [2]Spanish National Center for Cardiovascular Research (CNIC), Madrid, Spain

Background: Focal areas of cartilaginous metaplasia are frequent in murine atherosclerosis. They are produced by modulated smooth muscle cells (SMCs) converted to a chondroid phenotype characterized by the expression of the chondrocyte master regulator SOX9. We set out to block the development of cartilaginous metaplasia by SMC-specific deletion of the Sox9 gene and analyze the effects on atherosclerosis.

Methods: We generated mice with a floxed Sox9 gene and a transgene encoding inducible Cre recombinase under a SMC-specific promotor. Hypercholesterolemia and atherosclerosis were induced using a recombinant AAV vector encoding PCSK9 followed by feeding a high-fat diet.

Results: Recombination ratio of the floxed Sox9 gene was 82%. Plasma total cholesterol levels were elevated throughout the study period and no difference in cholesterol burden or en face quantification of aortic lesion areas was detected between the floxed and the control group. Histological examination of lesions in the brachiocephalic artery revealed similar plaque size, but the amount of cartilaginous metaplasia was reduced by 69% in mice with SMC-specific Sox9 deletion, showing the importance of SOX9 for SMC chondroid conversion. The reduced levels of metaplasia were accompanied by a 177% increased necrotic core size.

Conclusion: SOX9 expression in modulated SMCs is crucial for development of intraplaque cartilaginous metaplasia and decreases necrotic core formation in brachiocephalic artery lesions. This suggests a protective role of cartilaginous metaplasia against necrotic core formation. Manipulating this pathway could be a future target for stabilizing atherosclerotic plaques.

O01.02 Johanne   HYALURONIC ACID IS A NEGATIVE REGULATOR OF FIBROBLAST-
        Hovgaard   MEDIATED ENHANCEMENT OF HIV INFECTION
        Egedal

J.H. Egedal[1, 2, 3], T.A. Packard[2], A. Laustsen[1], G. Xie[2, 3], E.A. Thomsen[1], M. Nyegaard[1], W.C. Greene[2], M.R. Jakobsen[1], N.R. Roan[2, 3]

[1]Department of Biomedicine, Aarhus University, Aarhus, Denmark, [2]Gladstone Institutes of Virology and Immunology, San Francisco, USA, [3]University of California, San Francisco, San Francisco, USA

The majority of HIV infections are established via the mucosa. The cells of the mucosal tissue thus form the first line of defense against HIV; however, little is known about their role in transmission. We recently demonstrated that fibroblasts from mucosal transmission sites potently enhance HIV infection of CD4 T cells. Fibroblasts are not permissive to HIV infection but may be important mediators of transmission. Therefore, clarifying how

fibroblasts aid establishment of infection is essential in our battle against HIV.

Fibroblasts are surrounded by an extensive extracellular matrix (ECM). Here, we focused on hyaluronic acid (HA), which is a major component of the ECM, and how it affects the ability of fibroblasts to enhance HIV infection. Using CRISPR/Cas9, we knocked out HAS2, the major enzyme generating HA in fibroblasts. Interestingly, deletion of HAS2 in primary foreskin fibroblasts enhanced HIV infection of CD4 T cells more efficiently than control, HA-producing, fibroblasts. After just 24 hours of co-culture with fibroblasts prior to infection, the CD4 T cell infection rates were significantly increased (control: 3-fold, HAS2KO: 4.7-fold).

Our data suggest that fibroblasts directly modulate CD4 T cells to become more permissive to HIV. This effect is highly influenced by HA levels with a greater enhancement when HA production is reduced.

We are currently analyzing RNAseq data of CD4 T cells exposed to fibroblasts to map out specific genes or pathways that are important for HIV susceptibility. Knowing what makes CD4 T cells prone to infection and how the mucosal tissue acts as a modulator could be key to developing new strategies to prevent HIV infection.

O01.03   Estefano Pinilla   MODULATION OF TRANSGLUTAMINASE 2 CONFORMATION TO COUNTERACT VASCULAR DYSFUNCTION IN DIABETES AND AGING

E. Pinilla[1, 2], V. Matchkov[1], S. Comerma-Steffensen[1], L. Rivera[2], U. Simonsen[1]

[1]Department of Biomedicine, Aarhus University, [2]Department of Physiology, Faculty of Pharmacy, Complutense University of Madrid

Background: Transglutaminase 2 (TG2) open conformation possesses transamidase activity, which is associated with age and diabetes-related changes in vascular stiffness and endothelial function. In contrast, its closed conformation presents GTP binding activity playing a role in transmembrane signaling, opening K^+channels in the vascular smooth muscle (VSM) and it's linked with cell survival. Therefore, the hypothesis of this work is that the pharmacological induction of TG2 to its closed conformation will offer vasoprotective effects, improving endothelial function.

Methods and results: We performed 'ex vivo' measurements of vessel tension using isometric myographs in small arteries from rodents and human patients, as well as patch-clamp studies in isolated cells. These experiments revealed that induction of the closed conformation of TG2 by LDN-27219 potentiated acetylcholine (ACh)-induced vasodilation by increasing the VSM sensitivity to nitric oxide (NO) through the opening of K^+channels, increasing this effect with aging and diabetes. In contrast, drugs that lock TG2 into its open conformation decreased the response to ACh. 'In vivo' measurements of blood pressure (BP) revealed that infusion of LDN-27219 lowered BP more effectively older rats. Three-week 'in vivo' treatment with LDN-27219 prevented endothelial dysfunction to a higher degree than candesartan on a diabetic mice model.

Conclusion: Pharmacological induction of TG2 closed conformation improves endothelial function by VSM sensitization to NO through K^+channel opening. This effect increases with aging and metabolic

imbalance and could be a potential strategy to restore vascular function in patients.

O01.04   Khoa Manh Dinh   THE ASSOCIATION BETWEEN STAPHYLOCOCCUS AUREUS NASAL CARRIAGE, CCR5 Δ32 DELETION AND THE RISK OF INFECTIONS IN HEALTHY INDIVIDUALS: RESULTS FROM THE DANISH BLOOD DONOR STUDY

K.M. Dinh[1], L.T. Erikstrup[2], P.S. Andersen[3, 4], K.R. Nielsen[5], C. Erikstrup[1]

[1]Department of Clinical Immunology, Aarhus University Hospital, [2]Department of Clinical Microbiology, Aarhus University Hospital, [3]Bacteria, Parasites and Fungi, Statens Serum Institut, Copenhagen, [4]Department of Veterinary and Animal Sciences, University og Copenhagen, [5]Department of Clinical Microbiology, Aalborg University Hospital

Background: Staphylococcus aureus (SA) is a dominant pathogen in both community and healthcare settings. Meanwhile, 41% of the healthy population are carriers of SA in the nose. The mechanisms involved in the transition from carriage to infection and the effect of SA carriage among healthy individuals on the risk of subsequent infection are not completely understood.

We aimed to assess the association between SA nasal carriage and the C-C receptor 5 Δ32 deletion and assess the risk of infections.

Methods: Genotyping for CCR5-Δ32 and nasal swabs of 4,759 participants aged 18-67 years from The Danish Blood Donor Study were performed combined with questionnaire data. SA-related infectious diseases and redeemed antibiotics were identified by ICD-10 and ATC codes in the Danish National Registers. Multivariable logistic and cox hazards regression analysis with adjustments were used as statistical models.

Results: CCR5Δ32 homozygotes had a lower risk of SA nasal carriage compared with wildtype (odds ratio=0.76, 95% confidence interval: 0.42-1.35). SA carriage was associated with increased risk of redeemed fucidic acid, especially among men (hazard ratio=1.55, 95% CI: 1.18-2.05). An increased risk of redeemed dicloxacillin/flucloxacillin and hospital admission with SA infections among carriers were observed compared with non-carriers, but did not reach statistical significance.

Conclusion: This study is the first to demonstrate an inverse association between CCR5Δ32 homozygosity and SA nasal carriage. Further, our results indicate a higher risk of skin infections associated with SA nasal carriage. Longer follow-up time will reveal the risk of invasive diseases.

O01.05   Marie Vognstoft Hjortbak   INTERACTIONS BETWEEN INHERENT AEROBIC CAPACITY, MYOCARDIAL ISCHEMIA REPERFUSION AND CARDIOPROTECTION

M.V. Hjortbak[1], T.R. Lassen[1], N.R. Jespersen[1], J.M. Seefeldt[1], P.T. Tonnesen[1], R.V. Jensen[1], N. Jessen[2], M. Pedersen[3], H.E. Bøtker[1]

[1]Department of Clinical Medicine - Cardiology, [2]Department of Clinical Medicine - Steno Diabetes Center Aarhus, [3]Department of Clinical Medicine - Comparative Medicine Lab

Background: Aerobic capacity is a strong predictor of cardiovascular mortality, however, it is not clarified how inherent aerobic capacity affects myocardial ischemia and reperfusion (IR). We aimed to investigate how inherent aerobic capacity affects myocardial IR injury. In addition we wished to investigate how differences in inherent aerobic capacity influenced the effect of ischemic conditioning.

Methods: Rats developed by selective breeding to be either high (HCR) or low (LCR) capacity runners were used. The hearts were mounted in a Langendorff perfusion model, where they were subjected to IR injury. The two types of rats were randomised to one of three protocols: 1. contol, 2. local ischemic preconditioning (IPC) or 3. remote ischemic preconditioning (RIC). The primary endpoint was infarct size (IS). Secondary, mechanistic endpoints were hemodynamic recovery, phosphorylation of the AMPK-pathway, metabolic intermediates, and glucose uptake evaluation.

Results: LCR control animals had significantly smaller IS compared to HCR controls. In both HCR and LCR rats IPC significantly decreased IS compared to corresponding controls. RIC did not provide IS reduction. IPC tended to increase AMPK-phosphorylation equally in both phenotypes. Metabolic metabolites were affected differently by aerobic phenotype, but also by IPC. Most pronounced was increased interstitial concentration of citrate at end ischemia in LCR animals compared to HCR animals.

Conclusion: LCR animals were less sensitive to IR injury compared to HCR animals. IPC was effective independent of the phenotype. IPC activates AMPK similarly in both LCR and HCR animals, but responses in cellular metablism may differ.

O01.06   Mads Dam Lyhne COMBINATION OF RIGHT VENTRICULAR FUNCTION AND PULMONARY PRESSURE IMPROVES PREDICTION OF ADVERSE OUTCOME IN ACUTE PULMONARY EMBOLISM

M.D. Lyhne[1, 2, 3], C. Kabrhel[2], N. Giordano[2], A. Andersen[1], J.E. Nielsen-Kudsk[1], H. Zheng[4], D. Dudzinski[3]

[1]Department of Cardiology, Department of Clinical Medicine, Aarhus University Hospital, Denmark, [2]Department of Emergency Medicine, Massachusetts General Hospital, Boston, [3]Department of Cardiology, Massachusetts General Hospital, Boston, [4]Biostatistics Center, Massachusetts General Hospital, Boston

Background: Right ventricular (RV) failure causes death in acute pulmonary embolism (PE). RV failure is a consequence of mismatch between RV function and afterload. We derived an echocardiographic index of this mismatch: systolic function by tricuspid annular plane systolic excursion (TAPSE) divided by pulmonary arterial systolic pressure (PASP).

We hypothesized, that TAPSE/PASP in PE patients would predict outcome better than the two measurements separately.

Methods: Patients were from a single center Pulmonary Embolism Response Team registry 2012-2019 with confirmed PE and a formal echocardiogram performed within 3 days. All echocardiograms were analyzed blinded to the outcome. Primary endpoint was a composite of

7-day mortality or clinical deterioration. Secondary outcomes were 7- and 30-day all-cause mortality.

Results: A total of 627 patient were included in the analyses; 135 met the primary endpoint. In univariate analysis, the TAPSE/PASP predicted outcome with OR=0.028 (95%CI 0.010-0.087, p<0.0001) and did so significantly better than TAPSE or PASP alone. When adjusting for either elevated biomarkers or other echocardiographic findings of RV dysfunction, the TAPSE/PASP ratio still predicted primary endpoint.

In multivariate analysis, TAPSE/PASP independently predicted adverse outcome (OR 0.026, 95%CI 0.008-0.080, p<0.0001).

TAPSE/PASP predicted both 7-days and 30-days all-cause mortality, which TAPSE or PASP did not.

In conclusion, TAPSE/PASP is a stronger predictor of clinical deterioration and mortality in acute PE compared to TAPSE and PASP alone. This easily obtainable measurement may be useful in optimizing risk stratification of patients with acute PE.

O02.01   Line Stensig Lynggaard

ASPARAGINASE ENCAPSULATED IN ERYTHROCYTES - A PROMISING ALTERNATIVE TO PEG-ASPARAGINASE IN CASE OF HYPERSENSITIVITY IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA.

L.S. Lynggaard[1], S.G. Højfeldtst[1], G. Vaitkeviciene[2], C. Langenskiöld[3], A.K. Lehmann[4], P.M. Lähteenmäki[5], K. Lepik[6], K. Schmiegelow[7], B.K. Albertsen[1]

[1]Children and Adolescent Health, Aarhus University Hospital , [2]Centre for Pediatric Oncology and Hematology, Children's Hospital, Affiliate of Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania., [3]Department of Pediatrics, Institute of Clinical Sciences, University of Gothenburg, Gothenburg, Sweden., [4]Department of Oncology, Haukeland University Hospital, Bergen, Norway., [5]Department of Pediatric and Adolescent Medicine, Turku University Hospital and Turku University, Turku, Finland., [6]Department of Hematology and Oncology, Tallinn Childrens hospital, Tallin, Estonia, [7]Children and adolescent health, Rigshospitalet, Copenhagen

Asparaginase is an important part of the treatment of acute lymphoblastic leukemia (ALL) in children. Hypersensitivity is a common course of truncated therapy and may decrease disease free survival. Asparaginase encapsulated in erythrocytes (GRASPA®) is an alternative formulation in which the erythrocyte membrane protects the asparaginase against elimination and prevents activation of the immune system.

The aim of the study is to evaluate the safety and efficacy of GRASPA®.

NOR-GRASPALL 2016 is a Nordic/Baltic multinational multicentre single-arm study for non-high risk patients with ALL and hypersensitivity (clinical allergy or silent inactivation) to PEG-asparaginase. GRASPA® replaces the remaining doses of PEG-asp (1-7 doses, 150 IU/kg). Measurements of enzyme activity and amino acids in cerebrospinal fluid are used for treatment monitoring.

Preliminary results: 34 patients are included in the study (33 with clinical allergy, one with silent inactivation). 119 doses are administered. 87.8% of the patients had adequate enzyme activity (>100 IU/l) 14 days after

GRASPA® administration, 80.3% after 21 days and 60% after 42 days. The median activity levels were 710 IU/L [IQR: 406-1018], 505.5 IU/L [IQR: 173.5-772.3] and 184.5 IU/L [IQR:0-301.5] after 14, 21 and 42 days respectively.

One patient had a severe hypersensitivity reaction to GRASPA®. No severe adverse events with relation to GRASPA® have been reported.

The preliminary results indicate a good tolerance and safety profile of GRASPA®. Patients had enzyme activity above therapeutic target for a longer period compared to PEG-asp.

We expect to complete the study in 2020, when 50 patients are included.

O02.02   Sofia Spampinato

RISK FACTORS FOR URINARY INCONTINENCE AFTER RADIOTHERAPY IN LOCALLY ADVANCED CERVIX CANCER: AN EMBRACE ANALYSIS

S. Spampinato[1], L.U. Fokdal[1], R. Pötter[2], C. Haie-Meder[3], J.C. Lindegaard[1], M. Schmid[2], I. Jürgenliemk-Schulz[4], U. Mahantshetty[5], B. Segedin[6], K. Bruheim[7], P. Hoskin[8], B. Rai[9], F. Huang[10], R. Cooper[11], E. van der Steen-Banasik[12], E. van Limbergen[13], R. Nout[14], C. Kirisits[2], K. Kirchheiner[2], K. Tanderup[1]

[1]Aarhus University Hospital, Department of Oncology, Aarhus, Denmark., [2]Medical University/General Hospital of Vienna, Department of Radiation Oncology- Comprehensive Cancer Center, Vienna, Austria., [3]Gustave-Roussy, Department of Radiotherapy, Villejuif, France., [4]University Medical Centre Utrecht, Department of Radiation Oncology, Utrecht, The Netherlands., [5]Tata Memorial Hospital, Department of Radiation Oncology, Mumbai, India., [6]Institute of Oncology Ljubljana, Department of Radiotherapy, Ljubljana, Slovenia., [7]The Norwegian Radium Hospital- Oslo University Hospital, Department of Oncology, Oslo, Norway., [8]Mount Vernon Hospital, Mount Vernon Cancer Centre, Northwood, United Kingdom., [9]Postgraduate Institute of Medical Education and Research, Department of Radiotherapy and Oncology, Chandigarh, India., [10]Cross Cancer Institute and University of Alberta, Department of Oncology, Edmonton, Canada., [11]St James's University Hospital, Leeds Cancer Centre, Leeds, United Kingdom., [12]Radiotherapiegroep Arnhem, Department of Radiotherapy, Arnhem, The Netherlands., [13]UZ Leuven, Department of Radiation Oncology, Leuven, Belgium., [14]Department of Radiation Oncology, Leiden University Medical Center, The Netherlands.

AIM

To identify risk factors for urinary incontinence in Locally Advanced Cervical Cancer (LACC) patients treated with radiochemotherapy and Image-Guided Adaptive Brachytherapy (IGABT).

MATERIAL/METHODS

LACC patients within the EMBRACE I study (An international study on MRI-guided brachytherapy in LACC), that enrolled 1416 patients treated from 2008 to 2015, were analysed. Physician assessed (CTCAEv.3) and patient reported (EORTC) urinary incontinence was evaluated. Patient, disease and treatment parameters were tested as risk factors. Minimal dose to the most exposed 2cm^{3}of the bladder (D$_{2cm3}$) and ICRU bladder point (BP) dose were tested as dosimetric factors. Incidence of severe(G≥3) and moderate grade(G≥2) CTC, as well as "Very much" and "Quite a bit+Very

much" (≥Quite a bit) EORTC answers were investigated in univariate (UVA) and multivariable (MVA) analyses (Cox).

RESULTS

1153 and 884 patients had baseline and at least one follow-up assessed for CTC and EORTC, respectively. Median follow-up was 48(1-124) months. Crude incidences for CTC G≥3 and G≥2 were 1,4% and 10,9%, respectively. Crude incidences for EORTC Very much and ≥Quite a bit were 6% and 18,1%, respectively.

ICRU BP dose was a risk factor for CTC G≥2, G≥3 and EORTC Very much. Baseline incontinence and body-mass-index were risk factors for most CTC and EORTC scores. Age was significant in UVA, but correlated with ICRU BP dose and was not tested in MVA. Smoking was a risk factor for EORTC scores.

CONCLUSION

ICRU BP dose, rather than bladder D_{2cm3}, is a risk factor for severe/moderate incontinence. This finding emphasizes the importance of ICRU BP, which is closely related to structures responsible for incontinence.

O02.03   Mads Ryø Jochumsen   CAN TUMOR BLOOD FLOW ESTIMATE PROSTATE CANCER AGGRESSIVENESS?

M.R. Jochumsen[1, 2], B.G. Pedersen[3, 2], L.P. Tolbod[1], J. Frøkiær[2, 1], M. Borre[4, 2], K. Bouchelouche[1, 2], J. Sørensen[1, 2]

[1]Department of Nuclear Medicine and PET-Centre, Aarhus University Hospital, [2]Department of Clinical Medicine, Aarhus University, [3]Department of Radiology, Aarhus University Hospital, [4]Department of Urology, Aarhus University Hospital

Objective: Our previous studies suggest that tumor blood flow measured with[82]Rb Positron Emission Tomography (PET) is a potential biomarker of prostate cancer aggressiveness. The aim of the present study was to evaluate this in a larger cohort.

Methods: 102 patients were included prior to MRI-guided prostate biopsies.[82]Rb PET scan of the prostate gland was performed in all patients. Prostate cancer was biopsy-verified in 85 of the patients. Tumor segmentation was performed at all MRI scans and the segmentations were fused with the[82]Rb PET scans for measurement of tumor uptake.

Results: Tumor[82]Rb uptake correlated moderately with MRI-guided biopsy Gleason Grade Group, with SUVmax showing the best correlation (rho=0.57, p<0.0001). Mean[82]Rb uptake (SUVmax) in low-risk prostate cancer 2.87 with 95% CI [2.56 ; 3.17] was significantly lower than in both intermediate- 3.74 [3.53 ; 3.95] and high-risk prostate cancer 4.17 [3.63 ; 4.71] (p<0.001).

Conclusions: Tumor[82]Rb uptake and hence blood flow has a moderate correlation with prostate cancer aggressiveness and may be helpful in separating clinically significant from insignificant prostate cancer.

O02.04   Michael Brun Andersen

IMPACT OF SPECTRAL IMAGING IN PATIENTS SUSPECTED FOR OCCULT CANCER: A STUDY OF 93 PATIENTS

M.B. Andersen[1, 3], D. Ebbesen[1], J. Thygesen[1], M. Kruis[2], F. Rasmussen[1]

[1]Department of Radiology, Aarhus University Hospital, [2]Philips Denmark, [3]Copenhagen University Hospital

Purpose: To investigate the impact of spectral dual layer detector CT in cancer compared to CE-CT.

Methods and Materials: In a national work-up program for occult cancer ninety-three patients prospectively enrolled had a contrast enhanced Philips IQon Spectral CT scan. The readings were performed with and without spectral data available. A minimum of 3 months between interpretations were implemented to eliminate recall bias. The sequence of reads for the individual patient was randomised. Readers were blinded for patient identifiers and clinical outcome. Two radiologists with 9 and 33 years of experience performed the readings in consensus. If disagreement, a third specialist radiologist with 11 years of experience determined the outcome of the reading.

Results: Significantly more (probable) cancer findings were identified on the spectral reading (six vs. one, p=0.03). Eight probable cancer findings on CE-CT were excluded as cancer on spectral CT. In thirty-four possible cancer findings, spectral added to the diagnosis in nine-teen cases. For the possible cancer findings, spectral information was strongly correlated with a difference between the spectral and conventional reading (P<0.001).Hundred-and-four benign lesions were found on CE-CTand spectral datasets (multiple lesions per patient could be present). In the conventional readings, the radiologists were entirely certain about the benignity in 60% of the cases and in the spectral readings in 89% of the cases (p<0.0001).

Conclusion: In conclusion, we find that access to spectral data adds to find (probable) cancer or exclude the diagnosis. Furthermore, it increases the radiologists' certainty about benign lesions.

O02.05   Jakob Haldrup Jensen

FRMD6 IS A NOVEL TUMOR SUPPRESSOR GENE IN PROSTATE CANCER

J. Haldrup[1, 2], S. Strand[1, 2], C. Cieza-Borrella[3], M. Jakobsson[4], M. Riedel[5], M. Norgaard[1, 2], S. Hedensted[1, 1], F. Dagnaes-Hansen[5], B. Ulhoi[6], R. Eeles[3], M. Borre[7], J. Olsen[4], M. Thomsen[5], Z. Kote-Jarai[3], K. Sorensen[1, 2]

[1]Department of Molecular Medicine (MOMA), Aarhus University, [2]Department of Clinical Medicine, Aarhus University, Aarhus, Denmark., [3]Oncogenetics, Division of Genetics and Epidemiology, The Institute of Cancer Research, London, UK., [4]Novo Nordisk Foundation Center for Protein Research, University of Copenhagen, Copenhagen Denmark., [5]Department of Biomedicine, Aarhus University, Aarhus, Denmark., [6]Institute of Pathology, Aarhus University Hospital, Aarhus, Denmark. e

me)], [7]Department of Urology, Aarhus University Hospital, Aarhus, Denmark. me)]

Available tools for prostate cancer (PC) prognosis are suboptimal but may be improved by better knowledge about genes that drive tumor aggressiveness. Here, we identified FRMD6 (FERM domain-containing protein 6) as an aberrantly hypermethylated and significantly downregulated gene in PC. Low FRMD6 expression was associated with post-operative biochemical recurrence in two large PC patient cohorts. In overexpression and CRISPR-Cas9 based knockout experiments in PC cell lines, FRMD6 inhibited viability, proliferation, cell cycle progression, anchorage-independent colony formation, 3D spheroid growth, and tumor xenograft growth in mice. Transcriptomic and proteomic analyses revealed enrichment of c-MYC signaling, mitochondrial, and ribosomal biogenesis upon FRMD6 knockout. In addition, enrichment of Hippo/Yap signaling was identified in the corresponding phospho-proteomes. Connectivity Map analysis and drug repurposing experiments identified pyroxamide as a new potential therapy for PC with FRMD6 loss. Finally, we used CRISPR-Cas9 to knockout Frmd6 and Pten, or Pten only (control), in the mouse prostate. After 12 weeks, Frmd6/Pten double-knockouts presented with high-grade prostatic intraepithelial neoplasia (HG-PIN) and hyperproliferation, while Pten single-knockouts developed only regular PIN lesions and displayed lower proliferation. In conclusion, we identified FRMD6 as a novel tumor suppressor gene and prognostic biomarker candidate in PC.

O03.01 Benedicte Marie Winther Johannsen

SOMATIC MORBIDITY AND MORTALITY IN WOMEN WITH POSTPARTUM PSYCHIATRIC DISORDERS

B.M. Johannsen[1], T.M. Laursen[1], B.H. Bech[2], T. Munk-Olsen[1]

[1]National Centre for Register-based Research, Department of Economics and Business Economics, Aarhus University, [2]Department of Public Health, Aarhus University

Background:

Psychiatric patients have increased risk of somatic morbidity and mortality, but no study has systematically explored if this is also the case for women with mental disorders triggered by childbirth (postpartum psychiatric disorders: PPD). Therefore, the aim of this study was to investigate somatic morbidity and mortality in women with a spectrum of PPD.

Methods:

A register-based cohort study included Danish women born after Jan. 1st 1960 who were followed until Dec. 31st 2015. Exposure of interest was 1) mild-moderate PPD: first ever prescription of psychotropic medication (ATC codes: N03-N07) and 2) severe PPD: first ever in- or outpatient contact to a psychiatric facility, both within 6 months postpartum. Outcomes of interest were 1) hospital-registered chronic somatic morbidity and 2) mortality from natural and unnatural causes. We included 1,841,949 women representing 22,615,310 person years at risk.

Results:

Among 15,852 women with mild-moderate PPD and 4,266 women with severe PPD we found higher risk of subsequent somatic morbidity (mild-

moderate PPD: HR 1.25; 95%CI 1.20-1.31 and severe PPD: HR 1.35; 95%CI: 1.24-1.48) when compared to the female background population. Mortality from both natural and unnatural causes was also higher in both groups: Mild-moderate PPD: natural causes MRR 1.37; 95%CI: 1.17-1.61; unnatural causes MRR 1.52; 95%CI: 1.10-2.11), severe PPD: natural causes MRR 1.42; 95%CI 1.02-2.00, and unnatural causes MRR 5.05; 95%CI: 3.40-7.51.

Conclusions:

This first overview of somatic prognosis in PPD shows that women at either end of the spectrum are at increased risk of subsequent somatic morbidity and overall mortality.

O03.02 Sara Koed Badre-Esfahani

NEARLY ONE THIRD OF WOMAN WITH NON-NATIVE BACKGROUND, NEITHER ATTEND HPV-VACCINATION NOR CERVICAL CANCER SCREENING - A NATIONWIDE DANISH REGISTER-BASED COHORT STUDY

S. Badre-Esfahani[1, 2, 3], M.B. Larsen[2], L. Seibæk[1, 3], L.K. Petersen[4, 5], J. Blaakær[4, 6], B. Andersen[2]

[1]Department of Clinical Medicine, Aarhus University, [2]Department of Public Health Programmes, Randers Regional Hospital, [3]Department of Gynaecology and Obstetrics, Aarhus University Hospital, [4]Department of Gynaecology and Obstetrics, Odense University Hospital, [5]OPEN Open Patient data Explorative Network, University of Southern Denmark, [6]Department of Clinical Research, University of Southern Denmark

Background: Cervical cancer is preventable through routine Human Papilloma Virus vaccination (HPVV) and cervical cancer screening (CCS). However, due to socio-cultural barriers, it is likely that non-native women, especially from Middle-Eastern and North-African (MENA) countries, are more prone than native women, neither to attend HPVV nor CCS (combined non-attendance). We aimed to investigate differences in degree of combined non-attendance in Denmark; and to analyze association between country of origin and combined non-attendance adjusted for socio-economic status.Methods: Logistic regression was performed to estimate the adjusted odds ratio (OR) with 95% CI for combined non-attendance compared to some degree of attendance.Results: 170,158 women were included. Degree of combined non-attendance was 10.0 % [9.8-10.1] among natives and 27.1% [26.4-27.7] among non-natives. Among all regions, degree of combined non-attendance was highest for women from MENA region (30.1% [29.2-30.9]), with a large country specific variation. There was furthermore a strong association between MENA origin and combined non-attendance. Somali women showing the strongest association (adj. OR=7.5 [6.3-8.9].Conclusion: Denmark has relatively low degree of combined non-attendance. However, the HPVV and CCS programs seem to be better tailored to the needs of native women and may not be sufficiently cater for the needs of the fast-growing and diverse non-native population. In order to secure more equal attendance in cervical cancer prevention in the future, upcoming studies should address this apparent ethnic inequality as well as focus on developing interventions sensitive to socio-cultural factors.

O03.03 Maria Daniella Bergholt DO PATIENTS RECEIVE MORE APPROPRIATE HEALTHCARE IN ACCREDITED HOSPITALS?

M.D. Bergholt[1, 5], A.M. Falstie-Jensen[2], C. Von Plessen[3], S.P. Johnsen[4]

[1]Department of Clinical Epidemiology, Aarhus University Hospital, [2]The Danish Clinical Registries, [3]Department of Clinical Research, University of Southern Denmark, [4]Department of Clinical Medicine, Aalborg University, [5]Department of Anaesthesiology, Gentofte University Hospital

Introduction: Accreditation is an important quality improvement activity worldwide, however its evidence base is weak. Objective: This study aims to examine changes in the delivery of appropriate (in-line with evidence) patient care after meeting accreditation standards. Method: A pre-/post study based on medical record audits in all Faroe Islands hospitals. We compared the fulfillment of process performance measures before and after the first accreditation round. Patients with 1 of 7 clinical conditions were included if they were patients at the hospitals between 2012-2013 (before accreditation) or during 2017-2018 (after accreditation). Outcome measures: Appropriate healthcare defined as 67 process performance measures reflecting clinical guidelines recommendations. Process performance measures were assessed both as an opportunity-based composite score and an all-or-none score. Results: 475 inpatients and 392 outpatients from 3 hospitals participated in the study. The total opportunity-based composite score was marginally higher after the hospitals were accredited (adjusted difference percentage point, 4.4% [95% CI -0.7;9.6]) though the change did not reach statistical significance. Nevertheless, patients treated in a hospital after accreditation, had significantly higher probability of receiving all the appropriate healthcare (total all-or-none adjusted relative risk, (RR) 2.32 [95% CI 2.03;2.67]) compared to patients treated before accreditation. Conclusion: Patients treated in a hospital after it has been accredited received more appropriate healthcare in-line with the clinical guidelines, compared to patients treated in a non-accredited hospital.

O03.04 Malene Thygesen THE ASSOCIATION BETWEEN RESIDENTIAL GREEN SPACE IN CHILDHOOD AND DEVELOPMENT OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A POPULATION-BASED COHORT STUDY

M. Thygesen[1, 2, 3], K. Engemann[4, 8], G.J. Holst[1, 5, 8], B. Hansen[6], J. Brandt[7], C. Geels[7], C.B. Pedersen[1, 2, 3, 8], S. Dalsgaard[1, 2, 3]

[1]National Centre for Register-based Research, Department of Economics and Business, Aarhus University, [2]The Lundbeck Foundation Initiative for Integrative Psychiatric Research, iPSYCH, Aarhus and Copenhagen, [3]Centre for Integrated Register based Research, CIRRAU, Aarhus University, [4]Center for Biodiversity Dynamics in a Changing World (BIOCHANGE), Aarhus University, [5]Department of Public Health, Section of Environment, Occupation and Health, Aarhus University, [6]Geological Survey of Denmark and Greenland, GEUS, [7]Department of Environmental Science, Aarhus University, [8]Big Data Centre for Environment and Health, BERTHA, Aarhus University

Background: Access to green space may be associated with beneficial effects on children's mental well-being. In a nationwide cohort, we

investigated associations between residential green space and a clinical diagnosis of Attention-Deficit Hyperactivity Disorder (ADHD).

Methods: Individuals born in Denmark 1992-2007 (n=814 834) were followed for ADHD from age five, during 1997-2016. Exposure was measured as the normalized difference vegetation index (NDVI) averaged between birth and the 5[th]birthday at historically updated residential addresses. We estimated incidence rate ratios (IRRs) with 95% confidence intervals (CI) for ADHD, according to exposure-level, adjusted for calendar time, age, sex, obstetrical factors, mental disorders and parental socioeconomic status. Furthermore, we examined confounding effects of air pollutants.

Results: Individuals living in areas defined by sparse green vegetation (lowest decile of NDVI) had an increased risk of developing ADHD (IRR=1.35; 95% CI: 1.28-1.42), compared with children living in areas within the highest decile of NDVI. After adjusting for the traffic-related air pollutant nitrogen dioxide (NO_2) the association was attenuated (IRR=1.17; 95% CI: 1.11-1.24), while further adjustment for fine particulate matter ($PM_{2.5}$) did not change this result.

Conclusions: Our findings suggest that access to green space during early childhood may be associated with a lower risk of developing ADHD. However, the association was in part confounded by exposure to air pollution, suggesting that part of the association between green space and ADHD may be explained by the lower exposure to air pollution, especially NO_2, in greener areas.

O03.05 Signe Hjuler Boudigaard

OCCUPATIONAL EXPOSURE TO RESPIRABLE QUARTZ AND RISK OF SYSTEMIC SCLEROSIS: A COHORT STUDY OF THE DANISH WORKING POPULATION 1977-2015

S.H. Boudigaard[1], V. Schlünssen[2], K. Søndergaard[3], K. Tóren[5], H. Kromhout[4], H.A. Kolstad[1]

[1]Department of Occupational Medicine, Danish Ramazzini Centre, Aarhus University Hospital, [2]Department of Public Health, Danish Ramazzini Centre, Aarhus University, [3]Department of Rheumatology, Aarhus University Hospital, [4]Institute of Risk Assessment, Utrecht University, the Netherlands, [5]Occupational and Environmental Medicine, Sahlgrenska Academy, University of Goteborg, Sweden

Background

Exposure to respirable quartz may increase the risk of systemic sclerosis. The aim of this study was to examine the association between respirable quartz exposure and systemic sclerosis and to explore the exposure-response relationship.

Method

We followed 3 million workers 1977-2015. We assigned each worker a quartz exposure level for each year of work based on an international quantitative job exposure matrix (SYNJEM). Recent Danish quartz measurements showed a reasonable correlation with SYNJEM estimates for 2015. Cases were identified in national health registers, and gender-

specific exposure response relations by cumulative exposure in different time windows were investigated.

Results

A total of 300 000 workers held a quartz exposed job at some point during their work history. We identified 998 cases of systemic sclerosis. Analyses adjusted for age, educational level and history of another autoimmune rheumatic disease comparing highest cumulative exposure with null-exposure showed a statistically non-significant increased risk of systemic sclerosis among both sex´s. Internal analyses restricted to the exposed workers showed a 10 % increase in risk per 0.05 mg/m^3-years (p=0.04) among men but no trend among women. Cumulative exposure accrued more than 20 years prior were most influential for the exposure-dependent increasing risk-ratios for men (IRR =1.7, p=0.06) and women (IRR=2.3, p=0.07) when comparing highest with the null-exposed.

Conclusion

This study suggests an exposure-dependent association between occupational exposure to respirable quartz and risk of systemic sclerosis with a latency of about 20 years. Among exposed men the relation was log-linear.

O03.06 Daniel Borch Ibsen

REPLACING RED MEAT WITH ALTERNATIVE FOOD SOURCES OF PROTEIN ON THE RISK OF DEVELOPING TYPE 2 DIABETES - MODELLING DIETARY CHANGES IN A CAUSAL FRAMEWORK

D.B. Ibsen[1], M.U. Jakobsen[2], E.T. Parner[3], K. Overvad[1]

[1]Research Unit for Epidemiology, Department of Public Health, Aarhus University, [2]National Food Institute, Division for Diet, Disease Prevention and Toxicology, Technical University of Denmark, [3]Research Unit for Biostatistics, Department of Public Health, Aarhus University

Objective: We wanted to answer the question of whether decreasing the intake of red meat and simultaneously increasing the intake of alternative food sources of protein affects the risk of type 2 diabetes compared with no changes in the substituted foods. We also examined interaction with the age at which participants changed their diet.

Methods: We used the Danish Diet, Cancer and Health cohort including men and women, two measures of diet taken roughly 5 years apart and information on incident type 2 diabetes (n=39,349; aged 55 to 72 years at the second diet measure). The pseudo-observation method was used to estimate the average exposure effect of decreasing the intake of red meat (processed and unprocessed) while increasing the intake of either poultry, fish, cheese, eggs or whole grains compared with no changes in the substituted foods on the subsequent 10-year risk of developing type 2 diabetes.

Results: We found that replacing 1 serving/day (100 g/day) of red meat with 1 serving/day of eggs (risk difference -2.4, 95% confidence interval -3.7 to -1.1%; per 50g/day) or whole grains (-1.4, -2.2 to -0.6%; per 30 g/day) was associated with a reduced risk of type 2 diabetes. No effects were observed for other replacement foods. The lowest risk was observed

for replacements at age 55 years compared with older ages (up to 70 years) for all replacements.

Conclusion: Replacing red meat with eggs or whole grains may reduce the risk of type 2 diabetes compared with no changes in the substituted foods and changing diet in midlife may be more beneficial than at older ages.

O04.01 Jose Manuel Cerdan de Las Heras

TELE-REHABILITATION PROGRAM IN IDIOPATHIC PULMONARY FIBROSIS

J. Cerdan de las Heras[1], O. Hilberg[2], A. Løkke[2], S. Ekholm[3], E. Bendstrup[1]

[1]Department of Respiratory Diseases and Allergy, Aarhus University Hospital, [2]Department of Respiratory Diseases, Hospital Little Belt, [3]Physio RandD IVS - Copenhagen

BACKGROUND

In Idiopathic Pulmonary Fibrosis (IPF), pulmonary rehabilitation (PR) is recommended to improve quality of life (QoL) and exercise capacity (EC). Not all patients with IPF can participate in hospital based PR due to frailty and long travelling distances. Tele-rehabilitation (TR) might be an alternative solution. We investigated the feasibility and efficacy of TR on EC and QoL in patients with IPF.

METHOD

Single-center, prospective, randomized study, including stable patients with IPF for 3 months (3M) of TR: video and chat-consultations with a real physiotherapist and workout sessions with a virtual autonomous physiotherapist agent (VAPA). Forced vital capacity (FVC), diffusion capacity (DLCO) was registered at baseline (BL). EC evaluated with 6-minute-walk-test distance (6MWTD) and QoL with Kings Brief Interstitial Lung Diseases (KBILD) and St. George's Respiratory Questionnaire (SGRQ) at baseline, 3,6 and 9 months follow up. Control patients did not receive hospital-based PR.

RESULTS

29 patients were included, 15 in the intervention group (IN) (male 86.7%, mean age 69.7±8.7 years, FVC % 76.7±16.4, DLCO % 46.5±11), and 14 in the control group (CO) (male 57.1%, mean age 72±7.6 years, FVC % 90.8±16.5, DLCO % 55±14).Favorable 6MWTD difference for IN at 3 month +39.5m (P=0.03); 6 month +34.3m (P=0.02); 9 month +40.0m (P=0.15). QoL had no difference between groups.

CONCLUSION

Tele-rehabilitation with VAPA is feasible for IPF, exercise capacity was maintained at 3 and 6 months follow up while remarkable decrease was shown in the control group. No change in Quality of Life was shown.

O04.02 Søren Helbo Skaarup

INTRA LYMPHATIC ALLERGEN IMMUNE THERAPY.

S.H. Skaarup., J. Schmid, T. Skjold, H.J. Hoffmann

Department of Respiratory Medicine and Allergy. Aarhus University Hospital

Introduction:

Grass pollen allergy affects nearly 1 of 10 Danes. Allergen specific immunotherapy, AIT, is indicated when local acting antihistamine and steroid treatment insufficiently relive symptoms. Intra lymphatic AIT is a new administration form that is completed within 3 months. AIT is directed into the lymph nodes thus optimizing immune changes leading to symptom reduction.

We aimed to study the clinical effect of intra lymphatic allergen specific immunotherapy with a double-blinded randomized placebo-controlled study.

Methods:

Patients with grass pollen allergy were randomized into three groups of 12. They were treated with either grass allergen, ALK 225, or sterile isotone saline injected into inguinal lymph nodes under ultrasound guidance.

The primary outcome was self-reported combined score of allergy symptoms and medication, cSMS, during the next three grass pollen seasons.

Results:

32 patients were recruited.

cSMS score was reduced with 37% (95%CI 27%-43%), p=0.04 in the follow-up period. In the first pollen season, placebo scored 5.8 (95%CI 3.6-8) vs. intralymphatic immunotherapy score at 3.5 (95%CI 2.7-4.2), p=0.03. No significant difference was observed in the two following seasons. cSMS response to grass pollen exposure was different between groups, 1.4(95%CI 1.3-1.5) vs. 1.0 (95%CI 0.9 - 1.1) Correlation between cSMS and grass pollen exposure was different in the follow-up period.

Conclusion:

Intra lymphatic allergen specific immunotherapy reduces allergy symptoms use of rescue medicine and lowers response to pollen exposure. These results may lead to may change management of allergy.

O04.03 Gabriela Silote CANNABIDIOL AND S-KETAMINE ANTIDEPRESSANT EFFECTS ARE ASSOCIATED WITH GENE EXPRESSION CHANGES IN THE BRAIN OF THE FLINDERS SENSITIVE LINE RAT

G.P. Silote[1, 2], L. Reinert[3], J. Hasseltrøm[4], G. Wegener[2], S.R.L. Joca[1, 2, 5]

[1]School of Pharmaceutical Science of Ribeirão Preto, University of São Paulo, [2]Translational Neuropsychiatry Unit, Department of Clinical Medicine, Aarhus University, [3]Department of Biomedicine, Aarhus University, [4]Department of Forensic Medicine, Aarhus University, [5]Aarhus Institute of Advanced Studies, AIAS, Aarhus University

Cannabidiol (CBD) exhibit rapid antidepressant-like effects in rodent models, usually associated to neuroplastic changes in the prefrontal cortex (PFC) and hippocampus (HPC). However, the molecular mechanisms underlying these effects are not yet known. Thereby, we investigated herein the effects induced by CBD and S-ketamine (KET) effects, another fast-acting antidepressant, in stress-induced gene

expression in a genetic model of depression, Flinders Sensitive Line (FSL) rats.

Adult male FSL and their controls (FRL) were treated with CBD (30 mg/kg), S-ketamine (15 mg/kg) or vehicle and submitted to behavioral testing (open field and forced swimming, FST), 1h later. Animals were killed after testing to collect blood (CBD levels, LC-MS) and brain (PFC and HPC) samples for gene expression analysis: 48 genes (Fluidigm).

Both CBD and ketamine reversed the depressive-like phenotype of FSL animals. There was no correlation between CBD blood levels and immobility time in the FST. FSL-VEH group showed decreased gene expression of plasticity related genes, compared to FRL-VEH: BDNF, GSK-3β, TrkB (both regions), PSD-95, Vegfa, PKA (HIP), Nr2a (PFC) and increase expression of GluR2 (both regions). Interestingly, CBD attenuated the decreased expression of Nr2a and Vegfa in FSL rats, also KET increase Vegfa (PFC; p<0,05).

The results confirm impaired expression of genes related to neuroplasticity and synaptogenesis in FLS brain. Surprisingly, CBD and ketamine effects in gene expression were not overlapping, thus suggesting independent, but maybe convergent mechanisms associated to their antidepressant effects. Protein analysis in currently under investigation to test this hypothesis.

O04.04   Emil Gregersen   PRION-LIKE SPREADING OF PARKINSON'S DISEASE - THE ROLE OF USP19 IN EXCRETION AND CYTOTOXICITY OF ALPHA-SYNUCLEIN

E. Gregersen, L. Jiang, L.B. Lassen, P.H. Jensen

Danish Research Institute of Translational Neuroscience – DANDRITE, Department of Biomedicine, Aarhus University

To develop better treatment strategies for Parkinson's disease, we need a deeper understanding of the underlying pathology of the disease and the cellular pathways involved. A well supported hypothesis claims that the aggregation and prion-like spreading of the small neuronal protein, α-synuclein, is a critical factor in disease progression. However, the release-mechanism allowing the pathological aggregated α-synuclein to escape affected neurons and spread to healthy neurons in interconnected brain areas is still unknown. A newly identified cellular process named misfolding-associated protein secretion (MAPS) has been proposed as a potential pathway for the selective secretion of aggregated proteins. Here, the endoplasmic reticulum anchored deubiquitinase, USP19, will target misfolded proteins for secretion during conditions like proteasomal stress. This project aims to investigate the ability of USP19/MAPS to target and secrete aggregated α-synuclein as a potential pathological event in the prion-like spreading hypothesis.

I found that USP19 targets aggregated α-synuclein, but also monomeric α-synuclein and other cytosolic proteins, for secretion. Interestingly, a cytosolic isotype of USP19 increase expression and accumulation of pathological α-synuclein, further implicating USP19 in cellular regulation of α-synuclein protein levels. To characterize the in-cell-formed aggregated α-synuclein further, I am attempting to selectively purify them.

Next, I want to clarify if USP19-dependent excretion of α-synuclein can be part of the prion-like spreading of α-synuclein pathology.

O04.05 Asbjørn Petersen KNOCKOUT AND PHARMACOLOGICAL INHIBITION OF KCA3.1 CHANNELS COUNTERACT HYPOXAEMIA IN A VENTILATOR-INDUCED LUNG INJURY MODEL

A.G. Petersen[1], P.C. Lind[1], A. Granfeldt[2, 3], U. Simonsen[1]

[1]Department of Biomedicine, Aarhus University, [2]Department of Intensive Care, Aarhus University Hospital, [3]Department of Clinical Medicine, Aarhus University

Background: Acute respiratory distress syndrome (ARDS) is a life-threating condition where pulmonary oedema leads to impaired gas exchange and respiratory failure. At present, no effective pharmacological treatment against ARDS exists. Based on previous animal studies, we hypothesized that inhibition of calcium-activated potassium channels of intermediate conductance (KCa3.1) would prevent hypoxaemia in a ventilator-induced lung injury (VILI) model.

Methods: First, we performed ex vivo measurements of tension in isolated pulmonary arteries mounted in an isometric myograph. The vessels were incubated with a KCa3.1 channel blocker (either TRAM-34 or senicapoc) in increasing concentrations. Second, in a blinded fashion, we evaluated the protective effects of KCa3.1 deficiency (KCa3.1$^{-/-}$) or senicapoc-treatment using a VILI mouse model. The primary endpoint was an assessment of the hypoxaemia two hours after induction of VILI.

Results: TRAM-34 and senicapoc were able to effectively counteract KCa3.1 channel activity in isolated pulmonary arteries. In the in vivo experiments, both KCa3.1$^{-/-}$ and senicapoc-treated animals showed improvements in gas exchange when compared to their respective controls. These groups of animals were also found to have reduced oedema formation, bronchoalveolar protein content and infiltration of neutrophils. Histopathological damage was also reduced in the senicapoc-treated animals.

Conclusion: We are the first to report that KCa3.1 channel inhibition reduces the degree of hypoxaemia. These findings indicate KCa3.1 as a new therapeutically target for treatment of ARDS and may have future commercial potential.

O04.06 Agnes Hauschultz Witt A NOVEL NEUROPHYSIOLOGICAL METHOD MSCANFIT MUNE DETECTS LOSS OF MOTOR UNITS AND SIGNS OF REINNERVATION IN CHRONIC SPINAL CORD INJURED PATIENTS

A.H. Witt[1, 2], A. Fuglsang-Frederiksen[1, 2], H. Kasch[3], N.B. Finnerup[4, 2], H. Tankisi[1, 2]

[1]Department of Clinical Neurophysiology, Aarhus University Hospital, [2]Department of Clinical Medicine, Aarhus University, [3]Spinal Cord Injury Centre of Western Denmark, Department of Neurology, Regional Hospital of Viborg, [4]Danish Pain Research Center, Aarhus University

Background: Affection of the peripheral nervous system (PNS) after spinal cord injury (SCI) is poorly described apart from entrapment neuropathies

and immobilization atrophy. Since compound muscle action potential (CMAP) amplitude may be reduced in immobilization atrophy and motor unit potential analysis is problematic in paralytic muscles in SCI, PNS involvement cannot be sufficiently documented using conventional electrophysiological methods. Our aim in this study was to examine PNS involvement, including motor unit loss and reinnervation in chronic SCI using a new motor unit number estimation (MUNE) method, MScanFit MUNE.

Methods: Thirty chronic SCI patients (21 complete, 9 incomplete), mean age: 43±13, and 25 gender -and age matched healthy controls (HC) underwent nerve conduction studies and MScanFit of tibial and peroneal nerves if entrapment neuropathy was excluded.

Results: Nine patients had either entrapment of the peroneal nerve or sciatic neuropathy. In the remaining patients, MScanFit in tibial nerve showed significantly lower MScanFit MUNE values (median: 68, 1st quartile(Q1) - 3rd quartile(Q3): 44- 104) than HC (median: 138, Q1-Q3: 107-152), $p<0.0001$, and larger motor unit size as percentage of the compound motor action potential (median: 5.7, Q1-Q3: 3.8-8.4) compared with HC (median: 2.7, Q1-Q3: 2.3-3.4), $p<0.0001$. In the peroneal nerve we found the same pattern but less pronounced.

Conclusion: MScanFit MUNE showed motor unit loss and signs of reinnervation in chronic SCI.

O05.01   Andreas Engel Krag

ANATOMICAL STUDY OF THE DEPRESSOR ANGULI ORIS MUSCLE AND IMPLICATIONS FOR FACIAL PARALYSIS

A.E. Krag[1, 2], D. Dumestre[1], A. Hembd[1], S. Glick[1], A.J. Mohanty[1], S.M. Rozen[1]

[1]The University of Texas Southwestern Medical Center, Department of Plastic Surgery, Dallas, Texas, [2]Department of Clinical Medicine, Aarhus University

Objectives:

Patients with incomplete recovery after facial paralysis often present with a hyperactive depressor anguli oris (DAO) muscle, restricting the smile, and a weak depressor labii inferioris (DLI) muscle, paralyzing the lower lip, despite the anatomical overlap between these mimetic muscles. We investigated the nerve supply to the DAO and DLI muscles to explain this paradoxical phenomenon.

Methods:

Ten hemifaces from five fresh human cadavers were included in the study. Skin and subcutaneous tissue were elevated from the neck to the zygomatic arch. The entire perioral muscle complex was dissected with delineation of the facial nerve supply to the DAO and DLI muscles. The facial nerve branches were further dissected proximally to identify the origin of branches.

Results:

The DAO muscle received dual innervation from both buccal branches of the facial nerve and marginal mandibular branches of the facial nerve. The buccal nerve branches terminated in the DAO muscle whereas marginal mandibular nerve branches continued towards the DLI muscle.

In contrast to the DAO muscle, the DLI muscle received single innervation from marginal mandibular facial nerve branches.

Conclusions:

Dual innervation with buccal and marginal mandibular facial nerve branches to the DAO muscle likely explains the DAO muscle hyperactivity observed in incomplete facial paralysis patients, which is caused by abnormal nerve regeneration through the buccal facial nerve branches. The paradoxical DLI muscle weakness is caused by the single marginal mandibular nerve supply, which is notorious for poor regeneration.

O05.02   Samuel Levi Svinth C Svendsen

SECRETIN ACTIVATES CFTR AND PENDRIN-DEPENDENT HCO_3^- SECRETION IN β-INTERCALATED CELLS

S.L. Svendsen, J. Leipziger

Department of Biomedicine, Aarhus University

Background: The secretin receptor is expressed in the intercalated cells (IC) of the collecting duct. We have recently shown that secretin triggers a pronounced and rapid increase of urinary $[HCO_3^-]$ in mice. Importantly, this secretin effect was completely absent in pendrin KO and CFTR KO mice. We hypothesize that secretin directly activates β-intercalated cells (β-IC) of the collecting duct (CD) via stimulation of basolateral secretin receptors

Methods: We used isolated perfused cortical CDs and intracellular pH measurements in β-ICs to quantify the transport rate of pendrin. Tubules were loaded with the pH indicator dye BCECF-AM. The initial alkalization rate ($\Delta pH/\Delta t$) upon luminal chloride removal was taken as measure of pendrin activity in β-ICs. Analysis was performed in a strictly paired fashion in the single β-IC before and after secretin and this was compared to time controls

Results: Mean $\Delta pH/\Delta t$ was markedly increased with secretin (0.20 ± 0.038 pH/min vs. 0.43 ± 0.044 pH/min, $p<0.0001$). This increase was significantly different from time controls without secretin ($p=0.0022$)

$\Delta pH/\Delta t$ was lower in β-ICs from CFTR KO mice compared to WT (0.077 ± 0.0099 pH/min vs. 0.25 pH/min±0.17, $p<0.0001$). An apparent activation of pendrin function with secretin was not observed in CFTR KO CDs

Conclusion: These results show that basolateral secretin directly activates pendrin-dependent HCO_3^- secretion in β-ICs. Importantly, HCO_3^- secretion in β-IC is markedly reduced in CFTR KO mice. Thus, our previously demonstrated in vivo effects of secretin align well with those reported here in the isolated perfused CD. This shows that secretin triggers urinary HCO_3^- excretion by activating the β-ICs

O05.03   Anders Gyldenkerne

CANCELLED

THE OBJECTIVE QUALITY OF VISION FOR NEARSIGHTED PATIENTS FOLLOWING CORNEAL REFRACTIVE SURGERY

A. Gyldenkerne, A. Ivarsen, J. Hjortdal

Department of Ophthalmology J, Aarhus University Hospital

Purpose: To examine the consequence of corneal refractive surgery (small-incision lenticule extraction) for the objective quality of vision for severely nearsighted patients.

Setting: The Department of Ophthalmology, Aarhus University Hospital

Design: Prospective cohort study

Methods: 58 highly nearsighted eyes (min. minus 6 diopters [D]) of 58 patients were analyzed. Patients were measured before and three months after surgery. Measurements included visual acuity, contrast sensitivity (measured with the Pelli-Robson chart), stereopsis (measured with the Frisby test), ocular scatter (measured with a double-pass system), and whole-eye higher-order aberrations.

Results: Results are reported as mean±SD. The spherical equivalent changed from -7.45±1.14 D to -0.23±0.40 D ($p < 0.001$). Best-corrected visual acuity improved (-0.03±0.05 logMAR to -0.07±0.06 logMAR. $p < 0.001$), contrast sensitivity decreased (1.82±0.12 log(cs) to 1.77±0.11 log(cs), $p = 0.007$), stereopsis was unchanged (21.43±9.84 to 21.15±13.45 arcseconds, $p = 0.80$), scatter was unchanged as well (1.14±2.42 to 1.15±0.55 OSI, $p = 0.74$), and spherical aberration increased significantly from 0.05±0.05 mm to 0.08±0.07 mm ($p < 0.001$). However, the visual quality calculated with the Visual Strehl Ratio was unchanged (0.11±0.11 to 0.11±0.07, $p = 0.80$).

Conclusions: Following corneal refractive surgery, contrast sensitivity was significantly albeit only slightly decreased; furthermore, despite a significant increase in the higher-order aberration spherical aberration, the visual quality was unchanged. In conclusion, corneal refractive surgery does not clinically affect the objective quality of vision to a significant degree.

O05.04   Wenqian Gu

STEVIOL GLUCURONIDE, A METABOLITE OF STEVIOL GLYCOSIDES, POTENTLY STIMULATES INSULIN SECRETION FROM ISOLATED MOUSE ISLETS: STUDIES *IN VITRO*

W.Q. GU[1], A. Rebsdorf[1], C. Anker[1], S. Gregersen[1, 2], K. Hermansen[1, 3], P.B. Jeppesne[1]

[1]Department of Clinical Medicine, Aarhus University, [2]Steno Diabetes Center Aarhus, Aarhus University Hospital, [3]Department of Endocrinology and Internal Medicine, Aarhus University Hospital

Aims: Steviol glycosides are the sweet components extracted from medicinal plant Stevia rebaudiana Bertoni, which have anti-hyperglycaemic effects. Steviol glucuronide (SVG) is the metabolite excreted in human urine after oral administration of steviol glycosides. We aimed to clarify if SVG exerts direct insulin stimulation from pancreatic islets and to explore its mode of action.

Materials and Methods: Insulin secretion was measured after 60 minutes static incubation of isolated mouse islets with 1) 10^{-9}-10^{-5}M SVG at 16.7 mM glucose and, 2) 10^{-7}M SVG at 3.3-16.7 mM glucose. Islets were perifused with 3.3 or 16.7 mM glucose in the presence or absence of 10^{-7}M SVG. Gene transcription was measured after 72h incubation in the presence or absence of 10^{-7}M SVG.

Results: SVG dose-dependently increased insulin secretion from mouse islets with 10^{-7}M exerting the maximum effect in the presence of 16.7 mM glucose (P<0.001). The insulinotropic effect of SVG was critically dependent on the prevailing glucose concentration, SVG (10^{-7}M) enhanced insulin secretion at or above 11.1 mM glucose (P<0.001) and showed no effect at lower glucose concentrations. During perifusion of islets, SVG (10^{-7}M) had a long-acting and apparently reversible insulinotropic effect in the presence of 16.7 mM glucose (P<0.05). Gene-transcript levels of B2m and Gcgr were markedly altered.

Conclusion: This is the first report to demonstrate that SVG stimulates insulin secretion in a dose- and glucose-dependent manner from isolated mouse islets of Langerhans. SVG may be the main active metabolite after oral intake of steviol glycosides.

O05.05   Leonardo Bonetti   SPATIOTEMPORAL BRAIN DYNAMICS OF ACOUSTIC PATTERNS RECOGNITION

L. Bonetti[1], E. Brattico[1], F. Carlomagno[1], J. Cabral[4, 2], A. Stevner[1], N.T. Haumann[1], G. Deco[3], M. Pearce[1], P. Vuust[1], M.L. Kringelbach[1, 2]

[1]Center for Music in the Brain, Department of Clinical Medicine, Aarhus University and The Royal Academy of Music Aarhus/Aalborg, [2]Department of Psychiatry, University of Oxford, Oxford, United Kingdom, [3]Computational and Theoretical Neuroscience Group, Center for Brain and Cognition, Universitat Pompeu Fabra, Barcelona, Spain, [4]Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Portugal

Music is a universal non-verbal human language, built on logical structures and articulated in balanced hierarchies between sounds, offering excellent opportunities to explore how the brain creates meaning for complex spatiotemporal auditory patterns. Therefore, in this magnetoencephalography (MEG) study, we investigated the spatiotemporal fast-scale brain dynamics during the recognition of Johann Sebastian Bach's original and varied musical patterns. We detected high centrality of hippocampus, operculum, primary auditory cortex, putamen and pallidus within the whole brain network during the entire task. Even though the network appeared similar for both Bach's originals and variations, the strength of the connections between those brain areas, as well as the general level of brain synchronization, was higher when participants recognised Bach's original patterns compared to the variations. This study sheds new light on the dynamics of brain connectivity underlying memory processes and meaning creation for auditory patterns, highlighting the crucial role of fast-scale phase synchronisation analysis to understand complex cognitive processes.

O05.06	Mads Bisgaard Bengtsen	METABOLIC AND HORMONAL RESPONSES TO HYPOGLYCEMIA: A HUMAN RANDOMIZED CROSSOVER TRIAL INVESTIGATING TYPE 1 DIABETES MELLITUS PATIENTS AND HEALTHY CONTROLS

M. Bengtsen[1], M. Svart[1], N. Magnusson[1], N. Rittig[2], T.S. Voss[2], J. Støy[2], N. Jessen[2], N. Møller[1]

[1]Department of Endocrinology and Internal Medicine, Aarhus University Hospital, [2]Steno Diabetes Center Aarhus, Aarhus University Hospital

Hypoglycemia and insulin resistance are ascertain components in type 1 diabetes mellitus (T1DM) hindering optimal glycemic management. It is well established that T1DM patients have compromised counterregulatory hormone responses to hypoglycemia, as a consequence of long diabetes duration and following repeated episodes of hypoglycemia, but it is uncertain whether these deficits affect adequate counterregulatory activation of metabolic responsiveness i.e. gluconeogenesis, lipolysis, ketogenesis. Our study was designed to test i) whether metabolic responsiveness are affected by compromised counterregulatory hormone responses to hypoglycemia, ii) whether short (Material and methods

In a randomized, controlled crossover 2x2 factorial design, nine subjects with T1DM and nine matched healthy control subjects underwent an episode of hypoglycemia (plasma glucose Results

In T1DM subjects, insulin sensitivity was 30% lower compared with healthy controls. Following hypoglycemia, counterregulatory hormones were attenuated in the T1DM subjects with 75% lower glucagon, 50% lower adrenaline, and 40% lower lactate, while 3-hydroxy-butyrate was 5-10 fold higher compared with healthy controls. Palmitate fluxes and endogenous glucose production did not differ between groups. Antecedent hypoglycemia did not affect counter regulation.

Conclusion

Subjects with T1DM displayed severely comprimised counterregulatory hormone- and lactate responses, wheras the metabolic responsiveness was appropriate and preserved. These findings may suggest presence of protective insulin resistance in T1DM subjects.

P01.01	Søren Krogh Jensen	CAN MAGNETIC BRAIN STIMULATION IMPROVE RECOVERY AFTER SPINAL CORD INJURY?

S. Krogh[1, 2], U. Frandsen[3], P. Aagaard[3], H. Kasch[1, 2]

[1]Department of Clinical Medicine, Aarhus University, [2]Spinal Cord Injury Centre of Western Denmark, Regional Hospital Viborg, [3]Department of Sports Science and Clinical Biomechanics, University of Southern Denmark

Background: Repetitive transcranial magnetic stimulation (rTMS), in which a wire coil is placed on the scalp and a train of focal magnetic impulses are transmitted to excite a targeted area of the brain, can be applied to the motor cortex of spinal cord injured (SCI) patients, and perhaps modulate their nervous system to facilitate more intensive and rewarding rehabilitation efforts. This could, in turn, lead to improved functional capacity and increased QoL following discharge. In this sham-controlled RCT we investigate the effects of rTMS treatment during primary rehabilitation following SCI.

Methods: 20 patients with motor incomplete SCI admitted to primary rehabilitation at a specialized SCI rehabilitation centre are being consecutively recruited to undergo actual (active, n=10) or sham (sham, n=10) rTMS application over the leg primary motor cortex for 8 weeks, supplementary to usual care. Gait function, knee joint muscle strength and rate of force development, sensory function, spasticity and pain sensations are assessed before, during (4 wks) and after the intervention period.

Results: Preliminary data analyses (n=7 total) show that the active group have greater improvements in ambulatory function and leg muscle strength compared to the sham group. However, the data are still underpowered to prove any statistically significant effects.

Conclusion: Our preliminary results suggests that rTMS treatment may be able to improve functional recovery following SCI.

P01.02 Laura Øllegaard Johnsen

THE ROLE OF NCBE IN CEREBROSPINAL FLUID PRODUCTION

L.Ø. Johnsen, K.A. Friis, L.B. Ryø, J. Giehm, J. Prœtorius, H.H. Damkier

Department of Biomedicine, Aarhus University

Background:

The CSF is mainly produced by specialized ependymal cells in the choroid plexus (CP). If CSF accumulates inside the brain ventricles, either due to an obstructed drainage or due to an increased production rate, a hydrocephalic state will arise.

CSF production is a result of net transfer of water and solute into the ventricles. The Ncbe cotransporter (slc4a10) is localized at the basolateral membrane of the CP epithelium (CPE) and transports Na^+ and HCO_3^- into the cell. Studies have shown that Ncbe-overexpression results in increased CSF production causing hydrocephalus.

Hypothesis:

Ncbe is the main protein involved in CSF production and inhibiting Ncbe at the blood-CSF barrier will significantly decrease CSF production.

Methods:

Genetic modification methods are being explored. siRNA targeting different areas of the Ncbe mRNA product were designed and tested in vivo on mice. We will investigate whether this Ncbe knockdown mouse has an affected CSF formation rate by a CSF production rate assay.

Results:

Using intraventricular siRNA injections targeting Ncbe mRNA in mice, we found a small down regulation of Ncbe protein expression (app. 20%) after 48 hours. However, we expected that this knock down was insufficient to validate Ncbe as primarily responsible for CSF production.

Future perspectives:To establish a more permanent and stronger Ncbe knock down model, shRNA in a lentiviral vector targeting Ncbe mRNA will be delivered using the same procedure as the siRNA model and will initially be validated on primary CP cell cultures.

P01.03   Rolf Blauenfeldt   DO CHANGES IN RED BLOOD CELL DEFORMABILITY AND FUNCTION CAUSE SECONDARY ISCHEMIC INJURY IN ACUTE ISCHEMIC STROKE? - RATIONALE AND METHODOLOGY

R.A. Blauenfeldt[1, 2], G. Andersen[1, 2], A.M. Hvas[1, 3], D.C. Hess[4]

[1]Department of Clinical Medicine, Aarhus University, [2]Neurology and Danish Stroke Center, Aarhus University Hospital, [3]Thrombosis and Haemostasis Research Unit, Department of Clinical Biochemistry, Aarhus University Hospital, [4]Department of Neurology, Medical College Georgia and Augusta University, Augusta, USA

Rationale:

Healthy Red Blood Cell are highly deformable and must pass through the microvasculature half their diameter. RBCs carry Nitric Oxide (NO) as nitrosylated proteins, which improves their deformability. Nitric Oxide Synthetase 3 (NOS3) was conventionally thought of as present only in endothelial cells. However, RBCs also express functional NOS3 which may be a source for hypoxic vasodilation in brain microvasculature following stroke.

Aims:

To evaluate whether RBC deformability and NOS3 activation are associated with acute infarct growth and stroke severity in acute ischemic stroke patients.

Methods and design:

Predefined biomarker substudy to an ongoing Danish multicenter randomised, controlled study examining the effect of remote ischemic conditioning (RIC) in patients with acute stroke (RESIST). In brief, Adult patients with a putative stroke identified prehospital with symptom duration < 4 hours, who are independent in daily activities will be randomised 1:1 to RIC or Sham-RIC.

Blood samples will be drawn in the hyperacute prehospital phase (pre-allocation), and upon admission and after 24 hours at the stroke center. Fresh whole-blood EDTA will be used and analysed as soon as possible. Laser based ektacytometry (Rheoscan, AnD300, Rheomeditech) will be used to quantify the deformability index of RBCs. For the analytical flowcytometry (Cytoflex S, Beckmann Coulter), RBCs will be specifically stained using a conjugated antibodies to Glycophorin A and Hemoglobin Beta and activated $pNOS3^{Ser1177}$ and $AMPK\alpha1^{thr172}$ will be estimated.

The estimated biomarker sample size is 300. The biomarker sub-study started October 2019 and will run until the end of 2022.

P01.04   Simone Schandorf Elstrøm Nielsen   TRACKING THE TRANSFERRIN RECEPTOR IN THE BLOOD-BRAIN BARRIER

S.S.E. Nielsen

Department of Biomedicine, Health, Aarhus University

The blood-brain barrier (BBB) constitute an essential role in protecting the brain from xenobiotics, but also possess a challenge for brain drug delivery. It is well accepted that delivery is possible by the molecular trojan-horse strategy; receptor-mediated transcytosis of pharmaceutical

constructs. However, the delivered amounts are not considered enough to obtain effective therapeutic concentrations, and knowledge about how to optimize the current systems is therefore needed. Targeting the highly expressed Transferrin Receptor (TfR) in brain endothelial cells (BECs) of the BBB represents the golden standard, and has shown successful endocytosis for e.g. nanoparticles, liposomes and antibodies. However, there are knowledge gaps within the use of the TfR trafficking system. By studying the luminal vs. abluminal membrane expression, the intracellular trafficking and transcytosis capabilities of the receptor itself, we might elucidate important knowledge of how new generations of drug constructs should be designed.

P01.05 Meet Sanjaykumar Jariwala

THE GABA-ERGIC ENGRAM IN CENTRAL AMYGDALA FOR AVERSIVE LEARNING.

M. Jariwala[1, 2], W.H. Hou[5], A. Ricci[5], F. Ferraguti[3], C.C. Lien[4], M. Capogna[1, 2, 5]

[1]Center for Proteins in Memory, PROMEMO, Aarhus [2]Department of Biomedicine, Aarhus University [3]Department of Pharmacology, Innsbruck Medical University, Innsbruck, Austria, [4]Institute of Neuroscience, National Yang-Ming University, Taipei, Taiwan, [5]Danish Research Institute of Translational Neuroscience, DANDRITE, Aarhus

Memory recall plays an important role in governing immediate response to threat conditions, such as an electrical shock. One of the prominent regions involved in the relay of fear conditioning is the amygdala. This brain area receives thalamic and cortical sensory inputs and relay to downstream regions that regulates fear response, like freezing. Recent studies shed a new light on the active role of the central lateral amygdala (CeL) in fear learning. CeL contains mostly GABAergic neurons and includes two major cell populations that express either Protein Kinase C-delta (PKC-δ) or somatostatin (SOM). Therefore, the The functional output of CeL is tightly regulated by local inhibitory GABAergic transmission. However, how the CeL neurons encode for fear learning and whether inhibitory synaptic plasticity occurs, remains unexplored. Here, we applied a genetic strategy to label CeL neurons that are active during fear acquisition using a novel technique called Targeted Recombination in Active Populations (TRAP2). Preliminary immunohistochemistry results indicate that most of the TRAPed cells are mainly PKC-δnegative neurons. In addition, chemogenetically silencing TRAPed cells by application of an inhibitory synthetic agonist impairs fear memory retrieval. The genetic labelling of TRAPed cells identify for the first time the neuron populations that are activated by fear memory (engram). Consistently, in-vitro electrophysiology data show inhibitory synaptic plasticity onto SOMnegative neurons 24 hours and 7 days after fear learning. These results suggest that inhibitory synaptic plasticity onto a specific GABAergic population of the CeL plays a role on fear memory in rodents.

P01.06   Kristian Stœr   CORRELATION BETWEEN CORTICAL CHOLINERGIC DYSFUNCTION AND MICROGLIAL ACTIVATION IN THE SUBSTANTIA INNOMINATA IN REM SLEEP BEHAVIOUR DISORDER

K. Stœr[1], A. Iranzo[2, 3, 4], M.G. Stokholm[1], K. Østergaard[5], M. Serradell[2, 4], M. Otto[6], K.B. Svendsen[5], A. Garrido[3, 7], D. Vilas[3, 7], J. Santamaria[2, 3, 4], A. Møller[1], C. Gaig[2, 3, 4], D.J. Brooks[1, 8], P. Borghammer[1], E. Tolosa[3, 7], N. Pavese[1, 8]

[1]Department of Nuclear Medicine and PET Centre, Aarhus University Hospital, [2]Department of Neurology, Hospital Clínic de Barcelona, Spain, [3]Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Hospital Clínic, IDIBAPS, Universitat de Barcelona, Catalonia, Spain, [4]Multidisciplinary Sleep Unit, Hospital Clinic, Barcelona, Spain, [5]Department of Neurology, Aarhus University Hospital, [6]Department of Clinical Neurophysiology, Aarhus University Hospital [7]Movement Disorders Unit, Neurology Service, Hospital Clínic de Barcelona, Catalonia, Spain, [8]Division of Neuroscience, Newcastle University, England

Introduction

Our research group and collaborators have previously reported reduced cortical acetylcholinesterase activity, suggestive of cholinergic dysfunction, in patients with isolated REM sleep behaviour disorder (iRBD).

In this study we aimed to explore the relationship between cortical acetylcholinesterase activity and neuroinflammation, in the form of microglial activation, in the substantia innominata (SI), the major source of cholinergic projections to the cortex, in these iRBD patients.

Methods

We examined 19 iRBD patients with[11]C-PK11195 and[11]C-donepezil PET to assess the levels of activated microglia in their SI, and acetylcholinesterase activity, respectively.

[11]C-PK11195 binding potentials (BP_{ND}) and[11]C-Donepezil distribution volume ratio (DVR) values were correlated using the Pearson statistic.

Results

We found a significant negative correlation between[11]C-donepezil DVR in the cortex and[11]C-PK11195 BP_{ND}levels in the SI. A lower cortical[11]C-Donepezil DVR correlated with a higher[11]C-PK11195 BP_{ND}in the SI (r = -0.46, p = 0.024). Using Statistical Parametric Mapping, we identified clusters with the strongest negative correlations in the frontal and temporal lobes.

Conclusion

In conclusion, our study is compatible with inflammatory changes in the form of microglial activation in the SI of iRBD patients being a contributing factor in the development of cortical cholinergic dysfunction and possibly causing cognitive decline at a later stage, but the latter remains to be investigated.

P01.07   Victor Manuel   MUSICAL RHYTHM AND PLEASURE IN PARKINSON'S DISEASE
          Pando Naude

V. Pando-Naude[1], M. Witek[2], A. Højlund[4], S. Jackobsen[4], E. Johnsen[5], E. Garza-Villarreal[3], P. Vuust[1]

[1]Center for Music in the Brain, Aarhus University, [2]School of Languages, Cultures, Art History and Music, University of Birmingham, [3]Institute of Neurobiology, Universidad Nacional Autónoma de México, [4]Center for Functionally Integrative Neuroscience, Aarhus University, [5]Department of Neurology, Aarhus University

Background. Parkinson's disease (PD) is a neurological condition resulting from dopaminergic dysfunctions in the basal ganglia (BG) of the brain, with devastating consequences for motor and cognitive functioning. The method 'rhythmic auditory cuing' has been shown to improve motor deficits in PD patients, due to the ability of rhythm to stimulate the BG. However, this method may be limited by a rather simple rhythmic stimulation complexity, and therefore restricts its benefits to the motor domain. Syncopation is a form of rhythmic complexity related to pleasure and synchronized body-movement, referred to as groove. While healthy adults experience a pleasurable desire to move to stimulating music (medium syncopation), we do not know if PD patients respond in the same way. Does PD affect the pleasure experienced from rhythmically complex music? Can musical complexity be used to treat deficiencies in PD, and what level of rhythmic complexity would be most effective? Methods. Participants listened to short musical sequences that varied in rhythmic complexity (low, medium, high), and rated experienced pleasure and desire to move on a 5-point Likert scale. Results. PD patients without dopamine agonist (DA) medication rated higher scores on pleasure and desire to move for the low rhythmic complexity, while PD patients under DA medication and HC preferred medium complexity for pleasure and desire to move. Conclusion. PD patients prefer low complexity in music. This new knowledge can be used to design music which hits PD patients' rhythmic "sweet spot" , potentially helping their integral rehabilitation.

P01.08   Pernille Louise   DETECTING PRECLINICAL ALZHEIMER'S DISEASE WITH AMYLOID PET
          Kjeldsen   IMAGING TO ESTIMATE THE PREVALENCE OF INFLAMMATION AND TAU IN
                            RELATION TO COGNITIVE DECLINE

P.L. Kjeldsen[1, 2], R. Ismail[1, 2], P. Parbo[2], P.H. Nissen[3], K.V. Hansen[2], S.F. Eskildsen[4], M.F. Damholdt[1, 5], J.F.A. Aanerud[2], D.J. Brooks[1, 2, 6]

[1]Department of Clinical Medicine, Aarhus University, [2]Nuclear Medicine and PET, Aarhus University Hospital, [3]Department of Clinical Biochemistry, Aarhus University Hospital, [4]Centre of Functionally Integrative Neuroscience, Aarhus University, [5]Department of Psychology, Aarhus University, [6]Department of PET Clinical Science, Newcastle University

Alzheimer's disease (AD) is the most common cause of dementia, a debilitating neurodegenerative disorder, which primarily occurs in elderly individuals. AD is characterised by a brain pathology consisting of extracellular accumulations of a protein, beta-amyloid (Aβ), intracellular neurofibrillary tangles of another protein, tau, as well as cortical inflammation in the form of activated microglia. While the exact relationship between these pathologies remains to be established, findings point to Aβ being the first one of these to occur. The most significant genetic modifier of AD is the apoliprotein E (APOE) gene,

insofar that the ε4 allele of APOE increases the risk of developing AD by 2 to 4 times. One of the most consistently reported effects of APOE ε4 is that it influences Aβ deposition and clearance in the brain. In this study, we are studying healthy elderly individuals, who are carriers of APOE ε4 in order to relate the development of the different AD pathologies in the brain to their cognitive functioning. As part of the study, we have compared Aβ PET scans with[11]C-PiB of cognitively healthy APOE ε4 carriers above the age of 65 with age-matched cognitively healthy non-APOE ε4-carriers. We found that the APOE ε4-carriers generally had more Aβ aggregation irrespective of other factors. These Aβ-positive APOE ε4-carriers will be further examined with tau PET and microglia PET as well as cognitive measures in order to elucidate whether the APOE ε4-carriers with Aβ also have evidence of cortical inflammation and tau, and how this influences their cognitive functioning.

| P01.09 | James Isaac Lubell | NATURAL IMAGERY THROUGH THE RETINA: DOES THE RETINA ENCODE LOW-LEVEL STIMULUS FEATURES? |

J. Lubell, J. Alves, B.U. Westner, S.S. Dalal

NemoLab, Center of Functionally Integrative Neuroscience, Aarhus University

To date, there are few human studies investigating the nature of early retinal responses and their impact on cortical processes. Recent animal research demonstrated a close link between retinal and cortical activity patterns in different contexts. In the present study, we investigate how retinal activity might shape cortical visual responses in humans by examining activity patterns elicited by the spatial frequency content of natural imagery. We recorded retinal and cortical responses to grayscale natural images using electroretinography (ERG). The natural image stimuli were either unaltered or had their high or low frequency components enhanced. Comparing the stimulus conditions revealed higher peak amplitudes for natural stimuli and gamma-band activity in the ERG response. This gamma-band activity was modulated by low-level stimulus features. Higher spatial frequency components correlated with an ITC amplitude peak in the 60-75Hz bandwidth and a more narrow band response. Lower spatial frequency components correlated with an ITC amplitude peak in the 30-45Hz bandwidth and a more broad band response. Amplitudes in the 45-60Hz band had similar peak latencies, but had different response latencies to stimulus onset. Taken together, these results indicate that the retina is not only sensitive to low-level features comprising stimuli. Next steps will require assessing whether this retinal sensitivity also shapes cortical responses. Perliminarily, these results suggest that how the retina processes stimuli could account for more of the variance seen in cortical activity.

P01.10 Jeppe Lund Schaldemose

NEUROIMAGING BIOMARKERS OF COGNITIVE DECLINE IN ALZHEIMER'S DISEASE - A LONGITUDINAL PET-STUDY

J.L. Schaldemose[1], P. Parbo[1], R. Ismail[1], L.S. Madsen[1], M.F. Damholdt[2], D.J. Brooks[1]

[1]Department of Nuclear Medicine and PET Centre, Aarhus University Hospital, [2]Department of Psychology and Behavioural Science, Aarhus University

Introduction:

Alzheimer's disease (AD) causes progressive impairment of cognitive functions. The neuropathology of AD is characterised by amyloid-β plaque deposition and tau tangle formation along with a neuroinflammatory glial reaction. We are investigating the relationship between these neuroimaging biomarkers and cognitive decline in the progression of AD in subjects with mild cognitive impairment (MCI).

Methods:

We recruited 44 MCI, 23 HC and 5 AD participants. They underwent PET scans with ^{11}C-PiB, ^{18}F-AV-1451 and ^{11}C-PK11195 tracers to measure levels of amyloid-β, tau and inflammation reflected by translocator protein expression, as well as MR scans at baseline and 2 year follow up. Neuropsychological tests were administered at both times, targeting memory (MEM), executive function (EXE), attention (ATT), language (LAN) and visuospatial function (VIS).

Preliminary results:

Subjects were categorised as high or low amyloid-β according to their cortical PiB uptake, using a target:cerebellar uptake ratio threshold of 1.5 for abnormality. In the group of high amyloid-β MCI, we found negative correlations at baseline between levels of; Amyloid-β and MEM[2], EXE[2], ATT[2], VIS[2](n=22); Tau and MEM[1], EXE[1], ATT[1], LAN[1], VIS[1](n=12); Inflammation and MEM[1], EXE[1], ATT[1], LAN[2], VIS[1](n=22) ([1]$p<0.05$,[2]$p<0.001$).

Conclusion:

Raised amyloid-β, tau tangle and neuroinflammation levels are all associated with cognitive decline in prodromal AD - that is MCI cases with raised amyloid-β. Further analyses on the distribution and temporal time courses of these biomarkers are on-going, which will help reveal their individual roles in Alzheimer progression and the interactions between the pathologies.

P02.01 Cagla Cömert

A RECURRENT *DE NOVO HSPD1* VARIANT IS ASSOCIATED WITH HYPOMYELINATING LEUKODYSTROPHY

C. Cömert[1], L. Brick[2], D. Ang[3], J. Palmfeldt[1], M.F. Meaney[4], P. Fernandez-Guerra[1], M. Kozenko[2], C. Georgopoulos[3], P. Bross[1]

[1]Research Unit for Molecular Medicine, Aarhus University and Aarhus University Hospital, Aarhus, Denmark, [2]Division of Genetics, McMaster Children's Hospital, Hamilton, ON, Canada, [3]Department of Biochemistry, University of Utah School of Medicine, Salt Lake City, UT, 84112-5650,

United States, [4]Division of Pediatric Neurology, McMaster Children's Hospital, Hamilton, ON, Canada

Standardization of the use of next-generation sequencing for the diagnosis of rare neurological disorders has made it possible to detect potential disease-causing genetic variations, including de novo variants. However, the lack of a clear pathogenic relevance poses a critical limitation for translating this genetic information into clinical practice. Genetic screening is currently recommended in the guidelines for diagnosis and treatment of hypomyelinating leukodystrophies (HLDs). HLDs represent a group of rare heterogeneous disorders that interfere with the myelination of the neurons in the central nervous system. Seventeen genes are known to cause HLDs with different mechanisms, some of which are not fully understood. One of the HLD-related genes is HSPD1, encoding the mitochondrial chaperone heat shock protein 60 (HSP60), which functions as folding machinery for mitochondrial proteins. Disease-causing HSPD1 variants have been associated with two different inherited neurological disorders: a fatal HLD (HLD4; MIM 612233) and spastic paraplegia (SPG13; MIM 605280). In 2018, a de novo HSPD1 variant was reported as a potential disease-associated variant in a patient with HLD. Here, we present another case carrying the same disease-causing heterozygous de novo variation in the HSPD1 associated with the HLD phenotype. Our molecular studies show that the variant HSP60 is stably present in patient fibroblasts, and functional assays demonstrate that the variant protein lacks in vivo function, thus confirming its disease association. We conclude that de novo variations of the HSPD1 should be considered as potentially disease-causing in the diagnosis and pathogenesis of HLDs.

P02.02 Michael Nørregaard Vinkel

SENSORY DISTURBANCES AND PAIN IN YOUTH WITH CEREBRAL PALSY

M.N. Vinkel[1], G. Rackauskaite[2], H. Tankisi[3], A.J. Terkelsen[4], J.R. Østergaard[2], N.B. Finnerup[1]

[1]Danish Pain Research Center, Aarhus University Hospital, [2]Department of Pediatrics and Adolescent Medicine, Aarhus University Hospital, [3]Department of Clinical Neurophysiology, Aarhus University Hospital, [4]Department of Neurology, Aarhus University Hospital

Background

Cerebral Palsy (CP) is a movement disorder caused by damage to the immature brain. Pain is common in children and youth with CP with a prevalence of 14-76% and has an enormous impact on quality of life, but is underdiagnosed and undertreated. Furthermore, little knowledge of sensory disturbances and types of pain exists regarding patients with CP.

Objective

The aim of the study is to examine the prevalence of neuropathic pain in youth with CP. Additionally, we want to examine signs of sensory nerve damage e.g. hypoesthesia, hyperesthesia, allodynia and hyperalgesia.

Methods

Youth age 15-22 with CP were recruited from local pediatric departments and compared to age- and sex-matched healthy controls. Initial assessment of pain and sensory disturbances was performed through a

systematic interview and sensory mapping. An area with possible neuropathic pain or sensory disturbances was examined using quantitative sensory testing (QST) and evoked potentials. Findings were correlated with neuroimaging e.g. the location and size of the brain injury.

Results

Results are mainly descriptive, since the study is ongoing and currently includes six patients. Sensory disturbances can easily be assessed through a systematic interview and objective measures like sensory mapping and QST. Four of the patients had recurrent or chronic pain, which in all cases were diagnosed as musculoskeletal pain. Most patients had sensory abnormalities. Interestingly, several patients had never noticed a changed sensation to mechanical or thermal stimuli.

Conclusion

The study is ongoing and further results will be presented when ready.

P02.03   Julie Schjødtz Hansen   THE EFFECT OF MEDICAL CANNABIS ON NEUROPATHIC PAIN AND SPASTICITY   IN PATIENTS WITH MULTIPLE SCLEROSIS AND SPINAL CORD INJURY: A NATIONAL MULTICENTRE DOUBLE-BLINDED PLACEBO-CONTROLLED STUDY IN DENMARK.

J.S. Hansen[1, 6], H. Kasch[1, 6], N.B. Finnerup[3, 6], P.V. Rasmussen[1], R.M. Hansen[2], T. Petersen[1, 6], A.B. Oturai[4], F. Sellebjerg[4], E.A. Sædder[5], K.B. Svendsen[1, 6]

[1]Department of Neurology, Aarhus University Hospital, [2]Spinal Cord Injury Centre of Western Denmark, Viborg Regional Hospital, [3]Danish Pain Research Center, Department of Clinical Medicine, [4]Danish Multiple Sclerosis Center, Department of Neurology, Rigshospitalet, University of Copenhagen, [5]Department of Clinical Pharmacology, Aarhus University Hospital, [6]Aarhus University

Background:

Disease or acquired damage to the central nervous system may lead to invalidating spasticity and central neuropathic pain (NP). In multiple sclerosis (MS) and spinal cord injury (SCI), these symptoms are frequent and prominent. Patients with MS and SCI often possess a great desire for treatment with cannabis-based medicine (CBM). A Danish four-year trial has made prescription of CBM possible. However, knowledge about effects, side effects and doses of CBM remains limited and insufficient.

Objective:

To examine if CBM is a relevant and safe treatment for spasticity and NP for patients with MS or SCI.

Methods:

In a national multicentre study, we examine the effect of CBM on NP and spasticity in a double-blinded, parallel design. Patients will be randomized for treatment with either THC, CBD, a combination of THCandCBD or placebo. Treatment lasts seven weeks. Primary endpoints are patient-reported pain and spasticity on a numeric rating scale. Secondary endpoints include quality of life and sleep, registration of depression and

anxiety, relief of pain and spasticity and a range of clinical tests. Furthermore, the adverse event profile of CBM is described.

In a sub-study of 40 patients, the pharmacodynamics and pharmacokinetics of CBM are examined to gain more knowledge about blood concentration, duration of effect and drug excretion.

Discussion:

Knowledge regarding CBM use for NP and/or spasticity treatment is highly needed. The description of effects and adverse reaction profile may guide decisions to recommend future CBM treatment. CBM formulated as capsules can potentially ease the use of CBM compared to oral drops, sprays, tea or inhalation.

P02.04   Malene Overby   DISCOVERY OF NEURONAL VESICLE TRAFFICKING-ASSOCIATED PROTEIN 1 (NSG1) AS AN INTERACTING PROTEIN OF THE SORTILIN RECEPTOR - INSIGHTS INTO THE COMPLEXITY OF PROTEIN INTERACTIONS CONTROLLING NEUROLOGICAL AND PSYCHIATRIC DISORDERS

M. Overby, H. Müller

Department of Clinical Medicine, Translational Neuropsychiatry Unit, Aarhus University

The sortilin receptor (SORT) is an intriguing protein serving multiple functions as a sorting molecule and cell surface clearance receptor of a variety of ligands. SORT is recognized for its involvement in psychiatric and neurological disorders. For instance, SORT facilitates the transport of neurotrophins and acts as a regulator of their cognate receptors at the cell surface, thus playing an important role in neuronal survival and plasticity. However, the signals and proteins involved in organizing and regulating SORT-mediated targeting of neuronal proteins are poorly understood.

To gain insight into the regulation of SORT, we screened for interacting proteins of SORT and identified neuronal vesicle trafficking-associated protein 1 (NSG1). NSG1 repeatedly displayed a specific interaction with the cytoplasmic C-terminus of SORT in Y2H assays. Using Co-IP on cultured mammalian cells, and brain tissue from rats we confirmed the interaction between SORT and NSG1.

NSG1 is a single span integral membrane protein, which is highly and specifically expressed in neurons. NSG1 is involved in the recycling of important receptors including the AMPA receptor and the neurotensin receptors by preventing mislocalization of the receptors, thereby contributing to regulation of synaptic transmission and plasticity.

We aim to unravel the functional relevance of the interaction between NSG1 and SORT to provide further insight into the mechanisms controlling SORT trafficking and its sorting of neurotrophins and their cognate receptors. The results may gain novel insight for the development of new therapeutic drug using small molecule modulators targeting specific protein-protein interactions.

P02.05   Linda Karin M   MULTIPLE SCLEROSIS ALTERS WHITE MATTER MICROVASCULAR PERFUSIN
          Sundvall
          Germeys

L. Sundvall[1], I.K. Mikkelsen[2], S.F. Eskildsen[2], M. Nygaard[2], V.P. Rasmussen[1], L. Østergaard[2, 3], T. Petersen[1]

[1]Department of Neurology, Aarhus University Hospital, [2]Center of Functionally Integrative Neuroscience, Aarhus University, [3]Neuroradiology, Department of Radiology, Aarhus University Hospital

Introduction: Multiple sclerosis (MS) is an autoimmune disease characterized by blood-brain barrier disruption and demyelinating lesions. Capillary flow disturbances might reduce tissue oxygenation and may represent an important, but overlooked mechanism that increases the risk of MS-related brain damage. Dynamic susceptibility contrast-enhanced MRI (DSC) is a powerful new tool enabling brain oxygenation assessment by capillary transit-time heterogeneity (CTH) estimation. Therefore, DSC may have the potential to give new insight to MS disease activity.

Aims/Methods: To characterize brain microvascular alterations in newly diagnosed MS patients. MS-suspected patients are recruited consecutively on admission to the MS clinic. All subjects undergo a comprehensive MRI protocol with a 3 Tesla system. Diseased/control follow 2017 McDonald criteria.

Result: Inclusion is ongoing. Preliminary results, based on 19 MS subjects and 9 controls indicate elevated CTH*, long mean transit time of blood (MTT*) and increased oxygen extraction capacity (OEF^{max}*) in white matter lesions (WML) from MS subjects when compared to WML from controls, and when compared to MS normal appearing white matter (NAWM).MS contrast-enhancing WML have low CTH* and MTT* and increased estimated metabolic rate of oxygen* compared to MS NAWM WML (*$p<0.05$, adjusted for sex and age.).

Conclusion: Our results indicate that hyperemia is present in acute contrast-enhancing WML whereas susceptibility to oxidative stress emerge in quiescent non-enhancing WML. Elevated CTH in MS WML may indicate a high degree of microvascular shunting and suggests that elevated MTT may represent post-inflammatory vasodilation or angiogenesis.

P02.06   Katrine Tang   EXTRACELLULAR VESICLES RELEASED BY REMOTE ISCHEMIC
          Stenz   CONDITIONING AND BLOOD FLOW RESTRICTED EXERCISE IN STROKE
                           INCREASE ISCHEMIC TOLERANCE OF BRAIN MICROVASCULAR
                           ENDOTHELIAL CELLS

K.T. Stenz[1, 2, 3], J. Just[1, 2, 3], Z. Huang[2], Y. Yan[4], M.T. Venø[4], J. Kjems[4, 5], K. Vissing[6], X. Wang[2], K.R. Drasbek[1]

[1]Center of Functionally Integrative Neuroscience, Department of Clinical Medicine, Aarhus University, [2]Institute of Genetics and Developmental Biology, University of Chinese Academy of Sciences, [3]Sino-Danish Center, [4]Interdisciplinary Nanoscience Center - INANO-MBG, Aarhus University, [5]Department of Molecular Biology and Genetics, Aarhus University, [6]Department of Public Health, Section for Sport Science, Aarhus University

Stroke is a leading cause of death and disability worldwide. An ischemic stroke is characterized by an instant reduction in oxygen and nutrient delivery to the brain, leading to tissue damage. When treated, the

recanalization of blood vessels can lead to further tissue damage; together known as ischemia/reperfusion injury (I/R injury).

Novel therapeutics and neuroprotective strategies for early treatment are urgently needed in order to reduce disability after stroke. The aim of this study is to identify and utilize the body's own endogenous protective pathways against I/R injury by different conditioning methods; Remote Ischemic Conditioning (RIC) and Blood Flow Restricted Exercise (BFRE).

RIC has proven to protect against I/R injury in stroke. RIC is performed by 4 cycles of 5 min ischemia and reperfusion in a limb. Nano-sized Extracellular vesicles (EVs) which are released into the blood, are in part responsible for the remote protection induced by RIC. How this protective effect is mediated, remains unknown. EV-packaged miRNAs have the ability to alter target cell gene expression by gene repression through complementary base-pairing with mRNAs. Because of this, EVs and their miRNA cargo are particularly interesting from a functional point of view.

We have found that BFRE and RIC EVs elicits protection to endothelial cells in an in vitro stroke model and that miRNA-182 is upregulated after conditioning. Through in silico target prediction and in vitro validation, it was found that miRNA-182 can target mRNA of pro-apoptotic proteins for degradation. Which means that upregulation of miRNA-182 has an anti-apoptotic potential and thus protects against I/R injury.

P02.07   Christine Ahrends   DYNAMIC NETWORK CHANGES OF AUDITORILY BIASED DECISION-MAKING

C. Ahrends[1], A.B.A. Stevner[1], J. Cabral[1, 2, 3], F. Bravo[4], G. Deco[5, 6, 7, 8], M.A. Rohrmeier[9], P. Vuust[1], M.L. Kringelbach[1, 2]

[1]Center for Music in the Brain, Department of Clinical Medicine, Aarhus University and The Royal Academy of Music Aarhus/Aalborg, [2]Department of Psychiatry, University of Oxford, United Kingdom, [3]Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal, [4]Cognition and Consciousness Imaging Group, Division of Anaesthesia, Wolfson College, University of Cambridge, United Kingdom, [5]Center of Brain and Cognition, Universitat Pompeu Fabra, Barcelona, Spain, [6]Institució Catalana de Recerca i Estudis Avancats (ICREA), Barcelona, Spain, [7]Department of Neuropsychology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [8]School of Psychological Sciences, Monash University, Melbourne, Victoria, Australia, [9]Digital and Cognitive Musicology Lab, Digital Humanities Institute, École Polytechnique Fédérale de Lausanne, Switzerland

Human decisions are often irrational and subject to perceptual and cognitive noise. While research has identified visual confounding effects, evidence from the auditory domain is scarce. Moreover, the brain mechanisms underlying decision-making in multimodal settings are largely unknown. In the present study, we investigate whole-brain dynamic network changes associated with auditory bias in decision-making. We collected behavioural and fMRI data of 38 healthy participants while performing the Coloured Card Deck Paradigm. The neuroimaging data was first analysed in a traditional GLM-analysis to test differences in activation between experimental conditions. We then used LEiDA (Leading Eigenvector Dynamics Analysis) to identify patterns of dynamic functional connectivity associated with biased decision-making.

Several cortical clusters, each related to a specific experimental condition, were found in the GLM-analysis. We then used LEiDA on the parcellated BOLD-signal time series, which revealed a functional connectivity network with significantly higher probability of occurrence during the multimodal task. This task-specific dynamic functional connectivity network consisted of the same areas as those identified in the GLM-analysis. The combination of GLM and dynamic analysis of the fMRI data with LEiDA thereby revealed distinct spatio-temporal network activity associated with multimodal decision-making. Notably, this overlap was found between a hypothesis-driven analysis of activation and a data-driven analysis of functional connectivity. Our findings indicate that temporal dynamics of multimodal decision-making depend on interaction between functionally specialised nodes.

P02.08   Weine Dai   THE DYSFUNCTION OF INHIBITORY CONTROL IN HEROIN ADDICTION AND PROBLEM GAMBLING

W. Dai[1, 3, 4, 5], Q. Li[1, 2], X. Liu[1, 2], A. Møller[3]

[1]CAS Key Laboratory of Behavioral Science, Institute of Psychology, Beijing, China, [2]Department of Psychology, University of Chinese Academy of Sciences, Beijing, China, [3]CFIN and PET Center, Aarhus University, [4]Sino-Danish College, University of Chinese Academy of Sciences, Beijing, China, [5]Sino-Danish Center for Education and Research, Beijing, China

Heroin addiction, a type of substance addiction, is a brain disorder caused by in-taking heroin, is described as the most severe state of substance use disorder in DSM-V. Problem gambling, a type of behavioral addiction, is an urge to gamble continuously despite harmful negative consequences or a desire to stop. Researchers found that addiction may be caused by the failure of self-control. Based on the dual mechanisms of control framework, inhibitory control can be categorized into two types. Proactive inhibitory control (PIC) relies on anticipation and preparation for response in advance. But with the sudden requirement of stopping, reactive inhibitory control (RIC) detects conflict first and solve it almost simultaneously. Several studies found that RIC in people with addiction problems may be impaired. But only a few studies focused on PIC in addiction. We will use a conditional Stop-Signal task to examine whether PIC and RIC are impaired in heroin addictive patients. The same task will also be used for measuring PIC and RIC ability in problem gambling players. For both heroin addiction and problem gambling, we hypothesize that the stop-signal reaction time (SSRT) between patients and healthy control will show a significant difference, suggesting that reactive inhibitory control may be injured in problem gambling. On the other side, compared Preparation Cost between patients and healthy control, Preparation Cost was slower in patients than HC, indicating proactive inhibitory control may be impaired in patients with additive problems. We speculate that substance addiction and behavior addiction may show similar dysfunction of inhibitory control.

P02.09 Hannah Brogård EFFECT OF ADRENALINE ON SURVIVAL AND NEUROLOGICAL OUTCOME
Andersen IN A NEWBORN PIGLET MODEL OF HYPOXIC CARDIAC ARREST

H.B. Andersen[1], M. Andersen[1], T.C. Andelius[1], M.V. Pedersen[1], B. Løfgren[2, 3, 4], M. Pedersen[5], S. Ringgaard[6], K.J. Kyng[1], T.B. Henriksen[1]

[1]Department of Paediatrics, Aarhus University Hospital, [2]Department of Cardiology, Aarhus University Hospital, [3]Research Center for Emergency, Aarhus University Hospital, [4]Department of Internal Medicine, Regional Hospital of Randers, [5]Comparative Medicine Lab, Aarhus University Hospital, [6]The MR Research Centre, Aarhus University Hospital

Background

Guidelines for drug use in neonatal resuscitation are based on extrapolations from adult literature. Adrenaline is an integral component of all published neonatal resuscitation algorithms. However, the evidence on effect and safety of adrenaline in neonatal resuscitation is sparse. Therefore, it is crucial to determine, whether or not adrenaline improves survival and outcome. In a piglet model of neonatal cardiac arrest (CA) we investigated adrenaline vs. placebo on survival and brain lactate/N-acetyl-aspartate (NAA) ratio.

Methods

24 piglets <24 hours of age were anesthetised. Hypoxia was induced by clamping the endotracheal tube and maintained until CA or severe bradycardia. CA was defined as mean arterial blood pressure <20mmHg AND heart rate <60bpm. Cardiopulmonary resuscitation (CPR) was commenced 5 minutes after CA. The piglets were randomized to either CPR + adrenaline or CPR + placebo. The primary outcome was survival. Secondary outcome was lactate/NAA ratio, obtained by Magnetic Resonance Spectroscopy (MRS) 6 hours after resuscitation.

Results

We present preliminary results from the first 15 animals. Baseline- and CA characteristics were similar between study groups pre-randomization. Clinical arrest rhythms were asystoli (60%) and ventricular fibrillation (40%). Following randomization, survival rate was significantly higher with adrenaline administration (n = 7/8 (87.5 %)) than with placebo (n = 2/7 (28.6 %); P = 0.04)). MRI/MRS data are pending.

Conclusion

In this preliminary analysis, resuscitation involving adrenaline rather than placebo improved survival after neonatal hypoxic cardiac arrest. Data from the last 9 piglets are pending.

P03.01 Astrid Høeg THE ASSOCIATION BETWEEN ATTACHMENT INSECURITY AND POST-
Tuborgh CONCUSSION SYMPTOMS IN YOUNG ADULTS.

A. Tuborgh[1, 2], S.W. Svendsen[3], A. Elklit[4], J. Hunter[5], J.S. Jensen[6], A. Schröder[6], J.F. Nielsen[3], M.M. Thastum MM[6], E.T. Næss-Schmidt[3], C.U. Rask[1, 2]

[1]Department of Child and Adolescent Psychiatry, Research Unit, Psychiatry, Aarhus University Hospital, [2]Department of Clinical Medicine, Aarhus University, [3]Hammel Neurorehabilitation Centre and University

Research Clinic, Aarhus University, [4]Department of Psychology, National Center for Psychotraumatology, University of Southern Denmark, [5]Department of Psychiatry, Mount Sinai Hospital, University of Toronto, Canada, [6]Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital

Background

The incidence of hospital-treated mild traumatic brain injury is 100-300/100,000 person-years. 5-15% of the patients report long lasting post-concussion symptoms (PCS). The factors involved in the development of PCS are not fully determined. Anxious and avoidant attachment dimensions have been suggested to be a pre-exiting personality factor influencing the way patients manage long lasting symptoms.

Objectives

1) explore how attachment style is associated with self-reported PCS, and 2) if these associations are mediated by illness perceptions and illness behaviours.

Methods

The study was designed as a cross-sectional study embedded in a cohort study of adolescents and young adults (N=3080) with a recent concussion to investigate PCS 2-3 months post-injury (median 87 days, inter quartile range 66-107 days). Data were obtained from an administrative database and self-reported questionnaires. Linear regression models and structural equation models were used for statistical analyses.

Results

N=1190 (39%) responded on the questionnaires. Adjusted analysis revealed a significant association between attachment anxiety and PCS (β= 1.0 (95%CI 0.5 ; 1.5), p< 0.001) and between attachment avoidance and PCS (β= -1.7 (95%CI -2.6 ; -0.8), p< 0.001).

Negative illness perceptions and maladaptive illness behaviours mediated parts of the effect of attachment style on PCS.

Conclusion

Anxious and avoidant attachment dimensions could be pre-disposing factors indicating how patients with PCS report their symptoms. More studies are requested to investigate if attachment dimensions can be used as a predictive factor for developing PCS.

| P03.02 | Benjamin Mac Donald | PATTERNS OF TREATMENT IN SEVERE ANOREXIA NERVOSA. |

B. Mac Donald[1, 2], L. Petersen[3], J. Larsen[3], C. Bulik[4, 5], L. Clausen[1, 2]

[1]Department of Clinical Medicine, Aarhus University, [2]Department of Child and Adolescent Psychiatry, Aarhus University Hospital, [3]The National Centre for Register-based Research, Department of Economics and Business Economics, Aarhus University, [4]Center of Excellence for Eating Disorders, University of North Carolina at Chapel Hill, [5]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet

Background:

Severe anorexia nervosa (AN) is fraught with cost both socioeconomically and humanly. Hospital based involuntary treatment (IT) of severe AN can be needed and a subgroup of patients experience multiple episodes of IT. To optimize the ongoing focus on reducing IT this study aims at examining what characterizes the treatment course in severe AN that includes multiple episodes of IT.

Method:

This is a register based retrospective exploratory cohort study with minimum two years of follow-up from 1st admission with AN. The study population is all patients born after 1963 who have been admitted between the years 2000 to 2014 with an AN (DF50.0, DF50.1, DF50.8 og DF50.9) diagnosis registered. First patterns of treatment will be identified using variables including number of admissions with and without IT, temporal admission patterns, types of involuntary measures, and whether or not there is an AN diagnosis at admission. Next treatment pattern groups are compared on variables including age at diagnosis, age at 1st admission, age at 1st IT episode, time from diagnosis to 1st IT episode, psychiatric comorbidity, psychopharmacological treatment, and socioeconomic status.

Results:

Preliminary results are expected by January 2020.

Perspective:

The study is essential to promote identifiers of patients at risk of multiple IT episodes, which is needed to help clinicians identify these patients early and intervene to prevent and reduce IT.

P03.03 Bardia Varastehmoradi OPIOID SYSTEM HAS AN IMPACT ON HPA AXIS, COGNITIVE PROCESSES AND DEPRESSION

B. Varastehmoradi[1], K.L. Smith[2], C. Sánchez[1, 2], E. Robinson[3], G. Wegener[1]

[1]Translational Neuropsychiatry Unit, Department of Clinical Medicine, Aarhus University, [2]Department of Biology, Alkermes Inc., Waltham, MA, USA, [3]School of Physiology, Pharmacology and Neuroscience, University of Bristol, Bristol, UK

Negative cognitive affective bias(CAB) is one of the symptoms that appears in depression. As cognitive processing can be modulated by endogenous opioid peptides. The aim of this study was to investigate the role of opioid system on hypothalamic-pituitary-adrenal(HPA) axis in CAB and depression.

The CAB of corticosterone(CORT) and the kappa opioid receptor(KOR) agonist, U50488, was measured in the affective bias test(ABT) using female SD rats. During 4 pairing days, the animals chose a bowel which contained reward or not. The reward was buried with different substrates which were paired with drug or vehicle injection. In the preference test the animal chose one of the rewarded substrates during 30 trials. Based on the number of choices, the CAB was calculated. Moreover, the plasma level of dynorphin(DYN) and serum level of CORT in serum was measured by EIA and ELISA 30 minutes following CORT or U50488 treatment. The

effect of DIPPA(KOR antagonist) on CAB of CORT-treated animals was also assessed.

We found both U50488(5mg/kg) and CORT(10mg/kg) significantly induced negative biases, while DIPPA(5mg/kg) eliminated CORT-induced negative biases. No significant difference between DYN level in CORT-treated and control group was observed. However, the CORT concentration in serum was significantly higher in U50488-treated group than control(p<0.01).

This study show that KOR has an impact on HPA axis and depression related measures. The data supports that the opioid system, especially KORs, can be proposed as putative therapeutic targets in depression due to modulating cognitive functions, HPA axis and mood level.

Keywords: opioid, HPA axis, cognitive affective bias, depression

P03.04   Line Elmerdahl Frederiksen

HOSPITAL CONTACTS FOR MENTAL DISORDERS IN CHILDHOOD CANCER PATIENTS AND SURVIVORS IN A LONG-TERM PERSPECTIVE: A NATIONWIDE REGISTER-BASED COHORT STUDY

L.E. Frederiksen[1], F. Erdmann[1], H. Hasle[2], J.F. Winther[1, 3]

[1]Childhood Cancer Research Group, Danish Cancer Society Research Center, [2]Department of Pediatrics, Aarhus University Hospital, [3]Department of Clinical Medicine, Aarhus University

Introduction:

Substantial improvements in survival of childhood cancer have led to a steadily growing population of survivors. The diagnosis and its subsequent treatment may adversely impact the health of survivors in various aspects throughout the life course. We aimed to explore the long-term risk of hospital contacts for mental disorders after a childhood cancer diagnosis.

Materials and methods:

We conducted a nationwide register-based cohort study of children diagnosed with cancer before the age of 20 years in Denmark, a population-based comparison group and a sibling comparison group. Childhood cancer cases (n=9,859) diagnosed between 1943 and 2008 were identified from the Cancer Register and compared to a cohort of their siblings (n=17,221) and population comparisons (n=49,158). Information on hospital contacts were obtained from the Psychiatric Central Research Register (1970-1994) and the National Patient Register (1995-2017). We followed our study population from time of diagnosis until death, emigration or end of study and assessed hospital contacts for any mental disorder and for specific diagnostic groups.

Preliminary results:

Childhood cancer cases were slightly less likely to have an in-patient hospitalization of any mental disorder in later life than the population comparisons (4.05% vs 4.78%, p 0.002), but similar compared to siblings (4.05% vs 4.44%, p 0.128). However, childhood cancer cases were more often hospitalized for psychotic disorders and mental disorders due to known somatic conditions (e.g. dementia) than the two comparison

groups. Having been diagnosed with retinoblastoma or a CNS tumor increased the risk of a hospitalization for a mental disorder.

P03.05 Davide Ligato A COMPARISON BETWEEN CLASSICAL SINGERS, RHYTHMIC SINGERS, AND NON-SINGERS INVESTIGATING MUSICAL AND PHYSICAL TRAINING. CAN THESE AFFECT HUMAN SENSORY PERCEPTION?

D. Ligato, B.A. Kleber, E. Brattico, P. Vuust

Department of Clinical Medicine, Center for Music in the Brain, Aarhus University and RAMA

Background: The extent to which we perceive pain, air hunger, visceral sensations, but also other inner bodily sensations (interoception) may influence our own subjective experience: for example, trained singers constantly rely on interoception for their performance, processing feedback information almost in real time. Here, we investigate both the interoceptive skills and the performance (interoceptive accuracy) of trained singers and volunteers without vocal training, and to what extent musical skills and accumulated musical and physical training enhance interoception. Generally, interoception is tested with a heartbeat task, where participants judge the synchrony of external auditory stimulations with their own heartbeats. We therefore investigated interoception using a heartbeat task design including an auditory stimulation and a new stimulation using electrical stimuli.

Methods: 20 classical singers, 19 rhythmic singers, and 18 non-singers stated their individual musical and physical training and have been tested using two heartbeat tasks, the Musical Ear Test (MET; measures the participant's performance to a melodic and a rhythmic tests), and a questionnaire (GOLD-MSI; measures a participant's ability to engage with music) to assess music.

Results: 57 volunteers (age: 18-53, average: 29±8) participated. Results from the heartbeat tasks revealed no significant differences between groups. Rhythmic singers performed better on the MET (rhythmic); singers performed better on both the MET (melody) and on the GOLD-MSI.

As we were not able to replicate previous findings with the heartbeat tasks, further data analysis will aim to identify possible underlying factors.

P03.06 Katrine Ingeman Beck DEVELOPMENT OF THE HEALTH ANXIETY BY PROXY SCALE: A NEW MEASURE FOR EXCESSIVE PARENTAL WORRIES FOR CHILDREN'S HEALTH.

K. Ingeman[1], L. Frostholm[2], D. Hoffmann[2], K. Wright[3], E. Lockhart[4], E. Garralda[5], M. Kangas[6], C.U. Rask[1]

[1]Department of Child and Adolescent Psychiatry, Research Unit, Aarhus University Hospital Psychiatry, [2]Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, [3]Psychology, Faculty of Arts, University of Regina, Canada., [4]Royal Hospital for Children, Glasgow, UK, [5]Department of Medicine, Imperial College, London, UK, [6]Macquarie University, Sydney, Australia

Background: Health anxiety by proxy is defined as parents' obsessive worries about their child's health. The parents' intrusive and unpleasant thoughts about their child's health may cause physical examinations of

their child and an increased number of health care contacts. Thus, health anxiety by proxy is an important issue in both preventive and treatment settings. Still, no instrument exist to assess health anxiety by proxy and it often goes unnoticed.

Aim: This study aimed at developing the Health Anxiety by Proxy Scale (HAPYS), a measure for excessive parental worries for children's health.

Method: The development of the HAPYS involved three steps: 1. Qualitative interviews with 7 patients clinically judged to suffer from health anxiety by proxy, 2. Questionnaire development in close collaboration with an expert panel, and 3. Pilot testing of the HAPYS with both well parents and parents with health anxiety by proxy. The HAPYS was continuously adjusted to the feedback from experts and patients.

Results: The final version of HAPYS has 26 items with an additional impact section with five items. The items cover thoughts, feelings and behavior characteristic of health anxiety by proxy. HAPYS has shown to possess good face and content validity.

Discussion: Development of questionnaires should optimally be performed systematically and with patients involved. The HAPYS is the first systematically developed questionnaire to assess health anxiety by proxy. Results indicate that it is a valid tool to assess health anxiety by proxy, with the potential of helping clinicians with parents suffering from this condition. The HAPYS is currently being further evaluated in a larger sample.

P03.07   Nanna Weye   ALTERNATIVE METRICS TO QUANTIFY PREMATURE MORTALITY IN MENTAL DISORDERS. A POPULATION-BASED COHORT STUDY

N. Weye[1], N. Momen[1], K.M. Iburg[2], M. Christensen[1, 2], . Health Metrics Writing Group[1, 3], J. McGarth[1, 3, 4], O. Plana-Ripoll[1]

[1]National Centre for Register-based Research, Department of Economics and Business Economics, Aarhus University, [2]Department of Public Health, Aarhus University, [3]Queensland Brain Institute, Unviersity of Queensland, [4]Queensland Centre for Mental Health Research, the Park Centre for Mental Health, Queensland

The Global Burden of Disease (GBD) study uses Years of Life Lost (YLLs) to quantify premature mortality. This is a useful metric from many perspectives, however because GBD acknowledges only a small number of mental disorders as causes of death (CoDs), the true impact of mental disorders on premature mortality is underestimated. Recently, methods have been introduced that compare people with a disorder to the general population through Life Years Lost (LYLs). The aim of this paper was to present register-based estimates for mental disorders of both YLLs and LYLs.

Methods:

Nationwide register-based cohort study of all persons aged 0-94 years in Denmark in 2000-2015. Using the GBD approved set of mental health-related CoDs, YLLs were estimated. In addition, we calculated all-cause and cause-specific LYLs for 12 specific mental disorders and counts of comorbid mental disorders.

Results:

The leading causes of YLLs (rates per 100.000 person-years) were alcohol use disorder (men 568.7 YLLs, women 155.5), and especially suicide (men 590.1 YLLs, women 202.3). However, all mental disorders were associated with shorter life expectancies using LYLs. Men and women diagnosed with any mental disorder had respectively 11.1 (95% CI 11.0-11.2) and 7.9 (95% CI 7.7-8.0) years shorter life expectancies, and the difference increased in those with more comorbid mental disorders.

Conclusions:

Register-based studies allow the calculation of precise YLLs and LYLs, and both metrics are informative. The novel LYLs metric better captures the true impact of mental disorders on premature mortality in those with mental disorders and also facilitates the exploration of comorbidity and specific CoDs.

P03.08 Cecilie Marie Nielsen

HOW CAN WE IMPLEMENT MEASUREMENT-BASED CARE OF SCHIZOPHRENIA? CLINICAL VALIDATION OF PANSS-6, A BRIEF RATING SCALE TO MEASURE SYMPTOM SEVERITY

C.M. Nielsen[1, 2], P. Kølbæk[1, 2], C. Correll[3], O. Mors[1, 2], S.D. Østergaard[2, 4]

[1]Psychosis Research Unit, Aarhus University Hospital - Psychiatry, [2]Department of Clinical Medicine, Aarhus University, [3]Department of Psychiatry, The Zucker Hillside Hospital, Glen Oaks, NY, USA, [4]Department for Depression and Anxiety, Aarhus University Hospital - Psychiatry

Background: In psychiatry, systematic use of symptom rating scales to guide treatment decisions - so called Measurement-based care (MBC), has shown great promise in the treatment of mental disorders such as depression and anxiety. However, in the treatment of schizophrenia, which is considered to be the most disabling mental disorder, implementation of MBC is lacking. A key obstacle in the implementation of MBC for schizophrenia is the lack of a brief and valid rating scale to measure symptom severity.

The most widely used schizophrenia severity rating scale, the 30-item Positive And Negative Syndrome Scale (PANSS-30), takes approximately an hour to administer, which is too long for routine clinical use. Therefore, based on item response theory analysis, our group has extracted a 6-item scale (PANSS-6), which has promising psychometric properties, but lacks clinical validation.

Aim: The aim of this PhD study is to validate PANSS-6 by investigating the degree of correspondence between PANSS-6 scores rated based on a brief targeted interview (the Simplified Negative And Positive Symptoms Interview (SNAPSI)) and PANSS-6 scores extracted from PANSS-30 ratings obtained using the Structured Clinical Interview for PANSS (SCI-PANSS).

Methods: Consenting adults (n=75) with a diagnosis of schizophrenia, undergoing outpatient treatment, will be interviewed with both SNAPSI and SCI-PANSS within 24 hours (random order). Interviews will be conducted by two independent interviewers and followed by independent PANSS-6 and PANSS-30 ratings.

Perspectives: If our results demonstrate that PANSS-6 is clinically valid, this brief rating scale can aid implementation of MBC for schizophrenia.

P03.09 Maria Christensen

THE ECONOMIC BURDEN OF MENTAL DISORDERS: A SYSTEMATIC REVIEW

M.K. Christensen[1, 2], C. Lim[3], S. Saha[3], K.M. Iburg[2], D. Cannon[3], F. Presley[3], J.J. McGrath[1, 3, 4]

[1]National Centre for Register-based Research, Department of Economics and Business Economics, Aarhus University, [2]Department of Public Health, Aarhus University, [3]Queensland Center for Mental Health Research, Australia, [4]Queensland Brain Institute, University of Queensland, Australia

Background:

About a third of the world's population will develop a mental disorder over their lifetime. Having a mental disorder is a huge burden in health loss and cost for the individual, but also for society because of treatment cost, production loss and caregivers' cost.

Objective:

To synthesize the international published literature on the economic burden of mental disorders.

Material and methods:

Systematic literature searches were conducted in the databases PubMed, Embase, Web of Science, EconLit, NHS York Database and PsychInfo using key terms for cost and mental disorders. Searched were restricted to 1980 until May 2019. The inclusion criteria were: (1) cost-of-illness studies or cost-analyses; (2) diagnosis of at least one mental disorder (3) samples based on the general population; (4) outcome in monetary units.

13,640 hits were screened by their title/abstract and 439 articles were full-text screened by two independent reviewers. 113 articles were included from the systematic searches and 31 articles from snowball searching, giving a total of 144 included articles.

Results:

The preliminary results show a substantial variety in the methodology, costs component and outcomes in the included studies.

An online tool will be developed enabling the reader to explore the published information on costs by type of mental disorder, country, type of study and quality score.

Conclusion:

This paper will provide an important and comprehensive overview over the economic burden of mental disorders around the world, and the output will facilitate policymaking.

P03.10   Sanne Toft   INSOMNIA IN DEPRESSION AND THE EFFICACY AND APPROPRIATENESS
          Kristiansen   OF BALL BLANKETS: AN INDUSTRIAL PHD

S.T. Kristiansen[1, 2], P. Videbech[3], E.R. Larsen[4, 5], M.B. Bjerrum[1]

[1]Research Unit of Nursing and Healthcare, Department of Public Health, Aarhus University, [2]Protac A/S, Skanderborg, [3]Center for Neuropsychiatric Depression Research, Mental Health Centre Glostrup, [4]Mental Health Department Odense - University Clinic, Mental Health Service, Region of Southern Denmark, [5]Department of Clinical Research, University of Southern Denmark

Introduction

Depression affects approx. 4% of the global population and is often accompanied by insomnia. Medications used to treat insomnia can have side effects. Investigating the benefits of non-pharmacological treatment options is therefor highly relevant.

Aim

To investigate patients' experiences of sleep problems caused by depression and to test the efficacy and appropriateness of the Protac Ball Blanket™(PBB).

Methods

Study 1 is a systematic integrative review on the experience of sleep problems caused by depression. Both quantitative and qualitative studies will be included. Data will be analyzed using content analysis.

Study 2 is a crossover trial including 45 patients. Patients are randomized to either receive treatment with PBB in two weeks or to wait. Subsequently, patients switch either to wait or to receive PBB. The primary outcome is changes in Total Sleep Time. Secondary outcomes are changes in SOL, NA, WASO, per need medication, quality of sleep, insomnia severity and self-reported symptoms of depression and anxiety. Data collection methods: Actigraphy, sleep and medication diaries and questionnaires. We will perform a paired, two-sided t-test to compare the means of the differences in the outcomes.

Study 3 is a qualitative study of 20 patients. Aim: To investigate the patient perceived benefits and limitations of sleeping with PBB and to pursue any surprising results from the RCT that needs further explanation. Data will be collected using semi-structured interviews and analyzed using content analysis.

Perspectives

PBB is potentially a non-pharmacological supplement to sedatives, but evidence for the efficacy is needed before the treatment is implemented.

P04.01   Troels Græsholt-   SIGNS OF DANGER - A SYSTEMATIC REVIEW OF THE RISK OF CHILD
          Knudsen   ABUSE

T. Græsholt-Knudsen[1], C.U. Rask[2], S. Lucas[4, 5], M.V. Stadelhofer[3], W.M. Ullahammer[3], C. Gu[3], A.L. Bæk[3], M.F. Edelbo[3], C. Obel[1]

[1]Department of Public Health, Aarhus University, [2]Department of Child and Adolescent Psychiatry, Aarhus University Hospital, [3]Aarhus University, [4]Uppsala University, [5]Uppsala University Hospital

Why?

Physical child abuse has immediate and long-term detrimental effects. Consequently, screening tools and risk models to inform preventive measures are widespread. However, as the toxic nature of abuse limits the use of experimental methods, the evidence base for risk models is diverse and mainly observational. Former reviews on risk indicators are dated (2009) - or they make use of narrow search strategies.

Aims

We will provide a systematic, comprehensive overview of current knowledge from observational studies, using both keywords and free-text searches from scientific search engines covering health, social sciences, education and governmental reports. We will present all risk indicators found, including their effect sizes and, using the QUIPS rating tool, their strength of evidence. Data will be organized with inspiration from Bronfenbrenner's ecological framework and prior reviews on this subject.

Whom?

Results will be the first collection of risk indicators temporally separated from physical child abuse and collected from a comprehensive, cross-disciplinary search. They are expected to be useful for clinicians estimating risks, policy-makers and analysts doing predictive modeling or preventive legislation targeting physical child abuse, and other agents working for prevention of physical child abuse.

P04.02   Nina Mckinnon   THE IMPACT OF SOCIOECONOMIC STATUS ON THE INCIDENCE OF
          Edwards   TOTAL HIP ARTHROPLASTY DURING 1995-2018

N.M. Edwards, A.B. Pedersen

Department of Clinical Epidemiology, Aarhus University Hospital

Aim

To describe the association of socioeconomic characteristics on the incidence of THA.

To describe the time trends of these correlations between socioeconomic status (SES) and the risk of THA.

Method

Register-based study using the Danish Hip Arthroplasty Registry to identify all patients undergoing surgical procedure for a primary THA in Denmark from the 1st of January 1995 to the 31st of December 2017 with the primary diagnosis idiopathic arthrosis. The CPR registry was used to select 5 controls for each THA case, matched on sex, region of residence and

index date. Exposure was different SES markers. Adjusted odds ratios with 95% confidence intervals were calculated (aOR) using logistic regression.

Results

A total of 108,946 THA and 544,730 participants were enrolled. The aOR for the risk of THA for the youngest age group with the lowest education (ref highest) was 1.47 (1.36-1.58). The associations decreased with increasing age. The aOR for the youngest age group with the lowest liquid assets (ref highest) was 0.75 (0.7-0.81). This association was seen in all age groups. The aOR for the risk of THA with the lowest education (ref high) was 1.24(1.15-1.32) in the years 1995-2000 and decreased to 1.01 (0.97-1.05) in the years 2013-2017. For the lowest income the aOR was 1.22 (1.12-1.32) in 1995-2000 and decreased to 0.85 (0.8-0.9) in 2013-2017 (ref highest).

Conclusion:

Lower level of education was associated with a higher risk of THA but the association decreased with increasing age. The inequality seen in the risk of THA and in the level of acquired education suggest a time trend towards less social inequality.

P04.03   Jon Hagen   TESTING DYNAMIC MUSCLE FUNCTION USING ELECTRICAL STIMULATION
          Herskind   IN HUMANS.

J. Herskind, A. Gravholt, L.G. Hvid, K. Overgaard

Department of Public Health, Aarhus University

Background: Maximal voluntary isometric contraction (MVIC) testing is widely used as a measurement of muscle strength. To avoid influence from neural or psychological factors, previous studies have also utilized electrically evoked contractions to test muscle function. However, in most of these studies only modest forces are achieved compared to voluntary contractions. Furthermore, the isometric testing mode precludes assessment of the force-velocity relationship. Therefore, we here attempt to develop a method for testing dynamic muscle function of the quadriceps femoris using electrical stimulation with forces approaching those achieved during voluntary activation.

Methods: Subjects were seated in a dynamometer with one leg randomized for testing. Following MVIC testing, a series of electrically evoked dynamic and isometric contractions were performed at various frequencies. Force and velocity data were sampled during testing and subjective ratings of discomfort were reported using a numeric pain scale (NPS).

Results: The study is ongoing at the time of writing. Pilot data indicate that electrically induced contractions can yield force-velocity relationships resembling those of isolated muscle preparations. The maximal forces elicited by electrical stimulation reach 50-70 % of MVIC, while NAS scores indicate a moderate to high level of discomfort during stimulation. However, discomfort appears to decrease after habituation.

Conclusion: Based on pilot studies, the newly developed test can effectively assess dynamic muscle function. This may be particularly useful

in patient populations where muscular and neurological function need to be assessed separately.

P04.04 Karin Rosenkilde Laursen **INVESTIGATING POTENTIAL HEALTH EFFECTS OF EXPOSURE TO PASSIVE VAPE FROM E-CIGARETTES - A RANDOMIZED CONTROLLED CHAMBER STUDY**

CANCELLED

K.R. Laursen[1], G.J. Holst[1], S. Loft[2], T. Sigsgaard[1]

[1]Department of Public Health, Aarhus University, [2]Department of Public Health, University of Copenhagen

Background: The use of e-cigarettes is often permitted in otherwise smoke-free areas causing passive vape exposure for present individuals. Little is known about the potential adverse health effects of passive vape, and people with respiratory diseases may be more susceptible to vape exposure.

Objective: To investigate local and systemic effects of short-term passive exposure to vape from e-cigarettes among patients with mild or moderate chronic obstructive pulmonary disease (COPD).

Methods: Non-smoking COPD patients (n=16) participated in a double-blinded randomized controlled chamber study comprising exposures to: A) clean filtered air (control exposure), and B) vape from e-cigarettes using participants as their own controls. E-cigarette users were present in an adjacent chamber during both exposures, but only in situation B they were vaping and the vape-polluted air was passed on to the exposure chamber. The two exposure days were separated by 14 days, and participants were exposed to each of the exposures for four hours. Subjective symptoms were recorded using a questionnaire, while objective measures including spirometry and markers of inflammation in exhaled air and blood were examined prior to, after, and 24 hours after exposure. Data are analyzed using multivariate analysis of variance for repeated measures.

Results: Will be presented at PhD Day 2020.

Implications: The study will provide knowledge on possible health effects of passive exposure to vape from e-cigarettes which could be of relevance to the public and public health decision makers. Furthermore the study can inspire others on do's and don'ts when conducting an exposure study with e-cigarettes as exposure.

P04.05 Jakob Schöllhammer Knudsen **THE CHANGING FACE OF EARLY TYPE 2 DIABETES: HBA1C AND LIPID MANAGEMENT TRENDS, 2000-2017 A DANISH POPULATION-BASED STUDY**

J.S. Knudsen[1], A. Hulman[2, 3, 4], P.F. Rønn[5], T. Lauritzen[4], H.T. Sørensen[1], D.R. Witte[2, 3], R.W. Thomsen[1]

[1]Department of Clinical Epidemiology, Aarhus University, [2]Steno Diabetes Center Aarhus, [3]Danish Diabetes Academy, [4] Research Group for General Practice, Department of Public Health, Aarhus University, [5]Steno Diabetes Center Copenhagen

OBJECTIVE: Population-based data investigating long-term trends in diabetes management strategies are scarce. We examined 18-year changes in early HbA$_{1c}$and lipid testing and control among people initiating glucose-lowering drugs (GLD) in Northern Denmark.

METHODS: Population-based sequential cross-sectional study using healthcare databases covering the entire population of Northern Denmark. For all 94,175 GLD initiators 2000-2017, we examined the proportion with HbA$_{1c}$and lipid testing, lipid-lowering therapy, and achievement of glycemic and LDL cholesterol targets within a year.

RESULTS: The proportion of patients who had at least one HbA$_{1c}$test increased from 53% in 2000 to 95% in 2017. Lipid testing increased from 82% to 98% and lipid-lowering drug initiation quintupled from 12% to 61%. Pre-treatment HbA$_{1c}$declined substantially, from a mean of 9.2% in 2000 to 7.3% in 2011, but rose again after the new HbA1c diagnostic criteria to 7.9% in 2017. Post-treatment HbA$_{1c}$as a measure of treatment effectiveness decreased less; whereas pre- and post-treatment LDL cholesterol levels declined almost in parallel. The proportion achieving glycemic and cholesterol targets increased substantially over time.

CONCLUSION: The typical real-life patient with early type 2 diabetes has changed substantially over the past two decades. Monitoring and treatment of glucose and cholesterol has improved considerably, yet there is room for further improvements. The increasing pre-treatment HbA1c after 2011 suggests that the change in diagnostic criteria for diabetes may possibly preclude a substantial number of dysglycemic patients from initiating relevant treatment.

P04.06 Susanne Fogh Jørgensen

TIMELY FOLLOW-UP AND ADHERENCE TO FOLLOW-UP GUIDELINES AFTER CERVICAL SCREENING ABNORMALITIES: A NATIONWIDE REGISTER-BASED COHORT STUDY.

S.F. Jørgensen[1, 2], B. Andersen[1, 2], M. Rebolj[3], S.H. Njor[1, 2]

[1]Department of Public Health Programmes, Randers Regional Hospital, [2]Department of Clinical Medicine, Aarhus University, [3]Cancer Prevention Group, School of Cancer and Pharmaceutical Sciences, Faculty of Life Sciences and Medicine, King's College London, London, UK.

Background: Cancer screening can be hampered by unavailability of diagnostic services to investigate potential screen-detected abnormalities. We designed an extensive register-based study, mapping diagnostic and treatment services in the cervical cancer screening program to explore the availability and use of follow-up of potential screen-detected abnormalities.

Methods: We followed women aged 23-59 years with screen-detected abnormalities between 2012-2014 through their pathway of follow-up, determining the number of tests and treatments from different healthcare providers and their timing. We assessed variations in diagnostic and treatment resources to determine how and how often a woman's care deviates from the national recommendations and whether this is associated with age, geographic area or healthcare provider.

Results: Among women with inadequate or HSIL+ screening results, 48% and 93% had timely follow-up, respectively. Women with ASCUS/LSIL and a positive HPV-test, had a high proportion of timely follow-up (87%), while

having a negative HPV-test led to excessive testing beyond recommendations in approximately 32 % of cases. When including test type and provider in the assessment of adherence to the total follow-up pathway, only 50% of all women received exactly the recommended follow-up care. Higher age and the provider being a general practitioner were associated with better adherence.

Conclusions: In this evaluation we found that even though women adhere to screening and the first follow-up test, failures do happen later down the follow-up pathway, resulting in either insufficient treatment/surveillance or over-testing in 50% of all follow-up pathways.

P04.07   Susanne Boel   RISK FACTORS FOR REHOSPITALIZATION AND PREMATURE MORTALITY IN
         Graversen   ELDERLY AFTER AN ADMISSION FOR PNEUMONIA - A POPULATION-
                         BASED COHORT STUDY

S.B. Graversen[1, 2], H.S. Pedersen[1], A. Sandbaek[2, 3], C.H. Foss[4], A.R. Ribe[1]

[1]Research Unit for General Practice, Department of Public Health, Aarhus University, [2]Department of Public Health, Aarhus University, [3]Steno Diabetes Centre Aarhus, [4]Department of Geriatrics, Aarhus University Hospital

Background

Rehospitalization and premature mortality after an admission for pneumonia are common among the elderly. Knowledge on risk factors may prevent adverse events, yet small numbers and lack of generalizability have limited earlier studies. We examined risk factors for rehospitalization and mortality in elderly hospitalized for pneumonia.

Methods

Using the Danish nationwide registries, we identified all hospitalizations for pneumonia during 2000-2016 in individuals aged 65-99 years old. Hazard ratios for 30-day rehospitalization and 30-day mortality with 95% confidence intervals were calculated using a Cox proportional hazards model, adjusted for age, sex, calendar period, and time since discharge.

Results

Of the 298,559 pneumonia-related admissions, 23.0% were followed by rehospitalization and 8.1% by death within 30 days of follow-up. Overall, the majority of the potential risk factors were significantly associated with the outcomes. Number of comorbidities, concurrent pharmacological treatments and prior contacts to the health care system were associated with a higher risk of both rehospitalization and premature mortality in a dose-response relationship. Age above 80 years was associated with a higher risk of premature mortality but was associated with a lower risk of rehospitalization compared to age 65 years.

Conclusions

This study identified several potential risk factors for rehospitalization and premature mortality among elderly discharged after pneumonia. This knowledge is urgently needed to design targeted intervention in a cross-sectoral setting aimed at preventing excess rehospitalizations and premature mortality after pneumonia in these frail patients.

P04.08   Rikke Nørgaard Pedersen   THE LONG TERM RISK OF BREAST CANCER RECURRENCE IN DENMARK 1987-2018

R.N. Pedersen[1], L. Mellemkjær[2], S. Friis[2], B. Ejlertsen[3, 4], T.L. Lash[1, 5], M. Nørgaard[1], D.P. Cronin-Fenton[1]

[1]Department of Clinical Epidemiology, Department of Clinical Medicine, Aarhus University Hospital, [2]Danish Cancer Society Research Center, Danish Cancer Society, [3]Danish Breast Cancer Group, [4]Rigshospitalet, [5]Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA, USA

Background: Breast cancer (BC) may recur many years after primary diagnosis. We investigated the 30-year incidence of breast cancer recurrence (BCR) and identified risk factors for "late breast cancer recurrence" (≥10 years after primary surgery).

Methods: Using the Danish Breast Cancer Group's (DBCG) database, we identified all women with incident stage I-III operable BC diagnosed during 1987-2004. Information on early BCR (<10 years) was obtained from DBCG. We derived an algorithm to identify late BCR using Danish population-based registries. We are currently validating the algorithm. Follow-up began on the date of BC surgery and continued until BCR, death, emigration, second cancer or 31/12/2018. Crude incidence rates (IRs) per 1,000 person-years (PY) and cumulative incidence proportions (CIPs) were calculated for BCR. Furthermore, we investigated associations between clinico-pathological factors and late BCR, starting follow-up 10 years after primary surgery.

Preliminary results: Among 36,962 patients, 11,648 developed BCR. The IR was 25.7 (95%CI, 25.3-26.2) per 1,000 PY and the 30-year CIP was 34%. Ten years after primary diagnosis, 21,588 women were eligible; among these, 3,579 developed late BCR corresponding to an IR of 20.4 (95%CI, 19.7-21.1) per 1000 PY and a CIP of 21% after 20 years of follow-up (from year 10 to year 30 after primary surgery). The CIP was higher among patients with estrogen receptor (ER)+ tumors, stage III disease and high nodal status.

Conclusion: Our preliminary findings suggest BC patients are at risk of late BCR throughout the period from 10 to 30 years after primary diagnosis, and baseline tumor characteristics are associated with late BCR.

P04.09   Tina Lützen   PRELIMENARY RESULTS: GP ATTENDANCE IN PROXIMITY TO HPV VACCINATION

T.H. Lützen[1], C.U. Rask[2], N. Rolving[3], O. Plana-Ripoll[4], D. Rytter[1]

[1]Department of Public Health, Aarhus University, [2]Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, and Child and Adolescent Psychiatric Center Risskov, Aarhus University Hospital, [3]University Research Clinic for Innovative Patient Pathways Diagnostic Center, Silkeborg Regional Hospital, [4]National Centre for Register-Based Research, Department of Economics and Business Economics, Aarhus University

INTRODUCTION

Studies on girls experiencing suspected adverse events after HPV-vaccination show increased morbidity prior to vaccination compared to other HPV-vaccinated. This may indicate that their symptoms have not occurred recently, and it is therefore important to examine whether there is a temporal link between vaccination and experiencing symptoms.

OBJECTIVES

To examine whether possible changes in GP attendance occurs following vaccination, and whether possible changes in GP attendance occurs in temporal link to vaccination.

METHODS

Cases were referred to an HPV-center and matched with HPV-vaccinated controls on selected variables. Negative binomial regression were used to examine GP attendance patterns prior to and after vaccination. An interaction term between case/control status and GP contacts before/after vaccination was used to estimate possible changes in GP attendance. Analyses were stratified on vaccination year (2008-2009, 2010-2012 and 2013-2015).

RESULTS

GP contacts for cases rise in the first year after vaccination, with incidence rate ratios (IRR) between cases and controls increasing 41% [37% ; 45%] after vaccination compared to prior. Stratification on vaccination year show similar increases in IRR.

DISCUSSION AND CONCLUSIONS

This study shows that cases increase in GP contacts in close proximity to HPV-vaccination. It is however not possible to conclude a causal link to HPV-vaccination. Symptoms may be of temporal coincidence and would have occurred irrespectively, or vaccination may trigger unknown pathways for increased illness. Note this is preliminary results and should be cautiously interpreted.

P04.10   Gitte Hoff Valentin   SOCIO-ECONOMIC INEQUALITIES IN FRAGILITY FRACTURE OUTCOMES: A SYSTEMATIC REVIEW AND META-ANALYSIS OF PROGNOSTIC OBSERVATIONAL STUDIES.

G. V[2, 1], S. P[2], R. C[3], K. F[2], C. P[2], A. B[4], C. G[4], B. L[5, 1]

[1]Department of Clinical Medicine, [2]DEFACTUM, Central Denmark Region, [3]The Parker Institute, Bispebjerg and Frederiksberg Hospital and Research Unit of Rheumatology, [4]Musculoskeletal Research Unit, Bristol Medical School, Southmead Hospital, [5]Department of Diabetes and Hormone diseases

Purpose: Fragility fractures, especially of the hip, cause substantial excess mortality and impairment in health-related quality of life (HRQoL). This systematic review and meta-analysis aimed to investigate the association between socio-economic status (SES) and post-fracture mortality and HRQoL.

Methods: PubMed, EMBASE and CINAHL databases were searched from inception to the last week of November 2018 for studies reporting an association between SES and post-fracture mortality and/or HRQoL

among people aged ≥50 years. Risk ratios (RRs) were meta-analysed using a standard inverse-variance-weighted random effects model. Studies using individual-level and area-based SES measures were analysed separately.

Results: A total of 24 studies from 15 different countries and involving more than one million patients with hip fractures were included. The overall risk of mortality within one year post hip fracture in individuals with low SES was 24% higher than in individuals with high SES (RR 1.24, 95%CI: 1.19 to 1.29) for individual-level SES measures, and 14% (RR 1.14, 95% CI: 1.09 to 1.19) for area-based SES measures. The quality of the evidence for the outcome mortality was moderate. Using individual SES measures, we estimated the excess HRQoL loss to be 5% (95% CI -1 to 10%) among hip fracture patients with low SES compared with high SES.

Conclusions: We found a consistently increased risk of post hip-fracture mortality with low SES across SES measures and across countries with different political structures and different health and social care infrastructures. The impact of SES on post-fracture HRQoL remains uncertain due to sparse and low-quality evidence.

P05.01   Andreas Ladefoged Ebbehøj

ADRENAL TUMORS AND INCIDENTALOMAS IN A POPULATION-BASED STUDY: THE GOOD, THE BAD, AND THE ZEBRA

A. Ebbehøj[1, 2], C. Zhang[2], D. Li[2], R.J. Kaur[2], S. Singh[2], T. Li[2], S. Achenbach[2], E. Atkinson[2], S. Khosla[2], I. Bancos[2]

[1]Department of Endocrinology, Department of Clinical Medicine, Aarhus University, [2]Endocrine Division, Mayo Clinic, Rochester, Minnesota, US

Background: Adrenal tumors are a common incidental finding and reported in 5% of abdominal scans. Current literature suggest that 13-20% of "adrenal incidentalomas" are malignant or hormonally active. Our objective was to determine the incidence and clinical presentation of adrenal tumors in the largest population-based study to date.

Methods: Population based study of patients diagnosed with adrenal tumors from 1995 to 2017 in Olmsted County, MN, US (population 136,760). We used the Rochester Epidemiology Project, that allows access to all hospital and community medical records for Olmsted County residents, to identify the cohort. We calculated sex- and age-standardized incidence rates (:IR) of new patients diagnosed while living in the study area.

Results: Of 1287 patients diagnosed with adrenal tumors, median age was 62 years (IQR 52-72) and 713 (55%) were women. IR increased from 4.4 (CI95% 0.3-8.6) in 1995 to 47.8 (CI95% 36.9-58.7) in 2017.

Malignant adrenal mass was diagnosed in 8.7% patients (4 patients with adrenal cortical carcinoma (0.3%) and 108 (8.4%) patients with other malignant mass). 11 (0.9%) patients had pheochromocytoma and 53 (4.1%) had benign but hormonally active adenomas. Patients discovered incidentally (1050, 81.6%) had a lower rate of malignancy (3.4% vs 36%, p<0.001) and hormone excess (1.9% vs 22%, p<0.001) compared to patients with non-incidental discovery.

Conclusion: Adrenal tumors are becoming increasingly common due to incidental findings. Only a minority of incidentalomas seems to be of clinical significance compared to more than half of non-incidentalomas.

P05.02   Signe Mosegaard   NOVEL GENETIC DISCOVERIES DETECTED USING WHOLE EXOME SEQUENCING AND RNA TRANSCRIPTOMICS IN 14 PATIENTS DIAGNOSED WITH MULTIPLE ACYL-COA DEHYDROGENATION DEFICIENCY (MADD)

S. Mosegaard[1], M. Gusic[2], S. Stenton[2], S. Olpin[3], H. Nygaard[1], M. Sharrad[8], S. Korman[4], J. Sykut-Cegielska[5], A. Das[6], Y. Rahman[7], S. Beblo[8], E. Morava[9], L. Kluijtmans[10], N. Gregersen[1], H. Prokisch[2], R. Olsen[1]

[1]Research Unit for Molecular Medicine, Department of Clinical Medicine, Aarhus University and Aarhus University Hospital, [2]Institute of Human Genetics, Helmholtz Zentrum München, [3]Department of Clinical Chemistry, Sheffield Children's Hospital, Sheffield, [4]Department of Pediatrics, Shaare Zedek Medical Center, Jerusalem, [5]Department of Inborn Errors of Metabolism and Paediatrics, The Institute of Mother and Child, Warsaw, [6]Department of Pediatrics, Hannover Medical School, Hannover, [7]Centre for Inherited Metabolic Disorders, Guy's and St Thomas' Hospital NHS Foundation Trust, London, [8]University Hospital for Children and Adolescents, University of Leipzig, Leipzig, [9]Department of Clinical Genomics, Mayo Clinic, Rochester, Minnesota, [10]Translational Metabolic Laboratory, Dept of Laboratory Medicine, Radboud University Medical Center, Nijmegen

MADD is a heterogeneous inborn error of fatty acid and amino acid oxidation that is potentially treatable with riboflavin. The disease can be caused by genetic defects of the electron transfer flavoproteins, linking multiple acyl-CoA dehydrogenation reactions to the respiratory chain, or by genetic defects in the synthesis of riboflavin-derived catalyzing co-factors. Whole exome sequencing (WES) with RNA-sequencing (RNA-seq) as complementary tool is highly successful in expanding the genetic knowledge of MADD. However, there are still MADD patients that remain genetically unresolved, suggesting that the genetics of MADD is much more complex than previously assumed.

WES was performed on DNA from 14 patients with MADD-like acylcarnitine and organic acid patterns, but without identified bi-allelic variants in known MADD candidate genes. RNA-seq was performed on RNA from cultured fibroblasts from 8 of 14 patients.

In 5 patients, we identified likely disease-causing variants and implementation of RNA-seq led to the confirmation of variants' pathogenicity in 2 of 5 cases. We detected a large copy number variant in ETFDH, which was not detected previously due to limitations of Sanger sequencing. Additionally, we detected pathogenic variants in genes that previously have not been associated with diagnostic MADD metabolites.

Using WES we detected two new genes in MADD biochemistry and some of our results could indicate that MADD could be a disorder with synergistic heterozygosity and bigenic or polygenic as recently suggested. In accordance with recent years research, we show that genetics of MADD is very heterogeneous, and recommend using WES to genetically solve these patients.

P05.03 Marc Daniel Opfermann ACETOACETATE DERIVED METABOLIC CHANGES AND PROTEIN MODIFICATIONS

M. Opfermann, S. Thyssen, M. Johannsen

Department of Forensic Medicine, Aarhus University

Introduction:

Ketone bodies (acetoacetate [AcAc], β-hydroxybutyrate [BHB] and acetone) are upregulated during carbohydrate-restricted diets, fasting and prolonged exercise. Elevated levels of ketone bodies through ketogenic diets have been shown to be beneficial in certain diseases. Also, animal studies have demonstrated that caloric restriction can delay the onset of age-related diseases and extend longevity. The mechanisms behind these beneficial effects are not yet fully elucidated; however, it has been shown that ketone bodies may have other fates beyond the use as energy metabolites. For example, BHB is able to inhibit histone deacetylases and is further involved in modifying proteins through post-translational lysine β-hydroxybutyrylation.

Our studies have shown that AcAc and its more reactive metabolite AcAc-CoA are able to modify proteins on lysine and sulfenylated cysteine residues.

Aim:

We aim to identify a possible role of AcAc/AcAc-CoA in metabolism beyond the use as energy source. For this purpose, we aim to profile protein targets, identify specific binding sites and determine the functional changes of those proteins.

Methods:

For the influence on cellular metabolism, we use an untargeted metabolomics approach. For profiling of the protein targets, we use a chemical modified probe of AcAc-CoA, which can be used for protein pulldown and subsequently proteomics analysis.

Perspective:

Since the mechanism behind the beneficial effect of ketone bodies are not fully understood, our results may elucidate the affected pathways. It remains to be seen if the protein modifications are of biological relevance and if those can be used in a clinical setup.

P05.04 Mette Gude THE "STANNIOCALCIN-2 - PAPP-A - IGFBP-4 - IGF-I AXIS" IN ATHEROSCLEROSIS

M.F. Gude[1], R. Hjortebjerg[2], M. Bjerre[1], J. Frystyk[2]

[1]Medical Research Laboratory, Aarhus University Hospital, [2]Department of Molecular Endocrinology, University of Southern Denmark

Background

Atherosclerosis is a major cause of cardiovascular disease (CVD) worldwide. Lately there has been a growing interest for the role of the Insulin-like growth factor (IGF) system in atherosclerosis and CVD. Pregnancy-associated plasma protein-A (PAPP-A) is an enzyme that

activates IGF-I action through liberation of IGF-I when it is bound to IGF-binding protein-4 (IGFBP-4). Recently the protein stanniocalcin-2 (STC2) emerged as an inhibitor of PAPP-A, thereby preventing PAPP-A to activate IGF-I through enzymatic degradation of IGFBP-4. Numerous studies support that PAPP-A promotes atherosclerosis and a recent study in hypercholesterolemic mice demonstrated that overexpression of STC-2 reduced aorta atherosclerosis by 47 %.

Aim

To examine the local relationship and production of the IGF-I - IGFBP-4 - PAPP-A - STC-2 axis in human atherosclerotic plaque tissue.

Methods

We are in the process of collecting atherosclerotic plaques from patients undergoing endarterectomy from the carotid or femoral artery. Immediately after surgery, plaque tissue is incubated to estimate the basal secretion and activity of axis proteins. Furthermore, STC2 is added to examine whether the axis is modifiable. When the last incubations are completed, we will perform biochemical measurements of incubation-media samples: media content of total IGF-I, intact and fragmented IGFBP-4, PAPP-A and STC2 will be measured.

Expected outcomes

Human atherosclerotic plaque tissue produces STC-2 and PAPP-A that modulate local IGF action.

P05.05   Rasmus Espersen EFFECT OF CALCIUM CITRATE VS CALCIUM CARBONATE ON ELEVATED PARATHYROID HORMONE AFTER ROUX-EN-Y GASTRIC BYPASS. A DOUBLE-BLINDED, RANDOMIZED TRIAL.

R. Espersen[1, 2], L.R. Madsen[1, 2], L. Rejnmark[1, 2], B. Richelsen[1, 2]

[1]Department of Endocrinology and Internal Medicine, Aarhus University Hospital, [2]Department of Clinical Medicine, Aarhus University

Following Roux-en-Y gastric bypass (RYGB), elevated parathyroid hormone (PTH) levels potentially harmful to bone health are commonly observed. Owing to assumed superior absorption, calcium citrate is often recommended over calcium carbonate following RYGB for the treatment of elevated PTH. We aimed to investigate the impact of either calcium carbonate or calcium citrate in patients with elevated PTH levels following RYGB.

Design: Clinical, double-blinded, randomized controlled trial of a 12-week duration at a Danish University Hospital.

Patients and Measurements: Thirty-nine RYGB operated patients with elevated PTH levels (PTH > 6.9 pmol/L) and normal plasma levels of calcium and 25-hydroxyvitamin D were randomized to either calcium carbonate or calcium citrate (1200 mg elementary calcium daily). We assessed change in PTH as the primary outcome.

Results: The effect of the two calcium formulations on change in PTH was comparable and neutral: −1.9% (calcium citrate) vs +0.9% (calcium carbonate), P = 0.680. Compared to the carbonate-treated group, the following bone turnover markers decreased significantly in the citrate-

treated group: procollagen I N-terminal propeptide (–16.6% vs –3.2%, P = 0.021), osteocalcin (–17.2% vs –4.3%, P = 0.007) and bone-specific alkaline phosphatase (–5.9% vs 3.7%, P = 0.027) and remained significantly decreased after multivariable adjustment.

Conclusion: Increasing the dose of calcium supplementation in RYGB operated patients with slightly elevated PTH levels does not normalize PTH levels, regardless of the type of supplement. Our results do not support recommending supplementation with calcium citrate over calcium carbonate in RYGB patients.

P05.06 Katrine Brodersen

EFFECTS OF ROUX-EN-Y GASTRIC BYPASS SURGERY OR GASTRIC SLEEVE SURGERY ON INSULIN SENSITIVITY, INSULIN SECRETION AND WHOLE BODY GLUCOSE TURNOVER IN MORBIDLY OBESE SUBJECTS WITH TYPE 2 DIABETES

K. Brodersen[1, 2], N. Møller[2], B. Richelsen[2], M.F. Nielsen[1]

[1]Department of Surgery, Viborg Regionshospital, [2]Department of Endocrinology, Aarhus University

Background: Obesity surgery (Roux-en-Y Gastric Bypass) resolves diabetes in 70-80% of obese patients with type 2 diabetes. The effect of the surgery is evident immediately after surgery, and not as one would expect in line with the weight loss.

Gastric Sleeve surgery is a relatively new type of obesity surgery, witch entails reduced risk of long-term complication, compared to Roux-en-y Gastric Bypass surgery. Recent studies suggest that Gastric Sleeve surgery elicits the same response as regards diabetes as Roux-en-y Gastric Bypass. The cause behind this effect is still pending, but could be due to improved hepatic insulin resistance.

Method: 16 obese patients with type 2 diabetes, planned for either Roux-en Y Gastric Bypass or Gastric Sleeve surgery, are along with 8 healthy patients (BMI 25 kg / m2), included in the study. An oral glucose tolerance test (OGTT) and a two-step hyperinsulinaemic euglycœmisk glucose clamp (clamp) is performed prior to surgery, and at 2 and 12 months past surgery. Furthermore dual energy x-ray absorptiometry is performed and indirect calorimetry is measured during the clamp sessions.

Results: are pending.

Conclusion: With this study, we expect to be able to determine whether Gastric Sleeve surgery has the same significant effects on hepatic insulin sensitivity, insulin secretion and whole body glucose turnover, as Roux-en-Y Gastric Bypass surgery. The results can lead to an improved treatment of obese patients with type 2 diabetes.Abstract content (click to change me)

P05.07   Katrine Meyer Lauritsen

KETONE BODY INFUSION INCREASES CIRCULATING ERYTHROPOIETIN AND BONE MARROW GLUCOSE UPTAKE

K.M. Lauritsen[1, 2], E. Søndergaard[1, 2, 4], M. Svart[1, 2], N. Møller[1, 4], L.C. Gormsen[3]

[1]Department of Endocrinology and Internal Medicine, Aarhus University Hospital, [2]Danish Diabetes Academy, Odense University Hospital, [3]Department of Nuclear Medicine and PET Centre, Aarhus University Hospital, [4]Steno Diabetes Center Aarhus

Sodium-glucose cotransporter 2 inhibition (SGLT2i) was originally developed as a facile way of lowering blood glucose. However, clinical trials have demonstrated that SGLT2i also increases circulating ketone bodies and hematocrit. In this study, we investigated the possible association between erythropoietin and ketone bodies.

Seventeen healthy subjects undergoing either cardiac (study A) or brain (study B) PET/CT as part of protocols involving experimental hyperketonemia were investigated. Participants were infused with either 7.5% Na-3-β-hydroxybutyrate (3-OHB) or saline (0.9%). In study A, bone marrow palmitate and glucose uptake was measured with dynamic ^{11}C-palmitate and ^{18}F-FDG PET (n = 8). Bone marrow time-radioactivity curves were measured in two vertebrae in the spine. A serum sample from the end of each study day was analyzed for erythropoietin.

Erythropoietin concentrations were significantly greater during hyperketonemia than after saline infusions (mean ± SD 9.9 ± 1.1 vs. 7.6 ± 1.0 IU/L, P = 0.01). Hyperketonemia was also associated with 25% increased bone marrow ^{18}F-FDG uptake compared with the saline study day (mean ± SD 0.64 ± 0.08 vs. 0.51 ± 0.12 mL plasma/mL tissue, P = 0.04) but did not affect bone marrow ^{11}C-palmitate uptake (1.7 ± 0.4 vs. 1.9 ± 0.6 μmol/g/min, P = 0.62).

In conclusion experimental hyperketonemia results in ~30% concomitant increase in erythropoietin levels and bone marrow glucose uptake. Although the level of hyperketonemia in our study was markedly higher than what is typically observed during SGLT2i, our data provide a possible explanation for the unknown link between SGLT2 inhibitor treatment and increased erythropoiesis.

P05.08   Esben Stistrup Lauritzen

MELATONIN INHIBITS GIP SECRETION DURING AN ORAL GLUCOSE TOLERANCE TEST IN HEALTHY YOUNG MEN

E.S. Lauritzen

Medical Research Laboratory, Department of Clinical Medicine, Aarhus University

Introduction: Modern living is associated with an epidemic of type 2 diabetes mellitus (T2DM). Sleep disturbances such as insomnia or frequent awakenings are strong risk factors for T2DM with several studies indicating a central role of melatonin. Administration of melatonin immediately prior to an oral glucose tolerance test impairs glucose tolerance in both young and postmenopausal healthy women, but the mechanism remains unknown.

Methods: Fifteen healthy men were each examined four times: An oral glucose tolerance test (OGTT, 75 g) was performed on one day and an

isoglycemic intravenous glucose infusion (IIGI) aiming at replicating the blood glucose profile of the OGTT day was performed on a second day. This pair of study days were conducted both on melatonin treatment (10 mg/hour for four hours) (M) and on treatment with an identical placebo capsule (P). Melatonin or placebo treatment was started at t = -60 minutes, the OGTT or IIGI was started at t = 0 minutes.

Results: Glucose-dependant insulinotropic peptide (GIP) levels were significantly suppressed after melatonin compared with placebo (iAUC P<0.05) during OGTT, and post hoc analysis revealed a difference at t = 40, 90, and 120 minutes (M: 33±3, 34±4, and 28±3 vs P: 39±3, 39±4, and 36±4 pmol/l, P=0.02, 0.02, and <0.001). Melatonin compared with placebo did not affect glucose, insulin, C-peptide, and glucagon-like peptide 1 levels, or the incretin effect (insulin: M-OGTT/M-IIGI)/(P-OGTT/M-OGTT)).

Conclusions: Melatonin decreases GIP levels after an OGTT in healthy young men. This indicates that a decreased GIP secretion could underlie the previously reported deleterious effects of melatonin on glucose tolerance.

P05.09 Jeyanthini Risikesan

LIPID METABOLISM IN INDIVIDUALS WITH NAFL/NASH

J. Risikesan

Department of Clinical Medicine, Aarhus University

The overall aim of this PhD project, are to gain further insight into VLDL-TG metabolism using our VLDL-TG tracer method. VLDL particles are the quantatively most important transporter of TG in the postabsorptive state and studies of VLDL-TG metabolism may provide information regarding both TG metabolism and lipid metabolism in general in obese subjects with NAFL or NASH. In our laboratory we have developed a method for direct measurement of VLDL-TG secretion, oxidation and storage in healthy, NAFL and NASH individuals. This PhD project consists of three studies 1) splanchnic and systemic VLDL-TG and FFA balance, 2) exercise study and 3) storage study.

The aim of study 1 was to determine differences in:

Systemic and splanchnic FFA and VLDL-TG balances. Uptake and cellularregulation of FFA and VLDL-TG in fat and muscle tissue. Between subjects with biopsy-proven NAFL or NASH, by using catherization of the femoral artery and the hepatic vein to directly measure splanchnic (liver) VLDL-TG uptake and secretion, by measuring a-v differences of VLDL-TG across the liver, in combination with innovative tracer techniques. We use indocyanine to quantify the livers blood flow. FFA tracer as well as adipose tissue and skeletal muscle will be used to measure whole- body substrate turnover and flexibility as well as tissue specific substrate handling during fasting and hyperinsulinemic conditions. The purpose of study 2 was to determine the effect of an acute exercise on VLDL-TG kinetics in obese men and women with biopsy-proven NAFL and NASH. By using an ex vivo labeled VLDL-TG tracer that allowed us to directly measure the oxidation of VLDL-TG as well as plasma VLDL-TG kinetics.

P05.10   Katrine Bilde   EFFECT OF OVERWEIGHT AND AGE ON THE BLOOD-BRAIN-BARRIER

K. Bilde, R.H. Olesen, A. Larsen

Department of Biomedicine, Aarhus University

Neurodegenerative diseases have become a global problem affecting more than 60 million people and estimates are that these numbers will increase in the coming years. Old age in itself is one of the major risk factors. However, increasing evidence has also linked obesity and related metabolic stress factors such as type 2 diabetes to the development of neurodegenerative diseases.

The microenvironment of the brain is tightly controlled by the blood-brain-barrier (BBB) consisting of endothelial cells held together by tight junction proteins and junctional adhesion molecules supported by underlying pericytes and astrocytes and extracellular matrix proteins. Dysfunction of the BBB has been implicated in neurodegenerative diseases and BBB dysfunction is associated with loss of tight junctions, degeneration of pericytes and increased neuroinflammation.

In this explorative study the effect of increasing age and body mass index (BMI) has been studied on the stability of BBB genes. By using microarray data from sound individuals obtained from the BrainCloud database (Lieber Institute, USA) and analyzing 21 key genes associated to BBB stability, this study found 5 genes (CDH5, HSPG2, BSG, ARGN and PDGFRA) to be significantly regulated by increasing age and 4 genes (ZO-2, ZO-3, HSPG2, and PDGFC) to be significantly regulated by increasing BMI. These genes are highly related to cell adhesion, the extracellular matrix or cellular growth indicating that both increasing age and BMI has an impact on BBB integrity that might contribute to the risk of developing neurodegenerative diseases and also affect the response to medication.

P06.01   Mathilde Frost Kristensen   A CUSTOM ADJUSTABLE 3D PRINTED MICROFLUIDIC FLOW-CELL FOR MICROSCOPY ANALYSIS OF *IN SITU*-GROWN BIOFILMS

M.F. Kristensen[1], D. Leonhardt[1], M.L.B. Neland[2], S. Schlafer[1]

[1]Department of Dentistry and Oral Health, Aarhus University, [2]Department of Engineering, Science and Technology, Aarhus University

Biofilm phenomena ranging from metabolic processes, attachment and detachment to quorum sensing are likely to be influenced by the velocity of the liquid in contact with the biofilm. Therefore, biofilms should preferably be studied under flow conditions. In addition, to study biofilm and analyze it without disrupting the three-dimensional structure of the biofilm, in situ grown biofilms should be the samples of choice. Therefore, we searched for a commercial flowcell that allows for microscopy analysis of in situ grown biofilm under shear-control, but were unsuccessful. Thus, we designed a custom adjustable 3D-printed flowcell able to meet the aforementioned requirements. The flowcell consists of an in-port, an out-port and a central bottomless chamber for the sample. Sealing a coverslip to the flowcell creates a defined flowspace between sample and coverslip. As a proof of concept, we studied the impact of stimulated saliva flow on pH developments in three 72-hour biofilms grown in situ on custom-made glass slabs. Previous studies have shown the development of steep pH gradients inside dental biofilm within minutes after exposure

to sugar. However, these studies were conducted under static conditions, and hence they failed to take the impact of flow on pH into account. The results of this pilot study show how the acid production under static conditions leads to steep pH gradients but how the pH is neutralized and even slightly alkaline under flow conditions, with the biofilm still being exposed to sucrose. This study emphasizes the need for flow conditions when studying dental biofilm. Future studies will focus on different flowrates on pH developments in dental biofilms

P06.02   Andreas Steenholt Niklassen

DANISH VALIDATION OF SNIFFIN' STICKS OLFACTORY TEST FOR THRESHOLD, DISCRIMINATION, AND IDENTIFICATION

A.S. Niklassen[1, 2], T. Ovesen[1, 2], H. Fernandes[1], A.W. Fjældstad[1, 2]

[1]Department of Clinical Medicine, Aarhus University, [2]Ear, nose and throat Department, Regional Hospital West, Holstebro

Objectives: The aim was to validate the Sniffin' Sticks threshold, discrimination, and identification olfaction test.

Background: Olfactory disorders are very common. Olfactory testing is important for accurate diagnostics and treatment.

Methods: The study included 388 participants. First we performed a questionnaire study in which 238 adults rated their familiarity with 125 odour descriptors. Secondly, we evaluated the original Sniffin' Sticks in 75 participants. And last, we modified our odour descriptors into a new version which was used to test 75 new participants.

Results: 21 original odour descriptors were unfamiliar in the identification test and five odours had identification rates <75%. Using the new version, all odours had a successful identification rate>75%.

Conclusion: The original Sniffin' Sticks was not usable in Denmark. Modification resulted in improvement of familiarity and rate of identification, so the test is now valid for use in Denmark and can be used clinically in hospital departments and at private practitioners.

P06.03   Kevin Kris Warnakula Olesen

TEN YEAR RISK OF MYOCARDIAL INFARCTION DIABETES PATIENTS WITHOUT ANGIOGRAPHIC CORONARY ARTERY DISEASE

K.K.W. Olesen[1], M. Madsen[2], C. Gyldenkerne[1], P.G. Thrane[1], T. Thim[1], B.B. Løgstrup[1], L.O. Jensen[3], B. Raungaard[4], H.E. Bøtker[1], H.T. Sørensen[2], M. Maeng[1]

[1]Department of Cardiology, Aarhus University Hospital, [2]Department of Clinical Epidemiology, Aarhus University Hospital, [3]Department of Cardiology, Odense University Hospital, [4]Department of Cardiology, Aalborg University Hospital

Purpose: Patients with diabetes and no obstructive coronary artery disease (CAD) by coronary angiography (CAG) have a low risk of myocardial infarction (MI), similar that of non-diabetes patients without CAD. We estimated the risk of MI, ischemic stroke, and death in diabetes patients without CAD by CAG compared a random sample from the general population.

Methods: We conducted a cohort study of diabetes patients without obstructive CAD examined by CAG from 2003-2016 in Western Denmark. Diabetes patients without CAD were compared to an age- and gender matched comparison group sampled from the Western Danish general population without previous history of coronary heart disease. Endpoints were MI, ischemic stroke, and death. The 10-year risk differences (RD) in cumulative incidence proportions were estimated accounting for the competing risk of death. Adjusted hazards ratios (HRs) were estimated using stratified Cox regression.

Results: We identified 5,760 diabetes patients without obstructive CAD and 29,139 matched individuals from the general population. Median follow-up was 7.7 years. Diabetes patients without CAD had a similar absolute (RD 0.30%, 95% CI -0.31 - 0.92) and relative (adjusted HR 0.91, 95% CI 0.70-1.17) 10-year risk of MI compared to the general population. Diabetes patients without CAD had an increased risk of both ischemic stroke (adjusted HR 1.88, 95% CI 1.48-2.39) and all-cause death (adjusted HR 1.41, 95% CI 1.29-1.54).

Conclusions: Absence of obstructive CAD by CAG in patients with diabetes is associated with a similar risk of MI and an increased risk of ischemic stroke and death compared to the general population.

P06.04 Thorsten Rasmussen

CARDIOVASCULAR ADRENERGIC NEUROPATHY IN TYPE 2 DIABETES MELLITUS

T.K. Rasmussen[1], J. Hansen[3], P. Borghammer[2], N.B. Finnerup[1], T.S. Jensen[1], A.J. Terkelsen[1, 4]

[1]Danish Pain Research Center, Department of Clinical Medicine, Aarhus University, [2]Department of Nuclear Medicine and PET-centre, Aarhus University Hospital, [3]Department of Health Science and Technology, Aalborg University, [4]Department of Neurology, Aarhus University Hospital

Cardiovascular autonomic neuropathy (CAN) is a common complication of type 2 diabetes mellitus (T2DM). Symptoms can include orthostatic intolerance due to neurogenic orthostatic hypotension and/or insufficient heart rate (HR) regulation. The degree of CAN is typically evaluated through assessment of clinical parasympathetic nerve fiber function. Few studies have investigated the clinical assessment of the adrenergic branch of the autonomic nervous system (ANS), although modulation of adrenergic tone constitutes a promising field for medical treatment.

Aim:

This study aims to assess the adrenergic nervous system in T2DM patients through a standardized quantitative clinical test battery. Furthermore, we aim to assess the association between functional clinical measures and signs of 123-MIBG scintigraphy abnormalities and 24-hour blood pressure (BP) profiles.

Methods:

Forty T2DM patients will be investigated by a standardized test battery, evaluating adequacy of BP and HR responses to physical straining. Severity of autonomic adrenergic neuropathy will be indexed according to a composite autonomic scoring scale. Measures of resting HR variability

and 24-hour blood pressure variability will be collected. Patients will undergo 123-MIBG scintigraphy.

Data collection is currently ongoing.

Perspective:

We expect this extensive profiling of T2DM patients to further advance the understanding of the clinical assessment of the ANS function, with a particular focus on diagnosing potential adrenergic dysfunction. We anticipate that improved and concise ANS assessment tools will ease the diagnostic process of diabetic patients and aid health care personnel in treatment decision-making

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P06.05 Olesya Svystun

SEVERE IMAGE-STITCHING ARTEFACTS AND DISTORTION IN CCD-BASED CEPHALOGRAMS AND THEIR ASSOCIATION WITH SENSOR TYPE AND HEAD MOVEMENT. AN *EX-VIVO* STUDY

O. Svystun

Department of Dentistry and Oral Health, Aarhus University

Objectives: To assess presence and severity of image-stitching artefacts and distortion in lateral cephalograms acquired by CCD-based sensors and their association with movement.

Methods: A human skull on a robot simulating five head movements (antero-posterior translation/lifting/nodding/lateral rotation/tremor), at three distances (0.75/1.5/3mm), two patterns (skull returning/not returning to the initial position). Three cephalometric units, ProMax-2D (Planmeca Oy, Finland), one with Dimax-3 (D-3) and one with Dimax-4 (D-4) sensor, Orthophos-SL (ORT, Dentsply-Sirona, Germany), acquired cephalograms during the predetermined movements, in duplicate (54 with movement, and 28 controls with no movement per unit). Observer assessed the presence of an image-stitching line (none/thin/thin with vertical stripes or thick), misalignment between the anatomical structure display (none/<1/1-3/>3mm), and distortion in each image quadrant (present/absent), in duplicate. Severe image-stitching artefacts were pre-defined.

Results: Intra-observer reproducibility was >0.8. Severe image-stitching artefacts were scored in 70.4% and 18.5% of D-3 and D-4 movement images, respectively. Severe distortion was scored in 64.8% of D-3, 5.6% of D-4, and 37% of ORT movement images.

Conclusion: Sensor type, movement type, distance, and pattern affected presence and severity of image-stitching artefacts and distortion in CCD-based cephalograms.

P06.06 Johan Fridolf Hermansen

NOVEL ULTRASOUND TECHNIQUES FOR PREDICTION OF ACUTE KIDNEY INJURY

J.F. Hermansen[1], A. Hørlyck[2], D.V. Nielsen[1], P. Juhl-Olsen[1]

[1]Department of Anesthesiology, Aarhus University Hospital, [2]Department of Radiology, Aarhus University Hospital

Background

In cardiac surgery, acute kidney injury (AKI) is a frequent complication and an independent risk factor for increased mortality and morbidity. Renal function is governed by a complex interplay between several determinants, including volume status, cardiac output, mean arterial pressure and back pressure to venous outflow.

The most common strategy for improving perioperative renal function target increases in renal afferent flow by administration of fluid. However, this strategy is initiated without detailed knowledge on the individual patient's renal perfusion status or degree of renal venous congestion. Ultrasonography of renal vasculature and the portal vein may help to identify patients with renal congestion.

The aim of the study is to determine the correlation and optimal cut-off values for perioperative organ-specific flow rates and patterns for the development of AKI.

Methods

This is a descriptive, clinical, prospective study. Patients scheduled for on-pump cardiac surgery and with ≥ 1 risk factors for postoperative AKI are eligible for inclusion. Ultrasonography measures are performed on the day before surgery and on the first and fourth postoperative day. Endpoints include renal vein flow classification (primary), portal vein flow classification and renal arterial flow ratio (resistive index).

Results

Inclusion is ongoing and expected to be completed by fall 2019. The preliminary results from the first 40 patients will be presented at the PhD Day 2020.

Conclusions

The study will provide detailed information on the capabilities of ultrasonography flow measures in predicting the development of AKI.

P06.07   Ane Bull Iversen   KNOWLEDGE OF STROKE CORE SYMPTOMS, HELP-SEEKING BEHAVIOR AND PRE-HOSPITAL DELAY IN ACUTE STROKE

A.B. Iversen[1, 3, 4], R.A. Blauenfeldt[1], S.P. Johnsen[2], G. Andersen[1], M.B. Christensen[4, 3], B. Christensen[3]

[1]Department of Clinical Medicine, Neurology, Aarhus University, [2]Danish Center for Clinical Health Services Research, Department of Clinical Medicine, Aalborg University and Aalborg University Hospital, [3]Section for General Medical Practice, Department of Public Health, Aarhus University, [4]Research Unit for General Practice, Department of Public Health, Aarhus University

Reperfusion therapies have revolutionized acute stroke treatment and improved patient outcomes. However, only a minority of admitted ischemic stroke patients are eligible for acute treatment, mainly due to presentation outside the time-window. There are many causes for prehospital delay, but most are related to patient-dependent factors.

We conducted a cross-sectional study on admitted stroke patients, performing structured interviews on patients and their bystanders and collecting data from medical records and the Danish Stroke Registry. We aimed to investigate knowledge of stroke core symptoms (facial palsy, palsy of extremities and aphasia/dysarthria) help-seeking behaviour and the association to early hospital arrival and reperfusion therapy. The study will be repeated after a national stroke campaign, to evaluate the effect of the campaign.

Results: We included 435 patients and performed in total 384 interviews on patients and 264 on bystanders. Of patients, 54% could not mention any stroke core symptom, 22% could mention at least two. In bystanders the percentages were 28% and 53% respectively. Primary EMS-contact were made in 29 % of the cases only. In 28% their GP was the first contacted, in 21% the out-of-hours primary care, in 14% friends or family and in 9% other.

Conclusion: Stroke core symptom knowledge in our population was low, and significantly lower in patients than in bystanders. The stroke campaign will hopefully improve knowledge and help-seeking behaviour, reduce pre-hospital delay and increase the number of patients receiving treatment.

P06.08 Jelmer Sybren Westra

DIAGNOSTIC PERFORMANCE OF QUANTITATIVE FLOW RATIO FOR FUNCTIONAL ASSESSMENT OF CORONARY ARTERY DISEASE IN PROSPECTIVELY ENROLLED PATIENTS: AN INDIVIDUAL PATIENT-DATA META-ANALYSIS

J. Westra[1], S. Tu[2], G. Campo[3], S. Qiao[4], H. Matsuo[5], X. Qu[6], L. Koltowski[7], Y. Chang[2], T. Liu[8], J. Yang[9], B.K. Andersen[1], A. Eftekhari[1], E.H. Christiansen[1], J. Escaned[10], W. Wijns[11], X. Bo[4], N.R. Holm[1]

[1]Department of Cardiology, Aarhus University Hospital, [2]School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, [3]Cardiovascular Institute, Azienda Ospedaliero-Universitaria di Ferrara, Italy, [4]Fu Wai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences, [5]Department of Cardiovascular Medicine, Gifu Heart Center, Gifu City, Japan, [6]Huadong Hospital Affiliated to Fudan University, Shanghai,China, [7]1st Department of Cardiology, Medical University of Warsaw, Warsaw, Poland, [8]Department of Cardiology, Hagaziekenhuis, The Hague, The Netherlands, [9]Guangdong General Hospital, Guangzhou, China, [10]Department of Cardiology, Hospital Clinico San Carlos, Madrid, Spain, [11]The Lambe Institute for Translational Medicine and Curam, National University of Ireland Galway, Ireland

Objectives

We aimed to provide robust diagnostic performance estimates for Quantitative Flow Ratio (QFR) in assessment of intermediary coronary artery stenoses.

Background

Angiography-based functional stenosis assessment by QFR may be introduced as a cost saving and safe approach to expand the use of physiology-guided percutaneous coronary interventions. QFR was proven

feasible and showed good diagnostic performance in mid-sized studies with fractional flow reserve (FFR) as reference standard.

Methods

We performed a collaborative individual patient-data meta-analysis of prospective studies with paired assessment of QFR and FFR using the CE-marked QFR application. The main outcome was agreement of QFR and FFR using a two-step analysis strategy with a multi-level mixed model accounting for study and center level variation.

Results

Of 16 studies identified, four studies had prospective enrollment and provided patient level data reaching a total of 819 patients and 969 stenoses with paired FFR and QFR: FAVOR Pilot (n=73); WIFI II (n=170); FAVOR II China (n=304) and FAVOR II Europe-Japan (n=272). We found an overall agreement (mean difference 0.009±0.068, I^2=39.6) of QFR with FFR as reference. The diagnostic performance was sensitivity 84% (95%CI: 77 to 90, I^2=70.1), specificity 88% (95%CI: 84 to 91, I^2=60.1); positive predictive value 80% (95%CI: 76 to 85, I^2=33.4), and negative predictive value 95% (95%CI: 93 to 96, I^2=75.9).

Conclusions

Diagnostic performance of QFR was good with FFR as reference in this meta-analysis of high quality prospective studies. QFR could provide an easy, safe, and cost-effective solution for functional evaluation of coronary artery stenosis.

P06.09   Christian Stæhr   UPREGULATION OF ENDOTHELIAL $KIR_{2.1}$ CHANNELS LEADS TO DISTURBANCE IN NEUROVASCULAR COUPLING IN FAMILIAL MIGRAINE

C. Staehr[1], R. Rajanathan[1], D. Postnov[2,3], C. Aalkjaer[1], K. Lykke-Hartmann[1], S. Sandow[4], F.W. Bach[5], V. Matchkov[1]

[1]Department of Biomedicine, Aarhus University, [2]Bio Optical and Acoustic Spectroscopy, Boston University, [3]Department of Biomedical Sciences, University of Copenhagen, [4]Faculty of Science, Health, Education and Engineering, University of the Sunshine Coast, [5]Department of Clinical Medicine, Department of Neurology, Aarhus University Hospital

Background

It has been shown that neurovascular coupling (NVC) is primarily mediated through paracellular K^+ signaling and that endothelial K^+ inward rectifying 2.1 ($Kir_{2.1}$) channels play a central role in this communication. Disturbance in NVC has been observed in migraine patients but the underlying mechanism remains unknown. In this study, we aimed to investigate NVC in heterozygous mice bearing a mutation (G301R) of the α2 isoform Na^+,K^+-ATPase ($α2^{+/G301R}$), which is known to be associated with familial hemiplegic migraine type 2 in humans.

Methods

Age-matched $α2^{+/G301R}$ and wild type (WT) mice were studied. NVC was assessed in-vivo using laser speckle imaging and ex-vivo in brain slices using confocal microscopy. Arterial dilation in response to increased bath concentrations of K^+ was assessed in isometric myograph. Western blot

and immunohistochemical staining semi-quantified the protein level of $Kir_{2.1}$ channels in cerebral arteries.

Results

Whisker stimulation increased perfusion in the corresponding sensory cortex and this response was larger in $\alpha2^{+/G301R}$ than in WT mice. Neuronal excitation ex-vivo led to increased dilation of parenchymal arterioles from $\alpha2^{+/G301R}$ mice compared to WT. Cerebral arteries from $\alpha2^{+/G301R}$ mice dilated stronger than WT to increased K^+ concentrations. Endothelial denudation abolished the difference in K^+-induced vasodilation between genotypes. Endothelial $Kir_{2.1}$ channel expression was increased in middle cerebral arteries from $\alpha2^{+/G301R}$ mice in comparison with WT.

Conclusion

$\alpha2^{+/G301R}$ mice showed exaggerated increase in blood flow in response to neuronal activity. This was associated with an increased expression of endothelial $Kir_{2.1}$ channels.

P06.10   Martin Faurholdt Gude   PREHOSPITAL IDENTIFICATION OF LARGE VESSEL OCCLUSION BY PRESS (PREHOSPITAL STROKE SCORE) - A NEW COMBINED SYMPTOM SCORE

M.F. Gude[1], R.A. Blauenfeldt[2], A.B. Behrndtz[2], C.N. Nielsen[1], L.O.Z. Speiser[3], C.Z. Simonsen[2], S.P. Johnsen[4], H. Kirkegaard[1], G. Andersen[2]

[1]Prehospital Emergency Medical Services, Central Denmark Region, [2]Department. of Neurology, Aarhus University Hospital, [3]Departmen of Radiology, Aarhus University Hospital, [4]Department of Clinical Medicine, Aalborg University Hospital

Background

The success of effective acute stroke treatment relies on fast recognition and short delay to treatment. Prehospital identification might optimize visitation. Early identification of a suspected large vessel occlusion (LVO) can facilitate direct transfer to a comprehensive stroke center (CSC).

The Prehospital Stroke Score (PreSS) is a simple two-part symptom-based stroke score which has been implemented in the ambulance services in the Central Denmark Region. PreSS 1 aims at identifying stroke. (1 point in either face weakness, arm weakness or slurred speech.) PreSS 2 aims at identifying LVO. (2 points in arm weakness, gaze palsy, incorrect month and/or age.)

We aimed to investigate the ability of PreSS 2 to identify LVO prehospitally.

Methods

PreSS positive patients admitted to a stroke center were prospectively included (June-December 2018). The PreSS score was compared with neuroimaging determining LVO status. Initial NIHSS in LVO patients who were either PreSS positive or negative were compared.

Results

Among 832 patients evaluated for stroke, 63 had LVO (7.6 %). We found a PreSS 2 sensitivity of 57.1% and a specificity of 90.2%.

Median NIHSS was significantly higher in LVO patients identified with PreSS part2 (19 vs.14, p=0.007.)

Discussion

The high specificity ensures that very few patients with non-LVO risk a longer transfer to a CSC that could delay thrombolysis. PreSS 2 does not identify all patients with LVO, but the patients that are missed scores markedly lower on NIHSS and are PreSS 1 positive. It seems that PreSS 2 identifies patients with high NIHSS where the evidence for thrombectomy is strongest.

| P07.01 | Michal Frumer | NEW CONFIGURATIONS OF CANCER CONCERN. WHO CARES FOR WHAT? |

M. Frumer[1, 2], P. Vedsted[1], M.L. Tørring[3], R.S. Andersen[1, 3]

[1]Research Unit for General Practice, Department of Public Health, Aarhus University, [2]Department of Public Health, Aarhus University, [3]Department of Anthropology, Aarhus University

Predictive morphology, understood as the clinical practice that links specific changes in tissue to an increased danger of cancer in the future, is currently transforming into standard care in Denmark. Consequently, still more people come under routine surveillance for a risk of developing a cancer. This project is about the CT follow-up of such potential signs of lung cancer (the indeterminate pulmonary nodules) and it explores the configuration of concerns that are present in the clinic and beyond. Based on ethnographic fieldwork in two diagnostic outpatient lung cancer clinics, we ask: What is at stake from the inside of our health care system? How is the push for early detection managed and experienced in the clinic? When disease ontologies are increasingly heterogenic and boundless, what sorts of logics (or lack hereof) drives interpretation in the clinic? We argue that the concerns and uncertainties associated with this 'at risk' group materialises differently at different positions in the healthcare system. The radiologist, the specialised pulmonologist, and the lung cancer nurse have different objects of concern. Thus, we need to understand clinical specialists as more than pioneers of biomedicalisation. This enables us to see how 'the system' is itself diverse and describe the messiness of everyday clinical practice.

| P07.02 | Birgith Engelst Grove | A CONTENT AND FACE VALIDITY STUDY OF A NEPHROLOGY PRO QUESTIONNAIRE USED AS DECISION AID IN CLINICAL PRACTICE |

B. Grove[1], P. Iversen[2], N.H. Hjøllund[1, 3], A. De Thurah[4]

[1]AmbuFlex/WestChronic, Occupational Medicine, Regional Hospital West Jutland, [2]Department of Nephrology, Aarhus University Hospital, [3]Department of Clinical Epidemiology, Aarhus University Hospital, [4]Department of Rheumatology, Aarhus University Hospital

AIM The prototype of the PRO questionnaire used at the nephrology outpatient clinic has been developed based on a literature review and focus group discussions with clinical experts. The PRO questionnaire includes information on specific aspects of daily life with renal failure and comprises generic items from SF-36, and the kidney disease Quality of Life

questionnaire (KDQOL). The aim of this study was to evaluate the content and face validity of the PRO questionnaire used in the nephrology outpatient clinic for clinical decision-making

METHOD A systematic approach in accordance to the International Patient Decision Aid Standards (IPDAS) guideline constituted the background for this alpha-testing. Comprehensibility and usability, relevance and deficits of the instrument were assessed from patients and clinicians. In total 8 one-to-one semi-structured cognitive interviews was conducted to assess patients' views. A combination of 'think-aloud' and semi-structured probing techniques were applied. A focus group interview was conducted with 7 clinicians.

RESULTS This study resulted in a rephrasing of several items and essential domains emerged from the thematic analyse. As a consequence items covering pain and gastrointestinal function were included. Additionally, a free-text box allowing for patient´s preferences was added to the questionnaire.

CONCLUSION This study has demonstrated the usability of alpha testing according to the IPDAS criteria by cognitive interviews and focus group when evaluating content validity in a new PRO questionnaire for clinical use, embracing the different perspectives from clinicians and patients.

P07.03 Kristoffer Brix Olesen

CANCELLED

FROM HIGHER EDUCATION TO WORK: DO DANISH UNIVERSITIES IGNORE IMPORTANT EMPLOYABILITY SKILLS IN CURRICULUM?

K.B. Olesen[1], L.D. O´Neill[2], M.K. Christensen[1]

[1]Centre for Health Sciences Education, Aarhus University, [2]Centre for Teaching and Learning, University of Southern Denmark

Discrepancies between the skills taught in higher education and those valued by employers are recurrently noted. Several studies of the transfer from higher education to work have suggested that there is a skills gap between the employers' requirements and the outputs from higher education. Despite the focus on employability over the last years, the reality of students' acquisition of employability skills seems, at best, variable.

Employability skills are the skills that are directly pertinent to obtaining and maintaining work. According to Bridgstock (2009), employability skills are comprised of four components: (1) self-management skills, (2) career-building skills, (3) generic transferable skills, and (4) discipline-specific skills. Embedding employability skills into curriculum is recognized as a powerful strategy and an important first step for developing employability skills among students in higher education. Our aim is, therefore, to map ways in which curricula in Medicine and Public Health respectively declare students' acquisition of employability skills. This is achieved by utilizing curriculum mapping as a method where declared course learning outcomes in all Danish universities' Medicine and Public Health educations are aligned against the four components of employability skills.

The preliminary results suggest only a limited number of employability skills are embedded within the investigated educations. However, universities must recognize the importance of these skills because they are necessary for performance in any work situation. It is therefore

questionable in which way these educations explicitly prepare graduates for future employment.

P07.04   Mathilde Stærk   ARE BASIC LIFE SUPPORT INSTRUCTORS COMPETENT?

M. Stærk[1, 2, 3], L. Vammen[3, 4], C. Hansen[1, 2, 3, 5], K. Krogh[3, 4], B. Løfgren[2, 3, 6, 7]

[1]Clinical Research Unit, Randers Regional Hospital, [2]Department of Internal Medicine, Randers Regional Hospital, [3]Research Center for Emergency Medicine, Aarhus University Hospital, [4]Department of Anesthesiology and Intensive Care, Aarhus University Hospital, [5]Department of Cardiology, Herlev and Gentofte Hospital, [6]Department of Clinical Medicine, Aarhus University, [7]Department of Cardiology, Aarhus University Hospital

Background

Bystander basic life support (BLS) and automated external defibrillation (AED) improve survival after out-of-hospital cardiac arrest. Certified BLS/AED instructors are expected to master and disseminate these skills. This study aimed to evaluate certified BLS instructors' competencies in demonstrating cardiopulmonary resuscitation (CPR) and use of an AED.

Methods

Certified BLS instructors demonstrated CPR and use of an AED on a resuscitation manikin. Skill quality was evaluated with data collected from the manikin and video recordings and compared to international guidelines. Participants completed questionnaires regarding resuscitation guidelines and rating of their own skills.

Results

We analyzed data from 125 participants. Of all chest compressions, only 22% were within guideline recommendation regarding depth (mean depth 64 mm (7.3)). Instructors often misplaced the left AED electrode (median distance 7.6 cm (5.0;10.5), 25% placed correctly), while the right AED electrode usually was placed correctly (median distance 2.9 cm (1.5;4.0), 85% placed correctly). Nearly half of the participants failed to state correct answers regarding how to diagnose a cardiac arrest and where to place AED electrodes. Despite their performance, participants rated their own BLS skills high.

Conclusion

The majority of certified BLS instructors performed chest compressions with excessive depth. Instructors in general misplaced the left AED electrode and only half could correctly describe the recommended position of the AED electrodes. Overall, this study found severe gaps in BLS instructors' competencies, which indicates a need for revised BLS instructor education and faculty development.

P07.05   Mie Østergaard   INNOVATION - THE POLITICAL HEALTHCARE AGENDA IS ALL ABOUT IT, BUT WHAT IS THE ACTUAL UNDERSTANDING OF THE PHENOMENON? PRELIMINARY RESULTS FROM A QUALITATIVE EXPLORATION OF INNOVATION IN THE DANISH HEALTHCARE SECTOR

M. Østergaard[1], M. S. Vesterby[2], M. T. Høybye[1, 3], H. A. Søndergaard[4]

[1]Centre of Elective Surgery, Regional Hospital Silkeborg, [2]INNO-X Health, Department of Clinical Medicine, Aarhus University, [3]Interacting Minds Centre, Department of Clinical Medicine, Aarhus University, [4]Department of Management, School of Business and Social Sciences, Aarhus University

Purpose

There is a constantly growing expectation on the healthcare sector to reinvent and streamline health services and to be more efficient in the future. This tendency places great demands on healthcare professionals to act and think innovatively. Research from diverse fields of science supports this trend. Based on this, the field of healthcare innovation has become a top priority on the political agenda. However, the literature holds a wide spectrum of definitions on healthcare innovation complicating a consistent understanding and conceptualization of the phenomenon. Such inconsistency vouches for the importance of producing knowledge in the field in order to support the progress of the sector.

Main findings

Fifteen semi-structured interviews were conducted with managers from Danish hospitals spread across the country. The findings are conflicting. To some extent, an awareness of the need for innovation appears. However, inadequate knowledge and comprehension greatly challenges the phenomenon healthcare innovation, leading to different ways of conceptualizing it. This inconsistency, combined with the ecosystem surrounding the sector, influences negatively on the inclination to work innovatively. Special concerns include organizational structures, cultures, and political agendas.

Perspectives

Inconsistency in perception and conceptualization of healthcare innovation may have tremendous impact on the sector for managing challenges in the future. However, it is not only important to be aware of the differences in perception, but also what characterizes these diversities in order to succeed in making innovations sustainable across silos and borders of the system.

P07.06   Maria Louise Gamborg   CLINICAL DECISION-MAKING IN GERIATRIC EMERGENCY MEDICINE: A SYSTEMATIC REVIEW

M.L. Gamborg

Centre for Health Sciences Education, Aarhus University

Clinical Decision-Making (CDM) refers to cognitive processes and the ability to make competent clinical decisions. In Emergency Medicine (EM) this competency is challenged by uncertainty and task complexity and with a growing geriatric subgroup in EM, new challenges arise. This review

aims to describe how CDM is conceptualised in the literature on CDM in geriatric EM (GEM).

A systematic search was performed in PubMed, ProQuest, Scopus, EMBASE and Web of Science on search terms related to CDM, EM and geriatrics. Title and abstract were screened for 622 peer-reviewed manuscripts, ultimately including 45 in the analysis.

As studies were largely varied in their operationalization of CDM, it was not possible to perform a meta-analysis. Through narrative analysis, four overarching themes emerged of decisions operationalized as: (1) an outcome measure, (2) a cognitive phenomenon, (3) aided by tools, and (4) as clinical judgement. Overall findings suggested that CDM based on cognition alone led to negative outcomes, but improved with training. When investigating the effect of CDM aids, the majority of studies found support of using them.

The heterogeneousness of how CDM is operationalized indicate a lack of consensus on the cognitive processes underlying CDM in GEM. The concept of decision-making was often merely used as a proxy measure, or was most often ill-defined or lacking a theoretical framework. As such, it should be reconsidered, if this these types of studies are, in fact, decision-making literature. Further empirical work is needed to understand the cognitive, behavioral and contextual process involved.

P07.07   Simon Meyer Lauritsen

ACCURATE AND EXPLAINABLE ARTIFICIAL INTELLIGENCE FOR THE EARLY PREDICTION OF ACUTE CRITICAL ILLNESS

S.M. Lauritsen[1, 2], M. Kristensen[2], M.V. Olsen[4], M.S. Larsen[4], M.J. Jørgensen[1], J. Lange[1], B. Thiesson[2, 3]

[1]Department of Clinical Medicine, Aarhus University, [2]Enversion A/S, Aarhus, [3]Department of Engineering, Aarhus University, [4]Department of Biomedical Engineering and Informatics, Aalborg University

Acute critical illness is often preceded by the deterioration of routinely measured clinical parameters such as vital signs and blood tests. In clinics, the early prediction of acute critical illness is calculated as the weighted sum of selected clinical parameters such as the Early Warning Scores (EWS). The introduction of EWS shows a trend towards better clinical outcomes, but unfortunately, the performance of EWS yield a tradeoff between sensitivity and specificity, which can lead to negative outcomes for patients. Previous work shows promising results on using artificial intelligence (AI) trained on electronic health records for early prediction of acute critical illness. These AI models demonstrate high predictive ability, but at the expense of explainability. Here we present AI-EWS an explainable AI for early prediction of acute critical illness. To demonstrate the generalizability of the AI-EWS, we report results on sepsis, acute kidney injury, and acute lung injury. We developed the AI-EWS as a temporal convolutional network followed by an explanation module based on deep taylor decomposition. The AI-EWS achieved area under the receiver operating characteristic curve values of 0.81(0.79-0.83) to 0.86(0.83-0.89) 12 hours before acute critical illness onset across all three cases. In summary AI-EWS shows high predictive ability, while enabling the possibility of explaining the predictions in terms of input data to empower clinicians to understand the underlying reasoning of the prediction. Our results may lead to a wider adoption of AI in clinical

practice by facilitating trust and transparency - properties that also makes it easier to comply with CE regulations.

P07.08 Louise Sofia Madsen COMMUNITY-BASED REHABILITATION IN OUTDOOR SETTINGS: A SYSTEMATIC REVIEW OF QUALITATIVE ARTICLES ON PEOPLE WITH DISABILITIES AND PROFESSIONALS' EXPERIENCES AND PERCEPTIONS

L.S. Madsen[1, 2], C. Handberg[3], C.M. Jensen[2], C.V. Nielsen[1, 2]

[1]Department of Public Health, Aarhus University, [2]DEFACTUM, Central Denmark Region, [3]The National Rehabilitation Centre for Neuromuscular Diseases

Aim: To examine and synthesise qualitative articles of people with disabilities and professionals' experiences and perceptions on community-based rehabilitation (CBR) in outdoor settings. The objective was to expand the understanding of facilitators, barriers and potential benefits related to the intersection of CBR and outdoor settings.

Methods: Six electronic databases were searched (PubMed, Embase, Scopus, PsycINFO, CINAHL and Cochrane Library) for qualitative articles. The Critical Appraisal Skills Programme Checklist was used for quality assessment. The qualitative research methodology Interpretive Description was applied to synthesise and analyse the extracted data material.

Results: In total, 4029 abstracts were identified; nine articles were included for analysis. The synthesis revealed four themes; Ability to Overcome Challenges, Outdoor Adaptive Activities, Inclusive Social Communities and Culture of Reciprocal Interaction, representing central aspects of people with disabilities and professionals' experiences and perceptions of CBR in outdoor settings.

Conclusion: The intersection of CBR and outdoor settings provide opportunities to deal with real-life issues and thus empower people with disabilities to overcome challenges in everyday life. The outdoor setting seemed to strengthen a holistic approach to delivery of rehabilitation based in the community. However, for a sustainable development of CBR in outdoor settings initiatives need to expand beyond professional program context and strengthen focus on inclusion of the community as well. Future research should add focus on general community inclusion and development for CBR initiatives in outdoor settings.

P07.09 Sigurd Beier Sloth CANCELLED SELF-REGULATED VS. INSTRUCTOR-REGULATED TRAINING IN LAPAROSCOPY

S.B. Sloth[1], M. Seyer-Hansen[2], G. De Win[3], M.K. Christensen[1]

[1]Centre for Health Sciences Education, Aarhus University, [2]Department of Obstetrics and Gynaecology, Aarhus University Hospital, [3]Department of Urology, Antwerp University Hospital

Studies on proficiency-based training (PBT) have shown promising results on developing and retaining trainees' laparoscopic skills. However, PBT can be very time-consuming. Accordingly, home-based training on portable box trainers (BTs) has been proposed as a solution. But previous studies found that trainees lack motivation and incentives to engage in home-based training. In this study we compare home-based self-

regulated simulation training (SRST) to centralized instructor-regulated simulation training (IRST). We want to explore whether home-based SRST can be engaging and effective given the right training design.

We include first-year trainees in Surgery, Urology and Gynecology. Trainees are randomized to either SRST or IRST in basic laparoscopy. During the training program the SRST group train at home, while the IRST group engage in two centralized training sessions instructed by surgical experts. Trainees engage in PBT with validated proficiency tasks and protected training time. All participants train portable BTs connected to an online training platform providing feedback on metrics. Pre- and post-tests consist of validated exercises in camera navigation, hand-eye and bi-manual coordination.

Analysis of preliminary data show an overall pass rate of 78% (89% SRST, 67% IRST). All participants significantly improved their hand-eye and bi-manual coordination during the training. The preliminary findings reveal no significant inter-group differences.

Our preliminary results show improvements of basic laparoscopic skills regardless of allocated training program. A future aim of the study is to examine how training context and facilitation influences transfer of training.

P07.10 Camilla Lundquist

FROM RESEARCH TO CLINICAL PRACTICE. BARRIERS AND FACILITATORS FOR IMPLEMENTATION OF UPPER LIMB PREDICTION ALGORITHMS FOR PATIENTS WITH STROKE

C.B. Lundquist[1], H. Pallesen[2], T. Tjørnhøj-Thomsen[3], I. Brunner[2]

[1]Hammel Neurorehabilitation and Research Centre, Aarhus University, [2]Hammel Neurorehabilitation and Research Centre, Department of Clinical Medicine, Aarhus University, [3] National Institute of Public Health, University of Southern Denmark

Background

Stroke is a leading cause of long-term disability in the western world and upper limb (UL) impairments are common. Accurate prediction of recovery of UL function can lead to targeted, individualized rehabilitation.

Despite the potential benefit UL prediction models are rarely used clinically. A successful implementation requires that the algorithm seems useful to the clinicians.

Purpose: The purpose of this study is to gain insight in knowledge and use of UL prediction algorithms and to explore factors perceived important for use of UL prediction models.

Methods: This is a qualitative study using focus group interviews.

The Consolidated Framework for advancing Implementation Research (CFIR) was used as an explanatory framework guiding data collection and analysis. A semi-structured interview guide was developed based on the CFIR.

Focus group interviews were performed amongst physiotherapists and occupational therapists employed at Hammel Neurorehabilitation Centre and University Research Clinic (RHN).

The interviews were managed by a moderator who was aware of ensuring a confident atmosphere welcoming a diversity of opinions. A second researcher functioned as an observer, providing feedback to the moderator and observing interactions in the focus group.

The Interviews were audiorecorded, transcribed and imported to Nvivo12, a qualitative research software program. An inductive, explorative analysis was performed. Information gained from all interviews were synthesised. The authors were open to new themes emerging.

Results: Four focus group interviews were performed. Data will be analyzed Nov 2019- Jan 2020.

P08.01   Peter Bo Jørgensen

HIGHER EARLY PROXIMAL MIGRATION OF HEMISPHERICAL CUPS WITH ELECTROCHEMICALLY APPLIED HYDROXYAPATITE (BONEMASTER) ON A POROUS SURFACE COMPARED WITH POROUS SURFACE ALONE: A RANDOMIZED RSA STUDY WITH 53 PATIENTS

P.B. Jørgensen[1, 2], H. Daugaard[3], S.S. Jakobsen[1], M. Lamm[1], K. Søballe[1, 2], M. Stilling[1, 2]

[1]Department of Orthopedic Surgery, Aarhus University Hospital, [2]Department of Clinical Medicine, Aarhus University, [3]Department of Orthopaedic Surgery, Gentofte Hospital

Background and purpose -- BoneMaster (BM) is an electrochemically deposited hydroxyapatite (HA) implant-coating, which is evenly distributed, thin, and quickly resorbed. It is designed to stimulate osseointegration andearly implant stability and alleviate longer-term HA-induced third-body polyethylene wear. This study evaluates early cup migration and functional outcomes of cementless porous-coated hemispherical cups with or without BM.

Patients and methods -- In a patient-blinded, randomized, controlled trial 53 patients at mean 64 years (55-75) with coxarthritis were operated with an Exceed cup (Zimmer Biomet) and Bi-Metric stem (Zimmer Biomet) with porous and BM coating (PBM) or with porous coating alone (P). Follow-ups were performed postoperatively and at 3, 6, 12, and 24 months. Effect measures were cup migration measured with RSA and PROMs.

Results -- At 6-month follow-up, proximal cup migration in the PBM group (0.09 mm, 95% CI 0.02-0.20) was higher than in the P group (0.25 mm, CI 0.15-0.35). At 1- and 2-year follow-up, cup migration in all 6 degrees of freedom was similar between groups (p > 0.2). From before surgery to 2-year follow-up, Oxford Hip Score (OHS) increased by 17 points (CI 14-20). Hip disability and Hip disability and Osteoarthritis Outcome Score (HOOS) increased in all sub-scores, but was more pronounced for PBM cups compared with P cups in the Symptoms sub-score (p = 0.04).

Interpretation -- Contrary to expectations, PBM cups had higher early migration than P cups. At 2-year follow-up, migration was similar between groups. There seems to be no early benefit of BM coating on acetabular cups.

P08.02   Lea Lykke Harrits   MATERNAL THYROID DISEASES AND PUBERTAL DEVELOPMENT IN
          Lunddorf   DAUGHTERS AND SONS

L.L.H. Lunddorf[1], A. Ernst[1, 2], N. Brix[1], L.H. Arendt[1, 3], S.L. Andersen[4], J. Olsen[1, 5], C.H. Ramlau-Hansen[1]

[1]Department of Public Health, Research Unit for Epidemiology, Aarhus University, [2]Department of Urology, Aarhus University Hospital, [3]Department of Obstetrics and Gynecology, Regional Hospital Horsens, [4]Department of Clinical Biochemistry, Aalborg University Hospital, [5]Department of Clinical Epidemiology, Aarhus University Hospital

Background: Studies have shown secular trends in timing of puberty in both girls and boys have been shown, but the causes hereof are largely unknown. Thyroid diseases constitute the most common pregestational endocrine disorders in pregnant women and increase the risk of being born small for gestational age, which is linked to rapid catch-up growth and earlier puberty. Further, as normal levels of maternal thyroid hormones are essential for adequate fetal neurodevelopment, the HPG-axis is likely affected, potentially altering the timing of puberty later in life.

The aim of this cohort study was to investigate whether maternal thyroid diseases were associated with timing of puberty in daughters and sons.

Methods: Using the Puberty Cohort nested within the Danish National Birth Cohort, 15,819 mother-child pairs were included. Information on maternal thyroid diseases was collected through interviews twice during pregnancy as well as from the Danish National Patient Registry. Information on current pubertal status was collected half-yearly from the age of 11 years of age until full sexual maturation. Main outcome was mean difference in age at attaining each pubertal milestone as well as a combined pubertal marker in children of mothers with thyroid diseases with unexposed children as reference.

Results: Sons of mothers with hyperthyroidism entered puberty earlier than unexposed (combined marker: -2.8 (95% CI: -4.9; -0.7) months). Maternal hypothyroidism and goitre did not affect pubertal timing in sons. Any maternal thyroid diseases did not affect timing of puberty in daughters.

Conclusion: Maternal hyperthyroidism might accelerate pubertal development in sons.

P08.03   Thor Haahr   ABNORMAL VAGINAL MICROBIOTA IS SIGNIFICANTLY ASSOCIATED WITH
                        POOR CHANCE OF PREGNANCY IN PATIENTS UNDERGOING *IN VITRO* FERTILIZATION TREATMENT.

T. Haahr[1], J.S. Jensen[2], N. Uldbjerg[3], P. Humaidan[1]

[1]The Fertility Clinic, Regional Hospital Skive, Department of Clinical Medicine, Aarhus University, [2]Statens Serum Institut, Copenhagen, [3]Department of Obstetrics and Gynecology, Aarhus University Hospital

Introduction

The vaginal microbiota is considered healthy when dominated by one or more Lactobacillus species. In contrast, a Lactobacillus deficient vaginal microbiota is considered dysbiotic. Recent evidence challenges the paradigm of a "sterile" uterus, showing that dysbiotic vaginal bacteria can ascend to the endometrium and cause a biofilm infection. However, the

association between vaginal dysbiosis and poor reproductive outcome remain controversial due to equivocal results. We aimed to optimize the diagnosis of vaginal dysbiosis in IVF patients to predict which patients would be at risk of poor reproductive outcome due to an ascending infectious etiology.

Results

In a prospective cohort study, we identified 21% (27/130) of IVF patients with vaginal dysbiosis as based on the gold standard, using Gram stained smears. By using qPCR primers for hallmark vaginal bacteria, we established quantitative thresholds by ROC curve analysis (AUC=0.95) to identify patients with high loads of dysbiotic vaginal bacteria. More patients were found with abnormal vaginal microbiota (AVM) as based on the qPCR method, 28% (36/130). The clinical pregnancy rate in IVF patients with AVM was 9% vs 44% in the normal group, P=0.004. No significant associations to reproductive outcome was found based on standard 16S rRNA sequencing methods.

Conclusion

AVM is significantly associated with poor reproductive outcome, but this finding depends on the methods used to diagnose vaginal dysbiosis. A novel qPCR method was able to optimally dichotomize patients into normal and abnormal compared to gold standard. 16S rRNA sequencing methods did not improve diagnosis of vaginal dysbiosis.

P08.04 Pelle Emil Hanberg

PHARMACOKINETICS OF DOUBLE-DOSE CEFUROXIME IN PORCINE INTERVERTEBRAL DISC AND VERTEBRAL CANCELLOUS BONE - A RANDOMIZED MICRODIALYSIS STUDY

P. Hanberg[1, 2, 3], M. Bue[2, 3], A.R. Jørgensen[2], M. Thomassen[2], K. Öbrink-Hansen[4], K. Søballe[2, 3, 5], M. Stilling[2, 3, 5]

[1]Department of Orthopaedic Surgery, Horsens Regional Hospital, [2]Orthopaedic Research Unit, Aarhus University Hospital, [3]Department of Clinical Medicine, Aarhus University, [4]Department of Infectious Diseases, Aarhus University Hospital, [5]Department of Orthopaedic Surgery, Aarhus University Hospital

Background: Postoperative pyogenic spondylodiscitis is associated with prolonged antimicrobial therapy and high relapse rates. A previous study has indicated that a single dose of cefuroxime (1.5 g) provides insufficient spine tissue concentrations for spine procedures lasting more than 2-3 hours.

Purpose: To evaluate the time with concentrations above relevant minimal inhibitory concentrations (T>MIC) in plasma, subcutaneous adipose tissue, vertebral cancellous bone, and intervertebral disc after a twofold increase of the standard dosage of 1.5 g cefuroxime given as one double dose (1x3 g) or two single doses (2x1.5 g) with a four-hour interval.

Method: Sixteen pigs were randomized into two groups: Group 1 received one double dose of cefuroxime (1x3 g) as an intravenous bolus and Group 2 received two single doses of cefuroxime (2x1.5 g) as an intravenous bolus with a four-hour interval. Cefuroxime measurements

were obtained from plasma and the respective tissues for eight hours thereafter. Microdialysis was applied for sampling in solid tissues.

Results: The time with concentrations above the Staphylococcus aureus clinical breakpoint minimal inhibitory concentration of 4 µg/mL was higher in all compartments for Group 2 compared with Group 1. The mean T>MIC (4 µg/mL) in all compartments ranged between 47%-67% for Group 1 and 72%-92% for Group 2. Furthermore, a delayed tissue penetration into all tissues for both groups was demonstrated.

Conclusion: This study suggests that cefuroxime should be given at least 45 min prior to spine procedures and as two single doses at a maximum interval of four hours for extended spine procedures.

P08.05   Sara Bønløkke Simonsen

HPV IN THE BLOOD OF CERVICAL CANCER PATIENTS - CLINICAL IMPLICATIONS.

S. Bønløkke[3], J. Blaakær[2], B.S. Sørensen[4], M. Stougaard[3], G.B. Nyvang[6], J. Lindegaard[5], J. Bertelsen[3], T. Steiniche[3], K. Fuglsang[1]

[1]Department of Obstetrics and Gynecology, Aarhus University Hospital, [2]Department of Obstetrics and Gynecology, Odense University Hospital, [3]Department of Pathology, Aarhus University Hospital, [4]Department of Biochemistry, Aarhus University Hospital, [5]Department of Oncology, Aarhus University Hospital, [6]Department of Oncology, Odense University Hospital

Introduction

HPV is the main cause of cervical cancer. The virus can be detected in tissue samples, but in this study, we hypothesised that HPV DNA is released into the bloodstream from tumour cells, and that these fragments of HPV DNA are measureble in the blood.

Materials and Methods

Blood samples from patients diagnosed with cervical cancer at Aarhus and Odense University Hospital (June 2018 to December 2020) are collected. A baseline sample is collected before treatment, and follow-up samples are collected during and after treatment for up to two years.

Results

The study is ongoing, and currently we have results on blood samples from the first ten patients; four with localised cancer (stage IB), who have undergone surgery, and six with disseminated cancer (> stage IB), who have received radio- and chemotherapy. Analyses have shown that HPV DNA can be qualitatively and quantitatively measured in disseminated patients, and in follow-up samples, HPV DNA quantity decreases during treatment. For patients with localised cancer, HPV DNA has not been detectable.

Conclusion

DdPCR can detect HPV DNA in blood samples from disseminated cervical cancer patients, and preliminary results suggest that an HPV DNA measurement before treatment correlates to disease stage. For patients who develop a disease recurrence, we expect to see an increase in HPV DNA prior to this, and by analysing follow-up blood samples, we may have found a method to predict a recurrence, enabling us to start

treatment early. Since HPV also causes other cancer types, we expect the method to be applicable in these cancers too.

P08.06   Line Winther Gustafson

"SEE AND TREAT" IN AN OUTPATIENT SETTING IN WOMEN AGED 45 YEARS AND OLDER WITH CERVICAL DYSPLASIA

L.W. Gustafson[1, 3], A. Hammer[3, 2], L.K. Petersen[4], B. Andersen[1, 3], P. Bor[5, 3]

[1]Department of Public Health Programmes, Randers Regional Hospital, [2]Department of Obstetrics and Gynecology, Regional Hospital West Jutland, [3]Department of Clinical Medicine, Aarhus University, [4]Open Patient Data Explorative Network (OPEN) and Department of Gynecology and Obstetrics, Odense University Hospital, [5]Department of Obstetrics and Gynecology, Randers Regional Hospital

Introduction: Despite an organized cervical screening program, 370 Danish women are still diagnosed with cervical cancer every year, and 100 women die from the disease. Although cervical cancer incidence is high in older women, the incidence of cervical precursor lesions is low. This may be due to challenges in the diagnostic workup. The "see and treat" approach is a procedure, which includes colposcopy, biopsies, and a cone biopsy, allowing women to be diagnosed and treated in one visit.

Aim: To investigate if the implementation of "see and treat" in a gynecological outpatient clinic can optimize the diagnostic workup, clinical follow-up, and treatment of women ≥45 years with abnormal screening results.

Methods:

Study 1. Cross sectional study including women ≥45 years referred to gynecological departments in Central Denmark Region due to abnormal screening results. We will report the prevalence of HPV and cervical dysplasia, and calculate agreement rates between colposcopy, cervical punch biopsies, and cone biopsy.

Study 2. Proof of principle study to evaluate the accuracy of cytology and p16/Ki67 testing in detecting CIN2+ in women included in study 1.

Study 3. Prospective follow-up study, exploring the psychological impact of and patient's preferences with the "see and treat" approach using a validated questionnaire.

Perspective:

Our results will provide important knowledge on diagnostic, treatment and follow-up strategies in older women with abnormal screening results, including patient's preferences. The implementation of "see and treat" is thus expected to lead to more accurate diagnosis and more optimal treatment of older women.

P08.07   Helle Østergaard IS A ROTATOR CUFF TEAR A PROGNOSTIC FACTOR OF PHYSICAL
FUNCTION AND QUALITY OF LIFE IN PATIENTS WITH A PROXIMAL
HUMERUS FRACTURE? PRELIMINARY SUB-ANALYSIS FROM A NORDIC
MULTICENTER STUDY (NITEP)

*H. Østergaard[1, 3], A. Launonen[2], K. Døssing[1, 3], M. Vestermark[1], K. Søballe[4],
M. Mechlenburg[3, 4]*

[1]Department of Orthopaedic Surgery, Viborg Regional Hospital,
[2]Department of Orthopaedic Surgery, Tampere University Hospital,
[3]Department of Clinical Medicine, Aarhus University, [4]Department of
Orthopaedic Surgery, Aarhus University Hospital

Background

Proximal humerus fracture (PHF) is the third most common fracture in elderly people. The prevalence of rotator cuff tear in patients with a PHF is estimated to 10-50% and correlates with age and severity of fracture. However, only few studies have investigated whether the presence of rotator cuff tear impairs physical function and quality of life in patients who sustained a PHF, and reported results are inconsistent.

Objectives

We aimed to determine if the presence of rotator cuff tear impairs physical function and quality of life in patients with a PHF treated non-operatively.

Methods

The study is a preliminary sub-analysis nested in an ongoing randomized controlled trial. Patients (= 54) with a verified PHF, age 60 or older, were recruited in three Nordic hospitals. Presence of (full-thickness) rotator cuff tear was determined by ultrasound examination performed 3 months after injury. After 6 and 12 months, scores on Constant Score (CS), Disability of the Arm, Shoulder and Hand (DASH), and EuroQol-5 Domain (EQ-5D) were compared between the group with a rotator cuff tear and the group without rotator cuff tear.

Results

The prevalence of rotator cuff tear was 31%. At 12 months follow-up, we found a statistically significant difference in the CS between the groups (p=0.012). This was supported by a clinically relevant difference (14 points) between the groups. Neither at 6 nor at 12 months follow-up did we see significant differences between the groups on DASH score (p=0.10), EQ-5D$_{index}$(p=0.15) or EQ-5D$_{vas}$(p=0.80).

Conclusion

We find that rotator cuff tear impairs physical function after PHF and can be considered as a prognostic factor.

| P08.08 | Louise Lilleøre Kjeldsen | PELVIMETRY MEASURED BY MRI; IS PELVIC CAPACITY DEPENDENT ON PHYSICAL POSITION IN PREGNANT WOMEN? |

L.L. Kjeldsen[1, 2, 3], A.D. Blankholm[4], A.G. Jurik[4], R.D. Maimburg[1, 2]

[1]Department of Clinical Medicin, Aarhus University, [2]Department of Obstetrics and Gynaecology, Aarhus University Hospital, [3]Department of Midwifery, UCN, [4]Department of Radiology, Aarhus University Hospital

Background:Midwives encourage women to adopt various positions during childbirth to increase pelvic dimensions and thereby facilitate birth. Knowledge about various positions and its possibility to increase the pelvic dimensions and benefit labour progress is limited and mostly obtained from clinical experience. Despite the assumed positive effect of maternal upright position at birth a more sedentary behaviour using mostly supine position at birth has been implemented in the last 10-15 years. Supine position mayreduce the positive physiological process of labour and may be inconsiderate of women's comfort with a possible negative impact on the birth experience and the women's subsequent confidence

Objectives: To study antero-posterior and transverse pelvic dimension in pregnant women in kneeling squat, supine dorsal- and semi-lithotomy dorsal position in gestational week 20 and 32.

Methods: A diagnostic imaging study recruiting 50 pregnant women expecting their first child at their first appointment at Aarhus University Hospital, Denmark. MRI scans will be conducted in three different positions; kneeling position, supine dorsal position, and supine-lithotomy position obtaining three short MRI scan sequences.

Results: The study is ongoing and preliminary results will be presented. The hypothesis is that pelvic dimension is larger in the kneeling squat position compared to supine dorsal and semi-lithotomy dorsal positions.

Conclusion: There may be an unused potential to ease childbirth and reduced unnecessary interventions if midwives are supplied with more physiological knowledge about childbirth.

| P08.09 | Kris Chadwick Hede | CARGEL BIOSCAFFOLD IMPROVES CARTILAGE REPAIR AFTER BONE MARROW STIMULATION IN A MINIPIG MODEL |

K.C. Hede[1], B.B. Christensen[1, 3], M.L. Olesen[1], J.S. Thomsen[2], C.B. Foldager[1, 3], M.C. Lind[3]

[1]Orthopaedic Research Lab, Aarhus University Hospital, [2]Department of Biomedicine, Aarhus University, [3]Department of Orthopaedics, Aarhus University Hospital

Purpose

To compare cartilage repair with bone marrow stimulation combined with CARGEL Bioscaffold (CB) with bone marrow stimulation (BMS) alone in chondral defects in the knees of Göttingen minipigs.

Materials and methods

Six adult Göttingen minipigs received two chondral defects in each knee. The knees were randomized to BMS with CB or BMS alone. The animals were euthanized after 6 months. Follow-up consisted of

histomorphometry, immunohistochemistry, semiquantitative scoring of the repair tissue (International Cartilage Repair Society II), and μCT of the trabecular bone beneath the defect.

Results

Histomorphometry revealed significantly more fibrocartilage (80% vs 64%, p = 0.01) and less fibrous tissue in defects treated with CB (15% vs 30%, p = 0.02). Hyaline cartilage was seen in a small area in one defect treated with CB (1.2%). No differences were seen for bone (2% vs 5%, p = 0.29), or marrow (3% vs 1%, p = 0.30). For histological semiquantitative score (ICRS II), defects treated with CB scored lower on subchondral bone (69 vs. 44, p = 0.02) and basal integration (53 vs 71, p = 0.02). No significant differences were seen on the other parameters of the ICRS II. Collagen type II staining revealed a trend towards more positive staining in the CB group, but the difference was not statistically significant (p = 0.08). μCT revealed that the trabecular bone beneath the defect had thicker trabeculae (p = 0.029) and a higher bone material density (p = 0.028) in defects treated with CB.

Conclusion

Treatment of cartilage injuries with CB seems to lead to improved repair tissue and a more pronounced subchondral bone response compared with bone marrow stimulation alone.

P08.10   Christine Rohr Thomsen

NEW METHOD FOR EVALUATING THE STIFFNESS OF THE HUMAN UTERINE CERVIX BASED ON ELASTOGRAPHY AND A FORCE-MEASURING DEVICE

C. Rohr Thomsen[1, 2], P. Bor[1], P. Sandager[2], P. Hinge[3], N. Uldbjerg[2]

[1]Department of Obstetrics and Gynecology, RRA, [2]Department of Obstetrics and Gynecology, Aarhus University Hospital, [3]Department of Engineering, Aarhus University

Background

Preterm softening of the uterine cervix is a leading cause of preterm birth. Today we have no objective tool for measuring cervical softening.

Elastography is an ultrasound-based method for evaluating the consistency of a tissue.

The principle is based on the distance between the small pixels, which constitutes the ultrasound image. When applying the pressure on the tissue these distances change. Elastography uses this phenomenon when evaluating the consistency of a tissue.

The aim of this study was to evaluate elastography as a method for assessing cervical softening.Method

We used conventional vaginal ultrasound scanning in combination with elastography and a force-measurement device, developed in collaboration with Massachusetts Institute of Technology (MIT), USA.Results

The cervix is very heterogeneous; therefore, it is very important to use a standardized protocol for identification of the region of interest (ROI), i.e. the part of the cervix, which we examine. In normal pregnant women, this

technique demonstrate a more fold increase in cervical softening as pregnancy progress.Conclusion

Though our results are very preliminary, the method looks promising. We will now perform more scans in order to test and refine the method.

The perspective is better identification and treatment of pregnant women at risk of preterm delivery. In addition, the method could be used to plan induction of labor for post-term pregnancy.

| P09.01 | Jordan Nicolas Alves | **MOTION-RELATED ACTIVITY IN THE HUMAN RETINA ELICITED BY MOVING GRATINGS** |

J.N. Alves, J.I. Lubell, B.U. Westner, S.S. Dalal

Center of Functionally Integrative Neuroscience, Aarhus University

A multitude of studies across various species have demonstrated that motion induces synchronous activity in retinal amacrine and ganglion cell populations. However, evidence for retinal motion processing in humans is sparse and not consistent. Here, we investigate whether specific types of motion stimuli elicit motion related activity in the human retina that can be recorded using electroretinography. The participants passively viewed moving circular gratings with three different speeds, a stimuli category thathas been shown to result in massive cell activity synchronization in the mouse retina. Binocular retinal activity was recorded using DTL fiber electrodes and subsequently analyzed in the time and frequency domain. Contrasting the different speed conditions showed clear effects for the fastest moving grating stimulus: this condition elicited evoked potentials with larger amplitudes than slower motions. Time-frequency analysis revealed a power increase in high frequency activity (60-120 Hz) for the high speed condition compared to slower moving gratings. Taken together, this shows retinal activity elicited by moving stimuli, possibly reflecting retinal motion processing.

| P09.02 | Charlotte Ernst | **INTRAVASCULAR ADENOSINE TRIPHOSPHATE (ATP)-INDUCED CONTRACTION IS MEDIATED BY P2-PURINERGIC RECEPTORS AND THE A3-ADENOSINE RECEPTOR IN PORCINE RETINAL ARTERIOLES EX VIVO** |

C. Ernst[1], P. Skov Jensen[1], C. Aalkjaer[2], T. Bek[1]

[1]Department of Ophthalmology, Aarhus University Hospital, [2]Department of Biomedicine (physiology), Aarhus University

Title: Intravascular adenosine triphosphate (ATP)-induced contraction is mediated by P2-purinergic receptors and the A3-adenosine receptor in porcine retinal arterioles ex vivo

Purpose: ATP is a vasoactive compound assumed to be involved in the pathophysiology of retinal vascular disease such as diabetic retinopathy. ATP has been shown to induce vasoconstriction, but it is unknown which vascular receptors are involved in the vasoactive effect. Therefore, the aim was to investigate the diameter response of ATP on the arterioles, precapillary arterioles and capillaries during intravascular application of the compound with or without a receptor blocker.

Methods: Porcine superior hemiretinas (n=24) were mounted in a specially designed tissue chamber allowing diameter measurements of arterioles, precapillary arterioles and capillaries during intravascular application of vasoactive compounds without or with blocking of the P2-purinergic receptors (PPADS) or the A3-adenosine receptor (MRS 1523).

Results: Intravascular administration of ATP induced significant contraction ($p<0.01$) of retinal vessels at all three branching levels. The contraction of the arterioles was blocked by both PPADS ($p<0.01$) and MRS 1523 ($p<0.01$), in pre-capillary arterioles the contraction was blocked by PPADS ($p=0.03$), whereas the contraction of capillaries was blocked by MRS 1523 ($p=0.01$).

Conclusion: ATP can induce contraction after intravascular application on porcine retinal vessels ex vivo. The effect can be assumed to depend on both ATP and ATP degradation products due to involvement of both P2-purinergic- and adenosine receptors, and depend on the vascular branching level which is targeted.

P09.03   Søren Viborg Vestergaard

INCIDENCE, PREVALENCE AND MORTALITY OF NEPHROTIC SYNDROME IN ADULTS

S.V. Vestergaard[1], H. Birn[2], H.T. Sørensen[1], D. Nitsch[3], C.F. Christiansen[1]

[1]Department of Clinical Medicine, Aarhus University, [2]Department of Biomedicine, Aarhus University, [3]Department of Non-communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine

Background

To address a knowledge gap, we examined incidence, prevalence, and mortality of diagnosed nephrotic syndrome (NS) and biochemistry consistent with NS in adults.

Methods

From the Central Denmark Region (1997-2013), we sampled 1) persons with NS recorded in the Danish National Registry of Patients, and 2) persons with biochemistry consistent with NS (nephrotic proteinuria [urine albumin/creatinine-ratio >220 mg/mmol, OR urinary albumin loss >2.2 g/day, or corresponding proteinuria] and severe hypoalbuminemia [p-albumin <25 g/L]). We estimated the incidence rates (IRs) per 100,000 person-years during 2005-2013, and annual prevalence of diagnosed NS as well as biochemistry consistent with NS per 100,000 population with 95%-Cis., overall, and by age, and sex. We computed survival curves for the cohorts, overall and stratified by age-group.

Results

We identified 373 persons with first-time hospital-diagnosed NS and 462 persons with biochemistry consistent with NS corresponding to an IRs of 3.8 per 100,000 person-years (95%-CI: 3.7-3.9) and 4.7 per 100,000 person-years (95%-CI: 3.8-5.6), respectively. Among women, IRs of NS was highest in younger age-groups, whereas IRs increased across ages in men in both cohorts. Prevalence of NS and biochemistry indication NS was comparable. Five year survival was close to 75% in both cohorts, with decreasing survival across age-groups.

Conclusion

Incidence of biochemistry consistent with NS was slightly higher than diagnosed NS in adults, both showing overall increasing incidence across ages, and highest incidence in young women and elderly men. Survival of persons identified with NS and biochemistry consistent with NS was similar.

P09.04 Christina Voss Ernstsen

ACUTE PYELONEPHRITIS: THE EFFECT ON RENAL WATER CHANNELS

C.V. Ernstsen[1], J.R. Therkelsen[2], M.G. Christensen[2], A.B. Schelde[1], H.A. Prætorius[2], L.N. Nejsum[1]

[1]Department of Clinical Medicine, Aarhus University, [2]Department of Biomedicine, Aarhus University

Acute pyelonephritis (APN) is a bacterial infection in the kidney, which occurs due to bacteria ascending from the bladder to the kidney during a urinary tract infection. APN can lead to irreversible kidney damage and/or bacteria dissemination to the blood causing sepsis. Aquaporin (AQP) water channels are essential for regulation of body water homeostasis. In the kidney, AQP2 is responsible for fine-tuning of urine concentration in response to the hormone vasopressin. AQP2 dysregulation is involved in various renal diseases, including nephrogenic diabetes insipidus, acute and chronic kidney injury. However, renal AQP2 regulation during APN has never been investigated. Using a mouse model of APN, we performed immunohistofluorescence and advanced line scan analysis to investigate AQP2 expression, subcellular localization and post-processing during APN.

P09.05 Stine Julie Hyldal Tingskov

THE EFFECT OF TAMOXIFEN ON GENDER DIFFERENCES IN UNILATERAL URETERAL OBSTRUCTED RATS AND HUMAN KIDNEY SLICES

S.J. Tingskov, M.S. Jensen, R. Nørregaard

Department of Clinical Medicine, Aarhus University

Renal fibrosis is regarded as the most damaging process in chronic kidney disease (CKD). Interestingly, females are less prone to CKD, which might be due to estrogen. In this study, we will investigate the effect of tamoxifen (TAM), a selective estrogen receptor modulator, in a unilateral ureteral obstruction (UUO)-induced fibrosis model in female, male and ovariectomized (OVX) female rats. Furthermore, a recently develop model of human renal fibrosis was used to study multicellular pathological processes in human tissue.

Fibrosis was induced by 7 days of UUO. Female OVX rats had both their ovaries removed two weeks before UUO. Tamoxifen (25 mg/kg for female rats and 50 mg/kg for male rats) was given by oral gavage. Human precision-cut kidney slices were exposed to TGF-β for 48h in order to make the tissue fibrotic and afterwards treated with TAM for 6h.

Renal fibrosis was increased after UUO in both male, female and OVX rats. TAM treatment reduced the gene expression of fibrotic markers in female UUO rats, but not in male and in OVX rats. Yet, TAM significantly reduced the protein level of fibrotic markers and the kidney weight in response to UUO in both female as well as OVX and male rats.

Importantly, treatment with TAM has a tendency to reduce fibronectin in human kidney slices exposed to TGF-β from women but not in men.

These findings indicate that TAM reduces UUO-induced fibrosis in both female, OVX and male rats, but have different effects on gene levels of fibrotic markers and plasma data. Furthermore, our finding provide preclinical evidence that treatment with TAM affects men and women differently and the concentration of the drug must be adapted to the gender.

P09.06   Monica Dahlstrup Sietam   **THE ROLE OF SYNDECAN 2 IN VISUAL BEHAVIOUR**

M.D. Sietam[1, 2], S. Sajgo[1], B. Thomsen[1], K. Yonehara[1]

[1]DANDRITE, Aarhus University, [2]Department of Molecular Biology and Genetics, Aarhus University

The retina is comprised of five main cell classes organized into specific layers for processing of the visual input. Photoreceptors receives and transduce the visual stimuli, bipolar cells cells relay the visual information from the upstream to the downstream circuit, which is filtered and modulated by the horizontal and amacrine cells, while the retinal ganglion cells are the sole output to the brain. Disruption of the circuitry can lead to loss of specific visual features, relfexes or sight.

Finding and understanding genetic contributors and their link to visual processing or behaviours can provide an insight into disease mechanisms through identification of impaired circuit components.

The cell surface proteoglycan, Syndecan 2 (Sdc2), has, in a pilot study, shown to diminish the horizontal optomotor reflex when whole body expression was reduced. The same phenotype has previously been reported in mice for the gene Frmd7 that is known to cause congenital nystagmus in humans. Interestingly Sdc2 and Frmd7 share a common interaction partner Calcium/calmodulin-dependent serine kinase (Cask) involved in synapse formation and function. Moreover, mutations in Cask disrupting the interactions to Frmd7 has been linked to nystagmus as a secondary phenotype to X-linked mental retardation.

In this project, we aim to investigate the role of the Sdc2, in visual behaviors and retinal circuitry using a homozygous knock out mouse as a model. We plan to achieve this by applying multidisciplinary approaches such as behavioural analysis, electrophysiology, genome engineering, and viral vectors.

P09.07   Silja Hansen   **A NOVEL PORCINE MODEL FOR EXPERIMENTAL CNV**

S. Hansen[1], A. Askou[1], M. la Cour[3], T. Bek[2], T. Corydon[1]

[1]Deparment for Biomedicine, Aarhus University, [2]Department of Ophthalmology, Aarhus University Hospital, [3]Department of Ophthalmology, Copenhagen University Hospital

Background:

Current treatment of exudative age-related macular degeneration (eAMD) antagonizes the vascular endothelial growth factor (VEGF) which

is a known driver of choroidal neovascularization (CNV) in the disease. However, injections should be given repeatedly, whereas gene therapy has shown to be effective in a murine model after a single injection. This approach should be brought closer to clinical translation in a porcine model, but laser induced subretinal CNV in pigs have a low success rate, since the laser damages the neuroretina. Therefore, we developed a method using subretinal injection of saline prior to laser application, to protect the neuroretina from burns from the laser by separating it from the retinal pigment epithelium (RPE).

Methods:

In 30 freshly enucleated porcine eyes a subretinal cannula was forwarded through the vitreous body to penetrate the retinal surface. A retinal bleb was produced by injecting 0,05 ml saline. Subsequently, laser burns were applied to the retina in the area of the bleb. Ophthalmoscopy was performed to examine the neuroretina for possible damage.

Results:

In all eyes the subretinal injection of saline was successful, and ophthalmoscopy showed that the neuroretina was unaffected by the laser.

Conclusions:

Transvitreal subretinal injection of saline in porcine eyes can detach the neuroretina to protect it from laser burns intended to produce choroidal neovascularization. Further studies will have to evaluate this method in an in vivo porcine model. This may facilitate the development of experimental CNV with a high success rate in the porcine eye as a precondition for developing gene therapy to treat eAMD.

P09.08 Ann Mai Hindkjær Østergaard

THE EFFECT OF 0.9% NACL COMPARED WITH PLASMA-LYTE ON BIOMARKERS OF KIDNEY DAMAGE IN PATIENTS UNDERGOING PRIMARY UNCEMENTED HIP REPLACEMENT

A.M. Østergaard[1], A.N. Jørgensen[1], N.P. Ekeloef[2], S. Bøvling[3], F.H. Mose[1], J.N. Bech[1]

[1]University Clinic in Nephrology and Hypertension, Department of Medical Research, Regional Hospital Holstebro, [2]Department of Anesthesiology, Regional Hospital Holstebro, [3]Department of Orthopedic Surgery, Regional Hospital Holstebro

Background: 0.9% NaCl induces hyperchloremic acidosis and is suspected to increase the risk of acute kidney injury (AKI). Biomarkers such as NGAL and KIM-1 may have potential as early indicators of AKI.

Methods: In a double-blinded, placebo-controlled study, 38 patients undergoing primary hip replacement were randomized to 0,9% NaCl or Plasma-Lyte (PL). Infusion was given during surgery as 15 ml/kg the first hour and 5 ml/kg the following two hours. As surgery initiated, urine was collected over the course of 4 hours. Hereafter another urine collection proceeded until the following morning. Urine was analyzed for concentrations of NGAL and KIM-1. Blood samples for measurements of pH and plasma electrolytes were collected.

Results: NaCl induced an increase in P-Cl (111±2 mmol/L after NaCl and 108±3 after PL, p = 0.004) and a drop in pH (7.39±0.02 after NaCl and 7.43±0.03 after PL, p = 0.001). Urinary excretion of NGAL increased significantly in both groups (ΔNGAL: 5.5 [4.1;11.7] µg/mmol creatinine p=0.004 after NaCl vs. 5.5 [2.1;9.4] µg/mmol creatinine after PL, p<0.001). There was no difference in the increase between groups (p=0.839) Similarly, urinary excretion of KIM-1 also increased significantly in both groups (ΔKIM-1: NaCl 115.8 [74.1;156.2] ng/mmol creatinine, p<0.001 vs. PL 152.4 [120.1;307.9] ng/mmol creatinine, p<0.001). There was no difference in the increase between groups (p=0.064).

Conclusion: A hyperchloremic acidosis was present in the group receiving isotonic saline. NGAL and KIM-1 were significantly increased in both groups after surgery, despite no changes in eGFR. These results may indicate that surgery induced subclinical kidney damage.

P09.09 Linea Sandfeld Blichert-Refsgaard

TREATMENT OF NON-MUSCLE INVASIVE BLADDER CANCER: DO WE DESTROY THE BLADDER FUNCTION?

L. Blichert-Refsgaard[1], C. Graugaard-Jensen[1], M. Nørgaard[2], J.B. Jensen[1]

[1]Department of Urology, Aarhus University Hospital, [2]Department of Clinical Epidemiology, Aarhus University Hospital

Background:

In Denmark, approximately 1500 patients are diagnosed with non-muscle invasive bladder cancer (NMIBC) every year. The yearly recurrence rate is 35%.

The treatment is a combination of repeated transurethral resection of the bladder (TURB), follow-up cystoscopies and instillation therapy.

It is unknown how the treatment of NMIBC affects the bladder function, and thereby the bladder related quality of life.

Aim:

- To investigate a possible difference in functional bladder complications due to the different treatment of NMIBC (TURB and intravesical instillation therapies)

- To assess the bladder related quality of life associated with the treatment.Methods:A descriptive, explorative study with a study population of total 50 patients with NMIBC. The treatment is according to Danish guidelines, based on the histology of baseline TURB.

A full urodynamic examination is performed at 0 and 6 months and complemented with bladder diary and quality of life-questionnaires regarding bladder symptoms. Questionnaires is distributed right before treatment, after 6, 12 and 24 months.Outcomes:

The functional complications stratified according to the different type of bladder treatment.

Outcomemeasures are the urodynamic examination parameters and the self-reported complications in the questionnaires

Results:

The study is currently including patients. We expect primarily results to the PhD-day.

Perspectives:

The study will be the first to study functional aspects of NMIBC treatment. The evaluation of potential bladder function impact and quality of life issue will be crucial in future patient counselling and treatment.

P09.10   Sofie Schmøkel   DISSECTION OF THE TUMOR ECOSYSMTEN IN BLADDER CANCER

S.S. Schmøkel

Department of Molecular Medicine, Aarhus University Hospital

A clinical challenge in bladder cancer is to predict treatment response as 50% of patients fail chemotherapy, which is first-line treatment. A tumor is an ecosystem consisting of carcinoma cells, infiltrated immune cells, and cancer-associated fibroblasts. The ecosystem may support survival and progression of the tumor but have also shown to have an impact on treatment response.

We have developed protocols for single nuclei RNA-sequencing, which will be used to delineate the tumor ecosystem in connection with disease outcome and treatment response in tumors from 40 patients that have received chemotherapy.

Single nuclei are isolated from fresh frozen tumors and applied to the microfluidic platform, Drop-seq, which is used to generate droplets containing a nuclei and a bead. The beads are covered with oligo's comprising four parts:

1) A PCR handle located nearest the bead and used as a priming site for downstream PCR and sequencing.

2) A cell barcode identical for all primers on the same bead.

3) A Unique Molecular Identifier, which varies for all individual oligo's and makes it possible to identify PCR duplicates and count individual transcripts.

4) A oligo-dT sequence is located for capturing poly-adenylated mRNAs.

Within each droplet the nuclei is lysed and its mRNA content hybridize to the oligo's. Following, libraries are constructed and sequenced.

Eight tumors (8778 nuclei) have now been analyzed to an average sequencing depth of 589446 aligned reads per nuclei covering an average of 1256 genes. Data analysis is currently ongoing.

We believe that comprehensive analyses of the tumor ecosystem can be used to build better models predictive of treatment response.

P09.11 Signe Krejberg Jeppesen

THE RETINAL OXYGEN SATURATION MEASURED BY DUAL WAVELENGTH OXIMETRY IN LARGER RETINAL VESSELS IS INFLUENCED BY THE LINEAR VELOCITY OF THE BLOOD

S.K. Jeppesen, T. Bek

Department of Ophthalmology, Aarhus University Hospital

Introduction: Retinal oximetry allows the quantification of oxygen saturation in larger retinal vessels. It should be expected that the oxygen saturation would be the same in the first order arterioles shortly after their branching from the central retinal artery. Therefore, it has been unclear why the oxygen saturation of the first order arterial branches have been measured to differ shortly after the offbranching from the central retinal artery.

Materials and methods: In fourty normal persons the oxygen saturation were measured by oximetry (model T1, Oxymap, Reykjavik, Iceland) and the linear velocity of the blood determined by Doppler OCT (Dual-beam Doppler FD-OCT system, Center for Medical Physics and Biomedical Engineering, Vienna, Austria) in the upper and lower temporal and nasal arterioles and venules shortly after their branching from the central retinal artery and vein. The measured oxygen saturations was correlated with age, vessel diameter and blood linear velocity.

Results: The measured oxygen saturation (Sm) were (mean±SD) 97.8% ± 6.4% in the arterioles and 60.2% ± 8.8% in the venules. For both the arterioles and venules Sm correlated significantly with the linear velocity (v) of the blood (Sm, arterioles = 101.6-0.28*v, p<0.0001 and Sm, venules = 64.5-0.38*v, p = 0.002). After correction of the oxygen saturation for differences in the linear velocity from both arterioles and venules were significantly reduced.

Conclusions: Measurements of oxygen saturation in larger retinal arterioles and venules using dual wavelength oximetry can be improved by correcting for the influence of the linear velocity of the blood.

P10.01 Katrine Andersen

THE RELATIONSHIP BETWEEN SYNAPTIC DENSITY AND COGNITIVE DECLINE IN PARKINSON'S DISEASE (PD) AND EARLY DEMENTIA WITH LEWY BODIES (DLB)

K. Andersen, A.K. Hansen, P. Borghammer

Department of Nuclear Medicine and PET Centre, Aarhus University Hospital

Patients with PD often develop cognitive decline and dementia during the course of the disease; however, the underlying causes are poorly understood. The pathological processes in PD include a variety of synaptic alterations. Previously, these changes were thought to be limited to the dopaminergic system. Recent evidence, however, suggests a more generalized synaptic degeneration. Thus, an improved understanding of the overall synaptic loss in PD is needed.

Using in vivo high-resolution [^{11}C]UCB-J PET imaging, this study assessed the density of synapses in PD subjects (N=20), demented PD subjects, subjects with early DLB (N=9) and matched healthy controls (N=14).

Preliminary analyses revealed that when compared with healthy controls, a pooled group of PD, PDD, and DLB patients exhibited a trend of lower SV2A density in substantia nigra (SUVR -21%; one-sided p= 0.051). Substantia nigra contains the majority of dopaminergic neurons and these are known to degenerate in PD. Additional analyses interrogating frontal lobe [^{11}C]UCB-J SUVR values and Montreal Cognitive Assessment (MoCA) scores were performed to investigate the relationship between synaptic density and cognitive decline. Significant correlation was seen between MoCA score and frontal lobe^{11}C--UCB-J SUVR values (r^2=0.304,p=0.002).

Our preliminary results indicate that synaptic integrity measured by the radioligand [^{11}C]UCB-J is reduced in subcortical regions central to the pathogenesis of PD. Ongoing inclusion of additional subjects may reveal additional differences in cortical regions. Overall, SV2A imaging holds promise for in vivo imaging of synaptic loss and assessment of disease progression in PD patients.

P10.02   Peter Uhrbrand   PROLONGED OPIOID-USE AFTER PLANNED BACK SURGERY: A PROSPECTIVE STUDY

P. Uhrbrand[1, 2], L. Nikolajsen[1, 2]

[1]Department of Clinical Medicine, Aarhus University, [2]Department of Anaesthesiology, Aarhus University Hospital

Background with aim

Several studies have shown that an increasing number of patients continue using opioids even months to years after surgery, hence developing addiction and possible abuse behavior. The aim of this study was to investigate prolonged opioid use after planned back surgery, including frequency, causes and risk factors.

Methods

Three hundred spinal surgery patients aged 18 years or above were prospectively included from the Department of Orthopedic Surgery, Aarhus University Hospital.

Opioid consumption in morphine milligram equivalents (MME) and reasons (back pain, radicular pain, other pain conditions) were measured preoperatively and at discharge after surgery. Three and six months after surgery, a self-assessment questionnaire containing questions about pain and opioid consumption was filled out.

Results

One-hundred and thirty-nine patients (47%) were opioid-naïve prior to surgery. Of those, 16 patients (11%) still consumed opioids daily 3 months after surgery and 10 (7%) consumed opioids daily six months after surgery.

For both opioid-users and non-users, the reasons for continued opioid consumption after 6 months were back pain (69%), radicular pain (53%), to relax (11%), to sleep better (19%), to feel good (8%), other pain (18%) or other reasons (8%).

During the first 3 months after surgery, 94 patients (33%) experienced withdrawal symptoms. Six percent did not attempt to taper off opioids after the surgical procedure.

Conclusions

Seven percent of the opioid-naïve patients develop long-term opioid consumption after planned back surgery.

P10.03   Anna Holm   UMBRELLA REVIEW OF THE EVIDENCE: NURSES' COMMUNICATION WITH MECHANICALLY VENTILATED PATIENTS IN THE INTENSIVE CARE UNIT

A. Holm

Department of Intensive Care, Aarhus University Hospital

Aim: To conduct a review summarizing evidence concerning communication with mechanically ventilated patients in the intensive care unit focusing on nurse-patient communication.

Background: Patients undergoing mechanical ventilation in the intenisve care unit are unable to communicate verbally, causing many negative emotions. Due to changes in sedation practice, a growing number of patients are conscious and experience communication difficulties.

Design: The umbrella review method guided by the Joanna Briggs Institute was applied.

Data sources: A systematic search was done in the Cochrane Library, the Joanna Briggs Institute database, Cinahl, Pubmed, PsycINFO, and Scopus between January and April 2019. Peer-reviewed research synthesis from 2009-2019 were included.

Review Methods: A quality appraisal, data extraction, and synthesis were done.

Results: Seven research syntheses with results from 106 original studies were included. A total of 229 findings were extracted and synthesized into two main themes and 6 subthemes. 1) Characterization of the nurse-patient communication with a) Patients' communication and b) Nurses' communication; 2) Nursing interventions that facilitate communication with a) Communication assessment and documentation, b) Communication methods and approaches, c) Education and training of nurses, and d) Augmentative and alternative communication.

Conclusion: Nurse-patient communication is characterized by an unequal power relationship with a common experience - frustration. Four key interventions were identified and integration of these interventions may be key to designing and implementing future communication packages in the intenisve care unit.

P10.04   Jeppe Foged   MUSCLE METABOLISM AND FATIGUE DURING INTENSE INTERMITTENT
         Vigh-Larsen   EXERCISE IN ELITE MALE ICE HOCKEY PLAYERS

J.F. Vigh-Larsen[1], G. Ermidis[2, 3], V. Rago[2, 4], M.B. Randers[2], D. Fransson[5], L. Gliemann[6], F.V. de Paoli[7], K. Overgaard[1], T.B. Andersen[1], L. Nybo[6], P. Krustrup[2], M. Mohr[2, 5, 8]

[1]Section for Sport Science, Department of Public Health, Aarhus University, [2]SDU Sport and Health Sciences Cluster (SHSC), University of Southern Denmark, [3]Department of Movement and Wellness Sciences, University of Parthenope, [4]Centre for Research, Education, Innovation and Intervention in Sport, University of Porto, [5]Center for Health and Human Performance, University of Gothenburg, [6]Department of Nutrition, Exercise and Sports, University of Copenhagen, [7]Department of Biomedicine, Aarhus University, [8]Centre of Health Sciences, University of Faroe Islands

The purpose was to study skeletal muscle metabolism and fatigue during intense intermittent exercise using ice hockey as an experimental model. Players from the U20 male national team (n=30) participated and completed an experimental game. This consisted of three periods of 8 shifts of 1 min duration separated by 2 min recovery resulting in a total playing time of 24 min per player. Activity pattern and physical loading was monitored using heart rate recordings and a local positioning system. Muscle biopsies were obtained from m. vastus lateralis before and after the game (n=6) as well as instantly following shifts (n=7). Venous blood was drawn pregame and at the end of each period (n=14) followed by a repeated sprint test. In total, players covered 6015 ± 199 m including 109 ± 14 accelerations and decelerations and 2701 ± 251 m of high-intensity skating resulting in an average and peak on-ice heart rate of 84 ± 2 and 97 ± 2%HRmax. Muscle lactate rose from 7 ± 3 to 38 ± 20 mM/kg d.w. during the first period, but was unchanged during the third period. Blood lactate increased from 0.8 ± 0.3 to 4.7 ± 3 and 4.9 ± 3 mM/L following the first and third period. Muscle glycogen decreased from 400 ± 22 to 188 ± 43 mM/kg d. w. after the game while mean sprint time declined following the third period in association with a drop in explosive actions. In conclusion aerobic and anaerobic energy systems are highly active during intense intermittent exercise resulting in a markedly high utilization of muscle glycogen and fatigue development during the end of a game. This may at least partly be explained by the lowered muscle glycogen levels and a compensatory increased reliance on fat oxidation.

P10.05   Jacob Horsager   PARKINSON'S DISEASE STARTS IN THE GUT OR THE BRAIN - A MULTI-MODALITY IMAGING STUDY.

J. Horsager[1], K. Andersen[1], K. Knudsen[1], T.D. Fedorova[1], C. Skjærbæk[1], N. Okkels[1], M. Otto[2, 3], M. Sommerauer[4], K.B. Svendsen[3], J. Geday[5], J. Kraft[5], E. Bech[5], E.H. Danielsen[3], D.J. Brooks[1], P. Borghammer[1]

[1]Department of Nuclear medicine and PET, Aarhus University Hospital, [2]Department of Clinical Neurophysiology, Aarhus University Hospital, [3]Department of Neurology, Aarhus University Hospital, [4]Department of Neurology, University Hospital Cologne, Germany, [5]Privat practice, Neurology

Background

Patients with Parkinson's disease (PD) accumulate intraneuronal protein aggregates, called Lewy pathology (LP), leading to neuronal loss. Compelling evidence suggest that LP initiates in the terminals of the autonomic nervous system (ANS) in the gut and spreads centripetally to the brainstem. Patients with REM-sleep behavior disorder (RBD), a parasomnia related to neuronal loss in the pons, all develops PD or Dementia with Lewy Bodies and have a severely damaged ANS, but an intact substantia nigra. However, not all PD patients develop RBD, and postmortem neuropathological studies do not always find pathology in the ANS.

In this study we test the hypothesis that PD can be divided into two distinct subtypes:

1) "Brain-first": LP initiates in the brain, above the substantia nigra. Intact ANS. RBD-negative

2) "Body-first": LP initiates in ANS, below the level of substantia nigra. Damaged ANS. RBD-positive.

Methods

Following protocol is applied to all patients.

^{123}I-MIBG scintigraph: sympathetic innervation of the heart.

[11]C-donepezil PET/CT: parasympathetic innervation of the gut.

^{18}F-DOPA PET: dopaminergic innervation of putamen (from substantia nigra).

Polysomnography for evaluation of RBD status.

Results

Convincing, preliminary results indicate that patients without RBD ("Brain-first"), have a relatively intact ANS. Conversely, patients with RBD ("Body-first") have a damaged ANS. Final result will be presented at the PhD-day.

Conclusion

PD can probably be divided into a "Brain-first" and "Body-first" phenotype. This is important for our understanding of the disease and for selection of patients to future clinical trials with neuroprotective treatments.

P10.06   Tatyana D Fedorova

DECREASED PARASYMPATHETIC INNERVATION OF THE GUT IN VAGOTOMISED PATIENTS: AN *IN-VIVO* PET STUDY.

T.D. Fedorova[1], K. Knudsen[1], B. Hartmann[2], J.J. Holst[2], F.V. Mortensen[3], K. Krogh[4], P. Borghammer[1]

[1]Department of Nuclear Medicine and PET-center, Aarhus University Hospital, [2]NNF Center for Basic Metabolic Research and Department of Biomedical Sciences, University of Copenhagen, [3]Department of Surgery, Aarhus University Hospital, [4]Department of Hepatology and Gastroenterology, Aarhus University Hospital

Background

Patients with radically removed esophagus cancer have multiple long-term postoperative issues, possibly because they are vagotomised during

the surgery. However, no PET studies have assessed integrity of the vagus nerve after esophagectomy.

Purpose

To assess parasympathetic innervation and objective function of internal organs in patients who underwent esophagectomy.

Methods

Sixteen healthy controls and 12 patients, vagotomised due to esophagectomy, underwent ^{11}C-donepezil PET, measurement of colonic transit time and assessment of subjective long-term symptoms.

Results

Vagotomised patients had significantly decreased PET signal in the small intestine ($p=0.01$) and colon ($p<0.01$) compared with healthy controls. Vagotomised patients also displayed a significantly increased colonic transit time ($p<0.01$) and increased volumes of the small intestine ($p<0.01$) and colon ($p=0.01$). We observed no correlations between objective measurements and subjective complaints.

Discussion

Our findings show significant and persistent damage of the vagus nerve following esophagectomy. However, we did not find any correlations between subjective symptoms and objective dysfunction, possibly due to the small sample size. Therefore, future studies are needed to understand the causation between surgery, subsequent vagotomy and long-term symptoms.

In conclusion, this study sheds new light on integrity of the vagus nerve after esophagectomy and proposes a novel method for assessment of the parasympathetic nervous system using ^{11}C-donepezil PET.

P10.07   Mustafa Aykut Kural

LARGE SYNCHRONIZED BILATERAL CORTICAL NETWORKS GENERATING TRIPHASIC WAVES IN ENCEPHALOPHATIC EEG RECORDING

M.A. Kural

Neurology Department, Aarhus University Hospital

Background and Purpose: Triphasic waves (TWs) are peculiar EEG waveforms that have been described in patients with encephalopathy, for more than 50 years. However, their origin, the brain regions generating TWs remained largely unknown. The aim of this study was to determine the source of triphsic waves.

Method: From 2014-2019, 20 patients having 24 TWs with different morphology (asymmetric and symmetric) attributable to various encephalopathic etiologies were analysed. We did EEG source imaging using dipole modeling and brain distributed source analyses, to find the distribution of current sources in the underlying neural network.

Result: We found that TWs are generated by widespread, bilateral, synchronized neuronal networks over both frontal poles and temporal poles. Distributed source models were better in localizing these large

networks, since equivalent current dipoles were often misleading when pointing only the center of these widely distributed generators.

Conclusion: The widely distributed, synchronized, bilateral fronto-temporal networks generating TWs explain the altered consciousness in these encephalopathic patients.

P10.08   Sebastian Skejø   PREDICTING THROWING SPEED USING ACCELOMETERS: A FIRST STEP TOWARDS MONITORING THROWING LOAD IN HANDBALL

S. Skejø[1], M. Møller[2], J. Bencke[3], H. Sørensen[1]

[1]Department of Public Health, Aarhus University, [2]Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, [3]Human Movement Analysis Laboratory and Dep. Orthopaedic Surgery, Copenhagen University Hospital at Amager-Hvidovre

INTRODUCTION: Overuse shoulder injuries are very common in handball. Understanding why such injuries occur, likely requires accurate measurement of the volume and speed of throws a player makes in training and match. However, no technology that enables such measurements currently exists. The aim of this study was to develop a novel device that can measure the speed of handball throws.METHODS: 19 experienced handball players (11 males, 8 females) each threw five throws of each of five different types. For each throw, we measured the ball speed and recorded acceleration of the wrist using a high range accelerometer. Subsequently, we computed the peak total acceleration for each throw and predicted ball speed as a linear function of the logarithm of the peak total acceleration. We predicted ball speeds using 10-fold cross validation. Our performance measures were R^2, mean absolute error, mean calibration (calibration-in-the-large), weak calibration (calibration slope) and moderate calibration (visual inspection of the calibration plot). RESULTS AND DISCUSSION: The predictive model was well calibrated (mean calibration: 0.0 m/s, weak calibration: 1.00) and had a satisfying predictive accuracy (R^2: 0.71, mean absolute error: 1.82 m/s). Thus, our method provides a promising foundation for understanding why overuse shoulder injuries occur. Nonetheless, such understanding requires knowing both throwing speed and volume. The present work only addresses the former. Thus, future work should improve the method such that the number of throws can also be accurately determined by a wrist-worn accelerometer.

P10.09   Simon Kjeldsen   MEASURING DAYTIME RESTING PERIODS IN PATIENTS WITH SEVERE ACQUIRED BRAIN INJURY

S.S. Kjeldsen[1], O.K. Andersen[2], J.F. Nielsen[1], I. Brunner[1]

[1]Hammel Neurorehabilitation Centre and University Research Clinic, Aarhus University, [2]SMI®, Department of Health Science and Technology, Aalborg University

Introduction

Patients undergoing rehabilitation after severe acquired brain injury (sABI) are offered several daytime resting periods (DRPs) every day. DRPs are supposed to consolidate the patient's motor and cognitive learning and

counteract fatigue. These effects depend on the quality of rest (QoR) achieved during DRPs.

Therefore, it is of interest to assess whether QoR is measureable in patients who cannot express themselves.

As measures of QoR, this study explores the use of staff assessments and objective measures such as heartrate, heartrate variability and the motor rest ratio (MRR) which is the percentage of minutes where no motor activity is registered during DRPs.

Objectives

Our aim is to investigate associations between staff assessments and the objective measures of QoR. Our aim is also to determine whether heartrate, heartrate variability and MRR are useful and feasible outcome measures when studying interventions targeting QoR.

Methods

In this observational study, patients are recruited from a single rehabilitation ward rehabilitating patients in the subacute stage after sABI. Subjects are monitored with accelerometry and electrocardiography for 21 days during DRPs. QoR is documented by staff on a 4 point likert scale after each DRP. Associations will be analysed using a multivariable regression model. Analysis will be adjusted for relevant patient characteristics such as severity and type of injury, time since injury and age.

Results

Results are pending. 26 subjects have been included per Oct. 28th 2019.

Discussion

Measuring QoR in patients with sABI could be an important tool to guide rehabilitation staff in regards to timing and environment during DRPs.

P10.10   Troels Kjærskov Hansen   FRAILTY ASSESSMENT IN OLDER PATIENTS USING A RECORD-BASED MULTIDIMENSIONAL PROGNOSTIC INDEX IS RELIABLE

T.K. Hansen[1], E.M. Damsgaard[1, 3], S. Shahla[2], J.M. Bruun[3], M. Gregersen[1]

[1]Department of Geriatrics, Aarhus University Hospital, [2]Medical Department, Randers Regional Hospital, [3]Department of Clinical Medicine, Aarhus University

Background: Comprehensive Geriatric Assessment (CGA) is considered the gold standard of cumulative frailty assessment in older patients. The Multidimensional Prognostic Index (MPI) is a CGA-based, bedside prognostic tool. For research purposes, a retrospective frailty identification and quantification based on medical record data is desirable. We aimed to examine the reproducibility and diagnostic accuracy of a record-based MPI (RB-MPI) frailty assessment method.

Method: A total of 50 consecutively discharged medical patients aged ≥75 years was included from two medical wards. Frailty assessment was performed in patients who required personal assistance on a daily basis or had a Charlson Comorbidity Index (CCI) ≥1. The RB-MPI rating was done by two independent raters. Inter-rater reproducibility measures were

calculated. In the same patients, a bedside MPI rating (B-MPI) was performed and compared to the RB-MPI.

Results: Evaluating the RB-MPI inter-rater reproducibility; the mean difference was -0.02 points (95% CI -0.06 to 0.01, p=0.20). Intraclass Correlation Coefficient (ICC) was 0.71. Evaluating inter-method reproducibility; the mean difference was -0.02 (95% CI -0.04 to 0.01, p=0.18); ICC=0.83. Sensitivity was 100%, specificity 80%. The Area under the Receiver Operating Characteristic curve (AUROC) was 0.92 (95% CI 0.75-1.00).

Conclusions: The RB-MPI method has an acceptable inter-rater reliability and high agreement as compared to the reference standard, the B-MPI method. The diagnostic accuracy of the RB-MPI is considerable. We consider RB-MPI to be an applicable method for the use of retrospective identification and quantification of frailty for research purposes.

P11.01   Jesper Emil Jakobsgaard   SKELETAL MUSCLES FROM RATS SELECTIVELY BRED FOR DIVERSE RUNNING CAPACITY DISPLAY DIFFERENTIAL STRESS- AND METABOLIC-RELATED SIGNALLING IN RESPONSE TO FATIGUING ELECTROSTIMULATION

J.E. Jakobsgaard[1], T. Grønnebæk[1], M.V. Hjortbak[2, 3], H.E. Bøtker[3], F. de Paoli[4], K. Vissing[1]

[1]Section for Sport Science, Department of Public Health, Aarhus University, [2]Department of Clinical Medicine, Aarhus University, [3]Department of Cardiology, Aarhus University Hospital, [4]Department of Biomedicine, Aarhus University

Purpose: Rats artificially bred for high and low running capacity (HCR and LCR, respectively) has been used as a model to study the effects of intrinsic aerobic capacity on various clinical outcomes. However, little is known whether skeletal muscles in HCR and LCR rats display differential cellular sensitivity to imposed stress, such as prolonged muscle contractions. Therefore, the purpose of this study was to evaluate the acute activation of key transcriptional regulators involved in metabolic-, stress- and Ca^{2+}-related signalling, as a response to fatiguing electrostimulation, in skeletal muscles of HCR and LCR rats.

Methods: Soleus and extensor digitorum longus (EDL) muscles where excised from HCR and LCR rats and exposed to either 1) 30 min of isometric contractions provoked by prolonged low frequency electrostimulation (STIM), or 2) a time-matched control period.

Results: A similiar increase in phosphorylation of AMPK following STIM was observed in soleus muscles of both LCR and HCR. Only soleus muscles from LCR displayed an increase in acetyl-CoA carboxylase phosphorylation following STIM. No effects of STIM on CaMKII was observed in soleus from either rat type. EDL muscles from HCR displayed a greater phosphorylation of AMPK and p38MAPK elicited by STIM, whereas the same muscle type from LCR showed greater CaMKII phosphorylation.

Conclusion: While slow-twitch soleus muscles from both HCR and LCR rats displayed a similar metabolic-related signalling response to fatiguing muscle contractions, fast-twitch EDL muscles of HCR rats appeared more

responsive, in comparison to LCR. Ca^{2+}-sensitivity, as indicated by CaMKII activation, was greater in LCR EDL muscles.

P11.02   Ensieh Farahani   FUNCTIONAL ANALYSIS OF GENOME-WIDE RNA-SEQ DATA AFTER HSV1 INFECTION   REVEALS NOVEL INFLAMMATORY RESPONSE PATHWAYS

E. Farahani, S. Riis Paludan

Department of Biomedicine, Aarhus University

To elucidate the cellular functions affected by Herpes Simplex Virus Type 1 (HSV1) in human cells, we first investigated the differential gene expression at 3 different time-points (4h, 12h, 24h) across 3 cell lines (sh-sy5y, hacat and thp1) infected with HSV1 using RNA-seq. The mRNA expression differences in infected cells relative to uninfected cells resulted in a list of upregulated and downregulated genes.

Functional analysis of these genes using the Gene Ontology (GO) classification shows enrichment in antiviral cytokine/interferon responses as well as other biological processes such as regulation of MAP-kinases, apoptosis, cell cycle, cellular homeostasis in response to stress, hypoxia and external stimuli. We found 134 'core' genes commonly differentially expressed in all three cell lines. Using jasper and transfac enrichment analysis we discovered master regulators possibly controlling this set of core genes.

To further corroborate these findings, the same procedure was applied to cell-lines infected other viruses: the differential gene expression at 3 different time points in sh-sy5y cells infected with HSV2 and Polio virus were measured. The intersection between these three viruses reveals 498 genes which have some overlap with the core gene set.

One of the upstream regulators of the core set with an hitherto unclear role in the context of infection and cellular inflammatory responses is HIF1A. Based on the expression profiles, we derived enriched network clusters from existing protein-protein interaction (PPI) data. The resulting networks highlight novel pathways being modulated in HSV1-infected cells and provide the basis for further experimental validation.

P11.03   Josephine P Geertsen Keller   TOPOISOMERASES AS A REGULATOR OF PROMOTERS IN HUMAN PROTO-ONCOGENES THROUGH STABILIZATION OF G-QUADRUPLEXES

J.G. Keller[1, 2], M. Thorsager[2], B.R. Knudsen[2], M. Stougaard[1]

[1]Department of Clinical Medicine, Pathology, Aarhus University,
[2]Department of Molecular Biology and Genetics, Aarhus University

G-quadruplexes are non-canonical DNA secondary structures found in guanine rich sequences of human promotors. These sequences are prevalent in promoters of proto-oncogenes where formation of G-quadruplex structures have been observed to inhibit promoter activity, thereby preventing cancer development or progression. The in vivo regulation of G-quadruplex structures is not well understood. However, DNA topology and protein interaction have been suggested to be involved.

Human topoisomerases are key regulators of the DNA topological problems generated during transcription and replication. Moreover, topoisomerase I has demonstrated affinity towards G-quadruplexes in vivo. In preliminary studies, we have observed that downregulation of topoisomerase I increased the activity of a proto-oncogene promoter containing a G-quadruplex forming sequence. This stimulation is topoisomerase I specific, as downregulation of e.g. topoisomerase IIa or topoisomerase IIb did not show the same effect. Moreover, the stimulatory effect of topoisomerase I was not observed when the G-quadruplex forming sequence was mutated.

These results suggest that topoisomerase I may regulate promoter activity by influencing G-quadruplex formation. As topoisomerase I is targeted by anti-cancer drugs from the camptothecin family, it is possible that over-expression of proto-oncogenes due to downregulation of topoisomerase I may be a side effect of camptothecin treatment.

P11.04 Bertram Dalskov Kjerulff **USING ROUTINE WHITE BLOOD CELL COUNTS TO PREDICT INFECTIONS IN BLOOD DONORS**

B. Kjerulff

Department of Clinical Immunology, Aarhus University Hospital

Background and aim: Infections may skew the distribution of immune cells away from the normal profile. Inversely, a skewed immune cell distribution may increase susceptibility to infections. This project investigates if cell counts can predict the risk of infections among Danish blood donors.

Methods: A total of 1,187,252 white blood cell (WBC) counts from 181,653 Danish blood donors were merged with the National Patient Register (8,005 cases defined by ICD-10 codes) and the National Prescription Register (126,847 cases) to identify donors with infectious diseases up to six months after blood donation. Data was analysed using age and gender-adjusted recurrent event cox regression.

Results: In donors with a WBC count above the normal range, the risk of redeeming a prescription is 1.26 (95% CI 1.19-1.33) times higher in the first month after donation than in donors below the upper limit of the normal range. In the six months after a donation, this risk is 1.19 (CI 1.16-1.23). The increase in risk of having an infection related ICD-10 code is 1.40 (CI 1.12-1.75) within the first month and 1.26 (CI 1.14-1.40) within six months.

Discussion and perspectives: There is an association between WBC count and risk of infections but the clinical relevance is limited. Data for lymphocyte and neutrophil counts is currently being analysed along with further stratification of cell counts and adjustment for season, smoking and BMI. Further analysis may elucidate the usefulness of cell counts for predicting infections.

P11.05   Lixiang Jiang   REGULATION OF α-SYNUCLEIN TRANSCRIPTION BY THE PLK-2/GSK-3B SIGNALLING PATHWAY - A POTENTIAL MODULATOR OF PARKINSON'S DISEASE RISK

L.X. Jiang

Danish Research Institute of Translational Neuroscience

Parkinson's Disease (PD) is an incurable neurodegenerative disease characterized by neuronal cell death and presence of plentiful α-synuclein containing neuronal inclusions, known as Lewy bodies (LBs) and Lewy neurites (LNs). It is the second most common neurodegenerative disease, affecting 1-3% of the elderly population. Yet, there is no existing neuroprotective or neurorestorative therapy in the clinic for PD patients.

As the major component of LBs and LNs, α-syn is regarded as a pivotal player in the development of PD and increased α-syn levels represents a risk factor. Hence, downregulation of α-syn could be a therapeutic target in PD. Professor P. H. Jensen's laboratory had identified a kinase-dependent signaling axis comprising PLK-2 and GSK-3b that regulates α-syn mRNA transcription. During this one year, I confirmed this signaling axis in HEK293t cells and found a potential exon of SNCA that may be a target in this pathway, but still need to explore which transcription factors and the specific DNA domain that is involved and test its relevance in in vivo models and clinical samples. Characterization of this signalling pathway can lead to new potential drug targets and treatments for PD as well as genetic biomarkers for risk.

P11.06   Christina Valbirk Konrad   USING HIV-SPECIFIC SINGLE-CHAIN VARIABLE FRAGMENTS TO TARGET THE PERSISTENT HIV RESERVOIR

C.V. Konrad[1], M.H. Schleimann[2], K. Zuwala[2], J.D. Gunst[1], P.W. Denton[1, 2], O.S. Søgaard[1, 2], M. Tolstrup[1, 2]

[1]Department of Infectious Diseases, Aarhus University, [2]Department of Infectious Diseases, Aarhus University Hospital

The major challenge of HIV eradication is the extraordinary capacity of HIV for immune evasion as HIV forms a latent reservoir of persistently infected cells. To enable a cure for HIV it is thus essential to target the latent reservoir of HIV-infected cells.

Existing HIV-specific antibodies are important mediators of HIV neutralization and blocking of transmission but are unable to eradicate the remaining virus in infected cells. Recombinant single-chain variable fragments (scFv) may offer an improved strategy to the fight against the persistent HIV-infected cells. Due to their smaller size compared to full-length antibodies, scFv have the advantage of improved penetration of e.g. lymphoid tissue hiding persistently infected cells, and the ability to access masked epitopes that are otherwise escaping the antibody response, without compromising their ability to neutralize HIV and inhibit viral replication.

The goal of this PhD project is therefore to clone scFv from HIV-specific broadly neutralizing antibodies based on their ability to mediate potent and broad neutralization of free HIV and bind HIV-infected cells. The lead HIV-specific scFv will be explored to facilitate killing of HIV-infected cells upon binding to cell surface HIV envelope molecules. The anti-HIV

effector function of the cloned scFv will be assessed by in vitro cell killing assays, and the functional efficacy of the lead HIV-specific scFv will be validated in humanized mice infected with HIV.

HIV-specific scFv characterized in this study will be incorporated into future clinical trials with latency-reversing agents and lead to a potential novel immunotherapy against the latent HIV reservoir.

P11.07   Anne Borup   THE POWER OF PARASITES: EXPLORING THE IMMUNOMODULATORY PROPERTIES OF HELMINTH-DERIVED EVS

A. Borup[1], A.T. Boysen[1], B.W. Deleuran[2], P. Nejsum[1]

[1]Department of Clinical Medicine, Aarhus University, [2]Department of Rheumatology, Aarhus University Hospital

The incidence of autoimmune diseases have increased during the last decades, simultaneously the incidence of helminth infections have declined. An explanation for this inverse relationship is uncovered by evolution, stating that the human immune system has developed while being exposed to microorganisms and parasites such as helminths and lack of their presence leads to a dysregulated immune system. Helminths have been shown to produce immunomodulatory molecules that might play a role in this regulation, and recent discoveries show that helminths also release extracellular vesicles (EVs). These EVs hold strong potential as therapeutics since they modulate the host immune responses without having the health risk of an active infection. The field of helminth EVs is in its infancy and a standardized protocol for isolation of EVs with both high EV-yield while obtaining the most efficient immunomodulatory EVs is lacking. We compare size exclusion chromatography and ultracentrifugation in order to determine the most optimal procedure for isolating EVs from excretory/secretory products of the porcine roundworm Ascaris suum. Furthermore, we report that EVs from A. suum reduce a LPS-induced inflammatory response in macrophages in a dose-dependent manner.

P11.08   Michelle Mølgaard Thomsen   IDENTIFICATION OF NOVEL INNATE IMMUNODEFICIENCIES IN PATIENTS WITH SEVERE VARICELLA ZOSTER ENCEPHALITIS.

M. M. Thomsen[1, 2], M. Carte-Timofte[1, 2], M. Freytag[1], K. S. Hansen[1], T. H. Mogensen[1, 2]

[1]Department of Infectious Diseases, Aarhus University Hospital, [2]Department of Biomedicine, Aarhus University

Varicella zoster virus (VZV) is a very common and highly contagious human neurotropic DNA virus. It causes varicella (chickenpox) upon primary infection and establishes latency in the sensory ganglia, where it can reactivate and cause zoster (shingles). VZV may however in rare cases spread to the central nervous system (CNS) where it can cause severe complications such as encephalitis or vasculitis in otherwise healthy individuals. Recently, deleterious mutations in the DNA sensor POLR3 was found to cause severe VZV CNS infections in both children and adults that were otherwise healthy. We therefor hypothesize that additional novel single gene inborn errors of immunity may predispose to severe VZV infections in the CNS. We will investigate this by performing

whole exome sequencing on DNA from adult patients identified with VZV encephalitis in the Danish Study Group of Infections in the Brain (DASGIB). In the exomes of the patients we will try to identify possible disease causing mutations in patients DNA using different bioinformatics tools. We will then characterize the immune response in patient cells by infecting with VZV and measuring cytokine production and viral replication by qPCR and Flow Cytometry. Lastly, we will evaluate a molecular mechanism for altered function of the mutated molecule and reconstitute patient cells with the wild type protein to investigate if the phenotype can be rescued. This study will contribute with essential knowledge about the neuropathogenesis of VZV which can be used to improve vaccination as well as treatment of patients and genetic counselling of family members to the patients examined in the study.

P11.09   Signe Schöllhammer Knudsen

RHEUMATOID ARTHRITIS IN PREGNANCY AND OFFSPRING SCHOOL PERFORMANCE. A DANISH NATIONWIDE REGISTER-BASED STUDY

S.S. Knudsen[1, 2], J.F. Simard[2], B.W. Deleuran[5], J. Christensen[4], T.M. Laursen[3], B.H. Bech[1]

[1]Department of Public Health, Aarhus University, [2]Health Research and Policy, Stanford University, [3]Department of Economics and Business Economics, Aarhus University, [4]Department of Clinical Medicine, Aarhus University, [5]Department of Biomedicine, Aarhus University

ABSTRACT

Objectives:

To examine the overall cognitive development of children exposed to maternal rheumatoid arhtritis (RA) in utero by comparing their scores in national school tests, to those of their peers.

Methods:

Children born in Denmark 1995 - 2008, and listed in the Danish National School Test Register were included (n=738,862). Children exposed to maternal RA were identified through linkage of national registers. In separate analyses, exposure was subdivided according to maternal RA serostatus. Preclinical maternal RA was included as a separate exposure.

The Danish National School Tests are mandatory, standardized tests. Results from all reading tests (grades 2, 4, 6 and 8) and mathematics tests (grades 3 and 6) from 2010-2018 were included. Test scores were compared according to exposure to maternal RA , for each test separately using linear regressions, and by combining all grades for reading and mathematics separately, using mixed-effects models.

Results:

In total, 816 children were exposed to maternal RA in utero. There were no differences in scores in any reading test, between maternal RA exposed and unexposed children. RA exposed children scored poorer in mathematics tests (adjusted difference of mean score: -0.15 SD (-0.22; -0.08)). There was no appreciable difference between children by maternal RA serostatus. Children exposed to preclinical RA (n=472) showed the same pattern of performance as children exposed to RA.

Conclusions:

RA exposed children scored slightly poorer in mathematics tests, but performed as well as their unexposed peers in the reading tests. The results do not suggest that RA in pregnancy has a major impact on offspring school performance.

P11.10   Fanghui Ren   MECHANISM OF ACTIVATION OF AUTOPHAGY IN NEURONS BY HERPES SIMPLEX VIRUS

F.H. Ren

Department of Biomedicine, Aarhus University

Herpes simplex virus (HSV)-1 and -2 are neurotropic viruses, which can cause encephalitis, which is associated with high mortality if not treated. The innate immune system is a major determinant for the outcome of infection, and autophagy has been implicated as an innate immune mechanism against HSV infections. However, the mechanism governing HSV-induced autophagy in neurons remains unknown, and will be explored in this project. At this stage we have found a human neuron-like cell line in which HSV can induce autophagy. This occurs through in a time- and dose-dependent manner. HSV infection stimulates autophagy after 6h, and this further increases until 16h post infection. These findings provides us with a system to study HSV-induced autophagy in neurons. We are now generating a large panel of genome-edited cell lines using CRISPR/Cas9 technology, in order to identify the signaling pathway triggered by HSV in neurons to induce an important antiviral program in neurons.

P12.01   Erik Buch Jørgensen   ACCURACY OF IN VIVO DOSIMETRY BASED SOURCE-TRACKING IN HDR PROSTATE BRACHYTHERAPY

E.B. Jørgensen, G. Kertzscher, K. Tanderup, J.G. Johansen

Department of Oncology, Aarhus University Hospital

Purpose

To determine the accuracy of an in vivo dosimetry based source-tracking (ST) method for brachytherapy (BT).

Methods

Five prostate BT treatment plans previously performed at our institute were simulated in a water tank providing full scatter conditions. All irradiations were performed with an Ir-192 HDR Flexisource. Dosimetry was performed at a 20 Hz sampling rate using a radioluminescent crystal ($0.5x0.5x2mm^3$, Al_2O_3:C) coupled to a photo multiplier tube via a fiber-optic cable.

The expected dose-rates were calculated using the TG 43 algorithm. The measured count rates for dwell positions with dwell times above 1.2 s were calibrated to units of dose-rate. The calibration coefficients were determined in a small PMMA phantom before each treatment simulation.

The ST algorithm generated an expected position of each needle longitudinally (along the needle) and radially (towards - away from the detector needle) by minimising the least squares between the expected

and measured dose-rates. The expected dosimeter position of each treatment was corrected by the mean longitudinal positional shift and the ST algorithm was subsequently repeated.

Results

Irradiation was carried out at a total of 1048 dwell positions distributed in 88 needles and ST could be performed in 75 needles (85 %). The last 13 needles had less than 2 dwell positions with dwell times above 1.2 s

67 % / 97 % / 100 % of the absolute radial positions and 95 % / 97 % / 100 % of the absolute longitudinal positions was within than 1 mm / 2 mm / 3 mm.

Conclusion

The ST could determine the radial and longitudinal position for 85% of needles with accuracy better than 2 mm for the far majority (97 %) of needles.

P12.02   Simon Grund Sørensen

DO DEFECTS IN DNA DAMAGE RESPONSE GENES LEAD TO PATTERNS OF MUTATIONS ACROSS THE WHOLE CANCER GENOME?

S.G. Sørensen, J. Bertl

Department of Molecular Medicine, Aarhus University Hospital

DNA damages happen through exposure to exogenous and endogenous carcinogens, e.g. UV-light, smoking, and radical oxygen species. Most damages are reversed through the DNA damage responses (DDR). Losing the function of one or more DDR mechanisms typically cause an accumulation of mutations across the entire genome, possibly leading to cell death or cancer development. Losing the function of a DDR mechanism may however also sensitize the cancer cells to treatments inducing further DNA damage, as well as treatments blocking compensatory DDR mechanisms e.g. PARP-inhibitors. There is thus a clinical potential in better understanding the effect of DDR perturbations on the genome, and we aim to do this by looking at mutation patterns.

Data: 2,583 whole cancer genomes from the PCAWG project (under ICGC). Each patient has been annotated for loss of function variants in DDR genes. The study encompasses both somatic mutations and germline events and at various levels: point mutations, short insertions and short deletions, structural variants and copy-number changes.

We have identified apparent associations between perturbation of DDR genes and COSMIC cancer signatures. E.g., 38 patients in our data have perturbated the BRCA2 gene, and have a median increase of around 2000 mutations towards signature 3. This is expected for breast and ovary cancer, but we have found that the pattern expands across other cancer types. In perspective, such findings may improve our understanding of how faulty DDR mechanisms affect the genome across cancer types, which in return can help guide the application of cancer treatments as well as drive discovery of novel cancer drug targets.

P12.03   Signe Neldeborg   TURNING COLD TUMORS HOT

S. Neldeborg[1], C.K. Holm[3], B.R. Knudsen[2], M. Stougaard[1]

[1]Pathology, Department of Clinical Medicine, Aarhus University,
[2]Department of Molecular Biology and Genetics, Aarhus University,
[3]Department of Biomedicine, Aarhus University

Background:

Cancer patients with "cold" tumors, i.e. tumors lacking immune cell infiltration, do not respond well to treatment with immunotherapy, compared to patients with "hot" tumors, i.e. tumors with immune cell infiltration.

This lack of immune infiltration has been attributed to the low immunogenicity of the cancer cells, either in the form of low pro-inflammatory cytokine production or poor antigen presentation, but also due to upregulation of T-cell dismissive surface molecules such as PD-L1.

DNA damaging agents, like Topoisomerase (TOP) inhibitors, have been shown to stimulate an immunogenic response in cancer cells, but the underlying mechanism is not well understood.

The aim of this project is to investigate the response produced in cancer cells upon treatment with a low dose TOP1 inhibitor drug and better understand the underlying mechanisms.

Method:

I am verifying the immunogenic response to TOP1 inhibitor treatment in a broad range of cancer cell lines, to determine whether it is a general mechanism in cancer.

Furthermore, I am planning to do an extensive profiling of the gene expression and protein excretion from cancer cells treated with TOP inhibitors.

Results:

Analyses are ongoing, and so far, I have preliminary results confirming a response in a broad range of cancer cells. In my further studies, I expect to see an increase in immune-attracting chemokines, pro-inflammatory cytokines etc.. I also hope to discover new interesting pathways linked to the immunological response.

Conclusion:

If it is possible to induce an immune response in cancer cells, using TOP1 inhibitors, we can possibly develop a new strategy to make "cold" tumors "hot".

P12.04   Pernille Aaen   IN VIVO MOUSE MODEL OF HER2/ERBB2-INDUCED METASTATIC BREAST
          Sloth   CANCER AND CHARACTERIZATION OF LUNG METASTASES

P. Aaen[1], M.H. Vendelbo[1, 2], E. Bødtkjer[1]

[1]Department of Biomedicine, Aarhus University, [2]Department of Nuclear Medicine and PET-Center, Aarhus University Hospital

Breast cancer remains the second leading cause of cancer-related deaths among women. Metastasis is the most lethal aspect of the disease, but animal models that capture the complete carcinogenic and metastatic process are scarce. In this study, we develop new experimental tools to characterize the functional and molecular dynamics of primary breast carcinogenesis and metastasis and evaluate novel therapeutic targets.

In mice with HER2/ErbB2-induced breast cancer, we surgically remove primary breast carcinomas when they are 10-12 mm in size. Lung metastases appear around 4 months after initial tumor resection and are detectable by MRI.

The metastases are of up to a few mm in size and can be dissected from the lung tissue post-mortem. From primary breast carcinomas, lung metastases, and normal breast tissue, we enzymatically isolate multicellular epithelial organoids that can be used for assessing protein expression and the activity of pH-regulating transporters ex vivo.

This model of de novo metastatic breast cancer represents a promising tool for identifying functional adaptations from normal breast tissue to primary breast carcinomas and metastatic lesions. In particular, the developed model is promising for evaluating new therapeutic targets to interfere with breast cancer metastasis.

P12.05   Karen Schow Jensen

PRIMARY HEALTH CARE UTILIZATION AMONG SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA: A MATCHED COHORT STUDY

K.S. Jensen[1], B.K. Albertsen[1], H. Schrøder[1], P. Vedsted[2]

[1]Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital, [2]Research Unit for General Practice, Department of Public Health, Aarhus University

Background: More children survive acute lymphoblastic leukaemia (ALL) due to advances in diagnosis and treatment. Today, more than 90% of children with ALL are alive five years after their diagnosis. This means a growing population of childhood ALL survivors. However, intensive treatment for childhood ALL may have severe side effects. Register studies of long-term survivors of childhood cancer have shown an increased risk of hospitalisation compared with the general population. Still, the knowledge about non-hospital-based contacts with a doctor in childhood cancer survivors is scarce.

Objective: To compare the primary healthcare contact rates over time between ALL survivors and matched comparisons without ALL.

Methods: This is a population-based 1:10 matched cohort study using information from nationwide registries. Participants were a cohort of 692 childhood ALL survivors and 6920 matched references. Eligible patients were those who completed maintenance therapy in the time period from 01.01.1997 until 31.12.2017, were diagnosed with B-precursor ALL and T-ALL, were enrolled in the NOPHO ALL-92, ALL-2000 and ALL-2008 trials, and were treated at one of the four Danish paediatric oncology departments. The references were sampled randomly from the source population matched by age, sex and region and without a history of childhood cancer 2.5 years after the case was diagnosed.

Perspective: Improved understanding of the long-term healthcare utilisation of childhood cancer survivors is relevant as it can be seen as a proxy for the population's morbidity. And results may have an impact on the organization of follow-up programs.

P12.06 Rasmus Blechingberg Friis

SYMPTOM DEVELOPMENT FROM INITIAL TREATMENT TO PROGRESSIVE DISEASE IN PATIENTS WITH ADVANCED LUNG CANCER

R.B. Friis[1], N.H. Hjoellund[2, 3], H. Pappot[4], H. Skuladottir[1]

[1]Department of Oncology, Regional Hospital West Jutland, [2]AmbuFlex/WestChronic, Occupational Medicine, University Research Clinic, Aarhus University , [3]Department of Clinical Epidemiology, Aarhus University Hospital, [4]Department of Oncology, University Hospital of Copenhagen

Introduction

Cancer patients treated in the department of oncology at Regional Hospital West Jutland have, as a standard, since 2014 filled in an electronic questionnaire prior to any outpatient visit. The answers from the patients are used in clinical practice to improve dialogue and decision support.

The aims of this study were to explore the symptom development in lung cancer patients on a group level from initial 1st line palliative treatment to the time of progressive disease and, if possible, identify symptoms which could indicate early signs of progressive disease.

Methods:

Lung cancer patients who had filled in the questionnaire (EORTC QLQ-C30/LC13) at baseline and at the time of progression were eligible. Individual scales were converted to scores (0-100). Group mean changes in functional and symptom scores from baseline to the time of progression were compared by paired t-test to identify specific scores that deteriorate towards the time of progressive disease.

Results

Of 584 reviewed patients, 110 were eligible for the analysis. The scales most sensitive to change between baseline and the time of progressive disease were physical functioning (-10.2, p=.000), role functioning (-11.4, p=.000), social functioning (-9.4, p=.001), fatigue (11.4, p=.000) and pain (10.2, p=.001). Alopecia (13.7, p=.000) and peripheral neuropathy (8.7, p=.000) did also change significantly but were to a large extent caused by side effects to the treatment.

Conclusion

The results indicate that deteriorations in specific symptom scores could indicate early disease progression in advanced lung cancer. The results are, however, exploratively due to the retrospective analysis.

P12.07 Marie Louise Milo RADIOTHERAPY ASSOCIATED CORONARY ARTERY STENOSIS IN 87,550 PATIENTS WITH EARLY BREAST CANCER

M.L.H. Milo[1], L.B.J. Thorsen[1, 2], J. Alsner[1], K.M. Nielsen[3], S.P. Johnsen[4], B.V. Offersen[1, 5, 6]

[1]Department of Experimental Clinical Oncology, Aarhus University Hospital, [2]Department of Oncology, Aalborg University Hospital, [3]Department of Cardiology, Aarhus University Hospital, [4]Danish Center for Clinical Health Services Research, Department of Clinical Medicine, Aalborg University, [5]Department of Oncology, Aarhus University Hospital, [6]Danish Center for Particle Therapy, Aarhus University Hospital

Purpose: We aimed to evaluate the risk of coronary artery stenosis requiring intervention among early stage breast cancer (BC) patients treated with adjuvant radiotherapy (RT).

Material and methods: Women diagnosed with early BC in Denmark between 1990-2016 were identified from the register of the Danish Breast Cancer Group and information of coronary artery stenosis was collected from The Western Denmark Heart Registry. Incidence rate ratios (IRR) of coronary artery stenosis requiring intervention were calculated by comparing patients irradiated for left versus right-sided BC (LvsR).

Results: This study included 87,550 BC patients of whom 42,740 received RT: 51.1% on the left and 48.9% on the right side. Invasive procedures for coronary artery stenosis were preformed in 233 left-sided and 178 right-sided irradiated patients. The IRR for coronary artery stenosis requiring intervention, LvsR, among all irradiated patients was 1.2 (95% CI 0.99 - 1.46) and for patients irradiated before 2008 the IRR LvsR was 1.35 (95% CI 1.02 - 1.77) with the largest risk within the first five years and again 10 years after RT. For patients treated after 2008 the IRR LvsR was 1.05 (96% CI 0.79; 1.41) with no difference in time intervals after RT. No increased IRR LvsR was observed for patients treated with adjuvant chemotherapy, neither before nor after 2008.

Conclusion: To our knowledge this is the largest study investigating radiation associated coronary artery stenosis requiring intervention. RT for left-sided BC was associated with an increased incidence of coronary artery stenosis for patients treated before 2008 whilst no effect from RT was detected in patients treated after 2008.

P12.08 Andreas Gravgaard Andersen VALIDATION OF AN A PRIORI CONE-BEAM SCATTER CORRECTION APPLICATION FOR ONLINE PROTON THERAPY RANGE VERIFICATION

A.G. Andersen[1], Y.K. Park[2], B. Winey[3], U.V. Elstrøm[4], J.B.B. Petersen[1], L. Dong[5], L.P. Muren[1]

[1]Department of Medical Physics, Danish Centre for Particle Therapy, [2]Department of Radiation Oncology, UT Southwestern Medical Center, [3]Department of Medical Physics, Massachusetts General Hospital, [4]Department of Medical Physics, Aarhus University Hospital, [5]Department of Radiation Oncology, University of Pennsylvania

Purpose:

Anatomical changes and other set-up uncertainties can have a large impact on the dose distribution in proton therapy. Cone-beam (CB)

projections, are acquired just before treatment to verify position, however contains many artifacts, with implication for dose and range calculations.

We aim to provide an application for reliable scatter correction to eliminate the artifacts, allowing for accurate range calculations.

Material and Methods:

The algorithm used the planning CT as a priori input, which was registered rigidly (rigidCT) and deformably to the raw CB reconstruction (rawCBCT), and then forward projected to match the raw CB projections. The difference between the projection sets was then smoothed to create a scatter-map, which was then subtracted from the raw CB projections before a final reconstruction (corrCBCT).

Cone-beam projections from a Varian ProBeam Gantry of two phantoms were scatter corrected. The corrCBCT and the clinical reconstruction (varianCBCT) was compared against the rigidCT.

For the data analysis twelve segmentations of Catphan materials were made.

Water equivalent path length (WEPL) was calculated from every point on the posterior side of the image and towards the anterior side of an Alderson phantom.

Results:

In the Catphan segmentation the corrCBCT performed better than the varianCBCT in eight, nine and ten out of the twelve segmentations when considering the median, mean and SD values respectively.

For the WEPL results, the corrCBCT performed markedly better with median range differences, from the rigidCT, between -6.7 and 7.3 mm (SD: 2.5 to 5.5 mm). While the varianCBCT had median range differences from 6.0 to 37.4 mm (SD: 7.1 to 19.4).

P12.09   Nadia Øgaard   BLOOD-BASED DETECTION OF COLORECTAL CANCER USING DNA METHYLATION BIOMARKERS - CLINICAL APPLICATIONS FOR EARLY DETECTION AND PREDICTION OF POSTSURGICAL RELAPSE

N. Øgaard, S.Ø. Jensen, J.B. Bramsen, C.L. Andersen

Department of Molecular Medicine, Aarhus University Hospital

Objective

Blood-based analysis of circulating tumor DNA (ctDNA) provides a minimal-invasive avenue for colorectal cancer (CRC) detection. However, in certain clinical settings such as in early disease stages and post-surgery, the disease burden is low, hence, ctDNA detection requires extremely sensitive detection methods. The use of DNA methylation markers to identify trace amounts of ctDNA in blood is gaining prominence.

Here, we investigate the potential of methylation markers to identify CRC-released ctDNA in 1) early-stage patients, and 2) postsurgical patients to detect minimal residual disease and identify patients at risk of relapsing.

Results

A total of three CRC specific DNA methylation markers were identified in a biomarker discovery study based on methylation profiles from >5,000 tumor and blood samples. Methylation-specific droplet digital PCR assays were developed and validated. When applied on plasma from 113 CRC patients and 87 controls the methylation markers detected CRC with 78 % sensitivity and 99 % specificity (combined marker performance). In an independent cohort of 143 CRC patients and 91 controls, the markers were capable of discriminating CRC patients from controls with 85% sensitivity and 99% specificity.

For improved marker sensitivity, dual-strand assays were designed and validated. Ongoing analysis investigates if the DNA methylation markers have potential to be applied in postsurgical patients to detect minimal residual disease.

Conclusion

Three identified DNA methylation markers enabled detection of CRC-released ctDNA with high sensitivity and specificity, thus, show promise for numerous clinical applications in CRC detection and management

P12.10   Laura Patricia Kaplan

A NEW TOOL TO ASSIST IN CLINICAL COMPARISON OF RADIOTHERAPY TREATMENT PLANS

L.P. Kaplan[1, 2], S.S. Korreman[1, 2, 3]

[1]Department of Clinical Medicine, Aarhus University, [2]Department of Oncology, Aarhus University Hospital, [3]Danish Center for Particle Therapy, Aarhus University Hospital

Aim

An integral part of the radiotherapy workflow is selecting the optimal radiation treatment plan (RTP) from a group of possible plans. Comparing the quality of RTPs is a complex, and to some extent subjective, task. Using quantitative metrics to describe RTP quality lowers the degree of subjectivity and thus minimizes variations between observers. We propose a software tool that calculates and visualizes quantitative metrics for RTP quality as an aid in the clinical radiotherapy treatment workflow.

Methods

The Eclipse treatment planning software used at AUH offers the ability to run custom C# scripts from within the main user interface. Within this framework we developed several scripts for calculation and visualization of metrics. We use both custom and built-in functionality from the Eclipse Scripting Application Programming Interface (v 13.7) for calculations and the Oxyplot library (v 1.0) for visualization.

Status

So far, we have developed two scripts. When run, each displays a graphical user interface. Script 1 calculates and plots metrics for several plans at once. The user can choose from a range of metrics describing:

- Max, min, and mean dose to anatomical structures

- Dose conformality and homogeneity in the target

- Dose gradient

- Size and number of contiguous hot or cold volumes

- Robustness of dose towards geometrical and calibration errors

Script 2 calculates and displays normal tissue complication probability as a function of dose and highlights the achieved value for several plans at once. At present, models for xerostomia and dysphagia are implemented.

Perspectives

We will continue developing our tool and test it in various clinical settings and anatomical sites.

P12.11 Casper Gammelmark Muurholm

EXPERIMENTAL VALIDATION OF REAL-TIME ROTATION-INCLUDING DOSE RECONSTRUCTION DURING TUMOR TRACKING

C.G. Muurholm[1], T. Ravkilde[2], R. De Roover[3, 4], S. Skouboe[1], R. Hansen[2], W. Crijns[3, 4], P.J. Keall[5], T. Depuydt[3, 4], P.R. Poulsen[1, 6]

[1]Department of Oncology, Aarhus University Hospital, [2]Department of Medical Physics, Aarhus University Hospital, [3]KU Leuven, Department of Oncology, Leuven, Belgium, [4]University Hospitals Leuven, Department of Radiation Oncology, Leuven, Belgium, [5]ACRF Image X Institute, The University of Sydney, Australia, [6]Danish Center for Particle Therapy, Aarhus University Hospital

Hypofractionation in prostate radiotherapy increases the need for accurate treatment delivery, but motion deteriorates the delivered dose. Real-time motion adaptation adjusts for translational motion. The effects of residual uncompensated rotations are mostly unknown. In this study, we develop and demonstrate real-time rotation-including dose reconstructions performed during prostate radiotherapy phantom experiments.

DoseTracker is an in-house developed program which performs motion-including dose reconstruction based on streamed tumor positions and linac parameters. Its ability to predict dose errors was compared to film in three different scenarios: (1) No motion correction, and translational motion correction with (2) MLC tracking, and (3) couch tracking.

For each scenario three motion traces were applied to a pelvis phantom with embedded radiochromic film for experimental comparison between DoseTracker and measurement. The parameters used for comparison were the motion induced 2D 3%/2mm γ failure rate and the motion-induced reduction in D95% (ΔD95%) for the CTV and GTV and the motion induced increase in urethra D0.1cc (ΔD0.1cc).

Online real-time dose reconstruction was done in more than 80,000 calculation points at a rate of about 5Hz. The root-mean-square error of DoseTracker relative to film was 3.6% (γ failure rate), 0.12Gy (CTV ΔD95%), 0.28Gy (GTV ΔD95%), and 0.25Gy (urethra ΔD0.1cc).

Online real-time rotation-including motion-including dose reconstruction was performed for the first time. It agreed well with film measurements. It provides a valuable real-time QA tool that allows easy investigation of motion effects and the efficacy of compensation techniques.

F01.01 Emina Gültekin   CONSTRUCTIONS OF ETHNIC MINORITY PATIENTS: A CONSTRUCTIVIST GROUNDED THEORY APPROACH

E. Gültekin

Faculty of Health, Aarhus University

Background: Patients who belong to ethnic minorities are associated with negative health outcomes. Although attention has been drawn to the challenging character of intercultural character in the Danish health care system, little attention has been afforded the roles of both health professionals and the patients themselves in facilitating ethnic minority patients' access to health care and subsequent impact on health outcomes.Objective: The project's objectives are to observe the meeting between health professionals and ethnic minority patients and hence examine the construction of ethnic minority patients drawn upon by health professionals involved in the care of patients with non-Danish backgrounds and the patients themselves.Design: The qualitative design is based on a constructivist grounded theory approach with symbolic interactionism as the theoretical perspective.The research question will be investigated with use of varied methods and includes three sub studies.Methods:Participants will be selected through purposeful sampling as health professionals accustomed and knowledge about ethnic minority patients. The data collection comprises a combination of moderate participant observation inspired by ethnographic field research with parallel intensive interviewing. Data will consist of extensive fieldnotes about the observations, reflections, hunches, informal and formal conversations during admission to an emergency department. Analysis will run concurrently and consist of constant comparative method and theoretical sampling aimed at developing a theory that explains relevant factors, statements and actions by learning why, how and from what they originate.

F01.02 Kathrine Carstensen   QUALITY IMPROVEMENT COLLABORATIVES IN THE IMPLEMENTATION OF THE DANISH HEALTHCARE QUALITY PROGRAMME

K. Carstensen

DEFACTUM - Public health and health services research, Central Denmark Region

Internationally, quality improvement (QI) in healthcare has evolved into a major topic. Different approaches to QI have been deployed and quality improvement collaboratives (QICs) represent one widely applied approach. The effects of QICs in supporting QI are however unclear, and little is known about the mechanisms and components in QICs that are responsible for the varying effects. Establishment of such knowledge requires research that looks into the implementation process of QICs.

Against this backdrop, this PhD project aims to investigate how quality improvement collaboratives (QICs) function as an implementation approach to QI driven by healthcare professionals. This will be examined using the implementation of the national Danish Healthcare Quality Programme (DHQP), in which QICs are used as an implementation approach, as an empirical case.

The PhD project comprises three sub-studies wherein the functioning of QICs is studied at the organisational, professional and management level,

respectively. Methodologically, the PhD project is designed as a qualitative case study in which two strategically selected QICs are followed during their implementation. Data will be collected through a combination of literature and document studies, qualitative interviews and observations.

The results of the PhD project will provide a valuable basis for understanding the circumstances under which QICs are successful as an implementation approach. Such knowledge is essential in order to maximize the practical relevance of QIC as implementation approach in QI. Furthermore, the results will provide important knowledge on the capacity of healthcare professionals in fostering QI.

F01.03   Anne Timm   A PROCESS EVALUATION OF THE FAMILY LEVEL IN A COMPLEX HEALTH PROMOTION INTERVENTION

A. Timm[1], K. Kragelund Nielsen[2], H. Terkildsen Maindal, H[1, 2]

[1]Department of Public Health, Aarhus University, [2]Steno Diabetes Center Copenhagen

Background: Gestational diabetes mellitus (GDM) predisposes women and their offspring to a range of short- and long-term morbidities, including early onset type 2 diabetes (T2D). Studies have suggested that the women's diabetes risk can be reduced through structured lifestyle intervention. However, compared to their normoglycemic counterparts, women with GDM often face multiple barriers for healthy behaviours. As health behaviours tend to cluster within families and social support is a critical component of ensuring sustainable healthy behaviours, focusing on the family level rather than the individual level seems optimal. The Face it trial was developed as a health promoting intervention to meet this potential.

Methods: The first study will therefore be a realist review of behaviour change in families in order to reduce their cardiometabolic risk. The aim of the study will be to investigate how, for whom and under what circumstances BCTs were effective in promoting healthy behaviours. Studies 2 and 3 will investigate what motivates and challenges families in changing health behaviours and what hinders and motivates health visitors conduct health promoting activities with a qualitative approach

PhD: This PhD runs from July 2019 to June 2022. First results are expected in April 2020.

Perspectives The project is expected to generate novel knowledge on how and under which circumstances health promotion can be carried out in the family context. It will further result in a strengthening of the existing evidence on the use of BCTs in supporting health behaviour change and thereby paving the way for future intervention studies to be based on a solid theoretical foundation.

| F01.04 | Marie Ernst Christensen | FOOD AND EATING CHALLENGES AMONG ADOLESCENTS AND YOUNG ADULTS WITH CANCER UNDERGOING CHEMOTHERAPY |

M.E. Christensen[1, 3], P.R. Olsen[2], H.K. Rose[2], A. Haahr[3], A. Norlyk[1]

[1]Research Unit for Nursing and Health Care, Department of Public Health, Aarhus University, [2]Department of Oncology, Aarhus University Hospital., [3]Research Centre for Rehabilitation, VIA University College

Introduction:

In Denmark, the incidence of cancer among adolescents and young adults (AYAs) (age 15-29y) comprises app. 500 per year. Studies show that appetite, nausea and vomiting affects food intake in patients undergoing high-emetogenic chemotherapy, and that AYAs are particularly affected by these side effects compared to other age groups. Consequently, there is a risk of inadequate nutritional intake, which may cause unintended weight loss and obstruct development of the best conditions to withstand treatment and side effects. AYAs undergoing chemotherapy are an exceptionally vulnerable population. They undergo a complex developmental phase in life, they experience a growing autonomy, and when facing a cancer diagnosis, they experience an involuntary dependence in their next-of-kin, which further complicates the management of eating and give rise to eating-related conflicts and dilemmas. However, evidence on food and eating related challenges is sparse.

Aim:

The aim is to understand the food and eating challenges faced by AYAs, their next-of-kin, and healthcare professionals in hospitals as well as at home. The knowledge acquired from the clinical and the home settings will used to develop recommendations and youth friendly information material to support the healthcare professionals in the guidance of AYAs undergoing chemotherapy and their next-of-kin when facing food and eating challenges.

Methods:

The study is based on a qualitative research design inspired by Van Manen´s hermeneutical-phenomenological methodology.

Participants:

Recruited from the following oncology departments at Aarhus University Hospital: Adult Oncology, Child and Youth, Haematology.

| F01.05 | Anders Schmidt Vinther | PREVENTING ANABOLIC STEROID USE IN GYMS - WHAT WORKS? |

A.S. Vinther

Department of Public Health, Aarhus University

Anabolic steroids are potent drugs that can rapidly increase muscle size and strength way beyond the natural limits of the human body. It is therefore not surprising that these drugs have been widely used by elite athletes seeking to enhance their sporting performance and, more recently, by recreational gym users striving for a sizeable, muscular and lean physique. However, as with most other drugs, steroid use also comes

with a range of adverse health effects. For this reason, medical and public health authorities have long called for action to develop strategies that can prevent steroid use initiation. As research into the prevalence and health risks of steroid use has proliferated over the past three decades, so has the academic interest in developing effective behaviour change interventions. Despite this, however, two central questions remain unanswered: How can the use of anabolic steroids in and around gyms be prevented, and to what extent is it possible? This research project takes an explorative approach and seeks to address these questions through in-depth, qualitative interviews with three main groups of interest: 1) leading international experts within the field of steroid use and prevention, including researchers, public health commissioners, and anti-doping professionals, 2) intervention providers of a national, gym-based steroid prevention programme, and 3) young, male gyms users engaged in recreational strength training. At the heart of this project lies an ambition to more fully understand the limiting and promoting factors for steroid prevention and, ultimately, to pave the way for more effective prevention efforts.

| F01.06 | Lene Klem Olesen | A COMPLEX INTERVENTION STUDY ON A PALLIATIVE REHABILITATION BLENDED LEARNING PROGRAM TO SUPPORT RELATIVES AND HEALTH CARE PROVIDERS OF PEOPLE WITH ALS AND FTD IN COPING WITH CHALLENGES |

L. Klem Olesen

Department of Public Health, Aarhus University

Amyotrophic lateral sclerosis (ALS) is regarded as the most devastating of adult-onset neurogenerative disorders and affects approximately 130-150 people in Denmark every year. It is known that 80% of people with ALS are at risk of developing frontotemporal dementia (FTD-dysfunction).

Relatives of people with ALS and FTD-dysfunction (PALS/FTD) and health care providers (HCPs) are burdened by the challenges the diseases entails. Literature is sparse on the challenges that relatives and HCPs' experience and how these can be addressed and supported.

This project concerns a coordination of a palliative and rehabilitation approach, where information and support for relatives and HCPs have proved effective regarding making their daily lives more manageable.

The overall aim of this PhD is to involve relatives of deceased PALS/FTD-dysfunction and HCPs in developing and testing the feasibility of a targeted palliative rehabilitation blended learning program to support relatives of PALS/FTD-dysfunction and HCPs in coping with challenges. The design is qualitative using the Interpretive Description Methodology and the Salutogenesis as a theoretical framework.

The PhD will provide knowledge on challenges and needs of relatives and HCPs and contribute with know-how of the new intervention which hopefully will benefit other patients national and international.

F01.07	Anna Louise Skovgaard	THE WORK OF BEING A PATIENT

A.L. Skovgaard[1, 4], M. Johansson Jørgensen[1, 4], T. Tjørnhøj-Thomsen[3], M. Terp Høybye[2, 4]

[1]Horsens Regional Hospital, Department of Research, [2]Silkeborg Regional Hospital, Department of research, [3]Department of Health and Social Context, University of Southern Denmark, [4]Department of Clinical Medicine, Aarhus University

Background:

Living with chronic illness, as an increasing number of people are, implies long-lasting treatment pathways, which include activities that are to a greater extent handled by patients and their relatives themselves. This change in the division of labor between patient and health care system affects the duties and responsibilities of chronic patients in contemporary health care.

For patients, living with a chronic illness is about balancing everyday life, and in the best of circumstances, the health care system supports patients and their relatives in this endeavor. However, sometimes, the extent and complexity of the activities exceed the resources available and discourage patients from taking care of themselves.

Aim:

This anthropological study explores how patients with chronic illness and frequent acute hospitalizations negotiate duties and care in the Danish health care system. How is the balance between duties and resources addressed in the encounter with health care professionals and which forms of care are enacted in the process?

Methods:

Patients with chronic illness and frequent acute hospitalizations (n=10-15) are followed closely for an extended period of time (6-12 months) through methods of participant-observation and conversation/interview. The empirical material is analyzed using an abductive approach.

Perspectives:

Increasing our knowledge on how activities performed by the health care system may be perceived in the perspective of every day life of patients, qualifies discussion of these matters with patients, support balance, and promote meaningful collaboration between patients and professionals across health care sectors.

F01.08	Mia Hansen Mandau	NURSES' PRACTICES OF COORDINATING CARE BETWEEN EMERGENCY AND SPECIALIST HOSPITAL DEPARTMENTS - A MULTIPLE-CASE STUDY

M.H. Mandau

Department of Public Health, Aarhus University

Following a major health reform in 2007, Denmark has seen the introduction of large, integrated emergency departments (ED) with one single entry for all acutely ill patients coming to a hospital. Coordination of patient care across departments is paramount, as fragmentation can result in adverse outcomes and low patient satisfaction. Studies have

shown that nurses play a key role in the making of coordination and in securing continuity of patient care. Nevertheless, we lack knowledge about the practice of coordinating care for patients with a shared admission between ED and specialist departments. This study aims to investigate nurses' formal and informal coordination practices and to analyse how different organisational contexts facilitate or constrain coordination practices. The study applies a multiple-case study method. This allows investigating coordinating practices in their real-lifecontexts and the integration of multiple sources of data provides detailed information about coordination practices. The study includes document analysis, participant observations, focus group interviews and individual interviews. The study contributes with new empirical and theoretical knowledge about how nurses coordinate complex patient care between ED and specialist departments. In terms of practice, the study has important implications for better securing continuity of patient care and avoiding fragmentation. This applies to EDs with shared admissions well as other settings; the short time spans and high uncertainty typical of EDs offer the ultimate test for the sustainability of coordination practices.

F02.01   Signe Risbøl Vils   THROMBOEMBOLIC RISK IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

S.R. Vils[1], A. Troldborg[1, 2], A.M. Hvas[3], S. Thiel[1]

[1]Department of Biomedicine, Aarhus University, [2]Department of Rheumatology, Aarhus University Hospital, [3]Department of Clinical Medicine, Aarhus University

The purpose of the project is to investigate the increased risk of thrombosis seen in patients with Systemic Lupus Erythematosus (SLE) or Antiphospholipid Syndrome (APS) or both. Our hypothesis is that complement-dependent activation of platelets is one of the mechanisms involved in the formation of blood clots in these patients.

SLE and APS are chronic autoimmune diseases, which often overlap, where about 50% of SLE patients also suffer from APS. The significant reduction in life expectancy seen in these patients is mainly caused by thromboembolic events.

The complement system is an inflammation-generating part of the innate immune system and is known to be activated in patients suffering from SLE. A change in size of the platelets, which indicates activated platelets, is also observed in these patients. The presence of complement-activation and modified platelet-size, combined with a higher degree of immune-activating and dysfunctional endothelium seen in patients with SLE and/or APS, could contribute to the pro-thrombotic phenotype observed in these patients.

With this study, we will explore the interplay between the complement system and the platelets in patients with SLE, APS or SLE combined with APS, and compare it to a healthy control group.

We will use well-established methods to evaluate complement activation, platelet function and platelet activation. We will through these studies expand the knowledge about complement-platelet-interactions and the mechanisms behind immune-mediated blood clot formation.

F02.02	Cecilie Rud Budtz	SERIOUS PATHOLOGY IN PRIMARY CARE PHYSIOTHERAPY

C.R. Budtz

Department of Occupational Medicin, University research Clinic, Regional Hospital West Jutland

Background: Physiotherapists play a central role in the management of patients with musculoskeletal disorders in primary care. Although screening for serious pathology is part of the physiotherapy guidelines, little is known of the physiotherapists understanding of and knowledge on symptoms of serious pathology. The specific aims of the PhD study are therefor to 1) determine how many patients in primary care physiotherapy have a serious pathology, 2) investigate the physiotherapists' knowledge and understanding of symptoms of serious pathology, and 3) develop and pilot test a program that aims to enhance the physiotherapists awareness on symptoms of serious pathology.

Materials and methods: Study 1 is a register-based nationwide cohort study. Records of physiotherapy contact are linked to records of diagnoses identifying all incident cases of serious pathology within a six month period after first physiotherapy contact. Study 2 is a nationwide questionnaire survey. A short single-item questionnaire focusing on the physiotherapist's behavior when faced with patients showing signs of serious pathology will be developed, pilot tested and distributed electronically to primary care physiotherapists across Denmark. Study 3 is a two group pretest-posttest design. A smart and simple program is developed that enhances the physiotherapists' knowledge and awareness on symptoms of serious pathology. The program is based on the results from the questionnaire survey in study 2, a systematic literature review and consensus meetings with a clinical expert panel of physiotherapists and medical doctors. The program is pilot tested and adjusted accordingly.

F02.03	Angela Anna Paula Victoria Herengt	NRF2 CONTROL A NOVEL ANTI-VIRAL PROGRAM

A. Herengt

Department of Biomedicine, Aarhus University

We have previously shown that the cell-stress sensor Nrf2 negatively regulates expression of STING and reduces anti-viral interferon responses to cytosolic DNA.

Unexpectedly we have now discovered that activation of NRF2 initiates, in vivo and in vitro, a powerful anti-viral cellular program that works independently of STING and type 1 interferons.

| F02.04 | Diana Salomi Ponraj | SLOW GROWING GRAM-POSITIVE ANAEROBIC BACTERIA IN ORTHOPAEDIC IMPLANT ASSOCIATED INFECTIONS |

D.S. Ponraj[1], H. Brüggemann[2], T. Falstie-Jensen[3], C. Ravn[4], N. Pedersen Jørgensen[5], J. Lange[1, 6]

[1]Department of Orthopaedic Surgery, Regional Hospital Horsens, [2]Department of Biomedicine, Aarhus University, [3]Department of Orthopaedic Surgery, Aarhus University Hospital, [4]Department of Orthopaedic Surgery, Odense University Hospital, [5]Department of Infectious Diseases, Aarhus University Hospital, [6]Department of Clinical Medicine, Aarhus University

Background:

Implant associated infections (IAI) are a rare, but serious complication that occurs after orthopaedic surgeries. A small percentage of IAIs are caused by slow growing Gram-positive anaerobic bacteria (SGAB) like Cutibacterium species, Finegoldia species and Staphylococcus saccharolyticus. They have non-specific clinical and laboratory features. This, in combination with the tendency of these organisms to form biofilms and their slow growing nature make diagnosis by traditional methods difficult. Knowledge of the true frequency of SGAB from removed implants is consequently limited.

Aim:

The aim of this study is to identify the SGAB from removed orthopaedic implants using advanced microbiologic methods and to determine their frequency.

Method:

Orthopaedic implants removed for any indication are collected and processed by the vortex-sonication method to dislodge the biofilms. The sonication fluid is cultured in multiple culture media under anaerobic conditions with prolonged incubation time. The isolated organisms are identified by MALDI-TOF MS (Matrix-Assisted Laser Desorption/Ionization-Time of Flight Mass Spectrometry) and 16S rRNA gene sequencing. In addition, culture-independent methods like metagenomic sequencing will be done to get a complete picture of IAI-associated bacterial species and potentially identify unculturable species.

Results:

Preliminary data on the type and frequency of SGAB isolated from orthopaedic implants will be presented.

| F02.05 | Philip Therkildsen | POSITIVE PREDICTIVE VALUE OF THE GIANT CELL ARTERITIS DIAGNOSIS IN THE DANISH NATIONAL PATIENT REGISTRY: A VALIDATION STUDY |

P. Therkildsen[1], P.E. Hjort*[1], B.D. Nielsen[1], I.T. Hansen[1], A. Thurah[1], M. Nørgaard[2], E.M. Hauge[1]*

[1]Department of Rheumatology, Aarhus University Hospital, [2]Department of Clinical Epidemiology, Aarhus University Hospital

Background:

Giant cell arteritis (GCA) is the most frequent systemic vasculitis. Diagnosis is based on symptoms, histopathology, biochemistry, and imaging. In Denmark, all diagnostic codes from hospital contacts are registered in the Danish National Patient Registry (DNPR). Since GCA can be difficult to diagnose, we hypothesize that the overall positive predictive value (PPV) of GCA in the DNPR is low.

Objectives:

To investigate the PPV of GCA in the DNPR and to identify characteristics associated with high PPVs.

Methods:

In the period Jan. 2012 to Jan. 2018, 293 patients aged ≥50 years with newly-diagnosed GCA were included from the DNPR. Patients were sampled from three hospitals in the Central Region of Denmark. Two independent investigators reviewed all medical records, pathology reports, biochemistry, and imaging material, and determined the final diagnosis. Sub-analyses of the PPV were performed using number of glucocorticoid (GC) prescriptions and contacts.

Results:

A total of 183/293 patients were categorized as GCA, resulting in an overall PPV of 62% (95% confidence interval (CI): 57-68%). Combining with ≥3 GC prescriptions the PPV increased to 78% (95% CI: 71-83%) and included 166/183 (91%) GCA patients. The highest PPV of 93% (95% CI: 85-96%) was achieved by combining ≥3 GC prescriptions with ≥3 hospital contacts. However, this only included 88/183 (48%) GCA patients.

Conclusion:

This is the first study to validate the diagnostic code of GCA in the DNPR. The overall PPV of GCA in the DNPR is comparable to other medical diagnoses. Combining with number of GC prescriptions and contacts increases the PPV significantly, but also reduces the number of GCA patients.

F02.06 Susanne Gundersborg Sandbøl

THE EFFECT OF A NEWLY BUILT HOSPITAL ON INFECTION CONTROL

S. Sandbøl[1, 2], S. Ellermann-Eriksen[2, 3], E.N. Glassou[4], A. Haagerup[1, 3]

[1]NIDO|danmark, Staben Hospitalsenheden Vest, [2]Department of Clinical Microbiology, Aarhus University Hospital, [3]Department of Clinical Medicine, Aarhus University, [4]Department of Quality and Development, Staben Hospitalsenheden Vest

INTRODUCTION: High touch surfaces are well-known to contribute significantly to hospital-acquired infections. Current assessments of microbial burden are based on visual inspection such as INSTA 800. However, these methods do detect neither types, nor amounts of pathogen

AIM: This pilot study aimed to develop and validate an environmental microbial sampling method for assessment of types as well as amounts of pathogen on the high touch surfaces door handles, bedside tables and bedrails.

METHODS: Sampling was performed with nylon fiber swabs. 60 environmental samples were conducted in the period December 2018 to March 2019. Samples were manually streaked with 100 µl on ORI agar plates and incubated for >24 hours at 35°C. Identification of pathogens was assessed by visual inspection, and amounts of pathogens were assessed by counting the number of colony forming unit (CFU) per agar plate.

RESULTS: 40% of the door handles were positive for CoNS, Enterococcus, and Bacillus; 65% of the bedside tables were positive for Staphylococcus aureus, CoNS, Enterobacteriaceae, Enterococcus, and Bacillus; and 45% of the bedrails were positive for CNS, Enterococcus and Bacillus.

CONCLUSION AND PERSPECTIVES: This study successfully developed and validated a microbial environmental sampling method for determining Staphylococcus Aureus, CoNS, Enterococcus, Enterobacteriaceae, and Bacillus on door handles, bedside tables and bedrails. Moreover, the method revealed that pathogens occur on visually clean high touch surfaces. These findings shed new light on hospital cleaning and indicate a need for revising sanitary guidelines. However, future large-scale studies are needed.

F02.07 Frederik Holm Rothemejer

UTILIZING CRISPR/CAS9 TO PRODUCE ANTI-HIV CAR T CELLS

F.H. Rothemejer[1, 2, 3]

[1]Department of Infectious Diseases, Aarhus University Hospital, [2]Department of Biomedicine, Aarhus University, [3]Department of Clinical Immunology, Aarhus University Hospital

Antiretroviral therapy effectively suppresses HIV replication to undetectable levels in blood but cannot cure HIV infection due to integration of proviral DNA in memory T cells. Current efforts to cure HIV has not yet led to profound reductions in the size of the viral reservoir. Thus, there is an urgent need for novel approaches to eliminate latently infected cells. Chimeric antigen receptor (CAR) T cells have revolutionized hematological treatments and are currently being expanded to other fields. CAR T cells consist of an extracellular antigen-binding domain derived from a single chain variable fragment of an antibody fused to intracellular signaling domains. Anti-HIV CAR T cells have previously been studied in vitro but has had limited success. The previous studies have several shortcomings including ineffective targeting, exhaustion of the engineered cells, and few studies have tested the cells in vivo. The aim of this project is to utilize the site-specific gene delivery of the CRISPR/Cas9 system to produce novel anti-HIV CAR T cells by inserting the CAR cassette into specific genomic loci to evaluate the effect of these on cellular effector functions and exhaustion. As the antigen-binding domain, we will use two potent broadly neutralizing antibodies shown to suppress viremia in HIV-positive individuals. We will then produce anti-HIV CAR T cells from T memory stem cells, a highly effective T cell subset with stem cell-like properties to self-renew and differentiate. Lastly, we will test the engineered anti-HIV CAR T cells in vivo in a humanized mice model, thereby increasing the clinical translation of the results.

F02.08   Janne Møller   TRANSLATION AND INITIAL VALIDATION OF KING'S SARCOIDOSIS QUESTIONNAIRE

J. Møller[1], T.S. Prior[1], O. Hilberg[2], S.S. Birring[3], E. Bendstrup[1]

[1]Department of Respiratory Diseases and Allergy, Aarhus University Hospital, [2]Department of Respiratory Medicine, Vejle Hospital, [3]Division of Asthma, Allergy and Lung Biology, School of Transplantation, Immunology, Infection and Inflammation Sciences, Faculty of Life Sciences and Medicine, King's College London, UK

Introduction:

King's Sarcoidosis Questionnaire (KSQ) is a brief questionnaire assessing health status in patients with sarcoidosis. KSQ is developed and validated in an English sarcoidosis cohort. This study aimed to translate King's Sarcoidosis Questionnaire into Danish and conduct the initial validation.

Methods:

The questionnaire was translated into Danish following acknowledged guidelines. Initially, a forward translation was performed by two Danish native speaking translators. The two versions were merged, and consensus was reached in presence of differences between the two translations. A native English speaking translator blind to the original English version, back translated the merged version, and the original author reviewed the translation. Ten patients with sarcoidosis of different gender, age, radiologic stage and organ involvement completed the questionnaire followed by a semi-structured interview. Patient interviews were reviewed by an expert panel.

Results:

The initial translational process was smooth with only minor differences between the two forward translations. Consensus was easily reached, and the back translation was approved by the original author. Patients interviews demonstrated a high face and content validity for the Danish version of KSQ. Discussion of patient interview in the expert group did not necessitate any further adaptations of the Danish version.

Conclusions:

The translation of KSQ was easily completed. Patient interviews demonstrated high face and content validity. A study conducting further validation of the questionnaire in a Danish sarcoidosis cohort will follow the initial validation.

F03.01   Katarzyna Grycel   FUNCTIONAL AND STRUCTURAL ANALYSIS OF CRMP2 KNOCKOUT MOUSE MODEL

K. Grycel[1], J.R. Nyengaard[1], J. Midtgaard[2], Z. Xu[3]

[1]Department of Clinical Medicine, Core Center for Molecular Morphology,Section for Stereology and Microscopy, Aarhus University, [2]Department of Neuroscience, Motor Control, University of Copenhagen, [3]Institute of Genetics and Developmental Biology, Chinese Academy of Sciences

Schizophrenia is a debilitating psychiatric disease affecting many people worldwide and causes delusions, hallucinations, and other cognitive difficulties. It has been shown that brain structure is altered in Schizophrenia patients (Karlsgodt et al. 2010). Changes in brain connectivity (Kiparizoska et al. 2014) and in white matter structures (Kubicki et al. 2005) were shown. CRMP2 is a gene from the collapsing response mediator protein family, which plays a major role in axon formation. It has been shown that CRMP2 plays a role in Schizophrenia (Toyoshima et al. 2019). This project uses a tissue specific knockout model of CRMP2 in the central nervous system (Zhang et al. 2015). The model elicits schizophrenic behavioral symptoms as well as enlarged lateral ventricle consistent with Schizophrenia patients. The mice also show altered myelination, which has been linked to several neuropsychiatric disorders, Schizophrenia among others. This project investigates to what extent the myelination of CRMP2 deficient mice is affected through multielectrode electrophysiology recordings of field potentials in order to determine the conductivity of the affected brains. The focus is also on structural investigation of the largest white matter structure in the brain - corpus callosum. This part is conducted through a 3D reconstruction of electron microscopic images using a serial block-face FEI Teneo Volume Scope. Additionally, white matter structures will be investigated with fluorescent myelin staining (FluoroMyelin Red), clearing techniques and optical microscopy.

F03.02   Sine Mette   SOCIOECONOMIC DISPARITIES IN REVASCULARIZATION THERAPY FOR
          Øgendahl Buus   ISCHEMIC STROKE

S.M.Ø. Buus

Department of Neurology, Aarhus University Hospital

Background: Revascularization therapies (RT) for ischemic stroke (thrombolysis and thrombectomy) have vastly improved the prognosis after ischemic stroke. Several studies have demonstrated socioeconomic disparities in treatment and outcome after stroke. We need to investigate this matter further in order to ensure as many patients as possible to be eligible for, and subsequently receive RT, with the ultimate goal of achieving better outcomes after ischemic stroke, regardless of SES.

Methods: We will perform a cohort study on adult patients with ischemic stroke in Denmark during the years 2015 through 2018. The primary outcome is thrombolysis or thrombectomy received (yes or no), the primary exposure variable is defined by socioeconomic status measured by three different parameters (educational status, employment, and income), each presented in an ordinal categorical manner (low, medium, and high). Possible confounders will be assessed through directed acyclic graphs, and relevant confounders will be adjusted for in the final analyses. Possible confounders include: Age, sex, civil status, stroke severity, stroke etiology, comorbidity, ethnicity, hospital, smoking, alcohol, previous stroke, etc.

We will use multivariable logistic regression models to calculate risk ratios for receiving treatment. Numbers will be presented in both an unadjusted, mutually adjusted, and fully adjusted model. Mutual adjustment implies adjustment for the remaining SES parameters. We will furthermore perform separate mediator analyses to investigate the importance of

delay and anticoagulant therapy, as these could be important mediators of an association between SES and RT.

F03.03   Cecilie Siggaard Jørgensen

GENOME-WIDE ASSOCIATION STUDY OF NOCTURNAL ENURESIS IDENTIFIES RISK-LOCI ON CHROMOSOME 6 AND 13

C.S. Jørgensen[1], H.T. Horsdal[2], V.M. Rajagopal[2, 3], E. Agerbo[2], A. Børglum[2, 3], S. Rittig[1], K. Kamperis[1], J. Grove[2, 3], T.D. Als[2, 3], H. Stefánsson[4], B. Walters[4], D. Demontis[2, 3], J.H. Christensen[2, 3]

[1]1Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital, [2]iPSYCH, The Lundbeck Foundation Initiative for Integrative Psychiatric Research, [3]Department of Biomedicine, Human Genetics, Aarhus University, [4]Decode Genetics, Reykjavik, Iceland

Introduction:

Nocturnal enuresis (NE) is a common condition with a twin-based heritability estimate of 70%. Here we present the first genome-wide association study (GWAS) of NE based in iPSYCH2012. iPSYCH2012 is a large population-based Case-Cohort sample established to investigate major psychiatric disorders.

Methods:

Genotyped individuals in iPSYCH2012 included ~50,000 individuals with psychiatric disorders and 30,000 randomly selected individuals. Persons within iPSYCH2012 with NE (5-25 years) were identified either in the "The Danish National Patient Register" and "The Danish Psychiatric Central Register" based on ICD10 codes, or in the "The Danish National Prescription Registry" based on desmopressin prescriptions (3,882 NE cases and 31,073 controls). The GWAS was performed using logistic regression including relevant covariates e.g. psychiatric disorders.

Results:

We identified six common variants surpassing genome-wide significance in two independent loci. We estimate the NE liability scale single nucleotide polymorphism heritability to be 0.239-0.304 (P = 2.2×10^{-16}). In subsequent evaluation, our findings did not seem to be caused by comorbid psychiatric disorders. Our main results were replicated in an independent Icelandic cohort. 12 potential risk genes were mapped, which are important transcriptional regulators of neurodevelopment. PRDM13, SIM1, and EDNRB are of particular interest as they all have biological functions related to previously identified NE pathophysiological mechanisms.

Conclusion:

This study further demonstrates that NE has a strong genetic component and suggests that GWASs with larger sample sizes are likely to uncover more risk variants.

F03.04   Kirsten Nordbye-Nielsen   **RELIABILITY OF THE DANISH CHALLENGE: AN ADVANCED MOTOR SKILLS TEST FOR CHILDREN WITH CEREBRAL PALSY**

K. Nordbye-Nielsen[1, 2], T. Maribo[3], V. Wright[4, 5], O. Rahbek[1], B. Møller-Madsen[1, 2]

[1]Childrens Orthopaedics Research Department, Aarhus University Hospital, [2]Department of Clinical Medicine, Aarhus University, [3]Central Region Denmark, DEFACTUM, [4]University of Toronto, [5]Holland Bloorview Rehabilitation Hospital, Toronto, Canada

AIM: We translated and investigated the Reliability of the Challenge, a measurement of advanced motor skills in Danish children with cerebral palsy(CP)

METHOD: The Challenge was translated into Danish. Inter-rater studies were conducted with 45 participants, 19 girls, 26 boys; 5-18 y: mean (SD) 10 y 9 mo (4y) at Gross Motor Function Classification System (GMFCS) levels I and II. Forty-five children completed the Challenge of whom 15 children had their assessments video recorded for inter-rater reliability. Twenty-two children were assessed twice for test-retest reliability. We calculated ICC correalation coefficients for Inter-rater reliability on live assessments, from video recorded versus live assessments as well as from test-retest assessments. Minimal Detectable Change score (MDC_{90})was estimated. Four assessors scored the assessments.

RESULTS: Inter-rater reliability, Test-retest and Minimal Detectable Change (MDC90) estimates is to be reported on the Ph.d. Day

INTERPRETATION: This study calculated reliability of the Challenge after translation. Our results revealed ICC´s these have to be compared with results found in the original study. MDC_{90}estimated seems clinically relevant for interpretation. Physiotherapists can use the Challenge in live and video recorded assessments, after passing criterion-based training.

F03.05   Tobias Glaston Stærmose   **UNDERSTANDING ALS THROUGH MAGNETISM - A PRELIMINARY LOOK AT THE PLANS FOR THIS MEG BASED PHD-STUDY.**

T.G. Stærmose, J.U. Blicher

Center of Functionally Integrative Neuroscience, CFIN, Department of Clinical Medicine, Aarhus University

Introduction: Amyotrophic lateral sclerosis (ALS) is a motor neuron disease, in which loss of neurons in both the brain and in the spinal cord is the predominant characteristic. The pathogenesis of ALS is unknown and patients with ALS have various degrees of progressing loss of motor function, usually starting in a hand, a leg or in the bulbar muscles. This can quickly (years) progress to total loss of motor function and lead to death due to respiratory muscular failure. Currently there is no biomarker for ALS, and it is a clinical exclusion diagnosis, this often leads to a diagnostic delay of more than one year.

Objective: Understanding the changes in brain signals as ALS progresses, with the potential for future improvement to the now clinical diagnosis.

Methods and Goals: Aarhus University Hospital have the only Magnetoencephalography (MEG) scanner in Denmark. Using MEG in combination with EEG and MRI we hope to learn more about the

progression of ALS as well as new technics for classification of ALS. Furthermore, we plan to follow the patients with multiple scans as well as clinical assessments for up to 12 months in a longitudinal part of the study.

Taking advantage of the improved spatial signals from MEG we hope to more accurately pin point areas of disease progression and potentially predict progression before clinical signs to help improve the care of the patients.

Scanning patients at the time of referral (before the final diagnosis) will potentially also allow us to classify true ALS and mimics of ALS thus shortening diagnostic delay and allow for earlier treatment in the future.

F03.06   Alana Miranda Pinheiro

INJURY- RESPONSE OF SATELLITE GLIAL CELLS AND THEIR POTENTION AS TARGETS IN NEUROPATHIC PAIN TREATMENT

A.M. Pinheiro, C.B. Vægter, L.T. Pallesen

Department of Biomedicine, Aarhus University

Satellite glial cells (SGC) enclose the peripheral sensory neurons and are believed to modulate neuronal function at Neuropathic Pain (NP) conditions. NP is a poorly understood pathology that results from injury to or diseases of the peripheral sensory nerves, affecting 600 million people worldwide. SGCs respond to nerve injury by inducing activation of neighbor neurons, representing a new form of neuronal plasticity in the DRG contributing to pain hypersensitivity. Despite SGC participation at the pain pathway, little is known about the molecular details underlying the SGC-neuron crosstalk. Aiming to investigate how SGC respond to neuronal injury here will be established a combined transcriptional (scRNAseq) and proteomic (Mass Spectometry- MS) approach to identify regulated SGC genes and proteins after nerve injury. scRNAseq will uncover mRNA of rare and most complex SGC subpopulations and MS will add understanding of functional changes and the necessary strategies for targeted therapy. Additionally, due to these cells strategic location and function it will be explored SGC potential as a target to attenuate neuronal hyperactivation that might result in mechanical hyperalgesia. Meteorin (METRN), a novel SGC-targeting drug, will be investigated. Calcium imaging will be used as functional set up to analyze how METRN affects SGCs and how METRN- stimulated SGCs modulates neuronal signaling and function. Thus, representing a breakthrough at the NP therapy which currently available drugs are only restricted to symptomatic treatment. Data from this project will add significant insight into glia cells and potentially targets for the treatment of peripheral neuropathies.

F03.07   Kathrine Abildskov Friis

IN VITRO INVESTIGATION OF THE ROLE OF NCBE IN INFLAMMATION INDUCED CEREBROSPINAL FLUID HYPERSECRETION OF THE CHOROID PLEXUS

K.A. Friis, L.Ø. Johnsen, J. Praetorius, H.H. Damkier

Department of Biomedicine, Aarhus University

Introduction: Hydrocephalus is a well-known complication to subarachnoid hemorrhage (SAH) and is caused by an increased volume

of cerebrospinal fluid (CSF). CSF is mainly produced by the choroid plexus (CP) in the blood CSF barrier (BCSFB). It is known that SAH leads to inflammation of the CP that increases secretion of CSF. In rats the abundance of the $Na^+:HCO_3^-$ exchanger NCBE in CPE increases after SAH leading to the increased CSF production. This increased expression of NCBE may be mediated by the NF-Kβ pathway known to increase CSF-secretion after hemorrhage.

Hypothesis: Inflammation of the CPE increases expression of NCBE which causes an increased rate of CSF secretion similar to SAH-induced CSF hypersecretion. Inhibition of NCBE or the NF-Kβ pathway after an inflammatory response in the CPE leads to a decreased rate of CSF secretion, making it a potential target for treatment of hydrocephalus secondary to SAH.

Methods: In an in vitro model of the BCSFB we will imitate an SAH inflammatory response using proinflammatory cytokines, IL-1, IL-6 and TNFα. The expression of NCBE will be evaluated by qPCR, western blot and immunocytochemistry. The therapeutic effect of an NCBE- and NF-Kβ inhibitor is tested using siRNA targeting NCBE and Triptolide. To investigate if the NF-Kβ pathway mediates the expression of NCBE, the NF-Kβ pathway is inhibited followed by stimulating NCBE with TNFα.

Perspectives: If the hypothesis of this study can be substantiated, further investigations into the role of NCBE and NF-Kβ in the development of hydrocephalus secondary to SAH will elaborate the possibility of using NCBE and NF-Kβ pathway as future treatment targets.

F03.08   Helene Honoré   CRITERION VALIDITY OF AN ACCELEROMETER-BASED METHOD TO MONITOR PHYSICAL ACTIVITY IN DAILY LIFE ACTIVITIES AFTER ACQUIRED BRAIN INJURY

CANCELLED

H. Honoré

Hammel Neurorehabilitation Center and University Research Clinic

Background

Rehabilitation of physical function and activity performance are key elements in interdisciplinary rehabilitative interventions after acquired brain injury (ABI). Accelerometry is a novel technology frequently used to assess performed activity in a non-intrusive way. However, the validity of accelerometer algorithms varies, and the reliability of accelerometry measurement in both hospital and home-life settings remains largely unexplored. Consequentially, no accurate method exists to assess physical activity in during daily life activities following ABI. An algorithm to classify activity and activity intensity from accelerometer data was recently developed and automated on a sample of healthy people. Yet, the sensitivity and predictive value for people with ABI is unestablished.

Objective

To validate the psychometric sensitivity of an accelerometer-based activity monitor in a population of patients with ABI in a natural activity setting.

Methods

The sensitivity and predictive value of activity classifications and activity intensity will be determined for a group of 20-30 patients with ABI admitted to Hammel Neurorehabilitation Center and University Research Clinic. Activity monitoring will be performed mounting an accelerometer with non-allergenic tape on the lateral side of each participant's dominant or least affected leg while the patients performs daily life activities like walking, standing, sitting or lying down in a 15 minutes protocol.

F03.09 Anette Bach Jønsson

EFFECTS OF BLOOD FLOW RESTRICTED EXERCISE ON QUALITY OF LIFE, PHYSICAL FUNCTION AND NEUROMUSCULAR RECOVERY IN INDIVIDUALS WITH SPINAL CORD INJURY - A RANDOMIZED CONTROLLED TRIAL

A. Jønsson[1, 4], P. Aagaard[2], J. Blicher[3], H. Kasch[1, 4]

[1]Spinal Cord Injury Centre of Western Denmark, Viborg Regional Hospital, [2]Sport and Science and Clinical Biomechanics, University of Southern Denmark, [3]Center of Functionally Integrative Neuroscience, Aarhus University, [4]Department of Clinical Medicine, Aarhus University

Spinal cord injury (SCI) is a life-changing devastating condition. SCI implies reduced quality of life (QoL) and physical functioning (PF). Improvement of residual motor function and prevention of muscle loss are pivotal for a successful recovery. Low-intensity blood-flow restricted exercise (BFRE) is a promising new and safeform of low-tension muscle training. Increased muscle strength, hypertrophy and improved PF have been reported with BFRE in other patient groups with motor disability. Study Aim: To investigate the effects of BFRE on PF, QoL and neuromuscular recovery in tetraplegic SCI patients. Material and Methods: The study is designed as a double-blinded RCT with 12 participants allocated to pneumatic limb occlusion (BFRE group) and 12 participants assigned to sham BFRE (control group). Inclusion criteria are: Admitted at SCIWDK, diagnosis tetraplegia>1 month, 18-<70 years of age, grades 2,3 or 4 muscle function of the elbow flexors and wrist extensors. Exclusion criteria: severe arteriosclerosis, substance abuse, mental illness, coronary arterial disease, uncontrolled hypertension, autonomic dysreflexia, DVT, Ehlers-Danlos Syndrome, Marfan's Syndrome and day-time assisted ventilation. The intervention period will consist of 8 weeks of BFRE twice a week with follow-up assessments performed at 4, 8 and 12 weeks. Intervention is add-on to standard PT/OT rehabilitation procedures. Discussion: The study is expected to document the effect of BFRE in SCI patients on PF, QoL, muscle strength and hypertrophy, level of spasticity, pain, use of medication in addition to TMS measures of brain and spinal plasticity. The study is expected to be finalized in August 2021.

F03.10 Frederik Junge Egersgård

THE VASOACTIVE EFFECTS OF SEMAGLUTIDE ON PORCINE RETINAL RESISTANCE VESSELS EX VIVO

F.J. Egersgård, C. Ernst, T. Bek

Department of Ophthalmology, Aarhus University Hospital

Aim

Diabetic retinopathy is among the leading causes of visual loss in the Western World. It is characterised by retinal lesions leading to disturbances in retinal blood flow.

The GLP-1 analogue semaglutide is being used to control blood glucose levels in type 2 diabetic patients and has shown to protect against multiple systemic complications however at the expense of an increased occurrence of retinal complications. It is possible that these retinal complications are related to possible effects of the drug on retinal vessels. Therefore, the purpose of this study was to evaluate the vasoactive effects of semaglutide on retinal vessels.

Methods

The primary arteriole of a porcine retina (n=8) was cannulated and mounted in a specially designed tissue chamber. The retinal vasculature was perfused and recorded by a fluorescence microscopy during application of semaglutide intravascularly. The microscope allowed for diameter recording of retinal arterioles (<25 μm), precapillary arterioles (10-25 μm) and capillaries (<10 μm).

Results

Preliminary data suggest that intravascular application of semaglutide dilated retinal vessels in both arterioles (6.8% 95% CI 4.0%-9.7%) and precapillary arterioles (12.5% 95% CI 0%-25.6%). It appeared that there was no vasoactive effect at the capillary level.

Conclusion

From the preliminary data it appears that semaglutide applied intravascularly dilates porcine retinal vessels and that this effect is different between the 3 selected branching levels. Further studies will determine whether the vasoactive effects are mediated by different mechanisms.

Acknowledgements

F04.01   Rasmus Eich Hammer   THE EFFECT OF RECOMBINANT BOTULINUM NEUROTOXIN A ON NEUROPATHIC PAIN IN SPARED NERVE INJURY MOUSE MODEL

R.E. Hammer[1], M. Richner[2], C.B. Vaegter[2, 3], P. Karlsson[1, 4], J.R. Nyengaard[1, 5]

[1]Core Center for Molecular Morphology, Section for Stereology and Microscopy, Department of Clinical Medicine, Aarhus University, [2]Danish Research Institute of Translational Neuroscience, Nordic EMBL Partnership for Molecular Medicine, Department of Biomedicine, Aarhus University, [3]The International Diabetic Neuropathy Consortium, Aarhus University Hospital, [4]Danish Pain Research Center, Department of Clinical Medicine, Aarhus University, [5]Center for Stochastic Geometry and Advanced Bioimaging, Aarhus University

Background and aims

Neuropathic pain is a debilitating chronic pain disorder characterized by sensory abnormalities such as dysesthesia, hyperalgesia and allodynia. Diabetic polyneuropathy (DPN) and traumatic nerve injury are some of the

most common causes of neuropathic pain. The Db/Db model and the Spared Nerve Injury (SNI) model are validated animal models mimicking DPN and traumatic nerve injury, respectively. Published data indicate that botulinum toxin A (BoNT/A) has analgesic effects against peripheral neuropathic pain. This project aims to assess whether recombinant BoNT/A has analgesic effect on the two mouse models representing neuropathic pain.

Methods

A total of 64 mice will be used (32 control mice (C57BL/6) and 32 Db/Db mice). In each group, 16 mice will be SNI operated while the remaining 16 will be sham-operated. In each group of 16, eight will receive either vehicle or 3.2 pg BoNT/A pr. mouse. Pain threshold will be assessed using Von Frey filaments and possible effects on the spinal cord, sciatic nerve, dorsal root ganglion and brain will be evaluated using immunohistochemistry and quantitative light and electron microscopy.

Results

This is an ongoing study and the final results will be presented at the conference. We hypothesize that recombinant BoNT/A treatment will have analgesic effect on both mouse models of neuropathic pain, compared with littermates that received placebo.

Conclusions

If the hypotheses hold, this project will potentially lay the groundwork for clinical testing in human patients with neuropathic pain.

F04.02   Hamed Zaer   A NEW PORCINE MODEL FOR NEUROMODULATORY BRAIN RADIOSURGERY

H. Zaer[1], A. Nørgaard Glud[1], M.B. Schneider[3, 4, 6], E.S. Worm[5], M.B. Jensen[5], R. Hansen[5], L. Hoffmann[5], J.R. Adler[6, 3], M. Høyer[2], J.C. H. Sørensen[1], D. Orlowski[1]

[1]Centre of Experimental Neuroscience (Cense), Department of Neurosurgery, Aarhus University Hospital and Department of Clinical Medicine, Aarhus University, [2]Danish Center for Particle Therapy, Aarhus University Hospital, [3]Department of Neurosurgery, Stanford University School of Medicine, [4]Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, [5]Department of Oncology and Radiation therapy, Aarhus University Hospital and Department of Clinical Medicine, Aarhus University, [6]Zap Surgical Systems, Inc., San Carlos, California, USA

Introduction

Stereotactic radiosurgery has been used for decades in the treatment of epilepsy, arteriovenous malformation, and tumours to ablate the unhealthy tissues. However, some therapeutic radiation-induced changes in the remaining living cells is observed. Modulation of the neuronal activity without provoking the apoptosis/necrosis requires knowledge of radiation dose-tolerance in small tissue volumes. Thus, we aimed to document the thresholds for late-onset cell death after delivering high doses of irradiation to small brain volumes.

Methods

Six female Gottingen minipigs were used. The baseline MRI and PET were acquired. Five animals were irradiated stereotactically in the left primary motor cortex and the right cortical white matter. One animal remained as control. Follow-up MRI and PET scans were done at three weeks, three and six months post-irradiation. The histological analysis was done at 6 months post-radiation after euthanization and tissue fixation.

Results

We observed a dose-dependent gradient of cellular reaction to the radiation and spreading of inflammatory changes along the neural tracts in white matter. Necrotic changes in both MRI and histology were seen at 6 months post-radiation. The threshold of radio-destructive lesions was 100 Gy in cortical grey matter, and 60 Gy in white matter.

Conclusion

In this study, we defined the threshold of radiation-dependent necrotic changes in the brain. Radiosurgery has both direct dose-dependent effect and possibly indirect neuromodulatory effects. Neuromodulatory responses to radiation may be mediated by vascular changes, endogenous immunoreactive agents, as well as neuronal cell changes and glial cell remodelling.

F04.03   Anna Krogh Andreassen

A DEVELOPMENTAL PERSPECTIVE OF WORKING MEMORY IN CHILDREN AT FAMILIAL HIGH RISK OF SCHIZOPHRENIA OR BIPOLAR DISORDER - THE DANISH HIGH RISK AND RESILIENCE STUDY

A.K. Andreassen[1, 2], N. Hemager[2], A.N. Greve[1, 2], C.B. Knudsen[1, 2], L. Veddum[1, 2], J.M. Brandt[2, 3], M.F. Krantz[2, 3], M. Gregersen[2, 3], A. Søndergaard[2, 3], A.H. Carlsen[5], R. Lambek[8], J. McGrath[6, 7], A.E. Thorup[2, 4], M. Nordentoft[2, 3], O. Mors[1, 2], V.F. Bliksted[1, 2, 5]

[1]Psychosis Research Unit, Aarhus University Hospital, [2]The Lundbeck Foundation Initiative for Integrative Psychiatric Research, iPSYCH, [3]Mental Health Centre Copenhagen, Copenhagen University Hospital, Mental Health Services Capital Region, [4]Child and Adolescent Mental Health Center, Mental Health Services, Capital Region of Denmark, [5]Department of Clinical Medicine, Medical Sciences, Aarhus University, [6]National Centre for Register-based Research, Department of Economics and Business Economics, Aarhus University, [7]Queensland Brain Institute, University of Queensland, St Lucia, Queensland, Australia, [8]Department of Psychology, Aarhus University

BACKGROUND

It has been found that children at familial high risk of schizophrenia (FHR-SZ) have working memory (WM) deficits. This has not been found in children at familial high risk of bipolar disorder (FHR-BD). Deficits in working memory have been suggested to be part of a transdiagnostic phenotype associated with adverse outcomes, e.g. daily functioning. The development of aspects of working memory as a phenotype for schizophrenia is not thoroughly understood and have not been examined in a large cohort within a narrow age range.

OBJECTIVES

Aims:

1) Investigate the development of WM from age seven to age 11 across familial high risk groups in schizophrenia or bipolar disorder compared to population based controls (PBC).

2) Investigate if deficits in aspects of WM at age seven predicts lower level of daily functioning at age 11.

METHODS

VIA 11 is part of a nationwide cohort study - The Danish High Risk and Resilience Study consisting of 522 children who are either FHR-SZ (N=202), or FHR-BP (N=120) or PBC (N=200). The data collection ends summer 2020. WM is assessed using validated and age-appropriate neuropsychological tests targeting both spatial and verbal abilities, along with a multi-informant questionnaire.

RESULTS

At age seven children at FHR-SZ showed deficits in WM compared to PBC, while children at FHR-BP did not. We expect that deficits in working memory will remain stable at age 11 and that deficits in working memory at age seven will predict lower level of daily functioning at age 11.

PERSPECTIVES

We hope to enhance current knowledge about the development in deficits in WM in children at FHR-SZ and FHR-BP and the relation to daily functioning.

F04.04   Nadia Flensted   MUSIC AS A TREATMENT FOR PREGNANCY-RELATED INSOMNIA: A
         Høgholt   SYSTEMATIC REVIEW AND META-ANALYSIS

N.F. Hoegholt, K.V. Jespersen, A.B.A. Stevner, H.M. Fernandes, P. Vuust, M.L. Kringelbach

Center for Music in the Brain, Department of Clinical Medicine, Aarhus University and Hedonia: Transnational Research Group, Department of Psychiatry, the University of Oxford, UK, and The Royal Academy of Music Aarhus/Aalborg

Background: About 50-60% of all pregnant women suffer from insomnia during pregnancy. Pregnancy-related insomnia is associated with severe outcomes for both mother and child postnatally. This systematic review aims to evaluate the effectiveness of music listening as a means of treating pregnancy related insomnia.

Methods: We searched on 8 different electronic databases during March 2018. After screening and reviewing 303 studies only 2 randomized controlled trials testing the effect of music listening on insomnia were ultimately included. The risk of bias was analysed following the guidelines from Cochrane Handbook for Systematic Reviews of Interventions. The quality of the evidence was assessed using Grades of Recommendations, Assessment, Development and Evaluation(GRADE) and entered in the Gradepro 2014 software. Finally, a meta-analysis on the primary outcome, Pittsburgh Sleep Quality Index (PSQI), was carried out on the included studies using Review Manager version 5.3.

Results: All included studies had at least one domain with high risk of bias and were all graded as moderate quality of evidence. The meta-analysis showed an overall effect of a decrease in PSQI score of -1.93 (-3.29; -0.56) and a heterogeneity of $I^2 = 70\%$, indicative of a significant improvement in subjective sleep quality with greater effect over time.

Conclusion: Despite the moderate quality and sparse amount of studies on music treatment for pregnancy-related insomnia, our findings support the hypothesis of a beneficial effect of music listening for 2-4 weeks at bedtime in the third trimester. Furthermore, it seems that music listening at bedtime has an accumulating effect on insomnia symptoms.

| F04.05 | Kamilla My Thanh Lê Truong | CRYONEUROLYSIS' OUTCOME ON PAIN EXPERIENCE - A RANDOMIZED CONTROLLED BLINDED TRIAL |

K. Truong

Center for Experimental Neurosciense (CENSE), Aarhus University Hospital

BACKGROUND: Low back pain affects 800.000 people in Denmark. A review from 2007 found moderate evidence for short and long-term pain relief by cryoneurolysis on lumbar medial branch nerves. This study aims to investigate the effect of cryoneurolysis in lumbar facet joint pain syndrome and to compare it to standard treatments whilst investigating whether pre-defined parameters are independent factors for outcome.

METHODS: Participants will be recruited from Aarhus University Hospital and Silkeborg Spine Center. Eligible participants will be evaluated further according to anamnesis and neurology, MRI or CT confirming degenerative facet joint and diagnostic anesthetic block on the facet joint pain generator. If NRS score is reduced by >50% within 1 hour, they will be enrolled. A total of 315 participants will be randomized into 3 groups to undergo either one treatment of cryoneurolysis (cryo), radiofrequency ablation (RFA) or same setup but no active treatment (placebo). All groups will receive physiotherapy for one month. The primary outcome measure is the Numeric Rating Scale (NRS). Furthermore, Oswestry Disability Index, EQ-5D, SF-36, Patient Global Impression of Change, Pain Catastrophizing Scale and Major Depression Inventory. All measures are assessed at baseline and follow-up at day 1 and 1, 3, 6, and 12 months.

RESULTS: All forms will be collected in the Aarhus University REDCap database. T-test will be used on the group of units (Cryo, RFA or Placebo) that will be tested twice, before and after intervention to eliminate random between-patient variation.

CONCLUSION: Cryoneurolysis may be an alternative treatment option to patients with lumbar facet join pain syndrome.

| F04.06 | Caroline Juhl Arnbjerg-Nielsen | PSYCHOEDUCATION FOR PATIENTS WITH BIPOLAR DISORDER IN RWANDA |

C.J. Arnbjerg[1], E. Musoni-Rwililiza[1], D. Gishoma[2], L. Nyirazinyoye[2], J. Carlsson[3], P. Kallestrup[1]

[1]Center for Global Health, Department of Public Health, Aarhus University, [2]College of Medicine and Health Sciences University of Rwanda, [3]Competence Centre for Transcultural Psychiatry (CTP), Mental Health

Centre Ballerup, Ballerup and Department of Clinical Medicine, University of Copenhagen

Background: Mental health- and neurological disorders constitute 13% of the global burden of disease. Alarmingly this burden has risen by 41% in the last 20 years. In low-and-middle-income countries as few as 10% of people living with bipolar disorder receive care. In western countries the efficacy of psychoeducation, as an add-on treatment to pharmacotherapy in the treatment of symptoms and in relapse prevention initiatives with respect to bipolar disorder, is well documented. Yet, no studies on psychosocial interventions for bipolar disorder have been conducted in a low-income country.

Aim: To determine the effect, feasibility and acceptability of psychoeducation for patients with bipolar disorder on all three levels of the health care system in Rwanda - at the community health centre, district- and university hospital.

Methods: Patients will be randomized into either group A) group-psychoeducation at a referral hospital; or B) group-psychoeducation for both patients and relatives or C) waiting list. Moreover a district trial and a community trial will test the impact and feasibility of psychoeducation at the district and community level.

Outcomes: Reduction in symptom severity and incidence of relapse, improved quality of life, medical adherence and knowledge, as well as reduced self-stigmatization.

Perspectives: If proven successful, this is of importance for closing the huge treatment gap in mental health particularly affecting low- and middle-income countries and may reduce the mortality and increase quality of life in the population suffering from bipolar disorder. Furthermore, potential positive outcomes may be implemented in similar low-resource settings elsewhere.

F04.07 Maiken Krogsbæk Mikkelsen

THE EFFECT OF OLANZAPINE TREATMENT ON THE FEEDING REGULATING REGIONS OF HYPOTHALAMUS

M.K. Mikkelsen1, N.Y. Larsen1, C.S. Sanchez2, 3, J.R. Nyengaard1

1Section for Stereology and Microscopy, Clinical Medicine, Aarhus University, 2Translational Neuropsychiatric Unit, Clinical Medicine, Aarhus University, 3Alkermes Inc., Boston, USA

Olanzapine (OLZ) is the most commonly used 2. generation antipsychotic for the treatment of schizophrenia. Although OLZ has reduced extrapyramidal side effects compared to 1. generation antipsychotics, other side effects include increased feeding, decreased activity, obesity and metabolic dysfunction.

We have treated rats with OLZ for 48 hours and 28 days to investigate the acute and chronic side effects of OLZ on the hypothalamus. It is postulated that feeding regulating nuclei in this area are effected by OLZ, thus partaking to the observed side effects. Using immunohistochemical stains targeting different neuron subtypes (POMC, NPY, MC4R, Orexin A, MCH etc.), we are studying OLZs effect on neuron number and local neuron size of hunger and satiety stimulating neurons. In addition, using autoradiography we will study if the expression of opioid receptors are

changed as an effect of OLZ treatment. Opioid antagonistic treatment combined with OLZ leads to reduced weight gain compared to OLZ treatment alone. It will therefore be interesting to see if OLZ secondary causes dysfunctional opioid receptor signaling in the hypothalamus.

There is significant and constantly increasing weight gain and food intake after 72 hours of OLZ treatment. However, food intake stagnates to control levels after 14 days of treatment, and increased hunger stimulation are not believed to be solely responsible for the increased weight observed. Blood glucose levels are significantly increased after 48 hours of OLZ treatment indicating systemic metabolic changes.

Results from this study could help in the future creation of co-treatment strategies to reduce the debilitating side effects of OLZ treatment.

| F04.08 | Maja Fuhlendorff Jensen | GUT-FIRST AND BRAIN-FIRST PARKINSON'S DISEASE - STUDIES IN ANIMAL MODELS AND PRODROMAL HUMAN TISSUE SAMPLES |

M.F. Jensen, N.V.D. Berge, P. Borghammer

Department of Nuclear Medicine and PET-Centre, Department of Clinical Medicine, Aarhus University

Parkinson's disease (PD) is the second most common neurodegenerative disease and characterized by Lewy pathology consisting of alpha-synuclein (asyn)-enriched aggregates. These pathological, aggregated asyn (pAS) assemblies are believed to self-amplify and spread in a prion-like manner through neural connections by recruiting endogenous asyn protein. It has been postulated that pAS starts in the enteric nervous system (ENS) years before diagnosis and spreads to the brain through the autonomic nervous system. However, not all PD patients show pAS pathology in the ENS. An ongoing multi-modality imaging study of human patients conducted by my main supervisor indicates that PD can be divided into two subtypes: a gut-first subtype where the pAS arises in the gut and spreads to the brain, and and a brain-first subtype where the pAS arises in the brain and spreads to the gut. This project aims to study several aspects of PD etiology: (1) To create gut-first and brain-first rat models of PD by injecting preformed asyn fibrils (PFF) into the gut and the amygdala, respectively. (2) To study archived human gut tissue from PD patients, prodromal PD patients and matched healthy controls from the Danish Pathology Bank (PATOBANK). (3) To compare inflamed vs. non-inflamed appendices from PATOBANK from healthy controls and PD patients. These studies will improve our understanding about how and why ENS pAS may lead to PD in some conditions but not others. If the gut- and brain-first rat models closely resemble the evolution of symptoms and neuronal damage in PD patients, these models may be very useful for further studies of PD pathogenesis and for testing neuroprotective drugs.

| F04.09 | André Dias | DYNAMIC WHOLE BODY FDG PET/CT - NEXT GENERATION FUNCTIONAL IMAGING |

A.H. Dias, O.L. Munk, L.C. Gormsen

Department of Nuclear Medicine and PET Center, Aarhus University Hospital

Project Presentation:

Positron Emission Tomography (PET) using the glucose analog 2-deoxy-2-[18F]fluoro-D-glucose (FDG) is a mainstay of diagnostic work-up and treatment response in most malignancies.

FDG is taken up and phosphorylated by glucose consuming cells by the same membrane transporters and enzymes as endogenous glucose but does not undergo regular glycolysis, becoming retained in the cells. PET scans are usually performed as a 10-min static scan one hour after injection of FDG and thus represents a 'snapshot' of the distribution of glucose at a single late time-point.

This qualitative reading of the PET images is often supplemented by a semiquantitative assessment of glucose uptake, the standardized uptake value (SUV) but due to several technical drawbacks it has so far proved impossible to reach international agreement on what level of FDG uptake should be considered malignant.

These challenges can be overcome by dynamic parametric FDG PET/CT, where time-related changes in tissue radioactivity are detected throughout the entire duration of a 70-min scan. This scan protocol allows imaging of the metabolic rate of glucose and distribution volume of non-metabolized FDG that are less prone to inter-institutional variation and agreement on threshold values is therefore feasible. So far translation of this technique to a clinical setting has primarily been limited by the complexity of concurrent blood sampling and the long scan time.

The general purpose of this PhD project studies is to simplify the acquisition of dynamic parametric FDG PET/CT and to evaluate whether parametric FDG PET/CT improves diagnosis and treatment monitoring in select diseases.

F04.10 Casper Skjærbæk

DOES PARKINSON'S DISEASE START IN THE GUT - AN ESOPHAGEAL TRANSIT AND INTESTINAL DYSFUNCTION STUDY

C. Skjærbæk, K. Knudsen, P. Borghammer

Department of Nuclear Medicin and PET, Aarhus University Hospital

Parkinson's Disease (PD) is a neurodegenerative disease clinically characterized by bradykinesia, tremor and rigidity. Yet, non-motor symptoms including constipation and dysphagia are common. According to the body-first hypothesis PD may originate in the gastrointestinal tract and spread to the brainstem. Predilection sites for PD-related pathology include the vagal nerve and the lower part of the esophagus. However, most structures innervated by the autonomic nervous system are affected.

We aim to validate esophageal scintigraphy as a method for detecting esophageal dysfunction in early PD. Furthermore, we will study potential correlations among objective and subjective measures of gastrointestinal dysfunction. We hypothesize that dysfunction of the lower esophagus and colon will correlate and be markedly more prevalent in patients. Subjective measures are expected to underestimate the prevalence.

30 early-stage PD patients and 28 healthy controls (HC) are included. In addition to esophageal scintigraphy, colonic transit and volume are determined by CT-scanning after radio opaque marker ingestion. We

carry out olfaction tests, motor symptom evaluation and several questionnaires.

Here, we present preliminary data from 14 PD and 14 HC. These analyses indicate prolonged transit time in the lower part of the esophagus. By January 1st, we expect to have analyzed 30 PD and 28 HC.

The importance of investigating the gastrointestinal tract in PD is underlined if final conclusions from this study confirms that a subgroup of patients has widespread, clinically unrecognized gastrointestinal dysfunction in early stages of PD.

F05.01   Anne Østergaard Nannsen   "THE EFFECT OF LOW INTAKE OF NON-STARCHY VEGETABLES ON RISK OF COLORECTAL CANCER"

A.Ø. Nannsen[1], B.V. Andersen[2], K. Overvad[1], A. Olsen[3], A. Tjønneland[3], C.C. Dahn[1]

[1]Department of Public Health, Aarhus University, [2]Department of Food Science, Aarhus University, [3]Institute of Cancer Epidemiology, Danish Cancer Society

Aim: This study aims to investigate sustained low intakes of non-starchy vegetables and the risk of colorectal cancer.

Background: By 2018, colorectal cancer (CRC) was the third most common cancer in the world with over 1.8 million incident cases, only preceded by lung and breast cancer. Adequate consumption of vegetables may protect against cancer, partly due to high fibre content, folate, vitamin B, minerals and high antioxidant potential. Specifically non-starchy vegetables has been associated with decreased risk in CRC. The American Institute for Cancer Research (AICR) reported a significantly decreased risk of CRC for intakes of non-starchy vegetables above 300 g/day compared to intakes below 100 g/day, after adjusting for known risk factors such as red meat consumption and smoking.

Method: The study population comprised 57,053 people ages 55-64 living in Denmark at the time of invitation. Data on non-starchy vegetables was collected in a 192-item food frequency questionnaire (FFQ) mailed to each participant prior to their first visit to a study centre at baseline (1993-1997) and at follow up (1999-2002). Register linkage concerning incident CRC was performed via CPR-register, using definitions of CRC based on the International Classification of Diseases (ICD). Hazard ratios (HR) of CRC related to non-starchy vegetables will be estimated using crude and adjusted cox proportional hazard regression model.

Results: Results from the data analysis are expected primo 2020.

Keywords: vegetables, diet, colon cancer, rectal cancer, cohort study.

F05.02   Frederik Pagh Kristensen   STATIN THERAPY AND RISK OF NEUROPATHY IN DIABETES: A POPULATION-BASED COHORT STUDY

F.P. Kristensen[1, 2], D.H. Christensen[1, 2], B. Callaghan[2, 3], S.T. Knudsen[4], S.H. Sindrup[2, 5], E. Feldman[2, 3], L. Østergaard[2, 7], H. Andersen[2, 6], T.S. Jensen[2, 6], H.T. Sørensen[1], R.W. Thomsen[1]

[1]Department of Clinical Epidemiology, Department of Clinical Medicine, Aarhus University Hospital, [2]International Diabetic Neuropathy Consortium, Department of Clinical Medicine, Aarhus University, [3]Department of Neurology, University of Michigan, Ann Arbor, USA, [4]Steno Diabetes Center Aarhus (SDCA), Aarhus University Hospital, [5]Department of Neurology, Odense University Hospital, [6]Department of Neurology, Institute of Clinical Medicine, Aarhus University Hospital, [7]Department of Neuroradiology, Aarhus University Hospital

Aim

Diabetic polyneuropathy (DPN) affects up to 50% of all diabetes patients. Statin therapy may prevent DPN by lipid-lowering and pleiotropic anti-inflammatory effects, however, previous studies have suggested both decreasing and increasing risk of DPN with statin therapy. Thus, the association of statin therapy with risk of DPN remains uncertain.

Methods

We linked population-based medical databases to conduct a 15-year cohort study including all adult diabetes patients in Denmark, 2002-2016. Diabetes diagnosis was defined as the first occurrence of either a hospital contact for diabetes or a prescription of a glucose-lowering drug. Statin use was defined as ≥1 statin prescription within 180 days prior to and 180 days after first diabetes diagnosis and dived into new use (first-ever statin prescription within that period) and prevalent use (first statin prescription prior to that period). We followed patients from 180 days after initial diabetes diagnosis until first-time DPN, death, emigration, or study end, using Cox proportional hazard regression analysis to adjust for confounding factors.

Results

Among 282,292 incident diabetes patients, 59,641 (21%) were statin new users, and another 75,587 (27%) were prevalent statin users. Over a median follow-up of 6.3 years, incidence rates per 1000 person-years were 4.0 for new-users, 3.7 for prevalent users, and 3.5 for never users of statins. The adjusted hazard ratio for DPN was 1.04 (95% CI, 0.98-1.11) in new users and 0.95 (95% CI, 0.89-1.01) in prevalent users, as compared with never statin users.

Conclusion

Statin therapy, initiated before or around the time of diabetes diagnosis, was not associated with risk of subsequent DPN.

F05.03   Katrin Debes   DESCRIPTION OF SPORTS INJURY RATE OVER TIME: IS IT APPROPRIATE TO
          Kristensen   EXCLUDE SUBSEQUENT EVENTS?

K. Debes-Kristensen

Department of Public Health, Sports Science, Aarhus University

In sports, athletes often sustain multiple injuries over time. Despite this, much research on sports injuries analyses only the time until first sports injury when describing injury occurrence over time. This procedure may, however, lead results to be underestimated due to selection bias. In epidemiology, this is called the "healthy worker bias" because the athletes with the greatest predispositions towards injuries dominate the injury

incidence rate, if athletes are excluded after the first injury. The purpose of the present study is therefore to analyse multiple-injury data in novice runners to ascertain whether selection bias occurs when analysing only the time to first injury rather than all injuries. This study is a prospective, observational cohort study with a one-year follow-up. The shared frailty model was used for analysing data. We visually compared the cumulated baseline hazard ratios and the proportion of uninjured participants for first injury only and for all injuries together, revealing that differences between the analyses became more prominent over time. Specifically, the difference in proportion of uninjured participants between the two analyses was 2 percentage points when the one-year follow-up concluded. Thus, it seems selection bias might be present in analyses on sports injuries, when only the first sports injury is included. The severity of selection bias appears to be increasing with the length of follow-up. Hence forth, researchers wanting to describe sports injury occurrences over time should include all injuries in their analyses to reduce the risk of underestimation of injury incidence rates or hazard rates due to selection bias.

F05.04   Katrine Hjuler Lund

A PROSPECTIVE COHORT STUDY OF PERCEIVED STRESS AND SEMEN QUALITY

K. H. Lund[1], T. Wang[2], A.S. D. Laursen[1], E. E. Hatch[2], K. J. Rothman[2, 3], L. A. Wise[2], E. M. Mikkelsen[1]

[1]Department of Clinical Epidemiology, Aarhus University Hospital, [2]Department of Epidemiology, Boston University School of Public Health, Boston, MA, USA, [3]RTI Health Solutions, Research Triangle Park, Durham, NC

Background: The estimated prevalence of infertility for couples is 15-20% and male factors account for 50% of cases. In North America 18-21% of men of reproductive age report daily stress. A Danish study from 2017 showed that 23-24% of men aged 16-34 years reported high levels of perceived stress assessed by the 10-item Perceived Stress Scale (PSS). Previous studies on perceived stress and semen quality report inconsistent results.

Objective: To evaluate the association between perceived stress and semen quality. We hypothesize that high levels of perceived stress (≥ 20 points on the PSS) is associated with low semen volume, sperm motility and sperm concentration.

Methods: We will use self-reported data from two prospective preconception cohorts; Pregnancy Study Online (PRESTO) and SnartForaeldre.dk (SF). Men aged ≥ 21 (PRESTO) and ≥ 18 (SF) who completed a baseline questionnaire on sociodemographic and lifestyle factors as well as reproductive and medical history were invited to use Trak twice, 7-10 days apart. Trak is an FDA-approved test kit for in-home assessment of semen quality. We will use WHO cut off values to categorize low semen volume (<1.5ml), sperm motility (<40%) and sperm concentration (<15 10^6per ml). We will pool data from the two cohorts and use logistic regression models to compute odds ratios (ORs) with 95% confidence intervals and adjust for potential confounders.

Results: Preliminary data showed, that 328 men (PRESTO: 276 and SF: 52) provided 575 semen samples. In PRESTO the mean PSS score was 14.92 (SD 6.17) and 57 men had a score ≥20.

F05.05   Buket Öztürk   PRENATAL EXPOSURE TO ANTIDEPRESSANTS AND THE RISK OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDHOOD: FINDINGS FROM A NATIONWIDE COHORT STUDY

B. Öztürk, L. Pedersen, V. Ehrenstein, H.T. Sørensen

Department of Clinical Epidemiology, Aarhus University Hospital

Background: Recent studies have examined the causal effect of prenatal exposure to antidepressants on the risk of ADHD in childhood. However, they have shown inconsistent results.

Objectives: To examine the causal effect of prenatal exposure to antidepressants on the risk of ADHD in childhood, by triangulating results from different approaches where each approach has different key sources of potential bias.

Methods: We created a pool of all singleton live-born children in Denmark in 1997-2016 and performed following analyses: Restricted analyses, by comparing prenatally antidepressants exposed vs. unexposed restricted to, i) children of former antidepressants exposed mothers, ii) children of mothers with a diagnosis of depression. Sibling design analysis, by comparing prenatally antidepressants exposed vs. unexposed siblings. Active-comparator analysis, by comparing prenatally antidepressants exposed children vs. children of mothers exposed to talk therapy. Negative control analysis, by comparing paternally antidepressants exposed vs. unexposed children. We used Cox regression to calculate hazard ratios (HR) and 95% confidence intervals (CI) for the risk of ADHD.

Results: The pool consisted of 1,223,201 children. Restricted analyses resulted in HRs of i) 1.19 (1.09;1.29) and ii) 1.21 (1.00;1.45). Sibling design analysis resulted in a HR of 1.09 (0.89;1.33), active-comparator analysis in 1.26 (1.14;1.39) and the negative control analysis in 1.04 (0.93;1.15).

Conclusion: We found a small elevated risk of ADHD in children prenatally exposed to antidepressants compared with unexposed children. However, triangulation shows that this might be due to residual confounding.

F05.06   Philip Munch   IS THE RISK OF CARDIOVASCULAR DISEASE INCREASED AFTER LIVING KIDNEY DONATION?

P. Munch[1], C.F. Christiansen[1], H. Birn[2], M. Nørgaard[1]

[1]Department of Clinical Epidemiology, Aarhus University Hospital,
[2]Department of Renal Medicine, Aarhus University Hospital

Background:

Living kidney transplantation is considered the best treatment of end stage renal disease. However, it involves removal of a kidney from an otherwise healthy individual. Donor nephrectomy inevitably leads to a reduction in renal function. Since reduced renal function is a well-known risk factor for cardiovascular disease, we examined the risk of ischemic

cardiovascular disease (acute myocardial infarction, angina pectoris, ischemic stroke and transient ischemic attack) and atrial fibrillation after living kidney donation.

Methods:

In this nationwide cohort study, we included individuals who underwent living donor nephrectomy in the period 1996-2018 and followed them for cardiovascular diagnoses through medical registries. We compared the risk of cardiovascular disease in kidney donors with that in healthy sex and age-matched individuals from the general population using Cox-regression. Additionally, we compared the risks in kidney donors and blood donors using standardization.

Results:

Compared with the general population, kidney donors had a lower risk of both ischemic cardiovascular disease and atrial fibrillation. Compared with blood donors, kidney donors had similar risk of ischemic cardiovascular disease (standardized incidence ratio (SIR) = 1.08, 95%CI = (0.82-1.43)) and a slightly decreased risk of atrial fibrillation (SIR = 0.84, 95%CI = (0.53-1.34)).

Conclusion:

We did not find clearly higher risks of ischemic cardiovascular disease or atrial fibrillation after living kidney donation. These findings support the practice of living kidney donation among carefully selected donors.

F05.07   Lisa Fønss Rasmussen

EFFECTS OF TRANSITIONAL INTERVENTIONS BETWEEN HOSPITAL AND HOME ON READMISSIONS AMONG OLDER PATIENTS DISCHARGED FROM A MEDICAL WARD: A SYSTEMATIC REVIEW

L.F. Rasmussen[4], L.B. Grode[1], I. Barat[1], J. Lange[2, 4], M. Gregersen[3]

[1]Department of Medicine, Horsens Regional Hospital, [2]Department of Orthopedic Surgery, Horsens Regional Hospital, [3]Department of Geriatrics, Aarhus University Hospital, [4]Department of Research, Horsens Regional Hospital

Background

The proportion of older people and life expectancy will increase during the next decades. In Denmark, 20% of all older medical patients are readmitted within 30 days after discharge. This brings severe challenges to patients, caregivers and healthcare systems as older age is associated with higher utilization of healthcare services.

Aim

To identify, assess and synthesize the existing literature on transitional care interventions on readmission rate among older medical patients.

Method

Search strategy

Five bibliographic databases were searched in the period from 2007-2019. Also, a comprehensive hand search was conducted.

Study eligibility

P: Medical patients of 65+ years discharged from a medical ward or emergency department I: The transitional phase between hospital and home. Interventions include both pre- and post-discharge components C: Usual care O: Unplanned readmission Study selection

All steps were performed by two researchers independently. However, one researcher screened all titles for intervention eligibility.

Methodological quality

Two reviewers assessed risk of bias independently using "The Quality Assessment Tool for Quantitative Studies".

Data extraction

Data were extracted by two researchers independently.

Results

Study selection, study characteristics, risk of bias, results of individual studies, synthesized results and risk estimates will be presented.

Conclusion

A short and precise description of main conclusions will be presented.

Perspective

This insight may improve the quality of future transitional care interventions, thus benefiting patients, caregivers, healthcare professionals and healthcare systems.

F05.08   Line Thams   EFFECTS OF MILK PROTEIN AND VITAMIN D ON MUSCLE STRENGTH IN DANISH 6-8-YEAR-OLD CHILDREN: STUDY PROTOCOL

L. Thams[1], C.T. Damsgaard[2], N.K. Andersen[2], L.G. Hvid[1], A. Larnkjær[2], C. Mølgaard[2], M. Hansen[1]

[1]Section for Sport Science, Department of Public Health, Aarhus University, [2]Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen

Background and aim:

During winter, children living at Northern latitudes are at risk of vitamin D deficiency. Vitamin D supplementation can improve muscle strength in adults with low vitamin D status whereas in children, the few published studies show divergent results. It is well documented that protein intake can stimulate muscle protein synthesis, however we lack knowledge about the effect of protein supplementation on muscle strength in children. Since vitamin D and milk protein may both affect muscle strength, there is a potential for synergistic effects on muscle strength by combining these interventions. As a part of the larger D-pro study investigating children's bone health and growth, we here aim to assess the effects of milk protein and vitamin D on muscle strength in children.

Hypothesis:

1) Intake of milk protein will increase muscle strength.

2) Vitamin D supplementation will hinder the winter nadir in vitamin D status and improve muscle strength compared to placebo.

3) Intake of milk protein and vitamin D will have a synergistic, positive effect on muscle strength.

Method:

In a 2×2-factorial randomized controlled trial, 200 healthy 6-8 year-old Danish children were randomly allocated to receive 2.6 dl/day yoghurt with either high or medium protein content (25 vs. 9 g protein/day) and blinded tablets with either vitamin D (20 μg/day) or placebo for 24 weeks from sept-nov 2019. We measure serum 25-hydroxy-vitamin D (vitamin D status), muscle strength (isometric leg press, hand grip, squat jump, long jump, 30s sit-to-stand), body composition (DXA), and physical activity level (7-day tri-axis Axivity) at baseline and endpoint.

Clinicaltrials.gov ID: NCT03956732

F05.09 Anders Emil Ejskjær Gravholt THE EFFECT OF ELECTRICALLY EVOKED ECCENTRIC CONTRACTIONS ON MUSCLE HEALTH.

A. Gravholt, J. Herskind, L.G. Hvid, K. Overgaard

Department of Public Health, Section for Sport Science, Aarhus University

Background: Functional Electrical Stimulation (FES)has been proven to sustain muscle mass and assist in rehabilitation when physical activity is limited/impossible . In regular resistance training programmes (without FES), dynamic contractions are thought superior to static contractions, yet this has not been thoroughly tested for FES programmes.

Purpose: To assess feasibility, discomfort, and effects of a 5-week training intervention (electrically evoked eccentric contractions) on muscle function .

Methods: Healthy Volunteers are recruited for a 5-week training intervention using electrical stimulation of the quadriceps femoris muscles. The training protocol will focus on unilateral eccentric (lengthening) contractions in a dynamometer with the other leg acting as a passive control. Subjects will be tested prior to and following the intervention for changes in muscle thickness (via ultrasonography) and force output during electrically and voluntarily evoked contractions. During all electrical stimulation, discomfort will be assessed using a numeric pain rating.

Preliminary results: Preliminary data suggests that a high force output for eccentric contractions is both possible and tolerable (acceptable with regard to discomfort), indicating that the proposed intervention can be completed.

Perspectives: If feasible and superior, eccentric electrical training may aid in delaying deteriorating of physical function along with the associated adverse health events .

| F05.10 | Nanna Husted Jensen | IMPLEMENTATION OF A DIABETES PREVENTIVE PROGRAMME FOR WOMEN WITH PRIOR GESTATIONAL DIABETES AND THEIR FAMILIES: THE FACE-IT PROGRAMME |

N.H. Jensen[1], K.K. Nielsen[2], I.K. Dahl-Petersen[2], H.T. Maindal[1, 2]

[1]Department of Public Health, Aarhus University, [2]Steno Diabetes Center Copenhagen

Background: Women with prior gestational diabetes mellitus (GDM) (DK: 3-4 % of all births) have a seven-fold increased risk of type 2 diabetes (T2D). GDM is associated with adverse long-term outcomes in the offspring and partners to the women have a high risk of T2D, as they tend to share the same living conditions. Prevention of T2D is possible with health behaviour interventions. Yet, they are often ineffective in real-world practice because of deficient implementation.

Face-it is a novel intervention targeting women with prior GDM and their families. It includes three extra visits from health visitors and digital coaching focusing on health promotion and prevention of T2D.

This PhD aims to evaluate the implementation of Face-it, and to investigate i) reach among participants, ii) fidelity in intervention delivery, and iii) if retention is influenced by health literacy status.

Methods: 460 women and their partners will be recruited from three Danish hospitals. Study I, II, and III will be designed as prospective cohort studies. Data on health and sociodemographic characteristics will be collected from medical records, surveys among the women and their partners, and registers. Fidelity data will be collected from a survey answered by the health visitors and as tracked data from the digital coaching platform.

Results: The PhD runs from June 2019-May 2022. The first results are expected ultimo 2020.

Perspectives: Results will add evidence to establishment of practices for this high-risk group through its investigation of implementation likely to affect the success of Face-it. If proven effective, the results will guide scale-up of Face-it within healthcare sectors.

| F06.01 | Pia Johansson Heinsvig | DOPING AGENTS IN DENMARK - AN ANALYTICAL EXAMINATION OF THE DANISH DOPING MARKET |

P.J. Heinsvig[1], C. Lindholst[1], T.S. Nielsen[1], A.V. Christiansen[2]

[1]Department of Forensic Medicine, Aarhus University, [2]Department of Public Health, Section for Sport Science, Aarhus University

Over the years, the media have reported on many different doping cases within elite sports. However, doping is not only associated with elite sports but today it is also well-known phenomenon within the fitness and exercise environment, where it represents a potential risk for public health. Today, there are only a few data within the field of the Danish doping situation and the aim of this project is to provide more information in order to center and qualify Anti-Doping Denmark's (ADD) focus areas: prevention, control, and information. In the first part of the project, a LC-MS/MS method to detect doping agents in urine samples collected from people involved in different types of crime will be developed. This type of

information will be used to see if there is a pattern within the use of steroids and the type of crime. Furthermore, the same method will be used to analyze wastewater collected from different point sources. In order to target the method, all doping seizures from a one-year period collected by three police districts will be analyzed using GC-MS for their content including active ingredients, additives, and whether the products originate from either an original or a counterfeit production. Another and already developed method using LC-TOF with a library of over 700 compounds will be used as a supplement to the LC-MS/MS method in order to screen both urine and wastewater samples for the presence of selected doping substances. Both the LC-MS/MS and the LC-TOF methods will further be used to analyze wastewater from four fitness centers which do/do not cooperate with ADD analyzed two sports centers and three bigger sports events.

| F06.02 | Jeppe Damgren Vesterager | **HOSPITAL VARIATION IN POST-OPERATIVE INFECTIONS AMONG HIP FRACTURE PATIENTS** |

J. Vesterager[1], P. Kristensen[1,2], I. Petersen[1,3], A. Pedersen[1]

[1]Department of Clinical Epidemiology, Aarhus University Hospital, [2]Department of Clinical Medicine, Regionshospitalet Horsens, [3]Institute of Epidemiology and Health, University College London

Background: Postoperative infections after hip fracture are serious and challenging complications - adversely affecting mortality, quality of life, and hospital costs. Hospital variation in 30-day mortality after hip fracture cannot entirely be explained by patient characteristics, treatment, or hospital level factors. We therefore need to investigate variation in postoperative infections after hip fracture which may explain variation in mortality.

Purpose/aim: The objective was to examine variation in postoperative infection rates after hip fracture at Danish hospitals.

Materials and Methods: In this nationwide population-based cohort study, we included patients undergoing hip fracture surgery from 2012 to 2017 (n=29.736) registered in the Danish Multidisciplinary Hip Fracture Registry. Patients were followed 30 days from surgery. Postoperative infections were defined as any hospital-treated infection. Data on postoperative infections were obtained from the Danish National Patient Register. We used two statistical models; 1) A Poisson regression analysis accounting for individual patient covariates, 2) A multilevel Poisson regression analysis accounting for individual patient covariates nested within hospitals. We evaluated hospital variation using intra-class-coefficient (ICC) and median risk ratio (MRR).

Results: The overall infection incidence was 15.3 %. Male gender, high comorbidity, high age and underweight were strong predictors of postoperative infections. The final results on the variation analyses will be presented at the PhD-day.

F06.03 Mette Lauge Kristensen

THE INFLUENCE OF CERVICAL DYSPLASIA ON FEMALE FERTILITY.

M.L. Kristensen[1], M. Waldstrøm[2, 3], S.P. Ulrichsen[1], E.E. Hatch[4], L.A. Wise[4], K.J. Rothman[4, 5], E.M. Mikkelsen[1]

[1]Department of Clinical Epidemiology, Aarhus University Hospital, [2]Department of Pathology, Lillebœlt Hospital, [3]Department of Regional Health research, University of Southern Denmark, [4]Department of Epidemiology, Boston University School of Public Health, Boston, MA, USA., [5]RTI Health Solutions, Research Triangle Park, Durham, NC.

Background: Human papillomavirus (HPV) is a sexually transmitted virus, which can cause infection in the female genitalia. The prevalence of HPV infection is 25% in women under the age of 30. HPV infection can lead to cervical dysplasia. In 2018, abnormal cells were found in 7,5% of all performed cervical cytologies. About 15% of all couples experience infertility, and only a few risk factors are confirmed. Disruptions in the cervical ecosystem can change the mucus production and the immunological environment.The influence of cervical dysplasia on female fecundability, defined as the probability of conceiving per menstrual cycle, is not well determined.

Aim: To investigate the influence of cervical dysplasia on fecundability among Danish couples trying to conceive.

Methods: The study is a prospective cohort study (n=13,457) based on two Danish preconception cohorts, the "Snart Gravid" and the "Snart Forœldre". The women complete a screening questionnaire, a baseline questionnaire and bimonthly follow-up questionnaires for up to 12 months. The self-reported data provides information on socio-demographic, reproductive history, medical history, lifestyle, and pregnancy status etc. We will obtain data on cervical cytologies, biopsies and surgical procedures from The National Pathology Registry and The Danish National Patient Registry. We will analyse the association between cervical dysplasia and fecundability using a proportional probability regression model. The computed fecundability ratios and corresponding 95% confidence intervals express the difference in the per-menstrual cycle probability to conceive between women with and without cervical dysplasia.

F06.04 Christine Leonhard Birk Sørensen

MENTAL HEALTH THROUGH ADOLESCENCE AND EARLY ADULTHOOD

C.L.B. Sørensen[1], T.N. Winding[2], J.H. Andersen[2], J.K. Christiensen[3], K. Biering[2, 4]

[1]Health Sciences, Faculty of Health, Aarhus University, [2]Department of Occupational Medicine, Regional Hospital West Jutland, [3]Department of Educational Psychology, Aarhus University, [4]Department of Public Health, Aarhus University

Background: Poor mental health is increasing in adolescence all over the world and may have great consequences. Poor mental health in childhood is associated with inferior learning, educational dropout, risk-behavior, and selfharming behavior, which may affect the child's future negatively. This PhD project concerns resilience factors and mental health in adolescence and early adulthood.

Objectives: The aims of the 3 studies are: 1: to examine how mental health change during adolescence and early adulthood and how resilience factors are associated to mental health at different ages; 2: to compare mental health in parents and offspring in terms of self-reported mental health, psychiatric diagnosis and use of antidepressant medication; 3: to examine how the historical time and geographical neighborhood affect mental health.

Methods: The primary outcome is mental health measured by CES-D and CES-DC. Data origin from two youth cohorts (VestLiv and FOCA (Future Occupation of Children and Adolescents cohort)) and from Statistics Denmark. Study 1 and 2 includes data from all four waves of VestLiv and study 2 will be supplemented with data on parents' mental health from the initial Vestliv questionnaire. Study 3 compares self-reported mental health and use of antidepressant medication in the two cohorts collected in 2004 and 2017.

Perspectives: These studies will help to understand the resilience factors connected to mental health in a Danish perspective, thereby adding cultural/regional perspectives to the international research base. This knowledge is important in preventive work to secure better mental health and to reduce inequality in mental health.

F06.05 Søren Mose   TRAJECTORIES OF HEALTH CARE SERVICE UTILISATION IN PEOPLE WITH MUSCULOSKELETAL PAIN

S. Mose[1, 2], P. Kent[3], D.H. Christiansen[1], J.H. Andersen[1]

[1]Department of Occupational Medicine, University Clinic, Regional Hospital Herning, [2]VIA University College, School of Physiotherapy, [3]School of Physiotherapy and Exercise Science, Faculty of Health Sciences, Curtin University, Perth, Western Australia.

Background

Musculoskeletal pain is the most common cause of health care seeking in Denmark, even though only a minority of people with musculoskeletal pain seek care.

Health care seeking is influenced by a number of factors and mechanisms but little is known about (i) how pain characteristics are associated with care seeking and care costs, and (ii) what differentiates care seeking trajectories for persons with chronic musculoskeletal pain. Understanding both could help us identify modifiable factors associated with different care seeking trajectories and help health care professionals better manage musculoskeletal pain. The aims of this study are to:

Analyse how pain characteristics influence trajectories of health care seeking and related costs. Also, analyse how individual, socioeconomic, health, psychosocial, and work-related factors influence this association. Analyse what types of health care and which personal, work and health-related factors are associated with trajectories of high and low health care seeking among people with chronic pain. Explore qualitative differences in the experiences and understanding of patients with chronic pain who have trajectories of high care seeking compared with those with low care seeking.   Materials and Methods

The study is a mixed methods cohort study with ten years follow-up. The study population is a representative cohort of about 5000 Danes. Analysis is be based on questionnaire, register and interview data. Questionnaire data from 2008 will be linked to Danish National health and social registers via Statistics Denmark. Qualitative data will be collected though individual interviews.

F06.06   Birgitte Laier Bitsch

EFFECTIVENESS OF CARDIAC REHABILITATION FOLLOWING ACUTE CORONARY SYNDROME FOR PATIENTS WITH AND WITHOUT CONCURRENT DIABETES (A SYSTEMATIC REVIEW AND META-ANALYSIS

B.L. Bitsch[1, 8, 1], M.B. Ravn[1, 2, 5], L.H. Tang[2, 5, 4], P. Doherty[6], R. Taylor[7], A.D. Zwisler[2, 5], T. Maribo[1, 8, 3]

[1]DEFACTUM, Region Midtjylland, [2]REHPA- Knowledge Centre for Rehabilitation and Palliative Care (REHPA), [3]Department of Public Health, Aarhus University, [4]Department of Physiotherapy and Occupational Therapy Næstved-Slagelse-Ringsted Hospitals., [5]University of Southern Denmark and Odense University Hospital, [6]Department of Health Sciences, University of York, [7]Institute of health research, University of Exeter Medical School, [8]Centre for Rehabilitation Research, Aarhus

Introduction:

Cardiac rehabilitation (CR) is highly recommended after acute coronary syndrome (ACS) due to significant health benefits. However, studies evaluating CR interventions lack representation of patients living with multiple diseases. ACS and diabetes often occur together and therefore patients with both ACS and diabetes are highly prevalent in CR. There is conflicting evidence if patients with both ACS and diabetes improve physical function and quality of life to the same extent as patients without diabetes after CR. The study aims to examine: Is CR following ACS equally effective for patients with concurrent diabetes (type 1 or type 2) as for patients without diabetes?

Methods and material:

The study is a systematic review and meta-analysis. Searches are conducted in 5 electronic databases and will be conducted during November 2019. Studies that include patients participating in CR following ACS with and without diabetes are eligible for inclusion. Included study designs are: randomised controlled trials and observational study designs comparing effectiveness of CR between patients with diabetes versus patients without diabetes. CR has to consist of at least structured exercise sessions. Main outcomes are exercise capacity and health-related quality of life. Authors screen titles and abstracts for inclusion, extract data, and assess risk of bias. The systematic review is reported in accordance with the PRISMA statement. The body of evidence will be assessed by the GRADE approach. A quantitative meta-analysis is performed. Adjustments are planned for several variables.

| F06.07 | Kasper K Friedrichsen | REPEATED TRAUMATIC BRAIN INJURY AND RISK OF EPILEPSY |

K. Klingenberg-Lolk, J. W. Dreier, J. Christensen

Department of Neurology, Aarhus University Hospital and National Centre of Register-based Research, Aarhus University

Background: It is well established that traumatic brain injury (TBI) increase the risk of developing epilepsy. The risk is highest in close temporal proximity to trauma, but remains increased for more than 10 years after a brain insult. Much less is known about the impact of repeated TBI (rTBI) on the risk of epilepsy. We aimed at studying how rTBIs contributed to the long-term risk of epilepsy.

Methods: A nation-wide register-based cohort study was carried out for all Danish children born in the period from 1 Jan 1977 to 31 Dec 2016. Cohort members were followed from birth until epilepsy onset, death, emigration, loss to follow up or 31. December 2016. We estimated hazard ratios and cumulative risk of epilepsy. To estimate the cumulative risk of epilepsy in the population without TBIs, we matched five controls for each case among persons with no TBI.

Results: Compared to persons with no TBI, persons with a single TBI had an increased risk of epilepsy (HR 2.19, 95% CI 2.10-2.29). Risk of epilepsy was even higher in persons with rTBI (HR 4.67, 95% CI 4.21-5.18). The risk of epilepsy was highest immediately after both TBI and rTBI, but remained increased for at least 20 years compared to persons without TBI. The 20-year cumulative risk of epilepsy was 2.47% (95% CI 2.37% - 2.57%) following TBI compared with 1.28% (95% CI 1.25% - 1.32%) in the matched controls. The cumulative risk was 3.62% (95% CI 3.23% - 4.06%) following rTBI compared with 1.05% (95% CI 0.95% - 1.18%) in the matched controls.

Conclusion: Our results suggest that rTBIs are associated with a cumulative impact on the risk of epilepsy, and that this risk is increased for at least 20 years after TBI.

| F06.08 | Louise Ruby Høj Illum | REGIONAL DIFFERENCES IN ENDOMETRIOSIS IN DENMARK: WHO GETS THE DIAGNOSIS? |

L.R.H. Illum[1], A. Forman[2], D. Rytter[1]

[1]Department of Public Health, Aarhus University, [2]Department of Obstetrics and Gynecology, Aarhus University Hospital

Background: Endometriosis is a benign gynecological disease, which is highly underdiagnosed partly due to diagnostic challenges and to the lack of awareness among both patients and health care professionals. Geographical residence could be a potential determinant for diagnosis, because of regional differences in awareness, and differences in the referral process to a specialized endometriosis center depending on where you live. Hence, the objective of this study is to investigate, whether living in different regions of the country influences the probability of getting an endometriosis diagnosis.

Methods: A register based cohort study was conducted using data from Statistics Denmark and the Danish National Patient Registry. The study population consisted of all women aged 15-55 living in DK at some point in the period 1990-2017. Incidence rates of endometriosis diagnosis was

calculated for each municipality, stratified by age group and by period of time respectively.

Results: 2.188.720 women were included in the study, and during the follow-up period, 26.539 cases of endometriosis were identified. The preliminary results show a clear pattern in the geographical distribution, with higher incidence rates in the northern and eastern parts of Jutland compared to the rest of the country. Stratified results show the same geographical pattern, but with a marked increase in incidence rates after 2000, especially in the northern and eastern parts of Jutland.

Conclusion: The preliminary results indicate considerable regional differences in the incidence rates of endometrioses in DK, suggesting that some areas of the country might have a higher rate of underdiagnosing endometriosis.

F06.09   Nils Skajaa   STROKE IN YOUNG ADULTS - INCIDENCE AND PROGNOSIS: DANISH POPULATION-BASED COHORT STUDIES

N. Skajaa

Department of Clinical Epidemiology, Aarhus University Hospital

Background: Stroke is a leading cause of death and disability worldwide. Approximately 12,000 incident strokes occur in Denmark every year. Stroke primarily affects the elderly, but the incidence rate is increasing among young adults aged less than 50 years. The prognosis of young adults with stroke remains poorly understood.

Aim: To examine the incidence of stroke in young adults and the subsequent short- and long-term risks of mortality, morbidity, and social disability.

Methods: We will conduct nationwide, population-based cohort studies using Danish health and administrative registries. Our stroke cohort is comprised of data from the Danish Stroke Registry (2003-2019) and Danish National Patient Registry (1980-2019). From the Civil Registration System, we will construct a reference cohort from the general population. For these cohorts, we will obtain individual-level data on hospital contacts and medication prescription redemptions using the unique 10-digit identifier. Study one will examine trends in the incidence rate of stroke, comparing young with older adults. Study two will examine the short- and long-term mortality risk following stroke, comparing young adults with both older adults and the general population without stroke. Study three and four aim to investigate the cardiovascular, neurologic, psychiatric, and gastrointestinal risks associated with a stroke diagnosis, comparing young adults with older adults and the general population. For all studies, important prognostic factors to examine include stroke severity and comorbidity.

Conclusions: This PhD project will provide knowledge on the poorly understood prognosis of stroke in young adults.

F06.10   Jie Zhang   DOES GRANDPARENTAL BODY COMPOSITION INFLUENCE THAT OF THE GRANDCHILDREN?-A FAMILY LINKAGE STUDY ACROSS THREE GENERATIONS

J. Zhang[1], K. Overvad[1], A. Olsen[1, 2], D. Lawlor[3], C.C. Dahm[1]

[1]Department of Public Health, Aarhus University, [2]Danish Cancer Society Research Center, Copenhagen, Denmark, [3]Department of Social Medicine, University of Bristol, Bristol, UK

Background and aims

The worldwide prevalence of obesity has tripled since 1975, and nearly a third of the world's population is now classified as overweight or obese. New evidence suggests transgenerational effects that have far-reaching implications for the health of future generations. However, it remains unclear to which degree genetic and epi-genetic effects or shared environmental factors contribute. The purpose of this study is to examine grandparental associations with offspring BMI and other body composition indicators, assessing the extent to which parental BMI mediates this association, in order to assess the contribution of genetic or environmental cross-generational transmission by using the three-generation data from a Danish cohort study.

Materials and methods

The project will use data from the Diet, Cancer and Health (DCH), and DCH-Next generation cohorts. The main outcomes are body composition in grandchildren, including BMI (standardized by sex and age), waist circumference, waist-height ratio, and fat mass index. The exposure is grandparental body composition (same four indicators). Covariates include socioeconomic status, lifestyle, medical history, cardiometabolic markers, and family history of diseases. A mixed-model analysis that uses fixed and random effects will be conducted to explore the association for body composition across three generations.

Perspective

A better understanding of the etiology of obesity will help to identify possible preventative strategies. Furthermore, by evaluating the impact of family contributions to the development of obesity, new evidence for optimal tailoring of preventive or therapeutic intervention will be gained.

F07.01   Lotte Sørensen   MEASUREMENT PROPERTIES OF HAND-HELD DYNAMOMETRY FOR ASSESSMENT OF SHOULDER MUSCLE STRENGTH: A SYSTEMATIC REVIEW

L. Sørensen[1], L.G. Oestergaard[1], M. Tulder[1, 2], A.K. Petersen[1]

[1]Department of Physiotherapy and Occupational Therapy, Aarhus University Hospital, [2]Department of health Science, Amsterdam Movement Sciences research institute, Vrije University

Objective: To summarize the evidence of measurement properties of hand-held dynamometry (HHD) for assessment of shoulder muscle strength.

Methods: Cochrane Central Register of Controlled Trials (CENTRAL), Pubmed, EMBASE, and PEDro were searched up to April 2019. Inclusion criteria were studies 1) evaluating measurement properties of HHD used on shoulder muscles, 2) including individual's ≥18 years. Exclusion criteria were studies including patients with neurologic, neuromuscular, systemic

diseases or critical illness. Quality assessment and evidence synthesis followed the COSMIN guideline.

Results: In total, 5755 studies were screened for possible inclusion and 18 studies (684 patients) were included. More studies examined the internal and external rotation than the abduction, adduction, flexion and extension. The reliability results were sufficient with 99% of the reported Intra-class correlations coefficient (ICC) values ≥0.70. The measurement error results were not sufficient for any of the movements examined. Minimal detectable change (MDC) ranged between 0-49%, with only few results ≤15%. This means that HHD cannot measure changes less than 15%. Furthermore, the sensitivity analysis showed that it is questionable whether HHD can measure changes less than 20%. The quality of evidence was high or moderate for 10 out of 12 movements examined. Based on low and very low quality of evidence the convergent validity and discriminative validity were not sufficient.

Conclusion: The reliability of HHD was overall sufficient. The measurement error was not sufficient for any of the movements examined and evaluation of treatment effect should be interpreted with caution.

| F07.02 | Louise Binow Kjær | THE PATIENT, THE STUDENT AND THE EDUCATIONAL ENVIRONMENT: A MULTI-METHOD STUDY OF LEARNING IN STUDENT-RUN CLINCS |

L.B. Kjær[1, 2], M.K. Christensen[1], V. Hjortdal[3], T.B. Hansen[4], P. Strand[5]

[1]Centre for Health Sciences Education, Aarhus University, [2]Department of Clinical Medicine, Aarhus University, [3]Heart-Lung-Cardiovascular department T, Aarhus University Hospital, [4]Orthopedic Department, Hospital Unit West, Aarhus University Hospital, [5]Lund University, Sweden

Background:

Student-run clinic (SRC) is a clinical teaching format, where students have increased responsibility for patients. Recent studies conclude that student-run clinics have a strong focus on responsibility, authenticity, and collaboration, which enhances student motivation and patient-centered learning. There is a need for further research on how didactical and environmental features of different student-run clinics contribute to the development of patient-centeredness and how student-run clinics as a teaching format affects patients.

Purpose:

The purpose of this study is to create a thorough understanding of the educational practice in two student-run clinics and how this educational practice facilitate medical student learning of the transferable skill "patient-centeredness". The study will be conducted in three separate studies each focusing on a different perspective of the educational practice: 1) The patient perspective; 2) The student perspective; and 3) The educational environment perspective.

Methods:

A multi-method study using "Focused Ethnography" including observations, interviews and video; and the quantitative instrument "The Undergraduate Clinical Education Environment Measure".

Expected results:

Recommendations for designing student-run clinics and for patient participation in pre-graduate clinical education.

Perspectives:

The results will lay ground for reseach-based recommendations of didactical principles and teaching methods to be used in clinical education environments. Communication of the results to educational developers, teachers and universities can create a large impact on all hospitals in Denmark and potentially internationally.

| F07.03 | Sivaranjani Madhan | SYSTEMATIC ASSESSMENT OF ORAL FUNCTION, QUALITY OF LIFE AND CRANIOFACIAL MORPHOLOGY CHANGES IN ORTHOGNATHIC SURGICAL PATIENTS |

S. Madhan[1], M. Cornelis[1], E.M. Pinholt[3], P. Svensson[2], P.M. Cattaneo[1]

[1]Section of Orthodontics, Department of Dentistry and Oral Health, Aarhus University, [2]Section of Orofacial Pain and Jaw Function, Department of Dentistry and Oral Health, Aarhus University, [3]Department of Oral and Maxillofacial Surgery, Hospital of South West Denmark, University of Southern Denmark

Orthognathic surgery is indicated in severe cases of malocclusion and deformation of the jaws. When orthodontic treatment fails to achieve satisfactory orofacial functional and aesthetic results, orthognathic procedures are considered as an option to improve the patient appearance, psychosocial well-being and oral function. In the literature, many studies have assessed the outcome after orthognathic surgery; however, most of them do not include enough variables to assess the overall outcome of OS. Some of those studies also have the following limitations: lack of control subjects, heterogeneity in study design, a low sample size, short follow-up period, with most of them being retrospective studies. Given the lack of evidence regarding the long-term outcome after orthognathic surgery, the aim of the present project is to fill the existing gap by conducting a well-tailored study, which will systematically investigate the health-related quality of life, oral function, sleep-disordered breathing, temporomandibular disorder and pain and craniofacial morphology changes in orthognathic surgical patients.

| F07.04 | Cathrine Bell | INTEGRATING MEDICAL SPECIALTIES AND OUTPATIENT APPOINTMENTS - A NOVEL PATHWAY FOR MULTIMORBID PATIENTS ENCOUNTERING SEVERAL OUTPATIENT CLINICS |

C. Bell[1], C.W. Appel[1], A. Frølich[3], A. Prior[2], P. Vedsted[1, 2]

[1]Diagnostic Centre, University Research Clinic for Innovative Patient Pathways, Silkeborg Regional Hospital, Aarhus University, [2]Research Unit for General Practice, Aarhus University, [3]Knowledge Centre for Multimorbidity and Chronic Conditions, Slagelse Hospital, Copenhagen University

Introduction

Multimorbidity poses a major challenge to health care. It is prevalent in at least every fourth adult person and the rate is rapidly rising with increasing age. The everyday-life of multimorbid patients is often influenced by difficulties in managing their conditions, complex drug regimes and attending multiple appointments in a fragmented health system. Thus, optimal care for multimorbid patients necessitates a need for more coordination and interdisciplinary collaboration.

Aim

To reduce appointments to outpatient clinics, to integrate and coordinate tests, consultations and care, and to support medical specialties in coordinating care of multimorbid patients.

Method

We developed a pathway for multimorbid patients (PMP) seen in two or more outpatient clinics facilitating integrated care. Coordinators, assigned to improve the care flow, review and align appointments and tests in agreement with the patient's wishes. Outpatient consultations are arranged to take place the same day and schedules for care providers are coordinated. The patients' attendance in outpatient clinics are planned sequentially and involved care providers attend an interdisciplinary conference, resulting in a joint treatment plan, with feedback and notice of modifications.

Results

Until now, 140 patients (median age 72 years, 38% females) have been enrolled. We present results on feasibility by tracking the flow of PMP and acceptability by conducting surveys among patients and healthcare providers.

Conclusions

Practicalities of organising PMP are manageable. Integrating medical specialities requires prioritising in a complex re-organisation of existing approaches.

F07.05   Mikkel Bo Brent   PTH AND THE ACTIVIN TYPE IIA DECOY RECEPTOR IN PREVENTION OF IMMOBILIZATION-INDUCED BONE AND MUSCLE LOSS

M.B. Brent[1], A. Lodberg[1], F. Duch[1], B.C.J. van der Eerden[2], A. Brüel[1], J.S. Thomsen[1]

[1]Department of Biomedicine, Aarhus University, [2]Department of Internal Medicine, Erasmus MC, Rotterdam, The Netherlands

Immobilization or reduced voluntary movement is a hallmark symptom of neurological diseases like stroke and cerebral palsy. Immobilization results in a rapid and significant bone and muscle loss, increased risk of fractures, and reduced muscle mass. Parathyroid hormone (PTH) is one of the most potent bone anabolic drugs to counteract bone loss but is not able to promote muscle gain. ActRIIA-mFc is a new and promising activin type IIA decoy receptor that increases both bone and muscle mass. We investigated whether PTH and ActRIIA-mFc alone or in combination could prevent three weeks of Botulinum toxin A (BTX)-induced immobilization of hindlimb bone and muscle loss. Seventy-two 16-week-old female C57BL/6 mice were divided into the following groups based on their body

weight. Baseline, Ctrl (Control), BTX, BTX + ActRIIA-mFc (10 mg/kg), BTX + PTH (100 µg/kg), and BTX + ActRIIA-mFc (10 mg/kg) + PTH (100 µg/kg). Immobilization reduced rectus femoris muscle mass (−48%), trabecular bone volume fraction (−33%), cortical thickness (−13%), femoral neck strength (−57%), and tibial bone formation rate (−64%) compared to Ctrl. Treatment with Act-RIIA-mFC alone or in combination with PTH increased trabecular bone volume fraction (+36% and +114%), cortical thickness (+8% and +15%), and femoral neck strength (+47% and +58%) compared to BTX. In addition, the combination of Act-RIIA-mFc and PTH increased rectus femoris muscle mass (+15%) and tibial bone formation rate (+161%) compared to BTX. In conclusion, Act-RIIA-mFc monotherapy partly counteracted the loss of bone, while Act-RIIA-mFC in combination with PTH prevented both the bone and muscle loss after immobilization.

F07.06   Louise Hermann Poulsen

DOES 3D IMAGING CHANGE THE TREATMENT DECISION FOR WISDOM TEETH IN THE UPPER JAW?

L. Hermann, A. Wenzel, L. Schropp, L.H. Matzen

Department of Dentistry and Oral Health, Aarhus University

Background: Pathology such as external root resorption of the maxillary second molar caused by the wisdom tooth is more often observed in 3D radiographic imaging (CBCT) compared to 2D panoramic imaging. Presence of resorption may change the treatment of the patient. No evidence-based guidelines exist for when to perform a CBCT for maxillary wisdom teeth.

Objectives: To assess factors observed in CBCT influencing a change in treatment decision of maxillary wisdom teeth.

Methods: This retrospective pilot study included 111 impacted maxillary wisdom teeth in 86 patients (mean age 26 years) who had a panoramic image and CBCT performed (6x6-cm field-of-view, 0.13 mm voxel resolution). Assessment of radiographic images and patient files: 1) initial treatment plan based on panoramic image; 2) diagnoses based on CBCT; 3) treatment decision after information from CBCT was available.

Results: Seventy cases (63.1%) underwent treatment, while for 41 (36.9%) the decision was no treatment. A change in treatment plan was registered in 65 cases (58.6%) after CBCT. In 12 cases (10.8%) treatment changed from removal of the wisdom tooth to removal of the second molar, while 25 (22.5%) were scheduled for removal in the initial treatment plan; but after CBCT, the decision was not to treat. If resorption involved the pulp of the second molar, there was an almost 17 times higher risk that this tooth was removed instead of the wisdom tooth (logistic regression analysis: OR 16.8; P<0.001).

Conclusions: Findings in CBCT often changed the treatment plan. Severe external root resorption observed in CBCT was the main decisive factor for removing the maxillary second molar instead of the wisdom tooth.

| F07.07 | Tora Hauh | DEVELOPMENT AND VALIDATION OF A MONITORING ASSESSMENT TOOL FOR A NEW OPERATION TECHNIQUE, LAPAROSCOPIC COMPLETE MESOCOLIC EXCISION |

T. Haug[1, 2], A.H. Madsen[1, 2], D. Miskovic[3], L.H. Iversen[1], S.P. Johnsen[4]

[1]Department of Clinical Medicine, Aarhus University, [2]Surgical Research Department, Herning Regionshospital, [3]St. Mark's Hospital, London, [4]Department of Clinical Medicine, Aalborg University Hospital

BACKGROUND: A new surgical technique, Laparoscopic Complete Mesocolic Excision (LCME), has recently been associated with improved outcomes of patients with colon cancer. Although the procedure requires great technical skills, there is no established assessment tool for monitoring the surgical performance and hence, a lack of data on how the surgical performance can affect patient outcomes.

AIM: To develop and validate an assessment tool for monitoring oncological and clinical safety of LCME-surgeries.

METHOD: The Delphi method have been applied, a systematic forecasting method relying on a panel of 5 LCME experts. All experts have been interviewed and answered 3 rounds of questionnaires. Results of these have been integrated in an assessment tool named GASCOS (Global Assessment Score of Clinical and Oncological Safety for Laparoscopic CME).

A total of 30 video-recorded LCME-surgeries performed by surgeons with different level of expertise, has been collected for validation. All videos have been anonymized and scored by 5 different experts independently using GASCOS.

The surgical quality of the video-recorded cases has been determined according to pathological standards and CT-scans postoperatively.

ANALYSIS: Examining the validity and reliability of the GASCOS score.

These will be calculated by comparing grades achieved according to the GASCOS, to the level of expertise of the surgeon. In addition, scores of GASCOS will be compared to the level of surgical quality.

| F08.01 | Thomas Johannesson Hjelholt | ASSOCIATION OF CHA_2DS_2-VASC SCORE WITH STROKE, THROMBOEMBOLISM AND DEATH IN HIP FRACTURE PATIENTS WITH OR WITHOUT ATRIAL FIBRILLATION: A NATIONWIDE COHORT STUDY. |

T.J. Hjelholt[1], S.P. Johnsen[2], P.K. Brynningsen[3], A.B. Pedersen[1]

[1]Department of Clinical Epidemiology, Aarhus University Hospital, [2]Department of Clinical Medicine, Aalborg University, [3]Department of Geriatrics, Aarhus University Hospital

Background

Patients undergoing hip fracture surgery have a 10 times increased risk of stroke, compared to the general population.

Objectives

Evaluate the association of CHA_2DS_2-VASc score with the risk of stroke, thromboembolism and all-cause mortality in hip fracture patients with or without atrial fibrillation (AF).

Methods

We conducted a nationwide cohort study using data from the Danish Multidisciplinary Hip Fracture Registry. All incident hip fracture patients aged 65 years and older operated between 2004 and 2016 were included (n=78,096). We calculated incidence rates, cumulative incidences and hazard ratios (HR) with 95% confidence intervals (CI), by CHA_2DS_2-VASc score, stratified on AF history.

Results

The cumulative incidence of ischemic stroke 1 year after hip fracture increased with ascending CHA_2DS_2-VASc score, being 1.9% for patients with a score of 1 and 8.6% for patients with a score of ≥6 in the AF group. Corresponding incidences in the non-AF group were 1.6% and 7.6%. Compared with a CHA_2DS_2-VASc score of 1, adjusted HRs were 5.53 (95% CI: 1.37-22.24) among AF patients and 4.91 (95% CI: 3.40-7.10) among non-AF patients with a score of ≥6. A dose-response like association was observed for all cardiovascular outcomes. All-cause mortality risks and HRs were substantially higher for all CHA_2DS_2-VASc scores above 1 in both the AF and non-AF groups.

Conclusion

Among hip fracture patients, CHA_2DS_2-VASc score is associated with risk of stroke, thromboembolism and death in patients with and without AF. Patients with high CHA_2DS_2-VASc scores had almost similar absolute risks for cardiovascular outcomes, irrespective of AF.

F08.02   Niels Moeslund   IMPACT OF OXYGENATION DURING NORMOTHERMIC REGIONAL PERFUSION IN A DONOR AFTER CIRCULATORY DEATH IN A PORCINE MODEL

N. Moeslund[1, 2], P. Ryhammer[6], L. Ilkjær[4], M. Pedersen[5], H. Eiskjær[1, 3]

[1]Cardiology Research Department, Aarhus University Hospital, [2]Department of Clinical Medicine, Aarhus University, [3]Cardiology Department, Aarhus University Hospital, [4]Cardiothoracic Department, Aarhus University Hospital, [5]Comparative Medicine Lab, Department of Clinical Medicine, Aarhus University, [6]Anesthesiology Department, Aarhus University Hospital

Background: Organs for transplantation are sparse and every year patients die while on the waiting list for heart transplantation. Organs from circulatory dead donors are now used in many countries to increase the donor pool but not in Denmark. While normothermic regional perfusion (NRP) is an established method to optimize donor organs from circulatory dead donors, on, its use in thoraco-abdominal perfusion is debated. Knowledge about the oxygenation levels that are most favourable for thoraco-abdominal NRP is needed.

Aim: To find the optimal oxygenation strategy during NRP in a heart transplant setting from circulatory dead donors in a porcine model.

Methods: The study is performed as a randomized intervention-control study with 2 groups (8 pigs in 21% oxygenation group and 8 pigs in the 100% group). The primary endpoint-parameter is cardiac contractility after NRP compared to baseline measured by pressure-volume recordings and by thermodilution with a pulmonary catheter. Baseline measurements are recorded before disconnecting the ventilator (before asphyxia). When mechanical asystole is recorded, NRP is commenced after afifteen minutes no touch period. The heart is then resuscitated, and NRP is gradually weaned. The cardiac contractility is measured at 1, 2 and 3 hours after weaning. Myocardial biopsies are acquired for in vitro assessment of mitochondrial function by oxygraphy.

Perspectives: We believe that thoracoabdominal NRP in donors suffering from circulatory death may increase the number of available donor organs, and this study may provide information about the most optimal oxygenation settings.

F08.03   Malene   PERFORMANCE EVALUATION OF TEMPORARY EPICARDIAL PACE WIRE
         Enevoldsen   WITH INTEGRATED SENSOR FOR PACING, SENSING, AND CONTINUOUS
                         POSTOPERATIVE MONITORING OF MYOCARDIAL FUNCTION AFTER OPEN
                         HEART SURGERY

M.S. Enevoldsen

Cardiothoracic Research Department T, Aarhus University Hospital

Background: In monitoring heart function after open heart surgery, echocardiography is the golden standard. However, one limitation is the missing ability of ultrasound to provide continuous cardiac monitoring.

This study introduces a new direct measurement of epicardial velocity using a temporary pacemaker wire (TMEs) containing an accelerometer. This allows continuous monitoring of cardiac function during the surgical and post-operative period. The study is designed to assess the feasibility of the accelerometer containing TMEs and to compare this new technology with current ultrasound measurements.

Material and Methods: In this multicenter, international, open, non-controlled investigation, patients undergoing open heart surgery, will be equipped with the accelerometer containing TMEs. The accelerometer provides specific data of the myocardium's mean systolic velocity during heart contractions by coordinating mean and peak systolic velocity in three axes. From implantation and until removal, the accelerometer detects, transmits, and stores continuous heart contractility data. Contractility data will later be paired with a time schedule of events peroperatively and postoperatively, and with ultrasound examinations (transesophageal and transthoracic) performed during and after surgery.

Results: Pending results.

Conclusion: Pending results.

Perspectives: Continuous monitoring of ventricular contractility can ideally be used to identify the need for and optimization of inotropic support and allow early detection of onset of complications such as ischemia and myocardial dysfunction.

| F08.04 | Martin Sejr-Hansen | CLINICAL VALIDATION OF QUANTITATIVE FLOW RATIO IN EVALUATION OF CORONARY ARTERY STENOSIS -THE FAVOR III TRIAL |

M. Sejr-Hansen, T. Thim, A. Eftekhari, N. Holm, E.H. Christiansen

Department of Cardiology, Aarhus University Hospital

Background:

Evaluation of coronary artery stenosis requires objective evidence for its ischemic potential. Current guidelines recommend functional assessment of intermediary coronary stenosis by fractional flow reserve (FFR). The need for a pressure wire has limited the adoption of FFR due to risk of dissections and inadequate reimbursement programs.

Quantitative flow ratio (QFR) is a novel diagnostic tool to compute FFR based on angiographic images. QFR therefore allows for FFR estimation without use of a pressure wire or adenine.

Aim:

To evaluate the two-year clinical outcome in patients with stable angina pectoris and intermediate coronary stenosis managed with QFR or FFR----based diagnostic strategies.

Design:

Investigator initiated, 1:1 randomized, prospective, clinical outcome, non--inferiority, multi--center trial performed in collaboration with 35 European and Japanese heart centres.

A total of 2000 patients with stable angina pectoris or stabilized acute coronary syndrome and intermediate non--culprit lesions with indication for pressure----based physiological assessment of coronary stenosis are included. Clinical and angiographic in-- and exclusion criteria are detailed in the study protocol.

Primary endpoint: Patient oriented composite endpoint (PoCE: all--cause mortality, any myocardial infarction, any revascularization, and stroke).

Perspectives:

If QFR is non-inferior to FFR, QFR may become the preferred strategy for invasive functional evaluation of coronary artery stenosis and may expand the use of functional lesion evaluation in lower income countries.

| F08.05 | Salma Karim | EVALUATION OF CORONARY PRESSURE, FLOW AND RESISTANCE IN CHRONIC TOTAL OCCLUSIONS (CTO)-A SUB-STUDY OF THE NORDIC-SPANISH RANDOMIZED TRIAL ON THE PROGNOSTIC EFFECT OF REVASCULARIZATION OR OPTIMAL MEDICAL THERAPY OF CHRONIC TOTAL CORONARY OCCLUSIONS (ISCHEMIA-CTO) NCT03563417 |

S.R. Karim, A. Eftekhari, E.H. Christiansen

Cardiology Research Department B, Aarhus University Hospital

Background

A chronic total occlusion (CTO) found during diagnostic invasive coronary angiography is associated with worse outcome compared to non-occlusive coronary artery disease.

The ISCHEMIA-CTO trial will compare optimal medical therapy with percutaneous coronary intervention (PCI) in the treatment of coronary CTOs in endpoints such as long term major adverse cardiac and cerebrovascular events and life quality.

The CTO is supplied by collaterals from a donor vessel. Previous studies have mentioned short-term changes in fractional flow reserve (FFR), however there's no data beyond 4 months post-PCI. And the microcirculatory system has not been considered in earlier studies which is crucially important in regulating blood flow of the occluded vessel.

The aim of this study is evaluation of FFR, coronary flow reserve and index of microvascular resistance in the donor vessel and the CTO artery following PCI.

Methods

Patients randomized to PCI in the ISCHEMIA-CTO trial will be included in this study and undergo assessment of coronary physiology in the donor vessel prior and following PCI of the non-CTO lesion.

The CTO-vessel is assessed physiologically after the CTO-PCI. This is conducted through thermodilution using a combined coronary pressure and flow wire.

Symptomatic patients with ≥ 5% of myocardial ischemia will undergo a follow-up invasive CAG 1 year after CTO-PCI. Physiological measurements of the donor-vessel and the CTO-vessel will be performed once again.

Perspectives

The inclusion is ongoing and continues to primo 2023. We're hoping to contribute to the knowledge on CTO treatment and in time change clinical practise in treating and guiding patient with CTO.

F08.06   Anne Mette Dybro

THE EFFECT OF METOPROLOL ON MYOCARDIAL FUNCTION, PERFUSION AND HEMODYNAMICS IN SYMPTOMATIC PATIENTS WITH HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY

A. Dybro, T.B. Rasmussen, M.K. Jensen, S.H. Poulsen

Department of Cardiology, Aarhus University Hospital

BackgroundHypertrophic cardiomyopathy (HCM) is a hereditary heart disease characterized by a thickened but non-dilated left ventricle. The prevalence of the HCM phenotype in the general population is 0,2 % equivalent to 10.000 people in Denmark. Obstruction of the left ventricular outflow tract develops in 30-60% of HCM patients, and these patients have hypertrophic obstructive cardiomyopathy (HOCM). HOCM patients often experience advanced heart failure symptoms with exertional dyspnea, impaired exercise capacity, chest pain, and fatigue. No curable treatment exists for the condition. By consensus, the primary treatment option is pharmacological with the use of beta blockers despite limited evidence of the effect in HOCM patients. Clinical management is based

predominantly on the empirical use of beta blockers, observational cohort studies and analyses of registries rather than randomized controlled trials.

Aim

This study investigates myocardial function, perfusion and invasive hemodynamics in symptomatic patients with HOCM, and how treatment with metoprolol influences myocardial performance and exercise tolerance.

Method

A randomized, double blinded placebo-controlled crossover trial. Patients will be examined with blood pressure catheters in the chambers of the heart at rest and while conducting a bicycle load test. Echocardiographic evaluation will also be performed. Each patient is examined twice; during metoprolol and placebo treatment.

Perspectives

The results will 1) document the effects of metoprolol in HOCM patients 2) provide unique insight to disease mechanisms in HOCM, and 3) guide whether HOCM patients should be offered more invasive treatments.

F08.07   Kristian Hylleberg   HEMODYNAMIC EFFECTS OF ORAL KETONE SUPPLEMENTS IN PATIENTS
         Christensen   WITH CHRONIC HEART FAILURE AND REDUCED EJECTION FRACTION

K.H. Christensen, R.N. Nielsen, H. Wiggers

Department of Cardiology, Aarhus University Hospital

Background:

The Ketone Body 3-Hydroxubutyrate (3-OHB) is a naturally occurring energy substrate that is utilized in starvation, critical illness and chronic heart failure (CHF). We have demonstrated a 2 L/min (40%) increase in cardiac output following intravenous treatment with 3-OHB in CHF patients. It is unknown whether these effects can be obtained using oral 3-OHB supplements.

Aim:

In this study we aim to investigate if these beneficial effects can be obtained by use of commercially available oral ketone supplements.

Methods:

This is a randomized, placebo-controlled, single-blinded study in 8 patients with CHF. Participants will receive two different oral 3-OHB supplements (Perfect Keto® Base an HVMN Ketone Ester®) and one isocaloric carbohydrate-based placebo (Science in Sport® Go Energy). Patients are examined on three separate occasions using Swann-Ganz Monitoring, Echocardiography and biochemical markers of ketosis.

Primary outcome is cardiac output measured by the thermodilution method. Secondary outcomes include Pulmonary Capillary Wedge Pressure, Left Ventricular Ejection Fraction, Global Longitudinal Strain and Blood Ketone Levels.

Perspectives:

This study will potentially pave the way for larger trials, investigating the effect 3-OHB as a therapeutic agent in chronic heart failure. Furthermore we will gain important new insights in the metabolism of the failing heart.

F09.01   Lauge Vammen   DEVELOPING A CLINICALLY RELEVANT CARDIAC ARREST MODEL IN PIGS

L. Vammen[1], L.W. Andersen[2], B. Løfgren[2], A. Granfeldt[1, 2]

[1]Department of Intensive Care, Aarhus University Hospital, [2]Research Center for Emergency Medicine, Aarhus University Hospital

Background:

The survival rate after cardiac arrest is low around 10 %. In the post-cardiac arrest setting, we lack treatment options to improve outcomes and prognosis. Novel treatments are difficult to develop, as the majority of experimental cardiac arrest research lack clinical relevance, why positive results translate poorly to the clinical setting.

Aim:

To develop a clinically relevant cardiac arrest model in pigs with regards to etiology of cardiac arrest, cardio-pulmonary resuscitation, and post cardiac arrest intensive care.

Methods:

In anesthetized pigs, cardiac arrest is induced by myocardial infarction and after seven minutes of untreated cardiac arrest, resuscitation according to international guidelines is started. Upon successful resuscitation, animals undergo 48 hours of intensive care, including hemodynamic support and target temperature management. During the entire protocol, all animals are invasively monitored for cerebral parameters (intracranial pressure, regional partial oxygen pressure, and tissue metabolite concentration) and cardiovascular function (blood pressures, cardiac output, and left ventricular function assessed by pressure-volume measurements). After 48 hours, animals undergo a MRI scan for an evaluation of cerebral and cardiac injury.

Perspectives:

The above-described animal model will provide new insights into the pathophysiology of cardiac arrest. On short-term, we want to expand this into a survival model, which would allow for assessment of e.g. neurological function testing. This would be a solid testing ground for future promising treatments, and could aid translation and result in fewer futile clinical trials.

F09.02   Sivagowry
         Rasalingam Mørk   OUT-OF-HOSPITAL CARDIAC ARREST, CENTRAL DENMARK REGION: TEMPORAL USE OF MECHANICAL CIRCULATORY SUPPORT AND ASSOCIATED OUTCOME

S.R. Mørk[1], C. Stengaard[1], M.T. Bøtker[2], S. Christensen[3], C.J. Terkelsen[1]

[1]Department of Cardiology, Aarhus University Hospital, [2]Prehospital Medical Service, Central Denmark Region, [3]Department of Anestesiology and Intensive Care, Aarhus University Hospital

BACKGROUND

In Denmark approximately 5300 people experience out-of-hospital cardiac arrest (OHCA) each year. Despite various initiatives to improve public engagement and access to a significant number of automated external defibrillators, the 30-day survival rate is only 16%. Extracorporeal cardiopulmonary resuscitation (eCPR) may be considered for patients with refractory OHCA. With the use of eCPR the circulation can be restored immediately, providing time to diagnose and treat the underlying cause of the cardiac arrest. Despite eCPR being performed for more than 10 years in Central Denmark Region, detailed knowledge of the full cohort of patients treated with eCPR is sparse.

PURPOSE

To describe temporal use of eCPR and assess the factors associated with outcome. Primary outcome will be survival with good neurological function Cerebral Performance Category score (CPC score) 1 and 2 at hospital discharge.

METHOD

Patients who have received eCPR for refractory OHCA at Aarhus Universitiy Hospital from 2010 to 2018 will be included. This study will use data from the Danish Cardiac Arrest Registry combined with the cardiac invasive registries. Characteristics of those treated with eCPR versus those not treated with eCPR will be investigated and correlated with mortality and morbidity.

PERSPECTIVE

There is no data on the use of eCPR and only limited data on how to select the right patients for mechanical circulatory support. These data may improve the organization of the use of eCPR.

F09.03   Marte Holmen   THROMBOEMBOLIC RISK AMONG PATIENTS WITH ELEVATED
~~CANCELLED~~ HOMOCYSTEINE LEVELS

M. Holmen, J.F. Arendt, A.M. Hvas

Department of Clinical Biochemistry, Aarhus University Hospital

Elevated levels of plasma total homocysteine (tHcy) are suggested to induce an increased risk of thromboembolism. It is, however, persistently controversial whether treatment with homocysteine-lowering medicine such as folic acid, vitamin B_{12} and B_6 reduce this thromboembolic risk. We hypothesize that among patients with elevated tHcy levels , those who have not received prescription of vitamins, B_{12}, B_6 and folic acid have a higher risk of venous or arterial thromboembolic events compared with patients who have received prescriptions of these vitamins. We have identified 177,000 patients from Northern and Central Denmark in this population-based cohort study. All patients had a registered tHcy-measurement in the study period, 01.01.2000 to 31.12.2017. The diagnosis- and prescription history were collected, including thromboembolic events and prescription of homocysteine-lowering vitamin-treatment in the study population. We want to compare thromboembolic risk and treatment effect in patients with normal and elevated tHcy. The study will clarify treatment practice in patients with

elevated tHcy and their subsequent risk of arterial and/or venous thromboembolism. Decisions on treatment as well as strategies for follow-up in patients with elevated tHcy have previously not been standardized. A clarification on which patients will benefit from vitamin treatment may lead to a more personalized treatment regime and a better prognosis for patients with elevated tHcy.

F09.04   Katrine Berg   CARDIAC MITOCHONDRIAL STRUCTURE AND FUNCTION FOLLOWING
CANCELLED   HEART TRANSPLANTATION - ENERGY HTX

K. Berg, N.R. Jespersen, B.R.R. Nielsen, H. Eiskjær

Department of Cardiology, Aarhus University Hospital

Introduction

Following heart transplantation (HTx), acute cellular rejection (ACR) is a complication that compromises the survival-rate significantly. Endomyocardial biopsies (EMB) are performed as routine surveillance of ACR. However, assessment of mitochondrial function and integrity may prove to be a more sensitive marker of ACR than histopathological evaluation of the biopsies. In addition, the serial biopsies during the first year after HTx give a unique opportunity to examine if the improvement in cardiac function after HTx is related to changes in mitochondrial structure and function.

Objectives

In three different studies, it will be examined whether 1) cardiac mitochondrial function is related to primary myocardial function following HTx, 2) whether myocardial function improves over time in these patients, and 3) whether "Myocardial External Energy Efficiency" evaluated from 11C-acetate-PET scans can be used as a marker of mitochondrial function and thus ACR.

Methods

In all three studies EMBs will be examined with high resolution respirometry to assess mitochondrial oxidative capacity and electron microscopy to evaluate mitochondrial density and anatomy.

Patients in study 3 will be examined with 11C-acetate PET-scans twice to evaluate if PET-scans may replace EMBs as the screening-modality for ACR.

Assessment of mitochondrial function will be compared to cardiac function evaluated with echocardiography, invasive hemodynamic measurements and results from blood samples.

Perspectives

The study proposal will hopefully pave the way for an entire new approach to evaluate ACR. This may eventually evolve into a more individually tailored treatment regime following HTx.

F09.05	Steen Hylgaard Jørgensen	**METABOLIC ALTERATIONS IN THE FAILING HUMAN HEART**

S.H. Jørgensen[1, 2, 3], E. Hansen[3], S. Ringgard[3], C. Lausten[3], H. Wiggers[2]

[1]Department of Cardiology, North Denmark Regional Hospital, [2]Department of Cardiology, Aarhus University Hospital, [3]The MR Research Centre, Aarhus University

Background

Changes in cardiac metabolism are involved in the progression of chronic heart failure (CHF). Until recently, metabolic studies have been based on biopsies, disturbing metabolism or positron emission tomography imaging, which involve ionizing radiation and without the ability to trace downstream metabolites. Using a novel technique of hyperpolarized [1-13 C]-pyruvate cardiac magnetic resonance spectroscopy (MRS), it is possible to visualize cardiac metabolism in vivo. Our research group has published results from studies on pigs. A study on 4 healthy subjects has been published, confirming that the method is feasible in humans. The aim of this PhD is to visualize the metabolic flux in cardiomyocytes, in vivo, in CHF in humans for the first time.

Methods

Study 1: Twenty newly diagnosed patients with dilated cardiomyopathy (DCM), (LVEF: 10-45%) will undergo a hyperpolarized 13 C-pyruvate MRS.

Study 2: Patients from study 1 will undergo a hyperpolarized 13 C-pyruvate MRS after 3 months on optimal CHF medical therapy.

Study 3: Ten diabetic patients with DCM, on optimal CHF medical therapy will undergo hyperpolarized 13 C-pyruvate MRS.

Study 4: Patients from study 3 will have a SGLT-2-inhibitor added to medical therapy and undergo a hyperpolarized 13 C-pyruvate MRS after 3 months.

Perspectives

Hyperpolarized 13 C-MRS offers a real-time visualization of metabolic alterations in heart failure and possibly provides a "metabolic fingerprint" that can increase our understanding of metabolic alterations in CHF. It may lead to the development of targeted personalized medical therapy for CHF. We plan to begin the studies during november 2019.

F09.06	Simone Juel Dragsbœk	**LONG-TERM CARDIOPULMONARY RESPONSES TO PULMONARY EMBOLISM IN AN IN VIVO ANIMAL MODEL**

S. JD[1], M. DL[1], J. VH[1], C. CEP[2], F. SHM[3], J.E. NK[1], A. A[1]

[1]Department of Cardiology, Aarhus University Hospital, [2]Department of Forensic Medicine, Aarhus University, [3]Department of Pulmonary Medicine, Amsterdam University Medical Centers

Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is a serious complication to pulmonary embolism (PE). CTEPH is due to incomplete resolution of material from an acute PE with persistent increased pulmonary arterial pressure (PAP). The increased PAP causes right ventricular (RV) hypertrophy and dilatation, that may develop into a decompensated state of right heart failure. The pathophysiological

mechanisms in CTEPH are mainly unknown. To understand the pathophysiology and improve preventive and therapeutic strategies it is key to have an animal model that resembles the disease as closely as possible.

Aim: We aim to investigate the long-term effects of large, central, autologous PE on the cardiopulmonary system in pigs.

Methods: 60 kg pigs are anesthetized and ventilated and autologous blood clots created ex vivo will be introduced by a 26F sheath. 12 pigs will be randomized to an intervention group or a sham group. The intervention group will receive large PE until mean PAP has doubled. The pigs will be evaluated at baseline, after the acute embolization and 30 days later. The evaluation consists of: hemodynamic measurements, bi-ventricular pressure-volume loop recordings, blood samples, and Computed Tomography. After euthanisation, tissue samples are saved for further analyses.

Perspective: This study will describe the long-term cardiopulmonary changes in a porcine model of pulmonary embolism aiming to give novel insights into the transition from acute PE into CTEPH. This study has the potential to lead to the development of an animal model of CTEPH and thereby serve as a platform for testing pharmacological and transcatheter interventions in CTEPH.

F09.07   Andreas Lind Johannessen   LYMPHATIC FUNCTION AND MORPHOLOGY IN THE ARMS OF BREAST CANCER TREATED WOMEN - A FOLLOW-UP STUDY

A.L. Johannessen[1, 2], M. Alstrup[1], B.V. Offersen[2], V.E. Hjortdal[1, 3], S. Mohanakumar[1]

[1]Cardiothoracic Research Department T, Aarhus University Hospital, [2]Department of Experimental Clinical Oncology, Aarhus University Hospital, [3]Departement of Cardiothoracic Surgery, Rigshospitalet

Axillary surgery and radiation therapy (RT) are significant risk factors for developing breast cancer related lymphedema (BCRL). These interventions may partially obstruct lymph outflow from the ipsilateral arm, chronically raising the afterload of the lymphatic vasculature. Lymphatic contractile function is changed, and distinct pathological lymphatic patterns are described in women diagnosed with BCRL, but it is unknown whether these changes occur before clinical edema is detectable. The study population consists of 35 high-risk breast cancer patients examined at baseline a few weeks after ended RT and at follow-up 6-12 months later. Contraction frequency, velocity and pumping pressure of the lymphatic vessels are described using Near-Infrared Fluorescence (NIRF) imaging. Lymphatic stress-test is performed using hyperthermia. Blood is analyzed for endothelial growth factors and pro-fibrotic cytokines.

The preliminary results consist of 14 patients investigated at baseline. Two patients presented with lymphatic abnormalities. A 22% higher pumping pressure was observed in the ipsilateral arm compared to the contralateral in the remaining 12 patients (p=0.0105). The 2 patients with lymphatic abnormalities had reduced maximal pumping pressure in the ipsilateral arm compared to the contralateral.

The preliminary baseline results indicate that well-functioning lymphatic vessels in the ipsilateral arm are compensating for the cancer treatment

related obstruction by raised pressure. However, lymphatic vessels with lymphatic abnormalities generate lower pressures. These lymphatic abnormalities and reduced contractile function could be the initial phase in the development of BCRL.

F10.01   Omeed Neghabat

OPTICAL COHERENCE TOMOGRAPHY OPTIMIZED BIFURCATION EVENT REDUCTION - THE OCTOBER TRIAL

O. Neghabat, L.N. Andreasen, E.H. Christiansen, N.R. Holm

Department of Cardiology, Aarhus University Hospital

Background

Percutaneous coronary intervention (PCI) of bifurcation lesions is challenging with high risk of procedural and long-term complications. High ambiguity of coronary angiography and implantation of stents in vessel branch points constitute important difficulties that treating physicians need to overcome in about 15% of cases. Optical coherence tomography (OCT) is a high definition, intravascular imaging modality that may aid physicians in optimizing treatment results and potentially improve clinical outcomes if used routinely and systematically.

Methods

The OCTOBER trial is a 1:1 randomized, controlled, prospective, superiority trial randomizing 1200 patients with stable coronary artery disease located at a bifurcation to either standard angiography-guided PCI or OCT-guided PCI. 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. Patients are followed until 10 years.

Results

The trial is ongoing, and 549 patients have been randomized in 29 sites in Europe. Enrollment is expected to conclude in late 2020.

F10.02   Jakob Tobias Nyvad

THE IMPACT OF AORTIC CALCIFICATION ON CENTRAL BLOOD PRESSURE AND MARKERS OF HYPERTENSION MEDIATED ORGAN DAMAGE IN CHRONIC KIDNEY DISEASE

J. Nyvad[1], K.L. Christensen[2], M. Reinhard[1], N.H. Buus[1]

[1]Department of Nephrology/Clinic of Hypertension, Aarhus University Hospital, [2]Department of Cardiology/Clinic of Hypertension, Aarhus University Hospital

Background: Patients with chronic kidney disease (CKD) have a high incidence of cardiovascular events. Blood pressure (BP) in the aorta (CBP) has in some studies been found to be a better predictor of cardiovascular outcomes than brachial BP. Under normal conditions, brachial BP is significantly higher than CBP. However, with declining renal function, this difference decreases and may even be reversed. As CBP is the BP most directly affecting the heart, brain and kidneys, this increased CBP may play a role in the poor cardiovascular prognosis of CKD-patients. It has been proposed, that the reason for the difference is increased aortic

stiffness caused by aortic calcification, which is highly associated with CKD.Aim and hypothesis: The aim of this study is to identify physiological or biochemical factors predicting a higher than expected CBP in patients with CKD. We hypothesize that this difference relates to the vascular disease - in particular arterial calcification - that is associated with CKD.

Methods: This study will include 160 CKD-patients at various stages and 40 controls. Patients will be recruited prior to elective coronary angiography (CAG). During the CAG procedure, patients will undergo direct measurements of intra-aortic BP along with measurements of brachial BP with an oscillometric device and estimated CBP. Furthermore, Agatston-scoring of CT-scans of the thoracic and abdominal aorta will be conducted along with echocardiography and a range of blood-samples.

Perspectives: By identifying factors causing a higher than expected CBP, this study may be a step towards establishing more personal treatment of BP in patients with increased risk of elevated CBP.

F10.03   Rajkumar
          Rajanathan

MICE WITH MIGRAINE ASSOCIATED MUTATION IN THE NA$^+$,K$^+$-ATPASE α2 ISOFORM DEVELOP CARDIOMYOPATHY-LIKE CHANGES.

R. Rajanathan[1], C. Stæhr[1], K. Lykke-Hartmann[1], H.C. Beck[2], N.R. Jespersen[3], H.E. Bøtker[3], V.V. Matchkov[1]

[1]Department of Biomedicine, Aarhus University, [2]Department of Clinical Biochemistry and Pharmacology, Odense University, [3]Department of Clinical Medicine, Department of Cardiology, Aarhus University Hospital

Migraine with aura is recognized as a significant risk factor for cardiovascular disease. Familial Hemiplegic Migraine type 2 is a migraine with aura associated with reduced expression of the Na$^+$,K$^+$-ATPase α2 isoform due to point mutations in its gene. Accordingly, heterozygous mice bearing one of these mutations (α2$^{+/G301R}$) have a 50% reduction in the expression of cardiac Na$^+$,K$^+$-ATPase α2 isoform. Previous studies of α2 isoform knockdown mice suggest its importance for cardiac structure and function. Therefore, we hypothesized that migraine-associated mutation in the Na$^+$,K$^+$-ATPase α2 isoform leads to cardiac abnormalities in mice.

Approximately 4 and 8 months-old α2$^{+/G301R}$mice were compared with age-matched wild type littermates (WT). The hearts were weighed and left ventricles were dissected for proteomics analysis (iTRAQ LC-MSMS), mitochondrial respiration measurements (Oroboros respirometry) and lipid peroxidation assessment (malondialdehyde-quantification).

Proteomics analysis of elderly α2$^{+/G301R}$mice suggested a protein expression pattern characteristic for cardiomyopathies. Weight-to-body-weight ratio was increased in elderly α2$^{+/G301R}$mice in comparison with WT. The respiratory capacity was also increased in elderly α2$^{+/G301R}$mice suggesting an increased oxygen consumption and this was associated with an increased level of lipid peroxidation.

Migraine-associated mutation in the Na$^+$,K$^+$-ATPase leads to cardiomyopathy-like changes in elderly mice. The underlying mechanism remains to be identified and prompts for further investigation planned in my PhD project.

| F10.04 | Mia Klinkvort Kempel | THE IMPACT OF SOCIAL INEQUALITY AND INSECURITY ON THE RISK OF EARLY SIGNS OF CARDIOVASCULAR AND METABOLIC DISEASE |

M.K. Kempel[1], T.N. Winding[1], M. Böttcher[2], J.H. Andersen[1]

[1]Department of Occupational Medicine, University Research Clinic, Regional Hospital West Jutland, [2]Department of Cardiology, Regional Hospital West Jutland

Background: Cardiovascular disease remains a major cause of morbidity and mortality in western societies and is the number 1 cause of death globally. Poor socioeconomic conditions seem to increase the risk of cardiovascular and metabolic diseases. Some of this association may be explained by lifestyle but little is known about the potential impact of childhood and youth psychosocial factors.

Aim: To examine the prevalence of early signs of cardiovascular and metabolic disease in a cohort of young subject, and study the role of childhood socioeconomic position (SEP) and psychosocial factors.

Hypothesis: Psychological and emotional stress in childhood, due to lower SEP, can trigger biological processes leading to early signs of cardiovascular and metabolic disease.

Methods: In total, 264 participants, from an existing cohort, are currently undergoing clinical examinations evaluating early signs of cardiovascular and metabolic disease. The cohort is consisting of individuals born in 1989 and living in the county of Ringkøbing when the study initiated in 2004 (N=3681). They have been invited to answer questionnaires at age 15 and at three follow-ups. Register data about different aspects of parental SEP is also registered.

The clinical examinations are scheduled to complete in January 2020.

Perspectives: We expect to increase the understanding of the linkages between low SEP and disease. If early psychosocial factors impact the risk of cardiovascular and metabolic disease, there is additional evidence to support early interventions. Newly discovered social risk factors, and possibly also clusters of biomarkers, might further be applied to the primary healthcare sector.

| F10.05 | Johannes Enevoldsen | CARDIO-PULMONARY INTERACTION IN OPEN-CHEST CONDITIONS - PREDICTING THE RESPONSE TO FLUID ADMINISTRATION |

J. Enevoldsen[1, 2], P. Juhl-Olsen[1], T. Scheeren[3, 2], S.E. Rees[4], S.T. Vistisen[2]

[1]Department of Anaesthesiology and Intensive Care, Aarhus University Hospital, [2]Department of Clinical Medicine, Aarhus University, [3]Department of Anaesthesiology, University Medical Center Groningen, [4]Department of Health Science and Technology and The Faculty of Medicine, Aalborg University

Background: Fluid administration is the default treatment when a patient shows signs of circulatory impairment, and while intravenous fluids can be life-saving, they should not be used without caution. Fluids do not always correct the circulatory impairment and can have detrimental side-effects. To limit futile fluid loading, several methods have been developed to predict the circulatory response to fluid administration. One of the more accurate methods is ventilator-induced pulse pressure variation (PPV),

which utilizes cardio-pulmonary interactions during mechanical ventilation. This method is currently limited to closed-chest conditions, as it depends on the preload varying effect of swinging intrathoracic pressure. There may, however, still be some preload variation present in open-chest conditions, due to the effect of alveolar pressure on pulmonary vascular resistance. This study aims to identify the remaining PPV and to evaluate its use in predicting fluid responsiveness.Method: This study is a secondary analysis of data from 61 patients undergoing coronary artery bypass graft (CABG) surgery. In both closed- and open-chest conditions, a fluid challenge was performed and evaluated. With an exploratory approach, we will analyze the respiratory variance in various features of the arterial blood pressure waveform, and evaluate how they relate to the fluid response.Results: We aim to present preliminary results on the PhD Day.Conclusion: We hope this study will give valuable insights into how cardio-pulmonary interactions are affected by open-chest conditions, and help broaden the applicability of PPV as a reliable fluid responsiveness predictor in this condition.

| F10.06 | Daniel Julius Lauritzen | LONG-TERM EFFECTS OF ANESTHETIC DRUGS ON NEURODEVELOPMENT IN ADULTS OPERATED FOR ASD OR VSD. |

D.J. Lauritzen, J. Heiberg, V.E. Hjortdal, B. Asschenfeldt

Cardiothoracic Research Department T, Aarhus University Hospital

Introduction:

Neurodevelopmental outcome is impaired in young adults surgically treated for atrial (ASD) and ventricular septal defects (VSD). The cause of this is largely unknown. This study investigates whether specific anesthetic agents administered during corrective surgery for septal defect in early childhood negatively affect neurodevelopmental outcome in adulthood.

Methods:

In a prospective cohort study, two groups of participants were enrolled. One group of 34 ASD patients and another group of 32 VSD patients. All of whom had undergone corrective surgery for septal heart defect in the period from 1988-2003.

Anesthesiological data were collected retrospectively from patient anesthesia records along with blood samples drawn from patients in the pre-, intra-, and postoperative phase. Neurodevelopmental assessment is then performed on the participants, who are now adults, using the Wechsler Adult Intelligence Scale, Fourth Edition (WAIS-IV) and patient performances were compared within the ASD and VSD groups.

Results:

Pending.

Perspectives:

If this study succeeds in identifying risk factors during surgery for septal heart defects in childhood, steps can then be taken to avoid these and thus relieve these children of the neurodevelopmental complications they experience in adulthood.

F10.07   Cecilie Budolfsen NT-PROBNP MEASUREMENTS TO RULE-OUT HEART FAILURE AMONG ATRIAL FIBRILLATION PATIENTS: A PROSPECTIVE CLINICAL STUDY

C. Budolfsen[1, 2, 3], A.S. Schmidt[1, 2, 3], K.G. Lauridsen[1, 2, 3], D.T. Nguyen[1, 2], C. Bang[1, 2], C.B. Poulsen[4], H. Rickers[3], B. Løfgren[1, 3, 4, 5]

[1]Research Center for Emergency Medicine, Aarhus University Hospital, [2]Clinical Research Unit, Randers Regional Hospital, [3]Department of Internal Medicine, Randers Regional Hospital, [4]Department of Clinical Medicine, Aarhus University, [5]Department of Cardiology, Aarhus University Hospital.

Background: Heart failure and atrial fibrillation often co-exist and heart failure is important to identify. Performing an echocardiography is considered gold-standard for diagnosing heart failure, but echocardiography may not always be readily available. The biomarker N-terminal pro brain natriuretic peptide (NT-proBNP) can be used to rule out acute heart failure in patients with sinus rhythm, however, atrial fibrillation affects the level of NT-proBNP in the blood. The objective of this study is to identify an optimal NT-proBNP threshold for ruling-out heart failure among atrial fibrillation patients.

Methods: This is an observational clinical study including patients admitted to hospital with atrial fibrillation. We aim to include a total of 403 patients from The Emergency Department and Acute Heart Clinic at Randers Regional Hospital. Project examinations will include blood-sampling for quantification of NT-proBNP levels, an echocardiography, and a chest X-ray. Lastly, patients will be asked to answer a questionnaire regarding their symptoms. The primary endpoint will be the negative predictive value of the optimal NT-proBNP cut-off level for ruling out heart failure among atrial fibrillation patients.

Results: Results are pending and the study design will be presented at PhD Day 2020.

Conclusion: Early rule-out of heart failure will allow faster initiation of optimal treatment for atrial fibrillation patients admitted to hospital.

F11.01   Søren Gullaksen EFFECT OF EMPAGLIFLOZIN AND SEMAGLUTIDE ON CARDIO-RENAL TARGET ORGAN DAMAGE IN PATIENTS WITH TYPE 2 DIABETES - A RANDOMIZED TRIAL

S. Gullaksen[1, 2, 3], L.V. HALD[1, 3], K.L. Funck[4], E.G. Laugesen[3], P.L. Poulsen[1, 2]

[1]Department of Clinical Medicine, Aarhus University, [2]Steno Diabetes Center, Aarhus, [3]Diabetes and Hormone Diseases, Aarhus University Hospital, [4]Diagnostic Centre, Silkeborg Regional Hospital

Aim: We will perform a placebo-controlled double-blind randomized controlled trial to evaluate the effects of empagliflozin vs placebo. Parallel to this, we will perform a parallel group intervention open-label trial of semaglutide in combination with empagliflozin or empagliflozin-placebo. We will evaluate the effect on renal oxygenation as measured by blood oxygen level dependent magnetic resonance imaging (BOLD MRI).

Background: Diabetic kidney disease (DKD) is a common and serious complication in diabetes patients. New treatments including sodium-glucose co-transporter 2 inhibitors empagliflozin and glucagon-like

peptide 1 agonists semaglutide have shown reno-protective effects. The pathophysiological changes underlying DKD remain poorly understood, and data is scarce as regards renal oxygenation as evaluated by BOLD MRI in high-risk type 2 diabetes patients.

Methods: 120 high-risk type 2 diabetes patients will be enrolled in the ongoing study. They will be randomized to one of four arms (semaglutid+empagliflozin; semaglutid + placebo; placebo; empagliflozin). Patients are examined at baseline, by week 16 and by week 32. The primary outcome is change in renal oxygenation as measured by BOLD MRI. Secondary outcomes are glomerular filtration rate, renal plasma flow, change in corticomedullary sodium homeostasis, markers of the renin-angiotensin system and change in urinary albumin excretion.

Perspectives: An understanding of the disease mechanisms reversed by empagliflozin and semaglutide will provide important information regarding the renal physiology in high risk patients, and this may also provide impetus towards developing primary preventive measures.

F11.02   Gry Høst Dørflinger

DIABETIC NEPHROPATHY - AUTOATTACK AND IMPAIRED REGULATION OF COMPLEMENT

G.H. Dørflinger[1], J.A. Østergaard[1, 2], M. Bjerre[1, 2]

[1]Department of Clinical Medicine, Aarhus University, [2]Steno Diabetes Center Aarhus

Micro- and macrovascular complications significantly increase morbidity among patients with diabetes.Diabetic nephropathy (DN) affects 30% of these patients and is a significant contributor to the morbidity. More insight on the mechanisms leading to DN is needed to pursue novel therapeutics targeting DN.

Recent studies have linked the complement system to development of DN. We have shown that Mannan Binding Lectin (MBL) accumulates in the kidneys in a type-1 diabetic mouse model, but not in the non-diabetic control mice, suggesting that diabetes induce a pattern of carbohydrate on the cellular surfaces that is recognized by MBL.

Up on binding of MBL, MBL-associated serine proteases (MASPs) initiate downstream activation of the complement system, resulting in formation of a pore-forming complex (MAC) that disrupts the cell membrane and leads to cell lysis.

We hypothesize that high glucose concentrations, alter the pattern of carbohydrates present on the cell surface causing autoreactivity of the lectin pathway, complement activation and damage to the endothelial cells.

In this vitro study we will evaluate the binding of MBL to human vascular endothelia cells (HUVECs) and renal endothelia cells after 3 days in normo- and hyperglycemic conditions (5.5 mM vs 21.5 mM).

Furthermore, we will mimic the complement cascade to see whether hyperglycemic conditions are entailed by autoreactivity in MAC-induced cell-lysis that is not directly influenced by MBL.

Our preliminary data support that a diabetic milieu enables MBL to recognize such altered self-tissue and activate the lectin pathway. However, we need to elaborate further to predict whether autoreactivity bypasses binding of MBL.

| F11.03 | Zheer Husain | THE EFFECTS OF IMPROVED INSULIN SENSITIVITY ON BONE MARKERS AND BONE BIOMECHANICAL PROPERTIES IN INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS |

Z. Husain[1, 2], R. Viggers[3, 6], R.F. Nielsen[1, 2, 5], J.S. Linde[1, 2, 4], B.L. Langdahl[4, 2], P. Vestergaard[3, 6], S. Gregersen[1, 2, 4]

[1]Steno Diabetes Center Aarhus, Aarhus University Hospital, [2]Department of Clinical Medicine, Aarhus University, [3]Steno Diabetes Center North Jutland, Aalborg University Hospital, [4]Department of Endocrinology and Internal Medicine, Aarhus University Hospital, [5]Department of Internal Medicine, Regional Hospital Randers, [6]Clinical Institute, Aalborg University

Background: Type 2 diabetes mellitus is a disease of high blood sugar, in part due to diminished insulin sensitivity. Individuals with type 2 diabetes have a 30-40% higher risk of bone fractures than healthy individuals. This fracture risk is not sufficiently predicted by bone mineral density. In fact, bones of individuals with type 2 diabetes are denser than those of non-diabetics.

Instead, the ability to repair and replace old bone with new seems to be impaired. This lower state of turnover seems to be correlated to the level of insulin sensitivity.

Purpose: To investigate whether improved insulin sensitivity in type 2 diabetics leads to an increase in bone turnover and improved bone structure.

Method: A 12-week double-blinded, randomised, controlled trial will be undertaken on 104 participants with type 2 diabetes. Participants will be assigned to metformin or placebo and non-weight bearing exercise or no exercise in a 2x2 factorial design.

Outcomes are insulin resistance (assessed by Insulin Suppression Test), bone turnover markers (P1NP, CTX, sclerostin and osteoclastin) and bone scans (HRpQCT) for structural information.

Perspective: The study will give us more insight into the coupling between insulin resistance and bone remodelling. Thereby, we may elucidate the underlying cause of the increased bone fragility and whether this cause is reversible. This may help us better predict and prevent fractures.

| F11.04 | Christine Bodelund Christiansen | ARONIA IN THE TYPE 2 DIABETES TREATMENT REGIMEN |

C.B. Christiansen[1, 2], P.B. Jeppesen[1], K. Hermansen[1, 3], S. Gregersen[2]

[1]Department of Clinical Medicine, Aarhus University, [2]Steno Diabetes Center Aarhus, Aarhus University Hospital, Denmark, [3]Department of Endocrinology and Internal Medicine, Aarhus University Hospital

Background: Aronia has the highest antioxidant capacity among berries and a high content of bioactive polyphenolic compounds. In vitro and in

vivo studies have indicated aronia's beneficial effects on oxidative stress-driven diseases such as cardiovascular diseases and type 2 diabetes (T2D). Aronia also has a favorable effect on cholesterol in humans. We aim to develop a novel fermented aronia extract (FAE) in order to enhance the antioxidant capacity of aronia and to compare its effect to that of non-fermented aronia extract (NFAE) on T2D. FAE may exert beneficial effects, not only on T2D, but on oxidative stress-driven diseases in general due to improved accessibility of polyphenols. Also, aronia does not induce hypoglycaemia, thus, it has potential as adjunct therapy or treatment of T2D. Hypothesis: FAE improves glycaemia, lipidaemia, and insulin resistance in T2D more efficiently than both NFAE and placebo. Method: A double-blind triple cross-over study including 60 TD2 patients was designed to answer the hypothesis. The study will include three intervention periods of six weeks duration separated by washout periods of three weeks. In the intervention periods, the T2D patients receive placebo, FAE, or NFAE. The levels of HbA1c, glucose, insulin, glucagon, cholesterol, triglyceride, cytokines, C-reactive protein, incretins, and dipeptidyl peptidase-4 will be measured before and after each intervention period. Hyperglycaemia, lipidaemia, 24h-blood pressure, body mass index, metabolomics, and microbiomics will also be assessed.

F11.05   Julie Nielsen   NOVEL PHARMACOLOGICAL APPROACH FOR ACTIVATION OF DORMANT FOLLICLES

J. Nielsen

Department of Biomedicine, Aarhus University

The prevalence of female infertility is believed to be increasing. Today's fertility treatment is limited by lack of insights into signaling pathways that could drive activation of dormant follicles. This project seeks to understand if newly identified metabolic candidates are involved in activation of dormant follicles. We use ovaries isolated from mice as an experimental system. Whole ovaries from juvenile mice are cultured in vitro, and by using a pharmacological approach, we will evaluate if the identified metabolic candidates have an effect on follicle distribution in the ovary drug treatments. Additionally, we use molecular biology tools to address important parameters that can evaluate follicle quality after drug exposure. Towards this, we perform ROS and TUNEL assays to analyze the levels of ROS and apoptosis in treated ovaries. In line with this, we seek to confirm the quality of the drug-treated egg, by testing the end product of complete follicle maturation. Follicles will be isolated from the in vitro cultured ovaries and cultured individually. Culture of the follicles should conclude with mature eggs that are able to be in vitro fertilized and subsequently develop into an embryo. This will be tested in vitro, to observe that the fertilized eggs can develop in vitro for three days, and additionally, that we can implant the resulting embryo into a mouse model and obtain live pulps. Lastly, we wish to establish an in vivo mouse model, and by administering the compound to the ovaries of an adult mice, we will evaluate the results, and how it affects the reproductive health of the transgenerational litters.

F11.06   Tue Duy Nguyen   ATHE MECHANISTIC LINK BETWEEN THE NA,K-ATPASE ABUNDANCE AND BLOOD GLUCOSE HOMEOSTASIS

T. Nguyen

Department of Biomedicine, Aarhus University

The mechanistic link between the Na,K-ATPase abundance and blood glucose homeostasis

Nguyen, T, Stæhr, C, Rajanathan, R, Bendix, P. Vendelbo, M, Lykke-Hartmann, K and Matchkov, V.

Na,K-ATPase (NKA) is a housekeeping enzyme responsible for ion homeostasis and vital to cell function. Its ubiquitous α1 subunit is responsible for the enzyme's housekeeping function, while α2 and α3 subunits are tissue-specific and have distinctive functions. Dysregulations in NKA contributes to the pathogenesis of diabetes through unknown mechanisms.

The aim of this study is to elucidate the role of chronic reduction in the α2 subunit of NKA in the glucose metabolism. In this study, we used heterozygous mice bearing a mutation (G301R) of the α2 isoform NKA ($\alpha2^{+/G301R}$), which is known to be associated with familial hemiplegic migraine type 2 in humans. Our methods include the expression studies of glucose-uptake-specific proteins and physiological function of pancreatic islets. Furthermore, in-vivo studies include measurements of blood glucose dynamics with[18]FDG-PET/CT scans and glucose monitoring with telemetry. We plan to assess the relevant biochemical parameters involved in glucose-intolerance associated with G301R mutation.

We found glucose intolerance in elderly $\alpha2^{+/G301R}$mice compared to WT. We therefore hypothesize that dysregulation in NKA α2 isoform can lead to inadequate glucose uptake in peripheral insulin-sensitive tissues (such as skeletal muscle and adipocytes) and/or a reduced insulin secretion.

We will demonstrate the role of NKA in glucose metabolism and suggest the mechanism for potential restoration of NKA activity as a pharmacological target of metabolic disorders.

| F11.07 | Fredrik Brustad Mellbye | EFFECTS OF CAFESTOL, A POTENTIAL ANTIDIABETIC SUBSTANCE IN COFFEE, IN SUBJECTS AT RISK OF TYPE 2 DIABETES |

F.B. Mellbye[1, 2], K. Hermansen[2], P.B. Jeppesen[2], S. Gregersen[1]

[1]Steno Diabetes Center Aarhus, Aarhus University Hospital, [2]Department of Endocrinology and Internal Medicine, Aarhus University Hospital

Daily coffee consumption is inversely associated with the risk of type-2-diabetes (T2D). We discovered that cafestol, a bioactive substance in coffee, increases insulin secretion in rat beta cells and increases glucose uptake in a human skeletal muscle cell line. Subsequently, we found that daily intake of cafestol in a T2D model, the KKAy mice, can postpone or prevent the development of T2D and increases insulin sensitivity, lowers blood glucose and increases insulin secretory capacity from islets of Langerhans. This indicates that cafestol may contribute to the reduced risk of developing T2D in coffee consuming humans and has a potential role as a future antidiabetic drug or dietary supplement.

The planned project is a randomized, controlled intervention study in humans with large waist circumference at high risk of developing T2D.

Firstly, we will in a crossover study examine the acute effects of cafestol on glucose metabolism during an oral glucose tolerance test (OGTT); secondly we will carry out a 12-week parallel intervention study with daily intake of either cafestol or placebo, we will at start and end perform Insulin Suppression Tests, full body MRI-scans, mixed meal tests as well as fecal, urine and blood samples.

We hypothesize that cafestol administered to subjects at high risk of developing T2D, acutely will lower the blood glucose during the OGTT, and that a 12-week daily intake of cafestol will improve insulin sensitivity and glucose tolerance, reduce liver fat content as well as change the diversity of the microbiome and metabolomics.

Our hope is to demonstrate that cafestol may be used as an antidiabetic drug or a dietary supplement to prevent T2D.

F11.08   Johanne Blanner Jul   SEX-SPECIFIC ALTERATIONS IN HEPATIC GLYCEROL METABOLISM IN MICE FED A HIGH-FAT DIET

J.B. Jul, J.B. Vegger, J.S. Thomsen, A. Brüel, J. Lebeck

Department of Biomedicine, Aarhus University

In mice, high-fat diet (HFD) induces insulin resistance (IR) and obesity; females are less susceptible to the development of both. IR alters the hepatic triglyceride and glucose metabolism, and glycerol is a precursor of both. This study investigates possible sex-specific regulation of hepatic glycerol metabolism in HFD fed mice. Aquaporin 9 (AQP9) facilitates hepatic uptake of glycerol and perilipin-2 (PLIN-2) coat intracellular lipid droplets.

C57BL/6J mice were fed either a control or a 60% HFD for 12 or 24 weeks (n = 8-10 in each group). Body weight (BW) and blood glucose were monitored throughout the experiment. At euthanization liver weight (LW) was determined and samples for Western Blotting and immunohistochemistry were collected. Results are presented as mean ± SEM and statistically tested using ANOVA.

24 weeks of HFD increased the LW/BW ratio in males and decreased it in females and immunohistochemistry revealed more prominent hepatic steatosis in males. This was paralleled by an increase in hepatic PLIN-2 expression after both 12 (0.6 ± 0.2 vs. 3.0 ± 0.7 $p<0.05$) and 24 weeks of HFD (1.4 ± 0.2 vs. 3.8 ± 0.2 $p<0.05$) in males. In females this was found only after 24 weeks of HFD (1.0 ± 0.2 vs. 2.9 ± 0.5 $p<0.05$). No significant effect of HFD on hepatic AQP9 abundance was observed. However, female control mice had a higher AQP9 abundance than male control mice after 12 weeks (1.0 ± 0.2 vs. 0.2 ± 0.1, $p<0.05$).

HFD feeding causes a more marked hepatic steatosis in male mice compared to female mice. Our results suggest that AQP9 is not a major contributor to development of hepatic steatosis in HFD fed mice.

F12.01   Morten Daniel Jensen   AUTOIMMUNE HEPATITIS AND CANCER RISK

M.D. Jensen[1], L. Grønbæk[1], H. Vilstrup[1], P. Jepsen[1, 2]

[1]Department of Hepatology and Gastroenterology, Aarhus University Hospital, [2]Department of Clinical Epidemiology, Aarhus University Hospital

Background: Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease, and the chronic inflammation may cause cancer development. We examined cancer risk in a nationwide cohort.

Method: We identified all Danish citizens diagnosed with AIH between 1994 and 2018 and followed them through Danish healthcare registries. For each of the 2.904 patients with AIH we included 10 population controls matched on gender, age, and year of birth. We examined absolute and relative risks of hepatocellular carcinoma (HCC) and other cancers (non-HCC). Within the cohort of AIH patients, we assessed relative risks of HCC and non-HCC for patients with vs. without cirrhosis and on vs. off immunosuppressive treatment.

Results: For AIH patients and controls the 20-year risk of HCC was 1.9% [95% confidence interval (CI): 1.2-2.8] and 0.1% [95% CI: 0.0-0.2], respectively, and of non-HCC 19.8% [95% CI: 17.5-22.1] and 18.7% [18.0-19.5]. Having AIH was associated with hazard ratios of 54.2 [95% CI: 10.4-282.2] for HCC and 1.4 [95% CI: 1.2-1.6] for non-HCC as compared to age- and gender-matched controls, after adjustment. An association was seen between cirrhosis and HCC, with a hazard ratio of 4.18 [95% CI: 1.22-14.24], but not between cirrhosis and non-HCC or immunosuppressive treatment and HCC or non-HCC.

Conclusion: Having AIH was associated with a greater 20-year risk of HCC and non-HCC, but the increase in cancer was small in absolute terms: an excess 1.8% risk of HCC and an excess 1.1% risk of other cancers over 20 years. Among patients with AIH, cirrhosis was associated with an increased risk of HCC, but immunosuppressive treatment was not associated with either HCC or non-HCC.

F12.02   Mira Mekhael   COMPARISON OF TRANSANAL IRRIGATION AND GLYCEROL SUPPOSITORIES IN TREATMENT OF LOW ANTERIOR RESECTION SYNDROME: A MULTICENTRE RANDOMISED CONTROLLED TRIAL.

M. Mekhael[1, 3], T. Juul[1, 3], K. Krogh[2, 3], P. Christensen[1, 3]

[1]Department of Surgery, Aarhus University Hospital, [2]Department of Hepatology and Gastroenterology, Aarhus University Hospital, [3]Department of Clinical Medicine, Aarhus University

Background: Low anterior resection (LAR) is achievable in up to 80% of patients undergoing surgery for rectal cancer. However, the LAR Syndrome (LARS), which consists of various symptoms of bowel dysfunction, constitutes a major problem. Up to 90% will experience some degree of LARS, and 40-50% will experience major LARS in the long term. If conservative treatment for LARS fails, patients can be treated with transanal irrigation (TAI). Since it is unknown if conservative modalities such as suppositories, with a similar purpose of introducing scheduled defecation, are as effective as TAI, there is a need to investigate this in a randomised controlled trial.

Methods: The study will be conducted as a multi-centre, randomised, controlled, parallel-group trial. It will include rectal cancer patients treated

with a LAR, who still suffers from major LARS after conservative treatment. A total of 114 patients will be randomised to receive treatment with either TAI or glycerol suppositories for 12 weeks. Participants receiving TAI will irrigate once a day with gradually increasing volume of water. Participants treated with glycerol suppositories will administer one glycerol suppository daily. Primary outcome is change in the main symptom assessed by the Measure Yourself Medical Outcome Profile Score. Secondary outcomes are bowel, urinary and sexual function and quality of life (QoL). Outcomes will be assessed by the end of week 12.

Results: Inclusion started in September 2019 and results will be ready in 2022.

Perspectives: The results will improve the evidence base for treatment of LARS, potentially improving QoL for the increasing number of patients suffering from LARS.

| F12.03 | Astrid Højmark Andersen | PROTON PUMP INHIBITORS INCREASE RISK OF ORAL CANCER AMONG PATIENTS WITH ALCOHOLIC CIRRHOSIS |

A.H. Andersen, L. Bossen, P. Jepsen

Department of Hepatology and Gastroenterology, Aarhus University Hospital

Background and Aims: Proton pump inhibitors (PPIs) increase risk of complications in patients with liver cirrhosis, probably caused by alterations in the gut and oral microbiome. Risk of oral cancer (OC) is increased proportionally by alcohol intake and smoking, but oral microbiome alterations have also been suggested as a risk factor. We aimed to examine the association between PPI use among patients with alcoholic cirrhosis and the risk of OC.

Method: We conducted a registry-based nationwide historical cohort study including 17,632 patients diagnosed with alcoholic cirrhosis between 2000 and 2017. Follow-up started at the date of alcoholic cirrhosis diagnosis, and ended at OC diagnosis, death or 31 December 2017, whichever occurred first. Data on PPI use was collected from the Danish National Prescription Registry. Cox regression was used to estimate the hazard ratio (HR) of OC in PPI users vs. non-users, adjusting for confounding by gender, age, calendar year, severity of alcoholic cirrhosis and smoking. PPI use was set as a time-dependent exposure.

Results: At inclusion, 4,302 patients (24%) used PPIs, and 15,357 patients (87%) used PPIs at some point. OC was diagnosed in 131 patients, and 12,121 patients died during follow-up. The 10-year cumulative risk of OC was 0.98% (0.66-1.42) among PPI users vs. 0.89% (0.72-1.09) among nonusers. PPI users had a higher rate of OC than non-users (adjusted HR = 1.77, 95% CI 1.19-2.62), but PPI users did not die more often than non-users (adjusted HR = 1.04, 95% CI 0.99-1.08).

Conclusion: PPIs are widely used among patients with alcoholic cirrhosis. PPI use was associated with increased risk of OC, but the 10-year risk of OC was low.

| F12.04 | Ditte Emilie Munk | EFFICACY OF ZINC ON HUMAN GUT COPPER UPTAKE DEPENDING ON ZINC TYPE AND DOSE REGIMEN QUANTIFIED WITH $^{64}CUCL_2$PET/CT-SCAN |

D.E. Munk[1], T.L. Laursen[1], O.L. Munk[2], H. Vilstrup[1], P. Ott[1], L.C. Gormsen[2], T.D. Sandahl[1]

[1]Department of Hepatology and Gastroenterology, Aarhus University Hospital, [2]Department of Nuclear Medicine and PET-Centre, Aarhus University Hospital

Background and Aims: Zinc is used in the treatment of Wilson's disease (WD) and works by blocking intestinal copper uptake. Currently, zinc must be taken thrice daily with a 1 hour fast before and after. Different types of zinc salts exist but only one, zinc acetate (Zn-ac), is approved as treatment of WD. We aimed to investigate the effect of zinc type and dose regimen on copper uptake.

Methods: In an interim analysis, we included the first 17 healthy individuals. The individuals received a baseline 64-Cu PET/CT-scan to determine hepatic copper uptake and a follow-up scan after 4 weeks of treatment. They were randomised to 1 of 3 treatments: Zn-ac 50 mg x 3 daily, Zn-ac 150 mg x 1 daily, or zinc gluconate (Zn-glu) 150 mg x 1 daily. The effect was quantified as the relative difference in mean standard uptake value (SUV) in the liver.

Results: All seventeen trial participants completed the study. Two were excluded from the analysis due to issues with the baseline scan. The effect on copper uptake varied substantially among the individuals. The mean ratio was 0.39 (SD: 0.19) for Zn-ac 50 mg x 3, 0.60 (SD: 0.35) for Zn-ac 150 mg x 1, and 0.90 (SD: 0.23) for Zn-glu 150 mg x 1, indicating that all treatments lowered hepatic copper uptake. There was no significant difference in the effect on copper uptake between Zn-ac thrice or once daily, or between Zn-ac and Zn-glu once daily ($p > 0.05$). There was a difference between Zn-ac thrice and Zn-glu once daily ($p < 0.05$).

Conclusion: The effect of zinc treatment could be quantified by 64-Cu PET/CT scan and seemed highly variable. Zinc thrice daily was not significantly better than once daily as long as the zinc type was Zn-ac.

F12.05   Frederik Kraglund   DECREASING INCIDENCE OF ALCOHOLIC LIVER DISEASE IN DENMARK: A NATIONWIDE STUDY

F. Kraglund[1], T. Deleuran[1, 2], G. Askgaard[3], P. Jepsen[1, 4]

[1]Department of Hepatology and Gastroenterology, Aarhus University Hospital, [2]Department of Medicine, Randers Regional Hospital, [3]Department of Internal Medicine, Zealand University Hospital, [4]Department of Clinical Epidemiology, Aarhus University Hospital

Background and aims: Alcohol exposure has decreased in Denmark since 1994. We undertook this study to describe the recent developments in the national epidemiology of alcoholic liver disease.

Methods: We identified all Danish patients with a first-time diagnosis of alcoholic cirrhosis, hepatitis, steatosis or unspecified liver disease from 1977-2017. We computed standardised incidence rates, prevalence, hospitalisation rates, and survival for the period 1994-2017 by age and gender. Moreover, we computed incidence rates by 5-year birth cohorts (1950-1979). We used publicly available data to contrast our findings to per capita alcohol consumption.

Results: The overall standardized incidence rate of alcoholic liver disease was stable until 2009 but decreased from 362 (95% CI: 346-378) to 258 (95% CI: 245-271) per 1,000,000 population per year from 2009 to 2017. This decrease was most pronounced in men aged 15-44 and women aged 45-64. The 1950-1959 birth cohorts had the highest age-specific incidence rates, and the rates decreased sequentially with each following birth cohort. Both prevalence of alcoholic liver disease (0.22%) and average length of hospitalisation of patients with alcoholic liver disease (6 days) was stable from 2009 onwards. The 5-year survival after first-time diagnosis for alcoholic liver disease was 44.9% (95% CI: 44.3-45.4%) for men and 51.8% (95% CI: 51.1-52.6%) for women.

Conclusions: Incidence of alcoholic liver disease has decreased since 2009 in Denmark, mainly caused by a lower incidence rate in the population born after 1960. Yet, the prevalence of alcoholic liver disease is unchanged, and the overall survival is poor.

F12.06   Frederik Heiberg Brix   FIBRINOGEN LIKE-PROTEIN 1 AND LYMPHOCYTE ACTIVATING-GENE 3 IN ALCOHOLIC HEPATITIS

CANCELLED

F. Brix[1], B. Deleuran[2], T.D. Sandahl[1], S. Støy[1]

[1]Department of Hepatology and Gastroenterology, Aarhus University Hospital, [2]Department of Biomedicine, Aarhus University

Background: Alcoholic hepatitis (AH) is characterized by a destructive hepatic inflammation and a primed, but ineffective, immune system. Patients with AH therefore have an increased susceptibility to infections, which are amongst the leading causes of death. Lymphocyte-activation gene (LAG)-3 is an inhibitory receptor on activated T-lymphocytes that has been linked to T-cell exhaustion and immune paralysis. Recently fibrinogen like-protein (FGL)-1 was shown to bind to and potentiate the inhibitory properties of LAG-3. FGL-1 is a liver derived protein which is upregulated in response to liver inflammation and damage. We therefore want to investigate if FGL-1 and LAG-3 is involved in the immune paralysis in AH and related to infection and mortality.

Method: The study population consists of 40 patients with AH. Samples e.g plasma and Peripheral Blood Mononuclear Cells (PBMC) were taken at diagnosis and at days 7 and 90 following diagnosis. Liver LAG-3 and FGL-1 has been measured by RNA-sequencing. Soluble FGL-1 and LAG-3 will be measured with ELISA and the expression of LAG-3 and effect of FGL-1 stimulation will be carried out by flow cytometry.

Results: Preliminary results show that patients with AH have upregulated expression of FGL-1 in the liver compared with healthy controls (AH: 974(551;1398) vs HC 428(214;642), p<0.001) but the expression of LAG-3 is reduced (AH: 0.31(0.14;0.48) vs HC 0.85(0.46;1.24), p<0.001).

F12.07   Kristoffer Kjærgaard   COGNITIVE DYSFUNCTION IN NON-ALCOHOLIC FATTY LIVER DISEASE: A MECHANISTIC RAT STUDY

K. Kjærgaard[1], A.C. Mikkelsen[1], A. Landau[2, 3], P.L. Eriksen[1], N.E. Magnusson[4], C. Bay-Richter[3], K.L. Thomsen[1]

[1]Department of Hepatology and Gastroenterology, Aarhus University Hospital, [2]Department of Nuclear Medicine and PET-Centre, Aarhus University Hospital, [3]Translational Neuropsychiatry Unit, Aarhus University, [4]Medical Research Laboratory, Aarhus University Hospital

BACKGROUND

A key factor now recognized in non-alcoholic fatty liver disease (NAFLD) is impaired cognition, which may affect up to 70% of NAFLD cases with significant socio-economic impacts. Emerging data suggests a link between NAFLD and impaired urea synthesis, leading to hyperammonemia, which is highly involved in the pathogenesis of hepatic encephalopathy, the neuropsychiatric syndrome seen in liver failure. Importantly, chronic low-grade inflammation, postulated as mechanistically important in cognitive dysfunction, is a common feature in NAFLD.

The aim of this study is to address the hypothesis that cognitive dysfunction in NAFLD is mechanistically associated with impaired urea synthesis, compounded by chronic low-grade systemic and neuroinflammation.

METHODS

Using a well-established model of NAFLD representing "western diet", 40 Sprague Dawley rats (10 per group) will be fed either a high-fat, high-cholesterol diet for 2, 8 or 16 weeks or standard diet.

We will assess behavioral changes using validated neuropsychological tests. In the liver, NAFLD staging (histology) and urea cycle enzymes (qPCR and Western blots) are assessed. In the brain, neuroinflammation is assessed by autoradiography (activated microglia), immunohistochemistry (activated microglia and astrocytes) and measurements of cytokines in the cerebrospinal fluid.

PERSPECTIVES

This project will help provide mechanistic insight into the pathogenesis of cognitive dysfunction in NAFLD. With the dramatic increase in rates of NAFLD, the results of this study could potentially bring forward improved understanding and evidence for specific targeted disease intervention, an urgent clinical need.

F12.08 Frederikke Schønfeldt Troelsen

RISK AND PROGNOSIS OF POST-COLONOSCOPY COLORECTAL CANCERS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A DANISH POPULATION-BASED COHORT STUDY

F.S. Troelsen, R. Erichsen, L. Pedersen, H.T. Sørensen

Department of Clinical Epidemiology, Aarhus University Hospital

Introduction: Colonoscopy is considered the gold standard for detecting colorectal cancer (CRC); however, around 8% of all CRCs are diagnosed after a negative colonoscopy. These cancers are broadly referred to as post-colonoscopy CRCs (PCCRCs) and defined as CRCs diagnosed between 6 and 36 months after a preceding colonoscopy. PCCRC risk

may be particularly elevated in patients with inflammatory bowel disease (IBD). This could reflect complicated colonoscopies or a different molecular profile, but evidence is missing. Likewise, the impact of IBD on prognosis after PCCRC is unknown.

Aim: We will examine the impact of IBD on risk and prognosis of PCCRC.

Methods: We will perform a population-based cohort study in Denmark, linking prospectively collected, individual-level data from existing Danish registries during 1995-2015. We will identify all individuals recorded with a first-time colonoscopy and a previous or concurrent diagnosis of IBD. Individuals with a colonoscopy and without a diagnosis of IBD will serve as the comparison cohort. Study participants will be followed from 6 months after colonoscopy until PCCRC, death, emigration, or 36 months after the colonoscopy. We will calculate cumulative incidence proportions and relative risks of PCCRC. For the prognostic part, we will follow PCCRC patients with and without IBD to first occurrence of death, emigration, or study end. Survival will be evaluated using Cox regression analysis.

Results and Conclusion: Preliminary data show that we are able to identify roughly 2,000 cases of PCCRC, of whom approximately 150 have IBD. Construction of the dataset is ongoing, and results will be presented at the PhD day.

F12.09   Lotte Lindgreen Eriksen

INHIBITORY SKEWING OF T-LYMPHOCYTE PHENOTYPE IN ALCOHOLIC HEPATITIS

L.L. Eriksen[1], M.A. Nielsen[2], T.L. Laursen[1], H. Vilstrup[1], B. Deleuran[2], S. Støy[1]

[1]Department of Hepatology and gastroenterology, Aarhus University Hospital, [2]Department of Biomedicine, Aarhus University

Background and aim: Acute alcoholic hepatitis (AAH) has a high mortality due to liver failure and infection. Dysfunctional T-lymphocytes are thought to be involved in the high susceptibility towards infection. T lymphocytes have high expression of inhibitory receptors, but it is unknown whether this is balanced by a high expression of co-stimulatory receptors and how this relates to the risk of infections. We characterised the expression of the co-stimulatory receptor 4-1BB on T-lymphocytes and its inhibitory soluble form, s4-1BB, in relation to expression of the inhibitory receptor PD-1 and the presence of infections.

Methods: Blood from patients with AAH (diagnosis, day 7 and 90) was compared with healthy controls (HC). T-lymphocyte 4-1BB and PD-1 was quantified by flow cytometry and plasma s4-1BB by ELISA.

Results: The frequency of 4-1BB+CD4 (AH 74%(CI95% 71-78), HC 59%(46-71), $p<0.05$) and CD8 (AH 91%(88-94), HC 83%(74-92), $p<0.05$) T-lymphocytes were higher in AAH compared with HC. In patients with AAH, the frequency of PD-1+relative to 4-1BB+T-lymphocytes was increased ($p<0.005$). Also, the frequency of T-lymphocytes expressing both 4-1BB+ and PD-1 ($P<0.05$) and only PD-1 ($P<0.05$) was increased in AAH. Patients who developed infection at day 7 had a decrease in T-lymphocyte expression of 4-1BB and an increase in s4-1BB within the first week compared to those uninfected (both $p<0.05$). The same was found comparing those who had died by day 90 to those still alive.

Conclusion: In patients with AAH, the balance between co-stimulatory and inhibitory receptor expression are skewed towards an inhibitory phenotype on T-lymphocytes associated with infection and mortality.

F12.10   Charlotte Rud   ARE OUTPATIENTS WITH AN ILEOSTOMY SUB-CLINICALLY DEHYDRATED?

C. Rud[1], S.M.D. Jørgensen[1], J.F. Dahlerup[1], P.B. Jeppesen[2], S. Lal[3], C.L. Hvas[1]

[1]Department of Hepatology and Gastroenterology, Aarhus University Hospital, [2]Department of Gastroenterology and Hepatology, Rigshospitalet, [3]Intestinal Failure Unit, Salford Royal NHS Trust, Salford

BACKGROUND: Patients with an ileostomy may have low fluid and electrolyte status; however, this is not necessarily noticed. This study aimed to examine the quality of life (QOL), fluid and sodium balance in patients with an ileostomy.

METHODS: Stoma-QOL and EQ5D5L questionnaires were sent to patients with the diagnostic code for an ileostomy. Responders were invited to an examination of their fluid and sodium status by bioelectrical impedance analyses (BIA), blood and urine samples.

RESULTS: Of 621 identified patients (50% females), there were 412 responders (66%), of which 179 still had an ileostomy. Their mean Stoma-QOL score were 58 ($\pm$12) points, and EQ5D5L scores were statistically significantly higher than Danish normative data (0.09 ($\pm$0.17) points, 95%CI 0.05-0.12). Sodium and fluid status were examined in 49 patients. Forty-five % (95%CI 31-59) had a natriuresis $\leq$20mmol/l, 27 % (95%CI 15-41) had abnormally high p-aldosterone, and there was a strong relationship between the variables (X^2=21.72, p<0.001). Preliminary analyses indicate that the ileostomy group had lower TBW, and a higher ratio of extracellular water (ECW)/TBW, than a control group.

CONCLUSION: Patients with an ileostomy may appear healthy and have above normal QOL. However, this may be caused by nonresponse bias, and it is conceivable that the responders are among the healthiest of patients with an ileostomy. Nearly half of the patients were seemingly sub-clinically dehydrated. Their high ECW/TBW ratio could possibly indicate intracellular dehydration. More research in this patient group is warranted, including whether interventions that normalise natriuresis confer positive clinical outcomes.

F13.01   Søren Reinhold Jakobsen   PULMONARY MORPHOLOGY IN THE DECEASED - FORENSIC PULMONARY IMAGING

S.R. Jakobsen[1], K. Hansen[1], M. Thali[2], L.W.T. Boel[1]

[1]Department of Forensic Medicine, Aarhus University, [2]Zurich Institute of Forensic Medicine, University of Zurich

Background: Clinical diagnosis based on post mortem computer tomography (PMCT) scans of the lungs in the deceased is a challenge due to a significant amount of natural post mortem changes appearing as artefacts. Furthermore, limitations are present in the traditional qualitative analytical approach. Methods to improved scanning quality is key in forensic pulmonary imaging. Aim: To improve examination of non-pathological vs. pathological findings in forensic pulmonary imaging using

novel quantitative analytical techniques. Methods: Three experimental studies will be conducted. Study I and II will examine the effect of ventilation in deceased. Study III will consist of an experimental pig-model exposed to an approximated drowning scenario. A total of 40 deceased humans is estimated for study I and II. In study III 12 pigs is expected in each group. Study I: Develops a new and feasible access to post mortem ventilation and examines the effect of post mortem ventilation on interpretation of non-pathological lung tissue changes in PMCT. Study II: Examines the effect of post mortem ventilation on the branching of the airway tree in PMCT by measuring Airway Fractal Dimension. Study III: Examines the extent of pathological findings in swine lungs exposed to controlled experimental drowning. Perspectives: Proving significant effect of ventilated PMCT on artefacts is paramount for the future implication of ventilated PMCT as a standardized procedure. Furthermore, the quantitative analysis may aid other key areas of radiological imaging. Knowledge on lung findings in a controlled drowning scenario may facilitate the forensic scientist in the difficult diagnosis of drowning.

F13.02   Nicolai Toft   FUNCTIONAL REGULATION OF NA^+,HCO_3^--COTRANSPORT IN HUMAN
CANCELLED   BREAST CANCER: ASSOCIATION WITH HISTOLOGY, EXPRESSION OF HORMONE AND GROWTH FACTOR RECEPTORS, AND PROLIFERATIVE ACTIVITY

N. Toft[1], M. Mele[2], H. Pedersen[3], E. Balling[2], P. Christiansen[2], T. Johansen[3], E. Bødtkjer[1]

[1]Department of Biomedicine, Aarhus University, [2]Department of Surgery, Regionshospitalet Randers, [3]Department of Pathology, Regionshospitalet Randers

Breast cancer is the most frequent cancer in women worldwide and accounts for ~15% of cancer-related deaths. Accelerated cancer cell metabolism increases acidic waste production. However, due to increased net acid extrusion, intracellular pH of cancer cells is usually normal or even elevated compared to normal cells.

Breast carcinomas are classified by histological type, expression of sex hormone and HER2 growth factor receptors, and the Ki-67 proliferative index. We hypothesize that the molecular background for increased intracellular pH and net acid extrusion varies depending on the clinicopathological characteristics of individual patients.

Based on organoids enzymatically isolated from biopsies of normal breast tissue and breast cancer tissue from ~80 patients with breast cancer, we investigated intracellular pH by fluorescence microscopy using the pH-sensitive dye BCECF. We induced intracellular acidification with the NH_4^+pre-pulse technique.

Overall, steady state intracellular pH and net acid extrusion capacity are elevated in organoids from breast cancer compared to normal breast tissue. The dependency of intracellular pH on $CO_2/HCO_3^-$is greater in cancer tissue with high Ki-67 index, HER2 overexpression, and in invasive lobular carcinomas.

Supporting the key importance of HER2 signaling for acid-base transport activity, we show that the small-molecule HER2 inhibitor and Lapatinib

reduces HCO_3^--dependent net acid extrusion from breast cancer organoids.

In conclusion, we show that Na^+,HCO_3^--cotransport is upregulated in human breast carcinomas and propose that pharmacological targeting of this transport would cause intracellular acidification and inhibit tumor growth.

F13.03	Cathrine Overgaard	PRECLINICAL RELATIVE BIOLOGICAL EFFECTIVENESS (RBE) FOR NORMAL TISSUE DAMAGE IN ANIMAL MODELS

C. Bang Overgaard[1], B. Singers Sørensen[1], C. Grau[2], N. Bassler[1]

[1]Department of Experimental Clinical Oncology, Aarhus University Hospital, [2]The Danish Center for Particle Therapy

Introduction: 50% of all cancer patients receive radiotherapy, and the conventional treatment is radiotherapy with megavoltage x-rays. In January 2019, radiotherapy with protons became an option in Denmark, at the Danish Center for Particle Therapy (DCPT) in Aarhus. Both the physical and biological characteristics of proton beam differ from photons. The concept of RBE is used to quantify the biological differences between two radiation modalities. However, a key problem is to assess the biological effects in vivo and to determine the impact of these on normal tissue.

The aim of this study is to quantify the biological effects induced by proton irradiation on normal tissue in vivo. This includes effects of radiation dose, fractionation, energy deposition in tissue per unit distance and endpoints.

Methods: The right hind limb of mice will be proton irradiated in a single dose or in multiple fractions in different positions with increasing energy deposition and dose. Endpoints are acute skin-damages which will be assessed by a skin-scoring system, and fibrosis assessed by a leg contracture model. The acute skin-damages will be assessed daily for one month, followed by late effect assessments from day 60 to 356. Blood samples will be collected before and after irradiation to analyze immunological responses. Finally, the legs will be removed for histological purposes.

Perspectives: This study is expected to provide supporting in vivo data on the biological effects of proton irradiation in order to optimize proton radiotherapy. It will help us to better understand the acute and late effects after proton radiotherapy and provide data to help minimize normal tissue damage.

F13.04	Tenna Vesterman Henriksen	THE EFFECT OF SURGICAL TRAUMA ON CIRCULATING FREE DNA LEVELS IN CANCER PATIENTS - IMPLICATIONS FOR STUDIES OF CIRCULATING TUMOR DNA.

T.V. Henriksen[1], T. Reinert[1], E. Christensen[1], H. Sethi[2], K. Birkenkamp-Demtröder[1], M. Gögenur[3], I. Gögenur[3], B.G. Zimmermann[2], L. Dyrskjøt[1], C.L. Andersen[1]

[1]Department of Molecular Medicine, Aarhus University Hospital, [2]Natera Inc, San Carlos, USA., [3]Center for Surgical Sciences, Zealand University Hospital

Introduction

In patients with cancer, detection of circulating tumor DNA (ctDNA) post-treatment is an emerging marker of residual disease. ctDNA constitutes only a minor fraction of the cell-free DNA (cfDNA) circulating in cancer patients, which complicates ctDNA detection. This is exacerbated by trauma-induced cfDNA. To guide optimal blood sample timing, we investigated the duration and magnitude of surgical trauma-induced cfDNA in patients with colorectal or bladder cancer.

Methods

DNA levels were quantified in paired plasma samples collected before and up to six weeks after surgery from 436 patients with colorectal cancer and 47 patients with muscle invasive bladder cancer. For 91 patients, the cfDNA fragment size was analyzed. ctDNA data from 91 patients with colorectal cancer and 47 patients with bladder cancer was used to assess how trauma-induced DNA affects ctDNA detection.

Results

The total cfDNA level increased postoperatively - both in patients with colorectal cancer (mean 3-fold increase) and bladder cancer (mean 8-fold increase). The DNA levels were significantly increased up to four weeks after surgery in both patient cohorts ($P=0.0005$ and $P≤0.0001$). Short, but not long, cfDNA fragments showed increased levels postoperatively. Of 25 patients with radiological relapse, five were likely ctDNA negative due to trauma-induced cfDNA.

Conclusion

Surgery was associated with elevated cfDNA levels, persisting up to four weeks, which may have masked ctDNA in relapse patients. Size analysis could not differentiate trauma-induced from ordinary cfDNA. To avoid high cfDNA levels, it may be recommended to delay postoperative blood sampling until end of week 4.

F13.05   Mette Tiedemann Skipper

THE ACUTE LYMPHOBLASTIC LEUKEMIA SURVIVOR TOXICITY AND REHABILITATION (ALL-STAR) STUDY

M.T. Skipper[1, 2, 3], L. Andrés-Jensen[3], T.L. Frandsen[3], K. Schmiegelow[3], B.K. Albertsen[2, 1]

[1]Department of Clinical Medicine, Aarhus University, [2]Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital, [3]Department of Pediatrics and Adolescent Medicine, University Hospital, Rigshospitalet

Background: Acute lymphoblastic leukemia (ALL) is the most common childhood cancer. Treatment has improved dramatically over the last decades, improving survival rates to over 90%. However, intensive chemotherapy treatment has a cost. 50% experience at least one severe treatment-related acute toxicity (Toft N, BJH, 2012) and an overrepresentation of chronic health conditions was found in childhood cancer survivors (Bhakta N, lancet, 2017). However, the association

between acute toxicities and late adverse effects in a cohort as the present, has not yet been investigated.

Aim: Our primary aims are to examine the prevalence of late adverse effects in survivors of ALL treated according to a contemporary protocol (NOPHO ALL2008). Further, to identify risk markers including host genome variants, drug exposure and treatment-related acute toxicities to the development of late adverse effects.

Hypothesis: 1) Identification of at least one severe late adverse effect in at least 50% of survivors. 2) Host genome variants, drug exposure and acute treatment-related toxicities can predict risk of late adverse effects.

Method: Survey on somatic symptoms, medical history and health-related quality of life (HRQL). Clinical examinations including anthropometrics, cardiac function (echocardiography and MRI), pulmonary function, physical function, neuropathy, DEXA scan, ultrasound of liver, pancreas and kidney and multiple biochemical analyses. We include controls 1:1 matched on sex and age.

Perspectives: Our study will hopefully identify risk patterns and possible intervention points, enable an evidence-based follow-up program and ultimately reduce risk of late morbidity and improve HRQL.

F13.06   Jintao Ren   DEEP LEARNING FOR IMPROVED TUMOUR DELINEATION IN RADIOTHERAPY OF HEAD AND NECK CANCER

J. Ren[1], J. Nijkamp[1], J.G. Eriksen[2], S.S. Korreman[1, 3, 4]

[1]Department of Oncology, Aarhus University Hospital, [2]Department of Experimental Clinical Oncology, Aarhus University Hospital, [3]Danish Center for Particle Therapy, [4]Department of Clinical Medicine, Aarhus University

In radiation oncology, treatment planning is individually planned for each patient based on oncologist's delineation of radiation target (malignancy) in medical images (CT, MR and PET scans). The limiting factor is the identification of the radiation target in the medical images. It is well-known that there are significant uncertainties in this identification, and these uncertainties are presently handled by adding a margin to the delineated target volume, thereby enlarging it and adding the considerable risk of dose spill-over to nearby organs at risk (OAR). In recent years, advances in computer capabilities have made the development of automatic segmentation possible. The application of deep learning has been evaluated in Head and Neck Cancer (HNC) for OAR segmentation and has been attempted for target volume segmentation on CT and MR imaging separately.

We aim to establish accurate tumour and pathologic lymph node segmentation using a large dataset (>300) of HNC patients with 3D multi-modal imaging - CT, PET, and MRI. We hypothesize that such a multi-modal deep learning method will lead to a feasible clinical workflow where minimal interaction will lead to clinically acceptable segmentations. This will simultaneously translate into a reduction of the workload and most importantly of the inter-observer variation. This project aims to investigate and develop new computer-assisted tools for identification and delineation of radiation target volumes in medical images with support from start-of-the-art Convolutional neural

networks(CNN). The tools will be potentially useful for delineation in any cancer site, and hence the scope of impact is huge.

F13.07   Arththy Antony   NA$^+$,HCO$_3^-$-COTRANSPORTERS AS ANTI-CANCER THERAPEUTIC TARGETS

A. Antony

Department of Biomedicine, Aarhus University

Elevated metabolism leads to increased cellular acid loading of cancer cells. We hypothesize that the cancer cells export or neutralize the acidic waste products throughmembrane transporters, particularly Na$^+$,HCO$_3^-$-cotransporters,that elevate intracellular pH and decrease extracellular pH. We further propose that this compartmentalized acid-base distribution contributes to sustaining intermediary metabolism, proliferative activity, and extracellular matrix degradation in cancer tissue and facilitates metastasis.

This project aims at developing novel therapeutic strategies that disrupt acid-base homeostasis in cancer tissue by interfering with acid-base transporters in the cell membrane.

F13.08   Stine Høvring Godsk   IMPROVING THE PROSPECTS OF IMMUNOTHERAPY IN SARCOMA THROUGH INVESTIGATION OF SARCOMA-SPECIFIC IMMUNE-EVADING MECHANISMS

S.H. Godsk[1], K.R. Gammelgaard[1], N. Aggerholm-Pedersen[2], M.R. Jakobsen[1]

[1]Department of Biomedicine, Aarhus University, [2]Department of Oncology, Aarhus University Hospital

Sarcoma is a rare type of cancer developing in bone and soft tissue. In Denmark, sarcoma account for 1% of all newly diagnosed cancers. Yearly this includes approximately 45 cases of bone sarcoma and 220 cases of soft tissue sarcoma. The primary treatment today is surgery alone or in combination with radiation and/or chemotherapy. Despite the success of immunotherapy in cancers like malignant melanoma and lung cancer, the results in sarcoma patients have so far been disappointing.

The ability of a cell to establish an immune response is a key element in preventing cancer growth and progression. A possible key evasion mechanism of the immune system in sarcoma is the suppression of the innate immune system. Here, we know that the protein STING plays a central role in the innate immune response, as it senses DNA damage resulting from invading pathogens or from the host itself as a result of tumorigenesis. Thus, the level of STING expression and functionality may be important for a strong anti-tumor response.

The goal for this project is to identify possible immune-evading mechanisms responsible for the ability of sarcoma to prevent immune responses. This will be approached through investigation of tumor infiltrating immune cells in sarcoma biopsies and investigation of the STING pathway in sarcoma cell lines, primary sarcoma cells from fresh tissue and mesenchymal stem cells. Furthermore, a transcriptomic analysis together with cytokine expression profiling within cancer tissue and blood from sarcoma patients will be carried out to identify possible correlations

between immune expression patterns and disease progression as well as overall survival.

F14.01   Mads Sandahl   EARLY DETECTION OF CLINICALLY SIGNIFICANT PROSTATE CANCER

M. Sandahl[1], K. Dalsgaard[2], M. Borre[3], B. Ginnerup[1]

[1]Department of Radiology, Aarhus University Hospital, [2]Department of Molecular Medicine (MOMA), Aarhus University Hospital, [3]Department of Urology, Aarhus University Hospital

Background: The traditional investigation in Prostate cancer (PC) include prostate specific antigen (PSA) and transrectal ultrasound (TRUS) biopsy which are unspecific and random examinations. Genetics play an important role for the development of PC and genetic testing, using single nucleotide polymorphisms (SNPs), may replace PSA testing in the future. Multiparametric magnetic resonance imaging (mpMRI) of the prostate has a high negative predictive value for the detection of clinically significant PC and can guide targeted biopsy. Purpose: To assess the value of different mpMRI sequences in relation to the detection of PC; To evaluate SNP-testing in the triage of patients suspected of having PC. Materials and methods: 550 biopsy naive patients will form the basis for the analysis of the mpMRI sequences. 438 patients with elevated PSA and a negative TRUS biopsy will form the basis for the evaluation of SNP-testing. mpMRIs images will be analyzed regarding benefit from different sequences, and patient characteristics will be examined with a focus on genetics. Perspectives: Improved PC detection.

F14.02   Ninna Hinchely   NITRATE AND ARSENIC IN DRINKING WATER AND ADVERSE
         Ebdrup   REPRODUCTIVE OUTCOMES IN MEN AND WOMEN

N.H. Ebdrup[1, 2], C.H. Ramlau-Hansen[2], B. Bay[1], J. Lyngsø[2], J. Schullehner[2, 4, 3], U.B. Knudsen[1]

[1]Department of Obstetrics and Gynaecology, Fertility Clinic, The Regional Hospital in Horsens, [2]Department of Public Health, Research Unit for Epidemiology, Aarhus University, [3]Centre for Integrated Register-based Research, CIRRAU, Aarhus University, [4]Geological Survey of Denmark and Greenland (GEUS)

Background

Nitrate and arsenic are common pollutants in drinking water globally, but the influence of female and male reproductive health remains uncertain. Few animal and human studies have linked their exposure to spontaneous abortion and decreased sperm quality, but conclusions are challenged by few participants and methodological limitations. The main objective is to explore how these environmental factors affects reproductive health.

Methods

We have designed a series of case-control and cohort studies aiming to overcome some of the limitations of previous studies. By using two different cohorts varying in time and availability of covariates, it will be possible to estimate the association between individual and time-specific nitrate and arsenic exposure levels with a variety of outcomes on the

pathway from conception to birth (infertility, abortion, menstrual irregularities and time to pregnancy). This is possible by linking geocoded residential history with drinking water quality maps. Furthermore, our data allows long-term follow-up of large populations assessing large exposure contrast, even if concentrations are below the drinking water standard to identify small yet chronic effects on reproduction.

Perspectives

We contribute with the largest population-based study to date looking at drinking water nitrate and arsenic consumption and adverse reproductive outcomes in men and women. The project will contribute with important knowledge to a field where epidemiological studies are needed. By using detailed data we strive to generate new insights for the benefit of the couples struggling with subfertility and, in doing so, contribute to the prevention of infertility.

| F14.03 | Jacob Damgaard Eriksen | RISK FACTORS FOR ANASTOMOTIC LEAK IN PATIENTS UNDERGOING RECTAL RESECTION FOR CANCER. A RETROSPECTIVE, POPULATION-BASED STUDY |

J.E. Eriksen[1], A.H. Madsen[2], K.J. Emmertsen[3], T. Bachmann[1], N. Thomassen[1], L.H. Iversen[1]

[1]Department of Surgery, Aarhus University Hospital, [2]Department of Surgery, Regional Hospital West Jutland, [3]Department of Surgery, Randers Regional Hospital

Aim: To examine patient-related, surgical, and postoperative risk factors for anastomotic leak after anterior rectal cancer resection.

Method: In a population-based setting of 1.3 mill inhabitants, a retrospective two-center study was conducted in patients undergoing rectal cancer resection with a primary anastomosis between January 2013 and October 2017. Anastomotic leak was detected with CT-scan, endoscopy, or surgery if clinical symptoms. Data on demographics, preoperative treatment, surgery, and postoperative complications were retrieved from the Danish Colorectal Cancer Group Database and supplied with data from review of medical records. Differences in variables were tested by Chi-square test. Risk factors of leak were examined by logistic regression analysis, adjusting for covariates.

Results: Data collection is still ongoing. Expected number of patients: 650. Preliminary results of 292 patients operated at one center during 2013-2015 have shown a leak rate of 16.4% with comparable rates after TME (total mesorectal excision) and PME (partial mesorectal excision). In descriptive analyses, the anastomotic leak rate differed according to gender (male/female: 23.9%/3.7%), body mass index (BMI≥30.0/BMI 18.5-24.9: 24.4%/12.8%), and smoking status (current smokers/non-smokers: 24.4%/14.2%).

Conclusion: The anastomotic leak rate was unexpectedly high at one center during 2013-2015. Results of the entire study will be ready November 2019.

F14.04	Anna Louise Christ Vestergaard	VITAMIN D DEFICIENCY IN PREGNANCY - IS INCREASED SUPPLEMENTATION NEEDED?

A.L. Vestergaard[1, 2], M. Christensen[2], M.F. Andreasen[3], A. Larsen[4], P. Bor[1]

[1]Department of Obstetrics and Gynecology, Randers Regional Hospital, [2]Research Unit, Randers Regional Hospital, [3]Section for Forensic Chemistry, Department of Forensic Medicine, Aarhus University, [4]Department of Biomedicine, Aarhus University

Introduction: Vitamin D deficiency is associated with increased risk of pregnancy complications related to placental function like intrauterine growth restriction, pre-eclampsia and gestational diabetes, although the underlying mechanisms are far from elucidated. Pregnancy complications increase the risk of preterm delivery, perinatal and maternal morbidity and mortality. Accumulating evidence links exposure to pregnancy complications and vitamin D deficiency itself to long-term health problems.

Aim: To investigate if increased vitamin D supplementation in pregnancy can reduce the prevalence of intrauterine growth restriction, pre-eclampsia and gestational diabetes, and to perform in-depth analysis of the placental effects of increased vitamin D supplementation to improve our understanding of underlying risks and disease pathology.

Methods: A double blinded randomized trial testing two doses of vitamin D: 10 μg vs. 90 μg, combined with in-depth molecular analysis of placental tissue from selected groups (healthy and diseased pregnancies, obese, medicine users). A total of 2000 pregnant women seeking prenatal care at Randers Regional Hospital will be included in the study. Study materials include maternal blood samples, questionnaires describing life-style habits, placental tissue, umbilical cord blood and information on maternal and fetal outcomes from medical records.

Perspective: We expect to provide new knowledge about disease mechanisms and vitamin D's effect on perinatal health and provide the scientific evidence for determining if increased vitamin D supplementation constitutes a feasible, economically sustainable way of improving public health for future generations.

F14.05	Rosa Marie Østergaard Kiil	PREGNANCY-RELATED MRI FINDINGS AT THE SACROILIAC JOINTS IN FEMALES REFERRED WITH LOW BACK PAIN - A 4-YEAR MRI FOLLOW-UP STUDY

R.M. Kiil[1], B.A. Arnbak[2, 3], A. Zejden[1], B. Schiøttz-Christensen[4, 5], O. Hendricks[5, 6], A.G. Jurik[1, 5, 7]

[1]Department of Radiology, Aarhus University Hospital, [2]Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, [3]Department of Radiology, Hospital Lillebaelt, Vejle, [4]Research Department, Spine Centre of Southern Denmark, Hospital Lillebaelt, [5]Institute of Regional Health Research, University of Southern Denmark, [6]King Christian 10th Hospital for Rheumatic Diseases, [7]Department of Clinical Medicine, Aarhus University

Background:

Low back and pelvic pain are frequent during and after pregnancy. It can be related to changes at the sacroiliac joins (SIJ), which may be detectable by magnetic resonance imaging (MRI). Few studies have investigated possible pregnancy-related SIJ MRI findings.

The purpose of this study was to describe the prevalence and course of SIJ MRI findings, clinical signs and a potential axial spondyloarthritis (SpA) diagnosis in females with non-specific low back pain and relate the findings to pain elicited by pregnancy.

Methods and Materials:

A prospective longitudinal cohort study comprising 328 females referred with non-specific low back pain to a Danish outpatient care unit, who had MRI of the SIJs and filled in a questionnaire on symptoms and function at baseline and at 4-year follow-up. Furthermore, they were examined clinically and biochemically at baseline.

Results:

At baseline, 44 (14.5%) females reported debut of pain related to pregnancy.

Cross-sectionally at baseline, 'any SIJ MRI finding' and 'a potential SpA diagnosis' were statistically significantly more frequent in females reporting pregnancy-related pain compared to the remainders (48% vs. 31%, p = 0.031 and 27% vs. 15%, p = 0.047, respectively).

During time, the prevalence of females with a potential SpA-diagnosis tended to decrease in females with pregnancy-related pain (27% to 18%, p = 0.289).

Conclusion:

Females reporting pregnancy-related pain tended to have different SIJ MRI and clinical characteristics, both in cross-sectional and longitudinal analyses, compared to remainders. Clinicians should be cautious when diagnosing SpA to women reporting pregnancy-related pain.

F14.06   Anne Sophie Fischer

COGNITIVE LATE EFFECTS IN CHILDHOOD BRAIN TUMOR SURVIVORS

A.S.L. Fischer[1], H. Hasle[2], H. Schroeder[2], L.T. Henriksen[2], Y. Lassen-Ramshad[3], A. Amidi[4], L. Kenborg[5], J.F. Winther[6]

[1]Department of Pediatrics, Aarhus University, [2]Department of Pediatrics, Aarhus University Hospital, [3]Department of Clinical Oncology, Danish Centre for Particle Therapy, Aarhus University Hospital, [4]Department of Psychology and Behavioural Sciences, Aarhus University and Department of Oncology, Aarhus University Hospital, [5]Danish Cancer Society Research Center, [6]Danish Cancer Society Research Center and Department of Clinical Medicine, Aarhus University

Background: Every year, around 40 children are diagnosed with a brain tumor in Denmark. As the survival rate is approaching 70%, a growing population of survivors is facing long-term effects of cancer and its treatment. Proton therapy was implemented in Denmark in 2019, and there is a need to evaluate treatment-induced late effects related to conventional photon-based radiation therapy. Among the most common late effects are cognitive impairments due to irradiation, but also to

surgery, chemotherapy and the tumor itself. Cognitive impairments, such as impaired processing speed, attention, memory, and executive functioning, may have detrimental effects on patients' everyday life. We aim to investigate the extent of neurocognitive deficits in patients receiving irradiation compared with those not being irradiated. Furthermore, we will compare a subgroup of patients receiving focal irradiation with patients, who have undergone surgery or observation alone.

Methods: In total, 426 eligible patients diagnosed with a brain tumor from 1997-2015, <15 years old at diagnosis, will be invited to a neurocognitive assessment. 200 patients are expected to participate with a response rate of 50%. The supervised neurocognitive assessments with standardized neurocognitive tests include: The Trail-Making-Test; The Hopkins Verbal Learning Test; Conner's Continuous Performance Test; Coding and Digit Span from Wechsler's Adult Intelligence Scale-IV; and The Controlled Oral Word Association Test.

Results: So far, 11 patients have been enrolled.

Conclusion: This study will be important to highlight the impact of different tumor treatments on late effects in survivors of childhood brain cancer.

F14.07 Marie Tvilum   OPTIMAL INDIVIDUAL TREATMENT STRATEGY FOR EVERY LOCALLY
        Chadwick Hede   ADVANCED NON-SMALL CELL LUNG CANCER PATIENT

M. Tvilum[1], M.M. Knap[1], L. Hoffmann[2], C.M. Lutz[2], A.A. Khalil[1], K.M. Haraldsen[4], C. Grau[3], M. Alber[5], A. Appelt[6], D.S. Møller[2]

[1]Department of Oncology, Aarhus University Hospital, [2]Department of Medical Physics, Aarhus University Hospital, [3]Danish Center for Particle Therapy, Aarhus University Hospital, [4]Department of Clinical Medicine, Nuclear Medicine and PET, Aarhus University Hospital, [5]Department Of Radiation Oncology, Heidelberg University Clinic, [6]Institute of Oncology and Pathology, St. James University Hospital and University of Leeds

Lung cancer is one of the leading causes of cancer related deaths worldwide. The treatment of locally advanced non-small cell lung cancer (LA-NSCLC) consists of combined chemo-radiotherapy (cRT). The treatment struggles with both local and distant failure.

The aim of this study is to find the correlation between early treatment response and pattern of failure. We hypothesize that early tumour response will predict pattern of failure, and hence could be used as a prognostic tool to individualize treatment when treating LA-NSCLC-patients with curative intended cRT.

The study is divided in 3 subprojects:

Project 1: The relationship between early tumour response to chemotherapy and pattern of failure will be established by analysis of PET-scans before and after one series of chemotherapy in a cohort of 500 consecutively treated patients. Analysis will include both standard and advanced voxel-level image analysis.

Project 2: The relationship between early response to RT and pattern of failure will be established based on response measurements for 500 patients, who have ConeBeam-CT made during RT available for analysis.

Additionally, 100 patients included in a Danish phase III trial, NARLAL2, will have PET/CT-scans during RT available for analysis. Analysis will be similar to project 1.

Project 3: A predictive model including both baseline patient characteristics and early response to chemo- and radiotherapy will be established. We aim to have the model validated externally and anticipate that the model could be a supportive tool in the treatment of LA-NSCLC patients. This will allow oncologists to select the optimal curative treatment intensity for every individual patient.

F14.08   Camilla Ejlertsen   LOOK - YOUR BABY IS TALKING TO YOU

C. Ejlertsen[1], I. Kristensen[2], A.M. Nybo Andersen[3], A. Brødsgaard[4]

[1]Department of Gynecology and Obstetrics, University of Copenhagen, University Hospital Hvidovre, [2]Department of Public Health ,Section for Nursing, Aarhus University, [3]Section of Epidemiology, University of Copenhagen, [4]Department of Pediatrics, Copenhagen University Hospital Hvidovre

The formation of the early relation between parents and infant has a significant impact on the child's mental, social and cognitive development and competencies. Symptoms of mental illness can affect parenting capabilities. This study is a prospective mixed-method study consisting of three sub-studies with the main focus on developing and testing an intervention that will be carried out at the obstetric department at Copenhagen University Hospital Hvidovre (CUHH) and in transition to the primary healthcare sector using family focused nursing (FFN) and neonatal behavioral observational (NBO) The aim of the intervention is to facilitate family consciousness of their resources and increase parental sensitivity to foster the best possible prerequisites for a healthy early relationship formation between parent and infant. The study population consists of mothers diagnosed with anxiety and/or depression diagnosis giving birth at CUHH and enrollment will start autumn 2019. The implementation and evaluation of the intervention will determine whether the combination of FFN, NBO and improved transition to primary healthcare sector is associated with decreased prevalence of maternal depressive among parents in the intervention group (N=55) compared to the control group (N=55). Effect from baseline (24-48 hours post-partum) to follow-up (3 months post-partum) will be measured using internationally validated questionnaires. This study 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 FFN and NBO at the obstetric department which has never been done in a Danish context.

F15.01   Kristian Wiborg Antonsen   IS THE SOLUBLE PD-1 VARIANT (SPD-1) EXPRESSED BY HUMAN MACROPHAGES?

K.W. Antonsen, C.V.B. Hviid, M.K. Hagensen, H.J. Møller

Department of Clinical Biochemistry, Aarhus University Hospital

Soluble PD-1 (sPD-1) is the free circulating form of the PD-1 receptor. PD-1 is expressed on various activated cells of the immune system. sPD-1 can

originate from alternative splicing of PD-1 mRNA and could compete with PD-1 for PD-L1 binding. The activation state of tumour associated macrophages influence survival in cancer, and the PD-1/PD-L1 axis has been suggested to play a role in their regulation. This study investigated PD-1 and sPD-1 expression in activated macrophages. Human monocytes (THP-1 cells and CD14+ monocytes from healthy blood donors) were differentiated into macrophages with either PMA or M-CSF and GM-CSF respectively. Macrophages were polarized to either an M1 (IFN-γ and LPS) or M2 (IL-4 and IL-13) phenotype. Macrophage phenotype markers (CD14, CD11b, CD163, TLR-2, CD206 and CD80) and expression of PD-1 was assessed by flow cytometry. Expression of PD-1 and sPD-1 mRNA will be assessed by droplet digital PCR. Secretion of sPD-1 protein was assessed by electrochemiluminescence ELISA. Compared to untreated cells, M1 cells had significantly increased expression of CD80 and TLR-2 while M2 cells had significantly increased expression of CD11b and CD206 consistently across both THP-cells and monocyte-derived macrophages (MDM). No induction of PD-1+ macrophages was observed. sPD-1 protein was consistently measurable in the supernatant of M1 THP-1 cells after 72 hours of stimulation. In MDMs, sPD-1 protein was measurable in the supernatant of M1 cells derived from 2/4 donors and in M2 cells derived from 1/4 donors after 72 hours of stimulation. No secretion of sPD-1 was observed by unstimulated macrophages. Gene expression results are still awaited.

| F15.02 | Alexey Ferapontov | MOLECULAR REQUIREMENTS FOR B CELL RECEPTOR ENGAGEMENT, B CELL ACTIVATION AND RECEPTOR-MEDIATED ENDOCYTOSIS OF ANTIGEN |

A. Ferapontov[1, 3], M. Omer[2, 3], J. Nielsen[2, 3], S. Thiel[1, 3], J. Kjems[2, 3], S. Degn[1, 3]

[1]Department of Biomedicine, [2]iNANO, [3]CellPAT, DNRF Center for Cellular Signal Patterns

B cells are a central component of the adaptive branch of the immune system, responsible for humoral immunity through production of antibodies. The first step in B cell activation is a crucial process, underlying such essential and diverse aspects of immune function and dysfunction as humoral immunity, vaccine responses, and autoimmunity. Yet fundamental aspects of antigen engagement and B cell activation remain controversial.

To tackle the question of molecular requirements for B cell activation, including considerations of B cell receptor (BCR) affinity and avidity, we are utilizing a well-established knock-in BCR model (B1-8hi) combined with novel nanoparticle antigens. Lambda light-chain positive B cells from B1-8hi knock-in mice display high-affinity binding to the haptens NP (4-hydroxy-3-nitrophenyl acetyl hapten) and NIP (4-hydroxy-3-iodo-5-nitrophenylacetic acid). Combinatorial assembly of NP- or NIP-conjugated locked nucleic acid segments in stable Holliday junctions allows on-demand mix-and-match generation of model antigens to desired specifications. Naïve resting B1-8hi B cells are purified using magnet-activated cell sorting (MACS), and their binding to NP/NIP antigenic patterns on Holliday Junctions are studied using flow cytometry and Octet binding assays. Future studies are aimed at investigating minimal pattern requirements for BCR cross-linking, receptor-mediated endocytosis using

spinning disc confocal microscopy and Holiday junction based BCR activation using super-resolution microscopy.

F15.03   Jacob Thyrsted   LACTATE INHIBITS TYPE I IFNS TO PROMOTE INFLUENZA A VIRUS
           Jensen   REPLICATION IN HUMAN AIRWAY EPITHELIUM

J. Thyrsted, J. Storgaard, A.L. Hansen, C.K. Holm

Department of Biomedicine, Aarhus University

Increased cellular consumption of glucose and of secretion of lactic acid is a hallmark of most cancer cells and has also recently been described for immune cells that are stimulated with pathogen associated molecular pattern ligands such as lipopolysaccharide. Increased lactate concentration has recently been demonstrated to negatively regulate the interferon-response to cytosolic RNA by inhibiting the (RIG-I)-like receptor signaling. We used a model of primary human airway epithelium to test the importance of lactate production during infection with the human pathogen influenza A virus. Here, we report that lactate is released in response to infection with the RNA virus influenza A virus. Further, we demonstrated that the increased levels of lactate inhibited efficient RIG-I like receptor mediated induction of type I IFN in response to infection and promoted spread of the virus. Our data imply that glycolysis promotes influenza A virus replication by lactate-mediated inhibition of RIG-I like signaling in human airway epithelium.

F15.04   Mastaneh Afshar   INVESTIGATION ABOUT SLOW-GROWING BACTERIA AS CAUSATIVE
           CANCELLED   AGENTS OF IMPLANT-ASSOCIATED INFECTIONS: HOW TO DETECT A
                             WOLF IN SHEEP'S CLOTHING

M. Afshar[1], J. Lange[1, 2], H. Brüggemann[1]

[1]Department of Biomedicine, Aarhus University, [2]Department of Clinical Medicine, Aarhus University

Background: For many elderly patients, surgical implantation of medical devices can tremendously improve the quality of life. However, implantation of foreign devices also carries a considerable risk for infection. Such implant-associated infections (IAIs) are one of the most serious worries in orthopedic surgery. IAIs are frequently caused by Staphylococcus aureus. However, numerous other opportunistic pathogens can also cause IAIs, such as slow-growing bacteria that are difficult to identify. The aim of this project is to perform a full investigation about the properties of newly identified bacterial species associated with IAIs; the causality of such species in IAI is interrogated with an array of bacteriological tools and models.

Implants are collected and processed by sonication and subsequent microbial cultivation at hospitals in Denmark, Germany and Sweden. After species identification, selected species are thoroughly investigated; these include so far Corynebacterium macginleyi, Staphylococcus saccharolyticus, Cutibacterium spp. and Finegoldia spp. Biochemical characterization of these species will be done and biofilm-forming ability will be evaluated. Whole genome sequencing, and for selected species, transcriptome sequencing and proteome analyses will be carried out, to gain knowledge about host-interacting traits and virulence determinants.

The project will proceed with investigations in cell culture models, e.g. the inflammatory response of host cells upon bacterial encounter will be determined, as well as properties regarding their persistence and invasiveness. The project should help improving diagnosis, treatment and prevention of IAI in the future.

F15.05   Thomas Emmanuel

THE EFFECT OF DEAD SEA CLIMATOTHERAPY ON PSORIASIS SKIN

T. Emmanuel, D. Lybæk, C. Johansen, L. Iversen

Department of Dermatology, Aarhus University Hospital

Psoriasis is a chronic recidivating inflammatory skin condition believed to be caused by dysregulated T-cells. This results in a chronic inflammatory milieu which changes the cells normally present in the skin. Many treatment options exist ranging from topical treatment, systemic treatment, and Dead Sea Climatotherapy (DSC), to biologics that inhibit different pro-inflammatory signaling pathways. DSC is typically done by sending patients to Ein Gedi in Israel on a 4-week treatment program consisting of individualized sun- and mud exposure. The effectiveness in the short term is comparable to the newest biologics. Psoriasis patients treated with DSC constitutes a subpopulation of psoriasis patients that have not been widely studied.

This study aim of this study is to investigate the effectiveness of Dead Sea Climatotherapy on psoriasis associated parameters in the skin.

Biopsies and formalin-fixed paraffin-embedded tissue specimens from 18 psoriasis patients have already been collected. These were acquired both before-, after-, and at first visible signs of psoriasis. These biopsies will need to be analyzed using techniques employed in our laboratory such as western blotting, immunohistochemical staining, and real-time quantitative polymerase chain reaction to analyze proteins, immunopathology, and transcription of genes, known to be involved in psoriasis. In this way, the effectiveness of DSC on a molecular level can be assessed and elucidated. The results of this study will aid in comparing the effectiveness of DSC with other treatments and will lead to better treatment options for psoriasis patients.

F15.06   Kamilla Vandsø Petersen

DEVELOPMENT OF A LOW-TECHNOLOGICAL, FAST AND QUANTITATIVE DIAGNOSTIC METHOD FOR DETECTION OF TUBERCULOSIS IN SALIVA SPECIMENS

K.V. Petersen[1], K.N. Borg[2], B.R. Knudsen[2], C. Wejse[1, 3]

[1]Department of Clinical Medicine, Aarhus University, [2]Department of Molecular Biology and Genetics, Aarhus University, [3]Department of Public Health, Aarhus University

Infection from members of the Mycobacterium tuberculosis complex (MTC) is a serious threat to global health. Tuberculosis (TB) is the leading course of death caused by a single infectious agent, even ranking above HIV. WHO estimates that 10 million people fell ill with TB in 2018, which lead to nearly 1.5 million deaths.

Today, the gold standard for TB diagnosis is mycobacterial culturing which takes 4 to 8 weeks before giving a clear result. Faster methods can be

based on PCR approaches. However, such methods are often combined with culturing and require sputum which can be difficult to obtain from e.g. children and HIV patients. There is no fast and quantitative point-of-care (POC) TB test based on easy obtainable and non-invasive test material.

We want to investigate the possibilities to overcome this problem by using enzyme activities unique to MTC as biomarkers in the development of a new diagnostic test. The test is based on specific enzymatic conversion of DNA molecules to circular DNA products suitable for rolling circle amplification, which enables quantitative and sensitive detection, when combined with droplet microfluidic approaches for single cell analysis. Currently different DNA molecules and approaches for efficient extraction of active enzymes from mycobacteria are being tested using M. smegmatis as model organism. The final aim is to develop a TB test suitable for POC testing using only saliva as patient sample.

F15.07   Anne Sophie Schou

USING EXTRACELLULAR VESICLES AS A TEMPLATE FOR AUTOIMMUNE DIAGNOSTIC SCREENING

A.S. Schou[1, 2], K. Varming[1], R. Bæk[1], R.K. Jentoft Olsen[2], M. Møller Jørgensen[1]

[1]Department of Clinical Immunology, Aalborg University Hospital, [2]Research Unit for Molecular Medicine, Aarhus University

INTRODUCTION:

Extracellular vesicles (EVs) are bilayered organelles produced by various cell types, from which the EVs inherit biological material, as RNA, DNA and proteins when they are released to the extracellular space. Proteins as the G-protein coupled receptor (GPCRs) are cell-signaling transmembrane peptides, which in their native form comprise of seven segments embedded in the membrane, which structural advancement can be maintained in EVs. In autoimmune diseases, auto-antibodies towards GPCRs is not uncommon, and in order to detect plasma autoantibodies, EVs expressing GPCR will be used as a novel screening tool. First, the EVs' ability to bind in a microarray setup was analyzed.

METHODS:

EVs were printed (250μg/μl) on different types surfaces and various different print buffers was tested in a multiplex assay with different print setups. EV spots were stained with biotinylated antibodies followed by binding of Cy5-marked streptavidin and visualized on Innoscan 710AL (Innopsys).

RESULTS:

So far, the epoxy glass slide showed no antibody binding signal. However, both the polymer coated slide and the hydrogel slide showed increased signal, indicating attacthment of EVs. Thus, EV binding to hydrogel- and polymer-coated slide seemed more promosing in most printing buffers.

CONCLUSION and PERSPECTIVES:

It was possible to capture HEK293 EVs on polymer- and hydrogel coated slides, but not on epoxy slides. Future experiments will test EV attachtment

in MTP 96-well format, followed by utilization of EV microarray for autoimmune screening purpose.

F16.01 Thomas Karmark Dreyer

SURVEILLANCE OF HIGH GRADE NON-MUSCLE INVASIVE BLADDER CANCER USING XPERT®BLADDER CANCER MONITOR - SEALS XPERT

T. Dreyer[1, 2], A. Ernst[1, 3], L. Dyrskjøt[2, 4], J.B. Jensen[1, 2]

[1]Department of Urology, Aarhus University Hospital, [2]Department of Clinical Medicine, Aarhus University, [3]Department of Public Health, Section for Epidemiology, Aarhus University, [4]Department of Molecular Medicine, Aarhus University Hospital

Bladder cancer is among the most frequently diagnosed cancers worldwide. The majority of bladder cancer tumors are non-muscle invasive bladder cancer (NMIBC) and although the risk of progression is low (roughly 15%) they often recur after treatment, giving rise to the need for close follow-up regimens.

The gold standard for follow-up of NMIBC is urine cytology and flexible cystoscopy, but methods of detecting cancer in urine samples is under development as a non-invasive and more comfortable alternative. A urinary based biomarker test will need to have sufficient sensitivity and NPV to not miss tumor recurrences and thus risk progression to invasive bladder tumors. The Xpert®Bladder Cancer Monitor is a urinary biomarker that detects five mRNA targets often expressed in NMIBC and that has performed well in preclinical trials.

In order to test if the urinary biomarker Xpert®Bladder Cancer Monitor is feasible in a clinical setting we have set up a multicenter, two-arm, randomized, non-inferiority, intervention clinical trial utilizing Xpert®Bladder Cancer Monitor urinary marker. Patients with previous high-grade NMIBC coming for cystoscopy and cytology in the outpatient clinic and that have no recurrence of NMIBC will be randomized 1:1 between two arms. Patients in the control arm will adhere to current clinical guidelines for follow-up of NMIBC whereas patients in the interventional arm will have cystoscopies replaced with Xpert®Bladder Cancer Monitor test.

We hypothesize that some cystoscopies in follow-up of high grade NMIBC can be substituted by use of urinary biomarker Xpert®Bladder Cancer Monitor without risking disease progression and patient safety.

F16.02 Amanda Frydendahl Boll Johansen

THE ROLE OF CIRCULATING TUMOR DNA ANALYSIS IN THE POST-OPERATIVE MANAGEMENT OF COLORECTAL CANCER PATIENTS

A.F.B. Johansen

Department of Molecular Medicine, Aarhus University Hospital

Background

In Denmark, colorectal cancer (CRC) represents a significant health burden with ~5,000 new cases in 2018. Treatment and prognosis is highly dependent on stage of disease. Standard treatment for stage III patients is surgery followed by adjuvant chemotherapy. However, ~30% experience

relapse of disease, indicating that the post-operative management of CRC patients could be optimized.

Circulating tumor DNA (ctDNA) analysis is an emerging tool, which holds the potential to identify residual disease after chemotherapy. It is based on the observation that tumors shed DNA fragments into the blood. Since ctDNA has a half-life of less than two hours, operationally cured patients will not have ctDNA during follow-up, while patients with residual disease is likely to be ctDNA positive.

Objective

To investigate the benefit of ctDNA-guided management of stage III CRC patients compared to surveillance by standard-of-care CT-scans.

Study Design

ctDNA analysis is performed by ultra-sensitive digital droplet PCR and targeted next generation sequencing. The study will establish a prospective, randomized clinical trial where patients will be randomized into two arms:

Experimental: ctDNA analysis is performed at months 4, 8, 12, 16, 20 and 24 after surgery. At time of first positive ctDNA sample, patients are offered high-intensive radiological surveillance.

Control: Patients receive surveillance according to current guidelines with CT-scans at months 12 and 36.

Perspectives

Results from this project may motivate changes to the post-operative radiological surveillance program - namely with the use of ctDNA analysis to complement and guide CT-scans.

F16.03   Simone Weiss   GENOME-WIDE EXPLORATION OF LNCRNAS DRIVING PROSTATE CANCER PROGRESSION AND THEIR POTENTIAL AS NOVEL PROGNOSTIC BIOMARKERS

S. Weiss[1], J.S. Pedersen[1], M. Borre[2], B. Schmierer[3], K.D. Sørensen[1]

[1]Department of Molecular Medicine, Aarhus University Hospital, [2]Department of Urology, Aarhus University Hospital, [3]High Throughput Genome Engineering, Karolinska Institutet

BACKGROUND

Prostate cancer (PC) is the most common type of cancer among Danish men (4500 incidences/year). A large subset of PCs are non-aggressive (indolent), and may be managed safely by active surveillance alone. However, another subset of PCs are aggressive and will become deadly if not treated in time, while they are still localized. Unfortunately, today's prognostic biomarkers are inadequate, resulting in costly and harmful overtreatment of indolent PC and delayed treatment of aggressive PC. Thus, better prognostic biomarkers are urgently needed.

Long non-coding RNAs (lncRNAs) are parts of our genomes, and have shown initial potential as biomarkers in PC. However, they have not been investigated thoroughly. The versatile CRISPR-Cas9 system may be used

to activate or inhibit lncRNAs genome-wide, thus assessing the effect of thousands of individual lncRNAs on PC progression.

AIM

The aim of my project is to identify lncRNAs that play a role in PC progression and prognosis, and thus may serve as novel prognostic PC biomarkers. Such biomarkers will improve PC risk stratification and pave the way for personalized treatment of PC.

METHODS

I will:

1) Perform in vitro genome-wide activating and interfering CRISPR screening to identify lncRNAs regulating PC cell proliferation.

2) Perform in vivo genome-wide activating and interfering CRISPR screening to identify lncRNAs regulating PC metastasis.

3) Analyze RNA sequencing data from large PC patient cohorts to identify dysregulated lncRNAs with prognostic biomarker potential.

4) Integrate part 1, 2, and 3 results for functional characterization of selected clinically relevant top candidate lncRNA drivers of PC progression.

F16.04   Lise Skovgaard Svingel

ACUTE PYELONEPHRITIS: INCIDENCE AND MICROBIOLOGY

L.S. Svingel[1], C.F. Christiansen[1], K.K. Søgaard[1, 2], H. Birn[3, 4], M. Nørgaard[1]

[1]Department of Clinical Epidemiology, Aarhus University Hospital, [2]Department of Clinical Microbiology, Aalborg University Hospital, [3]Department of Renal Medicine, Aarhus University Hospital, [4]Department of Biomedicine, Aarhus University

Introduction: Acute pyelonephritis (APN) is a severe manifestation of urinary tract infection with a proposed annual incidence of approximately one per 1000 women per year. APN is typically caused by bacteria entering the bladder and ascending to the kidneys. Positive urine culture is considered the cardinal confirmatory diagnostic test in patients with APN symptoms. The increasing antimicrobial resistance in uropathogens is becoming a challenge in the treatment of APN. There is limited data on the incidence of APN among all populations, and on the prevalence of uropathogens and their antimicrobial resistance among patients admitted with APN.

Aim: To examine the incidence of first-time hospital-based diagnosis of APN in Denmark in 2000-2018 and to describe the distribution of uropathogens and their antimicrobial resistance.

Methods: The study is a descriptive population-based cohort study linking data from Danish registries using the civil personal registry number assigned by The Danish Civil Registration System. The study cohort will include patients with a first-time inpatient or outpatient diagnosis of APN in the Danish National Patient Registry from 2000 to 2018. For a subcohort comprising APN cases from the Central Denmark Region, we will identify urine cultures relating to the diagnosis of APN. We will compute the annual incidence rate (per person years) of first-time APN, overall and

stratified by sex and age group, using the Danish population at risk as denominator. For the subcohort, we will calculate the proportion of microbiologically confirmed APN diagnoses, and the distribution of uropathogens and their antimicrobial resistance.

F16.05 Maria Bisgaard Bengtsen

ACUTE URINARY RETENTION IN MEN: TRENDS IN INCIDENCE AND MORTALITY, 1997-2018

M.B. Bengtsen

Department of Clinical Epidemiology, Aarhus University

Background

Acute urinary retention is a severe complication to benign prostatic hyperplasia. In the mid-1990's medical therapy for benign prostatic hyperplasia was introduced, and rapidly replaced surgery as first choice of treatment. The long-term consequences including changes in incidence and mortality of acute urinary retention are sparsely documented.

Aim

To examine trends in incidence and mortality of acute urinary retention in men.

Methods

Through the Danish National Patient Registry, we included men with a first hospitalization for acute urinary retention during 1997-2018. We computed incidence rates of acute urinary retention age-standardized to the patient population in year 2000 and standardized 1-year mortality rates by calendar year. We will use Cox regression to estimate mortality rate ratios according to comorbidity as defined by Charlson Comorbidity Score.

Results

We identified 99.811 men with a first hospitalization for acute urinary retention during 1997-2018, median age was 75 years (IQR 67-82). The majority (78.5%) had at least one comorbidity and 61% had benign prostatic hyperplasia. Age-standardized incidence rate per 10.000 person years increased with 43% in the study period; from 26.6 (95% CI: 23.5-29.2) in 1997 to 38.0 (95% CI: 34.3-42.0) in 2004, and remained stable for the remaining study period. The 1-year mortality declined from 21.1% (95% CI: 20.9-21.4) in 1997 to 16.1% (95% CI: 15.9-16.4) in 2018.

Conclusion

The incidence of hospitalization for acute urinary retention increased with 43% during 1997-2018. The 1-year mortality decreased slightly in the study period; however, adjustment for comorbidity remains to be performed.

F16.06   Anna Cecilie   CIRCULATING FREE DNA IN ANAL CANCER: RELATION TO RISK FACTORS
          Lefèvre   AND RECURRENCE

A.C. Lefèvre[1], C.S. Kronborg[2, 3], E. Serup-Hansen[4], K.G. Spindler[1, 3]

[1]Department of Experimental Clinical Oncology, Aarhus University Hospital, [2]Danish Center for Particle Therapy, Aarhus University Hospital, [3]Department of Oncology, Aarhus University Hospital, [4]Department of Oncology, Herlev Hospital

Aim: Analyses of circulating free DNA (cfDNA) has set new frames for personalized treatment in oncology. The aim of this study was to present the first study on total cfDNA in anal cancer (AC), and relate results to risk factors and recurrence.

Patients and methods: We included 80 patients treated in Aarhus from 2016 -2019. P16 was measured by immune histochemical staining and serum cfDNA by direct fluorescent assay. Median values, Mann-Whitney and Chi-square test were used for statistical analyses.

Results: Samples were available at baseline (n=73), mid-therapy (n=74), end of therapy (n=67) and one year after treatment (1Y) (n=30). P16+ was found in 87% (n=55). T1 tumors comprised 19%, T2=59%, T3=10% and T4=12% respectively.

CfDNA was higher for P16- tumors (1.48) than for P16+ tumors (0.9, P=0.04). Data revealed a weak association between baseline cfDNA and numeric tumor size (R^2=0.07, P=0.05), and higher level with increasing T-stage (T1= 0.80, T2=0.94, T3=1.11, T4=1.3). Increasing cfDNA levels was found when performance status increased from zero to >zero (0.89 vs. 1.15, P<0.01).

CfDNA dropped from baseline to mid-therapy (0.92-0.78, P=0.01), and from end-therapy to 1Y (0.89-0.69, P=0.03). Patients with relapse (n=9) had a baseline level above the 25th quartile (p=0.05), which translated into difference in recurrence free survival, when using the 25% quartile as cut off although not significant.

Conclusion: Results indicates an association between cfDNA and risk factors in AC. Moreover, low baseline value may correlate to lower risk of recurrence. However, low number of events and short follow up (mean 21 months), does not yet allow for reliable statistical analysis.

F16.07   Peder Berg   THE CYSTIC FIBROSIS URINE TEST

P. Berg[1], S.L. Svendsen[1], M.V. Sørensen[1], S. Jensen-Fangel[2], M. Jeppesen[2], K. Kunzelmann[3], J. Leipziger[1]

[1]Department of Biomedicine, Aarhus University, [2]Department of Infectious Diseases, Aarhus University Hospital, [3]Department of Physiology, University of Regensburg, Germany

Cystic fibrosis (CF) patients commonly present with systemic electrolyte abnormalities and metabolic alkalosis, likely caused by renal dysfunction of base excretion. In mouse studies, we have identified the physiological mechanism of CFTR-dependent urine bicarbonate excretion in the collecting duct, which depends on functional pendrin and CFTR in β-intercalated cells. Remarkably, CFTR and pendrin knock-out mice cannot respond to increase their urine bicarbonate excretion during the first 3

hours following a defined acute gastric load. We have developed a human, non-invasive CF urine test that is simple and quantifies the ability to excrete bicarbonate with the urine. In human CF patients (homozygote for ΔF508, n=9), we can show a reduced ability (~ 40% as compared to normals) to excrete urinary bicarbonate after application of this CF urine test. We hypothesize that the CF urine test can verify and quantify therapy success in CF patients treated with the novel CF modulator drugs Orkambi®and Symkevi®. Currently, 3 and 6 CF patients have been studied before and after 4 weeks of treatment with Orkambi®or Symkevi®respectively. These preliminary results showed an increase of the urinary HCO_3^-excretion in all treated CF patients but one.

These results indicate that CF mice and human CF patients present with the inability/reduced ability to excrete an acute oral HCO_3^-load. Furthermore, our results suggest feasibility of a CF urine test to validate treatment efficacy of novel CFTR modulator drugs.

F16.08 Josephine Hyldgaard

INFLUENCE OF HORMONE TREATMENT IN BLADDER CANCER - INCIDENCE, PROGNOSIS AND FUNCTIONAL OUTCOME

J.M. Hyldgaard[1], J.B. Jensen[1, 2]

[1]Department of Clinical Medicine, Aarhus University, [2]Urology Research Department, Aarhus University Hospital

Background

Bladder cancer (BC) is one of the most frequent cancers in the world and more common in men than female. Gender-related factors may be involved in the pathogenesis of BC. Studies have suggested that androgen-receptors may be present in the bladder and potentially involved in BC aetiology, thus making BC susceptible for androgen deprivation therapy (ADT). Currently treatment for BC includes surgery or radiation therapy. ADT include Degarelix, which besides decreasing testosterone, has been shown to reduce the occurrence of BC in rats and promote stem cell recovery following radiation therapy.

Hypothesis

ADT will lower the incidence of BC, and the prognosis of BC will vary depending on the type of ADT used. Furthermore Degarelix administered during radiation therapy for BC will reduce the degree of fibrosis in the bladder thus decreasing adverse side effects.

Methods

A cohort of patients treated with ADT for PC will be compared to two cohorts of age-matched men with and without PC both without ADT. The incidence of BC will be recorded for every group. Furthermore, the cohort of patients with PC and ADT will be divided into subgroups, depending of the type of ADT they have received and the degree of deprivation. They will be compared in terms of incidence and prognosis of BC. Finally, a small pilot study will be conducted to investigate the effect of Degarelix when administered during radiation therapy for BC.

Perspectives

This will be one of the largest studies to investigate the potential influence of sex hormones in the development and prognosis of BC and potentially

lead to new treatment options and possibly a new way of reducing radiation side effects.

CH.01   Gro Grunnet Pløen

SMC PHENOTYPIC MODULATION - A TARGET FOR ALLOGRAFT VASCULOPATHY

G.G. Pløen, J.F. Bentzon, C.B. Sørensen

Atherosclerosis Research Unit, Department of Cardiology, Department of Clinical Medicine, Aarhus University

Background:

Allograft vasculopathy limits long-term function due to fibrous intimal hyperplasia, appearing along the entire length of the affected arteries. The intimal hyperplasia is caused by chronic immune-mediated injury to the vasculature of the transplanted organ, leading to intimal smooth muscle cell (SMC) accumulation, luminal narrowing, and eventually ischemic graft failure. The most recent investigations point towards phenotypic modulation, migration and proliferation of local donor SMCs as the driving force in allograft vasculopathy.

Methods:

We will use a mouse model in which male carotid arteries by end-to-end anastomoses are transplanted into the carotid arteries of female recipients leading to mild rejection because of the minor histocompatibility locus on the Y chromosome. To show whether local SMCs contribute, male Myh11-CreERT2-mT/mG vessels are transplanted into female WT mice. To show whether recipient cells contribute, male WT vessels are transplanted into female mT/mG mice. For studies of the clonal architecture of SMCs, male Myh11-CreERT2-Confetti vessels are transplanted into female WT mice. Transplants are cryosectioned and DAPI stained to determine cell origin by fluorescence microscopy.

Conclusion:

We envisage that our model can be used to understand the repertoire of SMC phenotypes involved, the clonal structure of SMCs, the functional importance of SMC modulation and aid in the development of targeted treatment for allograft vasculopathy.

CH.02   Kia Busch

BENCHMARKING PROTON THERAPY WATER EQUIVALENT PATH LENGTH CALCULATIONS AGAINST TPS ALGORITHMS

K. Busch[1, 2], A.G. Andersen[1, 2], J.B.B. Petersen[1, 2], P.S. Skyt[1, 2], O. Nørrevang[2], L.P. Muren[1, 2]

[1]Department of Oncology, Aarhus University Hospital, [2]Danish Centre of Particle Therapy, Aarhus University Hospital

Purpose/Objective: Proton therapy is sensitive towards inter-fractional organ motion and density variations due to the finite range of protons. Range variations can be estimated by water equivalent path length (WEPL) calculations. Our aim was to compare WEPL calculations with dose re-calculation using a treatment planning system (TPS) algorithm.

Material/methods: The in-house WEPL program calculated isodoses of 15%, 25%, 35%, 45% and 55% of the 78 Gy target dose, which were compared using Dice similarity coefficient to isodoses created using the CERR platform in Matlab. For the TPS calculations, a cube of water (0 Hounsfield units (HUs)) was created in Eclipse TPS with a cylindrical target in the middle. Two multi-field optimised proton plans were created and re-calculated on the same cube with one and/or two inserts of either bone (300 HU), air (-1000 HU) or water (0 HU) placed in front of each field. In total, each plan was re-calculated eight times.

Results: The WEPL-based isodoses were most similar to the dose re-calculation for isodoses of 15%, 25% and 35% with a median Dice value of 0.99 (range: 0.98-1.00) across all scenarios and plans. The largest difference between the two plans occurred for an isodose of 55%, due to different volume sizes. With a bony insert a median Dice value of 0.94 (range: 0.87-0.98) across both plans, while the median Dice value was 0.79 (range: 0.66-0.94) for an insert of air.

Conclusion: WEPL calculations show promising results, especially for low isodoses and small density changes. However, we need to investigate how WEPL calculations can be used for higher isodoses and more pronounced density changes.

CH.03   Millicent Addai Boateng

CULTURAL ADAPTATION AND PSYCHOMETRIC PROPERTIES OF THE HEALTH LITERACY QUESTIONAIRE (HLQ) IN A GHANAIAN LANGUAGE (AKAN-TWI)

M.A. Boateng[1], P. AGYEI-BAFFOUR[2], S. ANGEL[1], U. ENEMARK[1]

[1]Department of Public Health, Aarhus University, [2]School of Public Health, Kwame Nkrumah University of Science and Technology, Ghana

Introduction: As health care is gradually becoming more patient-centred, patients are sometimes expected to assume more responsibility for their care process and this calls for attention into promoting health literacy. In order to assess the health literacy levels of caregivers in Ghana, we adopted the use of the Health Literacy Questionnaire (HLQ). The questionnaire was translated into the most common language in Ghana (Akan-Twi). This paper reports on the psychometric properties and validation of the HLQ (Akan-Twi).

Method: We carried out cognitive interviews and a cross sectional survey from November 2017- December 2017. The study was carried out together with an assessment of a malaria programme for caregivers (with children under 5), from two communities. Analysis of the psychometric properties is based on data collected from 1234 caregivers. Analysis covered difficulty level of scales, composite reliability, Cronbach's alpha and confirmatory factor analysis.

Preliminary findings: Cognitive testing showed that some words were ambiguous and questions were rephrased. The health literacy levels of the caregivers in the two communities were averagely the same. Composite reliability and Cronbach's alpha were >0.7 for all scales except Cronbach alpha for Understanding Health Information (0.6). The differences in means between demographic groups across the 9 scales were small, although mostly statistically significant.

Conclusion: The Akan-Twi version of HLQ appears relevant in our description of the health literacy levels of the caregivers in our study but further work is needed to assess its psychometric properties among a fair representation of the Ghanaian population.

CH.04 Rune Nguyen Rasmussen A SEGREGATED CORTICAL STREAM FOR RETINAL DIRECTION SELECTIVITY

R.N. Rasmussen, A. Matsumoto, K. Yonehara

Danish Research Institute of Translational Neuroscience – DANDRITE, Aarhus University

Visual features extracted by retinal parallel circuits are streamed into higher visual areas (HVAs) after being processed along the visual hierarchy. However, how specialized neuronal representations of HVAs are built, based on retinal output channels, remained unclear. Here we addressed this question by determining the effects of genetically disrupting retinal horizontal direction selectivity on motion-evoked responses in visual stages from HVAs to the retina in mice. Direction-selective (DS) cells in the rostrolateral (RL) area that prefer higher motion speeds, and that change direction tuning as stimulus speed increases, are selectively reduced upon retinal manipulation. DS cells in the primary visual cortex projecting to the RL, but not to the posteromedial area, were similarly affected. Therefore, the specific connectivity of cortico-cortical projection neurons routes feedforward signaling originating from retinal DS cells preferentially to area RL. We thus identify a cortical processing stream for motion computed in the retina.

CH.05 Francesco Maria Iena THE IMPACT OF HIGH FAT DIET ON GLYCEROL METABOLISM IN ADIPOSE TISSUE IS INFLUENCED   BY SEX AND LIRAGLUTIDE TREATMENT.

F.M. Iena, J.B. Jul, J.B. Vegger, J.S. Thomsen, A. Brüel, J. Lebeck

Department of Biomedicine, Aarhus University

Adipose tissue (AT) releases glycerol through aquaglyceroporin 7 (AQP7) and lack of AQP7 has been linked to increased activity of glycerol kinase (GlyK) and increased triglyceride storage in AT. The regulation of AT AQP7 expression is sex-dependent and we here investigated whether the effect of high fat diet (HFD) on AT glycerol metabolism is sex-specific and influenced by liraglutide (LIR) treatment.

HFD or control diet were given for 12 and 24 weeks to male and females C57BL/6J mice. LIR was injected (SC, 1 mg/kg/day) in female mice in the last 12 of the 24 weeks. Body weight (BW) and blood glucose (BG) levels were monitored. Serum and perigonadal AT was collected for biochemical analysis, western blotting and histological examination.

At 12 weeks, HFD increased BW by 34% in females and by 49% in males. While serum glycerol (sGly) was increased in both sexes, BG levels were only significantly increased in male mice. AQP7 expression was increased in female mice only, whereas only males increased the expression of GlyK and the adipocyte size. After 24 weeks, HFD increased BW by 76% in female and by 49% in male mice. BG and sGly levels were significantly increased in both sexes. AQP7 was significantly increased in females and

both male and females demonstrated an increased expression of GlyK and increased adipocyte size. LIR treatment decreased both BW and BG levels and normalized the expression of AQP7 and GlyK in AT and the size of the adipocytes.

In conclusion, the effect of HFD on AT glycerol metabolism is sex-specific and a parallel increased in AT GlyK expression and adipocyte size was observed. LIR treatment normalizes the expression of AQP7 and GlyK in AT.

CH.06 Qichao Zhang THE MITOCHONDRIAL-PROCESSING PEPTIDASE SUBUNIT BETA INTERACTS WITH AMYLOID BETA AND EXACERBATE THE ALZHEIMER'S DISEASE

Q. Zhang

Department of Clinical Medicine, Aarhus University

Extracellular plaque accumulation consisting of amyloid beta (Aβ) and intracellular neurofibrillary tangles are the most essential pathological hallmark for Alzheimer's disease (AD). However, metabolic dysfunction, such as reduced glucose utilization, takes place earlier than accumulation of plaques and tangles in the brain of AD patients. Mitochondrial-processing peptidase (MPP) subunit beta (PMPCB) is a subunit of MPP located in mitochondrial matrix and this is involved in presequence processing. We found PMPCB interaction with Aβ identified by co-immunoprecipitation and immune-electron microscopy both inside and outside of neural mitochondria in AD drosophila flies. Moreover, accumulated Aβ within the central nervous system correlates to the amount of PMPCB suggesting that presequence processing of mitochondrial precursor proteins play an important role during AD development. This research contributes to our understanding of how Aβ deposits appear in mitochondria and explain the different roles of mitochondrial dysfunction in AD: increased reactive oxygen species, reduced ATP and morphological changed mitochondria.

CH.07 Maimaitili Muyesier DIRECT CONVERSION OF FLOOR PLATE CELLS INTO MESDA NEURONS

M. Maimaitili[1,2], M. Chen[1,2], L. Percaz[1], F. Febbraro[3], M. Denham[1,2]

[1]Danish Research Institute of Translational Neuroscience DANDRITE, Aarhus University, [2]Department of Biomedicine, Aarhus University, [3]Department of Health Science and Technology , Aalborg University

Mesencephalic dopaminergic (mesDA) neurons are the main cell type affected in Parkinson's disease (PD) that gradually die during the disease progression. As a potential method to treat PD, the generation of mesDA neurons from pluripotent stem cells (PSC) offers great potential not only for cell replacement therapies by replacing the lost neurons cells with healthy new ones, but also for disease modeling and drug discovery. The generation of mesDA neurons from PSC can be achieved by a stepwise differentiation method that follows the in vivo developmental extrinsic signaling cues. However, these protocols are not efficient, which suggests that additional factors are required. Our aim is to identify molecular mechanisms regulating the development of mesDA neurons, which can

then be used to develop more efficient methods for generating mesDA neurons in vitro.

In our study, we used a combined differentiation and direct conversion approach as a novel method for deriving mesDA neurons. Firstly, we generated midbrain floor plate (FP) cells using our previously published protocol. Secondly, we examined various transcription factors in a direct conversion approach to generate mesDA neurons from the FP cells. In our direct converting step, we investigated six key transcription factors that are involved in regulating cell fate and differentiation of mesDA neurons. Our result showed that the over-expression of a single transcription factor and specific combinations of factors were capable of generating mesDA neurons from FP cells.

CH.08   Tingting Gu   EVALUATING THE ROLE OF CONDITIONED EXTRACELLULAR VESICLES IN A TRANSIENT MURINE STROKE MODEL

T. Gu[1], J. Just[1], N.K. Iversen[1], Y. Yan[2], J. Kjems[2], K. Vissing[3], H.E. Bøtker[4], K.R. Drasbek[1]

[1]Center of Functionally Integrative Neuroscience, Department of Clinical Medicine, Aarhus University, [2]Interdisciplinary Nanoscience Center, Aarhus University, [3]Section for Sports Science, Department of Public Health, Aarhus University, [4]Department of Cardiology, Aarhus University Hospital

Current treatment for ischemic stroke is limited to removing the blood clots and inducing reperfusion despite of severe outcomes of the disease, like disabilities and death. Remote ischemic conditioning (RIC) is a promising, non-invasive treatment induced by repeated cycles of controlled ischemia-reperfusion in the arm or leg. It protects multiple organs including brain from ischemic injury. However, the protective mechanism of RIC remains unclear. It is hypothesized that extracellular vesicles (EVs), which are cell-derived nanosized particles that can carry effective cargos to remote area, might play an important role in the process. In my PhD study, I am examining the extracellular vesicles in a mice stroke model called transient middle cerebral artery occlusion (tMCAO). Firstly, the distribution of EVs in ischemic mice brain was examined with myoblast EVs, which are known to contain growth factors involved in development and tissue regeneration. More conditioned EVs were found in the ischemic brain compared to non-conditioned EVs. And more EVs homing to the ischemic hemisphere compared to the non-ischemic hemisphere. With EVs isolated from blood samples of healthy human subjects taken before (Pre) and after (Post) RIC treatment, the acute effects of conditioned EVs were further evaluated. Pre-EVs, Post-EVs or PBS were administered intravenously into mice after occlusion. Laser speckle imaging was used to measure perfusion changes and track the development of penumbra during occlusion and 4 hours' reperfusion. Our study will clarify the role of conditioned EVs in ischemic stroke and maybe provide new perspectives for potential neuroprotective treatments.

CH.09   Ole Søndergaard Schwartz   THE CELLS OF THE SUPERIOR COLLICULUS

O.S. Schwartz

DANDRITE, Department of Biomedicine, Aarhus University

In recent years the mouse has emerged as a promising model for vision research. Among other things these tools have been used to describe ~40 functionally unique types of retinal ganglion cells. The Superior Colliculus (SC), arguably the most prominent visual center in the mouse, receive input from ~90% of these ganglion cells but still only four cell types have been described in the SC.

For several reasons studying the SC holds the promise of addressing a fundamental question of neuroscience, namely what the relationship between the activity of individual cells and higher mental functions are. First, understanding the input to individual cells in the SC is greatly simplified by it being only one synapse away from the well described and accessible retinal ganglion cells. Second, we have a rich description of the organization, inputs and outputs of the SC. Finally, the advent of two photon imaging allows monitoring responses of large groups of cells simultaneously.

Given the high functional diversity of the retinal ganglion cells that project to the SC and that no comprehensive functional clustering of cells in the SC have been attempted, it is possible that many more cell types exist in the SC. In a brief pilot-study of GRP-KH288 cells, a marker of one of the known SC cell types, we were able to distinguish at least three different response types indicating that the known morphological and physiological classes could be comprised of several functional cell types. The aim of the current project is to use two photon imaging to gather responses from thousands of SC cells and through clustering identify the unique functional cell types in the SC.

CH.10   Nanja Holland Hansen

COMPASSION CULTIVATION TRAINING (CCT) FOR INFORMAL CAREGIVERS OF PEOPLE WHO SUFFER FROM A MENTAL ILLNESS.

N.H. Hansen

Danish Center for Mindfulness, Department of Clinical Medicine, Aarhus University

Background: The 8-week Compassion Cultivation Training course is a promising intervention for cultivating compassion and reducing suffering. Caregivers of people who suffer from mental illness are at raised risk for mental health difficulties, such as depression, stress and anxiety. Caregivers become "hidden patients" who are struggling with their own psychological and physical health as well as providing care for someone with mental illness. There is an impetus to study preventive interventions to support caregivers that increase their psychological and physical health.

Method: A total of 160 participants were recruited. We used block randomization with 20 participants in each group totaling 8 groups with four intervention and 4 WLC groups. Self-report questionnaires were used at baseline, post 8-week intervention, 3- and 6-month follow-up. The Primary psychological measure was the Depression Anxiety Stress Scales. Secondary psychological measures were: Perceived Stress Scale,the Emotion Regulation Questionnaire, the Self-compassion Scale-12, the Multidimensional Compassion Scale, theFive Facet Mindfulness Scale, the Brief Resilience Scale, and the World Health Organization Five Well-Being Index. Process measures used was the Working Alliance Inventory Short Form Revised and demographic baseline measures were asked.

Results and Conclusion: 92% of the caregivers completed the intervention and 74% completed 6 or more sessions. If we include caregivers who completed 5 or more session the percentage increase to 87,7%. We conclude that an intervention for informal caregivers, like CCT, is not only feasible, there is also very a low attrition rate.

CH.11   Janne Tidselbak Larsen

ANOREXIA NERVOSA AND INFLAMMATORY BOWEL DISEASES

J.T. Larsen[1, 2, 3], C.M. Bulik[4, 5, 6], L.M. Thornton[4], Z. Yilmaz[4, 7], P.B. Mortensen[1, 2, 3], L.V. Petersen[1, 2, 3]

[1]National Centre for Register-based Research, Department of Economics and Business Economics, Aarhus University, [2]Lundbeck Foundation Initiative for Integrative Psychiatric Research (iPSYCH), Aarhus University, [3]Centre for Integrated Register-based Research (CIRRAU), Aarhus University, [4]Department of Psychiatry, University of North Carolina at Chapel Hill, USA, [5]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Sweden, [6]Department of Nutrition, University of North Carolina at Chapel Hill, USA, [7]Department of Genetics, University of North Carolina at Chapel Hill, USA

Gastrointestinal complications in eating disorders are well documented; however, the nature and direction of the association is less clear. Gastrointestinal disturbances can emerge secondary to severe malnourishment, binge eating, and purging. Alternatively, inflammatory bowel diseases (IBD) cause inflammation of different areas of the digestive tract and can lead to malnutrition, fatigue, and weight loss that could increase risk of developing eating disorders.

In order to advance our understanding of the relationship between eating disorders and IBD, we are conducting an investigation of their association using genetic data and diagnostic information from Danish national registers. Based on genotype information from the iPSYCH/ANGI-DK sample, we calculate polygenic risk scores (PRS) for anorexia nervosa (AN) and IBD, including the subtypes Crohn's disease and ulcerative colitis, and combine the genomic data with diagnostic information from the registers for the proband and their parents. We examine the associations between AN and IBD register diagnoses, between AN and IBD PRS, and explore whether high PRS for each illness predict a diagnosis of the other disorder in the registers.

We found that having AN diagnosis was associated with significantly increased incidence rates of subsequent diagnosis of IBD, but prior IBD was not associated with later AN. However, parental history of IBD was associated with increased incidence rates of AN in the proband. AN PRS was not significantly associated with risk of IBD diagnosis, but risk of AN diagnosis increased with higher IBD PRS. Our results suggest shared genetic and/or environmental influences for AN and IBD.

CH.12   Sif Sund Blandfort

ANALGESIC AND PSYCHOACTIVE MEDICATIONS AND THE RISK OF FALLS IN RELATION TO DELIRIUM IN SINGLE-BED ROOMS COMPARED TO MULTIPLE-BED ROOMS IN GERIATRIC INPATIENTS.

S. Blandfort[1], M. Gregersen[1], K. Rahbek[1], S. Juul[2], E.M. Damsgaard[1]

[1]Department of Geriatrics, Aarhus University Hospital, [2]Department of Public Health, Aarhus University

Background: Previously, we demonstrated a substantial reduction of delirium incidence among geriatric patients after relocating from old hospital buildings with multiple-bed rooms to a new hospital with single-bed rooms.

Aims: To investigate whether 1) the reduced incidence of delirium in single-bed rooms was associated with a simultaneous change in medication use, 2) the relocation had affected the incidence of falls, 3) the use of analgesics and psychoactive medications was associated with the risk of delirium and falls.

Methods: We included 461 admissions to the old wards and 553 admissions to the new wards. Delirium was assessed by the Confusion Assessment Method. Data on drug use and falls during hospitalization were extracted from medical records.

Results: There was no difference in drug use between the wards. In the new wards, patients who had experienced delirium had a much higher risk of falls than patients without delirium, while in the old wards this contrast was small. The risk of delirium was increased among patients who received antipsychotic drugs and anti-dementia drugs, Patients who received these drugs had an insignificantly increased risk of falls.

Conclusion: Medication of analgesics and psychoactive drugs was similar in the old and new wards. In single-bed rooms, but not in multiple-bed rooms there was a much higher risk of falls among inpatients that developed delirium than among other patients. Patients who had used antipsychotics and anti-dementia drugs during hospitalization had increased risk of developing delirium and an insignificantly higher risk of falls.

CH.13 Mette Bisgaard Andersen — CYCLING REDUCES BLOOD GLUCOSE EXCURSIONS AFTER AN ORAL GLUCOSE TOLERANCE TEST IN PREGNANT WOMEN: A RANDOMIZED CROSSOVER TRIAL

M. Bisgaard Andersen, P. Glud Ovesen, M. Daugaard, E. Bjerre Ostenfeld, J. Fuglsang

Department of Obstetrics and Gynecology, Aarhus University Hospital.

Background: Maternal hyperglycemia is associated with increased risk of adverse maternal and fetal outcomes. Acute and regular exercise beneficially impact glucose responses during pregnancy, but the timing of exercise and effects are less clear.

Aim: To evaluate the effect of an acute bout of cycling immediately after oral glucose intake on blood glucose and insulin in pregnant women at risk for gestational diabetes mellitus (GDM).

Methods: A randomized crossover controlled design was used. Fifteen pregnant women at 27 to 30 weeks gestation with BMI $\geq$ 27kg/m^{2}underwent two oral glucose tolerance tests (OGTTs) ingesting 75-gram glucose followed by either 20 minutes of stationary cycling at moderate intensity (65-75% maximal heart rate) or rest. Blood was

sampled at baseline and after one and two hours for glucose, insulin and C-peptide determination. Using continuous glucose monitors, glucose was measured up to 48 hours after the OGTT.

Results: After an OGTT, blood glucose levels increased in both trials (p<0.001). One hour after glucose intake, mean blood glucose was significantly lower after cycling (7.9±1.7mmol/L) compared to rest (8.7±1.5mmol/L; p=0.002). Mean glucose peak level was significantly lower after cycling than after rest (8.1mmol/L vs. 8.8mmol/L; p=0.039). Lower levels of insulin and C-peptide were observed after one hour (p<0.005). Differences in glucose levels after two and up to 48 hours were not significant.

Conclusions: Twenty minutes of cycling at moderate intensity after glucose intake reduced blood glucose excursions in pregnant women at risk for GDM. Reducing blood glucose excursions, exercise may reduce risks associated with maternal hyperglycemia.

CH.14   Kata Wolff Pedersen   INVESTIGATING PORCINE CYP PROTEINS IN PLM BY TARGETED PROTEOMICS

K.W. Pedersen, J. Hansen, J.R. Jornil, J.B. Hasselstrøm

Department of Forensic Medicine, Aarhus University

Cytochrome P450 (CYP) enzymes in the liver are central to drug metabolism in all mammals. Information about their activities is thus valuable for forensic chemists who work with lethal intoxications. In living individuals, CYP activity can be estimated by a clinical setup; however, there is currently no method to estimate the activity in deceased individuals. The aim of this study is to investigate the post mortem stability of CYP protein using a targeted proteomics approach. Therefore, we developed a targeted proteomics method for quantification of four porcine CYP enzymes involved in the drug metabolism (CYP1A2, CYP2D25, CYP3A29 and CYP2E1). The developed method was used to quantify said CYP enzymes in three porcine livers stored at ambient temperature for up to 72 h. To evaluate our method, we performed conventional in vitro enzymatic assays with phenacetin (CYP1A2) and midazolam (CYP3A) as substrates on the same tissue samples. We found that three out of four of the CYP enzymes were quantifiable by the targeted proteomics up to 48 h post mortem, while the conventional enzyme assays were unable to quantify the tested CYP enzymes after 24 h of storage at ambient temperatures. In conclusion, we found that the targeted proteomics approach is better than in vitro enzyme assays at quantifying CYP protein levels in post mortem hepatic tissue, likely because the peptide-based quantification is more robust against post mortem degradation.

CH.15   Nick Yin Larsen   CHARACTERISATION OF MINICOLOUMNARITY AND VOLUME TENSORS OF NEURONS IN BRODMANN AREA 46 IN NORMAL, SCHIZOPHRENIC AND DEPRESSIVE HUMAN AUTOPSY BRAINS

N.Y. Larsen[1, 2, 3], F. Sun[5], E.B.V. Jensen[2, 4], G. Rajkowska[6], J. Sporring[7], J.R. Nyengaard[1, 2]

[1]Core Centre for Molecular Morphology, Section for Stereology and Microscopy, Department of Clinical Medicine, Aarhus University, [2]Center for Stochastic Geometry and Advanced Bioimaging,, [3]Sino Danish Center, Aarhus University, [4]Department of Mathematics, Aarhus University, [5]Center for Biological Imaging, Chinese Academy of Sciences, Beijing, China, [6]University of Mississippi Medical Center, Jackson, USA, [7]Department of Computer Science, University of Copenhagen

Schizophrenia and depression are neuropsychiatric diseases that affect a person's feelings and behaviour. Both mental disorders are influenced by environmental and genetic factors, which leads to social problems for the individual patient, family and friends as well as economic costs for the society.

fMRI and PET studies have shown abnormal activation of the dorsolateral prefrontal cortex (DLPFC) in Brodmann Area 46 (BA46), which is involved in the development of schizophrenia and depression.

This could be due to an altered 3-dimensional size, orientation, shape and organization of the neurons in BA46. Using autopsy human brains from 11 control subjects, 10 subjects with schizophrenia, 11 suicidal patients with a history of depression, and 8 subjects with major depression without committing suicide, advanced methods from stochastic geometry and 3-dimensional reconstruction will be implemented for the characterization of minicoloumnarity and volume tensors of neurons in BA46.

Besides knowing the 3-dimensional structural changes of schizophrenia and depression, we also discover the neuronal number and organization inside a human brain, which can help us to understand the neuronal changes associated with schizophrenia and depression.

BA46 will be identified from thick and thin histological sections and the sampling of cells will be carried out by various forms of optical microscopy and serial sectioning bright field microscopy.

Assuming a difference in number, organization or orientation of neurons in BA46 of normal subjects, and patients with schizophrenia or depression, it can give a better understanding of the pathophysiology behind schizophrenia and depression.

CH.16   Xiaowen Niu   NOVEL THREE-DIMENSIONAL METHODS TO ANALYSE THE MORPHOLOGY OF NASAL CAVITY AND UPPER AIRWAY

X. Niu, S. Madhan, M. Cornelis, P. Cattaneo

Department of Dentistry and Oral Health, Aarhus University

Aims: The objective was to assess the intra- and inter-examiner reliability of the novel semi-manual methods to segment the nasal cavity (NC) and upper airway (UA), and to determine the minimal cross-sectional area (MCS) and minimal hydraulic diameter (HD) of UA.

Methods: Cone-beam computed tomography (CBCT) scans of 10 subjects were randomly selected from a database that included 345 patients for orthodontic treatment from 2011 to 2018. Semi-manual segmentation methods were used to segment and visualize the NC and UA respectively using Mimics (Materialise, Belgium). The UA centerline was determined for each CBCT dataset individually, and it was used to assess the MCS and

HD. Two examiners measured the NC and UA volume, MCS and HD independently, while one examiner performed the measurements twice. The intraclass correlation coefficient (ICC) was used to assess reliabilities and measurement errors were assessed by Dahlberg's formula and paired t-test. The agreement was further assessed with the Bland-Altman plot.

Results: The results indicated excellent reliability for both intra- and inter-examiner assessments, except for the inter-examiner values for the paired t-test for the oropharynx and thus the total UA volume, displaying a significant difference. All the results of the measurement error are at an acceptable level. The MCS and HD were reliable measurements, with a minimal ICC of 0.922 and more restricted 95% limits of agreement.

Conclusions: These novel three-dimensional methods to segment and analyse NC and UA are reliable. The MCS and HD associated with the UA centerline showed excellent reliability, which is critical to detect the collapsible part of the UA.

CH.17   Maria Keilow   THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE AND STANDARDIZED ACADEMIC TESTS: RELIABILITY ACROSS RESPONDENT TYPE AND AGE

M. Keilow[1, 2], H.H. Sievertsen[3, 1], J. Niclasen[4, 5], C. Obel[2]

[1]VIVE - The Danish Center for Social Science Research, [2]Department of Public Health, Aarhus University, [3]Department of Economics, University of Bristol, [4]Frederikshøj skole og dagbehandling, Vanløse, [5]Steno Diabetes Center Copenhagen

Exploiting nation-wide data from the Danish National Birth Cohort, we show that children's emotional and behavioral problems measured by the Strengths and Difficulties Questionnaire (SDQ) are closely related to their performance in standardized academic tests for reading and mathematics in sixth grade. The relationship is remarkably linear across the entire distribution for both the total difficulties score and subscale scores of the SDQ; higher scores on the SDQ (more problems) are related to worse performance in academic tests. We assess the similarity across respondent type; parent (child age 7 and 11), teacher (child age 11) and self-reported scores (child age 11), and find that teacher and parent reported scores have very similar slopes in the SDQ-test score relationship, while the child reported SDQ in relation to the academic test performance has a flatter slope.

CH.18   Cathrine Hjorth Hansen   EXPLORING DEMENTIA CARE IN A PRIVATE NURSING HOME FOR PEOPLE LIVING WITH DEMENTIA. AN ETHNOGRAPHIC STUDY

C. Hjorth Hansen[1], M. Kirkevold[2], B. Martinsen[1]

[1]Department of Public Health, Nursing, Aarhus University, [2]Department of Nursing Science, Oslo University

Background: As a respond to the growing number of people living with dementia in nursing homes, the notion of nursing home is currently under development. New types of nursing homes are established both in Denmark as well as in other parts of Europe in an attempt to provide new innovative care environments that are more suitable for people living with

dementia. So far, only limited research has investigated these new types of nursing homes.

Purpose: The purpose of this study is to provide new knowledge about dementia care by exploring the care and everyday life in a new private nursing home for people with dementia.

Method: The study has an ethnographic research design, and the data material is collected by: Participant observations (170 hours), ethnographic interviews with staff members (16), and ethnographic interviews with relatives (9).

Results: The preliminary results indicate that everyday life in the private nursing home is organized to support a meaningful life for the residents by offering content and communion on a daily basis. A number of predetermined structures are used to ensure the continuation of an active and social life for the residents. The preliminary results also indicate that the provision of suitable levels of content and communion can be challenging, and that some level of flexibility is required within the regular daily structures.

Implications: The results from this study will be an important contribution to the ongoing debate on how to organize and conduct dementia care in nursing homes in the future.

CH.19   Sidsel Boie   THE CHILDBIRTH EXPERIENCE QUESTIONNAIRE (CEQ) - VALIDATION OF
~~CANCELLED~~ ITS USE IN A DANISH-SPEAKING POPULATION OF NEW MOTHERS STIMULATED WITH OXYTOCIN DURING LABOUR

S. Boie[1], H. Lauridsen[2], J. Glavind[3], M. Smed[4], N. Uldbjerg[3], P. Bor[1]

[1]Department of Obstetrics and Gynecology, Randers Regional Hospital, [2]Department of Sports Science and Clinical Biomechancis, University of Southern Denmark, [3]Department of Obstetrics and Gynecology, Aarhus University Hospital, [4]Department of Obstetrics and Gynecology, Rigshospitalet

Background

When determining optimal treatment regimens, patient reported outcomes including satisfaction are increasingly appreciated. It is well established that the birth experience may affect the postnatal attachment to the newborn and on the management of subsequent pregnancies and deliveries. As no robust validated Danish tool to evaluate the childbirth experience exists, we aimed to perform a transcultural adaptation of the Swedish Childbirth Experience Questionnaire (CEQ).

Methods

In accordance with the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN), we translated the CEQ from Swedish to Danish. The CEQ was tested for content validity among 10 new mothers. In a population of women who have had their labour induced with oxytocin, we assessed the questionnaire for validity and reliability using factor analytical design, hypothesis testing, and internal consistency. We also determined criterion, construct responsiveness, and floor and ceiling effects.

Results

The content validation resulted in minor adjustments. The questionnaire was completed by 377 of 495 women (76.2%). An exploratory factor analysis revealed a three-dimensional structure in our Danish population. The internal consistency ranged between 0.75 and 0.89 and the ICC between 0.68-0.93. We found ceiling effects of 57.6% and 25.5% in two domains.

Conclusion

This study offers a transcultural adaptation of the CEQ to a Danish context. The 3-dimensional Danish version of the CEQ demonstrates construct validity and reliability. Our results revealed ceiling effects, which needs to be acknowledged when considering implementing the CEQ into trials and clinical practice.

CH.20   Bodil Karen Bæksted Jørgensen

EARLY TELEREHABILITATION OF GERIATRIC PATIENTS AFTER DISCHARGE FROM ACUTE CARE

B.B. Jørgensen[1], M. Gregersen[1], S.H. Pallesen[2], E.S. Damsgaard[1]

[1]Department of Geriatric, Aarhus University Hospital, [2]Center for Assisted Living Technology, Community of Aarhus,

Introduction: Exercise at home and improvement of the ability to undertake daily tasks are highly valued by older people after hospitalization. New telerehabilitation technologies make it possible to supervise and communicate with exercising participants by video conferencing equipment. This technology has shown to be both acceptable and effective in Danish COPD patients regarding basic mobility, safety and patient perception. Aim: Examine whether it is feasible to use telerehabilitation as home exercises in groups of max. 4 persons and compare this to the traditional exercise programs offered by a community center for older people. Methods: Both medical- and hip fracture community-dwelling 65+ years older geriatric patients acutely admitted to the Emergency Department (ED) and Department of Geriatrics, Aarhus University Hospital (AUH), were consecutively asked to participate in the study just before their discharge. Inclusion criteria: Dependence of a walking aid and familiar with the use of a computer. Exclusion criteria: Terminal illness, inability to walk independently with a walking aid, dementia, acute stroke, inability to complete the exercise program without a great risk of falling. Results: A total of 330 patients were consecutively screened for participation. Of these, 295 were excluded. At discharge 33 patients met with the inclusion criteria and were familiar with the use of a computer. Five patients agreed to participate but four of them withdrew during the first weeks after discharge. The overall explanation was exhaustion following the hospitalization.

Conclusion: Telerehabilitation may not be a feasible offer to recently discharged geriatric patients.

CH.21   Haiyun Qi

ASSESSING THE SEX DIFFERENCES OF RENAL FUNCTION AND METABOLISM BY USING HYPERPOLARIZED [1-^{13}C] PYRUVATE

H.Y. Qi[1], Y.B. Wen[1, 2], C. Østergaard Mariager[1], P. Mose Nielsen[1], L. Bonde Bertelsen[1], H. Stødkilde-Jørgensen[1], C. Laustsen[1]

[1]Department of Clinical Medicine, Aarhus University, [2]The First Affiliated Hospital of Zhengzhou University, Zhengzhou University, China

Metabolic sex difference are gaining increasing attension as an important factor in the onset and progress of disease and the tailoring treatment strategies. However, sex differences of pyruvate metabolism in kidney have not been reported. Therefor we applied hyperpolarized [1-^{13}C]pyruvate MR and dynamic contrast enhanced (DCE) MRI to invest metabolic and functional differences between healthy male and female Wistar rats.

Healthy male and female Wistar rats were included in this study. MR examinations were performed in a 9.4 T pre-clinical MR system (Agilent, UK) using a dual tuned ^{13}C/^{1}H volume rat coil (Doety Scientific, US). Hyperpolarize [1-^{13}C]pyruvate scanning was used to assess the metabolic difference and was started at the beginning of injection. BOLD and DCE scanning were used to assess the functional hemodynamic differences between male and female rats. After MR scanning, samples of arterial blood, urine and kidney tissue was harvested for further laboratory experiments. Unpaired two-tailed Student's test was used to compare the difference between age-matched male and female. Two-way ANOVA and Turkey's multiple comparisons test was used to a multiple comparisons between groups.

The results show a 50.6% higher renal lactate production and 58.5% higher fractional perfusion of lactate in male rats compared to age-matched female rats, while female rats had higher GFR. Moreover, volume-matched male rats showed also higher renal lactate production.

In conclusion, there is a metabolic shift between the male and female Wistar rats, while male rats showed elevated metabolic activity. Consideration of sex difference is needed when kidney disease research are designed.

CH.22   Karen Baden Alstrup

ABSTRACT TITLE (CLICK TO CHANGE ME) CHARACTERISTICS OF PATIENTS TREATED BY THE DANISH HELICOPTER EMERGENCY MEDICAL SERVICE FROM 2014-2018: A NATIONWIDE POPULATION-BASED STUDY

K. Alstrup[1], T. Møller[4], L. Knudsen[2, 3], T.M. Hansen[3], J.A.K. Petersen[2, 3], L. Rognås[1, 2, 3], C. Barfod[3, 4]

[1]Research and Development, Pre-hospital Emergency Medical Services, Central Denmark Region, [2]Department of Anaesthesiology, Aarhus University Hospital, [3]The Danish Air Ambulance, [4]Copenhagen Emergency Medical Services, University of Copenhagen

Background

Recently, a national Helicopter Emergency Medical Service (HEMS) was introduced in Denmark to ensure the availability of physician-led critical care for all patients regardless of location.

Proper dispatch of HEMS is known to be complex, and resource utilisation is a highly relevant topic. Population-based studies are fundamental when evaluating and optimising a system. The aim of this study was to describe

demographics, pre-hospital diagnostics, severity of illness or injury, and the critical care interventions performed for patients treated by HEMS.

Method

Retrospectivenationwide population-based study including patients encountered by HEMS between October 1st2014 and April 30th2018.

Results

Of 13,391 dispatches we included 7,133 missions: 4,639 patients were air lifted to hospital, 174 patients were escorted to hospital by the HEMS physician in an ambulance, and in 2,320 cases HEMS assisted the ground crew on scene but did not escort the patient to hospital. The median age was 60 years (range 0-99 years) and 64% were men.

The main diagnostic groups were cardio-vascular emergencies, trauma and neurological emergencies. In 61% of the cases, the patient was critically ill/injured, and in one third of the missions a critical care intervention was performed.

Conclusion

The national Danish HEMS primarily attends severely ill or injured patients and often perform critical care interventions. Patients with cardio-vascular emergencies, trauma and neurological emergencies are among those patient groups most commonly seen.

We conclude that the overall dispatch profile appears appropriate but emphasise that continuous development and refinement is essential.

CH.23   Mads Valdemar Anderson   GENOME EDITING BY TRACELESS CRISPR-CAS9 DELIVERY USING LENTIVIRUS-DERIVED NANOPARTICLES.

M.V. Anderson, E.A. Thomsen, K.A. Skipper, J.G. Mikkelsen

Department of Biomedicine, Aarhus University

Somatic cell genome editing with the CRISPR-Cas9 system can potentially transform the lives of patients living with severe diseases. Efficient genome editing with DNA-free delivery of CRISPR-Cas9 RNPs (ribonucleoprotein complexes), resulting in transient exposure to the RNA-guided nucleases, have already shown potential for treatment of ex vivo treatment of hematopoietic stem cells. For in vivo treatments however, the advantages of RNP delivery are outweighed by strong limitations of physical or chemical methods for delivery. Opposed to delivery of RNPs, viral vectors are routinely used for delivery of genes encoding Cas9 and sgRNA in vitro and in vivo. This however, results in prolonged expression of CRISPR-Cas9 that may cause unspecific cleavages and depletion of gene-corrected cells by the immune system.

Lentiviral vectors are capable of entering cells and deliver their genetic cargo to the nucleus. By utilizing different envelope proteins, such vectors can be pseudotyped to broaden or restrict the cell types that are transduced by the vector. With the aim of achieving safe and efficient genetic repair, we developed LNPs (lentivirus-derived nanoparticles) as carriers of endonuclease proteins, including Cas9. In this project I am developing LNPs for potent, traceless delivery of Cas9 and sgRNAs.

CH.24   Liv Marie Duus   COMPARISON OF WHOLE BLOOD AND PLASMA FOR DETECTION OF
         CANCELLED   CYTOMEGALOVIRUS DNA IN TRANSPLANT PATIENTS.

L. Duus, K. Handberg, S. Ellermann-Eriksen

Department of Clinical Microbiology, Aarhus University Hospital

Background:

Cytomegalovirus (CMV) remains one of the most important viral pathogens in hematopoietic stem cell transplant (HSCT) and solid organ transplant (SOT) patients. When whole blood is analysed rather than plasma, the intracellular CMV DNA is measured in addition to the extracellular CMV DNA in plasma.

Aim:

To compare whole blood and plasma for detection of CMV DNA in transplant patients in relation to clinical data.

Methods:

Whole blood and plasma from 196 SOT or HSCT patients were analysed for CMV on cobas® 6800. Before the analysis, whole blood was diluted 1:5 in Specimen Pre-Extraction Reagent (Roche Molecular Systems, Inc.) and heated on a thermomixer for 10 min, 56°C, 1000 rpm. Clinical data were collected from medical records.

Results:

Until now we have enrolled 196 SOT or HSCT patients and 1200 corresponding plasma and whole blood samples. CMV DNA was detected in 25 % of the plasma samples. Viral load was found to be 7.3 times higher in whole blood than in plasma in SOT patients, but only 2.9 times higher in HSCT patients. The mean number of leucocytes in SOT patients is $7.9*10^9$/l but only $4.6*10^9$/l in HSCT patients. Viral loads were seen in relation to antiviral treatment, immunosuppression and symptomatic disease.

Conclusions:

SOT and HSCT patients have different patterns in their viral loads in whole blood and plasma. The reason could be the difference in number of leucocytes. This must be taken into account when cutoff values for antiviral treatment are settled.

CH.25   Lene Wulff   ARE UNEXPLAINED HEALTH EVENTS FOLLOWING HPV VACCINATION
         Krogsgaard   ASSOCIATED WITH PRIOR EBV INFECTION? -A DANISH REGISTERBASED
                           CASE CONTROL STUDY

L.W. Krogsgaard[1], I.G. Helmuth[3], B.H. Bech[1], T. Lützen[1], O. Plana-Ripoll[4], R.W. Thomsen[2], K. Mølbak[3], D. Rytter[1]

[1]Department of Public Health, Research Unit for Epidemiology, Aarhus University, [2]Department of Clinical Epidemiology, Aarhus University Hospital, [3]Statens Seruminstitut, [4]National Centre for Register-based

Research, Department of Economics and Business Economics, Aarhus University

In Denmark, the vaccination program against HPV has been threatened by reports of suspected adverse events (AE). EBV infection is associated with long lasting symptoms similar to the reported AE's. The aim of this study was to examine if Epstein Barr Virus (EBV) is a risk factor for experiencing AE's after HPV vaccination.

The study was a nationwide register-based matched case-control study. Cases were HPV vaccinated girls in the period 2011 throughout 2017 who experienced AE's. For each case, five controls were selected among all HPV vaccinated girls. Information about EBV was obtained from the Danish Microbiology Database and assessed for the time periods 1) Before HPV vaccination, 2) Around HPV vaccination 3) The whole study period. Logistic regression was used to calculate OR's (95% CI) for the association between EBV and experienced AE's adjusting for matching variables and region of residence.

We identified 1,217 cases and 6,085 controls. A higher proportion of cases 204 (16.8 %) than controls 287 (4.7 %) were tested for EBV in the study period. Around time of HPV vaccination cases had elevated odds for testing EBV positive OR 4.52 (2.68;7.63) and EBV negative OR 20.99 (5.81; 75.79). Only five females were classified with acute/recent EVB infection in this period.

In conclusion, EBV infection is not a leading explanation for Danish females experiencing severe adverse events after HPV vaccination. EBV cannot be excluded as an explanatory factor for a small proportion of females. However, the findings are more likely explained by the fact that a larger proportion of females experiencing adverse events were tested for EBV.

CH.26   Maja Bendtsen Sharma   SUBSTANTIAL LONG-TERM DOSE-DEPENDENT MORBIDITY AFTER RADIOTHERAPY FOR SINONASAL CANCER. A CROSS SECTIONAL STUDY

M.B. Sharma[1], K. Jensen[2], J. Johansen[3], A. Amidi[4], M. Funding[5], S.F. Urbak[5], D. Bechtold[7], S.F. Eskildsen[6], C. Grau[8]

[1]Department of Oncology, Aarhus University Hospital, [2]Danish Center for Particle Therapy, Aarhus University Hospital, [3]Department of Oncology, Odense University Hospital, [4]Unit for Psychooncology and Health Psychology, Institute of Psychology, Aarhus University, [5]Department of Ophthalmology, Aarhus University Hospital, [6]Center for Functionally Integrative Neuroscience, Aarhus University, [7]Department of Ophthalmology, Odense University Hospital, [8]Department of Oncology and Danish Center for Particle Therapy, Aarhus University Hospital

Purpose: This study aimed to estimate incidence and severity of late morbidity after intensity modulated radiation therapy (IMRT) for sinonasal carcinoma (SNC).

Material and methods: Eligible patients were treated with IMRT in two Danish institutions for SNC from 2008 - 2016. Late morbidity was evaluated with a battery of neurocognitive tests, cerebral MRI, objective ophthalmological examination, blood samples, and olfactory function testing. Patient reported outcome was collected.

Results: Twenty-seven of 43 eligible patients were enrolled; median age was 67 years (range 47-83). Cognitive function: Patients scored lower than normative data on several domains. Poorer working memory and verbal fluency performance was significantly associated with higher mean doses to several cerebral substructures. Ocular toxicity: Seven patients (26%) had radiation-induced ocular toxicity, one being enucleated. We found correlations between grade 3 radiation-induced visual acuity impairment (CTCAE 4.0) and maximum dose to the optic nerve (p=0.037). Pituitary toxicity: Six patients (22%) had abnormal hormonal functioning; one exhibited insufficiency in all axes and initiated substitutional therapy. Olfactory function: Sixteen patients (59%) had impaired olfactory function. MRI: Voxel-wise analyses on MRI diffusion parameters will be undertaken, and morphology and white matter lesions will be examined in relation to dose. Patient-reported outcomes: The most affected domains of the global QoL analysis were social and emotional functions.

Conclusion: We found substantial long-term morbidity after IMRT. A nationwide prospective registration of morbidity SNC has now been initiated.

CH.27   Mette Eline Brunbjerg

IMMEDIATE IMPLANT-BASED BREAST RECONSTRUCTION. COMPARISON OF TWO SURGICAL METHODS.

M.E. Brunbjerg[1, 3], T.B. Jensen[1], P. Christiansen[1], J. Overgaard[2], T.E. Damsgaard[3]

[1]Department of Plastic and Breast Surgery, Aarhus University Hospital, [2]Department of Experimental Clinical Oncology, Aarhus University Hospital, [3]Department Clinical Medicine, Aarhus University

Background:

Increasing incidence and decreasing mortality of breast cancer results in more women living with the consequences of treatment. The aim of this study was to evaluate complication rate and patient- and investigator reported aesthetic result after implant-based breast reconstruction (BR) performed with two different techniques.

Methods:

Observational cohort study with 40 participants admitted for immediate, implant-based BR following skin-sparing mastectomy. N=20 underwent BR with a two-stage technique and n=20 underwent BR with a one-stage technique using acellular dermal matrix. Follow-up time was 2 years.

Results:

The risk for at least one major complication (breast level) in the one-stage group was 29% (CI: 10.7%-47.3%) compared to 12% (CI: -0.7%-24.7%) in the two-stage group. The risk for at least one minor complication (breast level) was 3.2% (CI: -3.1% - 10%) in the one-stage group but 44% (CI: 22.3% - 65.7%) in the two-stage group. The risk for implant removal (breast level) was 25% and equal between the groups.

Patients in both treatment groups underwent in average 1.5 surgical corrections to obtain a satisfying aesthetic result. Patient and investigator assessed aesthetic outcome was high in both groups.

Conclusion:

With equal rates of implant removal, aesthetic corrections and satisfaction with the result between the two groups the one-stage approach is feasible and allows the patient to achieve BR in one operation.

| CH.28 | Julie Jacoby Petersen | NAVIGATING THE COMPLEXITY: NURSES' EXPERIENCES WITH CROSS-SECTORIAL COLLABORATION AND PATIENT INVOLVEMENT |

J.J. Petersen[1], B. Østergaard[2], E.K. Svarvarsdottir[3], S.J. Rosenstock[1], A. Brødsgaard[4]

[1]Department of Gastroenterology, Copenhagen University Hospital, Amager Hvidovre, [2]Department of Clinical Research, University of Southern Denmark., [3]School of Health Science, University of Iceland, [4]Nursing and Health Care, Department of Public Health, Aarhus University

Background: Care transitions are a significant and inevitable part of healthcare systems worldwide where policies and organizational structure set the terms for integration between care settings. Previous studies indicate that cross-sectorial collaboration and involvement of patients and families are crucial to ensure safety and continuity in care transitions. However, barriers and a growing number of elderly patients causes the complexity in care transitions to increase. Limited is known about nurses' experiences even though they play a key role in care transitions.

Aim: To explore nurses' experiences on cross-sectorial collaboration and involvement of patients and families related to transitional care.

Design: A qualitative descriptive exploratory design.

Method: Data were collected from two focus group interviews with 16 nurses from three hospital wards and three municipalities. A semi-structured interview guide was designed based on a literature search. The data were analyzed using Qualitative Content Analysis inspired by Graneheim and Lundman.

Findings: One overall theme emerged: Navigating the complexity. The theme contained three categories; 1) Knowledge gap between sectors 2) Handling the ambiguities in the healthcare system 3) Involvement as a balancing act.

Conclusion: Our findings imply that cross-sectorial collaboration and involvement of patients and families are challenged due to internal and external aspects. Uncoordinated care causes a gap between healthcare sectors where patients and families are "in-between" sectors. We found nurses to be key players in care transitions, and their experience and knowledge should be utilized and applied in practice.

| CH.29 | Helle Elisabeth Andersen | CARING RESPONSIBILITY FROM THE PERSPECTIVES OF OLDER PERSONS WHOSE ADULT CHILDREN ARE THEIR CARERS - A PHENOMENOLOGICAL-HERMENEUTIC STUDY |

H.E. Andersen, B. Hoeck, D.S. Nielsen, J. Ryg, C. Delmar

Nursing and Health Care, Department of Public Health, Aarhus University

Aim: To develop lifeworld insights into the phenomenon of caring responsibility from the perspectives of persons aged 80+ years living alone with chronic illness, physical frailty and dependency on adult children following a recent hospitalisation.

Design: A qualitative study based on a phenomenological-hermeneutic approach inspired by reflective lifeworld research.

Method: Eleven semi-structured lifeworld interviews with older persons were conducted following discharge. The interviews were analysed using the methodological principles of reflective lifeworld research.

Findings: We identified the essential meaning and four constituents illuminating different aspects inherent in the complex phenomenon of caring responsibility; 'A life-constraining transition', 'Trusting the children to fill the gaps and be the glue', 'Tacit responsibility, negotiations and acceptance' and 'Depending on the children and knowing they are burdened by you'.

Conclusions: Caring responsibility is based on a trusting relationship and tacit negotiations indicating an understanding of interdependence and acceptance of dependence on adult children. However, a paradox appears when older persons express a deep-rooted perception of autonomy and independence as they have difficulties with their growing dependency and feelings of being burdensome. Older persons try to balance the continuum of autonomy, their existential self-image and actual capability. The practical part of caring responsibility dominates and affects the parent-child relationship leaving less time for meaningful togetherness.

CH.30   Morten Aagaard Nielsen

CHITINHEPTOSE - A NOVEL ANTIGENIC GLYCAN LINKED TO DIAGNOSIS AND DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS

M.A. Nielsen[1], A.Y. Metha[2], T.W. Kragstrup[1, 3], T.R. Mckitrick[2], B. Deleuran[1, 3], R.D. Cummings[2]

[1]Department of Biomedicine, Aarhus University, [2]Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, National Center for Functional Glycomics, USA., [3]Department of Rheumatology, Aarhus University Hospital

Introduction

Rheumatoid arthritis (RA) is a systemic inflammatory autoimmune disease, affecting 1% of the population. The etiology of RA remains unknown. However, glycan antigens have appeared as promising diagnostic and prognostic markers in autoimmune diseases.

Methods

Plasma samples from newly diagnosed, early RA (eRA) patients (OPERA trail, n=60)[1]and matched health controls (HC, n=60) were analyzed for antibodies towards glycans on the NCFG v.2 array.

The printing, binding, and scanning conditions have been described previously[2]. Briefly, diluted plasma (1:50) was applied to slides at RT for 1 h, followed by an anti-IgG antibody (PE). Positive signal was measured

by the mean fluorescent intensity minus the background (RFU) of four replicates.

Results

The relative IgG signal intensities (RFU) between the glycans differed between HC and eRA patients. The RFU levels of IgGs bound to chitin oligosaccharides were higher in eRA compared with HC (p<0.01). The RFU levels of IgGs recognizing chitoheptaose (C7) were elevated in eRA patients compared with HC (p< 0.05). The levels of IgG binding to C7 correlated with joint pain (ρ=0.42, p<0.01) and disease activity (ρ=0.29, p<0.05) after 1 yr. Treatment did not affect the RFU levels of IgG recognizing C7 neither did addition of an TNF inhibitor.

Conclusions

This study reveals that the SI levels of IgG binding to C7 are elevated in eRA patients compared with HC. These levels are correlated with both joint pain and disease activity after 1 yr. These observations support the hypothesis that IgG recognition of C7 could be of both diagnostic and prognostic value in RA.

1) Hørslev-P.K et al. 2013

2) Heimburg-Molinaro et al. 2011

CH.31   Cecilie Blenstrup   MID-UPPER ARM CIRCUMFERENCE IS A PREDICTOR OF TUBERCULOSIS
         Patsche   WASTING

C.B. Patsche[1, 2], C. Wejse[1, 2, 3]

[1]Center for Global Health, Department of Public Health, Aarhus University, [2]Bandim Health Project, INDEPTH Network, Guinea-Bissau, [3]Department of Infectious Diseases, Aarhus University Hospital

Background: Body mass index (BMI) 2 is used to determine nutrition therapy eligibility of patients with tuberculosis. A simpler measure of nutritional status, such as mid-upper arm circumference (MUAC), is desirable in low-resource settings. The objective of this study was to identify MUAC cut-offs predicting BMI 2 and BMI 2.

Methods: A prospective observational study was conducted at the urban health and demographic surveillance site in Guinea-Bissau. Newly diagnosed adult patients with tuberculosis were enrolled from three health centres and the national tuberculosis reference hospital, between November 2003 and August 2017. MUAC and BMI were measured at treatment initiation. Pearson's correlation, univariate regression analysis, and receiver operating characteristics (ROC) area under the curve were used to analyze data.

Results: A total of 1833 patients with tuberculosis aged ≥18 years were eligible for this study. Exclusion criteria were: multi drug-resistance tuberculosis, pregnancy, edema, and missing MUAC and/or BMI values. MUAC were strongly correlated with BMI (r=0.76), and for each BMI unit increase MUAC increased with 0.67 cm. ROC area under the curve for MUAC predicting BMI 2 was 0.87 and for MUAC predicting BMI 2 it was 0.89. A MUAC cut-off of 24.2 cm best identified BMI 2 (SENS 79.4%, SPEC

78.8%) and a MUAC cut-off of 22.0 cm best identified BMI 2 (SENS 87.9%, SPEC 75.0%).

Conclusion: MUAC is well-correlated with BMI in patients with tuberculosis in Guinea-Bissau and can be used as a nutritional status indicator. The findings suggest that MUAC can be used in place of BMI if BMI measurements propose a challenge.

CH.32   Sara Raquel Almeida Ferreira   INVOLVEMENT OF THE CD163 RECEPTOR IN THE ALPHA-SYNUCLEIN INDUCED NEURODEGENERATION IN PARKINSON'S DISEASE

S.A. Ferreira[1, 2], A. Etzerod[1, 4], I. Klœstrup[1, 2], C. Betzer[1, 2], P. Svedsen[1, 3], A. Panhelainen[5], M. Saarma[5], P.H. Jensen[1, 2], S.K. Moestrup[1, 3], M. Romero-Ramos[1, 2]

[1]Department of Biomedicine, Aarhus University, [2]Danish Research Institute of Translational Neuroscience – DANDRITE, Aarhus University, [3]Department of Cancer and Inflammation Research, Syddansk University, [4]Aix Marseille University, CNRS, INSERM, CIML, Marseille, France, [5]Biotechnology Institute, University of Helsinki, Helsinki, Finland

Inflammatory changes in the brain and periphery in Parkinson's Disease (PD) patients has been documented, but how the brain and the peripheral immune system interact and consequences of this interaction is yet unknown. We hypothesize that the immune system is involved in the neurodegeneration associated to alpha-synuclein (a-syn) in PD, therefore, its modulation may have a therapeutic potential. CD163 is a monocytic-scavenger receptor expressed in macrophages but not in brain microglia. CD163 has an increased expression in certain inflammatory conditions. We have observed infiltration of CD163+ cells into the brain in a PD toxic rat model. Moreover, we have data showing changes of CD163 (cellular and soluble) in PD patients. This strongly suggest a role for the CD163 macrophages in PD that we believe might be a key population involved in the crosstalk between brain and periphery. Here, we aim to determine if the CD163 receptor is directly involved in the immune response in PD and how it might relate to a-syn pathology and associated degeneration. To do so, we injected fibrillar a-syn into the striatum of CD163 knockout (KO) animals and wild-type (WT) littermates. Mice were analysed for motor and cognitive behaviour, a-syn pathology, immune response and dopaminergic degeneration at short (1 month) and long term (6 months) post-injection. Our preliminary data suggest that a-syn fibrils injection leads to significant a-syn pathology and neuronal degeneration associated to motor defects and linked to a significant increase in MHCII immune activity, on a gender dependent manner. Our data suggest that CD163 has a relevant role in the a-syn induced pathology and immune response.

CH.33   Martin Kinnerup   COGNITIVE IMPAIRMENT IN PARKINSON'S DISEASE

M.B. Kinnerup[1], J. Schaldemose[1], K. Stœr[1], R. Ismail[1], J. German[5], M. Sommerauer[1], A. Højlund[2], M. Chakravarty[5, 6, 7], D.J. Brooks[1, 3, 4], A. Nahimi[1]

[1]Nuclear Medicine and PET Centre, Aarhus University Hospital, [2]Center of Functionally Integrative Neuroscience, [3]PET Clinical Science, Newcastle University, [4]Department of Medicine, Imperial College London, [5]Brain

Imaging Centre, Douglas Institute, [6]Department of Psychiatry, McGill University, [7]Department of Biomedical Engineering, McGill University

Introduction

Parkinson's Disease patients suffer from approximately 8 non-motor symptoms (NMS) during the disease duration. The cause of the severity and the manifestation of NMS remain unclear, but they have been related to neuronal loss in locus coeruleus(LC). LC is one of the main sources of noradrenaline in the brain and changes to the integrity of neurons in this part of the brain could drive the NMS that we see in Parkinson's. Importantly, the loss of noradrenergic neurons may appear before the hallmark motor symptoms are clinically detectable, which underline the importance of knowing its role in the brain.

Methods and materials

In the current study, we use a multimodal approach to elucidate the relation between several imaging biomarkers of the PD patients' current cognitive function and how the cognitive function changes over time. Visualization of noradrenergic deficits is performed with PET, structural and morphological changes with MRI, functional and connectivity changes with M/EEG.

Expected outcomes

Changes to the noradrenergic system has proven to impact response inhibition, which is one of the core symptoms in Parkinson's. Further, changes to the brain oscillations have been associated with dementia in Parkinson's disease, more specifically the theta band has proven to be of high importance. Studies with electric stimulation of LC has shown an increase in synchronisation in the theta band, driving a connection between the noradrenergic system and theta band activity.

CH.34   Pauline Cantou   NEGATIVE CUES MODULATE CONFLICT PROCESSING: AN FMRI STUDY IN EARLY-ADOLESCENTS

P. Cantou, B. Kleber, S. Kotz, P. Vuust, E. Brattico

Center for Music in the Brain (MIB), Department of Clinical Medicine, Aarhus University and The Royal Academy of Music Aarhus/Aalborg

Adolescence is a transitional period between childhood and adulthood marked by heightened sensation-seeking behaviors and impulsive decision making. Previous studies suggest that those behaviors result from an imbalance between high emotional reactivity and low inhibitory control, especially in affectively charged situations. Specifically, adolescents performed better on conflicting tasks in an affect-free context than in an emotional context, suggesting that emotional cues interfered with cognitive control processes.

At the brain level, this adolescent-specific developmental pattern may be explained by the dual-system model proposing an imbalance between a hyperactive subcortical network and an immature prefrontal network during this period of life.

While this interaction between inhibitory control and emotional processes has been mainly investigated using rewarding cues, less is known about how inhibitory control is altered by stimuli of negative valence.

Here, we tested 25 early-adolescents on a color flanker task using emotionally neutral and negative words while they were scanned with functional MRI.

As expected, incongruent stimuli resulted in higher reaction time compared to congruent stimuli, which is a typical response to conflict processing due to more involvement of executive functions.

Emotion prolonged reaction time when processing incongruent stimuli but not congruent stimuli, suggesting that negative cues only modulate conflict processing.

Moreover, emotion increased subcortical activation (especially the left insula) in conflict trials that may reflect a takeover of emotional cues over cognitive processes.

CH.35   Rasmus H. Olesen   **OBESITY INCREASE MRNA EXPRESSION OF INFLAMMATORY GENES IN HEALTHY HUMAN BRAINS**

R.H. Olesen, A. Larsen

Department of Biomedicine, Aarhus University

Obesity has been declared a pandemic by WHO. Obesity constitutes a burden for the individual as well as the society. Obesity is a major risk factor for severe diseases, including cancer, cardiovascular diseases as well as type 2 diabetes mellitus. Studies shows that obesity are related to an increased risk of developing vascular dementia and Alzheimer' disease. This relationship might be related to the increased chronic low-grade inflammation as well as the alterations in the glucose metabolism. Here we examine the relationship between changes in mRNA expressions with increasing BMI. We utilized the Lieber Institute' polyA++ Brainseq database. The data consist of RNA-Seq data from 150 neurological and psychiatric sound human brains. The samples for analysis was taken from prefrontal cortex. The RNA-Seq data was analyzed with Limma, DEseq2 and qSVA., implementing the workflow described by the authors of the software. For the analysis, several possible confounders were considered, this includes subject with known diabetes or known use of pharmaceutical known to affect glucose metabolism. Possible confounders in the analysis were smoking, race, sex, PH and postmortem interval. Several of the top genes differential genes related to inflammation were discovered. This suggest a relationship between increasing BMI and inflammation. There were no clear relationship to previous described pathways, found in the GO or KEGG databases. However, we have found several genes, there is not described previously.

In conclusion, our results suggest an increase in levels of inflammatory genes. However, more research is needed to identify the mechanisms linking obesity and neurodegeneration.

CH.36   Simon Bang Kristensen   **BIVARIATE LOGISTIC MIXED EFFECT REGRESSION MODELS BASED ON LATENT VARIABLES**

S.B. Kristensen

Department of Public Health, Aarhus University

Bivariate observations of binary and ordinal data arise frequently in clinical trials and the cognitive sciences. Consider for example an efficacy-toxicity study for some drug, in which efficacy is binary and toxicity is measured as side-effects on an ordinal scale. While robust methods offer the possibility to evaluate drug effects taking into account the correlation between efficacy and toxicity, a bivariate modelling approach is required in scenarios where one is interested in aspects of the marginal distributions in themselves along with the association between the two. For example, we may be interested in efficacy and toxicity as separate outcomes but also wish to estimate the probability of benefiting from a positive treatment outcome while not experiencing a high degree of side-effects as a function of dosage.

We consider methods for constructing such bivariate models with logistic marginals and propose a model based on the Ali-Mikhail-Haq bivariate logistic distribution. We motivate the model as an extension of that based on the Gumbel type 2 distribution as considered by other authors and as a bivariate extension of the logistic distribution which preserves certain natural characteristics.

Basic properties of the obtained model are studied and the proposed method is exemplified by analysis of a cognitive experiment of visual recognition and awareness.

CH.37   Mette Jørgine Kirkeby

ANALYSING THE ROLE OF CHILDHOOD NEGATIVE LIFE EVENTS AND DIVERGENSES FROM NORMAL BIOGRAPHY ON LABOUR MARKET TRAJECTORIES OVER THE THE LIFE-COURSE

M.J. Kirkeby[1], C.D. Hansen[1, 2], J.H. Andersen[1]

[1]Department of Occupational Medicine, Herning Hospital, [2]Department of Sociology and Social Work, Aalborg University

Protocol:

Background: The transition from school to work is important for influencing trajectories throughout the life-course. The aim of this study is to investigate to what extent childhood negative life events and divergences from normal biography (as measures of vulnerability) are associated with differences in labour market trajectories from age 15 to 35 in a birth cohort of all Danish citizens born in 1983.

Methods:Information on social history, labour market participation, educational events and public transfers from all Danish adolescents born in 1983 (n = 50,110) is used to describe a normal biography, derive sequences in 7 state spaces monthly from age 15 to age 35. Cluster analysis on the sequences identifies distinct groups of adolescents with similar labour market trajectories. Clusters are compared by divergences from normal biography and negative life events to identify vulnerable groups.

CH.38   Martin Rune   EXPOSURE TO ORGANOPHOSPHATE INSECTICIDES IS ASSOCIATED WITH
         Hassan Hansen   DECREASED LUNG FUNCTION: A SHORT-TERM FOLLOW-UP STUDY IN
                             UGANDA

M.R.H. Hansen[1, 2], E. Jørs[3], A. Sandbæk[1, 4], D. Sekabojja[5], J. Ssempebwa[6], R. Mubeezi[6], P. Staudacher[7, 8], S. Fuhrimann[9], V. Schlünssen[1, 2]

[1]Department of Public Health, Aarhus University, [2]National Research Center for the Working Environment, [3]Odense University Hospital, [4]Steno Diabetes Center Aarhus, [5]Uganda National Association of Community and Occupational Health, [6]Makerere University, [7]Eawag, Swiss Federal Institute of Aquatic Science and Technology, [8]Institute of Biogeochemistry and Pollutant Dynamics, ETH Zurich, [9]Utrecht University

Introduction

Exposure to some classes of insecticides may be causally related with poor lung function. The purpose of this project was to investigate the association in a follow-up study with objective measures of exposure.

Methods

From September 2018 to February 2019, we conducted a short-term cohort study in a population of 364 small-scale farmers in Uganda. Participants were examined before, during and after the main pesticide-spraying season. At each visit, we measured each participant's lung function and acetylcholine esterase (AChE) activity. Organophosphate insecticides inhibit AChE, meaning low AChE can be used as a measure of exposure. Lung function was quantified as forced expired volume in 1 second (FEV_1), forced expiratory capacity (FVC) and FEV_1/FVC. We took the effects of gender, age and height into account by normalizing the FEV_1, FVC and FEV_1/FVC into Z-scores. The effect of AChE levels on lung function was analyzed using a multivariate random coefficient model that took into account the repeated measurements, possible non-linear exposure-response relationships, and known risk factors for lung disease.

Results and discussion

Lower AChE (higher exposure to organophosphate insecticides) was statistically significantly associated with decreased FEV_1 Z-score: $\Delta(FEV_1 Z)$ = -0.56 [-1.11 ; -0.01] for lowest compared to highest observed AChE. A similar, but statistically non-significant relationship was seen for FVC Z-score. No association was demonstrated between AChE and FEV_1/FVC Z-score.

Conclusion

The study suggests that occupational exposure to organophosphate insecticides may lead to an mixed obstructive/restrictive decrease in lung function.

CH.39   Louise Lindholdt   MENTAL HEALTH ACROSS TWO GENERATIONS - IS MENTAL HEALTH
                                 STATUS PASSED ON FROM PARENTS TO THEIR CHILDREN?

L. Lindholdt[1, 6], M. Labriola[2, 6], T. Lund[3, 4, 6], J.H. Andersen[5, 6]

[1]Department of Public Health, Aarhus University, [2]NORCE, Norwegian Research Centre, Bergen, Norway, [3]Centre for Social Medicine, Frederiksberg and Bispebjerg Hospital, [4]Department of Public Health,

University of Copenhagen, [5]Department of Occupational Medicine, Danish Ramazzini Centre, University Research Clinic, Regional Hospital West Jutland, [6]Research Centre for Youth and Employment, Regional Hospital West Jutland, University Research Clinic

Objective

Early psychosocial problems and mental symptoms are important factors of health and social inequality throughout life. Offspring of mentally ill parents is deemed particularly predisposed to social and mental problems in the long term, and is therefore at a higher risk of developing low mental health later in life.

The aim of this study will be to investigate whether mental illness among parents is associated with self-rated health (SRH) among their adolescent children.

Methods

The study will use questionnaire data from a nationwide youth cohort, the FOCA cohort (N=13,100), on adolescent's SRH measured by one item from SF-36. Information on parent's mental health will be obtained from The Danish National Prescription Registry where medicine use will be used as a proxy for mental illness combined with diagnoses on mental and behavioural disorders from the Danish National Patient Registry. Information will be examined in a five-year period before the adolescents completed the questionnaire. Also, a question devised specifically for the FOCA cohort questionnaire about mental illness among the adolescents' parents will be used.

Regression analyses will be used to examine the potential association between adolescents' SRH and parental mental illness. Adjustments will be made for relevant covariates as comorbidity and socioeconomic factors.

Results

No results yet.

Conclusion:

The study will address a current issue within public health, where it expects to indicate the importance of focusing on mental health across generations, and to provide evidence that can prove relevant when planning future interventions aimed towards adolescents with mental health problems.

CH.40   Lotte Levison   PEDIATRIC GUILLAIN-BARRÈ SYNDROME IN A 30-YEAR NATIONWIDE COHORT

L.S. Levison[1], R.W. Thomsen[2], L.K. Markvardsen[1], D.H. Christensen[2], S.H. Sindrup[3], H. Andersen[1]

[1]Department of Neurology, Aarhus University Hospital, [2]Department of Clinical Epidemiology, Aarhus University Hospital, [3]Department of Neurology, Odense University Hospital

Abstract

Objective

To examine epidemiological aspects of pediatric Guillain-Barré syndrome (GBS) over the past 30 years in a Northern European country, including diagnostic validity, incidence, risk factors, and initial clinical characteristics.

Methods

In the Danish National Patient Registry (DNPR) we identified all children (N=212) diagnosed with GBS and admitted to any Danish department of pediatrics between 1987 and 2016. 145 (68%) medical files could be retrieved and reviewed, enabling classification of patients as true GBS versus non-GBS. The nationwide GBS incidence rate (IR) was calculated and stratified by age, gender, time-periods and season. Risk factors and initial GBS characteristics were assessed by medical record review.

Results

The positive predictive value of GBS diagnosis codes was 86% (95% confidence interval (95% CI): 80-91%). The crude GBS IR was 0.69 per 100,000 person years (95% CI: 0.60-0.79) and peaked at two years of age; IR: 1.36 (95% CI: 0.89-1.99). The IR was higher among males 0.80 (0.66-0.95) than females 0.58 (0.47-0.72) and was relatively stable over the 30-year period. No seasonal difference of the IR was found. Of the 125 GBS cases; 63% were preceded by infection whereas none were preceded by surgery or malignant disease. Medically treated pain was documented in 70%, mainly confined to the lower extremities.

Conclusions

Pediatric GBS diagnoses in the DNPR have high validity. Pediatric GBS incidence peaks at the age of two and is preceded by infection in two-thirds of children. Lower extremity pain is a common clinical presentation in the acute setting.

CH.41   Andreas Halgreen Eiset   THE HEALTH STATUS OF NEWLY ARRIVED ASYLUM-SEEKING MINORS IN DENMARK - A NATIONWIDE REGISTER-BASED STUDY

A.H. Eiset[1], A.L. Loua[2], A. Kruse[2, 3], M. Nørredam[2, 4]

[1]Centre for Global Health (GloHAU), Department of Public Health, Aarhus University, [2]Section of Immigrant Medicine, Department of Infectious Diseases, Copenhagen University Hospital, [3]Department of Paediatrics, Copenhagen University Hospital, [4]Danish Research Centre for Migration, Ethnicity, and Health (MESU), Section for Health Services Research, Department of Public Health, University of Copenhagen

Objectives: Asylum-seeking minors are known to be at increased risk of physical and mental diseases compared to both native children and adult asylum-seekers. We present a nationwide register-based study based on the health assessment of 7210 newly arrived minors in Danish asylum centres from January 1st 2011 to December 31st 2015. Methods: We describe socio-demographic characteristics, trauma history and symptoms

of physical and mental health. To associate the reporting of traumatic events and signs of anxiety or depression we performed a logistic regression analysis. Results: We found a high, albeit varying, prevalence of traumatic experiences, sleeping and eating problems, and head- and toothache. In the subgroup that was assessed according to 'The Child Scale' more than two of every five minors were in need of immediate support. In the subgroup examined by a doctor, one of every four had at least one abnormal finding. Conclusion: The prevalence of trauma and mental health symptoms and the association of the two were striking. Our findings underline that timely recognition and appropriate treatment of childhood traumas should be given high priority in the receiving communities.

CH.42   Mette Kaasgaard HETEROGENEITY OF DANISH LUNG CHOIRS AND THEIR SINGING LEADERS - *A STUDY OF PERFORMANCE, EXPERIENCES, AND ATTITUDES IN AN EMERGING FIELD*

M. Kaasgaard[1, 2], I.C. Andersen[1, 4], P. Vuust[2], O. Hilberg[3, 4], A. Lokke[3, 4], U. Bodtger[1, 4]

[1]Respiratory Research Unit Region Zealand, Department of Respiratory Medicine, Naestved Hospital, [2]Center for Music in the Brain, Department of Clinical Medicine, Aarhus University, [3]Respiratory Dept., Hospital Lillebaelt, [4]Department of Regional Health Research, University of Southern Denmark

Background:

Lung choirsgain increasing attention as a beneficial leisure time intervention. In United Kingdom a standardized training program is offered to singing leaders by the British Lung Foundation. A similar program is not available in Denmark. This study investigates current variety in setting and approach in Danish lung choirs.

Methods:

An online survey was performed among Danish lung choir singing leaders, comprising 25 questions. Quantitative variables were counted, and inductive content analysis approach was used for the qualitative component.

Results:

Totally, 20 (67%) of 33 identified singing leaders responded. The lung choirs were heterogenous concerning setting, form, content and approach. Most singing leaders held high educational degrees in music, but lacked skills in lung diseases. The choirs were traditionally led with low levels of physical activity. However, singing leaders experienced lung choirs as a highly meaningful, and perceived that participants benefitted physically, psycho-socially, and musically. The study also identified concurrent tension fields, spanning from enthusiasm concerning perceived potentials of the field of "arts-and-health", and experiences of insecurity and isolation among the singing leaders.

Interpretation:

Danish singing leaders to do not have insight into disease specific aspects of singing in lung choirs, and lead the choirs without using techniques endorsed by the best documented singing leader training program (from

UK). Nevertheless, the responding singing leaders found their activity highly meaningful.

CH.43   Jakob Hansen   USING OPTICAL MOTION CAPTURE TO MEASURE PELVIS KINEMATICS DURING SIT-TO-STAND

J. Hansen[1, 2], H. Sørensen[2], J.F. Nielsen[1]

[1]Hammel Neurorehabilitation Centre and University Research Clinic, [2]Department of Public Health, Aarhus University

Background: 3D optical motion capture has been widely used to quantify the sit-to-stand (STS) movement. However, measuring the pelvic movement can be difficult due to markers being covered by adipose tissue or parts of the chair.

Aim: To compare three different pelvic marker protocols for measuring STS movement from a chair.

Method: 14 healthy subjects were tested in this study. Camera positioning was optimized in relation to the chair to increase the reflective markers visibility. Three different marker protocols were tested. 1) A marker protocol considered the golden standard for gait analysis (MP1). 2) A marker protocol with additional markers on the pelvic segment to ensure visibility (MP2). 3) A marker protocol developed specifically for this study, where a rigid pin with three markers was used to track the anterior superior iliac spine based on the principle of collinearity (MP3).

Preliminary results: MP1 is unable to track the pelvis segment throughout the complete STS movement. MP2 is able to track the complete movement of the pelvis, however, it underestimates the pelvic tilt angle compared to MP1. MP3 covers the full pelvic movement and pelvic tilt angles are comparable to MP1.

Implications: The results of this study provides a new method for measuring STS using optical motion capture. This results in a more robust and precise marker protocol that can be used for further biomechanical analysis of the STS movement and to investigate differences between certain populations.

CH.44   Birgit Refsgaard Iversen   THE EFFECTS OF IMPLEMENTING A CROSS-SECTORIAL LUNG TEAM FOR PATIENTS WITH COPD AT HIGH RISK OF EXACERBATION: A RETROSPECTIVE FOLLOW-UP STUDY

B.R. Iversen[1], L.Ø. Rodkjær[2], V. Bregnballe[3], A. Løkke[4]

[1]Department of Respiratory Diseases and Allergy; Aarhus University Hospital, [2]Department of Infectious Diseases, Aarhus University Hospital, [3]Department of Public Health, Aarhus University, [4]Department of Medicine, Vejle Hospital

Background

Chronic Obstructive Pulmonary Disease (COPD) is a progressive disease, and exacerbations become more frequent as severity of COPD increases. In 2018, the number of admissions in Denmark due to COPD was 34,961. The readmission rate (within 30 days) was 19%. The aim of this study was

to evaluate the effect of a cross-sectorial lung team (LT) for patients at high risk of exacerbation.

Methods

In 2016, 49 patients participated in a pilot study affiliated to a LT. The patients were able to contact the LT day and night, and the LT could pay home visits, initiate treatment and education at the patient's home. Data regarding admissions and length of stay were collected. Based on retrospective data from the same patients in the three preceding years (2013 to 2015), a prediction for 2016 of admissions and length of stay were calculated using a Poisson Regression Model and compared with the actual findings.

Data on health status were collected using COPD assessment test (CAT).

Results

COPD related admissions were significant lower for patients affiliated with a LT compared with the predicted numbers of admissions (0.54 (95% CI [0.32-0.90], p = 0.0192)). COPD related length of stay was also significant lower for patients affiliated with a LT compared with the predicted length of stay (0.41 (95% CI: [0.22-0.76], p = 0.0046)). A numerical, but not statistical significant improvement in total CAT-score of 1.10 (95% CI [-0.71-2.91], p = 0.226) was observed.

Conclusion

Affiliation to the LT seems to reduce COPD related admissions and length of stay but further research is needed to examine the effects of LT in a larger sample including e.g. the patients' level of health literacy.

CH.45   Morten   EXERCISE AS AN ADJUVANT TREATMENT STRATEGY EARLY IN THE
         Riemenschneider DISEASE COURSE OF MULTIPLE SCLEROSIS

M. Riemenschneider[1], T. Petersen[2], E. Stenager[3, 4], U. Dalgas[1]

[1]Section for Sports Science, Department of Public Health, Aarhus University, [2]Multiple Sclerosis Clinic, Department of Neurology, Aarhus University Hospital, [3]Department of Regional Health Research, University of Southern Denmark, [4]Multiple Sclerosis Clinic, Department of Neurology, Clinic of Southern Jutland

Background: In the recent years research from basic science have suggested disease-modifying effects of exercise in animal models of multiple sclerosis (MS). Despite the potential disease-modifying effects of exercise, a recent review pointed out that exercise solely have been applied late in the disease course of MS - and that an overlooked "window of opportunity" for exercise therapy exist early in the disease course of multiple sclerosis.Aim: To investigate the effects of exercise as an adjuvant treatment strategy early in the disease course of MS - specifically focusing on Magnetic Resonance Imaging (MRI) markers of disease-activity and progression.Methods: Randomized controlled trial including patients with < 2 years since diagnosis with relapsing remitting MS. The intervention is 48 weeks of supervised aerobic exercise, whereas the control group receive standard treatment and basic educational sessions on physical activity. Moreover, registry based data on disease activity and progression will be obtained from the Danish MS registry for comparison.

The primary outcome is whole brain atrophy, obtained by MRI. Secondary outcomes are measures of disease activity, progression, physical function, and cognitive function.Results: 84 patients have been included in the study, but as this is a long term intervention the study is still ongoing and we do not have results at this point.Discussion: This is the first study to investigate the effects of exercise therapy early in the disease course of MS and if exercise therapy shows to be a beneficial adjuvant treatment strategy it holds the potential to change and optimize the current clinical practice.

CH.46   Eva Forsom   THE EFFECT OF ANTIPSYCHOTIC TREATMENT ON BONE MINERAL DENSITY BASED ON QCT ANALYSIS OF AN AUTOPSY POPULATION

E. Forsom[1], J. Thygesen[2], L.W.T. Boel[1]

[1]Department of Forensic Medicine, Aarhus University, [2]Department of Clinical Engineering, Central Denmark Region

Background: Patients with schizophrenia have been found to have lower bone mineral density (BMD) compared to the background population. This has been linked to treatment with antipsychotics (APs), although the evidence for this is inconclusive. Previous studies have used DXA-scanning to investigate the correlation between BMD and APs in living patients. An autopsy-based study allows for quantitative CT-scanning of cases and controls. QCT yields volumetric BMD, which has been shown to be more sensitive to change than areal BMD resulting from DXA.

Aim: To investigate if people positive for APs at autopsy have lower lumbar spine BMD compared to a control group with no known antipsychotic treatment tested negative for APs at autopsy.

Methods: Cases consist of CT-scans of approx. 260 adult autopsied at the Department of Forensic Medicine at AU or UCP between 2013-2015 and 2017-2018, tested positive for antipsychotic medication at autopsy. Controls are scans of sex- and age- matched individuals autopsied at AU from 2016-2019, with no known history of schizophrenia or AP treatment and tested negative for APs at autopsy. Mindways QA and calibration phantoms are scanned on the CT scanners regularly in order to allow for asynchronous QCT analysis with Mindways software in order to obtain the vBMD of L1-L3. The results of cases and controls will be compared using paired t-test.

Perspectives: Knowledge of the potential negative effects of APs on BMD allows doctors to take preventative measures when starting patients on the medication. It further encourages future research to develop medication with lesser or no negative impact on bone health.

CH.47   Ana C.G. Ebsen   IMMUNO-CELLULAR AGING IN FEMALES REPORTING DEVELOPMENT OF ME-LIKE SYMPTOMS AFTER EXPOSURE TO HPV VACCINATION

A.C. Gonzalez Ebsen[1], H.N. Madsen[2], K. Pors[3], M.M. Jørgensen[2], O.H. Larsen[4], L. Brinthe[5], J. Mehlsen[3], N. Gregersen[1], P. Fernandez-Guerra[1], R.K.J. Olsen[1]

[1]Research Unit for Molecular Medicine, Department of Clinical Medicine, Aarhus University and Aarhus University Hospital, [2]VIA University College,

[3]Hjertemedicinsk Afdeling, Bispebjerg Frederiksberg Hospital, [4]Department of Molecular Medicine, Aarhus University and Aarhus University Hospital, [5]Klinisk Fysiologisk og Nuklearmedicinsk Afdeling, Gentofte Hospital

The shortening of telomeres and mitochondrial dysfunction are associated with aging and early senescence. Mitochondrial dysfunction produces indiscriminate amounts of reactive oxygen species (ROS) that can lead to oxidative stress. Under oxidative stress, high levels of ROS can oxidize telomeres, which can then lead to accelerated shortening. Patients with chronic diseases and mitochondrial dysfunction have been shown to have shorter telomeres. Myalgic Encephalomyelitis (ME) is a debilitating illness characterized by persisting fatigue not relieved by rest. Studies have shown systemic mitochondrial dysfunction in ME patients, that could contribute to fatigue.We looked at a cohort of patients that have developed ME-like symptoms,such as fatigue, after receiving the human papilloma virus (HPV) vaccination. The aim of this study is to investigate telomere length in DNA from peripheral blood mononuclear cells, by qPCR, in 19 HPV vaccinated females between 18-30 years old, that developed ME-like symptoms after the vaccination. The controls are 20 age-and-gender matched controls, HPV vaccinated, without symptoms. We found that telomere length in females with ME-like symptoms is shorter (0.74) than controls (p-value: 0.02). We further evaluated telomere length correlations with age and found a negative correlation between age and telomere length in the control group that is not observed in the patients. In conclusion, we report that females with ME-like symptoms, after exposure to HPV vaccination, have shorter telomeres independently of their age. Thus, illustrating the idea that these young females have an aged cellular system, which could explain their ME-like symptoms.

CH.48   Stine Karlsen   TERT MUTATED CIRCULATING TUMOR DNA IS A USEFUL BIOMARKER AND PREDICTS POOR PROGNOSIS IN DANISH HCC PATIENTS

S. Karlsen[1], M.S. Clement[2], B. Weber[3], N.K. Aagaard[1], G.E. Villadsen[1], H. Grønbæk[1], S.J. Hamilton-Dutoit[4], B.S. Sørensen[2], J. Kelsen[1]

[1]Department of Hepatology and Gastroenterology, Aarhus University Hospital, [2]Department of Clinical Biochemistry, [3]Department of Clinical Oncology and Danish Centre of Particle Therapy, [4]Department of Pathology

Background

No biomarker is able to diagnose hepatocellular carcinoma (HCC) with high sensitivity and specificity or provide clinically useful prognostic guidance. Circulating tumor DNA (ctDNA) with tumor-specific mutations is an attractive biomarker. The Telomerase Reverse Transcriptase (TERT) C228T promotor mutation is the most prevalent tumor-associated mutation in HCC.

Material and methods

We analyzed plasma DNA Danish patients, 95 with HCC and 45 with liver cirrhosis without HCC for TERT promotor mutations using droplet digital PCR. In 34 HCC cases we also analyzed DNA from the corresponding primary tumors. We investigated association to survival.

Results

Plasma TERT mutation was detected in 41/95 HCC patients (43%), but in none of the non-HCC patients. Moreover, TERT mutation was detected in 23/34 tumor samples (68%). In HCC patients, TERT mutations were associated with increased mortality when detected in plasma ctDNA (OR 4.62, P=0.0008), but not in tumor DNA (OR 2.275, P=0.27). Analysis of TERT mutations in plasma and tumor DNA from the same patient was concordant in 21/34 cases (62%; kappa value 0.31, P=0.014), 11 being double-positive and 10 double-negative. In the 13 non-concordant cases, TERT mutations were found in tumor DNA from 12 patients (92%) but not in their plasma DNA.

Conclusion

Plasma TERT mutation was found in 43% of Danish HCC patients and was associated with increased mortality. Moreover, plasma TERT mutation was specific for HCC patients, not being identified in non-HCC cirrhotic patients. We suggest TERT C228T mutation in ctDNA as a promising biomarker in HCC for both diagnosis and prognosis.

CH.49   Anders Schwartz Vittrup   URINARY AND GASTROINTESTINAL FISTULAS, BLEEDING AND STRICTURES AFTER IMAGE-GUIDED ADAPTIVE BRACHYTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER

A.S. Vittrup[1], K. Kirchheiner[2], K. Tanderup[1], N.B.K. Jensen[1], S. Spampinato[1], L.U. Fokdal[1], C. Kirisits[2], C. Haie-Meder[3], J.C. Lindegaard[1], M. Schmid[2], A. Sturdza[2], U. Mahantshetty[4], I.M. Jürgenliemk-Schulz[5], P. Hoskin[6], B. Segedin[7], K. Bruheim[8], B. Rai[9], E. Wiebe[10], E. van der Steen-Banasik[11], R. Cooper[12], E. Van Limbergen[13], M. Sundset[14], B.R. Pieters[15], R. Nout[16], R. Pötter[2]

[1]Department of Oncology, Aarhus University Hospital, [2]Department of Radiation Oncology, Comprehensive Cancer Center, Medical University of Vienna/General Hospital of Vienna, [3]Department of Radiotherapy, Gustave-Roussy, Villejuif, [4]Department of Radiation Oncology, Tata Memorial Hospital, Mumbai, [5]Department of Radiation Oncology, University Medical Centre Utrecht, [6]Cancer Centre, Mount Vernon Hospital, Northwood, [7]Department of Radiotherapy, Institute of Oncology Ljubljana, [8]Department of Oncology, The Radium Hospital, Oslo University Hospital, [9]Department of Radiotherapy and Oncology, Postgraduate Institute of Medical Education and Research, Chandigarh, [10]Department of Oncology, Cross Cancer Institute and University of Alberta, Edmonton, [11]Department of Radiotherapy, Radiotherapiegroep, Arnhem, [12]Leeds Cancer Centre, St James's University Hospital, [13]Department of Radiation Oncology, UZ Leuven, [14]Clinic of Oncology and Women's Clinic, St. Olavs Hospital, Trondheim, [15]Department of Radiation Oncology, Amsterdam University Medical Centers, University of Amsterdam, [16]Department of Radiation Oncology, Leiden University Medical Center

Background

Image-guided adaptive brachytherapy (IGABT) has improved local control and survival in locally advanced cervical cancer (LACC). This report aims to describe gastrointestinal and urinary fistula, bleeding and stricture events in the prospective intErnational study on MRI-guided

BRAchytherapy in locally Advanced CErvical cancer (EMBRACE), and analyze them according to FIGO stage.

Material/methods

In 1246 patients with available follow-up from 3 months onwards, gastrointestinal and urinary fistula, bleeding, and stricture grade 3-5 events (CTCAE v. 3.0) were summarised as maximum grade per patient (crude incidences). In addition, they were analysed according to FIGO stage (I-II, III, IVA, IVB) with chi-square test or Fischer's exact test.

Results

Median follow-up was 48 months (IQR 20-61). In total, 8.2% experienced grade 3-5 events. In stage I-II, the incidence was 5.2%, vs 18.7% in stage III, and 36.7% in stage IVA ($p<0.001$). For single endpoints, the incidences ranged from 0.5% to 2.8%. The incidences of ureter strictures and fistulas were 0.8% and 1.3% in stage I-II vs 8.3% and 7.7% in stage III, and 16.7% and 20.0% in stage IVA ($p<0.001$). Bleeding and gastrointestinal strictures were not significantly related to stage.

Conclusion

EMBRACE is the largest prospective study on radio(chemo)therapy with MR IGABT for LACC to date This report shows limited grade 3-5 gastrointestinal and urinary bleeding, strictures and fistulas, particularly in FIGO stage I-II. The risk of fistulas and ureter strictures increased with higher FIGO stage.

The incidences reported here, compare favourably with reports on conventional brachytherapy, and will benchmark future studies.

CH.50   Helle Kristensen   VALIDATION OF THE COLOSTOMY IMPACT SCORE IN PATIENTS OSTOMIZED FOR A BENIGN CONDITION

H.Ø. Kristensen[1], M. Krogsgaard[2], P. Christensen[1], T. Thomsen[3]

[1]Mave- og Tarmkirurgi Forskning, Aarhus University Hospital, [2]Center for Kræft og Organsygdomme, Rigshospitalet, [3]Department of Anesthesiology, Herlev and Gentofte Hospital

Background: Diseases of the colon and rectum may require surgery involving the formation of a fecal stoma for relief or cure. It is well-established that a stoma can cause practical difficulties and affect daily living and health-related quality of life (HRQL). In 2016 the Colostomy Impact-Score (CI-score) was developed on rectal cancer survivors with a permanent colostomy to identify colostomates with stoma-related reduced HRQL. The purpose of this study was to validate the CI-Score in patients with a colostomy after surgery for a benign condition.

Method: Colostomates in the Capital Region of Denmark were sent the CI-score and SF-36 during fall/winter 2018. Construct validity and discriminative validity were assessed by hypothesis testing and convergent validity between CI-score and SF-36 domain was assessed using correlation coefficients.

Results: 231 and 21 of the respondents had a colostomy for benign and malignant diseases respectively. Response rate was 65%. Correlations between CI-score and SF-36 domains in patients ostomized for a benign

condition were acceptable and comparable to patients ostomized after surgery for a malignant disease.

Conclusion: The CI-score is a valid measure of stoma-related impact on HRQL in patients with a colostomy after surgery for a benign condition. All colostomates regardless of underlying disease can be screened quickly and effectively with this instrument for stoma related reduced quality of life.

CH.51   Thomas Buus   DIFFUSION GRADIENT NONLINEARITY BIAS CORRECTION REDUCES BIAS OF BREAST CANCER BONE METASTASIS ADC VALUES

T.W. Buus[1], A.B. Jensen[2], E.M. Pedersen[1]

[1]Department of Radiology, Aarhus University Hospital, [2]Department of Oncology, Aarhus University Hospital

Background: Diffusion gradient nonlinearity (DGNL) bias causes apparent diffusion coefficient (ADC) values to decrease with increasing superior-inferior (SI) offset. This is a concern when performing quantitative diffusion-weighted imaging (DWI).

Purpose: To investigate if DGNL ADC bias can be corrected in breast cancer bone metastases using a clinical DWI protocol and an online correction algorithm.

Methods: A diffusion phantom (Model 128, High Precision Devices, Boulder, CO) was used for in vitro validation. To assess DGNL correction in vivo, twenty-three women with bone-metastasizing breast cancer were enrolled. DWI was performed on a 1.5T MRI system as single-shot, spin-echo, echo-planar imaging with short-tau inversion recovery (STIR) fat-saturation. From the b50 and b800 images, ADC maps with and without DGNL correction were created. Uncorrected and DGNL-corrected ADC values were measured in phantom and bone metastases by placing regions of interest on b800 images and copying them to the ADC map. The corresponding SI offset was recorded.

Results: In the diffusion phantom, DGNL correction increased SI offset, where ADC bias was lower than 5%, from 7.3 cm to 13.8 cm. Of the 23 patients examined, six had no metastases in the covered regions. In the remaining patients, 79 bone metastases were assessed. Bias of uncorrected bone metastasis ADC values was 19.1% (95% CI: 15.4-22.9%) at 14 cm SI offset. After DGNL correction, ADC bias was significantly reduced to 3.5% (95% CI: 0.7-6.3%, P < 0.001), reducing bias due to DGNL by 82%.

Conclusion: Online DGNL correction corrects DGNL ADC value bias and allows station length to be increased in the SI direction.

CH.52   Marianne Ørum   IMPACT ON COMPREHENSIVE GERIATRIC ASSESSMENT AND TAILORED FOLLOW-UP ON ABILITY TO COMPLETE CANCER TREATMENT - A RANDOMSED CONTROLLED TRIAL

M. Ørum[1], S.V. Eriksen[2], A.R. Jensen[2], K. Jensen[3], M. Gregersen[1], P. Meldgaard[2], M. Nordsmark[2], E.M. Damsgaard[1]

[1]Geriatric Department, Aarhus University Hospital, [2]Department of Oncology, Aarhus University Hospital, [3]Danish Center for Particle Therapy

Introduction

The impact of Comprehensive Geriatric Assessment (CGA) offered to older patients with cancer has been a matter of discussion in the latest years. We present the results of a randomized controlled trial comparing CGA offered as a single-visit to CGA including tailored follow-up (TFU).

Methods

Participants: Patients aged 70 years or more with a primary tumour in the head and neck (HN), lung (LC), upper gastrointestinal tract (UGI) or colo-rectal (CRC). Patients had a CGA performed by a geriatrician and a nurse on the same day as they were assessed by oncologists in an Oncology Department. Solely the frail and vulnerable patients were offered participation in the study. Patients were randomized 1:1 to CGA or CGA+TFU.

Results

From January 2016 to February 2019, 363 patients were included in the study.

Mean age was 76 years. Primary tumour site was HN: 4%, LC: 43%, UGI: 27 and CRC: 26%. A total of 302 patient initiated oncology treatment. In the CGA+TFU group 61% completed treatment as compared to 56% in the CGA group, RR: 1.16 (95% CI: 0.95; 1.42), p=0.14. The tendency was more pronounced in the palliative setting: RR: 1.29 (95%CI: 0.98; 1.70), p=0.07. The impact varied among primary tumour sites: In patients with HN and CRC, we found no impact of CGA+TFU: RR was 1.0 and 0.95 respectively. The impact in LC: RR was 1.28 (95%CI: 0.96; 1.71), p=0.10 and UGI: RR: 1.54 (95% CI: 0.81; 2.95), p=0.19.

Key conclusion

CGA combined with a tailored follow-up had a tendency towards improved adherence to cancer treatment in older patients. The impact varied with stage and tumour-site.

CH.53   Samuel Joseph Windross

THE ROLE OF STING DIMERISATION IN HSV INFECTION

S.J. Windross, T. Prabakaban, S.R. Paludan

Department of Biomedicine, Aarhus University

STING exists in an equilibrium as a monomer and also a non-covalent/covalent dimer/tetramer, which is mediated by disulphide brides at C64 and C148. Interestingly, STING in patients with SAVI mutations require dimer/tetramer formation for the activation of STING signalling. This suggests, dimer and tetramer formation is not required for cGAMP binding but is more important for signalling/trafficking. We have also shown that DNA/cGAMP transfection and HSV infection, shifts the equilibrium from predominantly monomeric STING to non-covalent/covalent dimer formation. In contrast to recent publications on STING oligomerisation, activation and signalling, this project aims to elucidate the importance in the formation of non-covalent/covalent STING dimer/tetramer interactions in the context of infection. Previous studies have noted the importance of the hydrophobic interface, lysine residues involved in ubiquitination, and oligomerisation enabling interaction with TBK1 and IRF3. However, in contrast to these studies, we

aim to elucidate the importance and exact mechanism of STING dimerisation and oligomerisation in response to infection. We aim investigate factors that mediate covalent STING dimer/tetramer formation, and the structural basis for covalent STING dimerisation. We will also look at the importance of STING oligomerisation in trafficking, and TBK1 interaction. Finally, we aim investigate how ER stress and UPR could alter covalent STING oligomerisation in response to infection. We will evaluate whether DNA stimulates the classical ER stress pathways, IRE1, AFT6, and PERK, and whether ER oxidoreductin 1 (Ero1) is responsible for covalent STING oligomerization.

CH.54   Anne Mette Fløe Hvass

ARE REFUGEES A NON-IMMUNE RESERVOIR FACILITATING SPREAD OF MEASLES? A CROSS SECTIONAL SURVEY OF MEASLES SEROLOGY IN NEWLY ARRIVED REFUGEES.

A.M.F. Hvass[1, 2, 3], M. Kragh Thomsen[4], C. Wejse[1, 2]

[1]Department of Infectious Diseases, Aarhus University Hospital, [2]Department of Clinical Medicine, Aarhus University, [3]Department of Social Medicine, Aarhus Municipality, [4]Department of Microbiology, Aarhus University Hospital

In 2018, Europe faced the highest number of Measles cases in a decade. In Denmark, childhood vaccination program covers approximately 90% of Danish children. To eliminate the disease, vaccine coverage needs to be above the immunity threshold of 95%. This can be even more difficult to obtain, when vaccination programs break down due to war, natural disaster etc. and concern has been raised, that unvaccinated refugees could facilitate spread of measles when migrating.

In order to address this concern, we tested 513 newly arrived refugees and family reunified refugees aged between 0 and 69 years for measles IgG antibody between May 1st, 2016 and October 31st, 2018. In the cohort, 50% were male. The majority came from Syria (55%) and the rest came from Iran, Iraq, Afghanistan, Pakistan, Eretria, Ethiopia, Somalia Kenya, Lebanon, Pakistan, Russia, Palestine, Morocco and Jordan.

We found 85% of the total group of refugees to have immunity against measles. In the 15% lacking antibodies, we did not find any country of origin to be significantly overrepresented. Also, we found lacking immunity in all age groups below 50 years.

Based on the results from this study, we found that refugees have a relatively good coverage against measles. They are not a non-immune reservoir. However, there is still a gap before reaching the herd immunity threshold. We recommend that vaccination is offered to refugees, who are not able to document immunizations from their country of origin or a refugee camp, in order to help stop the spread of measles in Europe.

CH.55   Marlene Louise Nielsen

DIAGNOSTIC YIELD OF THE POLYCYSTIC KIDNEY DISEASE GENE-PANEL

M.L. Nielsen[1], D.L. Lildballe[2], M. Rasmussen[2], H. Birn[1, 3], L. Sunde[4]

[1]Department of Biomedicine, Aarhus University, [2]Department of Clinical Genetics, Vejle Hospital, [3]Department of Renal Medicine, Aarhus University Hospital, [4]Department of Clinical Genetics, Aalborg University Hospital

Background

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a disease characterized by formation and growth of fluid filled cysts. In genetically resolved cases the disease is mainly caused by variants in PKD1 (~75%) and PKD2 (~25%). Since 2014, the department of Clinical Genetics at Aarhus University Hospital has offered genetic analysis of a polycystic kidney disease gene-panel. Here, we present the diagnostic yield of this analysis.

Methods

The panel comprises the genes PKD1 and PKD2 analyzed using Targeted Next Generation Sequencing (NGS). Data was filtered using an in-house pipeline, and variants were classified according to ACMG classifications. When a causative variant was identified within a family, subsequent family members were analyzed using Sanger sequencing. If no causative variant was identified using the NGS panel, Multiplex Ligation-dependent Probe Amplification (MLPA) was performed to identify larger deletions and duplications.

Results

During a five-year period, 131 patients suspected of ADPKD were analyzed with the panel, and 142 family members were analyzed using Sanger sequencing. Among patients analyzed with NGS, 72 patients had a causative variant within PKD1, 33 within PKD2 and 26 remained unresolved. In total, 113 potential causative variants were identified using the panel and 52% (59) of these were novel.

Conclusion

The total diagnostic yield of the polycystic kidney disease gene-panel including MLPA was ~80% (105/131). In the Danish cohort, 69% (72/105) of resolved cases was caused by a variant within PKD1 and 31% (33/105) within PKD2. Danish founder mutations in PKD2 may account for this shift in distribution.

CH.56   Berit Bargum Booth   ACCURACY OF COLPOSCOPY-DIRECTED BIOPSY VERSUS DYNAMIC SPECTRAL IMAGING DIRECTED BIOPSY IN CORRECTLY IDENTIFYING THE GRADE OF CERVICAL DYSPLASIA IN WOMEN UNDERGOING CONIZATION, A METHODOLOGICAL STUDY.

B.B. Booth[1, 2, 3], L.K. Petersen[4, 5], J. Blaakaer[4, 6], T. Johansen[7], H. Mertz[7], K. Dahl[2], P. Bor[1, 3]

[1]Gynecology and Obstetrics, Randers Regional Hospital, [2]Gynecology and Obstetrics, Aarhus University Hospital, [3]Department of Clinical Medicine, Aarhus University, [4]Department of Gynecology and Obstetrics, Odense University Hospital, [5]OPEN Open Patient data Explorative Network, University of Southern Denmark, [6]Department of Clinical Research, University of Southern Denmark, [7]Department of Pathology, Randers Regional Hospital

Aim: Compare the histological diagnosis of Colposcopic-Directed Biopsies (CDB) to Dynamic Spectral Imaging (DSI)-directed biopsies in women undergoing conization, using the histological diagnosis of the cone biopsy as gold standard.

Methods: Women referred to colposcopy were prospectivly included at Randers Regional Hospital. All had four cervical biopsies taken. The first biopsy was taken from the area that appeared most abnormal by conventional colposcopy (i.e. CDB) and the second biopsy from the area indicated by the DSI map. An additional two biopsies were taken. Biopsies were analyzed separately. If any biopsies revealed cervical dysplasia of such a degree that excisional treatment was recommended the patient was referred for conization. Subsequently, we compared the histological diagnosis of CDB and DSI-directed biopsies to that of the cone biopsy.

Results: Out of 573 enrolled women, 170 underwent conization. In women with an adequate colposcopy and representative biopsies (n=124) there was no deviance between the worst biopsy diagnosis (of any four) and the cone diagnosis in 95.2% (95% CI 89.8-98.2). CDB diagnosis matched the cone diagnosis in 80.6% (95% CI 72.6-87.2) and DSI-directed biopsy matched the cone diagnosis in 83.9% (95% CI 76.2-89.9). The difference was however not significant (p=0.54). Taking four biopsies increased the detection rate of cervical dysplasia significantly compared to both CDB (p=0.0008) and DSI-directed biopsy (p=0.0053).

Conclusions: We found no significant difference in the ability to identify cervical dysplasia between CDB and DSI-directed biopsies. A greater detection rate of cervical dysplasia was achieved through four biopsies.

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