PHD DAY
HEALTH

PROGRAMME & ABSTRACTS
25 JANUARY 2019

AARHUS
UNIVERSITY

PHD DAY 2019 PROGRAMME

LOCATION: THE LAKESIDE LECTURE THEATRES   25 JANUARY 2019

8.30   **Welcome by the Vice dean**
Lise Wogensen Bach, Vice dean, The Faculty of Health, Aarhus University

8.40   **Welcome and presentation of the programme by the chairman of the PHD Association**
Kasper Glerup Lauridsen, PhD student, Chairman of the PhD Association, Health, AU

8.50   **"Excel, Explain, Excite", keynote lecture**
Thomas F. Lüscher, Professor of Pharmacotherapy and Cardiology, and Editor-in-Chief of the European Heart Journal.
Introduced by Helene Nørrelund, Head of the Graduate School, Health, AU

09.50   **Coffee/tea and fruit break / networking**

10.15   **Poster and Flash talk presentations**
Poster: The Lakeside Lecture Theatres, the Bartholin Building (build. 1241) and the Skou Building
            (build. 1116)
Flash talk: The Skou Building (build. 1116)

11.45   **Lunch /poster viewing / networking**
The Lakeside Lecture Theatres, the Bartholin Building (build. 1241) and the Skou Building (build. 1116)

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

14.00   **Coffee/tea and cake break / networking**

14.15   **"Excel, Explain, Excite", keynote lecture**
Barry Stainthorp. Communications specialist and co-founder of the renowned Partners in Training.
Introduced by Helene Nørrelund, Head of the Graduate School, Health, AU

15.15   **Break / networking**

15.30   **Fogh-Nielsen Competition**
Chaired by Professor Søren K. Moestrup, Chairman of the Fogh-Nielsen board and co-chairman
Julie Brogaard Larsen, PhD student, Health, AU

16.15   **Awards; Poster, oral and flash talk presentations**
Professor, Vibeke E. Hjortdal and PhD student, Sebastian Udholm, Chair and Co-chair of the Organizing Committee, PhD Day 2019

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

16.30   **The programme for the day ends**

18.30   **Dinner and awards ceremony for the JCD prize and the Fogh-Nielsen Competition**
Centralværkstedet, Aarhus C.
Festive speech
Sebastian Udholm, PhD student, Health, AU

AARHUS
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Aarhus University
Graduate School of Health

PHD DAY
25 JANUARY 2019

Practical Information

- Posters should be hung up between 16:30 and 19:00 on 24 January or between 7:30 and 8:00 on 25 January. Posters may be removed from 12:30 on 25 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 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 25 January to save their presentation onto the auditorium hard disk

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

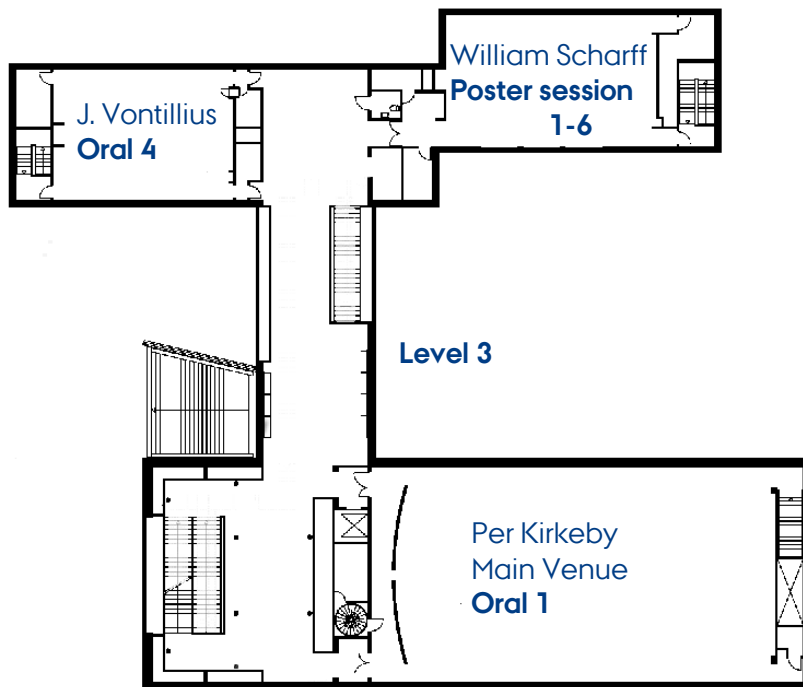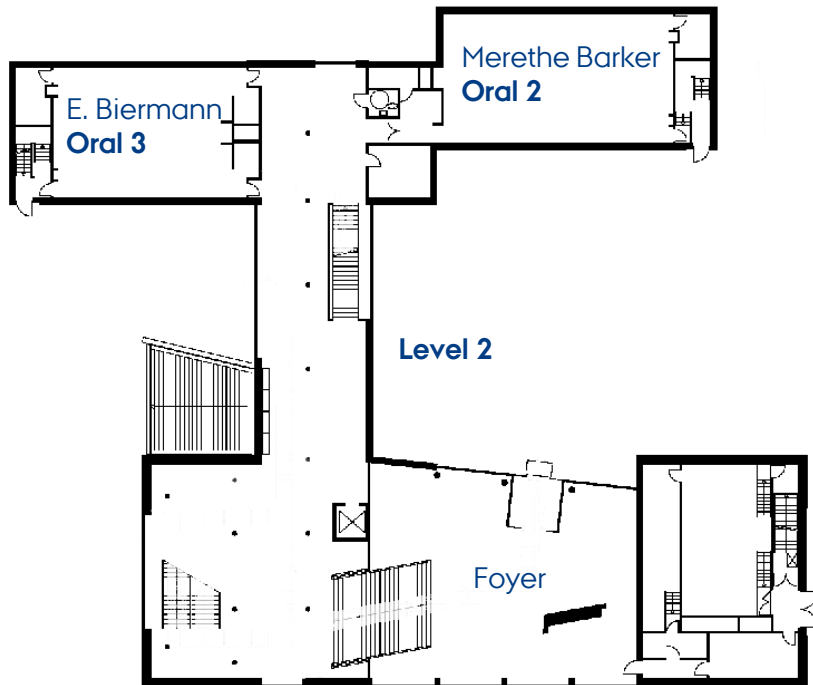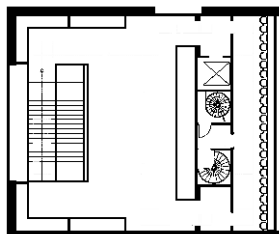|	
Oral session 1:	Lakeside Lecture Theatres, Per Kirkeby Auditorium
Oral session 2:	Lakeside Lecture Theatres, Merethe Barker Auditorium
Oral session 3:	Lakeside Lecture Theatres, Eduard Biermann Auditorium
Oral session 4:	Lakeside Lecture Theatres, Jeppe Vontilius Auditorium
Oral session 5:	Bartholin building, Auditorium 1
Poster session 1-6:	Lakeside Lecture Theatres, William Scharff Auditorium
Poster session 7-17:	Bartholin building, (building: 1240-1241) Auditorium 2, 3, 4, Studyroom and the Gardenroom
Poster session 18-22:	Skou building, (building 1116) Floor 0 and Floor 1
Flash talk session 1-2:	The Skou building, Oval meeting room no 1, Floor 3
Flash talk session 3-4:	The Skou building, Oval meeting room no 2, Floor 3
Flash talk session 5:	The Skou building, Oval meeting room no 3, Floor 4
Flash talk session 6:	The Skou building, Oval meeting room no 4, Floor 4

Organizing committee for PhD Day 2019:

- *Vibeke E. Hjortdal, Clinical Professor, Department of Clinical Medicine, Chairman*
- *Sebastian Udholm, PhD student, Department of Clinical Medicine, Co-chairman*
- *Alice Knudsen, PhD student, Department of Biomedicine*
- *Bente Pedersen, PhD administrator, The Graduate School*
- *Camilla Gunderstofte Nielsen, PhD student, Department of Biomedicine*
- *Helle Mellerup, Course administrator, The Graduate School,*
- *Jacob Thyrsted Jensen, PhD student, Department of Biomedicine*
- *Julie Brogaard Larsen, PhD student, Department of Clinical Medicine*
- *Kathrin Weyer, Postdoc, Department of Biomedicine*
- *Khoa Manh Dinh, PhD student, Department of Clinical Medicine*
- *Lene Baad-Hansen, Associate Professor, Department of Dentistry and Oral Health*
- *Martin Nors Skov, PhD student, Department of Clinical Medicine*
- *Pernille Thomasen, PhD student, Department of Biomedicine*
- *Rasmus Bysted Møller, Assistant Professor, Department of Public Health - Sport Science*
- *Simin Berenji Ardestani, PhD student, Department of Clinical Medicine*
- *Søren Dinesen Østergaard, Professor, Department of Clinical Medicine*

Social media: Facebook: PhD Association Health

Lakeside Lecture Theatres

E. Biermann
Oral 3

Merethe Barker
Oral 2

Level 2

Foyer

William Scharff
Poster session 1-6

J. Vontillius
Oral 4

Level 3

Per Kirkeby
Main Venue
Oral 1

Level 4

Bartholin Building (building: 1240/1241)
- Oral 5
- Poster session: 7-17

Skou Building, (building 1116)
- Poster session 18-22
- Flash talk : 1-6

Practical Information

Session overview:

Oral session	**1**:	Lakeside Lecture Theatres, **Per Kirkeby Auditorium**
Oral session	**2**:	Lakeside Lecture Theatres, **Merethe 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 (building: 1241/135), **Auditorium 1**
Poster session	**1-6**:	Lakeside Lecture Theatres, **William Scharff Auditorium**
Poster session	**7-10**:	Bartholin building, (building: 1241/211), **Studyroom,** (Floor 1)
Poster session	**11**:	Bartholin building, (building: 1241/231), **Gardenroom**, (Floor 1)
Poster session	**12-13**:	Bartholin building, (building: 1241/125+129), **Auditorium 2**
Poster session	**14-15**:	Bartholin building, (building: 1241/119), **Auditorium 3**
Poster session	**16-17**:	Bartholin building, (building: 1241/114), **Auditorium 4**
Poster session	**18-20**:	Skou building, (building 1116), **Floor 1**
Poster session	**21-22**:	Skou building, (building 1116), **Floor 0**
Flash talk session	**1-2**:	Skou building, (build. 1116, 1116348A), **Oval meeting room no 1** (Floor 3)
Flash talk session	**3-4**:	Skou building, (build. 1116, 1115343), **Oval meeting room no 2** (Floor 3)
Flash talk session	**5**:	Skou building, (build. 1116, 1116448A), **Oval meeting room no 3** (Floor 4)
Flash talk session	**6**:	Skou building, (build. 1116, 1115443), **Oval meeting room no 4** (Floor 4)
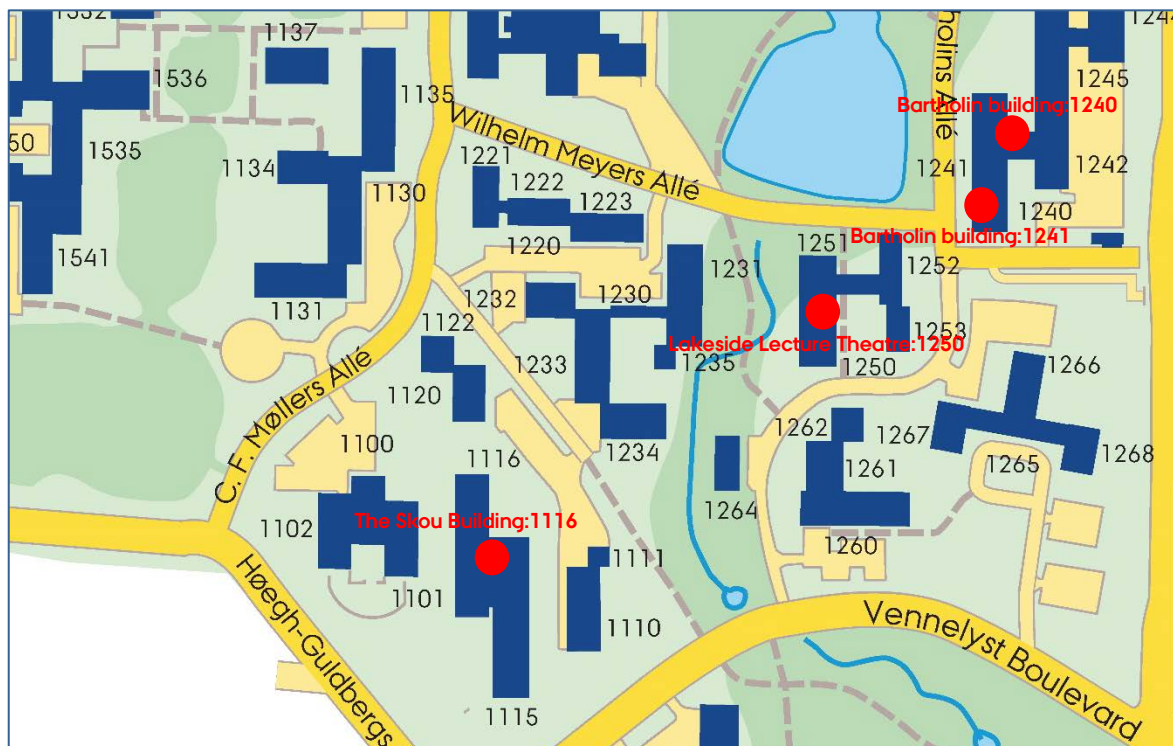
Excel, Explain, Excite!

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 2019.

This year's theme provides a broader perspective on research presentation and the dialogue between the scientific community and society. We should strive to excel, not only in our research but also in our communication, and thus bring the excitement of science to a broader audience. In total, 285 PhD, Research Year and Research Honours Programme students will present their research during the PhD Day. We are looking forward to seeing you excite and inspire your fellow students and senior colleagues!

Consistent with the theme, we have the pleasure to welcome two keynote speakers, who indeed know how to excel, explain and excite in their respective fields.

Professor Thomas Lüscher is a highly distinguished cardiovascular researcher and Editor-in-Chief of the European Heart Journal. We will benefit from his experience with the world of publishing and on how to improve scientific communication to allow your research results to create maximal impact.

Barry Stainthorp is a co-founder of the renowned Partners in Training, which has delivered communication and presentation training programmes for companies, government organisations and NGO's all over the world.

We are looking forward to an inspiring lecture which will undoubtedly leave us better qualified to explain our research and excite our audience. In addition, Mr. Stainthorp will provide feedback to presenting PhD students during selected oral sessions at the PhD Day.

A warm thank you to everybody who has participated and helped create a highly scientific, inspiring and exciting programme for the PhD Day 2019.

Vibeke Hjortdal, Professor
Chairman of the Organizing Committee
Health, Aarhus University

Sebastian Udholm, PhD student
Co-chairman of the Organizing Committee
Health, Aarhus University

Helene Nørrelund,
Head of Graduate School
Health, Aarhus University

Kasper G. Lauridsen, PhD student
Chairman of the PhD Association
Health, Aarhus University

The Keynote Lecture

Professor Thomas F. Lüscher, MD, FRCP, FESC

Professor Lüscher studied medicine at the University of Zurich and obtained the board certification in internal medicine and cardiology. He trained in cardiovascular research and in cardiology and specifically in echocardiography at the Mayo Clinic in Rochester, MN, USA and was later Professor of Pharmacotherapy at the University of Basel, then Professor of Cardiology at the University of Berne, before assuming a position as Professor and Chairman of Cardiology and Director of the University Heart Center at the University Hospital Zurich and Director of the Center for Molecular Cardiology at the University of Zurich, Switzerland. He is now Director of Research, Education & Development and Consulting Cardiologist at the Royal Brompton & Harefield Hospital Trust and the Imperial College in London.

Professor Lüscher is an active general and interventional cardiologist with a broad clini-cal scope and large experience in prevention, coronary and valvular heart disease, percutaneous interventions and heart failure. He has sucessfully taken care of cardiac patients for many years from many countries.

Professor Lüscher has been a mentor of numerous physicians and scientists from many countires. His research is translational in nature and focuses on coronary artery disease, specifically on the role of endothelium-derived mediators in the regulation of vascular tone and structure, platelet-vessel wall interactions, coagulation in aging, hy-pertension, lipid disorders and atherosclerosis. More recently, inflammatory pathways in coronray artery disease and particularly in acute coronary syndromes has been at the center of his interest. Professor Lüscher has published extensively, authoring or co-authoring over 500 original research articles and more than 200 reviews, book chapters and monographs including the ESC Textbook of Cardiovascular Medicine.

By the Institute for Scientific Information he has been rated as one of the 0.5% most cited scientists worldwide. He has obtained numerous research prizes and prestigious lecturerships worldwide. He is a member of many editorial boards and was Associate Editor Europe of Circulation (Journal of the American Heart Association) from 2004 to 2008. Since 2009 he is chairman of the publications committee of the European So-ciety of Cardiology (ESC) and an ex-officio member of the ESC board as well as editor-in-chief of the European Heart Journal.

The Keynote Lecture

Barry Stainthorp, Communications specialist

Barry Stainthorp is a communications specialist and was a founder of Partners in Training Ltd, a UK training consultancy and course provider.

He has spoken at conferences and symposia all over the world, in sectors as diverse as finance, telecommunications, politics, entertainment and science.

His work in the medical sector covers all situations where a person interacts with an audience. These can include the doctor/patient setting; dealing with the media in live or pre-recorded situations; creating and coaching the delivery of high quality presentations – posters, oral and plenary; facilitating advisory boards, investigator and results meetings, and preparing speakers for FDA Advisory Committees.

Barry is regularly invited to train specialist speakers for regional and local meetings as well as the major annual events in diabetes, cardiology, pulmonology and oncology. Barry also acts as a personal coach for international thought leaders in industry and public life.
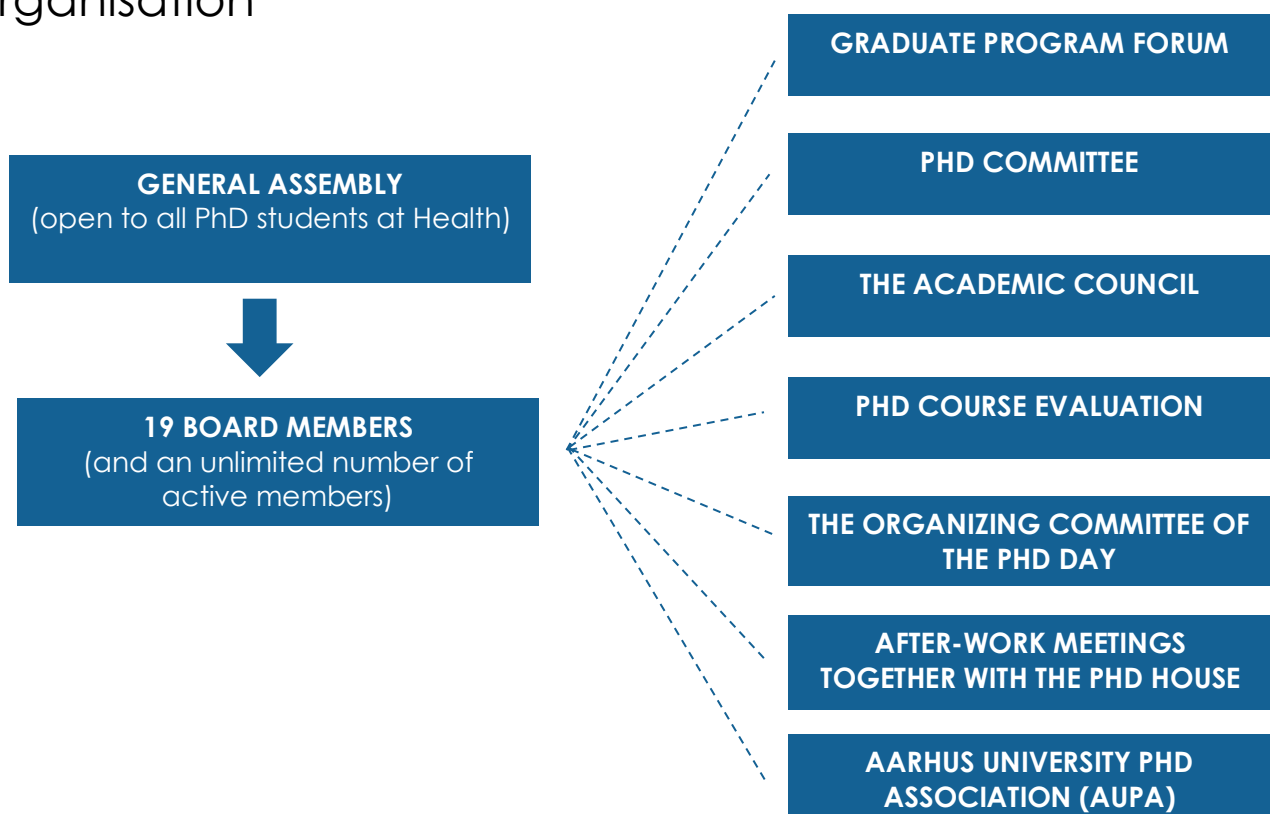
PhD Association
Health, Aarhus University

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

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Organisation

GENERAL ASSEMBLY
(open to all PhD students at Health)

↓

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

GRADUATE PROGRAM FORUM

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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!

Working hard for you!

phdassociation.dk

NorDoc

is going to launch its

3rd Nordic Summit

(including an intriguing PhD course programme 26th – 28th August)

for Doctoral Students

at your university

Aarhus University, 29-30th August 2019

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

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: Kathrine Arlander & 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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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.

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HE Studies
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E-mail: rkp@au.dk

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

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HEALTH SCIENCES

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    - Copyright and Open Access

- Support and help for systematic literature search designed for your specific project

- Regular PhD courses 'Literature Search in Medical Databases'

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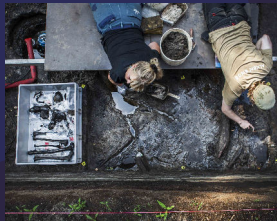DK-8000 Aarhus C
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AU Career PhD & JR
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Ph.D. Career Consultant
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Email: jamm@au.dk

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AU **CAREER**
PHD & JR

Graduate School of Health

MEDICAL INNOVATION DAY

To take place on
27 September 2019

at Aarhus University Hospital, Skejby

Two tracks

A. Challenges

You solve a defined challenge
from a company
(26 – 27 September 2019)

B. Innovative Ideas

You propose your idea to
investors
(27 September 2019)

So **take up a company challenge** or **present your own ideas**!

We offer you the opportunity to meet like-minded colleagues, get inspired to
innovative thinking and start new collaborations. Learn more about Medical
Innovation Day at **http://phd.health.au.dk/aboutus/mid/**

Registration opens in spring 2019

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

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PhD Association
Health, Aarhus University

The Graduate School of Health

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Danish Diabetes Academy: empowering diabetes research. Want to join?

With a new five-year grant (2018-2022) from the Novo Nordisk Foundation, the Danish Diabetes Academy (DDA) is on course for new heights in the education and training of young diabetes researchers.

We at the DDA are working constantly to enhance the opportunities for PhD students and postdocs to carry out research on diabetes in collaboration with academia, hospitals and the life science industry.

Our clear aim is to act as a development centre for diabetes research, and we therefore see it as a natural task for us to forge constructive links between all stakeholders in the field.

It is in the Danish Diabetes Academy's DNA always to aim high. For that reason, it is our ambition at all times to recruit the most talented Danish and international PhD students and postdocs. In free and open competition, of course.

Twice a year, the DDA advertises grants for PhD students and postdocs. In 2019, the deadlines are **8 February** and **23 August**.

The DDA has recently helped fund three industrial postdoc positions. Such positions will be a major cornerstone of the academy going forward, and we also expect to be able to offer grants for industrial PhDs in the near future.

The DDA always has a packed diary. We offer a unique, wide selection of educational events aimed specifically at PhD students and postdocs. Always with tutors and speakers of a high professional calibre.

In 2019, the events on offer will include:

- Summer School for PhD students, 26-29 August
- Winter School for postdocs, 3-6 November
- Basal Metabolism Course for PhD students, 25-28 November

The DDA is always pleased to invite new stakeholders into the community. At our website, https://www.danishdiabetesacademy.dk/ , you can join the Academy or sign up for our monthly newsletter.

As you'd expect, the DDA has a social media presence. Find us on Twitter, Facebook, LinkedIn and YouTube, where you can keep up with all the latest and get to know us better.

To find out more about the DDA, or to suggest new initiatives for the Academy, please contact the Managing Director, Tore Christiansen, tel: 29 64 67 64 or email: tore.christiansen@rsyd.dk .

PhD Day 2019
Excel, Explain, Excite!

Do you strive to achieve scientific excellence? Are you keen on communicating and explaining your research in the best way possible? Do you want to transfer your enthusiasm and excitement about science to society?

The PhD Day is an annual event arranged by the PhD Association Health in collaboration with the Graduate School of Health, Aarhus University. The theme of the PhD Day 2019 is: *Excel, Explain, Excite!*

To gain an impact on society, excellence in science is important. It can be argued, however, that the ability to explain the significance of your research in a way that excites and inspires a wider audience is almost as important.
As researchers, we should therefore focus on the conduct of high-quality, high-impact science with passion – but also on the communication of our results and their importance to potential future collaborators and stakeholders both in and outside of academia. If we succeed in communicating our knowledge and enthusiasm for our scientific work to others, we can increase the impact of our work and gain a stronger foothold in setting the scene for science in today's society.

Within this framework, the PhD day 2019 will focus not only on how to excel in science but also how to explain it to your audience in an exciting way. The PhD Day 2019 offers lectures by key note speakers experienced in the art of scientific communication and gives PhD and Research Year Students the opportunity to present their own research through oral or poster presentations, or to co-chair sessions.

We look forward to welcoming you!

The Organizing Committee 2019
Graduate School of Health, Aarhus University

We welcome
all our PhD students to
PhD Day 2019

PHD DAY 2019
Abstracts and sessions overview

Session chairmen

Fogh-Nielsen competition	Søren Kragh Moestrup (chairman) & Julie Brogaard Larsen (PhD student)
O1	Vladimir Matchkov, Rikke K.J. Olsen, Kristina Laugesen (PhD student) & Thomas Lassen (PhD student)
O2	Maja Ludvigsen, Peter Nejsum, Kristian Juul-Madsen (PhD student) & Nanna-Sophie Brinck Andersen (PhD student)
O3	Mikkel Mylius Rasmussen, Jane H. Christensen, Ted Carl Kejlberg Andelius (PhD student) & Filomena Iannuzzi (PhD student)
O4	Francesco d'Amore, Else Marie Damsgaard, Anders Kindberg Boysen (PhD student) & Julie Nelly Christensen (PhD student)
O5	Niels Uldbjerg, Vera Ehrenstein, Mai-Britt Hägi-Pedersen (PhD student) & Line Kolding (PhD student)
P1	Andrea Toth, Mathias Johan Holmberg (PhD student), Trine Ørhøj Barkholt (PhD student) & Louise Nissen (PhD student)
P2	Morten Bøttcher, Jacob Gammelgaard Schultz (PhD student), Marie Veje Knudsen (PhD student) & Kasper Glerup Lauridsen (PhD student)
P3	Dorte Rytter, Yutao Lu (PhD student), Maria Riedel (PhD student) & Malou Eva Maria Pinto Barbosa (PhD student)
P4	Mariane Schleimann, Thomas Falstie-Jensen (PhD student) & Alon Illy Schneider Hait (PhD student)
P5	Janne Lebeck, Pernille Glahn Wernlund (PhD student) & Tea Lund Laursen (PhD student)
P6	Jørgen Feldbæk Nielsen, Denise Fabienne Happ (PhD student) & David Ricardo Quiroga Martinez (PhD student)
P7	Gregers Wegener, Casper Schmidt (PhD student), Maj Ulrichsen (PhD student) & Saida Said (PhD student)
P8	Dennis Graversen (PhD student), Simin Berenji Ardestani (PhD student) & Sandra Sif Gylfadottir (PhD student)
P9	Jacob Johansen, Stine Bak (PhD student), Anders Damgaard Møller Schlünsen (PhD student) & Kristine Jepsen Bennedsgaard (PhD student)
P10	Anders Bonde Jensen, Anita Tranberg Simonsen (PhD student), Veera Manikandan (PhD student) & Patricia Alves da Mota (PhD student)
P11	Jesper Grau Eriksen, Lene Haldbo-Classen (PhD student) & Sanne Jensen (PhD student)

P12	Jeppe Lange, Anne Mette Schmidt (PhD student), Maj Haubuf (PhD student) & Anne-Birgitte Blavnsfeldt (PhD student)
P13	Niels Okkels, Thomas Skovhus Prior (PhD student), Andreas Aalkjær Danielsen (PhD student) & Hanan Amadid (PhD student)
P14	Konstantinos Kamperis, Jeanette Finderup (PhD student), Takwa Shaiman Aroankins (PhD student) & Maria Elkjær (PhD student)
P15	Deirdre Cronin Fenton, Inge Schjødt (PhD student) & Michael Bertelsen (PhD student)
P16	Vassilis Sevdalis, Andreas Ernst (PhD student), Maria Dietz Toppenberg (PhD student) & Katja Krustrup Pedersen (PhD student)
P17	Anna Starnawska, Per Mose Nielsen (PhD student) & Elin Rakvaag (PhD student)
P18	Henning Grønbœk, Charlotte Arp Sørensen (PhD student), Martin Lund (PhD student) & Anne Ankerstjerne Rasmussen (PhD student)
P19	Simon Fristed Eskildsen, Daniel Gramm Kristensen (PhD student) & Karolina Snopek Khan (PhD student)
P20	Michael Winterdahl, Rasmus Wulff (PhD student) & Mia Glerup (PhD student)
P21	Rubens Spin-Neto, Susanna Botticelli (PhD student), Stine Derdau Sørensen (PhD student) & Luca Bordoni (PhD student)
P22	Mette Madsen, Jakob Kirkegård (PhD student), Anne Vestbjerg Thyø (PhD student) & Mette Winther Klinge (PhD student)

F1	Bo Løfgren, Stine Andersen (PhD student) & Mikkel Giehm-Reese (PhD student)
F2	Bent Deleuran, Anna Halling Folkmar Andersen (PhD student) & Elias Didrik Francis Zachariae (PhD student)
F3	Martin Nors Skov (PhD student), Jibrin Danladi (PhD student) & Camilla Højland Knudsen (PhD student)
F4	Charlotte Runge & Lone Kirkeby (PhD student) & Nis Brix (PhD student)
F5	Karin Birkenkamp-Demtröder, Pernille Byrialsen Elming (PhD student) & Rikke Smedegaard Rosbjerg (PhD student)
F6	Tine Brink Henriksen, Sara Birch (PhD student) & Anna Sofia Elisabeth Aaby (PhD student)

Session overview

Fogh-Nielsen competition

Chairmen: Søren Kragh Moestrup & Julie Brogaard Larsen (PhD student)

Anne Louise Hansen. SUPER-FATS ELIMINATE STING-ING INFLAMMATION

Ole Köhler-Forsberg. STATIN TREATMENT AND THE RISK OF DEPRESSION

Mette Lise Lousdal. NEGATIVE CONTROLS TO DETECT UNMEASURED CONFOUNDING IN OBSERVATIONAL STUDIES OF MAMMOGRAPHIC SCREENING

Oral session 1

Chairmen: Vladimir Matchkov, Rikke K.J. Olsen, Kristina Laugesen (PhD student) & Thomas Lassen (PhD student)

O01.01   Jenny Diana Grove. ARTERIAL STIFFNESS AND BLOOD PRESSURE IN PATIENTS NEWLY DIAGNOSED WITH GRAVES' DISEASE COMPARED TO EUTHYROID CONTROLS

O01.02   Astrid Johannesson Hjelholt. GENE AND PROTEIN EXPRESSION OF LIPOLYTIC REGULATORS IN CONSECUTIVE HUMAN ADIPOSE TISSUE BIOPSIES AFTER EXPOSURE TO A BOLUS OF GROWTH HORMONE

O01.03   Simon Riis. PERSISTENT MOLECULAR ADAPTATIONS IN HUMAN SUBCUTANEOUS ADIPOSE TISSUE AFTER TEN WEEKS OF ENDURANCE EXERCISE TRAINING IN HEALTHY MALES

O01.04   Estefano Pinilla. EFFECT OF TRANSGLUTAMINASE 2 CONFORMATIONAL MODULATION ON AGE-RELATED CHANGES IN ENDOTHELIAL FUNCTION

O01.05   Sebastian Udholm. LIFELONG BURDEN OF SMALL UNREPAIRED ATRIAL SEPTAL DEFECT: RESULTS FROM THE DANISH NATIONAL PATIENT REGISTRY

O01.06   Anders Hostrup Larsen. METFORMIN REDUCES MYOCARDIAL OXYGEN CONSUMPTION AND IMPROVES CARDIAC EFFICIENCY IN INSULIN RESISTANT HEART FAILURE PATIENTS

Oral session 2   (Presentation Skills evaluated by Keynote Speaker Barry Stainthorp)

Chairmen: Maja Ludvigsen, Peter Nejsum, Kristian Juul-Madsen (PhD student) & Nanna-Sophie Brinck Andersen (PhD student)

O02.01   Katrine Schou Sandgaard. UNDERSTANDING THE IMPACT OF ANTIRETROVIRAL THERAPY INTERRUPTION ON THE IMMUNE SYSTEM IN CHILDREN WITH HIV

O02.02   Julie Brogaard Larsen. MANNOSE-BINDING LECTIN-ASSOCIATED SERINE PROTEASE (MASP)-1 AND DISSEMINATED INTRAVASCULAR COAGULATION IN SEPTIC SHOCK

O02.03   Anne Hald Rittig. DIFFERENCES IN THE MIRNA EXPRESSION PROFILES OF ERYTHRODERMIC MYCOSIS FUNGOIDES AND SÉZARY SYNDROME

O02.04   Asta Linauskas. POSITIVE PREDICTIVE VALUE OF FIRST-TIME RHEUMATOID ARTHRITIS DIAGNOSES IN THE DANISH NATIONAL PATIENT REGISTRY

O02.05   Madalina Elena Carter-Timofte. THE ROLE OF RNA POLYMERASE III MUTATIONS IN PATIENTS WITH SEVERE VARICELLA ZOSTER VIRUS (VZV) CENTRAL NERVOUS SYSTEM (CNS) INFECTION

O02.06   Didde Haslund. DOMINANT NEGATIVE INTRACELLULAR RETENTION OF C1 INHIBITOR IN HEREDITARY ANGIOEDEMA

Oral session 3

Chairmen: Mikkel Mylius Rasmussen, Jane H. Christensen, Ted Carl Kejlberg Andelius (PhD student) & Filomena Iannuzzi (PhD student)

O03.01   Rasha Hyder. PASSIVE NEUROMAGNETIC RESPONSES AS BIOMARKERS OF LANGUAGE PROCESSING IN THE BRAIN

O03.02   Alexander Gramm Kristensen. NERVE EXCITABILITY FINDINGS IN NEUROPATHIC TYPE 2 DIABETICS

O03.03   Majken Thomsen. IMAGING SYNAPTIC DENSITY IN RAT AND PIG BRAIN USING [11C]UCB-J PET

O03.04   Martin Langeskov Christensen. CAN AEROBIC EXERCISE IMPACT DISEASE PROGRESSION IN MULTIPLE SCLEROSIS?

O03.05   Lasse Reimer. AGE-RELATED SULFOXIDE-CONTAINING METABOLITES STIMULATE AGGREGATION AND SPREADING OF NEURODEGENERATORY PROTEIN α-SYNUCLEIN

O03.06   Rajath Pillai. FEASIBILITY AND RELIABILITY OF INTRAORALLY-EVOKED 'NOCICEPTIVE-SPECIFIC' BLINK REFLEX

Oral session 4

Chairmen: Francesco d'Amore, Else Marie Damsgaard, Anders Kindberg Boysen (PhD student) & Julie Nelly Christensen (PhD student)

O04.01   Maja Halgren Olsen. SOCIOECONOMIC INEQUALITY IN HEAD AND NECK CANCER SURVIVAL - A POPULATION-BASED STUDY FROM DAHANCA

O04.02   Simon Skouboe. FIRST CLINICAL REAL-TIME MOTION-INCLUDING TUMOR DOSE CALCULATION DURING RADIOTHERAPY DELIVERY

O04.03   Trine Block Mattesen. MOLECULAR SUBTYPING AND PROGNOSTICATION OF COLORECTAL CANCER FROM FORMALIN-FIXED PARAFFIN-EMBEDDED TISSUE USING GENE EXPRESSION SCORES IMPUTED FROM DNA METHYLATION

O04.04   Martin Fogtmann Berthelsen. THE CRISPR-CAS9 MINIPIG - A TRANSGENIC TOOLBOX PIG TO PRODUCE SPECIFIC GENOME EDITING IN DESIGNATED TISSUES

O04.05   Sarah Østrup Jensen. NOVEL DNA METHYLATION BIOMARKERS SHOW HIGH SENSITIVITY AND SPECIFICITY FOR BLOOD-BASED DETECTION OF COLORECTAL CANCER - A CLINICAL BIOMARKER DISCOVERY AND VALIDATION STUDY

O04.06   Stine Overvad Fredslund. ADJUVANT TREATMENT OF BREAST CANCER RELATED TO CARDIOTOXICITY AND DYSFUNCTIONAL ENDOTHELIUM: THE ABCDE STUDY

Oral session 5

Chairmen: Niels Uldbjerg, Vera Ehrenstein, Mai-Britt Hägi-Pedersen (PhD student) & Line Kolding (PhD student)

O05.01   Mads Sørensen Larsen. EFFECTS OF PROTEIN INGESTION PRIOR TO TRAINING LOW.

O05.02   Yulia Olsen. AIRBORNE ALTERNARIA AND CLADOSPORIUM SPORES AND ASTHMA IN DENMARK

O05.03   Julie Lyngsø. DOES LOW-TO-MODERATE ALCOHOL CONSUMPTION IMPAIR SUCCESS IN FERTILITY TREATMENT? RESULTS FROM A DANISH COHORT STUDY

O05.04   Jonas Boysen Fynboe Ebert. FAST ACCESS TO OUT-OF-HOURS TELEPHONE TRIAGE BY AN EMERGENCY ACCESS BUTTON: A RANDOMIZED CONTROLLED TRIAL EXPLORING PATIENT SATISFACTION, FEELING OF SAFETY, RELEVANCE AND FREQUENCY OF USE

O05.05   Mads Riiskjær. BOWEL ENDOMETRIOSIS SYNDROME: A NEW SCORING SYSTEM FOR PELVIC ORGAN DYSFUNCTION AND QUALITY OF LIFE

O05.06   Marzieh Katibeh. MODELLING AND EVALUATION OF A COMMUNITY-ORIENTED MHEALTH-BASED SCREENING AND PROMOTIONAL PROGRAM FOR IMPROVING EYE HEALTH IN IRAN

Poster session 1

Chairmen: Andrea Toth, Mathias Johan Holmberg (PhD student), Trine Ørhøj Barkholt (PhD student) & Louise Nissen (PhD student)

P01.01   Nicklas Vinter. TWENTY-YEAR TIME TRENDS IN USE OF EVIDENCE-BASED HEART FAILURE DRUG THERAPY IN DENMARK

P01.02   Lejla Islamagic. BIOMECHANICAL PROPERTIES OF CORMATRIX COMPARED WITH NATIVE MITRAL VALVE LEAFLETS

P01.03   Pernille Gro Thrane. 15-YEAR FOLLOW-UP OF THE DANISH ACUTE MYOCARDIAL INFARCTION 2 (DANAMI-2) TRIAL - PRIMARY PERCUTANEOUS CORONARY INTERVENTION VERSUS FIBRINOLYSIS IN ST-ELEVATION MYOCARDIAL INFARCTION

P01.04   Mads Dam Lyhne. IMMEDIATE CARDIO-PULMONARY RESPONSE IN ACUTE, CENTRAL PULMONARY EMBOLISM

P01.05   Johnni Rudbeck-Resdal. LONG-TERM OUTCOMES IN PATIENTS WITH ATRIO-VENTRICULAR BLOCK OF UNKNOWN AETIOLOGY IDENTIFIED BEFORE THE AGE OF 50 YEARS - A NATIONWIDE DANISH STUDY

P01.06   Ane Bull Iversen. STROKE AWARENESS AND HELP-SEEKING BEHAVIOUR: PREDICTORS FOR PREHOSPITAL DELAY IN STROKE

P01.07   Benjamin Asschenfeldt Arlander. NEUROCOGNITIVE IMPAIRMENTS IN ADULTS OPERATED FOR SEPTAL DEFECTS IN CHILDHOOD

P01.08   Omeed Neghabat. RANDOMIZED COMPARISON OF AN EVEROLIMUS-ELUTING BIORESORBABLE SCAFFOLD VERSUS EVEROLIMUS-ELUTING METALLIC STENT IN PRIMARY PERCUTANEOUS CORONARY INTERVENTION OF ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

P01.09   Asbjørn Petersen. THE KCA3.1 CHANNEL BLOCKER SENICAPOC PREVENTS THE DEVELOPMENT OF LUNG OEDEMA AND HYPOXEMIA IN A VENTILATOR-INDUCED ACUTE INJURY MODEL

P01.10   Mette Marie Astrup Søndergaard. IMPACT OF CHEMOTHERAPY AND RADIATION THERAPY ON LEFT VENTRICULAR SYSTOLIC AND DIASTOLIC FUNCTION IN PATIENTS WITH CANCER IN ESOPHAGUS AND GASTROESOPHAGAEL JUNCTION - A PROSPECTIVE STUDY DESIGN

Poster session 2

Chairmen: Morten Bøttcher, Jacob Gammelgaard Schultz (PhD student), Marie Veje Knudsen (PhD student) & Kasper Glerup Lauridsen (PhD student)

P02.01   Frederik Boe Hansen. MESENTERIC AND CEREBRAL ENDOTHELIAL FUNCTION IN THE POST-CARDIAC ARREST PERIOD

P02.02   Rafael Sobrano Fais. ALDOSTERONE-INDUCED NLRP3 ACTIVATION PROMOTES ENDOTHELIAL DYSFUNCTION DEPENDENT TO THE LYMPHOCYTES RECRUITMENT

P02.03   *CANCELLED* Rikke Lund Sønderbæk. THE EFFECT OF HIGH VERSUS LOW DIETARY SODIUM INTAKE ON ERYTHROCYTE SALT SENSITIVITY AND SHEDDING OF ENDOTHELIAL GLYCOCALYX IN A RANDOMIZED, DOUBLE-BLINDED, PLACEBO- CONTROLLED CROSS-OVER STUDY IN HEALTHY SUBJECTS

P02.04   Nanja Holland Hansen

P02.05   Lene Andreasen. RATIONAL DESIGN AND CURRENT STATUS ON THE OCTOBER TRIAL: A EUROPEAN TRIAL ON OPTICAL COHERENCE TOMOGRAPHY OPTIMIZED BIFURCATION EVENT REDUCTION

P02.06   Camilla Dalby Salvig. BIOMECHANICAL IN VITRO ASSESSMENT OF THE PORCINE AORTIC ROOT

P02.07   Anders Sjørslev Schmidt. CARDIOVERSION OF ATRIAL FIBRILLATION: CAN WE PREDICT SUCCESS USING COPEPTIN?

P02.08   Torben Hoffmann. REDUCING READMISSION TO HOSPITAL AFTER HEART SURGERY

P02.09   Christine Gyldenkerne. ASSOCIATION BETWEEN ANTI-DIABETES TREATMENT AND CARDIOVASCULAR RISK IN DIABETES PATIENTS WITH AND WITHOUT CORONARY ARTERY DISEASE

P02.10   Marc Daniel Opfermann. ISCHEMIA-HYPOXIA RELATED SMALL METABOLITES UPREGULATED SMALL ORGANIC ACIDS IN ISCHEMIA AS A NOVEL ENDOGENOUS PROTECTION SYSTEM AGAINST REPERFUSION INJURY

Poster session 3

Chairmen: Dorte Rytter, Yutao Lu (PhD student), Maria Riedel (PhD student) & Malou Eva Maria Pinto Barbosa (PhD student)

P03.01   Mette Bisgaard Andersen. PHYSICAL ACTIVITY IN PREGNANCY; EFFECTS OF BODY MASS INDEX AND WEIGHT GAIN

P03.02   Anne Staub Rasmussen. SURGERY DURING PREGNANCY AND BIRTH OUTCOMES

P03.03	Ida Charlotte Bay Lund. INTRODUCTION OF NON-INVASIVE PRENATAL TESTING IN DENMARK
P03.04	Mette Schou Mikkelsen. CYTOREDUCTIVE SURGERY COMBINED WITH HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC): A SAFE PROCEDURE WHEN USED IN OVARIAN CANCER TREATMENT
P03.05	Anne Rahbek Zizzo. NON-INVASIVE FETAL ELECTROCARDIOGRAPHY (FECG) IN 2ND AND 3RD TRIMESTER
P03.06	Eva Rydahl. CESAREAN SECTION ON A RISE: DOES ADVANCED MATERNAL AGE EXPLAIN THE INCREASE? A POPULATION-BASED REGISTER STUDY
P03.07	Sidsel Boie. CONTINUED VERSUS DISCONTINUED OXYTOCIN STIMULAITON OF LABOUR IN A DOUBLE-BLIND RANDOMISED CONTROLLED TRIAL: STATUS OF AN RCT
P03.08	Berit Bargum Booth. CERVICAL DYSPLASIA: HOW CAN WE IMPROVE THE DIAGNOSTICS?

Poster session 4

Chairmen: Mariane Schleimann, Thomas Falstie-Jensen (PhD student) & Alon Illy Schneider Hait (PhD student)

P04.01	Camilla Gunderstofte Nielsen. IRG1 PROTECTS HUMAN MONOCYTE-DERIVED MACROPHAGES FROM CELL DEATH
P04.02	Kathrine Kjær. QUANTIFICATION OF INDIVIDUAL TRANSCRIPTIONAL ACTIVE HIV PROVIRUSES DURING ANTIRETROVIRAL THERAPY IN ABSENCE OR PRESENCE OF ERADICATION THERAPY
P04.03	Anne Borup. MODULATION OF INFLAMMATION BY HELMINTH-DERIVED EVS
P04.04	Christina Valbirk Konrad. ISOLATION AND VALIDATION OF NOVEL HIV-SPECIFIC EFFECTOR ANTIBODIES FOR IMMUNE-MEDIATED TARGETING OF THE LATENT HIV RESERVOIR
P04.05	Sandra Maria Skovdal. STAPHYLOCOCCUS EPIDERMIDIS DOES NOT RELY ON POLYSACCHARIDES WHEN FORMING BIOFILMS IN HUMAN PLASMA
P04.06	Sidsel Dahl Andersen. IMMUNE MODULATORY EFFECTS ON INNATE IMMUNE RESPONSES BY ADULT BODY FLUID FROM THE PARASITIC WORM, ASCARIS SUUM
P04.07	Amin Zakeri. IMMUNOSUPPRESSIVE EFFECTS OF HELMINTH ANTIGENS ON TLR-MEDIATED INDUCTION OF INFLAMMATORY RESPONSES IN MACROPHAGE
P04.08	Fanghui Ren. THE POTENTIAL MECHANISM OF HSVS-INDUCED AUTOPHAGY IN NEURONS
P04.09	Johanne Hovgaard Egedal. HYALURONIC ACID IS A NEGATIVE REGULATOR OF FIBROBLAST-MEDIATED ENHANCEMENT OF HIV INFECTION
P04.10	Mette Christensen. DOES BLOCKING OF P2Y RECEPTORS ON THROMBOCYTES CHANGE THE OUTCOME OF URO-SEPSIS IN MICE?

Poster session 5

Chairmen: Janne Lebeck, Pernille Glahn Wernlund (PhD student) & Tea Lund Laursen (PhD student)

P05.01   Tine Vrist Dam. THE ANABOLIC EFFECT OF EXOGENOUS ESTROGEN ON THE SKELETAL MUSCLES IN POSTMENOPAUSAL WOMEN

P05.02   Mai Christiansen Arlien-Søborg. INSULIN SENSITIVITY IMPROVES AFTER DISEASE CONTROL IN ACROMEGALY IRRESPECTIVE OF TREATMENT MODALITY AND DESPITE AN INCREASE IN INTRAHEPATIC LIPID CONTENT: AN INVESTIGATOR-INITIATED PROSPECTIVE TRIAL

P05.03   Jonas Brorson Jensen. INFLUENCE OF NICOTINAMIDE RIBOSIDE AND PTEROSTILBENE SUPPLEMENTATION ON MUSCLE REGENERATION IN ELDERLY HUMANS

P05.04   Tine Billeskov. DOES GROWTH HORMONE REPLACEMENT THERAPY UNMASK INSULIN-LIKE EFFECTS IN PATIENTS WITH GROWTH HORMONE DEFICIENCY AND PROMOTE MUSCLE STEM CELL PROLIFERATION?

P05.05   Anne Sophie Koldkjær Sølling. TREATMENT WITH ZOLEDRONIC ACID SUBSEQUENT TO ODANACATIB PREVENTS BONE LOSS IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS

P05.06   Mads Bisgaard Bengtsen. COUNTER-REGULATORY RESPONSES TO HYPOGLYCEMIA IN SUBJECTS WITH TYPE 1 DIABETES AND HEALTHY CONTROL SUBJECTS

P05.07   Maike Mose. A NEW MODEL OF INFLAMMATORY DISEASE COMBINING ENDOTOXEMIA, FAST AND BED REST IN HEALTHY YOUNG MEN: A RANDOMISED CROSSOVER STUDY

P05.08   Thomas Skjærlund Grønnebæk. SKELETAL MUSCLE MITOCHONDRIAL PROTEIN SYNTHESIS AND RESPIRATION INCREASE WITH LOW-LOAD BLOOD FLOW RESTRICTED AS WELL AS HIGH-LOAD RESISTANCE TRAINING

P05.09   Francesco Maria Iena. SEX-SPECIFIC EFFECTS OF HIGH FAT DIET ON ADIPOSE TISSUE GLYCEROL METABOLISM IN MICE

P05.10   Liv Hald. VASCULAR EFFECTS OF ASPIRIN IN PATIENTS WITH TYPE 2 DIABETES WITHOUT CARDIOVASCULAR DISEASE AND NON-DIABETIC MATCHED CONTROLS

Poster session 6

Chairmen: Jørgen Feldbæk Nielsen, Denise Fabienne Happ (PhD student) & David Ricardo Quiroga Martinez (PhD student)

P06.01   Simone Schandorf Elstrøm Nielsen. TRANSCYTOSIS OF THERAPEUTIC TRANSFERRIN RECEPTOR ANTIBODIES IN BRAIN ENDOTHELIAL CELLS

P06.02   Abdel-Rahman Al-Absi. SYNAPTIC DYSFUNCTION IN THE PREFRONTAL CORTEX OF DF(H15Q13)/+ GENETIC MOUSE MODEL OF SCHIZOPHRENIA

P06.03   Thorsten Rasmussen. EARLY DETECTION OF SMALL FIBER POLYNEUROPATHY AND AUTONOMIC DYSFUNCTION IN TTR AMYLOIDOSIS

P06.04   Maimaitili Muyesier. INVESTIGATING THE ROLE OF CIRCULAR RNA IN MESENCEPHALIC DOPAMINERGIC NEURONS DERIVED FROM HUMAN PLURIPOTENT STEM CELLS

P06.05 Sérgio Eduardo Costa Almeida. NEURON-SPECIFIC RECEPTOR-MEDIATED SORTING OF THE FTLD RISK FACTOR PROGRANULIN

P06.06 Giulia Monti. LOCAL SYNAPTIC TRANSLATION OF A NOVEL SPLICE-VARIANT OF THE ALZHEIMER'S DISEASE RISK GENE SORL1

P06.07 Emil Gregersen. THE ROLE OF USP19 IN THE EXCRETION AND CYTOTOXICITY OF ALPHA-SYNUCLEIN AND THE PRION-LIKE INTERCELLULAR SPREADING OF ALPHA-SYNUCLEIN PATHOLOGY

P06.08 Sara Raquel Almeida Ferreira. INVOLVEMENT OF THE CD163 RECEPTOR IN THE ALPHA-SYNUCLEIN INDUCED NEURODEGENERATION IN PARKINSON'S DISEASE

P06.09 Pernille Louise Kjeldsen. A STUDY OF THE TEMPORAL DEVELOPMENT OF BETA-AMYLOID, TAU, INFLAMMATION, AND VASCULAR CHANGES IN PRECLINICAL ALZHEIMER'S DISEASE AND THE INFLUENCE OF THE NORADRENERGIC SYSTEM ON COGNITIVE DECLINE

P06.10 Martin Kinnerup. PROGRESSION OF COGNITIVE IMPAIRMENT IN PARKINSON'S DISEASE

Poster session 7

Chairmen: Gregers Wegener, Casper Schmidt (PhD student), Maj Ulrichsen (PhD student) & Saida Said (PhD student)

P07.01 Jordan Nicolas Alves. CHANGES OF RESTING-STATE OSCILLATORY NETWORK DYNAMICS AFTER MOTOR LEARNING: AN M.E.G. DEVELOPMENTAL STUDY

P07.02 Anders Gyldenkerne. OPTICAL AND VISUAL QUALITY AFTER SMALL-INCISION LENTICULE EXTRACTION (SMILE) FOR NEARSIGHTEDNESS

P07.03 Pauline Cantou. NEGATIVE CUES MODULATE CONFLICT PROCESSING: AN FMRI STUDY IN YOUNG ADOLESCENTS

P07.04 Simone Hyldgaard Andersen. THE NUCLEAR ANATOMY AND FIBER CONNECTIONS OF THE GÖTTINGEN MINIPIG AMYGDALA

P07.05 Charlotte Ernst. ATP-INDUCED DIAMETER CHANGES IN THE RETINAL VASCULAR TREE EX VIVO DEPEND ON THE BRANCHING LEVEL

P07.06 Hao Zhou. THE SPATIOTEMPORAL DYNAMICS OF TEMPORAL CONTEXT EFFECT IN HUMAN EARLY VISUAL CORTEX

P07.07 Jakob Hansen. USING OPTICAL MOTION CAPTURE TO MEASURE KINEMATICS DURING SIT-TO-STAND

P07.08 Sidsel Rugberg Alsing. TUNABLE EXPRESSION OF DICER INDEPENDENT SHRNAS FOR POTENT, DURABLE, AND SPECIFIC KNOCKDOWN OF VEGF

P07.09 Simon Bang Kristensen. REGRESSION METHODS FOR ORDINAL DATA IN METACOGNITION

P07.10 Ole Søndergaard Schwartz. ROLE OF INDIVIDUAL CELL TYPES IN THE SUPERIOR COLLICULUS OF THE MOUSE

Poster session 8

Chairmen: Dennis Graversen (PhD student), Simin Berenji Ardestani (PhD student) & Sandra Sif Gylfadottir (PhD student)

P08.01   Jacob Horsager. CARDIAC ^{11}C-DONEPEZIL BINDING INCREASES WITH AGE IN HEALTHY HUMANS - POTENTIALLY SIGNIFYING SIGMA-1 RECEPTOR UPREGULATION

P08.02   Mette Vestergård Pedersen. NEONATAL HYPOXIC ISCHEMIC ENCEPHALOPATHY AND HEART RATE VARIABILITY: A STUDY IN PIGLETS

P08.03   Jelena Stankovic. FOOD NEOPHOBIA AMONG DANISH ADOLESCENTS WITH AND WITHOUT AN ADHD DIAGNOSIS

P08.04   Camilla Lundquist. FROM RESEARCH TO CLINICAL PRACTICE: APPLYING AN ALGORITHM FOR PROGNOSIS AND TREATMENT OF UPPER LIMB PARESIS IN PATIENTS WITH SUBACUTE STROKE

P08.05   Tingting Gu. BIODISTRIBUTION OF HYPOXIA CONDITIONED MYOBLAST-EXTRACELLULAR VESICLES IN STROKE MICE

P08.06   Katrine Tang Stenz. BENEFICIAL EFFECTS OF REMOTE ISCHEMIC CONDITIONING AND BLOOD FLOW RESTRICTED EXERCISE IN STROKE

P08.07   Julie Linding Kjerulff. INFLUENCE OF TRANSPORT, TIME AND STORAGE TEMPERATURE ON S100B VALUES

P08.08   Cathrine Hjorth Hansen. WHAT CONSTITUTES DEMENTIA CARE? AN ETHNOGRAPHIC STUDY IN DAGMARSMINDE - A PRIVATE NURSING HOME FOR PEOPLE LIVING WITH ADVANCED DEMENTIA

P08.09   Anne Nielsen. AUTOMATIC DIFFUSION LESION OUTLINING IN ACUTE ISCHEMIC STROKE USING DEEP LEARNING

P08.10   Rolf Blauenfeldt. REMOTE ISCHEMIC CONDITIONING IN PATIENTS WITH ACUTE STROKE: A MULTICENTER RANDOMIZED, PATIENT-ASSESSOR BLINDED, SHAM-CONTROLLED STUDY (RESIST)

Poster session 9

Chairmen: Jacob Johansen, Stine Bak (PhD student), Anders Damgaard Møller Schlünsen (PhD student) & Kristine Jepsen Bennedsgaard (PhD student)

P09.01   Anne-Sofie Skou. OVEREXPRESSED GENES FOR EARLY DETECTION OF RELAPSE IN CHILDHOOD ACUTE MYELOID LEUKEMIA

P09.02   Michelle Simone Clement. THE ROLE OF MIR-200C IN MET-TKI RESISTANCE

P09.03   Marie Vognstoft Hjortbak. CARDIOPROTECTIVE EFFECT OF LOCAL AND REMOTE ISCHEMIC CONDITIONING IN COMBINATION WITH MILD HYPOTHERMIA

P09.04   Line Bager Andersen. ASSESSMENT AND VALIDATION OF NOVEL IMMUNE SYSTEM BIOMARKER CANDIDATES FOR PROSTATE CANCER USING TISSUE MICROARRAYS

P09.05   Trine Vilsbøll Larsen. PD-L1 DNA METHYLATION CORRELATES NEGATIVELY WITH PD-L1 EXPRESSION IN NSCLC

P09.06   Trine Strandgaard. INVESTIGATION OF THE FIELD EFFECT IN BLADDER CANCER PATIENTS

P09.07	Maibritt Nørgaard. DEEP SEQUENCING OF CIRCULATING TUMOR DNA FOR PREDICTION AND MONITORING OF ENZALUTAMIDE AND ABIRATERONE TREATMENT RESPONSE IN CASTRATION RESISTANT PROSTATE CANCER
P09.08	Jesper Geert Pedersen. INVESTIGATION OF PLASMA CYTOKINE LEVELS AND CIRCULATING TUMOUR DNA AS POTENTIAL BIOMARKERS FOR DISEASE STATUS IN METASTATIC MELANOMA PATIENTS DURING IMMUNOTHERAPY
P09.09	Emma Kirstine Bollmann Laursen. CIRCULAR RNAS IN PROSTATE CANCER AND THEIR POTENTIAL AS CLINICAL BIOMARKERS TO IMPROVE PROSTATE CANCER DIAGNOSIS AND RISK STRATIFICATION FOR MORE INDIVIDUALIZED MANAGEMENT

Poster session 10

Chairmen: Anders Bonde Jensen, Anita Tranberg Simonsen (PhD student), Veera Manikandan (PhD student) & Patricia Alves da Mota (PhD student)

P10.01	Laura Virginie Toussaint. TEMPORAL LOBE SPARING RADIOTHERAPY FOR COGNITIVE PRESERVATION IN PEDIATRIC BRAIN TUMOR PATIENTS
P10.02	Laura Patricia Kaplan. INTER-OBSERVER VARIATIONS IN RADIOTHERAPY PLAN EVALUATION
P10.03	Anders Schwartz Vittrup. LATE, PERSISTENT, SUBSTANTIAL AND LIKELY TREATMENT-RELATED SYMPTOMS (LAPERS): A REPORT FROM THE EMBRACE STUDY
P10.04	Nina Jensen. RISK FACTOR ANALYSIS AND DOSE-VOLUME EFFECTS FOR LATE BOWEL MORBIDITY IN LOCALLY ADVANCED CERVICAL CANCER
P10.05 CANCELLED	Raúl Argota Perez. ROBUSTNESS OF PROTON RADIOTHERAPY PLANS TOWARDS ANATOMICAL VARIATIONS IN NASOPHARYNGEAL CANCER
P10.06	Andreas Gravgaard Andersen. EVALUATION OF AN A PRIORI SCATTER CORRECTION ALGORITHM FOR CONE-BEAM CT PROJECTIONS IN PHOTON VS. PROTON THERAPY GANTRIES
P10.07	Maja Bendtsen Sharma. RADIATION THERAPY OF SINONASAL CARCINOMA: FUNCTIONAL ASSESSMENT OF LATE TOXICITY AND QUALITY OF LIFE
P10.08	Marie Louise Milo. DBCG COR: THE RISK OF RADIOTHERAPY INDUCED HEART DISEASE IN WOMEN TREATED FOR EARLY STAGE BREAST CANCER

Poster session 11

Chairmen: Jesper Grau Eriksen, Lene Haldbo-Classen (PhD student) & Sanne Jensen (PhD student)

P11.01	Jakob Haldrup Jensen. NOVEL TUMOR SUPPRESSOR FUNCTION AND PROGNOSTIC POTENTIAL OF FRMD6 IN PROSTATE CANCER
P11.02	Margarita Sergeyevna Melnikova. CHARACTERIZATION OF EPITHELIAL CELLS IN COLORECTAL CANCER
P11.03	Thomas Buus. WHOLE BODY MRI FOR DETECTING ADVANCED BREAST CANCER
P11.04	Maria Skydt Lindgren. NEOADJUVANT SHORT-TERM INTENSIVE CHEMORESECTION VS. STANDARD ADJUVANT INTRAVESICAL INSTILLATIONS OF NON-MUSCLE INVASIVE BLADDER CANCER - NICSA

P11.05 Malene Blond Ipsen. IDENTIFYING MECHANISMS OF PARP INHIBITOR RESISTANCE AND SENSITIVITY IN PROSTATE CANCER BY GENOME WIDE CRISPR-CAS9 SCREENING

P11.06 Signe Neldeborg. EFFECT OF LOW-DOSE CHEMOTHERAPY ON IMMUNE-MEDIATED KILLING OF CANCER CELLS

P11.07 Josephine P. Geertsen Keller. TOPOISOMERASE 1 AS A TARGET FOR ANTI-CANCER THERAPY

P11.08 Mads Ryø Jochumsen. [82]RUBIDIUM PET/CT - A NEW METHOD FOR TUMOR BLOOD FLOW IMAGING IN PROSTATE CANCER?

Poster session 12

Chairmen: Jeppe Lange, Anne Mette Schmidt (PhD student), Maj Haubuf (PhD student) & Anne-Birgitte Blavnsfeldt (PhD student)

P12.01 Kris Chadwick Hede. COMBINED BONE MARROW ASPIRATE AND PLATELET-RICH PLASMA FOR CARTILAGE REPAIR - RESULTS AT TWO-YEAR FOLLOW-UP

P12.02 Caroline Marie Andreasen. RESPONSE TO EARLY-ONSET PAMIDRONATE TREATMENT IN SEVERE CHRONIC NON-BACTERIAL OSTEOMYELITIS:
A RETROSPECTIVE SINGLE CENTER STUDY

P12.03 Cecilie Linneberg Matthiesen. EXTRACELLULAR SUPEROXIDE DISMUTASE - ASSOCIATED WITH BONE DEVELOPMENT IN ZEBRAFISH. A ROLE IN HUMAN BIOLOGY?

P12.04 Eva Forsom. ANTIPSYCHOTIC TREATMENT AND THE BONE MINERAL DENSITY OF THE LUMBAR SPINE

P12.05 Morten Aagaard Nielsen. GALECTIN-3 ASSOCIATES WITH OUTCOME IN RHEUMATOID ARTHRITIS

P12.06 Rasmus Klose-Jensen. DIFFERENCES AND SIMILARITIES OF THE FEMORAL HEAD'S BONE-CARTILAGE UNIT IN PATIENTS WITH OSTEOARTHRITIS AND PATIENTS WITH RHEUMATOID ARTHRITIS

P12.07 Sebastian Mosegaard. PREOPERATIVE RISK FACTORS FOR LOW PATIENT REPORTED SATISFACTION AFTER CARPAL TUNNEL RELEASE

P12.08 Laura Houstrup Therkelsen. FEW COMPLICATIONS FOLLOWING PERCUTANEOUS NEEDLE FASCIOTOMY FOR DUPUYTREN CONTRACTURE

P12.09 Jeanette Trøstrup. A SHOULDER-CAFÉ INTERVENTION TO REDUCE SHOULDER COMPLAINTS IN EMPLOYEES WITH HIGH MECHANICAL SHOULDER EXPOSURES AND SHOULDER COMPLAINTS: STUDY PROTOCOL

P12.10 Emil Toft Nielsen. A NOVEL CLINICAL METHOD FOR NON-INVASIVE QUANTIFICATION AND GRADING OF PIVOT-SHIFT TEST

Poster session 13

Chairmen: Niels Okkels, Thomas Skovhus Prior (PhD student), Andreas Aalkjær Danielsen (PhD student) & Hanan Amadid (PhD student)

P13.01 Sara Højslev Avlund. ASSOCIATION OF COMORBIDITY, MEDICATION USAGE AND FAMILY PSYCOPATHOLOGY ON QUALITY OF LIFE IN A COHORT OF ADOLESCENTS REFERRED ON SUSPICION OF AUTISM SPECTRUM DISORDER IN CHILDHOOD

P13.02   Janne Tidselbak Larsen. GENETIC RISK FACTORS FOR ANOREXIA NERVOSA

P13.03   Pernille Kølbæk. CLINICAL VALIDATION OF THE GLASGOW ANTIPSYCHOTIC SIDE-EFFECT SCALE (GASS)

P13.04   Katrine Ingeman Beck. DEVELOPMENT OF ASSESSMENT AND TREATMENT OF HEALTH ANXIETY BY PROXY: AN UNRESOLVED CLINICAL PROBLEM

P13.05   Astrid Høeg Tuborgh. ATTACHMENT STYLE AND SYMPTOM REPORTING IN YOUNG PERSONS WITH CONCUSSION

P13.06 CANCELLED Tina Thorborg. HOW PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS EXPERIENCE FINDING ADEQUATE INFORMATION ABOUT THEIR DISEASE AND LIFE OPPORTUNITIES

P13.07   Birgit Refsgaard Iversen. PREVENTATIVE CARE AND HOME TREATMENT IN PATIENTS AT RISK OF HOSPITALISATION DUE TO EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

P13.08   Jose Manuel Cerdan de Las Heras. "VAPA" - AN INNOVATIVE TELE-REHABILITATION TOOL FOR HOME USE: PATIENTS' PERCEPTION AND EXPECTATIONS

P13.09 CANCELLED Christina Bruun Knudsen. NEUROCOGNITION IN OFFSPRING OF PARENTS WITH SCHIZOPHRENIA OR BIPOLAR DISORDER: THE DEVELOPMENT FROM SEVEN TO 11 YEARS OF AGE

P13.10   Cecilie Marie Nielsen. CLINICAL VALIDATION OF PANSS-6 SCHIZOPHRENIA SEVERITY RATINGS AMONG PATIENTS UNDERGOING OUTPATIENT TREATMENT

Poster session 14

Chairmen: Konstantinos Kamperis, Jeanette Finderup (PhD student), Takwa Shaiman Aroankins (PhD student) & Maria Elkjær (PhD student)

P14.01   Samuel Levi Clement Svendsen. A SINGLE GASTRIC K^+LOAD INDUCES ACUTE DIURESIS IN MICE

P14.02   Kristine Fogh Andersen. HEMATURIA AND LONG-TERM RISK OF CHRONIC KIDNEY DISEASE: A DANISH POPULATION-BASED COHORT STUDY

P14.03   Søren Viborg Vestergaard. VALIDITY OF THE CODING OF NEPHROTIC SYNDROME DIAGNOSES IN DENMARK

P14.04   Marie Houmaa Vrist. PRELIMINARY RESULTS FOR THE USE OF NA18F PET/CT IN RENAL OSTEODYSTROPHIA

P14.05   Ann Mai Hindkjær Østergaard. THE EFFECT OF ORALLY ADMINISTRATED NITRATE ON RENAL AND SYSTEMIC HAEMODYNAMICS, WATER AND SALT REGULATION, TUBULAR TRANSPORT PROTEINS AND VASOACTIVE HORMONES IN A RANDOMIZED, PLACEBO-CONTROLLED, CROSSOVER STUDY IN HEALTHY SUBJECTS

P14.06   Marlene Louise Nielsen. CHARACTERIZATION OF CYST ORIGIN IN ADPKD

P14.07   Christian Østergaard Mariager. EX-VIVO INVESTIGATION OF RENAL METABOLIC HETEROGENEITY USING HYPERPOLARIZED ^{13}C-PYRUVATE MRI

P14.08   Birgith Engelst Grove. TELE FOLLOW-UP USING PATIENT-REPORTED OUTCOMES (PRO) MEASURES IN PATIENTS WITH CHRONIC KIDNEY DISEASE - THE PROKID STUDY: A STUDY PROTOCOL FOR A NON-INFERIORITY RANDOMISED CONTROLLED TRIAL

P14.09   Stine Lohmann. EX-VIVO INTRA-ARTERIAL ALLOGENIC MSC THERAPY PRIOR TO TRANSPLANTATION IN A PORCINE DCD MODEL DOES NOT LEAD TO IMPROVED GRAFT FUNCTION

P14.10   Stine Sundgaard Langaa. DETERMINATION OF RENAL BLOOD FLOW BASED ON PET/CT-RUBIDIUM-82 TECHNOLOGY IN HEALTHY SUBJECTS

Poster session 15

Chairmen: Deirdre Cronin Fenton, Inge Schjødt (PhD student) & Michael Bertelsen (PhD student)

P15.01   Malene Thygesen. EXPOSURE TO AIR POLLUTION AS A RISK FACTOR FOR THE DEVELOPMENT OF ADHD IN CHILDREN

P15.02   Daniel Borch Ibsen. CHANGES IN INTAKE OF DAIRY PRODUCT SUBGROUPS AND TYPE 2 DIABETES: MODELLING SPECIFIED FOOD SUBSTITUTIONS IN THE DANISH DIET, CANCER AND HEALTH COHORT

P15.03   Jose Omar Silverman Retana. FAMILIAL DIABETES STATUS AND THE RISK OF INCIDENT TYPE 2 DIABETES IN DENMARK

P15.04   Louise Lindholdt. DOES LABOUR MARKET PARTICIPATION AMONG PARENTS AFFECT SELF-RATED HEALTH OF THEIR CHILDREN? A STUDY OF 11,267 ADOLESCENTS AND THEIR PARENTS

P15.05   Emely Blæhr. SMALL-AREA VARIATION IN SUPPLY OF PSYCHIATRIC CARE: A REGISTER-BASED STUDY

P15.06   Mette Hansen Viuff. SEX HORMONE REPLACEMENT THERAPY IN TURNER SYNDROME AND THE IMPACT ON MORBIDITY AND MORTALITY

P15.07   Nanna Weye. ALTERNATIVE METRICS TO QUANTIFY PREMATURE MORTALITY IN MENTAL DISORDERS

P15.08   Helle Elisabeth Andersen. ADULT CHILDREN WITH CARE RESPONSIBILITY FOR A PARENT AGED 80+ YEARS LIVING ALONE WITH COMPLEX CARE REQUIREMENTS: A QUALITATIVE STUDY

P15.09   Sophie Amalie Glenvad Tind Hamann. ASSOCIATION BETWEEN BMI AMONG SCHOOL CHILDREN AGED 9-17 YEARS AND SOCIO-ECONOMIC STATUS OF THEIR HOUSEHOLD IN LEKHNATH, NEPAL

P15.10   Sofie Sand Jensen. IN UTERO EXPOSURE TO GLUCOCORTICOIDS AND TIMING OF PUBERTY IN BOYS AND GIRLS: A POPULATION-BASED COHORT STUDY

P15.11   Tina Kissow Lildal. A FEASIBILITY STUDY OF THE NOX T3 HOME SLEEP POLYGRAPHY FOR THE DETECTION OF OBSTRUCTIVE SLEEP DISORDERED BREATHING IN CHILDREN

Poster session 16

Chairmen: Vassilis Sevdalis, Andreas Ernst (PhD student), Maria Dietz Toppenberg (PhD student) & Katja Krustrup Pedersen (PhD student)

P16.01   Lene Wulff Krogsgaard. HOSPITAL CONTACTS AND DIAGNOSES FIVE YEARS PRIOR TO HPV VACCINATION AMONG FEMALES REFERRED FOR SUSPECTED ADVERSE VACCINE EFFECTS: A DANISH NATIONWIDE CASE-CONTROL STUDY

P16.02   Lotte Levison. GUILLAIN-BARRÉ SYNDROME IN DENMARK: VALIDATION OF DIAGNOSTIC CODES AND A POPULATION-BASED NATIONWIDE STUDY OF THE INCIDENCE IN A 30-YEAR PERIOD

P16.03   Karen Baden Alstrup. THE DANISH HELICOPTER EMERGENCY MEDICAL SERVICES DATABASE - HIGH QUALITY DATA WITH GREAT POTENTIAL

P16.04   Mette Kielsholm Thomsen. CAN WE SCREEN MORE PRECISELY?

P16.05   Maria Daniella Bergholt. APPROPRIATENESS OF HEALTHCARE, PATIENT OUTCOMES AND EXPERIENCES AMONG PATIENTS IN THE FAROE ISLANDS HOSPITALS BEFORE AND AFTER THEIR FIRST ACCREDITATION

P16.06   Nina Mckinnon Edwards. TOTAL HIP ARTHROPLASTY: THE ASSOCIATION BETWEEN SOCIOECONOMIC FACTORS, COMORBIDITIES, POSTOPERATIVE COMPLICATIONS, AND QUALITY OF LIFE

P16.07   Astrid Julie Bønnelykke. THE MANAGEMENT OF PATIENTS WITH ANAEMIA, THE RISK OF CANCER AND CANCER-RELATED ANAEAMIA SUBTYPES

P16.08   Sara Koed Badre-Esfahani. HPV VACCINATION IS ASSOCIATED WITH PARTICIPATION IN CERVICAL CANCER SCREENING - A NATIONAL REGISTER-BASED COHORT STUDY

P16.09   Line Stjernholm Tipsmark. ORGANISATION OF EMERGENCY DEPARTMENTS: THE DANISH CASE

P16.10   Signe Hjuler Boudigaard. A FOLLOW-UP STUDY OF OCCUPATIONAL STYRENE EXPOSURE AND RISK OF SYSTEMIC SCLEROSIS, RHEUMATOID ARTHRITIS, AND OTHER SYSTEMIC AUTOIMMUNE RHEUMATOLOGICAL DISEASES

Poster session 17   (Presentation Skills evaluated by Keynote Speaker Barry Stainthorp)

Chairmen: Anna Starnawska, Per Mose Nielsen (PhD student) & Elin Rakvaag (PhD student)

P17.01   Alexandra Golabek Christiansen. PREVENTION OF DERMATITIS IN EPOXY EXPOSED LAMINATION WORKERS PRODUCING WIND TURBINE BLADES: AN INTERVENTION STUDY USING FLUORESCENCE VISUALIZATION

P17.02   Mads Valdemar Anderson. TARGETED GENOME EDITING BY LENTIVIRAL PROTEIN TRANSDUCTION OF CRISPR-ASSOCIATED ENDONUCLEASES

P17.03   Randi Istrup Pedersen. GENOME-WIDE ANALYSIS OF SITE-SPECIFIC HOTSPOTS IN CANCER

P17.04   Laura Barrett Ryø. EXPLORING DOMINANT NEGATIVE DISEASE MECHANISMS IN HEREDITARY ANGIOEDEMA - FROM MAN TO MICE

P17.05   Alexander Kristian Damm Grevsen. PLATELET FUNCTION IN PRETERM NEONATES

P17.06   Cagla Cömert. A CELL MODEL FOR MODELLING DIFFERENT LEVELS OF OXIDATIVE STRESS AND MITOCHONDRIAL DYSFUNCTION

P17.07   Jacob Thyrsted Jensen. GENETIC ENGINEERING IN HUMAN EX VIVO LUNG MODEL

P17.08   Jon Hagen Herskind. THE EFFECT OF LOW FREQUENCY FATIGUE ON DYNAMIC MUSCLE FUNCTION

P17.09   Emil Aagaard Thomsen. EXPLORING R-CHOP RESISTANCE IN CANCEROUS B-CELLS BY FORWARD GENETIC CRISPR/CAS9-BASED SCREENING OF THE GENOME

Poster session 18

Chairmen: Henning Grønbæk, Charlotte Arp Sørensen (PhD student), Martin Lund (PhD student) & Anne Ankerstjerne Rasmussen (PhD student)

P18.01 Anne Beck. FROM WAITING TO PREPARING: A QUALITATIVE FEASIBILITY STUDY OF CANCER PATIENTS' PERSPECTIVES ON PREHABILITATION

P18.02 Christina Søndergaard Duvald. THE CHINCHILLA AS A NOVEL ANIMAL MODEL OF GESTATIONAL DIABETES

P18.03 Julie Jacoby Petersen. FAMILY NURSING - A WAY TO IMPROVE FAMILY FUNCTION AND QUALITY OF LIFE?

P18.04 Sigurd Beier Sloth. COURSE TO CLINIC TRANSFER BETWEEN SIMULATION-BASED AND OR-BASED SURGICAL TRAINING

P18.05 Nanna Holt Jessen. INVESTIGATIONS IN THE YEAR PRECEDING A DIAGNOSIS OF AN ABDOMINAL CANCER

P18.06 Helene Mathilde Larsen. CLINICAL EVALUATION AND TREATMENT OF CHRONIC DIARRHOEA FOLLOWING CANCER IN THE COLON AND PELVIC ORGANS

P18.07 Rikke Buus Bøje. STRUCTUAL CONTRADICTIONS IN NURSES' COLLABORATION IN TRANSITIONS OF OLDER ADULTS BETWEEN HOSPITAL AND PRIMARY CARE

P18.08 Helle Kristensen. SYSTEMATIC REVIEW OF THE IMPACT OF SOCIOECONOMIC, DEMOGRAPHIC AND RELIGIOUS FACTORS ON QUALITY OF LIFE IN OSTOMIZED COLORECTAL CANCER SURVIVORS

P18.09 Ingrid Villadsen Kristensen. EXPERIENCES OF LIVING WITH END-STAGE RENAL DISEASE PRIOR TO A KIDNEY TRANSPLANTATION

P18.10 Sif Sund Blandfort. CAN SINGLE-BED ROOMS PREVENT DELIRIUM IN GERIATRIC PATIENTS?

Poster session 19

Chairmen: Simon Fristed Eskildsen, Daniel Gramm Kristensen (PhD student) & Karolina Snopek Khan (PhD student)

P19.01 Uwe Martin Pommerich. DEFINING THE MINIMAL CLINICALLY RELEVANT CHANGE OF THE SIX SPOT STEP TEST IN PERSONS WITH MULTIPLE SCLEROSIS

P19.02 Jan Lykke Scheel Thomsen. FIXED MUSCULAR DEFICITS IN MYASTHENIA GRAVIS

P19.03 Charlotte Maria Jensen. EXPERIENCES AND PERSPECTIVES OF GOAL SETTING IN SPINAL CORD INJURY REHABILITATION: SYSTEMATIC REVIEW OF QUALITATIVE STUDIES

P19.04 Angela Pärn. THE ROLE OF PCSK9 IN BRAIN DEVELOPMENT AND BEHAVIOR

P19.05 Morten Riemenschneider. AN OVERLOOKED "WINDOW OF OPPORTUNITY" IN MULTIPLE SCLEROSIS EXERCISE THERAPY - THE MS EARLY EXERCISE STUDY

P19.06 Victor Manuel Pando Naude. BRAIN FUNCTIONAL CONNECTIVITY CORRELATES OF MUSIC-INDUCED ANALGESIA IN FIBROMYALGIA

P19.07	Søren Krogh Jensen. THE EFFECTS OF SYSTEMATIC REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION IN REHABILITATION AFTER INCOMPLETE SPINAL CORD INJURY: NEUROMUSCULAR ADAPTATIONS AND RECOVERY OF LOWER LIMB MUSCLE STRENGTH
P19.08	Lotte Hardbo Larsen. UNDERSTANDING THE MECHANISMS OF CRITICAL ILLNESS MYOPATHY BY USE OF A NOVEL ELECTROPHYSIOLOGICAL METHOD - MUSCLE VELOCITY RECOVERY CYCLES (MVRCS)
P19.09	Mustafa Aykut Kural. CLINICAL VALIDATION OF CRITERIA FOR IDENTIFICATION OF EPILEPTIFORM EEG DISCHARGES IN SENSOR SPACE AND SOURCE SPACE
P19.10	Signe Fruekilde. CONSIDERATIONS WHEN STUDYING NEUROVASCULAR COUPLING IN AWAKE UNANESTHETIZED MICE

Poster session 20

Chairmen: Michael Winterdahl, Rasmus Wulff (PhD student) & Mia Glerup (PhD student)

P20.01	Mathias Alstrup. LYMPHATIC FUNCTION AND MORPHOLOGY IN WOMEN WHO HAVE UNDERGONE BREAST CANCER TREATMENT
P20.02	Aska Drljevic-Nielsen. RESPONSE EVALUATION CRITERIA IN METASTATIC RENAL CELL CARCINOMA: IMPROVED ASSESSMENT OF RESPONSE AND PROGRESSION BY SPECTRAL CT
P20.03	Morten Krogh Herlin. MULTI-OMICS ANALYSIS OF PEDIATRIC ACUTE MYELOID LEUKEMIA, NOT OTHERWISE SPECIFIED BY THE CURRENT WHO CLASSIFICATION
P20.04	Marianne Agerlund Petersen. 15-COLOUR PANEL FOR CHARACTERIZING LEUKEMIC STEM CELLS IN CHILDREN WITH ACUTE MYELOID LEUKAEMIA
P20.05	Solveig Kärk Abildtrup Larsen. MRI WITH DIFFUSION WEIGHTED IMAGING (DWI) FOR FOLLOW-UP OF PATIENTS TREATED FOR TESTICULAR CANCER STAGE I
P20.06	Michael Brun Andersen. CAN TEXTURE ANALYSIS HELP DIFFERENTIATE BETWEEN MALIGNANT AND BENIGN LYMPH NODES IN PATIENTS SUSPECTED OF LUNG CANCER
P20.07	Astrid Lindman. HIGHLY MOTIVATED, BUT DECEIVED AND EXHAUSTED BY REPEATED, ABRUPT COMPLICATIONS: IMPLICATIONS FOR REHABILITATION WHEN TREATED WITH STEM CELL TRANSPLANTATION
P20.08	Jesper Pedersen. CROSS-MODALITY APPLICABILITY OF RECTAL RADIOTHERAPY DOSE RESPONSE MODELS FROM PHOTONS TO PROTONS

Poster session 21

Chairmen: Rubens Spin-Neto, Susanna Botticelli (PhD student), Stine Derdau Sørensen (PhD student) & Luca Bordoni (PhD student)

P21.01	Mathilde Frost Kristensen. PH MEASUREMENTS OF DENTAL BIOFILM UNDER FLOW CONDITIONS - THE IDEA BEHIND THE PROJECT
P21.02	Arwa Gera. TRANSLATION AND ADAPTATION OF THE DANISH VERSION OF OHIP-14
P21.03	Pankaj Taneja. MODULATION OF EXPERIMENTAL FACIAL PAIN VIA AFFECTIVELY DIFFERENT SOMATOSENSORY STIMULI

P21.04   Julie Suhr Villefrance. DOES CBCT CHANGE THE CLASSIFICATION OF EXTERNAL CERVICAL RESORPTION COMPARED TO INTRAORAL IMAGING?

P21.05   Xiaowen Niu. ASSOCIATION BETWEEN RAPID MAXILLARY EXPANSION AND NOCTURNAL ENURESIS IN CHILDREN: A RANDOMIZED CONTROLLED CLINICAL TRIAL

P21.06   Carolina Bizelli Silveira. STRONTIUM ENHANCES PROLIFERATION AND OSTEOGENIC BEHAVIOR OF BONE MARROW STROMAL CELLS OF DIFFERENT EMBRYONIC ORIGINS IN VITRO

P21.07   Stine Julie Hyldal Tingskov. TAMOXIFEN ATTENUATES DEVELOPMENT OF LITHIUM-INDUCED NEPHROGENIC DIABETES INSIPIDUS IN RATS

Poster session 22

Chairmen: Mette Madsen, Jakob Kirkegård (PhD student), Anne Vestbjerg Thyø (PhD student) & Mette Winther Klinge (PhD student)

P22.01   Marianne Ørum. DOES COMPREHENSIVE GERIATRIC ASSESSMENT (CGA) IMPROVE THE 90-DAY MORTALITY IN OLDER CANCER PATIENTS?

P22.02   Pernille Christiansen Skovlund. PATIENT INVOLVEMENT IN THE RESEARCH PROCESS

P22.03   Rasmus Blechingberg Friis. PROWIDE – PATIENT-REPORTED OUTCOMES USED FOR WEEKLY INTERNET-BASED DETECTION OF PROGRESSIVE DISEASE IN LUNG CANCER: A RANDOMIZED CONTROLLED TRIAL

P22.04   Kristoffer Brix Olesen. TRANSFERABLE SKILLS IN HEALTH SCIENCES EDUCATION: GLOBAL, LOCAL, AND CLASSROOM DISCOURSES

P22.05   Sofia Spampinato. RISK FACTORS FOR BLADDER FISTULA, BLEEDING AND CYSTITIS IN CERVIX CANCER: AN EMBRACE ANALYSIS

P22.06   Anna Holm. DEVELOPMENT AND TEST OF A COMMUNICATION STRATEGY FOR THE MECHANICALLY VENTILATED INTENSIVE CARE UNIT PATIENT (ICU-COM)

P22.07   Mie Østergaard. ENHANCING INNOVATIVE COMPETENCES IN THE DANISH HEALTH CARE SECTOR - A MIXED METHODS STUDY

P22.08   Jeppe Foged Vigh-Larsen. PERFORMANCE DIFFERENCES BETWEEN ELITE AND SUB-ELITE ICE HOCKEY PLAYERS WITHIN THE BEST AND SECOND BEST DANISH ICE HOCKEY LEAGUE

Flash talk session 1

Chairmen: Bo Løfgren, Stine Andersen (PhD student) & Mikkel Giehm-Reese (PhD student)

F01.01   Jacob Nicolaisen. MECHANICAL PERFORMANCE AND HEALING PATTERNS OF THE NOVEL SIROLIMUS-ELUTING BIORESORBABLE FANTOM SCAFFOLD IN LONG CORONARY LESIONS

F01.02 CANCELLED Rubina Attar. CLINICALLY MANIFESTED PERIPHERAL ARTERY DISEASE IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

F01.03   Kevin Kris Warnakula Olesen. PROGNOSTIC ASSESSMENT OF CORONARY ARTERY DISEASE BY COMPUTED TOMOGRAPHY ANGIOGRAPHY IN DIABETES AND NON-DIABETES PATIENTS: A STUDY FROM THE WESTERN DENMARK CARDIAC COMPUTED TOMOGRAPHY REGISTRY

F01.04   Christian Stæhr Frederiksen. MIGRAINE ASSOCIATED MUTATION IN THE α2 ISOFORM
              NA^+,K^+-ATPASE LEADS TO DISTURBANCE IN NEUROVASCULAR COUPLING

F01.05   Charlotte Brinck Holt. PLASMA LEVELS OF LECTIN PATHWAY PROTEINS HAVE NO
              PROGNOSTIC VALUE IN SHORT-TERM CARDIAC OUTCOMES AFTER MYOCARDIAL
              INFARCTION

F01.06   Zarmiga Karunanithi. ATRIAL SEPTAL DEFECT - EXERCISE CAPACITY AND PULMONARY
              HYPERTENSION

F01.07   Anne Brink Behrndtz. TRANSPORT STRATEGY IN PATIENTS WITH LARGE VESSEL
              OCCLUSION? TRIAGE STROKE: TREATMENT STRATEGY IN ACUTE LARGE VESSEL
              OCCLUSION: PRIORITIZE IV OR ENDOVASCULAR TREATMENT

F01.08   Lisa Carlson Hanse. PULMONARY CUSP REPAIR OF CONGENITAL HEART SURGERY: IN
              VITRO EVALUATION

F01.09   Mikkel Bundgaard Skotting. REGIONAL BRAIN VOLUMES IN NEWBORNS WITH
              CONGENITAL HEART DEFECTS

Flash talk session 2

Chairmen: Bent Deleuran, Anna Halling Folkmar Andersen (PhD student) & Elias Didrik Francis
Zachariae (PhD student)

F02.01   Kathrine Agergård Kaspersen. USE OF ORAL IRON SUPPLEMENTATION IS NOT
              ASSOCIATED WITH RISK OF INFECTIONS: RESULTS FROM THE DANISH BLOOD DONOR
              STUDY (DBDS)

F02.02   Signe Mosegaard. FATTY ACID OXIDATION (FAO) MODULATES INFLAMMATORY
              RESPONSES; IMPLICATIONS FOR INBORN ERRORS OF FAO AND SEPSIS DEVELOPMENT

F02.03   Esben Stistrup Lauritzen. CHRONIC METABOLIC EFFECTS OF MELATONIN

F02.04   Lene Thorup. VITAMIN D DEFICIENCY IN RHEUMATIC HEART DISEASE PATIENTS AND
              MATCHED HEALTHY CONTROLS IN NEPAL

F02.05   Aimi Danielle Munk Hamilton. GROWTH OF UROPATHOGENIC ESCHERICHIA COLI IN
              HUMAN URINE

F02.06   Jacob Rudjord Therkildsen. LACK OF $P2X_7$ RECEPTORS PROTECTS AGAINST RENAL
              FIBROSIS AFTER PYELONEPHRITIS WITH A-HEMOLYSIN PRODUCING ESCHERICHIA
              COLI

F02.07   Thea Cæcilie Viborg Vestergaard. THE INFLUENCE OF ANTI-TNF-ALPHA TREATMENT
              ON PLACENTAL FUNCTION AND PREGNANCY OUTCOME IN PATIENTS WITH CHRONIC
              INFLAMMATORY DISEASE

F02.08 CANCELLED Benjamin Kelly. MORPHOLOGICAL LYMPHATIC CHANGES IN PATIENTS WITH A
              UNIVENTRICULAR CIRCULATION

F02.09   Laura Boysen Dall. HELMINTH-MEDIATED MODULATION OF INFLAMMATORY
              RESPONSES IN SYSTEMIC LUPUS ERYTHEMATOSUS

Flash talk session 3

Chairmen: Martin Nors Skov (PhD student), Jibrin Danladi (PhD student) & Camilla Højland Knudsen (PhD student)

F03.01 ~~CANCELLED~~ Mathias Kaas Ollendorff. THE ALZHEIMER'S DISEASE RISK-FACTOR SORLA IS IMPLICATED IN THE AETIOLOGY OF ANXIETY

F03.02 Malene Overby. DISCOVERY OF NOVEL INTERACTING PROTEINS OF THE SORTILIN RECEPTOR - MECHANISTIC INSIGHTS INTO THE REGULATION OF A KEY PROTEIN INVOLVED IN NEUROLOGICAL AND PSYCHIATRIC DISORDERS

F03.03 Helene Honoré. TRACKING ACTIVITIES OF PATIENTS WITH ACQUIRED BRAIN INJURY WITH ACCELEROMETRY

F03.04 James Isaac Lubell. SEEING IS BELIEVING: HOW NEURAL OSCILLATIONS OF THE RETINA AND CORTEX TOGETHER MEDIATE HUMAN VISION

F03.05 Asbjørn Johan Krom-Thaysen. THE NUCLEAR ANATOMY AND FIBER CONNECTIONS OF THE GÖTTINGEN MINIPIG SEPTUM

F03.06 Davide Ligato. CAN MUSICAL TRAINING CHANGE HUMAN SENSORY PERCEPTION? A COMPARISON BETWEEN RHYTHMIC SINGERS, CLASSICAL SINGERS, AND NON-SINGERS

F03.07 Rune Rasmussen. DYNAMIC SPEED-DEPENDENT ENCODING OF MOTION DIRECTION IN MOUSE VISUAL CORTEX

F03.08 Bardia Varastehmoradi. THE OPIOID SYSTEM PLAYS A ROLE IN COGNITIVE PROCESSES AND DEPRESSION

F03.09 Meet Sanjaykumar Jariwala. DEVELOPING A METHOD TO IDENTIFY THE INPUTS DURING ACTIVATION OF DIFFERENT MEMORY CIRCUITS

Flash talk session 4

Chairmen: Charlotte Runge, Nis Brix (PhD student) & Lone Kirkeby (PhD student)

F04.01 Cæcilie Deisting Skejø. INCREASED PLASMA LEVELS OF SOLUBLE T-CELL IMMUNOGLOBULIN AND MUCIN DOMAIN 3 (TIM-3) IN EARLY RHEUMATOID ARTHRITIS CORRELATE WITH DISEASE ACTIVITY AND PROGRESSION

F04.02 Selim Kilic. A PROSPECTIVE STUDY OF HIGH-RESOLUTION ULTRASOUND IN LOWER EXTREMITY NERVES IN PATIENTS WITH COMMON FIBULAR COMPRESSION NEUROPATHY AND IN HEALTHY CONTROLS

F04.03 ~~CANCELLED~~ Sebastian Skejø. PREDICTING THROWING VELOCITY USING ACCELEROMETERS

F04.04 Andreas Steenholt Niklassen. OLFACTORY TRAINING AND BRAIN PLASTICITY

F04.05 Simon Meyer Lauritsen. EARLY SEPSIS DETECTION WITH DEEP LEARNING ON EHR EVENT SEQUENCES

F04.06 Josefine Slater. STEADY-STATE BONE PHARMACOKINETICS OF RIFAMPICIN COMBINED WITH MOXIFLOXACIN DETERMINED BY MICRODIALYSIS

F04.07	Peter Uhrbrand. PROLONGED OPIOID USE: A FREQUENT COMPLICATION AFTER SURGERY?
F04.08	Olesya Svystun. IMAGE-STITCHING ARTEFACTS IN CCD-BASED CEPHALOGRAMS AND THEIR ASSOCIATION WITH HEAD MOVEMENT: AN EX VIVO STUDY USING THREE CEPHALOSTATS

Flash talk session 5

Chairmen: Karin Birkenkamp-Demtröder, Pernille Byrialsen Elming (PhD student) & Rikke Smedegaard Rosbjerg (PhD student)

F05.01	Elena Dudukina. VAGINAL BLEEDING IN EARLY PREGNANCY AND RISK OF OCCULT CANCER
F05.02	Andreas Ladefoged Ebbehøj. MORBIDITY AND MORTALITY IN PATIENTS WITH PHEOCHROMOCYTOMA: DANISH NATIONAL DATA OVER A PERIOD OF 40 YEARS
F05.03	Casper Gammelmark Muurholm. DOSE-GUIDED MOTION MANAGEMENT DURING LIVER RADIOTHERAPY DELIVERY USING REAL-TIME RECONSTRUCTED TUMOR DOSE-VOLUME HISTOGRAMS
F05.04	Frederikke Schønfeldt Troelsen. COLORECTAL NEOPLASMS IN NEW USERS OF LOW-DOSE ASPIRIN WITH LOWER GASTROINTESTINAL BLEEDING: A DANISH NATIONWIDE MATCHED CROSS-SECTIONAL STUDY
F05.05	Erik Buch Jørgensen. DELIVERED DOSE RECONSTRUCTION BASED ON IN VIVO DOSIMETRY FOR PROSTATE BRACHYTHERAPY
F05.06	Simon Grund Sørensen. PREDICTING DNA REPAIR ERROR FROM MUTATIONAL PATTERNS IN WHOLE CANCER GENOMES AND EXOMES
F05.07	Peter Preben Eggertsen. MEMANTINE, AN ALZHEIMER'S DRUG, WITH POTENTIAL FOR CANCER THERAPY
F05.08	Cathrine Fonnesbech Hjorth. GENETIC VARIATION IN TAXANE METABOLISM AND RISK OF BREAST CANCER RECURRENCE AND MORTALITY: A POPULATION-BASED COHORT STUDY IN DENMARK

Flash talk session 6

Chairmen: Tine Brink Henriksen, Sara Birch (PhD student) & Anna Sofia Elisabeth Aaby (PhD student)

F06.01 ~~CANCELLED~~	Anna Sandager Hansen. SUBCLINICAL VAGINAL INFECTIONS AND ADVERSE PREGNANCY OUTCOME
F06.02	Maria Christensen. THE COST OF TREATED MENTAL DISORDERS: A RECORD-LINKAGE STUDY BASED ON DANISH REGISTERS
F06.03	Tara Ballav Adhikari. COMMUNITY-BASED MANAGEMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN NEPAL: STUDY PROTOCOL FOR A CLUSTER-RANDOMIZED CONTROLLED TRIAL
F06.04	Alexandra Lahtinen. DNA METHYLATION IN BLOOD LEUKOCYTES AS PUTATIVE BIOMARKERS FOR INSUFFICIENT SLEEP

F06.05   Charlotte Hansen Gabel. ARE WE CHANGING HEALTH WHILE RE-MODELLING SOCIAL HOUSING ESTATES? AN INTERDISCIPLINARY MULTIPLE SITES FOLLOW-UP STUDY IN DENMARK

F06.06   Maria Louise Gamborg. CLINICAL DECISION-MAKING IN GERIATRIC EMERGENCY MEDICINE: CURRENT PRACTICE AND TRAINING OBJECTIVES FOR RESIDENTS

F06.07   Aamod Dhoj Shrestha. CAN LAY HEALTH WORKERS HELP INCREASE CERVICAL CANCER SCREENING UPTAKE IN NEPAL?

F06.08   Karin Rosenkilde Laursen. ACUTE HEALTH EFFECTS OF FINE AND ULTRAFINE PARTICLES IN INDOOR AIR - A HUMAN EXPOSURE STUDY AMONG VULNERABLE POPULATION SUBGROUPS

PhD student chairmen

CH.01   Kristina Laugesen. CLINICAL INDICATORS OF IATROGENIC ADRENAL INSUFFICIENCY FOLLOWING DISCONTINUATION OF ORAL GLUCOCORTICOID THERAPY: A SELF-CONTROLLED CASE SERIES

CH.02   Thomas Lassen. EFFECT OF PAROXETINE ON LEFT VENTRICULAR REMODELING IN AN IN VIVO RAT MODEL OF MYOCARDIAL INFARCTION

CH.03   Kristian Juul-Madsen. CLEARANCE OF EXTRACELLULAR AGGREGATED α-SYN THROUGH COMPLEMENT RECEPTOR 3

CH.04   Nanna-Sophie Brinck Andersen. HOST GENETICS, INNATE IMMUNE RESPONSES, AND CELLULAR DEATH PATHWAYS IN POLIOMYELITIS PATIENTS

CH.05   Ted Carl Kejlberg Andelius. CHANGE IN INTRACEREBRAL MEASURES DURING THE FIRST 24 HOURS AFTER HYPOXIA-ISCHEMIA IN HYPOTHERMIC AND NORMOTHERMIC NEWBORN PIGLETS

CH.06   Filomena Iannuzzi. NEW CHALLENGES FOR ALZHEIMER'S DISEASE THERAPY: INSIGHTS FROM APP TYR$_{682}$ RESIDUE

CH.07   Anders Kindberg Boysen. CELL-FREE DNA AND HEPATIC ARTERIAL INFUSION OF OXALIPLATIN PLUS SYSTEMIC CAPECITABINE FOR PATIENTS WITH COLORECTAL CANCER LIVER METASTASES

CH.08   Julie Nelly Christensen. MEGALIN REGULATES PROGRESSION-RELATED EVENTS IN MELANOMA CELLS BY CONTROLLING DIFFERENTIATION STAGE AND EMT STATUS

CH.09   Line Kolding. SSRI EXPOSURE DURING PREGNANCY AND FETAL CARDIAC FUNCTION

CH.10   Mai-Britt Hägi-Pedersen. MULTICENTRE RANDOMISED STUDY OF THE EFFECT OF AN EARLY IN-HOME PROGRAMME (PREHOMECARE) FOR PRETERM INFANTS USING VIDEO CONSULTATION AND SMARTPHONE APPLICATIONS COMPARED WITH IN-HOSPITAL CONSULTATIONS

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CH.12   Mathias Johan Holmberg. GUIDELINE REMOVAL OF ATROPINE AND SURVIVAL AFTER IN-HOSPITAL CARDIAC ARREST

CH.13   Trine Ørhøj Barkholt. BENCH TESTING OF A DRUG-ELUTING BIORESORBABLE MAGNESIUM SCAFFOLD AND COMPARISON WITH POLYMERIC SCAFFOLDS AND METALLIC DRUG-ELUTING STENTS

CH.14   Jacob Gammelgaard Schultz. TERLIPRESSIN INCREASES SYSTEMIC AND LOWERS PULMONARY ARTERIAL PRESSURE IN EXPERIMENTAL ACUTE PULMONARY EMBOLISM

CH.15   Marie Veje Knudsen. FEASIBILITY OF IMPROVING PATIENTS' SELF-MANAGEMENT SKILLS WITHIN A MULTIDISCIPLINARY AND SUPERVISED CARDIAC TELE-REHABILITATION PROGRAMME

CH.16   Kasper Glerup Lauridsen. RESUSCITATION TEAM CHALLENGES DURING IN-HOSPITAL CARDIAC ARREST: A PROSPECTIVE MULTICENTER STUDY

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CH.18   Malou Eva Maria Pinto Barbosa. LONG-TERM FUNCTIONAL OUTCOMES FOLLOWING
               EARLY SECONDARY REPAIR OF OBSTETRIC ANAL SPHINCTER INJURY AND ITS IMPACT
               ON QUALITY OF LIFE

CH.19   Yutao Lu. BLADDER FIBROSIS: EARLY MOLECULAR CHANGES AFTER COMPLETE
               URETHRAL OBSTRUCTION

CH.20   Thomas Falstie-Jensen. DIAGNOSING CHRONIC PERIPROSTHETIC INFECTION OF THE
               SHOULDER WITH 18F-FDG PET CT

CH.21   Alon Illy Schneider Hait. THE GENETIC BASIS FOR RECURRENT HERPES VIRUS
               MENINGITIS - A ROLE FOR DEFECTIVE AUTOPHAGY?

CH.22   Pernille Glahn Wernlund. CGMP IN HEALTHY ADULTS

CH.23   Tea Lund Laursen. IMPROVED METABOLIC LIVER FUNCTION IN PATIENTS WITH
               CHRONIC HEPATITIS C AND ADVANCED LIVER DISEASE FOLLOWING SUCCESSFUL
               SOFOSBUVIR-BASED DIRECT-ACTING ANTIVIRAL THERAPY

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               AND PPD RESPONSE IN HOUSEHOLDS WITH AND WITHOUT TUBERCULOSIS CASES

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               NON-MUSICIANS DURING MUSIC LISTENING

CH.26   Denise Fabienne Happ. EFFECTS OF PREFRONTAL CORTEX AND NUCLEUS
               ACCUMBENS LESIONS ON AFFECTIVE BEHAVIOR IN RATS

CH.27   Saida Said. VOLTAGE CLAMP FLUOROMETRY STUDIES OF GAT-1

CH.28   Casper Schmidt. IMPULSIVITY AND COMPULSIVITY: THE ROLES OF DOPAMINE AND
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CH.29   Maj Ulrichsen. SORTILIN AND SORCS2 IN PERIPHERAL NERVE REGENERATION

CH.30   Simin Berenji Ardestani. EVALUATION OF HIGH PRESSURE NEUROLOGICAL SYNDROME
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CH.84   Anna Sofia Elisabeth Aaby. HEART SKILLS - A HEALTH LITERACY PROFILE OF 161
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Abstracts

Anne Louise
Hansen

SUPER-FATS ELIMINATE STING-ING INFLAMMATION

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The adaptor molecule STING (stimulator of interferon genes) is essential for the immune response against DNA, either from pathogenic sources or aberrant "self"-DNA. The usual immune reaction results in release of type I Interferons (IFN), but excessive release is thought to be a central driver in several devastating interferonopathies, including systemic lupus erythematosus (SLE), Aicardi-Goutières Syndrome (AGS), and STING-associated vasculopathy with onset in infancy (SAVI). However, whether STING can be directly inhibited has until now been unknown.

We recently identified a group of novel bioactive lipids, nitro-fatty acids (NFAs), which directly bind STING, and thus hinder STING activation and dampen type I IFN release. The following methods were employed to assess the actions of NFAs on STING: in vitro cell culture and in vivo infection models, mass spectrometric detection of NFAs and its targets, measurements of type I IFN levels, and protein expression assays.

We identified NFAs as novel, endogenously formed, inhibitors of STING signaling. In conclusion, the potential to inhibit STING signaling and the subsequent type I IFN release might decrease the pathology of several interferonopathies as ASG, SLE, and SAVI.

Fogh-Nielsen
competition

Ole Köhler-
Forsberg

STATIN TREATMENT AND THE RISK OF DEPRESSION

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Background: The effect of statin treatment on the risk of developing depression remains unclear. We aimed to assess the association between statin treatment and depression in a nationwide register-based cohort study with up to 20 years of follow-up.

Methods: We identified all statin users among all individuals born in Denmark between 1920 and 1983. One non-user was matched to each statin user based on age, sex and a propensity score taking several potential confounders into account. Using Cox regression, we investigated the association between statin use and: I) redemption of prescriptions for antidepressants, II) redemption of prescriptions for any other drug, III) depression diagnosed at psychiatric hospitals, IV) cardiovascular mortality and V) all-cause mortality.

Results: A total of 193,977 statin users and 193,977 non-users were followed for 2,621,282 person-years. Statin use was associated with I) increased risk of antidepressant use (hazard rate ratio (HRR)=1.33; 95% confidence interval (95%CI)=1.31-1.36), II) increased risk of any other prescription drug use (HRR=1.33; 95%CI=1.31-1.35), III) increased risk of receiving a depression diagnosis (HRR=1.22, 95%CI=1.12-1.32), but not after adjusting for antidepressant use (HRR=1.07, 95%CI=0.99-1.15), IV) reduced cardiovascular mortality (HRR=0.92, 95%CI=0.87-0.97) and V) reduced all-cause mortality (HRR=0.90, 95%CI=0.88-0.92).

Conclusions: These results suggest that statin users and non-users appear to be equally likely to develop depression, but the depression is more often detected/treated among statin users.

Fogh-Nielsen
competition

Mette Lise
Lousdal

NEGATIVE CONTROLS TO DETECT UNMEASURED CONFOUNDING IN
OBSERVATIONAL STUDIES OF MAMMOGRAPHIC SCREENING

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Estimates of reduction in breast cancer mortality from mammography
screening may be biased due to poor baseline comparability when
comparing participants and non-participants. We used apparently
unrelated causes of death and preventive measures to detect
unmeasured confounding.

We designed a closed cohort study of Danish women invited to a
mammography screening program at age 50-52 years in Copenhagen or
on Funen during 1991-2001. Women had to participate in their 1st
invitation round with a negative result. Based on their 2nd invitation round,
women were divided into participants and non-participants and followed
until death, emigration, or Dec 31, 2014, whichever came first. We
estimated hazard ratios (HRs) of death from breast cancer, other causes
excluding breast cancer, and external causes. We added dental care
participation as a covariate to test for an independent association with
breast cancer death. We adjusted for civil status, parity, age at first birth,
education, income, and hormone therapy use.

Participants had a lower hazard of breast cancer death (HR 0.43, 95%
confidence intervals (CI) 0.30-0.62) compared with non-participants.
Participants also had a lower hazard of death from other causes (HR 0.42,
95% CI 0.39-0.46) and external causes (HR 0.36, 95% CI 0.24-0.54).
Reductions persisted after covariate adjustment. Dental care participants
had a lower hazard of breast cancer death (HR 0.76, 95% CI 0.57-1.01),
independent of mammography participation.

Death from other causes and use of preventive measures may serve as
proxies for general health status. Even after adjustment for several
confounders, negative control associations remained, which could
indicate unmeasured confounding.

O01.01   Jenny Diana Grove

ARTERIAL STIFFNESS AND BLOOD PRESSURE IN PATIENTS NEWLY DIAGNOSED WITH GRAVES' DISEASE COMPARED TO EUTHYROID CONTROLS

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Hyperthyroidism, including Graves' Disease (GD), is associated with increased risk of cardiovascular disease (CVD). The possible mechanisms are not fully understood. Arterial stiffness (AS) is a well established risk marker of CVD. The association between AS and GD remains elusive.

We aimed to investigate whether AS differs in patients newly diagnosed with GD compared to euthyroid controls.

34 patients with GD and 31 age- and sex-matched controls were included. Ambulatory 24h blood pressure (BP), pulse wave velocity (PWV), and central augmentation index (AIX) were measured on the non-dominant arm using the Arteriograph. Office PWV and AIX were measured in the supine position after 10 minutes of rest and 8 hours of fasting using the SphygmoCor Exel. Differences between groups were assessed using multiple regression analysis.

Patients were hyperthyroid and had higher heart rate (HR). Mean arterial BP (MAP) was comparable between groups. Office measurements of PWV were similar among groups, whereas 24h PWV was increased in GD (9.2 m/s (95% CI 8.6-9.6) vs 7.6 m/s (95% CI 7.2-8.0)). This difference remained significant in a multiple regression analysis adjusted for age, sex, 24h HR, 24h MAP, and smoking: GD vs controls 1.0 (95% CI 0.6-1.6) m/s. Brachial and central pulse pressure was significantly increased in GD, both in office and 24h measurements, when adjusting for age, sex, 24h HR, bmi, and smoking. AIX was comparable between groups.

AS is increased in patients newly diagnosed with GD. 24h measurements revealed increased PWV that was undetectable in office measurements. Our data may add a piece to the puzzle of understanding excess cardio-vascular morbidity in hyperthyroidism, including GD.

O01.02   Astrid Johannesson Hjelholt

GENE AND PROTEIN EXPRESSION OF LIPOLYTIC REGULATORS IN CONSECUTIVE HUMAN ADIPOSE TISSUE BIOPSIES AFTER EXPOSURE TO A BOLUS OF GROWTH HORMONE

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Background: Circulating free fatty acids (FFAs) released from triglycerides in adipose tissue (AT) via lipolysis induce insulin resistance in skeletal muscle and liver. Growth hormone (GH) is a potent stimulator of lipolysis,

and serum FFA levels increase in a distinct temporal pattern in response to GH, characterized by a 1 h lag phase and a peak after 3 h followed by a gradual return to baseline. The molecular mechanisms underlying this lipolytic effect remain elusive. We aimed to study gene and protein expression of lipolytic regulators in consecutive human AT biopsies after a GH bolus.

Methods: Nine obese men were studied on two occasions: 1) After an IV GH bolus [GH], and 2) after injection of a GH receptor antagonist (pegvisomant) to block peripheral GH effects [control]. Serum FFAs were measured. Four biopsies from subcutaneous AT were obtained at t=0, t=60, t=180 and t=300, and gene and protein expression of putative lipolytic regulators were studied by RT-qPCR and western blotting.

Results: Serum FFAs increased one hour after GH exposure and peaked after three hours. In AT STAT5b phosphorylation and increased expression of cytokine-inducible SH2-containing protein (CISH), mRNA were recorded, indicative of GH signaling. Furthermore, GH exposure altered gene expression of the regulatory, lipolytic proteins G0/G1 switch gene 2 (G0S2) and phosphatase and tensin homolog (PTEN).

Conclusions: 1) Exposure to a GH bolus elevates serum levels of FFAs in a specific temporal manner. 2) This is accompanied by GH signaling in AT together with altered gene expression of lipolytic, regulatory proteins. 3) We speculate that GH stimulates lipolysis at the level of gene expression.

O01.03   Simon Riis

PERSISTENT MOLECULAR ADAPTATIONS IN HUMAN SUBCUTANEOUS ADIPOSE TISSUE AFTER TEN WEEKS OF ENDURANCE EXERCISE TRAINING IN HEALTHY MALES

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Endurance exercise training (END) induces adaptations in metabolically active organs in order to optimize metabolic function and performance, but adaptations in human subcutaneous adipose tissue (scAT) remain to be investigated. Based on animal studies, we hypothesized that END would increase the expression of proteins involved in lipolysis and glucose uptake in scAT.

To test these hypotheses, nineteen young and healthy males were randomized to either END (TR) or a non-exercising control group (CON). Abdominal subcutaneous fat biopsies and blood were obtained at rest pre and post intervention. By using Western Blotting and PCR, we determined expression of lipid droplet-associated proteins, various proteins involved in substrate metabolism, and transcription of cell-surface G-protein-coupled receptors (GPCRs). Plasma insulin and non-esterified

fatty acids at rest were used to estimate insulin sensitivity in adipose tissue based on adipose tissue insulin resistance index (Adipo-IR).

Adipo-IR improved in TR compared to CON (p=0.03). This was accompanied by increased insulin receptor (IR) protein expression in scAT with a 1.54 (SD 0.79) fold change from pre in TR versus 0.85 (SD 0.30) in CON (p=0.007). Hexokinase II (HK II) and succinate dehydrogenase complex subunit A (SDHA) protein increased in TR compared to CON (p=0.006 and p=0.04, respectively). We did not observe changes in lipid droplet-associated proteins or mRNA levels of GPCR's.

Collectively, END improved adipose tissue insulin sensitivity, which was associated with persistent changes in IR, HKII and SDHA protein expression. We suggest that these adaptations contribute to an improved metabolic flexibility.

O01.04   Estefano Pinilla   EFFECT OF TRANSGLUTAMINASE 2 CONFORMATIONAL MODULATION ON AGE-RELATED CHANGES IN ENDOTHELIAL FUNCTION

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Background and hypothesis: Transglutaminase 2 (TG2) open conformation possesses transamidase activity, which is associated with age-related changes in cardiovascular stiffness and endothelial function. On the other hand, its closed conformation presents GTP binding activity, which plays a role in transmembrane signaling and opening K^+ channels in the vascular smooth muscle (VSM). Therefore, our hypothesis was that the pharmacological induction of TG2 to its closed conformation would be associated with antihypertensive effects and might improve endothelial function.

Methods and results: We performed 'ex vivo' measurements of vessel tension using isometric myographs in small mesenteric arteries from wistar rats and patch-clamp studies in isolated cells. These experiments revealed that induction of the closed conformation of TG2 by LDN-27219 had a direct vasodilatory effect and potentiated acetylcholine (ACh)-induced vasodilation by increasing the VSM sensitivity to nitric oxide (NO) through the opening of large conductance Ca^{2+}-activated K^+ channels (BK_{Ca}); this effect increased with the age of the animals. In contrast, drugs that lock TG2 into its open conformation did not affect vessel tension and decreased the response to ACh. In vivo measurements of blood pressure (BP) revealed that jugular infusion of LDN-27219 decreased BP; an effect that was larger in older animals.

Conclusion: Pharmacological induction of the closed conformation of TG2 leads to improved endothelial function by VSM sensitization to NO through BK_{Ca} channel opening. This effect increases with the age of the animal and could be a potential strategy to restore age-related changes in endothelial function.

O01.05 Sebastian Udholm

LIFELONG BURDEN OF SMALL UNREPAIRED ATRIAL SEPTAL DEFECT: RESULTS FROM THE DANISH NATIONAL PATIENT REGISTRY

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Background: Adult patients with small, unrepaired atrial septal defects (ASD) have higher late mortality than the background population. Moreover, they have an increased risk of pneumonia, atrial fibrillation and stroke. In this nationwide study, we characterise the late natural history of adults with small, unrepaired ASD.

Methods: Using the Danish National Patient Registry, we identified all Danish patients aged 18-65 years and diagnosed between 1953 and 2011 with an unrepaired ASD. All patients were invited for echo-cardiography, spirometry, and a 6-minute walking test. Patients also completed a general health survey for comparison with the general population.

Results: We identified 723 patients with a small unrepaired ASD. Since the time of diagnosis, 182 patients had died, with an average lifespan of 63 years (current average Danish lifespan: 81 years). The most common cause of death was heart failure. Furthermore, ASD patients had a higher burden of chronic disease than the general population (38.2% vs. 26.9%; p=0.005), particularly lung disease (3.6% vs. 0.9%; p=0.008). A total of 153 patients (mean age: 32 years) underwent additional testing. On echocardiography, an open defect was verified in 19.6% (n=30) of the patients, of which half subsequently underwent intervention. Interestingly, 6-minute walking distance was markedly reduced.

Conclusions: Patients with small, unrepaired ASD in adult life have reduced lifespan, more chronic diseases, impaired submaximal exercise capacity, and higher levels of stress than the general population. The current guidelines for intervention and follow-up may need to be reconsidered.

O01.06 Anders Hostrup Larsen

METFORMIN REDUCES MYOCARDIAL OXYGEN CONSUMPTION AND IMPROVES CARDIAC EFFICIENCY IN INSULIN RESISTANT HEART FAILURE PATIENTS

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Background: Heart failure (HF) is characterized by mitochondrial dysfunction and reduced cardiac efficiency (CE = stroke work/oxygen consumption). Metformin has direct mitochondrial effects, and the drug is associated with improved survival in HF registry studies. We investigated the effects of metformin on cardiac oxygen consumption and CE in insulin resistant HF patients.

Methods: In a double-blinded design, 36 insulin resistant HF patients were randomized to 3 months of treatment with metformin (n = 19) or placebo (n = 17) on top of standard HF therapy. All subjects underwent ^{11}C-acetate positron emission tomography (PET), comprehensive transthoracic echocardiography, and cardiopulmonary exercise testing. The primary endpoint was change in CE derived from ^{11}C-acetate PET and echocardiography.

Results: Mean age was 63 ± 9 years; mean ejection fraction (EF) was $37 \pm 8\%$. Compared to placebo, metformin treatment reduced cardiac oxygen consumption with -1.6 mL $O_2 \cdot 100$ $g^{-1} \cdot min^{-1}$ (95%CI: -2.8 to -0.4; p = 0.01) and increased CE with 1.0 mmHg $\cdot$ mL $\cdot$ m$^{-2} \cdot 10^6$ (95%CI: 0.1 to 1.8; p = 0.03), equivalent to a 20% relative CE increase. Stroke work was preserved, -1.8 J (95%CI: -10.9 to 7.3; p = 0.69). Metformin treatment reduced HbA1c with -1.7 mmol/mol (95%CI: -3.0 to -0.3; p = 0.02) and body weight with -2.2 kg (95%CI: -3.6 to -0.8; p = 0.003). EF and exercise capacity (VO_2max) did not differ between groups.

Conclusions: Metformin treatment improved cardiac efficiency through reduced cardiac oxygen consumption in insulin resistant HF patients. These direct mitochondrial, energy-sparing effects of metformin encourage further large-scale investigations in prediabetic HF patients.

O02.01   Katrine Schou Sandgaard

UNDERSTANDING THE IMPACT OF ANTIRETROVIRAL THERAPY INTERRUPTION ON THE IMMUNE SYSTEM IN CHILDREN WITH HIV

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Background: Antiretroviral therapy (ART) interruptions in adults with HIV lead to decreases in CD4^{+}T cells and an increase in mortality. In contrast, the loss of CD4^{+}T cells in children with HIV can usually recover with ART. How exactly the immune system recovers, and which specific T cell receptor (TCR) clonotypes are important is unknown. In this study, we have investigated the impact of ART interruption on critical immune parameters in children with HIV.

Methods: TCR repertoire diversity and specific TCR clonotypes were estimated by Next Generation Sequencing. Thymic output was measured using a mathematical model to combine naive CD4^{+}T-cell proliferation rates with DNA PCR quantification of TCR excision circles. Samples were

drawn from a randomized controlled trial, where one cohort of children with HIV remained on ART, and the other had treatment withdrawn for 48 weeks.

Results: TCR repertoire and TCR clonotype profiles were similar before treatment interruption and 3 years after ART re-introduction. Specific T cell clonotypes were seen to drastically expand and being highly shared between children in response to ART interruption. Both thymic output and T cell proliferation were found to increase rapidly when ART was stopped, both returning to pre-interruption levels when the children re-started ART. No changes were observed in these immune parameters in the HIV children receiving continuous treatment.

Conclusions: Importantly, we found that critical immune parameters returned to pre-interruption levels. This indicates that the high levels of thymic output and specific protective TCR clonotypes in children may be sufficient to reverse the impact of ART cessation.

O02.02   Julie Brogaard Larsen

MANNOSE-BINDING LECTIN-ASSOCIATED SERINE PROTEASE (MASP)-1 AND DISSEMINATED INTRAVASCULAR COAGULATION IN SEPTIC SHOCK

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Background: Septic shock is life-threatening, especially if complicated by disseminated intravascular coagulation (DIC). Complement system activation is part of the dysregulated host response in sepsis. Mannose-binding lectin-associated serine protease (MASP)-1, a part of the complement system's lectin pathway, activates prothrombin and induces fibrin formation in vitro, but its role in the development of sepsis-related DIC has not been investigated previously.

Aim: To explore the association between MASP-1 and coagulation in septic shock.

Methods and materials: We included septic shock patients (n=36) from the intensive care unit. MASP-1 plasma concentrations were analysed with time-resolved immunofluorometric assay. Platelet count, international normalised ratio, fibrinogen, fibrin d-dimer, antithrombin and thrombin generation (Calibrated Automated Thrombogram®) were measured. DIC score was calculated according to the International Society of Thrombosis and Haemostasis.

Results: Low MASP-1 plasma concentration was associated with DIC (median 6,168 ng/ml vs 9,279 ng/ml in patients with DIC vs patients without DIC, p=0.02) and with decreased antithrombin concentration (Pearson's r=0.41, p=0.01). Low MASP-1 plasma concentration was also associated with impaired thrombin generation, which was indicated by lower endogenous thrombin potential and peak thrombin concentration and by prolonged lag time and time to peak.

Conclusion: Low MASP-1 concentration was associated with more pronounced coagulation disturbances in septic shock patients. This

indicates that MASP-1 modulates coagulation in sepsis. Thus, it could be a potential future biomarker or treatment target in sepsis-related DIC.

O02.03   Anne Hald Rittig   DIFFERENCES IN THE MIRNA EXPRESSION PROFILES OF ERYTHRODERMIC MYCOSIS FUNGOIDES AND SÉZARY SYNDROME

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Background: The most prevalent clinical forms of cutaneous T-cell lymphoma are mycosis fungoides (MF) and the more aggressive leukemic variant, Sézary syndrome (SS). Early stage MF comprises patches and plaque skin lesions, whereas advanced stages involve skin tumors and erythrodermic MF (eMF). Due to similar clinical and histologic features, it is difficult to distinguish between eMF and SS. Expression profiles and regulation of microRNA (miRNA) have previously been described in MF and SS. Multiple studies have investigated the use of miRNAs in discriminating clinically similar diseases.

Aim: The main purpose of our study was to investigate if a miRNA expression profile of skin could discriminate eMF from SS. Moreover, we wanted to investigate if the miRNA expression profile of eMF skin is more comparable to the miRNA expression profile of SS skin rather than early-stage disease.

Methods: We collected the specific skin biopsy used for the first early-stage/SS/eMF diagnosis of patients. We extracted the RNA and performed a qRT-PCR-based analysis of 380 human miRNA.

Results: Twenty-seven miRNAs were significantly differentially expressed (fold difference >1.5 and $P < 0.05$) between SS and eMF. Conducting an ANOVA analysis, we found that the differences in the miRNA expression profile of eMF skin were more comparable to that of early-stage disease rather than SS, despite the clinical similarities between eMF and SS.

Conclusions: eMF and SS have clinical similarities, but they are two different disease entities based on the miRNA expression profile. The discriminatory miRNA signature may potentially differentiate between these two disease entities.

O02.04   Asta Linauskas   POSITIVE PREDICTIVE VALUE OF FIRST-TIME RHEUMATOID ARTHRITIS DIAGNOSES IN THE DANISH NATIONAL PATIENT REGISTRY

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Purposes: To assess whether the positive predictive value (PPV) of first-time rheumatoid arthritis (RA) diagnosis registration in the Danish National

Patient Registry increases when data are linked to the RA treatment codes.

Patients and methods: Participants from the Danish Diet, Cancer and Health cohort with at least one RA diagnosis registered at one of the hospitals in the Central Denmark Region and recorded in the Danish National Patient Registry during the period 1977-2016 were identified. Register-based RA diagnoses were verified by scrutinizing medical records against RA classification criteria or clinical case RA. PPVs for 'overall RA' were calculated for two models: first-time RA diagnosis registration ever in the Danish National Patient Registry and first-time RA diagnosis registration ever, where a prescription had subsequently been redeemed for a synthetic disease-modifying antirheumatic drug (sDMARD).

Results: Overall, 205 of 311 first-time register-based RA diagnoses were verified (PPV 61.9%; 95% CI 56.9-67.0). When register-based RA diagnosis codes were linked to RA treatment codes, the PPVs increased substantially: the PPV for 'overall RA' was 87.7% (95% CI 82.5-91.5).

Conclusion: The first-time RA diagnoses in the Danish National Patient Registry should be used with caution in epidemiology research. However, linking registry-based RA diagnoses to the subsequent RA treatment codes increases the probability of identifying true RA diagnoses.

O02.05   Madalina Elena Carter-Timofte   THE ROLE OF RNA POLYMERASE III MUTATIONS IN PATIENTS WITH SEVERE VARICELLA ZOSTER VIRUS (VZV) CENTRAL NERVOUS SYSTEM (CNS) INFECTION

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Varicella Zoster Virus (VZV) is a herpes virus that can cause distinct pathologies in the human host: varicella (chicken pox) upon primary infection and herpes zoster (shingles) following reactivation. In rare cases, the virus may spread to the central nervous system (CNS), where it can cause a wide range of severe complications, such as encephalitis or CNS vasculitis. We hypothesise that, in these patients, host genetics is the main determinant of exacerbated disease manifestations. Using whole exome sequencing (WES) of patients with severe VZV CNS infection, we identified various missense mutations in different sub-units of the innate cytosolic DNA sensor RNA polymerase III (POL III). In order to study the role of POL III mutations in VZV disease pathogenesis, we isolated patient peripheral blood mononuclear cells (PBMCs) and stimulated with the POLIII agonist as well as a broad range of viruses. Functional analysis of patient cells identified an impaired ability to mount an efficient anti-viral immune response in the form of interferon gene expression (IFN) compared to immune cells isolated from healthy controls, in response to the POL III ligand, poly(dA:dT). We also observed increased VZV gene expression in patient cells, suggestive of failing viral control in patient PBMCs. In conclusion, we have provided increasing evidence that defects in POL III confer selectively increased susceptibility to VZV infection. This knowledge may be used in the management of patients in terms of

prophylaxis (vaccination, antiviral treatment) and genetic testing of family members to identify individuals with susceptibility to VZV and increased risk of severe VZV infection in the CNS.

O02.06   Didde Haslund   DOMINANT NEGATIVE INTRACELLULAR RETENTION OF C1 INHIBITOR IN HEREDITARY ANGIOEDEMA

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Hereditary angioedema (HAE) is an autosomal dominant disease characterized by very painful, unpredictable and potentially life-threatening edema attacks. HAE results from variations in the SERPING1 gene encoding C1 inhibitor (C1INH), a serine protease inhibitor (serpin) that plays a critical role in regulation of the contact system. Thus, reduced plasma levels of functional C1INH lead to uncontrolled activation of the contact system, triggering high levels of bradykinin and increased vascular permeability. Most HAE type I patients are heterozygous carriers of an HAE-causing SERPING1 variant, but present with C1INH levels that are lower than the expected 50% of the normal level. Until now, mechanisms explaining this phenomenon have not been described. Here, we show that C1INH protein encoded by a subset of HAE-causing SERPING1 alleles affects secretion of normal C1INH protein in a dominant negative fashion by triggering formation of protein-protein interactions between normal and mutant C1INH. Such interactions lead to formation of larger intracellular C1INH aggregates that are trapped in the endoplasmic reticulum (ER), thus inducing cellular retention and reduced secretion of normal C1INH protein. Notably, intracellular aggregation of C1INH and ER abnormality are observed in fibroblasts from a heterozygous carrier of a dominant negative SERPING1 gene variant, but the condition can be ameliorated by viral delivery of the SERPING1 gene. Collectively, our data link abnormal accumulation of serpins, a hallmark of serpinopathies, with dominant negative disease mechanisms that affect C1INH plasma levels in HAE type I patients and pave the way for new genetic treatments of HAE.

O03.01   Rasha Hyder   PASSIVE NEUROMAGNETIC RESPONSES AS BIOMARKERS OF LANGUAGE PROCESSING IN THE BRAIN

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Assessing the brain activity related to language comprehension is required in a range of situations (e.g. clinical or developmental assessment). Particularly in cases when the subjects' cooperation with instructions cannot be guaranteed (neurological patients), a protocol is needed that could be independent from overt attention and behavioural tasks. In Study 1 of this dissertation, we designed a novel paradigm, which allows quantifying a range of neurolinguistic processes in the absence of directed attention towards sound stimuli and without relying on any overt behavioural responses by recording the brain's responses to different speech sounds with carefully manipulated linguistic properties. This procedure is carried out using magnetoencephalography combined with individual MR images to guide the source reconstruction of the MEG signals. This paradigm has been tested in healthy young participants, who were presented with a non-attend sequence of speech stimuli while focusing on watching a silent movie. The results of the first study in healthy young participants validated the usability of our proposed paradigm for an objective assessment of language functions in clinical populations and unresponsive participant groups. Currently, this paradigm is being applied in healthy elderly participants to explore the influence of aging on human cortical activations related to language processing, before it will be applied to patients diagnosed with Parkinson's disease to investigate possible alterations in their cerebral processing of language. We will discuss implications of this approach to the study of neurolinguistics processing in healthy ageing and in neurological conditions.

O03.02   Alexander Gramm Kristensen   NERVE EXCITABILITY FINDINGS IN NEUROPATHIC TYPE 2 DIABETICS

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The aim of this study is to elucidate the changes in distal nerve axons in diabetic polyneuropathy (DPN) and correlate the findings with clinical neurophysiologic measures. Nerve excitability testing (NET) is a method of testing the function of axonal ion channels.

We included 128 patients and 50 controls, prospectively. All participants were examined with Nerve Conduction Studies (NCS) on three motor (tibial, peroneal and median) and three sensory (sural, bilateral and median) nerves. Motor NET was performed on 128 patients, sensory NET on 76. All controls had both motor and sensory NET.

The patients were divided into two groups, patients with neuropathy (DPN+) and patients without neuropathy (DPN-). Motor NET showed significant differences in several depolarizing parameters in the DPN+

group compared with the healthy controls (e.g. the measure "threshold electrotonus depolarizing for 10-20 ms", p=0.00574). These parameters correlated with NCS measures used in the diagnosis of DPN. Sensory NET showed significant differences in depolarizing and hyperpolarizing measures across the three groups and also correlated with diagnostic NCS measures.

While significant, the differences between these three groups are too slight to signify any functional changes for the motor nerves. The changes in sensory nerves are slightly larger, but due to the varied composition of sensory nerve fibers, it is hard to say if the changes are due to ion channel functionality or simply changes in the relative number of certain sensory nerve fiber types.

These findings, combined with findings from our first study, suggest the nerve fibers in DPN are damaged at the nerve terminals or the cell body.

O03.03   Majken Thomsen   IMAGING SYNAPTIC DENSITY IN RAT AND PIG BRAIN USING [11C]UCB-J PET

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Synapses facilitate neuronal signaling and are vital for neuronal function. Reduced synaptic density is linked to neurodegenerative diseases. A novel positron emission tomography (PET) tracer, [11C]UCB-J, binds to the synaptic vesicle 2A (SV2A) transporter, located in presynaptic secretory vesicles in the brain, and allows, for the first time, the assessment of synaptic density as a marker of synaptic function in vivo.

Here we investigate the potential of [11C]UCB-J as an in vivo biomarker of regional cerebral synaptic function in naïve rat (n=6) and pig (n=6) brain. We performed blocking experiments by injecting levetiracetam (LEV), an antiepileptic SV2A ligand, iv prior to the [11C]UCB-J PET scan in order to obtain specific binding. We also examined the ability of [11C]UCB-J to detect synaptic loss in rodent models of acute Parkinsonism and Huntington's disease induced using 6-hydroxydopamine (6-OHDA) (n=3), and quinolinic acid (QA) (n=6), respectively.

The brains showed high and fast [11C]UCB-J uptake in both species. The volume of distribution in the striatum was 38-54 in rat and 20-38 in porcine brain, and specific binding was observed when blocking with LEV (20-30 and 60 mg/kg in pigs resulted in 65% and 90% occupancy, respectively, while 100 mg/kg in rats resulted in 82% occupancy). In rats uni-laterally injected with 6-OHDA or QA, we detected synaptic losses of 7.5% and 50%, respectively, in the ipsilateral compared to contralateral side.

[11C]UCB-J PET is a promising tool to non-invasively image synaptic density and to detect loss of synaptic function induced by injection of

neurotoxins in vivo. It may provide a means for assessing future neuro-protective strategies.

O03.04 Martin Langeskov Christensen

CAN AEROBIC EXERCISE IMPACT DISEASE PROGRESSION IN MULTIPLE SCLEROSIS?

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Background: Multiple sclerosis (MS), a chronic disease of the central nervous system, is characterised by accelerated brain atrophy, impaired cognitive performance and reduced aerobic capacity, which relate to disease progression. Progressive aerobic exercise (PAE) represents a promising approach towards preserving or restoring these symptoms.

Aim: To investigate how PAE affects total brain volume, specific brain regions, blood biomarkers, cognitive performance and clinical measures of disease progression in MS.

Methods: This study was a 24-week randomised controlled crossover trial, including an Exercise (n=43, 24 weeks of PAE followed by self-guided physical activity) and Waitlist group (n=43, 24 weeks of habitual lifestyle followed by PAE). Assessments at 0, 24 and 48 weeks included magnetic resonance imaging (MRI: lesion load, global brain volume, regional brain volumes, cortical thickness), cognitive performance (The Brief Repeatable Battery of Neuropsychological Tests), blood samples (serum neurofilament light) and clinical measures (e.g. aerobic and walking capacity).

Results: After 24 weeks, 72 participants were included in a per protocol analysis of cognitive performance. This study failed to demonstrate any beneficial effects on cognitive performance in MS after 24 weeks of PAE. However, the aerobic capacity increased significantly in the Exercise group vs. the Waitlist group.

Perspectives: MRI and blood sample results will be ready shortly. In case of positive findings, this will provide the first human evidence for a disease-modifying effect of PAE in MS. Thus, the project has the potential to change clinical practice and current guidelines on how to treat MS.

O03.05 Lasse Reimer

AGE-RELATED SULFOXIDE-CONTAINING METABOLITES STIMULATE AGGREGATION AND SPREADING OF NEURODEGENERATORY PROTEIN α-SYNUCLEIN

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Synucleinopathies are a group of neurodegenerative diseases, including Parkinson's disease, multiple system atrophy and dementia with Lewy bodies, with the common characteristics of accumulation of intracellular inclusions in the central nervous system largely made up from aggregated

α-synuclein (α-syn). α-syn itself is a small natively unfolded monomeric protein that in the event of disease is converted into large insoluble disease-causing β-sheet-rich aggregates. Unravelling the underlying events causing this transformation is of great interest to the research field. The etiology of synucleinopathies are largely unknown, but the incidence increases steeply with age. Another age-related event is the accumulation of oxidized species, such as methionine sulfoxide. In this study, we show that exposure of α-syn to sulfoxide-containing metabolites, dimethyl sulfoxide and methionine sulfoxide greatly accelerates in vitro aggregation of α-syn into large insoluble β-sheet-rich fibrils. Addition of these fibrils to cells initiates aggregation of endogenous cellular α-syn, proving the potency of the aggregates. These findings are supported by increased aggregation-specific immunodetection of α-syn both in vitro and in SH-SY5Y cells exposed to sulfoxide-containing metabolites. An enlarged particle size of α-syn was also confirmed by dynamic light scattering. We are currently assessing the aggregation-promoting effect of oral dimethyl sulfoxide treatment in a transgenic α-syn mice model. Our results suggest a novel mechanism, whereby exposure of age-related sulfoxide species play a role in the conversion of monomeric α-syn into larger complexes associated with synucleinopathies.

O03.06   Rajath Pillai   FEASIBILITY AND RELIABILITY OF INTRAORALLY-EVOKED 'NOCICEPTIVE-SPECIFIC' BLINK REFLEX

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The "nociceptive-specific" blink reflex (nBR) test has been used to assess the trigeminal nociceptive processing in extraoral and intraoral nerve damage, and the nBR responses have been elicited by extraoral electrical stimulation, regardless of the site of nerve damage. The aims of this study were to test the feasibility of nBR on intraoral stimulation (nBR$_I$), to compare nBR$_I$ with extraoral stimulation (nBR$_E$), and to assess the intrarater and interrater reliability of nBR$_I$ for the maxillary (V2) and mandibular (V3) branches of trigeminal nerve. In 16 healthy participants, nBR was elicited in two extraoral and two intraoral sites by two operators, and repeated by one operator to test the interrater and intrarater reliability. The outcome variables were: pinprick pain thresholds (I$_P$), ipsilateral and contralateral nBR R2 responses (R2i, R2c), and pain scores on a 0-100 numerical rating scale for stimulus intensities from 100% to 400% of I$_P$. Intraclass correlation coefficients (ICC) were used to assess the reliability. Significantly higher pain scores were seen with increasing stimulus intensity, corresponding to the significant increase in R2 values on the V2, but not V3 (V2: $P < 0.004$, V3: $P > 0.391$). No significant differences were seen in the I$_P$ and pain scores between nBR$_E$ and nBR$_I$ for both the branches ($P > 0.386$). However, the R2i, R2c measures were significantly lower on nBR$_I$ for both the branches ($P < 0.014$). Overall, the ICCs of nBR$_I$ were higher for the V2 branch with the V3 branch showing poor intrarater and interrater

reliability. In conclusion, intraoral V2 sites can be used to elicit nBR, which may be clinically useful when assessing nerve damage in the upper jaw.

O04.01 Maja Halgren Olsen

SOCIOECONOMIC INEQUALITY IN HEAD AND NECK CANCER SURVIVAL - A POPULATION-BASED STUDY FROM DAHANCA

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Background: Nations with free access to health care observe a large and increasing socioeconomic inequality in survival after cancer, which is particularly pronounced for Head and Neck Squamous Cell Carcinoma (HNSCC). We investigate where in the trajectory of HNSCC the socio-economic inequality arises.

Materials and methods: Clinical information on all patients (n=15 248) diagnosed with HNSCC between 1992 and 2014 in Denmark, born >1920, aged ≥30 years at diagnosis, and registered in the nationwide and population-based clinical database DAHANCA were linked to nationwide, administrative registries to obtain information on socioeconomic factors and vital status. By fitting Cox proportional hazards and logistic regression models, we estimated the effect of socioeconomic position on HNSCC survival and a wide spectrum of prognostic and life-style factors.

Results: The hazard ratios for overall survival and the odds ratios for: advanced stage at diagnosis, not having a HPV-positive oropharynx cancer, not being curatively intended treated, having more than one comorbid disease, and being a smoker at diagnosis were increased among patients with shorter education, lower income, and those living alone or in rural areas.

Conclusion: This large-scale population-based study reveals significant socioeconomic differences in the most important determinants for HNSCC survival, which could possibly explain a considerable part of the excess burden of HNSCC deaths among deprived patients. The study stresses that it is of major importance to take into account differences in sub-sites, stage at diagnosis and HPV status in order to correctly estimate and monitor socioeconomic inequality in HNSCC survival.

O04.02 Simon Skouboe

FIRST CLINICAL REAL-TIME MOTION-INCLUDING TUMOR DOSE CALCULATION DURING RADIOTHERAPY DELIVERY

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Background: Respiratory-induced tumor motion during radiotherapy treatments for cancer can deteriorate the delivered dose. Here, we present the first real-time calculation of the dose while it is being delivered to a moving tumor. It provides a powerful tool for quality assurance (QA) and treatment adaptation.

Methods: In-house developed software, DoseTracker, was created to calculate the dose to a moving tumor. Seven patients treated with radiotherapy for hepatocellular carcinoma or metastases in the liver had gold markers implanted near the tumor. During treatment, the tumor motion was determined by X-ray imaging of the gold markers. The tumor positions and radiotherapy machine parameters were live-streamed to DoseTracker, which calculated the tumor dose in real-time. Post-treatment, the tumor dose deficit calculated in real-time by DoseTracker was compared with non-real-time, but more accurate, verification calculations.

Results: DoseTracker calculated the tumor dose at a frequency of 9.5 Hz using a mean of 3194 calculation points. The dose distributions were in good agreement with the post-treatment validation calculations, both spatially and temporally. DoseTracker calculated the reduction of the tumor dose coverage (difference in the so-called D95) caused by motion with a root-mean-square error of 2.0%-points.

Conclusions: The world's first clinical real-time motion-including tumor dose calculation during radiotherapy was demonstrated. This milestone marks a significant step towards real-time monitored radiotherapy with important potential applications of real-time QA, e.g. halting the treatment in case of gross deviations from the planned treatment.

O04.03   Trine Block Mattesen

MOLECULAR SUBTYPING AND PROGNOSTICATION OF COLORECTAL CANCER FROM FORMALIN-FIXED PARAFFIN-EMBEDDED TISSUE USING GENE EXPRESSION SCORES IMPUTED FROM DNA METHYLATION

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Background: Colorectal cancer (CRC) is characterized by marked inter-tumor heterogeneity, both molecularly and clinically. Patient stratification using RNA expression based subtyping has shown promise to resolve the heterogeneity and guide future precision medicine. However, it requires high quality RNA, which cannot be obtained from clinically collected formalin-fixed paraffin-embedded (FFPE) samples. Consequently, it is not applicable to most CRC patients.

Aim: To establish a subtyping approach based on DNA methylation profiles, which can be obtained from both fresh and FFPE tissue, and use this to improve patient prognostication.

Methods: Using paired genome-wide expression and DNA methylation profiles from 394 CRCs, we established, for each gene, a set of 200 genomic loci whose methylation levels correlated closely with expression. Next, we devised an approach, "methCORR", which uses only DNA methylation data to impute gene expression.

Results: The imputed gene expression profiles robustly reproduced real RNA expression profiles and enabled robust stratification of two fresh (n=231, n=203) and two FFPE CRC cohorts (n=113, n=56) into two molecularly distinct subtypes. Both the cancer cells and the immune and stroma cell types in the microenvironment distinguished the subtypes. The biological characteristics associated with metastatic dissemination were unique to each subtype. In accordance, methCORR-derived subtype-specific prognostic biomarkers were better at predicting outcome than universal prognostic biomarkers and TNM staging.

Conclusion: methCORR enables analysis of fresh and FFPE tissue, which facilitates subtyping and enables improvement of prognostication.

O04.04   Martin Fogtmann   THE CRISPR-CAS9 MINIPIG - A TRANSGENIC TOOLBOX PIG TO PRODUCE
         Berthelsen   SPECIFIC GENOME EDITING IN DESIGNATED TISSUES

M.F. Berthelsen

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The aim of the project is to generate a toolbox pig model. This is being done because the pig probably is the best non-primate model in trans-lational medicine. Unfortunately, pig models have proven difficult to produce. The two main complications have been the cloning of viable pigs and that just a few genes are altered, which is rarely sufficient to induce the desired disease. Especially, models based on multiple genetic modifications of the pig genome, e.g. cancer, are challenging to generate. This was changed with the development of the CRISPR-Cas9 technology, which made it possible to perform multiple in vivo gene editing.

We have cloned an inducible Cas9 expressing minipig and have obtained healthy F1 offspring. The Cas9 expression is mediated by a ubiquitous promotor, which also co-expresses fluorescent proteins for expression analysis. Transgenic Cas9 expression is observed in all major organs. The genetic design was validate in vitro by successful gene editing in cells obtained from the transgenic pig.

To validate the model, lung cancer has been induced in nine pigs by alteration of three or four key genes, respectively, known from human lung cancer. The pigs are being followed by PET/CT scanning. Preliminary data indicates abnormalities/cancer initiation in the pigs six months after induction.

In conclusion, an inducible Cas9 expressing minipig allows rapid gene editing to study different scenarios of human cancer in a pig model. The development of the Cas9 pig will extend the variety of pig disease

models, both to generate a model of lung cancer as proposed, but also models for other cancers, metabolic, cardiovascular, and neurological diseases.

O04.05 Sarah Østrup Jensen

NOVEL DNA METHYLATION BIOMARKERS SHOW HIGH SENSITIVITY AND SPECIFICITY FOR BLOOD-BASED DETECTION OF COLORECTAL CANCER - A CLINICAL BIOMARKER DISCOVERY AND VALIDATION STUDY

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Background: Screening for colorectal cancer (CRC) using Fecal Immuno-chemical Testing (FIT) can be life-saving because early detection greatly increases the chances of successful treatment. However, FIT may not be the best approach; first, because population acceptance is low due to unpleasantness of fecal sampling; second, because bowel tumors bleed only intermittently, which limits FIT sensitivity. Development of a blood-based screening approach may alleviate these problems.

Aim: To develop and validate novel blood-based biomarkers to achieve high patient compliance, sensitivity and specificity.

Methods & materials: Three CRC-specific DNA methylation biomarkers were identified using a genome-wide discovery strategy based on DNA methylation arrays from >4,000 samples. Digital droplet PCR was used to detect the biomarkers in two large and independent plasma cohorts of CRC patients and colonoscopy-confirmed healthy controls. Cohort 1 included 113 CRCs and 86 controls. Cohort 2 included 143 CRCs and 91 controls.

Results: In cohort 1, a positive test was observed in 88/113 CRCs (78% sensitivity) and only in 1/86 controls (99% specificity). Sensitivity was 62%, 81%, 77% and 86% for stage I-IV, respectively. The results were confirmed in cohort 2, which showed a sensitivity of 90% (92%, 88%, 97% and 90% for stage I-IV, respectively) and a specificity of 99%.

Discussion: We identified three DNA methylation markers with superior performance in plasma compared to FIT. To establish the potential of our test in a screening population, we will evaluate their performance in plasma samples collected from >40,000 asymptomatic individuals enrolled in the Danish national CRC screening program.

O04.06 Stine Overvad Fredslund

ADJUVANT TREATMENT OF BREAST CANCER RELATED TO CARDIOTOXICITY AND DYSFUNCTIONAL ENDOTHELIUM: THE ABCDE STUDY

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Background: Adjuvant treatment of breast cancer (BC) patients is associated with several unfavorable medical conditions, potentially leading to cardiovascular disease and/or the metabolic syndrome (MetS)

The aim of our study was to investigate metabolic late effects of adjuvant treatment in premenopausal and postmenopausal BC patients.

Material and Methods: 20 postmenopausal and 13 premenopausal women with early stage BC were examined prior to, immediately after, and one year after ended chemotherapy. For each patient, we included one healthy control matched by age and menopausal status.

24-hour blood pressure, hs-CRP, lipid profile, glucose metabolism, and anthropometrics (incl. DEXA scans) were determined.

Results: We found several significant changes in parameters related to cardiovascular and metabolic disease. Waistline increased significantly in both premenopausal ($p=0.008$) and postmenopausal women ($p=0.03$). In premenopausal women, we also found a significant increase in body fat ($p=0.01$), triglycerides ($p=0.03$), and diastolic blood pressure ($p=0.04$) from baseline to end of follow-up. In postmenopausal women, HDL cholesterol decreased significantly ($p=0.05$). At baseline, BC patients were not significantly different from healthy controls.

Conclusion: Several parameters related to MetS and cardiovascular disease changed significantly during chemotherapy. After one year, several key parameters remained pathologically changed. Premenopausal women were especially prone to develop these unfavorable changes.

To reduce the risk of MetS in patients with BC, lifestyle interventions and more strict metabolic control may be a useful approach.

O05.01   Mads Sørensen Larsen

EFFECTS OF PROTEIN INGESTION PRIOR TO TRAINING LOW

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Background: Training with low carbohydrate availability (training low) promotes the physiological adaptations to endurance training, but may influence net muscle protein balance negatively. Thus, repeated exposure to this training strategy may lead to loss of muscle mass and potentially impair physical performance. Studies suggest that ingestion of protein before commencing 'training low' does not attenuate the metabolic benefits of this strategy and at the same time provides substrate for muscle protein synthesis.

Purpose: We investigated how ingestion of protein before 'training low' influences muscle protein turnover and muscle signaling during exercise and recovery.

Methods: In a crossover design, 9 endurance athletes ingested either a protein (PRO) supplement (~35g) or a non-caloric placebo (PLA) before completing a 90 min bike ride with reduced glycogen stores. Muscle protein metabolism were assessed by using stable isotope tracer techniques, continuous blood sampling and muscle biopsies before, immediately, 1 and 4h after exercise.

Results and conclusion: Phosphorylation of mTOR was increased immediately one hour after exercise in PRO vs PLA ($p<0.05$). However, this did not translate to enhancements in protein synthesis rates ($p>0.05$). The mean protein net balance for both PLA and PRO was negative throughout the day with no difference between treatments (nmol/[100ml* min]: -6.7 ± 1.2 PLA & -5.6 ± 1.6 PRO, $p>0.05$). Our results suggest that protein ingested prior to 'training low' support a stabilization of blood glucose levels and thus energy availability via gluconeogenesis during exercise, more so than promoting muscle protein remodeling/synthesis.

O05.02   Yulia Olsen   AIRBORNE ALTERNARIA AND CLADOSPORIUM SPORES AND ASTHMA IN DENMARK

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Airborne Alternaria and Cladosporium spores contain aeroallergens associated with increased asthma severity in sensitized persons. We provide the first report of Alternaria and Cladosporium air spores concentrations for the Western part of Denmark (Viborg) and compare them with the concentrations routinely monitored in Copenhagen. During four studied years (2012-2015), clinically relevant concentrations of airborne Alternaria spores occurred more often and with larger values in western Denmark than in eastern Denmark. In 2015, the remote sources in the Baltics, northern Poland, and southern Sweden were associated with increased Cladosporium concentrations at both stations, whereas peak concentrations in Viborg were affected by the yield from the local sources situated in eastern Jutland. We found that distant sources located in northern Germany, northern/central Poland, and southern Sweden are possible contributors to the higher Alternaria concentrations at both stations. However, higher airborne Alternaria spore concentrations in Viborg support the hypothesis that local sources, such as grain fields during harvesting, cause the main load of airborne Alternaria in Denmark. We demonstrated that airborne Alternaria and Cladosporium spore concentrations can reach higher values in western Denmark. This implies that monitoring solely in Copenhagen is not sufficient and that the quality of the daily national report would benefit from an additional routine monitoring in Viborg. Further investigations are needed to quantify the

contribution from the remote and local sources for the spore air concentrations to model and develop a warning system for sensitized individuals.

O05.03   Julie Lyngsø   DOES LOW-TO-MODERATE ALCOHOL CONSUMPTION IMPAIR SUCCESS IN FERTILITY TREATMENT? RESULTS FROM A DANISH COHORT STUDY

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Background: Alcohol consumption is common among women of reproductive age. Yet, despite one in six couples struggle with infertility, it is still unclear whether low-to-moderate levels of alcohol consumption and alcohol binge drinking impair success in fertility treatment. Therefore, we aimed to investigate whether a weekly average alcohol intake and binge drinking affect the clinical pregnancy and live birth rate during fertility treatment.

Methods: A cohort study with prospectively collected exposure data. We included 1,708 women/couples undergoing fertility treatment at the fertility clinic at Aarhus University Hospital in 2010-2015. Female alcohol intake was self-reported and categorized as total weekly alcohol consumption (0, 1-2, 3-7 and >7 drinks/week). Outcome measures were clinical pregnancy and live birth in consecutive treatment cycles obtained from the Danish national health registries.

Results: Compared to a low average alcohol intake of 1-2 drinks/week, the adjusted odds ratios for achieving a live birth among abstainers, 3-7 and >7 drinks/week were 0.67 (95%CI: 0.31;1.44), 1.31 (0.65;2.63) and 1.12 (0.22;5.62), respectively, among women initiating the first IUI treatment cycle, and 1.13 (0.84;1.51), 1.04 (0.75;1.45) and 1.22 (0.58;2.59), respectively, among women initiating the first IVF/ICSI treatment cycle. The odds of achieving a live birth in the first IUI or IVF/ICSI cycle was unrelated to the number of binge drinking episodes in the month preceding baseline.

Conclusion: Low-to-moderate weekly alcohol drinking and binge drinking were not associated with neither clinical pregnancy nor live birth rates among women and couples receiving fertility treatment.

O05.04   Jonas Boysen Fynboe Ebert   FAST ACCESS TO OUT-OF-HOURS TELEPHONE TRIAGE BY AN EMERGENCY ACCESS BUTTON: A RANDOMIZED CONTROLLED TRIAL EXPLORING PATIENT SATISFACTION, FEELING OF SAFETY, RELEVANCE AND FREQUENCY OF USE

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Objectives: Out-of-hours (OOH) services are intended to help citizens in urgent need of healthcare outside normal office hours. All citizens must wai for their turn in the telephone waiting line, even if they perceive the health problem as highly urgent or life threatening. In these cases, pro-longed waiting time might cause harm. We have tested an emergen-cy acces button (EAB) that allowed callers to bypass the telephone waiting line if they perceived their health problem as severe. We aimed to investingate the frequency of use, the relevance of use and if the EAB would increase the citizens feeling of safety and satisfaction with the OOH service.

Design: Randomized controlled trial. Questionnaires answered by OOH service callers, questionnaires answered by OOH service triage professionals.

Setting: OOH services in two major healthcare regions.

Participants: OOH service callers contacting from September to mid-December 2017.

Results: 3 percent of callers used the EAB. Triage professionals found that only 22-30% of contacts that had used the EAB were "not relevant". EAB users were more satisfied with the OOH services and felt more safe that EAB non-users.

Conclusion: The emergency access button offers a novel way of providing fast access to OOH medical advice to citizens with urgent health care needs. Low frequency of use combined with a reported 22-30% frequency of irrelevant use suggests a level of misuse lower than 1% for the general population. As a result of this study, OOH services in Copenhagen have decided to implement the EAB into its daily services.

O05.05   Mads Riiskjær   BOWEL ENDOMETRIOSIS SYNDROME: A NEW SCORING SYSTEM FOR PELVIC ORGAN DYSFUNCTION AND QUALITY OF LIFE

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Background: Endometriosis is a heterogeneous disease with extensive variation in anatomical and clinical presentation, and symptoms do not always correspond to the disease burden. Current endometriosis scoring systems are mainly based on anatomical and surgical findings and do not take the patients' symptoms into account. The aims of the study were to develop and validate a simple, reproducible score for clinical evaluation of the severity of Bowel Endometriosis Syndrome (BENS) based on patient-reported symptoms.

Methods: The score was developed and validated from a cohort of 525 women with medically or surgically treated bowel endometriosis. Patients filled in questionnaires on pelvic pain, quality of life and urinary, sexual and bowel function. Items were selected for the final score using clinical and criteria and mulivariate analysis. Individual score values formed the BENS score, which was divided into "no BENS," "minor BENS," and "major BENS." Internal and external validation was performed.

Results: The six most important items were "pelvic pain", "use of analgesics", "dyschezia", "straining to urinate", "faecal urgency", and "satisfaction with sexual life". The range of the BENS score (0-28): no BENS, minor BENS, major BENS. External validation showed a significant association between BENS score and QoL ($p=0.0001$).

Conclusion: The BENS scoring system is the first endometriosis classification system to be based directly on the symptomatology of the patient. It offers the opportunity to compare clinical effects of medical and surgical treatment in an easily applicable manner. Validation in other languages will promote comparison of treatments and results across borders.

O05.06   Marzieh Katibeh   MODELLING AND EVALUATION OF A COMMUNITY-ORIENTED MHEALTH-BASED SCREENING AND PROMOTIONAL PROGRAM FOR IMPROVING EYE HEALTH IN IRAN

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Blindness is a global health issue and the majority of causes are still avoidable. This PhD project aims to establish a screening program to improve eye health in Iran.

We initially designed the screening program and mHealth tool via a participatory qualitative study. Then, we evaluated the program through a community trial in 4 districts of Iran. Primary health care workers (PHCWs) were trained to collect data and test visual acuity (VA) in the field. Participants with a VA≤20/40 in either eye were referred to an eye doctor. An ophthalmic assistant conducted retinal imaging at the local PHC units. Retinal specialists in a central reading centre reviewed retinal images and, if necessary, made further referral plans.

The community trial had three main arms: 1) mHealth intervention: using mobile application for data collection and screening tests, 2) Conventional intervention: using paper-based forms, Snellen chart for measuring VA and fundus photography equipment for fundus imaging, and 3) Control arm: using paper-based forms, no further intervention.

Of 3312 residents aged ≥50 who were invited to this program, 92.1% in the control, 78.4% in the mHealth and 57.7% in the conventional group agreed to participate. Sex, literacy and employment had association with the coverage of the mHealth intervention.

Around one third of participants had no previous ophthalmology (28%) or optometry (34%) exam. The referral rate among those who fulfilled the screening program was 59.2% (46.1% based on VA and 13.1% based on retinal images). These results show a high level of need for eye care among the studied population, which can be effectively tested and communicated by PHCWs using the mHealth tool.

P01.01   Nicklas Vinter   TWENTY-YEAR TIME TRENDS IN USE OF EVIDENCE-BASED HEART FAILURE DRUG THERAPY IN DENMARK

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Aims: European guidelines for heart failure (HF) have been updated repeatedly, with a continuous incorporation of new evidence from landmark studies. We aimed to explore the time trends in utilisation of pharmacological treatment for HF and in dispensing the recommended dosages among patients discharged with a first-time diagnosis of HF.

Methods and Results: We performed a historical cohort study of all patients with a first-time HF diagnosis from 1997 to 2015 identified in the Danish National Patient Registry. The patients were followed for dispensed treatment for HF, including angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), beta-blockers, mineralocorticoid receptor blockers (MRAs), digoxin, and diuretics. Furthermore, we estimated the proportion of patients receiving the recommended target dosages 1 year after the diagnosis. We noted an increase in utilisation correlated with publications of landmark studies, with the most marked increase pertained to beta-blockers. Among patients diagnosed in 2015, approximately 2 out of 3 received ACEIs/ARBs and beta-blockers, respectively. Less than half of the patients redeeming prescriptions for ACEIs, ARBs, beta-blockers, or MRAs received the recommended target dosages.

Conclusion: The utilisation of pharmacological therapy for HF appears to be correlated with the publications of landmark Phase III clinical trials. However, a high proportion of patients do not receive the recommended target dosages. Despite improvements over time, a substantial gap appears to remain between the evidence-based guideline recommendations and the pharmacological care received by HF patients in routine care.

P01.02   Lejla Islamagic   BIOMECHANICAL PROPERTIES OF CORMATRIX COMPARED WITH NATIVE MITRAL VALVE LEAFLETS

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Background: In severe primary mitral valve regurgitation, valve repair is preferred over replacement. CorMatrix (porcine small intestinal submucosa extracellular matrix) has been considered as a new mitral leaflet patch material due to the promising results conducted in low-pressure systems. Studies performed using the material in a high-pressure system (left ventricle) show conflicting results. Thus, the use of the material here is still subjected to significant uncertainties. This might be due to

different thickness-specific mechanical properties of CorMatrix compared with those of the native mitral leaflets.

Objectives: To characterize the biomechanics of the two native mitral leaflets and CorMatrix (2-layer and 4-layers) at physiological frequencies to investigate differences in behaviour.

Methods: Porcine hearts will be obtained from an abattoir. Samples from the anterior and posterior leaflets will be excised in radial and circumferential directions. All leaflet and CorMatrix samples will be cut with a puncher and mounted in the Bose ElectroForce 3200. Dynamic mechanical testing and a uniaxial test until rupture will be performed to determine properties such as elasticity, loss and storage modulus.

Results: The model has been tested and proven functional in a pilot study. Results are pending.

Perspective: By characterizing the biomechanics of the four sample groups, we wish to investigate if CorMatrix possess properties that resemble those of the native leaflets. This will aid in clarifying what biomechanical properties are required of biological graft tissue for mitral valve repair and if CorMatrix is suited as a surgical repair material.

P01.03   Pernille Gro Thrane

15-YEAR FOLLOW-UP OF THE DANISH ACUTE MYOCARDIAL INFARCTION 2 (DANAMI-2) TRIAL - PRIMARY PERCUTANEOUS CORONARY INTERVENTION VERSUS FIBRINOLYSIS IN ST-ELEVATION MYOCARDIAL INFARCTION

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Background: The landmark DANAMI-2 study showed that primary percutaneous coronary intervention (pPCI) was superior to fibrinolytic therapy in patients with ST-elevation myocardial infarction (STEMI).

The study found that pPCI-treated patients had reduced 30-day risk of the composite endpoint of death, re-infarction and stroke compared to patients treated with fibrinolysis. This study will investigate whether pPCI reduces nonfatal cardiovascular events and long-term mortality after 15 years of follow-up.

Hypothesis: We hypothesize that pPCI-treated patients have reduced rate of the composite endpoint of death and myocardial re-infarction compared to fibrinolytic-treated patients.

Methods: 1,572 STEMI patients were enrolled: 1,129 patients at referral hospitals and 443 patients at invasive centers. The patients enrolled at referral hospitals were randomly assigned to either transportation to pPCI at an invasive center or on site fibrinolytic therapy. Patients will be followed up for at least 15 years after randomization. The primary outcome will be a composite of all-cause mortality and myocardial re-

infarction. Outcome information will be obtained through the Danish National Patient Registry.

Perspective: This study will be the first to provide a very long-term perspective on death and cardiovascular events when comparing pPCI with fibrinolytic therapy in STEMI patients. This knowledge might enable us to optimize the acute treatment of STEMI patients and to emphasize the need for establishing STEMI centres with pPCI facilities, especially in less developed countries.

P01.04   Mads Dam Lyhne   **IMMEDIATE CARDIO-PULMONARY RESPONSE IN ACUTE, CENTRAL PULMONARY EMBOLISM**

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Background: Acute pulmonary embolism (PE) is a frequent but potentially fatal condition. Death often occurs within hours after the event. PE affects both the respiratory and the circulatory systems. The immediate physiological changes are important to know to support the patients.

Methods: We use a porcine model of large, autolouges PE. Respiratory and circulatory evaluation is measured using information from the respirator, arterial and central venous blood gasses, pulmonary and systemic pressure measurements and bi-ventricular pressure-volume loop recordings. After baseline, a number of PEs will be injected until the pulmonary pressure has doubled. The mentioned evaluation methods are performed 1, 2, 5 and 13 minutes after each introduced PE. If doubled pulmonary pressure has not been reached at 13 minutes, another PE will be introduced 2 minutes later. Evaluations are repeated 30, 60, 90, 120, 150, 180, 360, 540, and 720 minutes after the last embolus.

Results: Preliminary results are expected before presentation.

Perspective: Obtaining a better understanding of the cardiopulmonary responses in a succumbing patient is important for clinicians in order to support the respiratory and circulatory systems.

P01.05   Johnni Rudbeck-Resdal   **LONG-TERM OUTCOMES IN PATIENTS WITH ATRIO-VENTRICULAR BLOCK OF UNKNOWN AETIOLOGY IDENTIFIED BEFORE THE AGE OF 50 YEARS - A NATIONWIDE DANISH STUDY**

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Background: In the young, atrio-ventricular block (AVB) is rare. In half the patients, the aetiology is not identified during the preimplantation work-up. Long-term morbidity and mortality in these patients are unknown.

Purpose: To assess morbidity and mortality in young patients with AVB of unknown aetiology.

Methods: Patients were identified from Danish Pacemaker and ICD Registry. We identified all patients below 50 years at the time of first pacemaker implantation due to AVB in the period 1996-2015. Medical records were reviewed, and patients with AVB of unknown aetiology were included. We established a control group consisting of 10 controls per case, matched on gender, month and year of birth and alive at the time of pacemaker implantation. Patients and controls were followed using the Danish National Patient Registry, the Civil Registration System and the Register of Causes of Death. The primary outcome was a composite endpoint consisting of 1) death from any cause, 2) heart-failure hospitalization, 3) ventricular tachyarrhythmia hospitalization and 4) cardiac arrest with successful resuscitation.

Results: We included 517 patients with unexplained AVB and 5,170 controls. At baseline, the mean Charlson Comorbidity Index score was 0.34 among patients and 0.11 among controls. After a mean follow-up of 10.09 years (IQR 5.41-14.29 years), the primary endpoint had occurred in 15.09% of the patients and in 3.83% of the controls (hazard ratio 3.68; 95% CI 2.74 to 4.93; P<0.001).

Conclusion: Atrio-ventricular block of unknown aetiology presenting below the age of 50 years and treated with pacemaker implantation was associated with a significant 3-4 fold higher rate of serious cardiac events.

P01.06   Ane Bull Iversen   STROKE AWARENESS AND HELP-SEEKING BEHAVIOUR: PREDICTORS FOR PREHOSPITAL DELAY IN STROKE

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Background: Acute reperfusion therapies have revolutionized stroke treatment. However, only 20% of Danish patients are eligible, mainly due to presentation outside the time window. Numerous attempts to reduce prehospital and in-hospital delay have been made, but much time is still lost in the prehospital phase. Many patients do not recognize their symptoms as signs of stroke or do not understand the importance of calling the Emergency Medical Services (EMS) immediately. Others cannot call for help unless they have a bystander. Educational campaigns can enhance knowledge, improve behaviour and increase the number of patients eligible for reperfusion. TrygFonden is planning a national Danish stroke campaign in 2019.

Aims: To explore the knowledge of stroke in stroke patients and bystanders and investigate the association between stroke knowledge, help-seeking behaviour and receiving revascularization. To evaluate the effect of the national campaign.

Methods:

Study 1: A cross-sectional study of consecutive patients with acute stroke and Transient Ischemic Attack (TIA) admitted at one primary and one comprehensive stroke centre in the Central Denmark Region between January 28th and May 10th 2018. Structured interviews of 654 patients and bystanders were performed. We used the Danish Stroke Register to map the patient's route from onset of symptoms to admission to stroke centre, hereunder contact to general practitioner (GP), out-of-hours GP or EMS. Eligible patient were > 18 years, independent in daily activities, and with stroke onset-to-interview ≤7 days.

Study 2: We will evaluate the effect of the national campaign by conducting a similar study in 2020 when the campaign has been running for six months.

P01.07   Benjamin Asschenfeldt Arlander

NEUROCOGNITIVE IMPAIRMENTS IN ADULTS OPERATED FOR SEPTAL DEFECTS IN CHILDHOOD

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Introduction: Neurocognitive outcome is impaired in young adults with complex congenital heart disease. It is unknown whether the same holds for atrial (ASD) and ventricular septal defects (VSD). The present study examines the hypothesis of impaired neurocognitive outcome in adults who have undergone corrective surgery for septal defects in early child-hood.

Methods: In a prospective cohort study, two groups of participants were enrolled: 1) patients who had undergone corrective surgery for an isolated ASD or VSD and 2) healthy controls matched on age, gender, and education. The Wechsler Adult Intelligence Scale, Fourth Edition (WAIS-IV) was employed, and patient performances were compared to the control group and the expected population mean.

Results: A total of 21 ASD patients, 22 VSD patients, and 16 healthy controls were enrolled. Mean age was 27.4 (± 6.3) years in the ASD group and 24.2 (± 2.7) years in the VSD group. The Full Scale Intelligence Quotient (FSIQ) was lower in the ASD group (93.8 ± 11.7) compared with the control group (103.9 ± 9.9; $p = 0.01$) and with the expected population mean (100 ± 15.0; $p = 0.02$). The FSIQ was not significantly different in the VSD group (95.8 ± 15.2) compared with the control group (103.7 ± 10.8; $p = 0.09$) nor with the expected population mean ($p = 0.21$). However, the VSD group demonstrated significantly lower performances on two of four index scales compared to the expected population mean ($p < 0.05$).

Conclusions: Surgically corrected congenital septal defects may be associated with lower intelligence quotient scores in adulthood. The extent of the neurocognitive challenges needs to be clarified.

P01.08 Omeed Neghabat RANDOMIZED COMPARISON OF AN EVEROLIMUS-ELUTING BIORESORBABLE SCAFFOLD VERSUS EVEROLIMUS-ELUTING METALLIC STENT IN PRIMARY PERCUTANEOUS CORONARY INTERVENTION OF ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

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Background: Patients with ST-segment elevation myocardial infarction (STEMI) could be suitable for implantation of bioresorbable scaffolds (BRS) as patients are younger and lesions often are focal with low degree of calcium. We aimed to compare acute performance and 12-month healing response of an everolimus-eluting BRS (Absorb, Abbott Vascular, USA) compared to a permanent drug-eluting metallic stent (DES) (Xience, Abbott Vascular, USA).

Methods: The trial was a 1:1 randomized, non-blinded, non-inferiority study with planned inclusion of 120 patients with STEMI. Acute performance and healing patterns were evaluated by angiography and optical coherence tomography (OCT) at baseline and 12-month follow-up. The primary endpoint was minimum flow area (MFA) assessed at 12-month follow-up with a non-inferiority margin of 0.72 mm^2. Coronary stent healing index was investigated to assess healing over 12 months.

Results: A total of 66 patients were included before the Absorb BRS was discontinued due to safety concerns by regulatory bodies. All 66 patients had baseline OCT, 58 had 12-month follow-up OCT, 5 of these had unanalyzable OCT, and 53 entered matched analysis. One death occurred in each group; none were scaffold-related. Analysis is ongoing and will conclude in late November. Results of the primary endpoint will be presented at PhD Day 2019.

Conclusion: The present study will add valuable information on the use of BRS in STEMI settings and possibly justify further investigation of BRS compared to DES in large randomized trials with clinical endpoints.

P01.09 Asbjørn Petersen THE KCA3.1 CHANNEL BLOCKER SENICAPOC PREVENTS THE DEVELOPMENT OF LUNG OEDEMA AND HYPOXEMIA IN A VENTILATOR-INDUCED ACUTE INJURY MODEL

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Endothelial ion channels expressed in the pulmonary tissue have been shown to be crucial mediators of acute lung injuries (ALI). Mice genetically deficient of the calcium-activated K channel with intermediate conductance, KCa3.1, were found to be protected against lung damage in a pharmacological induced injury model. Inspired by this finding, we examined the effects of KCa3.1 channel blockers in mice exposed to injurious mechanical ventilation.

For functional studies, cumulative concentrations of two different KCa3.1 ion channel blockers (senicapoc (SE) and TRAM-34) were tested on isolated mouse pulmonary small arteries (PA) mounted in isometric myographs. In an ALI animal model, adult male mice were anesthetized and underwent tracheotomy. Thirty minutes before induction of ALI, the animals were administered SE (10-70 mg/kg) or vehicle by intraperitoneal injection and then ventilated for 2 hours with a high peak inspiratory pressure.

SE as well as TRAM-34 concentration-dependently reversed NS309-induced relaxations in the PAs. In the murine model, exposure to SE completely counteracted the development of hypoxemia when compared to vehicle. Furthermore, SE attenuated the formation of lung oedema measured as wet to dry lung weight and lowered BAL protein content.

In summary, our results suggest involvement of KCa3.1 channels in pulmonary vasodilatation and that senicapoc protects against ALI in mice exposed to mechanical overventilation. These findings lend further support for a critical role of calcium-activated K channels of the KCa3.1 type in mechanisms of tissue injury and as pharmacological target for tissue protection.

P01.10   Mette Marie Astrup Søndergaard

IMPACT OF CHEMOTHERAPY AND RADIATION THERAPY ON LEFT VENTRICULAR SYSTOLIC AND DIASTOLIC FUNCTION IN PATIENTS WITH CANCER IN ESOPHAGUS AND GASTROESOPHAGAEL JUNCTION - A PROSPECTIVE STUDY DESIGN

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Background: Patients with cancer in esophagus and gastroesophageal junction (EGEJ) treated with chemoradiotherapy (chemoRT) have increased risk of cardiovascular disease. EGEJ patients often have frailty and pre-existing cardiovascular disease. This may disqualify them for standard trimodal curative treatment and offer surgery alone, chemoRT alone or palliative treatment only. The current understanding of radiation induced heart disease (RIHD) in EGEJ patients is limited. Hence, there is a need for additional studies. Proton-based radiation therapy (RT) is a new alternative to standard photon-based RT, which is likely to reduce the risk of cardiovascular complications.

The aim: Firstly, to investigate the influence of chemoRT on ventricular function and myocardial capacity in EGEJ patients and evaluate the cardiac prognosis. Secondly, to identify potential high-risk patients who might benefit from proton-based RT instead of photon-based RT.

Method: Based on power calculations, we plan to include 56 patients within two years. Inclusions criteria: biopsy verified EGEJ cancer supported by findings from gastroscopy, PET CT scan and with the final diagnosis locally advanced, non-metastatic. Serial cardiac investigations will be performed to evaluate if they develop impairment of the heart function during or after chemoRT. Electrocardiogram, cardiac biomarkers and echocardiographic examinations of ventricular function and myocardial

capacity will be performed. To evaluate the influence of treatment on physical performance, CPX test is performed at rest and during peak exercise using a semi-supine ergometer bicycle.

Status: Inclusion has started in June 2018. So far, 11 patients are included.

P02.01 Frederik Boe Hansen

MESENTERIC AND CEREBRAL ENDOTHELIAL FUNCTION IN THE POST-CARDIAC ARREST PERIOD

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Introduction: Cardiac arrest has a poor prognosis; primarily due to brain injury. The brain injury progresses over time following resuscitation and is aggravated by hemodynamic instability and impaired cerebral circulation. We hypothesize that mesenteric and cerebral endothelial dysfunction plays a key role in the impaired circulation.

Objective: To investigate whether endothelial dysfunction is present in cerebral and mesenteric arteries in the post-cardiac arrest period.

Methods: Male Sprague-Dawley rats (n=40, 350-450 g) are anaesthetized, orally intubated, and ventilated. Subsequently, rats are randomized into four groups: two cardiac arrest groups observed for either 120 minutes (n=10) or 240 minutes (n=10) after resuscitation and two corresponding control groups. Following 7 minutes of asphyxial cardiac arrest, the animals are resuscitated using adrenaline, ventilation, and chest compressions. Noradrenaline is administered if mean arterial pressure <50 mm Hg after resuscitation.

Animals are euthanized by the end of the observation period. Mesenteric and middle cerebral arteries are extracted in order to conduct K_{Ca} channel expression studies and to functionally test the arteries in a wire myograph. Mesenteric and cerebral artery segments are mounted in oxygenated physiological saline. Subsequently, vessel segments are incubated with either vehicle (control), L-NAME (NO synthase inhibitor), or Senicapoc and UCL (K_{Ca}-blockers). The endothelium-dependent and independent vasodilation is examined by adding acetylcholine/bradykinin, NS309 (K_{Ca}channel activator), and sodium nitroprusside (NO analogue).

Results: Data collection will be completed by December 2018.

P02.02 Rafael Sobrano Fais

ALDOSTERONE-INDUCED NLRP3 ACTIVATION PROMOTES ENDOTHELIAL DYSFUNCTION DEPENDENT TO THE LYMPHOCYTES RECRUITMENT

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Erectile function (EF) depends on the tone of the corpora cavernosa (CC). Aldosterone is an important inflammatory modulator and impairs EF. The

nucleotide-binding oligomerization domain-like receptor 3 (NLRP3) is responsible for the release of pro-inflammatory cytokines that induce inflammation, and it is implicated in vascular dysfunction. Aldosterone induces NLRP3 activation in vascular beds. However, the role of NLRP3 in the modulation of CC tonus is unknown. Therefore, we hypothesize that Aldosterone-induced NLRP3 activation recruits lymphocytes and impairs EF. Male C57BL/6 (WT) and NLRP3 (NLRP3$^{-/-}$) knockout mice were used. Bone marrow was transplanted from WT to WT (WT->WT) and NLRP3$^{-/-}$ (WT->NLRP3$^{-/-}$) or from NLRP3$^{-/-}$ to WT (NLRP3$^{-/-}$->WT) mice with 10 to 12 weeks treated with vehicle or aldosterone (600 µg.kg^{-1}.day^{-1} for 14 days) while receiving 1% saline to drink. Reactivity of CC was performed. Approved by CEUA 012/2013-1. Aldosterone infusion reduced the endothelium-dependent relaxation to acetylcholine (ACh), but not endothelium-independent relaxation to sodium nitroprusside, and increased the lymphocytes infiltration in the CC. The absence of NLRP3 prevented these changes. Also, bone marrow transplantation from NLRP3$^{-/-}$ to WT mice prevented aldosterone-induced impairment of relaxation, but the transplantation from WT to NLRP3$^{-/-}$ did not. In conclusion, NLPR3 mediates the aldosterone-induced impairment of relaxation in the CC. In addition, NLRP3 in lymphocytes contributes to the effects of aldosterone on functional responses in CC. Thus, NLRP3 inhibition may represent a new therapeutic target to treat erectile dysfunction.

P02.03 Rikke Lund Sønderbæk ~~CANCELLED~~

THE EFFECT OF HIGH VERSUS LOW DIETARY SODIUM INTAKE ON ERYTHROCYTE SALT SENSITIVITY AND SHEDDING OF ENDOTHELIAL GLYCOCALYX IN A RANDOMIZED, DOUBLE- BLINDED, PLACEBO- CONTROLLED CROSS-OVER STUDY IN HEALTHY SUBJECTS

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Background: The endothelium is lined with endothelial glycocalyx (EG). EG protects the endothelium and functions as a barrier between blood and endothelium. Due to negative charges, EG has a strong ability to buffer sodium. In vitro studies indicate that sodium overload can damage the EG and reduce the sodium buffer capacity. This could cause endothelial dysfunction and might lead to cardiovascular disease. EG can be measured by the erythrocyte salt sensitivity (ESS) and shedding of glycocalyx.

Purpose: We aimed to examine the effect of dietary sodium balance on EG in healthy subjects.

Methods: In a double-blinded, randomized, placebo-controlled crossover study, 27 healthy subjects received a four-day sodium-reduced diet and treatment with NaCl or placebo in randomized order. Afterwards, the subjects were further sodium- and volume-loaded with 1 L isotonic NaCl intravenously. Changes in ESS and blood pressure were measured.

Results: After both low sodium (LS) and high sodium (HS) diet, ESS increased during the diet intervention. The increase after HS was significantly higher than after LS (ΔESS HS 25±22%, ΔESS LS 14±23%, p=0.02). After isotonic NaCl, ESS increased significantly in both groups (HS:

p<0.001, LS: p<0.001), but with no difference between the groups (ΔESS HS 17±13%, ΔESS LS 16±13%, p=0.895).

Conclusion: High sodium intake has a direct negative effect on EG and reduces the buffer capacity, but does not change the relative response in ESS to an acute sodium load.

P02.04   Cancelled   CANCELLED

P02.05   Lene Andreasen   RATIONAL DESIGN AND CURRENT STATUS ON THE OCTOBER TRIAL: A EUROPEAN TRIAL ON OPTICAL COHERENCE TOMOGRAPHY OPTIMIZED BIFURCATION EVENT REDUCTION

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Background: Treatment of coronary bifurcation lesions by percutaneous coronary intervention constitutes a technical challenge. Lesions with significant disease in the main and the side branch often require treatment by complex stenting techniques prone to suboptimal treatment results and poor clinical outcome. Intravascular optical coherence tomography (OCT) is a light-based imaging modality that is able to detect correctable factors not visible by standard angiography. OCT allows for improved procedural control and optimized stent implantation. The aim is to compare median two-year clinical outcome after OCT guided vs. standard angiographic guided revascularization of patients requiring complex bifurcation treatment.

Method: The OCTOBER Trial is a randomized, investigator-initiated, multicenter, superiority trial with planned inclusion of 1200 patients from 40 centers in Europe. Patients are randomized 1:1 to either OCT guided or standard guided revascularization. Inclusion criteria are stable or unstable angina pectoris, or clinically stable non-STEMI, and indication for re-vascularization of a complex coronary bifurcation. Treatment of patients randomized for OCT guiding treatment follows a systematic OCT protocol. All sites receive on-site training visits and are required to perform testcases to get certified for enrollment. The primary outcome measure is a median 2-year composite endpoint of major adverse cardiac events (MACE).

Conclusion: A positive outcome of the OCTOBER trial may establish OCT as a routine tool for optimization of complex PCI. By October 2018, a total of 211 patients have been randomized. Estimated final enrolment day is December 31st, 2019.

| P02.06 | Camilla Dalby Salvig | BIOMECHANICAL IN VITRO ASSESSMENT OF THE PORCINE AORTIC ROOT |

C.D. Salvig

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Aortic root aneurysms are defined as localized expansions of the aorta root with a presumably change in the biomechanical properties. It is thought that successfully repair depends on the ability to mimic and maintain the properties of the native aortic root. The aim of this study is to investigate the biomechanical properties of different segments of healthy native porcine aortic roots before tissue from patients with aortic root aneurism is examined.

Circumferential aortic wall specimens were cut out at the level of aortic annulus, sinus and sinotubular junction (STJ). Each of these specimens were further divided into three segments in relation to the right-coronary (RC), left-coronary (LC) and non-coronary (NC) commissures (nine samples in total). The biomechanical characterization (stress-strain relations) was obtained using a uniaxial dynamic test system. All tests were performed in the circumferential direction of the tissue and with a standardized sample width of 3.5 mm.

For the sinus level, the maximum stress was significantly larger for the NC compared to the RC sinus (3.37 ± 1.6 MPa and 1.70 ± 0.8 MPa, respectively). Likewise, the maximum stiffness was significantly larger for the NC compared to the RC (5.87 ± 3.1 N/mm and 2.69 ± 1.4 N/mm). For the aortic annulus and STJ levels, there were no significant differences between the commissural segments. Despite no significance, the same pattern was recognized for STJ.

These preliminary data suggest that the biomechanical strength and characteristics are significantly different along the circumferential part at the aortic sinus level. Although not significant, these inhomogeneities were also found at the STJ level.

| P02.07 | Anders Sjørslev Schmidt | CARDIOVERSION OF ATRIAL FIBRILLATION: CAN WE PREDICT SUCCESS USING COPEPTIN? |

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Introduction: This study aims to investigate if successful outcome after electrical direct current cardioversion of atrial fibrillation be predicted based on the biomarker copeptin. Cardioversion is an important treatment option, which aims to reduce disease burden. However, cardioversion is not always successful, and recurrence of atrial fibrillation is present in 50-80% of patients after one year. Copeptin is a novel biomarker associated with cardiovascular morbidity. In this study, we aimed to investigate the

association between copeptin and outcomes after cardioversion of atrial fibrillation.

Methods: Patients undergoing elective cardioversion of atrial fibrillation were included. The level of copeptin was determined before cardioversion and at 90-day follow-up.

Results: In total, 116 patients were included of which 85 (73 %) were male. Baseline characteristics were not statistically significantly different between the groups. Patients with a successful cardioversion had a mean copeptin level of 6.3 pmol/L (95% confidence interval (CI): 5.4-7.4) and this was 5.9 pmol/L (95% CI: 4.7-7.4) for unsuccessful cardioverted patients; ratio: 1.1 (95% CI: 0.8-1.4), p = 0.64. Patients in sinus rhythm at 90-day follow-up had a mean copeptin level of 5.8 pmol/L (95% CI: 4.9-7.0), and for patients with atrial fibrillation at follow-up this was 6.5 pmol/L (95% CI: 5.3-7.9); ratio: 1.1 (95% CI: 0.7-1.2), p = 0.44.

Conclusions: Copeptin levels were not associated with outcomes after cardioverting atrial fibrillation.

P02.08 Torben Hoffmann

REDUCING READMISSION TO HOSPITAL AFTER HEART SURGERY

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Epidemiologic studies have showed that the 30-day mortality after heart surgery has improved through the past 12 years, although the 1-year mortality has not been equally improved. Heart death is the main cause of death in the first year after heart surgery, and nearly every fifth patient was readmitted to the hospital in the first 30 days after surgery, though mostly because of uncomplicated conditions such as suboptimal medical treatment, infection or pleural effusion. This indicates a potential for improvement in timely post-operative follow-up.

We believe that closer post-operative follow-up after heart surgery will have a positive benefit on the patients' physical capacity, pleural and pericardial effusion, heart and lung function, wound infection, correct medicine, admission time, readmission frequency, 1-year mortality as well as general function level.

Therefore, we have established an outpatient student-run clinic, where we do postoperative follow-up two and four weeks after the surgery. The effect of intervention will be measured by a 6MWT, direct spirometry, focused ultrasound examination of the heart and pleura cavities, wound inspection, control of the subscribed medicine and a questionnaire about quality of life. Wounds will be clinically examined and photo documented, and differences in skin temperature will be measured in order to detect early signs of infection. The length of hospitalization, numbers of readmissions and potential death will be registered up to 1 year after initial discharge from surgery. Endpoints include readmissions to a hospital, the degree of heart failure and general functional level.

The intervention group will be compared to a control group.

P02.09   Christine   ASSOCIATION BETWEEN ANTI-DIABETES TREATMENT AND
         Gyldenkerne   CARDIOVASCULAR RISK IN DIABETES PATIENTS WITH AND WITHOUT
                        CORONARY ARTERY DISEASE

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Background: Coronary artery disease (CAD) is a major cause of cardio-vascular morbidity and mortality in patients with diabetes mellitus. Still, guidelines differ on the definition of high-risk diabetes patients and thus on who should receive primary prophylactic treatment.

Objective: To examine the risk of myocardial infarction (MI) associated with diabetes treatment strategy among diabetes patients with and without obstructive CAD after coronary angiography (CAG).

Methods: A registry-based cohort study of diabetes patients undergoing CAG from July 2004 to July 2012 was conducted. Patients were stratified by presence/absence of obstructive CAD and by diabetes treatment strategy: insulin (± non-insulin anti-diabetes medication), non-insulin diabetes medication, and dietary treatment. Endpoints were MI and all-cause death.

Results: The study included a total of 12,030 diabetes patients. Median follow-up-time was 3.0 years. Among patients with obstructive CAD, those treated with insulin had the highest risk of MI (adjHR 7.91, 95% CI 3.51-17.82), followed by patients receiving non-insulin diabetes medication (adjHR 5.42, 95% CI 2.40-12.22), and those treated with diet (adjHR 3.79, 95% CI 1.61-8.88), using patients with no CAD treated with diet as reference. This incremental risk of MI was significant ($p_{trend}<0.001$). Among diabetes patients without obstructive CAD, MI risk was similar and low in the three treatment groups ($p_{trend}=0.81$).

Conclusions: The presence of obstructive CAD defines the risk of MI in diabetes patients. Type of diabetes treatment, in particular insulin, was associated with risk of MI only in the presence of CAD.

P02.10   Marc Daniel   ISCHEMIA-HYPOXIA RELATED SMALL METABOLITES UPREGULATED SMALL
         Opfermann   ORGANIC ACIDS IN ISCHEMIA AS A NOVEL ENDOGENOUS PROTECTION
                        SYSTEM AGAINST REPERFUSION INJURY

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Background: For the last 15 years, ischemic heart disease has been the leading cause of death worldwide. Ischemia is characterized by restricted blood supply to tissues, which causes a deficiency in oxygen and nutrients. During recent studies at our department, we have discovered that two relatively unknown small organic acids, α-hydroxybutyrate (AHB) and α-hydroxy-β-methylbutyrate (HMB), were highly upregulated during

ischemia: up to 15-25 fold. Further preliminary experiments revealed that the cell permeable methyl-ester of AHB was cardioprotective in an ischermia/reperfusion (I/R) injury model. We hypothesize that the two small metabolites could be part of a novel endogenous protection system against I/R injury.

Aim: The aim of this project is to identify the mechanisms underlying the formation of AHB and HMB during ischemia, unravel their biological function, and finally examine in detail whether they are part of a hitherto unrecognized endogenous protection system against I/R injury.

Methods: The in vitro ischemia model is carried out on rat heart myoblasts (H9C2) and HL-1 mouse cardiomyocytes. With an untargeted metabolomics approach using LC-qTOF-MS, we are going to identify the triggers of AHB and HMB formation. Cardioptotective effects will be assessed in a cell based I/R injury model and tested in an ex vivo Langendorf heart assay. Subsequently, we will try to identify the mechanism of action of these compounds, with focus on mitochondrial metabolism and posttranslational modification.

Perspectives: If these compounds are indeed part of an endogenous protection system, it is highly relevant to further examine whether they can be used therapeutically.

P03.01   Mette Bisgaard Andersen   PHYSICAL ACTIVITY IN PREGNANCY; EFFECTS OF BODY MASS INDEX AND WEIGHT GAIN

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Introduction: Studies indicate that physical activity in pregnancy is preventive of pregnancy-related disorders. Pre-pregnant overweight may impair the physical activity in pregnancy and hereby increase the risk of complications. However, the knowledge in this field is sparse.

Objective: To examine effects of pre-pregnant BMI and weight gain during pregnancy on physical activity.

Methods: A cohort study of 400 singleton pregnant women who attended Aarhus University Hospital, Denmark (2010-2015). Physical activity was monitored for 1 week each trimester using Sensewear Armband. Physical activity was measured as daily metabolic equivalent task (MET) level. Women were classified according to BMI as normal weight (BMI<25), overweight (BMI 25-29.9) and obese (BMI≥30). The women were then grouped according to weight gain during pregnancy: i) <10 kg, ii) 10-15 kg and iii) >15 kg. Mean MET level across groups of BMI and weight gain were tested using one-way ANOVA. Development in MET levels during pregnancy was assessed using repeated measurements.

Results: Overweight and obese women had lower MET levels (1.2 and 1.0) compared to normal weight (1.4), (p <0.000). Women with a weight gain of 10-15 kg had a higher MET level (1.3) compared to women with lower (MET 1.2) and higher (MET 1.2) weight gain (p<0.004).

Daily MET level decreased during pregnancy in a similar, but not exactly the same, pattern for all groups of BMI and weight gain.

Conclusion: Physical activity during pregnancy was inversely related to pre-pregnant BMI. Women gaining 10-15 kg in pregnancy, corresponding to recommendations for normal BMI, had a higher level of physical activity in pregnancy than women with a lower or a higher weight gain.

P03.02   Anne Staub Rasmussen

SURGERY DURING PREGNANCY AND BIRTH OUTCOMES

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Objective: Abdominal surgery during pregnancy is of great concern for patients as well as health care professionals. This study aimed to examine the association between non-obstetric abdominal surgery during pregnancy, preterm delivery and being born small for gestational age in a population-based matched cohort study.

Materials and methods: Female citizens aged 15-54 years giving birth in Denmark in 1996-2015 were included in this study. Exposure was non-obstetric abdominal surgery during pregnancy. For each surgically treated pregnancy, we randomly selected 100 pregnant women with the same gestational age as the exposed at time of surgery in exposed pregnancies. The comparison cohort was pregnancies without surgery at or before time of exposure. Outcome measures were being born small for gestational age (SGA), defined as birth weight below -2SDs of the mean for a gender and gestational age specific reference, preterm delivery (born with gestational age < 37 weeks) or very preterm delivery (born with gestational age <32 weeks).

Results: The study included 1,184,589 pregnancies. Abdominal surgical procedures were conducted at least 14 days before delivery in 3,875 pregnancies, in 3,964 pregnancies before gestational week 37, and in 3,595 pregnancies before gestational week 32. In the surgically treated cohort, the risk of SGA was 3.9% compared with 2.7% in the comparison cohort, the risk of preterm delivery was 9.8% compared with 0.5%, and the risk of very preterm delivery was 2.5% compared with 0.02%.

Our population-based data showed an increased risk of being born SGA, preterm and very preterm when non-obstetric abdominal surgery was conducted during pregnancy.

P03.03   Ida Charlotte Bay Lund

INTRODUCTION OF NON-INVASIVE PRENATAL TESTING IN DENMARK

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Background: Non-Invasive Prenatal Testing (NIPT) enables screening for fetal trisomy 21, also known as Down syndrome, through sequencing of cell-free fetal DNA in maternal plasma. We wanted to describe the introduction of NIPT for trisomy 21 in Denmark.

Method: Data from NIPT and validation samples (chorionic villus, amniotic fluid, postpartum tissue or postnatal blood) were retrieved from The Danish Cytogenetics Central Registry and The Astraia Database from March 2013 to June 2017. Private providers of NIPT were contacted by email or phone.

Results: A total of 3,445 NIPT tests have been performed clinically through public Fetal Medicine Units. 84% of NIPT tests have been offered as an alternative to invasive testing for women at high risk (≥1:300 for trisomy 21) after combined first trimester screening. Overall, the sensitivity for trisomy 21 was 96.6% and the specificity 99.9%. One false negative NIPT test of trisomy 21 has been reported. Out of 31 high-risk NIPT results for trisomy 21, five women chose to continue pregnancy without further prenatal testing. Three of these five cases had postnatal confirmatory blood samples; two live births had no follow-up.

From June 2014, women have had the opportunity to seek a private provider of NIPT. Data from 658 NIPT tests have been included from seven private clinics. Six out of seven cases identified as high-risk for trisomy 21 were confirmed by invasive testing through public health care.

Conclusion: It is of paramount importance that all positive NIPT results are followed up by validation samples. Good registry practice is essential in order to optimize fetal diagnostics and postnatal care for those born with Down syndrome.

P03.04   Mette Schou Mikkelsen

CYTOREDUCTIVE SURGERY COMBINED WITH HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC): A SAFE PROCEDURE WHEN USED IN OVARIAN CANCER TREATMENT

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Introduction: Ovarian cancer is the most lethal of the gynecological cancers with more than 150,000 annual deaths worldwide. In an attempt to improve survival, cytoreductive surgery (CRS) combined with hyper-thermic intraperitoneal chemotherapy (HIPEC) is increasingly used in ovarian cancer treatment. HIPEC consists of perfusion of the abdominal cavity with a heated solution containing a cytotoxic agent. Most published studies evaluating the morbidity of CRS combined with HIPEC are retrospective. Our aim was to evaluate the short-term morbidity and mortality using a prospective study design.

Material and methods: We performed a prospective feasibility study from January 2016 to December 2017. Twenty-five patients with primary advanced stage ovarian cancer (FIGO III-IV) received upfront (no chemotherapy before surgery) or interval (received chemotherapy before surgery) CRS combined with carboplatin HIPEC at dose 800 mg/m^2. Our outcome measurements were grade 3-5 adverse events within 30 days according to Common Terminology Criteria for Adverse Events (CTCAE).

Results: Fourteen patients had upfront CRS and 11 patients had interval CRS. No grade 5 adverse events (deaths) or grade 4 adverse events (life-threatening events) occurred within 30 days. Eleven patients (44.0%) experienced at least one grade 3 adverse event (severe or medically

significant but not life-threatening events). The most common were infection (n=7, 28.0%) and transient neutropenia (n=3, 12.0%).

Conclusion: Our small-scale prospective feasibility study supports that CRS combined with carboplatin HIPEC used for primary advanced stage ovarian cancer is feasible with acceptable short-term morbidity.

P03.05   Anne Rahbek Zizzo

NON-INVASIVE FETAL ELECTROCARDIOGRAPHY (FECG) IN 2ND AND 3RD TRIMESTER

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Aim: To detect accurate fetal R-waves by noninvasive fetal electro-cardiography (fECG) in 2[nd]and 3[rd]trimester.

Background: Because of its isolating effect, the vernix caseosa complicates noninvasive fECG, especially between weeks 28-34. It is crucial to this new fetal surveillance method that recordings are reliable through 2nd and 3rd trimester. Reliable analyses of beat-to-beat fetal Heart Rate Variability (fHRV) depend on R-wave detection with milliseconds of accuracy, why ultrasound and conventional cardiotocography (CTG) is not suitable.

Methods: A new high-performance and high-accuracy bio-signal amplifier (Viewcare A/S) with a sampling rate at 8000 Hz will be used. FECG will be detected by five electrodes placed on the maternal abdomen. Data will be collected in a portable device and transmitted wireless to a computer. 30 healthy pregnant women will be included and divided into 3 gestational age groups. Detection rates of fetal R-waves will be shown for each group.

Results: This far, 18 data acquisitions have been performed. When 50 Hz noise and maternal QRS complexes were removed, fetal R-waves were visually detected throughout recordings in 85% of term pregnancies and 50% of the difficult weeks (28-34). More filtering needs to be applied. Furthermore, an algorithm for automatic detection of fetal R-waves is being developed.

Conclusions: These high-quality non-invasive fetal ECG recordings may form the basis of exact beat-to-beat fHRV analyses and improvement in fetal surveillance. Although some recordings and more work with the algorithm for fetal R-wave detection needs to be performed, these preliminary results bring optimism to the field of fetal surveillance with fECG.

P03.06   Eva Rydahl

CESAREAN SECTION ON A RISE: DOES ADVANCED MATERNAL AGE EXPLAIN THE INCREASE? A POPULATION-BASED REGISTER STUDY

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Background: In Denmark, the cesarean section (CS) rate has increased by 49% between 1998 and 2015 and accounts for 21% of all births. Post-ponement of pregnancy has been suggested as a contributing factor to this increase. The proportion of women giving birth at 35 years or above increased from 15% (1998) to 21% (2015). Advanced maternal age at childbirth is related to increased pre-pregnancy morbidity and associated risk factors that may contribute to increased risk of CS.

Methods: A national cohort study of all Danish births in 1998-2015 (N=1,122,964). Age <30 years serves as reference against age: (30-34 years), (35-39 years), and (+40 years). Primary outcome was CS. Multivariate regression with adjustment for demographic, health, pregnancy, fetal, and obstetric characteristics were performed and stratified by parity.

Results: A positive association between advanced maternal age and CS was found. Only minor changes in the risk estimate occurred after adjustment for confounders. In comparison with the reference category, e.g nulliparous aged 35-39 years had an adjusted odds ratio (aOR) 2.18 for CS (95% confidence interval (CI) [2.11-2.26]), whereas for women aged +40 years, the risk was more than tripled (aOR 3.64, 95% CI [3.41-3.90]). Same pattern was found among multiparous, although less pronounced.

Conclusions: This study finds of a strong association between increased maternal age and CS. Adjustment for maternal and obstetric risk factors had minor influence on the association. This leads the authors to add culture to the list of risk factors. Further research is needed on a possible age-related decrease in the ability to maintain progression of labor.

P03.07   Sidsel Boie   CONTINUED VERSUS DISCONTINUED OXYTOCIN STIMULAITON OF LABOUR IN A DOUBLE-BLIND RANDOMISED CONTROLLED TRIAL: STATUS OF AN RCT

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Oxytocin is an effective drug to induce labour, but it is also associated with adverse effects of which uterine tachysystole, fetal distress, and the need for immediate delivery are the most common. Discontinuation of oxytocin in the active phase could reduce the risk of adverse effects.

The objective of our study is to compare the caesarean section rate in women where oxytocin stimulation is discontinued or continued in the active phase of induced labour.

CONDISOX is a double-blind multicentre RCT conducted at 8 Danish and Dutch delivery wards. Recruitment initiated in April 2016.

CONDISOX includes pregnant women at term, stimulated with oxytocin to induce labour. Women are randomised to study medication containing

either oxytocin (continuous group) or placebo (discontinued group) infusion in the active phase of labour.

Based on a clinically relevant reduction of 7% in the caesarean section rate (α of 0.05, β of 80%), we aim to include 1200 participants.

Our primary outcome is caesarean section rate. Secondary outcomes include uterine tachysystole, postpartum haemorrhage, admission to the neonatal intensive care unit, umbilical arterial pH, and birth experience.

Status per October 2018: 550/1200 women included. Nearly 40 women are included per month. Two additional sites start inclusion in 2018.

The Committee on Health Research Ethics in the Central Denmark Region, the Danish Health Authority, and the Medical Research Ethics Committee of the Amsterdam UMC have approved the trial.

The high frequency of oxytocin use and the potential risks of both maternal and fetal adverse effects emphasise the need to determine the optimal regime of oxytocin stimulation.

Trial registration Number: NCT0255322

P03.08   Berit Bargum Booth

CERVICAL DYSPLASIA - HOW CAN WE IMPROVE THE DIAGNOSTICS?

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Background: Before cervial dysplasia develops, pre-malignant stages are present. Proper diagnosis of cervical dysplasia is essential to ensure efficient and correct management and treatment. Cervical dysplasia is examined through colposcopy. Sensitivity for colposcopy has been found as low as 50%. This is believed to be improved when using a new technology in combination with regular colposcopy. The Dynamic Spectral Imaging (DSI) technology is a digital instrument, which aids the examiner in choosing areas of the cervix for biopsy.

Aim: The aim of this project is to improve the diagnostic process of cervical dysplasia for each individual women.

Methods: 1500 women referred with cervical dysplasia will be examined with DSI technology at the Department of Gynaecology, Randers Regional Hospital and Aalborg University Hospital. 1500 women will be examined without this technology at Horsens Regional Hospital and a private gynaecology clinic. All women will have 4 biopsies taken, in accordance with the national guideline. Trained nurses, residents and consultants perform these examinations. Women with high grade dysplasia are referred to conisation of the cervix. The histological diagnosis of the conisation is regarded as the true dysplasia grade.

We examine:

- How much do we gain in sensitivity by using the new DSI colposcopy?

- Do the biopsies correlate to the diagnosis in the conisation material?

- Are there any differences in the biopsies taken by nurses, residents or consultants?

Perspective: With improved diagnostics of cervical dysplasia, we aim to reduce undertreatment and overtreatment and related side effects as well as, in the worst case, the undiagnosed development of cervical cancer.

P04.01 Camilla Gunderstofte Nielsen

IRG1 PROTECTS HUMAN MONOCYTE-DERIVED MACROPHAGES FROM CELL DEATH

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Metabolic reprogramming of macrophages is known to cause accumulation of citrate. Citrate is metabolized into aconitate and further into itaconic acid. Cis-aconitate decarboxylase is required for this conversion and is encoded by immunoresponsive gene 1 (IRG1). A recently published paper shows that itaconate is able to activate the transcription factor Nrf2, which is involved in the antioxidant immune response. Several studies have reported that IRG1 plays a role in the regulation of some pathogens; IRG1 reduces the infectivity level of West Nile virus, a neurotropic virus, it prevents immunopathology by M.tuberculosis, and Respiratory syncytial virus-induced lung injury is prevented in absence of IRG1. We will examine the role of IRG1 on cell viability and susceptibility to Herpes simplex virus and Dengue virus infection. We recently showed that Nrf2 represses STING expression, a critical antiviral signalling protein, during metabolic reprogramming in human cells. Besides these results, we observed that primary human monocyte-derived macrophages died in absence of IRG1. Our preliminary data indicates that the cell death is necroptosis-dependent, and our hypothesis is that IRG1 is protecting the cells from death by preventing necroptosis. We will investigate the importance of IRG1 in connection to cell viability using human primary macrophages and look at viability when activating Nrf2 or IRG1 using electroporation process, silencing RNA, plasmid transfection or different Nrf2 and IRG1 inducers. We will also examine what happens when we induce necroptosis. The project will show the importance of IRG1 when it comes to cell survival and perhaps even in eradication of virus.

P04.02 Kathrine Kjær

QUANTIFICATION OF INDIVIDUAL TRANSCRIPTIONAL ACTIVE HIV PROVIRUSES DURING ANTIRETROVIRAL THERAPY IN ABSENCE OR PRESENCE OF ERADICATION THERAPY

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Establishment of latently infected cells is considered the major obstacle to HIV eradication. Early during infection, HIV creates a reservoir of latently infected cells that harbour proviruses to ensure viral persistence and low-level HIV transcription despite treatment with antiretroviral therapy (ART). Manipulation of this ongoing transcription is used as the primary treatment

efficiency biomarker in latency-reversing agent (LRA)-based HIV eradication trials. Our research department has shown that administration of the LRA romidepsin to HIV-infected patients on ART can induce significant increases in HIV transcription in CD4^{+}T cells. Since the observed increases have only been measured in total cell populations, the actual number of infected cells contributing to transcription remains unknown. Therefore, we have implemented a novel digital droplet PCR system that allows high resolution analysis of individual active proviruses. We will use this system to determine the contribution of single proviruses to HIV transcription in patient mCD4^{+}T cells during ART and determine how adjunct eradication therapy with romidepsin alters the transcriptional activity from the individual proviruses in HIV-infected patients. Since eradication approaches to date has failed to eliminate the pool of latently infected cells, one is questioning whether we are effectively targeting the HIV reservoirs during such approaches. This study will give a robust readout to this question and provide the field with a better understanding of the latent reservoir during suppressive therapy supporting significant advances in curative approaches for HIV.

P04.03   Anne Borup   MODULATION OF INFLAMMATION BY HELMINTH-DERIVED EVS

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Developed countries have, for several decades, experienced a dramatic increase in the incidence of autoimmune diseases, while the incidence of infectious diseases has markedly decreased. The inverse relationship between immune dysregulation and exposure to microorganisms suggests that our immune system needs to be exposed to a variety of pathogens, including parasitic worms (helminths) in order to maturate in a proper way. Recent discoveries show that helminths produce anti-inflammatory and/or immunomodulatory compounds that can balance a dysregulated immune system. A promising component with great therapeutic potential is Extracellular Vesicles (EVs) due to their heterogeneous cargo containing bioactive proteins and nucleotides participating in cell-communication. Despite the great potentials of EVs, a major challenge relates to EV-isolation. Optimized protocols for EV isolation, which give both high yield and enrichment of the most potent immunomodulatory EVs, still need to be established. Improved characterization and classification of EVs from helminths are, therefore, needed in order to achieve sufficient EV isolation. In this study, I will establish a 'gold standard' for isolation of EVs from the helminth Ascaris suum by comparing the often used isolation methods ultracentrifugation and size exclusion chromatography and compare their ability to recover the highest number of EVs with lowest protein contamination. Furthermore, I will test the immunomodulatory ability of the helminth-derived EVs in vitro by stimulating immune cells with different subpopulations of EVs in order to identify the most potent EV fraction.

| P04.04 | Christina Valbirk Konrad | ISOLATION AND VALIDATION OF NOVEL HIV-SPECIFIC EFFECTOR ANTIBODIES FOR IMMUNE-MEDIATED TARGETING OF THE LATENT HIV RESERVOIR |

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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 shortly after initial infection. To enable a cure for HIV, it is thus essential to target the latent reservoir of HIV-infected cells.

Due to their ability to neutralize free virus and facilitate effector cell-mediated killing of infected cells, antibodies may be an important tool in the quest for HIV eradication. Existing HIV-specific antibodies have been selected based on their ability to neutralize free virus particles. These antibodies are capable of blocking transmission of HIV but are unable to eradicate the remaining virus in infected cells. The goal of this PhD project is, therefore, to clone novel HIV-specific antibodies selected based on their ability to mediate virus-infected cell destruction. These HIV-specific antibodies will be isolated and cloned from an HIV-infected clinical trial participant capable of prolonged immune control of his HIV infection during treatment interruption.

The anti-HIV effector function of the novel antibodies will be assessed by in vitro antibody-mediated cell killing assays, and the functional efficacy of the lead effector antibodies will be validated in humanized mice infected with HIV. Promising anti-HIV effector antibodies found in this study will be incorporated into future clinical trials and lead to a potential novel immunotherapy against the latent HIV reservoir that may bring us closer to a cure for HIV.

| P04.05 | Sandra Maria Skovdal | STAPHYLOCOCCUS EPIDERMIDIS DOES NOT RELY ON POLY-SACCHARIDES WHEN FORMING BIOFILMS IN HUMAN PLASMA |

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Staphylococci predominate in biofilm infections as they are excellent biofilm formers. The matrix of S. epidermidis was thought to consist mainly of polysaccharides (PIA), encoded by the icaADBC operon. However, many isolates do not have this operon, and this led to the discovery of the matrix-binding protein (Embp) that may be crucial for in vivo biofilm. We study the importance of Embp and PIA for biofilms in lab media and in in vivo-like media with human plasma.

S. epidermidis1585 (PIA-deficient) and derivative strains that either lacked Embp, expressed Embp, or expressed PIA were grown in lab media (BHI)

or BHI with human plasma. Confocal microscopy determined biofilm structure; antibiotic binding was visualised with bodipyFL-vancomycin, and minimal biofilm eradication concentrated (MBEC) was measured.

Imaging revealed that S. epidermidis biofilms only require poly-saccharides in absence of plasma. Embp-expressing, PIA-negative strains that were biofilm-negative in lab media formed biofilm in plasma similar to the PIA-positive strain. Vancomycin penetrated all biofilms, regardless of composition, and there were no difference in MBEC. However, not all cells bound vancomycin, which suggests cell-to-cell variation in activity and susceptibility and possibly persister cells.

The importance of polysaccharides for S. epidermidis biofilms is an artefact from growing biofilms in standard lab media void of human proteins. S. epidermidis employs diverse mechanisms for biofilm formation, which can be activated under different conditions. Thus, we must go back to study how S. epidermidis incorporates self-produced and host-derived matrix components to form antibiotic-resistant biofilms in vivo.

P04.06   Sidsel Dahl Andersen   IMMUNE MODULATORY EFFECTS ON INNATE IMMUNE RESPONSES BY ADULT BODY FLUID FROM THE PARASITIC WORM, ASCARIS SUUM

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Parasitic worms are known as strong modulators of their host immune responses. They suppress multiplesignaling pathways of the immune system and induce an anti-inflammatory environment, which increases their survival in the host. Interestingly, this immune modulation has shown to cause positive bystander effects in the host, as evident from murine models of autoimmune disorders like inflammatory bowel disease, psoriasis and allergies. However, the specific mechanisms behind this immune modulation remain elusive.
Here, we try to isolate the responsible parasitic molecules from the soil-transmitted helminth, *Ascaris suum*, that interfere with the innate immune pathways regulated by toll-like receptors (TLRs). To elucidate this, we challenge human macrophages with adult body fluid from *A. suum*, prior to stimulation with various stimulus. Interestingly, we find that helminth product suppresses the production of cytokines from macrophages. To further dissect the active components in the adult body fluid, we cleanup the helminths fractions with DNAse, RNAse and proteases and validates the immune responses following stimulation of macrophages.
If we can identify the intracellular pathways targeted by helminth-derived molecules, this may pave the way for novel agents that can modulate as dysregulated immune system. In addition, our work will contribute to the limited knowledge on the field of immunomodulatory effects of parasitic worms.

P04.07   Amin Zakeri   IMMUNOSUPPRESSIVE EFFECTS OF HELMINTH ANTIGENS ON TLR-MEDIATED INDUCTION OF INFLAMMATORY RESPONSES IN MACROPHAGE

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Toll-like receptors (TLRs) are an important compartment of the innate immunity and highly expressed by macrophages. TLRs are able to initiate inflammatory signals and polarize macrophages toward overactivation that leads to onset of an autoimmune condition. Helminth-derived antigens are masterful modulators of host inflammatory responses. This intervention can be mediated via manipulating TLRs' signalling and modifying extracellular vesicle (EV)-associated immune cells' communication. In this study, we explore the effects of Trichuris suis antigens on mouse bone-marrow derived macrophages (BMDM) in the presence of different TLRs agonists. Also, our investigation on the effect of parasite antigens on macrophages exosome is undertaken to assess whether the parasite antigens are able to modify macrophages to release regulatory EVs.

Method: Bone marrow (BM) cells were isolated from 8- to 12-week-old female C57BL/6 for generation BMDM. BMDMs were pre-treated with T. suis antigens for 0.5h and then stimulated with different TLRs agonists. After 24h, cytokine production was assessed by ELISA. In order to produce helminth-induced EVs, BMDMs were stimulated with T. suis antigens for 48h, then EVs were isolated by size exclusion chromatography.

Results: T.suis antigens were found to significantly attenuate most TLR-induced IL-6 and TNFa production in BMDM, while IL-10 was increased. Our preliminary data show that isolated EVs also are able to alter macrophage responses.

Conclusion: This study has so far demonstrated that T. suis antigens can interrupt with TLR signalling in BMDMs. In addition, we showed that EVs derived from T. suis-treated BMDM might potentially alter inflammatory responses.

P04.08   Fanghui Ren   THE POTENTIAL MECHANISM OF HSVS-INDUCED AUTOPHAGY IN NEURONS

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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 in a time- and dose-dependent manner. HSV infection stimulates autophagy after 6h, and this further increases until 16h post infection. These findings provide 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.

| P04.09 | Johanne Hovgaard Egedal | HYALURONIC ACID IS A NEGATIVE REGULATOR OF FIBROBLAST-MEDIATED ENHANCEMENT OF HIV INFECTION |

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The majority of HIV infections are established via the mucosa. We recently found that primary stromal fibroblasts isolated from mucosal sites potently enhance HIV infection of CD4 T cells and may thus be mediators of HIV transmission. Fibroblasts are not permissive to HIV infection, but they increase infection of T cells by both trans-infection and increasing the permissivity of CD4 T cells. As fibroblasts have an extensive and dynamic extracellular matrix (ECM), we hypothesized that parts of the ECM affect fibroblast-mediated enhancement of HIV infection.

Here, we focused on whether fibroblast-produced hyaluronic acid (HA), a major component of the ECM, affects the ability of primary human mucosal fibroblasts to enhance HIV infection of CD4 T cells. We found that cleavage of HA with hyaluronidase increased fibroblast-mediated enhancement. We used CRISPR/Cas9 to deplete HAS2, the major enzyme generating high molecular weight (HMW) HA. HAS2KO fibroblasts enhanced HIV infection of CD4 T cells more potently than wildtype controls.

HA can have differential immunomodulatory properties, with HMW HA being anti-inflammatory and LMW being pro-inflammatory. Stimulation of fibroblasts with TLR-agonists and cytokines alter the levels of HA on fibroblasts, which could modulate the ability of these cells to promote HIV infection of CD4 T cells. We propose that inflammatory signals may promote HIV infection, in part by increasing the ability of mucosal fibroblasts to enhance infection of CD4 T cells. Our ongoing work seeks to determine whether co-infections associated with increased HIV trans-mission risk increase fibroblast-mediated enhancement of HIV infection via altered HA regulation.

| P04.10 | Mette Christensen | DOES BLOCKING OF P2Y RECEPTORS ON THROMBOCYTES CHANGE THE OUTCOME OF URO-SEPSIS IN MICE? |

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Urinary tract infections are exceedingly common and, when severe, the infections are often caused by a-haemolysin (HlyA)-producing E. coli. HlyA releases cellular ATP directly through its membrane pore, and many of the biological effects of HlyA, including erythrocyte lysis, are completely prevented by blocking ATP-signalling. HlyA is known to activate thrombo-

cytes during sepsis, causing a decrease in thrombocyte count and intra-vascular coagulation. Therefore, we speculated whether inhibition of the ATP and ADP sensitive P2Y-receptors may prevent the decrease in thrombocyte count and potentially better the prognosis of sepsis.

Sepsis was induced by injection of 30 million HlyA-producing E. coli (WAM1824) into the tail vein of anaesthetised mice. The mice received continuous infusion of either MRS2500 (P2Y$_1$-antagonist) or Cangrelor (P2Y$_{12}$-antagonist). The mice were either monitored for survival and occurrence of haematuria for 6 hours or terminated after 2.5 hours for blood sample collection.

Continuous infusion with MRS2500 increased survival compared with vehicle-infused mice. MRS2500 did not affect the levels of pro-inflammatory cytokine levels (TNF-a, IL-6, KC and IL-1b), and the mice treated with MRS2500 did not show an increase in circulating thrombocytes. Cangrelor did not affect survival or the degree of haematuria, but data on cytokines and thrombocyte count are pending.

The increased survival rate in mice treated with the P2Y$_1$ receptor anta-gonist points towards a potential benefit from antagonising P2Y-receptors on thrombocytes. However, more experiments need to be done since we were not able to see any difference in cytokines or thrombocyte levels.

P05.01   Tine Vrist Dam   THE ANABOLIC EFFECT OF EXOGENOUS ESTROGEN ON THE SKELETAL MUSCLES IN POSTMENOPAUSAL WOMEN

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Background: After menopause, women experience an accelerated loss of skeletal muscle mass, and the response in muscle protein synthesis rate to anabolic stimuli, such as exercise and protein feeding, is lowered compared to young women and age-matched elderly men. The above-mentioned changes can be caused by the change in sex hormone status.

Aim: This study aims to investigate the effect of exogenous estrogen administration on skeletal muscle adaptations to 12 weeks of resistance exercise in postmenopausal women.

Design & Methods: The trial was designed as a randomized, controlled double-blinded intervention study, where 31 healthy postmenopausal women perform 12 weeks of resistance exercise. Half of them were randomized to transdermal estrogen administration (17 beta estradiol, 100 mg per 24 hours) during the training period. The other half received placebo patches. Primary endpoint: Muscle cross-sectional area of quadriceps femoris, measured by MRI.

Results: At baseline, there were no significant differences between groups in the cross-sectional area of quadriceps femoris (p-value 0,44), measured 15 cm above tibia plateau. A significant different in muscle growth was seen between groups after 12 weeks of resistance exercise (p-value 0,019), where the largest response was seen in the estrogen group.

Conclusion: After 12 weeks of resistance exercise, a larger response measured at the cross-sectional area of quadriceps femoris was seen in the estrogen group.

Perspectives: The results from the present study will help to elucidate the influence of estrogen on the degenerative changes in skeletal muscle, which takes place when women enter menopause.

P05.02   Mai Christiansen   INSULIN SENSITIVITY IMPROVES AFTER DISEASE CONTROL IN
            Arlien-Søborg   ACROMEGALY IRRESPECTIVE OF TREATMENT MODALITY AND DESPITE AN
                               INCREASE IN INTRAHEPATIC LIPID CONTENT: AN INVESTIGATOR-
                               INITIATED PROSPECTIVE TRIAL

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Background: Acromegaly induces insulin resistance and glucose intolerance despite a lean phenotype, both of which reverse by curative surgery. The impact of somatostatin analogue (SA) treatment on insulin sensitivity is less certain due to its suppressive effect on insulin secretion.

Aim: To study glucose metabolism and body composition in newly diagnosed patients with acromegaly before and after successful surgical or medical treatment.

Methods/materials: 21 patients (10 surgically cured and 11 SA controlled) were studied with a hyperinsulinemic, euglycemic glucose clamp (HEC), an Oral Glucose Tolerance Test, dual X-ray absorptiometry scan, and MR spectroscopy.

Results: IGF-I levels (μg/l) before and after treatment were 696 ± 90 and 221 ± 33 with no treatment-specific difference ($p=0.11$). Insulin sensitivity assessed by glucose infusion rate (GIR) during the HEC (mg/kg/min) increased after treatment ($p=0.001$), regardless of modality ($p=0.505$) [GIR: 3.3 ± 0.4 (before) vs. 4.7 ± 0.5 (after)]. SA treatment induced glucose intolerance compared to curative surgery ($p=0.036$). Disease control induced a 17% increase in total body fat ($p=0.001$) and 8% decrease in lean body mass ($p<0.000$). Intrahepatic lipid content increased after disease control ($p=0.04$), regardless of modality.

Conclusions: 1) The improvement in insulin sensitivity and the change in body composition after disease control of acromegaly do not depend on treatment modality, but SA treatment impairs glucose tolerance, 2) The data illustrate the powerful and direct insulin antagonistic effects of GH, 3) Our data extend and support the notion that IHL is regulated by GH, which may have implications beyond acromegaly.

P05.03   Jonas Brorson   INFLUENCE OF NICOTINAMIDE RIBOSIDE AND PTEROSTILBENE
            Jensen   SUPPLEMENTATION ON MUSCLE REGENERATION IN ELDERLY HUMANS

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Background: Successful skeletal muscle regeneration depends on a functional pool of muscle stem cells, termed satellite cells (SC). SC are in a quiescent state through adulthood, but undergo cycles of proliferation and self-renewal in response to muscle damage. During aging, there is a loss of SC quiescence, and SC more readily enter an ageing-state with impaired function. A common denominator for increasing SC function and activity is Sirtuin activation. Sirtuins are a family of metabolic sensors using nicotinamide adenine dinucleotide (NAD^+) as co-enzyme and are involved in mitochondrial biogenesis, autophagy etc. Stimulators of Sirtuins include Nicotinamide Riboside (NR) (a NAD^+precursor) and the polyphenol Pterostilbene (PT). In this study, we aim to investigate if NR+PT supplementation will promote skeletal muscle regeneration after muscle damage in elderly humans by enhanced recruitment of SC.

Methods: 32 healthy subjects >55 years are randomized to NR/PT (500/100 mg) or placebo twice daily for 45 days. 14 days after initiation, muscle damage is induced by electric stimulation and eccentric work in a dynamometer. Skeletal muscle biopsies will be collected before treatment initiation and 2 h, 2 days, 8 days and 30 days post stimulation. The primary endpoint represents amount of SC in skeletal muscle biopsies evaluated by IHC.

Perspectives: Muscle mass is a predictor for longevity in elderly and inversely correlated to metabolic syndrome and cardiovascular disease. The present study will help to identify factors important for muscle regeneration following muscle damage in humans, and explore if NR/PT can influence this process and help prevent morbidity in elderly humans.

P05.04   Tine Billeskov   DOES GROWTH HORMONE REPLACEMENT THERAPY UNMASK INSULIN-LIKE EFFECTS IN PATIENTS WITH GROWTH HORMONE DEFICIENCY AND PROMOTE MUSCLE STEM CELL PROLIFERATION?

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Aim: To investigate insulin-like effects of growth hormone (GH) in patients with GH deficiency (GHD) and the effect of GH and insulin-like growth factor I (IGF-I) on skeletal muscle stem cells (SCs).

Background: Maintenance of healthy skeletal muscle mass is essential for regulation of whole body metabolism. SCs are essential for muscle re-generation. Previous studies have demonstrated impaired SC function in type II diabetes. Thus, defect SC function may contribute to a vicious cycle exacerbating insulin resistance. Cell culture studies demonstrate that GH elicits insulin-like effects in GH-deprived cells. In rats, GH administration increases the SC number in cross-sections of muscle fibres, and fiber type composition is altered in muscle from animals with GHD. This indicates that GH plays an important role in regulation of substrate metabolism and SC function.

Hypothesis: Insulin-like effects of GH can be umasked in treatment naive GHD patients. Moreover, wholebody metabolic dysfunction in GHD patients is associated with impaired proliferative capacity of SCs, which can be reversed by GH.

Methods: 12 adults with newly diagnosed GHD will be studied before initiation of GH treatment and after GH-replacement therapy (>3 month). On each day, they will receive an intravenous bolus of 0.5 mg GH. Muscle and fat biopsies will be obtained. Analyses include western blot, real-time qRT-PCR, cell cultures of SC proliferation, tracers of substrate metabolism, DEXA-scan, spectroscopy and strength test. SCs will be isolated by fluorescence-activated cell sorting and cell culture experiments performed to evaluate the effects of GH and IGF-1 on SCs ex vivo.

P05.05   Anne Sophie Koldkjær Sølling

TREATMENT WITH ZOLEDRONIC ACID SUBSEQUENT TO ODANACATIB PREVENTS BONE LOSS IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS

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Purpose: The development of odanacatib (ODN), a cathepsin K inhibitor, was discontinued due to an increased risk of cardiovascular events. As the treatment is considered reversible, participants from the "Long-Term Odanacatib Fracture Trial" in Aarhus were offered treatment with zoledronic acid (ZOL).

Methods: Sixty-seven postmenopausal women (mean age: 78) accepted treatment with ZOL 5 mg and were followed for 12 months. Of these, 39 had received ODN for 7 years (ODN group), and 28 had received placebo for 5 years and ODN for 2 years (placebo ODN group). Bone turnover markers (BTM) were measured 3, 6 and 12 months after ZOL, and DXA of spine and hip were performed at the time of ZOL treatment and after 12 months.

Results: Within the entire study population, bone mineral density (BMD) at the lumbar spine increased significantly by $2.8\pm0.9\%$ (mean ± SEM) ($p<0.01$) from baseline to month 12. There was no significant change in BMD at the total hip ($p=0.17$) or femoral neck ($p=0.39$). There was no difference in the changes in BMD from baseline to 12 months between the two groups at any site ($p\geq0.20$ for all). The BTMs were in the lower half of the reference range for postmenopausal women 3 months after ZOL. C-terminal collagen crosslinks increased by $106.9 \pm 9.4\%$ ($p<0.001$), pro-collagen type I N-terminal propeptide by $101.8 \pm 16.2\%$ ($p<0.001$), osteocalcin by $32.3 \pm 5.7\%$ ($p=0.001$) and bone specific alkaline phosphatase by $78.9 \pm 37.2\%$ ($p=0.001$) between 3 and 12 months after ZOL. At month 12, BTMs were still within the premenopausal reference range.

Conclusion: Treatment with ZOL 5 mg maintained BTMs in the pre-menopausal range and prevented bone loss in women previously treated with ODN.

P05.06   Mads Bisgaard
          Bengtsen

COUNTER-REGULATORY RESPONSES TO HYPOGLYCEMIA IN SUBJECTS WITH TYPE 1 DIABETES AND HEALTHY CONTROL SUBJECTS

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Background and aim: Hypoglycemia is a dreaded condition among patients with type 1 diabetes (DM1) and is a limiting factor for optimal glycemic management. Diabetes duration and recent episodes of hypoglycemia impair the normal counter-regulatory response to hypoglycemia. The aim of our clinical trial was to compare counter-regulatory responses to hypoglyceia in patients with DM1 and healthy control subjects.

Material and methods: We designed a randomized crossover trial with nine male DM1 subjects and nine male healthy control subjects. In randomized order, they underwent 1) one episode of hypoglycemia and 2) two consecutive episodes of hypoglycaemia (below 2.9 mmol/L) preceeded and were followed by a hyperinsulinemic euglycemic glucose clamp.

Primary outcome: Insulin sensitivity (M-value)
Secondary outcomes: Counter-regulatory hormones.

Results: During hypoglycemia, plasma glucose levels reached a nadir of ~2.55 mmol/L. M-value was significantly different between the two groups (p<0.05). Control subjects produced a glucagon response with mean peak of 17 pmol/L±8.2 SD on day 1 and 14 pmol±5.2 SD on day 2 (NS difference). The DM1 subjects did not produce a glucagon peak response to hypoglycemia, and levels remained low with a mean concentration of 3.8 pmol/L±1.9 SD on day 1 and 3.8 pmol±1,8 SD on day 2 (NS difference)

Conclusion: Subjects with DM1 had defective counter-regulatory glucagon responses to hypoglycemia and were more insulin resistant compared to control subjects.

P05.07   Maike Mose

A NEW MODEL OF INFLAMMATORY DISEASE COMBINING ENDOTOXEMIA, FAST AND BED REST IN HEALTHY YOUNG MEN:
A RANDOMISED CROSSOVER STUDY

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Background and aim: Inflammatory disease causes insulin resistance, increased lipolysis and loss of muscle mass due to a combination of bed rest, insufficient food intake and ongoing inflammation. Great heterogeneity amongst patients complicates metabolic studies, which highlights the need for a new Model of Inflammatory Disease.

Material and methods: In a randomised crossover design, 6 healthy lean young men were subjected to the interventions: "Healthy" (overnight fast) or "Diseased" (LPS 1 ng/kg + 36 hour fast and bed rest). Insulin resistance was quantified by hyperinsulinemic euglycemic clamp technique and

protein, glucose and fat metabolism was investigated with tracer methodology.

Results: LPS induced a transient rise in CRP in "Diseased" compared to "Healthy" (mean ± SE, 30.57 ± 4.08 mg/l versus 1.03 ± 0.19, respectively.) Insulin sensitivity showed a 42% decrease in "Diseased" compared to "Healthy" conditions (mean ± SE, 4.15 ± 0.23 mg/kg/min and 7.18 ± 0.95 mg/kg/min, respectively, paired t-test, p = 0.01). Lipolysis increased by 72% ± 15% (median ratio ± SE, p = 0.004, Two-way repeated measures ANOVA) in "Diseased" compared to "Healthy", with a 78% ± 2% (median ratio ± SE, p < 0.0001, Two-way repeated measures ANOVA) reduction in both groups during hyperinsulinaemic conditions. We found no significant difference in the protein synthesis, breakdown or net balance between the two groups.

Conclusion: This new Model of Inflammatory Disease induced inflammation and catabolism with increased lipolysis and insulin resistance in both muscle and fat, while no alterations in protein metabolism were observed.

P05.08   Thomas Skjœrlund Grønnebœk

SKELETAL MUSCLE MITOCHONDRIAL PROTEIN SYNTHESIS AND RESPIRATION INCREASE WITH LOW-LOAD BLOOD FLOW RESTRICTED AS WELL AS HIGH-LOAD RESISTANCE TRAINING

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Purpose: Low-load blood flow restricted resistance exercise (BFRE) has emerged as an effective alternative to stimulate muscle growth for those who are unable to perform traditional high-load resistance exercise (HLRE). However, it is unknown whether BFRE, similar to HLRE, can also stimulate muscle mitochondrial biogenesis and respiratory function to support healthy skeletal muscle.

Methods: To study this, 34 healthy previously untrained individuals (24±3 yr.) participated in BFRE, HLRE, or non-exercise control intervention (CON) 3 times per week for 6 weeks. Skeletal muscle biopsies were collected; (1) before and after the 6-week intervention period to assess mitochondrial biogenesis and respiratory function, and; (2) during recovery from single-bout exercise to assess myocellular signaling involved in transcriptional regulation of mitochondrial biogenesis. During the 6-week intervention period, deuterium oxide was continuously administered to the participants to label newly synthesized skeletal muscle mitochondrial proteins.

Results: Mitochondrial protein synthesis rate was higher with BFRE (1.19 %/day) and HLRE (1.15 %/day) compared to CON (0.92 %/day) (P < 0.05), but similar between exercise groups. Coupled respiration supported by complex I and II substrates improved similarly with BFRE (38%) and HLRE

(24%) (P < 0.01). Training did not alter citrate synthase activity compared to CON. BFRE and HLRE elicited similar myocellular signaling responses.

Conclusions: These results demonstrate that BFRE can promote skeletal muscle mitochondrial adaptations, which have important implications for populations in whom exercise with high loading is untenable.

P05.09   Francesco Maria   SEX-SPECIFIC EFFECTS OF HIGH FAT DIET ON ADIPOSE TISSUE GLYCEROL
         Iena   METABOLISM IN MICE

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Background and Aim: AQP7 is an aquaglyceroporin that mediates glycerol efflux in adipose tissue (AT). Its low expression has previously been linked to obesity, a major risk factor for type 2 diabetes, in a sex-specific manner. This project aimed to investigate whether the AT glycerol metabolism is sex-specific after high fat diet (HFD).

Methods: Male and female C57BL/6J mice were fed a control or a HFD for 12 or 24 weeks. Blood glucose (BG) levels and body weight (BW) was monitored throughout the study. Perigonadal AT was used for western blotting and immunohistochemical analysis. Results are expressed as mean ± SEM and analyzed using ANOVA.

Results: BW increased by 34% in females and 49% in males and by 76% in females and by 48% in males, compared to controls, after 12 and 24 weeks of HFD, respectively. BG levels increased significantly in males ($p < 0.05$) after 12 weeks of HFD, while they increased significantly in both females ($p < 0.05$) and males ($p < 0.05$) after 24 weeks of HFD. Total AT AQP7 protein abundance increased after 12 ($p < 0.05$) and 24 ($p < 0.05$) weeks of HFD in female mice, whereas no significant changes were observed in male mice. This was paralleled by a decreased expression of lipolytic enzymes and an increased expression of glycerol kinase that phosphorylates glycerol into glycerol-3-phosphate.

Conclusions: Female mice were less susceptible to develop insulin resistance in response to HFD than male mice. Moreover, it was only in female mice that the expression of AQP7 increased in response to HFD. No parallel increase in the expression of lipolytic enzymes was observed. These findings support a sex-specific regulation of AT glycerol metabolism in mice fed a HFD.

P05.10   Liv Hald   VASCULAR EFFECTS OF ASPIRIN IN PATIENTS WITH TYPE 2 DIABETES
                      WITHOUT CARDIOVASCULAR DISEASE AND NON-DIABETIC MATCHED
                      CONTROLS

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Introduction: In this study, we investigated whether the effect of low-dose aspirin on endothelial-dependent vasodilation and arterial stiffness is different in patients with type 2 diabetes (T2DM) without known cardiovascular disease compared to a control group. Further, we examined the effect after the first ingested tablet, after 1 week of treatment and during a 24-hour dosing interval.

Method: We included 21 patients with T2DM and 21 age- and sex-matched controls. Endothelial-dependent vasodilation was assessed as the logarithmic reactive hyperemia index (lnRHI) measured by peripheral arterial tonometry and arterial stiffness assessed as pulse wave velocity (PWV) measured by applanation tonometry. Measurements were performed at baseline and 1 h after administration of 75 mg of aspirin. Participants were then treated for 6 days with once-daily aspirin, and measurements were repeated 24 h and 1 h after aspirin intake.

Results: Overall, there was no difference in the effect of aspirin on lnRHI or PWV in patients with T2DM compared to controls. After one week of treatment, both groups had an increase in lnRHI ($p<0.01$), but no change was seen in PWV. The control group had an immediate increase in lnRHI after the first aspirin tablet, but this was not observed in T2DM patients and was statistically significantly different between the groups ($p=0.046$). The effect of aspirin on lnRHI decreased during the 24-hour dosing interval in T2DM patients ($p=0.046$), but not in controls ($p=0.84$).

Conclusion: We did not detect any differences in the effect of aspirin treatment on endothelial-dependent vasodilation or arterial stiffness in patients with T2DM when comparing to a matched non-diabetic control group.

P06.01 Simone Schandorf Elstrøm Nielsen

TRANSCYTOSIS OF THERAPEUTIC TRANSFERRIN RECEPTOR ANTIBODIES IN BRAIN ENDOTHELIAL CELLS

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Brain endothelial cells (BECs) forming the blood-brain barrier (BBB) constitute an essential role in protecting the brain from xenobiotics, but also possess a challenge for transport of pharmaceutical antibodies to the central nervous system, where they are intended as treatment for neurodegenerative diseases. It is well accepted that delivery of therapeutic antibodies (e.g. for Alzheimer's and Parkinson's disease) to the brain is possible by receptor-mediated transcytosis, e.g. by use of the transferrin receptor (TfR), but successful delivery is still limited. Recent studies have shown that optimization may be possible by altering the antibody binding properties. Since most research has focused on cell uptake mechanisms, the subcellular transport and secretory mechanisms remain unexplained and will be the focus of this PhD study. It is our hypothesis that a detailed study of these mechanisms will provide guidance on ways to design and target new generations of brain drugs. Using an in vitro (ex vivo) BBB model with primary cells and high-resolution imaging, I will investigate whether engineering therapeutic antibody affinity and avidity can optimize brain uptake. I aim to characterize the intracellular mechanisms

for trafficking and transcytosis, and it is our hypothesis that such elucidations will provide important knowledge of how new generations of drug constructs should be designed.

P06.02 Abdel-Rahman Al-Absi

SYNAPTIC DYSFUNCTION IN THE PREFRONTAL CORTEX OF DF(H15Q13)/+ GENETIC MOUSE MODEL OF SCHIZOPHRENIA

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The recurrent 15q13.3 microdeletion is a 1.5 mega-base gene deletion on the human chromosome 15 that includes six genes. Findings from schizophrenic patients and animal models suggest that a dysfunction in more than one of the 15q13.3 genes is considered a risk factor for developing schizophrenia. Recently, a mouse model Df(h15q13)/+ of the 15q13.3 syndrome was generated by microdeletion on chromosome 7. Even though that etiology of schizophrenia is still poorly understood, emerging candidate risk genes for schizophrenia, along with clinical findings, implicate various aspects of GABAergic and glutamatergic neurotransmission deficit with the various symptoms of schizophrenia.

RT-qPCR and western blot were used to investigate number of GABA synaptic markers in the prefrontal cortex (PFC) in this mouse model. Furthermore, a structural study using Golgi staining and 3D reconstruction of pyramidal neurons from the same brain region has been employed to investigate spines and dendrites.

Results show a decrease in GAD65, but not GAD67, at both the mRNA and the protein levels in the PFC of Df(h15q13)/+ mice. Additionally, we found a decrease in both number and head volume of dendritic spines of the pyramidal neurons from the same brain region in Df(h15q13)/+ mice. GAD65 is known to be localized at the presynaptic terminal of the inhibitory synapses, and therefore to reflect their function. Furthermore, spine number and spine morphology of the pyramidal neurons are suggested to correspond to number and function of the excitatory synapses. Together, these results suggest a synaptic deficit at both the inhibitory and the excitatory synapses in the PFC region of Df(h15q13)/+ mice.

P06.03 Thorsten Rasmussen

EARLY DETECTION OF SMALL FIBER POLYNEUROPATHY AND AUTONOMIC DYSFUNCTION IN TTR AMYLOIDOSIS

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Introduction: Transthyretin-related (TTR) amyloidosis is a rare hereditary disease characterized by deposition of insoluble aggregates of proteins and fibrils in body tissues and organs. Active TTR amyloidosis results in irreversible progressive peripheral sensorimotor and autonomic neuropathy as well as non-neuropathic changes of cardiomyopathy and nephropathy. The diagnosis is based on the finding of amyloid deposits in body tissues with a clinical correlate and a pathogen variant in TTR. In at risk family members, pre-symptomatic individuals can be detected by genetic testing. Currently, asymptomatic individuals with genetically verified TTR amyloidosis are followed by a watchful-waiting approach, with treatment being initiated at the onset of clinical symptoms.

Aim: To asses early signs of neuropathy induced by amyloid deposits in patients with TTR.

Methods: Patients with verified TTR amyloidosis will be investigated by a standardized autonomic test battery assessing the function of the small fiber sympathetic and parasympathetic branches of the autonomic nervous system.

Perspectives: We expect that this novel approach in the assessment of TTR amyloidosis in gene-mutations carriers may detect the transformation to active-state amyloidosis at an earlier stage, allowing for fast initiation of treatment before the presence of symptomatic irreversible organ damage.

P06.04 Maimaitili Muyesier

INVESTIGATING THE ROLE OF CIRCULAR RNA IN MESENCEPHALIC DOPAMINERGIC NEURONS DERIVED FROM HUMAN PLURIPOTENT STEM CELLS

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Parkinson's Disease (PD) is the second most common neurodegenerative disorder. Despite the ongoing effort to understand the disorder, the cause is still unknown, with 90% of the cases being sporadic and only 10% linked to known coding gene mutations. Broader approaches are, therefore, required to investigate other regulatory mechanisms that may control mesencephalic dopaminergic (mesDA) neuron development or that are involved in disease processes. Circular RNA (circRNA) are abundantly expressed in the brain and highly conserved between species. However, the precise role for many of these circRNAs is still unknown. The few circRNA that have been investigated have been shown to be capable of controlling gene expression.

Therefore, elucidating the function circRNA in mesDA neurons may reveal novel neuroprotective strategies for Parkinson's disease. Using human pluripotent stem cells, we have produced mesencephalic dopaminergic neurons in vitro and examined the expression of circRNA using next-generation sequencing. Lentiviral agoshRNA knockdown was used to inhibit specific circRNA without altering their linear counterparts and, using this system, we are now investigating the role of circRNA in the regulation

of mesDA neuron cell fate. The results from this project will significantly contribute towards our understanding of how circular RNAs regulate gene expression in disease development and disease states.

P06.05 Sérgio Eduardo Costa Almeida

NEURON-SPECIFIC RECEPTOR-MEDIATED SORTING OF THE FTLD RISK FACTOR PROGRANULIN

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Frontotemporal lobar degeneration (FTLD) is the most common neuro-degenerative disorder under the age of 65, characterized by selective atrophy of the frontal and temporal lobes of the brain. The major cause of familial FTLD is heterozygous loss-of-function mutation in the GRN gene. GRN encodes a secreted glycoprotein known as progranulin (PGRN) that up until now has an undefined biological function. Recently, it was discovered that homozygous loss-of-function mutations in GRN cause a lysosomal storage disorder called neuronal ceroid lipofuscinosis (NCL), implicating PGRN in a lysosomal function and pointing out that sustaining or elevating PGRN levels is an appealing strategy for treating FTLD and NCL. The present project is based on our discovery of a CNS-specific receptor that, in our preliminary data, appears to regulate PGRN levels and location in different models. Based on this, we aim to investigate further into the interaction between these two proteins in the context of lysosomal function and potential therapeutic value for FTLD.

P06.06 Giulia Monti

LOCAL SYNAPTIC TRANSLATION OF A NOVEL SPLICE-VARIANT OF THE ALZHEIMER'S DISEASE RISK GENE SORL1

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SORLA is a neuronal receptor implicated in Alzheimer's disease (AD). Several single nucleotide polymorphisms within SORL1, the gene encoding SORLA, are associated with late-onset AD. Recently, rare SORL1 variants with premature stop-codons were identified in families with early-onset AD. These findings suggest that SORL1 genetic variants represent a major contributor of AD risk, now proposed to be considered next to variants in APP, PSEN1-2.

Here we describe a SORL1 transcript containing a novel exon located between exon 38 and exon 39, named exon 38B, encoding a truncated protein. We have identified this novel SORL1 transcript in several human tissues, including the brain, showing the strongest expression in the cerebellum. qPCR analysis showed that the novel transcript is reduced by >50% in the cerebellum of AD patients compared to controls. Notably, expression of SORL1 transcript encoding full-length SORLA was not changed, in line with results from previous studies showing unaffected levels in AD cerebellum. Immunostaining on human cerebellum showed

that only a subset of cerebellar Purkinje cells (PCs) expresses the truncated receptor, compared to an even distribution of the full-length SORLA. This result was confirmed by in-situ hybridization. Interestingly, almost 50% of SORL1-38B transcripts was found in dendrites of PCs, whereas full-length SORL1 transcripts locate >90% to the soma.

Our findings suggest that the specific cerebellar localization might be related to new independent functions of this SORL1 transcript. SORL1-38B represents a new interesting splice form, but further studies are necessary to elucidate the role played by this transcript in human cerebellum.

P06.07   Emil Gregersen   THE ROLE OF USP19 IN THE EXCRETION AND CYTOTOXICITY OF ALPHA-SYNUCLEIN AND THE PRION-LIKE INTERCELLULAR SPREADING OF ALPHA-SYNUCLEIN PATHOLOGY

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Parkinson's disease is currently treated purely symptomatic. To develop better treatment strategies, we need to better understand the underlying pathology of the disease. Increasing evidence supports the aggregation and prion-like spreading of the small neuronal protein α-synuclein as a key factor in disease progression. The release-mechanism of pathological oligomer α-synuclein species, promoting the spread of pathology between interconnected brain areas of healthy neurons, is unknown. Moreover, the size and composition of the transferred α-synuclein are poorly studied. My project aims to investigate a newly identified process termed misfolding-associated protein secretion (MAPS) as a potential pathway for the selective secretion of aggregated α-synuclein. The endoplasmic reticulum anchored deubiquitinase, USP19, has a key role in MAPS by targeting misfolded proteins for secretion under proteasomal stress. My data suggest USP19 targets aggregated α-synuclein, which are excreted to the extracellular media. Interestingly, a cytosolic isotype of USP19 has the opposite effect and causes accumulation of pathological alpha-synuclein. Based on this, we are aiming to identify potentially novel cell-made oligomer species excreted by MAPS. Furthermore, we want to explore the effects of the excretion on α-synuclein-dependent cytotoxicity in cell models and primary neurons. In the end, we hope to answer if USP19-dependent excretion of α-synuclein can be part of the prion-like spreading of α-synuclein pathology.

P06.08   Sara Raquel   INVOLVEMENT OF THE CD163 RECEPTOR IN THE ALPHA-SYNUCLEIN
          Almeida Ferreira INDUCED NEURODEGENERATION IN PARKINSON'S DISEASE

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The occurrence of inflammatory changes in the brain and periphery in Parkinson's disease (PD) patients have been documented. How the brain and the peripheral immune system interact, and the consequence of this

interaction in disease, is still undetermined. We hypothesize that the immune system is actively involved in the neurodegenerative process associated to alpha-synuclein in PD, thus its modulation may have therapeutic potential. CD163 is a scavenger receptor expressed in macrophages but not in brain microglia. It is overexpressed in certain inflammatory conditions, but its role in the immune system remains unknown. We have observed infiltration of CD163+ cells into the brain in a PD toxic rat model and changes of CD163 (at cellular and soluble level) in PD patients, strongly suggesting a role for CD163 macrophages in disease. We aim to determine whether the CD163 receptor is directly involved in the immune events occurring in PD and explore how it relates to alpha-synuclein. To do so, we have injected aggregated fibrillar alpha-synuclein into the striatum of CD163 knock-out (KO) animals and wild-type (WT) littermates. Mice were analysed to evaluate behaviour, alpha-synuclein pathology, immune response and dopaminergic degeneration at short (1 month) and long term (6 month) post-injection. The injection of alpha-synuclein fibrils lead to significant alpha-synuclein pathology and neuronal degeneration associated to motor defects. This was linked to a significant increase of MHCII immune activity that appeared different in the KO mice. Our data suggest that CD163 has a relevant role in the alpha-synuclein induced pathology and immune response.

P06.09   Pernille Louise   A STUDY OF THE TEMPORAL DEVELOPMENT OF BETA-AMYLOID, TAU,
          Kjeldsen   INFLAMMATION, AND VASCULAR CHANGES IN PRECLINICAL
                           ALZHEIMER'S DISEASE AND THE INFLUENCE OF THE NORADRENERGIC
                           SYSTEM ON COGNITIVE DECLINE

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Alzheimer's disease (AD) is the most common form of dementia, affecting more than 5 million people worldwide. It is characterized by a brain pathology consisting of extracellular deposits of beta-amyloid protein (Aβ), intracellular bundles of tau protein (tangles), brain inflammation in the form of activated microglia, and possibly changes in the brain's capillary blood flow. The order in which Aβ, tangles, inflammation, and vascular changes occur in the brain is still unclear, although Aβ is believed to occur first, many years before there are overt symptoms. So far, attempts to stop the pathologies with medications have been unsuccessful, possibly because by the time people start showing symptoms and are referred to treatment, there has already been too much brain damage. Thus, if people could be identified before they show symptoms, people with preclinical AD could perhaps be protected. We propose to recruit participants who have a genetic disposition for developing the disease as carriers of a certain genotype, ApoE4, and who, on a PET scan, show elevated Aβ deposition. We will then ask these participants to undergo further PET scanning for tau and inflammation as well as perfusion MRI scanning for vascular changes. The noradrenergic system in a brain area called locus ceruleus may be able to control inflammation. We will, therefore, also ask participants to undergo PET scanning for noradrenaline levels. This will reveal the order in which the

different pathologies occur in the brain, and how they influence each other in preclinical AD, as well as elucidate whether noradrenaline should be a target for future neuroprotective treatments.

P06.10   Martin Kinnerup   PROGRESSION OF COGNITIVE IMPAIRMENT IN PARKINSON'S DISEASE

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Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder, with approximately 1% of the population over 60 afflicted by the disease. The hallmark symptoms of PD are motor symptoms of rigidity, bradykinesia, tremor and postural instability.

On average, PD patients experience ~8 non-motor symptoms (NMS) during the disease duration. Among the reported NMS, we find: autonomic dysfunction, psychiatric (most common) and sleep disorders. The cause of the severity and the manifestation of NMS remain unclear, but they have been related to neuronal loss in locus coeruleus (LC). Importantly, NMS and the loss of noradrenergic neurons may appear before the hallmark motor symptoms are clinically detectable, which is in line with classical Braak staging of PD.

Through projections to cortical and subcortical structures, LC modulate various cognitive functions, such as perception, attention, learning and memory. With strong links between LC and cognition, quantification of the in vivo noradrenergic integrity could potentially be a predictive biomarker for cognitive progression in PD. In recent PET imaging studies, [^{11}C]MeNER showed, indirectly, a significant decrease of noradrenergic neurons in locus coeruleus, thalamus, nucleus ruber, hypothalamus, dorsal raphe and median raphe.

In the current study, I 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.

P07.01   Jordan Nicolas Alves   CHANGES OF RESTING-STATE OSCILLATORY NETWORK DYNAMICS AFTER MOTOR LEARNING: AN M.E.G. DEVELOPMENTAL STUDY

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Neuroimaging studies have shown that the motor learning induced alterations of the functional connectivity assessed during Resting State Networks (RSN) is age-dependent in adults. Motor learning relies on the build-up of new sensori-motor representations, which has been studied using the "bar-man task" in adults and in children. The aim of this study was to investigate the modulations of functional connectivity after a motor learning task in the child's resting state network.

20 children aged 7 to 12 (12 boys; mean 9y 9m; sd 1y et 8m) took part in the study. The RS tasks consisted of a 3x45s session. In the load-lifting motor learning task the participant was asked to lift a weight using the right hand, which triggered the fall of a weight attached to the left arm. We recorded the neuromagnetic signals using a CTF-MEG system. Coherency analyses have been conducted in the alpha and beta frequency bands. Results have been analysed using permutation statistic ($\alpha < 0.005$).

The behavioural performances were assessed by a learning curve model throughout the trials and revealed a significant global learning effect ($F_{(7;19)} = 50,62$; $p < 0,0001$). In the alpha band (8-12Hz): Analysis showed an increase of the connectivity in the RSN. In the beta band (15-29Hz): Significant increase of the functional connectivity in the somatosensory cortex and in the precuneus gyrus. Interestingly, we found that connectivity measured in pairs of brain areas in the pre-learning RSN was predictive of the behavioural performance.

After a motor learning task, the functional connectivity measured in the RSN increased between the regions involved in the build-up of sensori-motor representations in children.

P07.02   Anders Gyldenkerne

OPTICAL AND VISUAL QUALITY AFTER SMALL-INCISION LENTICULE EXTRACTION (SMILE) FOR NEARSIGHTEDNESS

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Purpose: To examine the relation between corneal higher-order aberrations (HOAs), scatter, and residual refraction with visual symptoms and visual acuity following small incision lenticule extraction (SMILE) for nearsightedness.

Setting: The Department of Ophthalmology, Aarhus University Hospital

Design: Prospective cohort study

Methods: 51 eyes of 51 patients treated with SMILE for nearsightedness were examined before and at 1 day, 7 days, 1 month, and 3 months after surgery.

Results: Preoperative refraction was -7.08±1.17 diopters (D). Postoperative uncorrected distance visual acuity (UDVA) at 3 months was -0.03±0.11 logMAR, and the postoperative refraction was -0.17±0.33 D.

Scatter increased by 0.22±0.53 (p=0.06), and the HOA coma increased by 0.1±0.1 mm (p<0.001); the HOA spherical aberration did not change significantly (p=0.35). The severity of patients' self-reported visual symptoms decreased following surgery; neither scatter, corneal HOAs, nor residual refraction was correlated with the degree of visual symptoms. Postoperative UDVA was significantly predicted by the residual refraction (adj. R^2=0.16, p=0.02 at Day 1 to adj. R^2=0.55, p<0.001 at 3 months). Scatter and corneal HOAs were not associated with postoperative uncorrected visual acuity.

Conclusions: Despite statistically significant changes in scatter and corneal HOAs, the severity of self-reported visual symptoms decreased following SMILE. The residual refraction proved highly successful in predicting postoperative uncorrected visual acuity, whereas scatter and corneal HOAs did not; the post-operative residual refraction plays a pivotal role for the visual quality.

P07.03   Pauline Cantou   NEGATIVE CUES MODULATE CONFLICT PROCESSING: AN FMRI STUDY IN YOUNG ADOLESCENTS

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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 individuals in early adolescence 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.

In view of these results, we hypothesize that emotion will increase sub-cortical activation (especially in the amygdala) in conflict trials, which may reflect a takeover of emotional cues over cognitive processes.

P07.04   Simone Hyldgaard Andersen

THE NUCLEAR ANATOMY AND FIBER CONNECTIONS OF THE GÖTTINGEN MINIPIG AMYGDALA

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Background: The amygdala receives multisensory input and is involved in the interpretation of these external and internal stimuli, assigning them emotional valence. Animal studies have shown the role of amygdala in the pathophysiology of different psychiatric diseases, e.g. major depression, anxiety and PTSD. Knowledge about anatomy and fiber connections of the amygdala is pivotal in order to conduct functional neurosurgical studies to find possible therapeutic interventions.

Aim: This study aims to describe the anatomy and connectivity of the amygdala and its subnuclei in the Göttingen Minipig (GM).

Method: 6 GM brains are embedded in HistOmer before being cut either coronally, horizontally or sagitally. The slabs are sliced and stained with Nissl or TH followed by microscopic analysis in order to identify the nuclei of the amygdala. Hereafter, 6 GM are mounted to a stereotaxic frame and MR-scanned. The MR-scan coordinates are used to inject anterograde or retrograde tracer in the specific regions of the amygdala. After 4 weeks, the GMs are anesthetized, euthanized and perfused with para-formaldehyde, brains are removed, prepared histologically and analyzed. Finally, the tracing study will be compared to DWI tractography.

Future Significance: Animal studies show that deep brain stimulation (DBS) of the basolateral amygdaloid nucleus can relieve some of the symptoms seen in animal models of PTSD. Furthermore, based on case studies of DBS as a means of treating autism refractory to medical treatment, it is hypothesized that DBS of the amygdala can help decrease symptoms of self-injurious behavior and improve cognitive function.

P07.05   Charlotte Ernst

ATP-INDUCED DIAMETER CHANGES IN THE RETINAL VASCULAR TREE EX VIVO DEPEND ON THE BRANCHING LEVEL

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Background: Disturbances in the retinal blood flow regulation are a critical cause of vision loss. In order to develop new therapies for vision-

threatening diseases, knowledge of the mechanisms underlying retinal blood flow and diameter regulation of the retinal blood vessels is required. Adenosine triphosphate (ATP) is known to be one of the key mediators of vasodilatation in the arterioles, but the vasoactive effects of ATP in the precapillary arterioles and capillaries are unknown.

Method: Porcine hemiretinas with a complete vascular segment were studied using the retinal fluorescence perfusion method. The diameter regulation of the retinal blood vessels was examined after intravascular and extravascular applications of the non-degradable ATP analogue ATP-γS.

Results: Extravascular ATP-yS induced vasodilatation of retinal arterioles (p=0.01), but not in precapillary arterioles and capillaries (p>0.30). Intravascular ATP-yS induced vasoconstriction in precapillary arterioles (p=0.02) but did not change the diameter in either arterioles or capillaries (p>0.29).

Conclusion: ATP-yS has both vasodilatory and vasoconstriction properties, with a different vasoactive effect on the different branching level of the retinal blood vessels. Extravascular ATP-yS induces vasodilatation in retinal arterioles, and intravascular ATP-yS induces vasoconstriction in retinal precapillary arterioles. Further investigations should elucidate which signal pathways mediate these effects.

P07.06   Hao Zhou   THE SPATIOTEMPORAL DYNAMICS OF TEMPORAL CONTEXT EFFECT IN HUMAN EARLY VISUAL CORTEX

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The human nervous system is highly adaptive and context sensitive. A short flash could be perceived brighter when offset synchronized with a nearby long flash than onset synchronized, leading to the so-called "Temporal Context Effect (TCE)" (Eagleman et. al., Nature, 2004). The goal of the current study is to delineate the neural correlates of this illusory effect, with a particular focus on the potential neural circuitry among early visual areas. We reconstructed sources of the brain magneto-encephalography (MEG) data recorded from observers experienced the Temporal Context Effect. Together with fMRI retinotopic mapping data, signals from different occipital lobe areas were extracted to investigate whether different early visual areas have differential representation of the onset vs. offset synchronized short flash. Our data revealed that, in the early time window of 100-200ms, the first neural response of TCE was observed in hV4, followed by V1/V2/V3, and later in V3a. In the time window of 200-250ms, besides V1/V2/V3/V3ab, LOC elicited strong visual awareness negativity (VAN) signals to TCE. These results indicate that the neural circuitry of TCE is instigated in hV4, followed by connection or confirmation with early visual area V1/V2/V3 and V3ab, and final perceptual output in LOC.

P07.07   Jakob Hansen
USING OPTICAL MOTION CAPTURE TO MEASURE KINEMATICS DURING SIT-TO-STAND

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Background: The method of 3D optical motion capture has been widely used to quantify the sit-to-stand (STS) movement. However, most motion capture studies of the STS movement report the use of a chair without armrest and backrest, which is in contrast to most chairs in everyday life. Further, no studies describe the use of a customized camera setup or marker protocol used specifically for the STS movement.

Aim: To compare different marker protocols to measure sit-to-stand from a regular chair.

Method: Cameras were positioned close to the subject in positions where the chair covers the reflective markers the least. However, the reflective markers located at the pelvis and thigh were still an issue due to the armrest of the chair and the hip flexion of the subject. Therefore, a specific marker set was developed, using collinear markers on a rigid pin, allowing the markers to be moved away from the covered area. To determine the validity of the developed marker set, it was compared to a standard gait marker protocol and a marker protocol where additional markers are used to track the pelvis segment.

Results: The overall ability to capture the markers' trajectories during STS will be evaluated. Further, the precision of calculated angles of the pelvis, hip and knee during STS will be compared. The study will result in a proposal for a new camera setup and marker protocol to be used when evaluating the STS movement for either clinical or research purposes.

P07.08   Sidsel Rugberg Alsing
TUNABLE EXPRESSION OF DICER INDEPENDENT SHRNAS FOR POTENT, DURABLE, AND SPECIFIC KNOCKDOWN OF VEGF

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RNA interference (RNAi) is a powerful and versatile tool which may be used for both research and gene therapy purposes. MicroRNA (miRNA) mimics and short hairpin RNAs (shRNAs) have been shown to efficiently downregulate a selected target. These species are processed by the enzyme Dicer to yield both a guide strand, which mediates knockdown of the selected target, as well as a passenger strand. The guide strand is incorporated into the RNA induced silencing complex (RISC), where it mediates targeted knockdown. The passenger strand may, however, also be incorporated into the RISC, resulting in potentially harmful off-target silencing. It has been discovered that miR-451 is processed in a non-canonical Dicer independent manner, yielding only a guide stand and no passenger strand. Using structural features which define miR-451, we have designed Dicer independent shRNAs (DIshRNAs), targeting vascular endothelial growth factor (VEGF), and which are embedded in long miRNA scaffolds and driven by an RNA polymerase II (pol II) promoter. This allows for controlled, tissue specific, and/or inducible expression of

the RNA inhibitor, with no passenger strand off-target effects. Our results show that our pol II driven DIshRNAs exhibit no passenger strand effects, while they specifically target and robustly reduce the level of VEGF, even in the absence of Dicer. VEGF is overexpressed in exudative age-related macular degeneration (AMD), and we hypothesize that the therapeutic use of DIshRNAs in gene therapy approaches may be able to potently reduce VEGF levels in a safe, specific, and long-lasting manner and hence ameliorate the disease phenotype.

P07.09   Simon Bang   REGRESSION METHODS FOR ORDINAL DATA IN METACOGNITION
          Kristensen
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A broad class of experiments performed in cognitive sciences can be summarised as follows. In a single trial, a subject must complete a task and then quantify her/his, for example, confidence in or control over the performed task. Such a trial is then repeated under various configurations, such as task difficulty or brain region stimulation. An objective of such experiments could be to measure metacognition, i.e. a person's ability to reflect on her/his actions and choices. Signal detection theory (SDT) is a popular and widely used model for analysing outcomes from cognitive experiments. However, two shortfalls of the model remain: 1) it is unclear how to account for the often complex designs of the experiment, and 2) it does not provide any direct estimates of metacognition. Recently, a measure of metacognitive sensitivity was introduced, called meta-d' ("meta d prime"), which is intended to quantify the metacognitive ability from the SDT model, but the need for a flexible model to accommodate the design persists. One solution in the SDT may be to realise that the standard SDT model is in fact statistically equivalent to the Proportional Odds model, a well-known regression technique for ordinal data. Using this, the experimental design can be adequately modelled. Using the same idea, we have defined an extension of SDT, which incorporates meta-d'. The mathematical definition of this model using latent variables is flexible, which makes it easy to expand, so that we can define a regression model to estimate metacognitive sensitivity while accounting for the design. Additionally, we have written a software package in the open-source statistical language R, which implements the model.

P07.10   Ole Søndergaard ROLE OF INDIVIDUAL CELL TYPES IN THE SUPERIOR COLLICULUS OF THE
          Schwartz   MOUSE

O. Schwartz

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In recent years, the mouse has emerged as a promising model for vision research, but much about how vision is processed in the mouse is still unknown. The Superior Colliculus (SC) receives input from ~90% of retinal ganglion cells and is assumed to play a central role in this processing. Yet, on the level of the individual cell, the SC is relatively undescribed. Since such knowledge is the foundation for understanding the circuitry of and ultimately the computations performed by the SC, our project is focused on identifying and characterizing individual collicular cells. To this end, we

have reviewed the cre-recombinase labelled cell lines in the GENSAT database, and singled out the lines where the morphology and laminar position of the cre-expression is compatible with it labelling a single cell type in the SC. We intend to analyze each of these in terms of their function, connectivity and role in behavior. To assess the function of the cells, we inject a floxed calcium indicator and gain visual access to the SC by inserting a cranial window in the skull and displacing the overlying sinus with a silicone plug. This setup allows us to measure the calcium responses of the cells with two-photon microscopy. In parallel, we are infecting the cre cells with a retrograde virus, resulting in labelling of any connected retinal ganglion cells. Last, we will be performing behavioral analyses on mice with an ablation of cre cells in the SC.

By combining functional calcium imaging of the cell lines with an analysis of connectivity to known RGCs and the consequence on behavior of ablation of the cells, we aim to obtain a strong indication of what role the cells play in mouse vision.

P08.01   Jacob Horsager   CARDIAC ^{11}C-DONEPEZIL BINDING INCREASES WITH AGE IN HEALTHY HUMANS - POTENTIALLY SIGNIFYING SIGMA-1 RECEPTOR UPREGULATION

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Background: Donepezil is an acetylcholinesterase inhibitor used for cognitive impairment in dementia. Recently, donepezil was associated with cardioprotection, but the mechanism is unknown. In our[11]C-donepezil positron emission tomography (PET) study of patients with Parkinson's disease and healthy controls, we observed a substantially higher PET signal in the heart of the older subjects, suggesting an upregulation of a donepezil target-protein with age.

In this observational report, we suggest that the cardioprotection is mediated through sigma-1-receptor upregulation, which is a receptor known to protect against myocardial hypertrophy and is abundantly expressed in the human heart.

Methods: We included 57 subjects with cardiac[11]C-donepezil PET data, all with no history of cardiovascular disease. Linear regression analysis was performed to explore the correlation between cardiac[11]C-donepezil standard uptake value (SUV) and age. Multiple linear regression analysis was performed to study potential confounders.

Results: The linear regression analysis revealed a significant positive correlation between cardiac[11]C-donepezil uptake and age ($r^2= 0.63$, P< 0.0001). The average increase was 1.25 SUV per decade and a 2-fold increase in SUV from age 30 to 65 years. The multiple regression analysis revealed no other significant predictors for[11]C-donepezil uptake.

Conclusion: Cardiac[11]C-donepezil SUV increases robustly with age in humans. We postulate that the increased[11]C-donepezil binding is caused

primarily by sigma-1 receptor upregulation. If our interpretation is correct, it shows that sigma-1 receptors may represent an overlooked target for pharmacological intervention studies.

P08.02   Mette Vestergård   NEONATAL HYPOXIC ISCHEMIC ENCEPHALOPATHY AND HEART RATE
          Pedersen   VARIABILITY: A STUDY IN PIGLETS

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Background: Heart rate variability (HRV) may be a novel biomarker of neonatal hypoxic ischemic encephalopathy (HIE). However, the association needs thorough systematic scrutiny, in particular with respect to the influence of treatment for HIE; therapeutic hypothermia (TH). We aimed to compare HRV parameters in piglets subjected to hypoxia-ischemia (HI), with or without TH, and healthy control piglets.

Materials and Methods: Piglets < 24-hours old were anesthetized and mechanically ventilated. A standardized hypoxic-ischemic insult was induced for 45 minutes. Six piglets were then randomized to TH (33.5 °C), and 6 piglets were randomized to normothermia (38.5 °C). Five control piglets were anaesthetized but had no HI. All piglets were observed for 24 hours after hypoxia. Electrocardiogram was recorded continuously. The HRV parameter standard deviation of normalized RR-interval (SDNN) was calculated in 5-minute epochs using Kubios Premium®.

Results: At baseline, no differences between groups were detected. SDNN was supressed during hypoxia. In normothermic piglets, SDNN remained supressed during the first hour after hypoxia. Hypothermic piglets had an increased SDNN in the first 5 hours after hypoxia, corresponding to the decreasing heart rate caused by the cooling process. At 5 hours, SDNN in hypothermic piglets plateaued, but it remained increased compared to both controls and normothermic piglets.

Conclusion: Our preliminary results show that HRV is supressed during and immediately after a standardized hypoxic ischemic insult and that therapeutic hypothermia increases HRV during cooling and after target temperature is reached.

P08.03   Jelena Stankovic   FOOD NEOPHOBIA AMONG DANISH ADOLESCENTS WITH AND WITHOUT
                             AN ADHD DIAGNOSIS

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Background: A high level of Food Neophobia (avoidance of novel foods) is associated with a deficiency in several nutrients. The same spectrum of nutrients has been established to be deficient among adolescents with ADHD, and this deficiency is associated with pronounced symptoms of ADHD. Other psychiatric diagnoses have been associated with an altered perception in olfaction and gustation, whereas such descriptions have not been described for ADHD. If there is an association between food

neophobia and the eating habits of adolescents diagnosed with ADHD based on an altered olfaction/gustation, it will create a whole new target for intervention/treatment since the "neophobic" eating behaviour is associated with pronounced symptoms of ADHD.

Aim: The aim of the present study is to investigate the level of food neophobia in healthy adolescents (without any established diagnoses) compared with adolescents diagnosed with ADHD. Further, we want to investigate whether the sense of smell and the sense of taste correlate with the level of food neophobia.

Methods: Two hundred Danish adolescents in aged 13-16 years will be enrolled: 100 without an established ADHD diagnosis and 100 with the diagnosis. This study will be performed as two consecutive studies. The first study will be a survey consisting of two questionnaires evaluating the eating behavior. The top 10% in both groups with the most neophobic eating behavior will be invited to participate in the second study. Here, we will perform a behavioral test to see how the participants actually behave when presented to novel foods. Further, the olfaction and gustation will be assessed as well as a quality-of-life questionnaire.

P08.04 Camilla Lundquist

FROM RESEARCH TO CLINICAL PRACTICE: APPLYING AN ALGORITHM FOR PROGNOSIS AND TREATMENT OF UPPER LIMB PARESIS IN PATIENTS WITH SUBACUTE STROKE

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Background: Accurate prediction of recovery of upper limb (UL) function can lead to targeted rehabilitation after stroke. The PREP2 algorithm predicts UL function based on clinical assessments combined with information on age, severity of stroke and transcranial magnetic stimulation. Despite the potential benefit, PREP2 is not used clinically. A main obstacle is that PREP2 must be applied within the first 72 hours after stroke.

Study 1. Prediction of UL function

Aim: Assess the accuracy of PREP2 when applied 14 days post stroke.

Method: A prospective cohort study. Ninety stroke patients are included consecutively at Hammel Neurorehabilitation Center. At baseline, patients are assessed according to PREP2, and UL function at three months post stroke is predicted in four categories.

Main outcome measure: Action Research Arm Test to assess UL function at 3 months.

Statistics: Correct Classification Rate.

Study 2. Prediction of real-life UL use.

Aim: Examine to what extent predicted PREP2 categories are associated with actual, real-life UL use.

Method: Patients included in study 1 wear triaxial accelerometers on both wrists at follow-up.

Primary outcome: Use ratio between affected and unaffected UL and magnitude ratio.

Statistics: Multiple linear regression.

Study 3. Future implementation.

Aim: Preparation of future implementation of PREP2.

Methods: Semi-structured focus group interviews with key staff in neuro-rehabilitation will be conducted to explore feasibility, acceptability and perceived usefulness of prediction models for UL function.

P08.05   Tingting Gu   BIODISTRIBUTION OF HYPOXIA CONDITIONED MYOBLAST-EXTRACELLULAR VESICLES IN STROKE MICE

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Remote ischemic conditioning (RIC) is a non-invasive treatment induced by repeated cycles of controlled ischemia-reperfusion in the limb. It has been proven to protect the brain from ischemia and reperfusion injury. However, the protective mechanism of RIC remains unclear. It is hypothesized that RIC might stimulate the release of extracellular vesicles (EVs) in the limb, which are cell-derived nano-particles that can carry different cargos to the remote ischemic area. In vitro data from our collaboration group has shown that EVs derived from hypoxia-reoxygenation conditioned myoblasts (undifferentiated cells that can develop into muscle cells) can promote angiogenesis and cell viability. In this study, we tested the biodistribution of EVs derived from the conditioned myoblasts in a stroke mouse model to see if there was a specific accumulation of conditioned EVs in the ischemic hemisphere. Mice were subjected to 45min middle cerebral artery occlusion to induce ischemia in the left hemisphere. EVs were isolated from hypoxia-reoxygenation (H-EVs) or normoxia (N-EVs) conditioned myoblasts, fluorescently labeled and then injected intravenously during occlusion. After 10 minutes of reperfusion, mice were sacrificed and the brain, heart, liver, spleen, and kidney were removed and stored in 4% PFA for later scan in the in-vivo imaging system (IVIS). The results showed that most EVs accumulate in the liver, kidney, and spleen. A trend of more accumulation of H-EVs in the stroke brain was found compared with N-EVs, and H-EVs seem to prefer the ischemic hemisphere. These results indicate a potential role of EVs in RIC.

P08.06   Katrine Tang Stenz   BENEFICIAL EFFECTS OF REMOTE ISCHEMIC CONDITIONING AND BLOOD FLOW RESTRICTED EXERCISE IN STROKE

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

blood vessels often leads to reperfusion injury; together known as ischemia/ reperfusion injury (I/R injury).

The aim of this study is to utilize the body's own endogenous protective pathways against I/R injury by different conditioning methods. These include remote ischemic conditioning (RIC), blood flow restricted exercise (BFRE), and traditional resistance training (TRT). We hypothesize that RIC, BFRE and TRT can induce cytoprotection through conditioned extracellular vesicles (EVs) released into circulation.

EVs are important for cell-to-cell communication over long distances, as they are stable in e.g. blood. Upon conditioning, these EVs change characteristics like; surface charge, surface proteins and miRNA content.

Studies: 1) Identify the surface proteins and the miRNAs of conditioned EVs; 2) Predict mRNA targets for miRNA gene regulation; 3) Investigate the protective impact of EVs from RIC, BFRE, and TRT during anoxia/ reperfusion in vitro model of brain derived human cells.

The objective is to elucidate the pathways of the protective mechanism underlying conditioned EVs and investigate ways to utilize it for future treatments.

P08.07 Julie Linding Kjerulff

INFLUENCE OF TRANSPORT, TIME AND STORAGE TEMPERATURE ON S100B VALUES

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Background: The biomarker S100B is routinely used for rule-out of intracranial lesions in patients suffering mild-moderate head trauma in emergency departments. It is currently investigated if S100B can be used in the prehospital setting by sampling of blood in the ambulance, where environmental disturbances may affect the validity of the measurement. Thus, before clinical application, it is important to investigate if S100B results in blood samples drawn into non-standard tubes at various temperatures and transported during a non-standardized period of time are comparable to in-hospital reference samples.

Aim: To compare S100B values in blood samples handled in a simulated pre-hospital setting to standardized in-hospital blood samples.

Hypotheses: Mean S100B values in blood samples are equivalent within predefined limits when

1. Drawn Sarstedt Monovettes compared to BD tubes

2. Stored at ambient temperature summer/winter (29/15 °C) compared to standard temperature (21 °C)

3. Transported for 30 min compared to samples stored in the laboratory for 30 min

4. Stored for 30 min compared to samples stored for 60 minPrimary outcome: Mean statistical difference (P>0.05) of serum S100B values between groups.

Methods: 30 patients with expected levels of S100B during surgery will be sampled at Department of Neurosurgery, Aarhus University Hospital. Blood samples will be stored in different tubes, under various temperatures, for a different time span and transported.

Discussion: If S100B results are equivalent across tubes, temperatures, transport and time to analysis, it may enable future research targeting development of point-of-care testing methods for biomarkers of traumatic brain injury.

| P08.08 | Cathrine Hjorth Hansen | WHAT CONSTITUTES DEMENTIA CARE? AN ETHNOGRAPHIC STUDY IN DAGMARSMINDE - A PRIVATE NURSING HOME FOR PEOPLE LIVING WITH ADVANCED DEMENTIA |

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Background: Due to demographic changes, the number of people living with dementia is rapidly increasing. The course of dementia is progressive, and people with advanced dementia require support to maintain everyday life. The majority of this support is provided by caregivers in nursing homes. At present, evidence-based recommendations advise against prescription of psychotropic medications for people living with dementia. However, these medications are still used in many Danish nursing homes. In this study, we investigate the care in the first Danish dementia-specific nursing home, where all types of psychotropic medications are continuously removed from the daily care.

Aim: The aim of the study is to provide new knowledge on how to care for the growing number of people living with advanced dementia in nursing homes.

Method: A reflexive ethnographic research approach described by Hammersley & Atkinson (2007) is used to investigate the care in Dagmarsminde. The empirical data is collected through participant observations (162 hours) and ethnographic interviews with staff members (13), managers (2), and relatives (10).

Analysis: A qualitative thematic analysis of all the empirical data is in progress.

Results: Pending.

Implications: In Denmark, as well as internationally, there are concerns about the quality of dementia care in nursing homes. The results from this study will be transformed into specific recommendations and can thereby contribute to an improved practice of dementia care in the future.

Keywords: Ethnography, nursing home, dementia.

P08.09   Anne Nielsen   AUTOMATIC DIFFUSION LESION OUTLINING IN ACUTE ISCHEMIC STROKE USING DEEP LEARNING

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Background and purpose: Every year, 13 million people in the world suffer acute ischemic stroke. Diffusion-weighted magnetic resonance imaging (DWI MRI) is considered a proxy-marker for ischemic core lesion and an important factor for treatment candidate identification. However, manual outlining of the ischemic core has several shortcomings; it is time-consuming, reader-dependent, and require expert neuroradiologists. In this study, we present a convolutional neural network (CNN) to make expert-standard DWI lesion outlinings in a fast, reproducible, user-independent way.

Methods: A total of 847 patients from three different studies were included. A CNN (CNN_{ACUTE}) and thresholding on the apparent diffusion coefficient (ADC_{THRES}) were used to outline acute DWI lesions and compare these to expert-based outlines by visual assessment, area under the receiver operating characteristic curve (AUC) and volumes (using Pearson correlation coefficient (PCC)).

Results: Overall, CNN_{ACUTE} was in good agreement with the expert-based delineations, yielding high AUC, high Pearson correlation coefficients, and no significant difference between the expert-based and the automatic volumes. Furthermore, CNN_{ACUTE} (AUC: 0.95±0.09, PCC: 0.982) was significantly superior to ADC_{THRES} (AUC: 0.72±0.10, p<0.00001, PCC: 0.286, p<0.00001). ADC_{THRES} tends to overestimate the lesion volumes.

Conclusion: The study showed highly accurate acute DWI lesion delineations using CNN_{ACUTE} with the potential to accelerate treatment initiative and decrease expert dependence, hopefully leading to better patient outcome.

P08.10   Rolf Blauenfeldt   REMOTE ISCHEMIC CONDITIONING IN PATIENTS WITH ACUTE STROKE: A MULTICENTER RANDOMIZED, PATIENT-ASSESSOR BLINDED, SHAM-CONTROLLED STUDY (RESIST)

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Background: Stroke is the second leading cause of death worldwide and a leading cause of serious, long-term disability. The most common type is ischemic stroke (AIS) in 85% of cases.

Novel therapeutics and neuroprotective strategies that can be started ultra early after symptom onset are urgently needed to reduce disability in stroke. Ischemic conditioning is one of the most potent activators of endogenous neuroprotection.

Remote ischemic conditioning (RIC) can be applied as repeated short-lasting ischemia in a distant tissue that results in protection against subsequent long-lasting ischemic injury in the target organ. RIC is commonly achieved by inflation of a blood pressure cuff to induce 5-minutes cycles of limb ischemia alternated by 5-minutes of reperfusion.

In the RESIST trial, our primary aim is to investigate whether remote ischemic conditioning applied in hyperacute prehospital phase and continued in-hospital can improve long-term recovery in acute stroke patients as an adjunct to standard treatment.

Methods: RESIST is a multicenter, prospective, randomized, patient-assessor blinded and sham-controlled study. Adults with a prehospital putative stroke, symptom duration < 4 hours and who are independent in daily activities of living will be randomized 1:1 to RIC or control.

The primary study endpoint is functional outcome (modified Rankin Scale) at 3 months in acute stroke patients (ordinal logistic regression).

A sample size of 1500 (prehospital randomized) will be required to achieve 1000 patients with a target diagnosis of acute stroke (estimated effect 6%, significance level of 5% and power of 80%).

Study start/end date: 16 March 2018/December 2022.

P09.01   Anne-Sofie Skou   OVEREXPRESSED GENES FOR EARLY DETECTION OF RELAPSE IN CHILDHOOD ACUTE MYELOID LEUKEMIA

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Overexpressed genes may be employed as targets for minimal residual disease (MRD) monitoring in the large proportion of childhood acute myeloid leukemia (AML) patients without leukemia-specific targets.

We investigated the expression of 4 leukemia-associated genes (SPAG6, ST18, PRAME, GAGED2) in hematologically healthy children (n=53) during suspected infection (n=90) and bone marrow regeneration (n=13). Gene expression in AML at diagnosis (n=53) and during follow-up (n=20) was compared with age-specific reference values.

At AML diagnosis, 64% had high expression of at least 1 of the 4 genes defined as >20-fold overexpression compared to hematologically healthy children. Nine out of 10 patients (90%) without established molecular MRD targets or high WT1 expression had high expression of at least 1 of the 4 genes. Gene expression was quantified in 99 peripheral blood (PB) samples during follow-up in 20 patients with distinct overexpression at diagnosis. All 10 patients with PB sampling performed within 100 days of disease recurrence displayed expression above normal by a median of 1.6 months (range 0.5-6) before hematological relapse. Only 1 of 96 (1%) post-therapy follow-up analyses performed in 9 patients in continuous CR for >5 years after diagnosis had expression above normal. We found no

clinically relevant influence of fever on gene expression levels, except for GAGED2, where 21% of febrile children had expression above normal.

Sequential post-therapy monitoring of overexpressed genes in PB can predict relapse in childhood AML patients and facilitate molecular MRD monitoring in the majority of patients without a leukemia-specific target or WT1 overexpression.

P09.02   Michelle Simone Clement

THE ROLE OF MIR-200C IN MET-TKI RESISTANCE

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Acquired resistance to targeted therapy is a major challenge in non-small cell lung cancer (NSCLC). One of the possible mechanisms causing this is epithelial-to-mesenchymal transition (EMT). This phenotypic transition involves loss of cell polarity and cell-cell adhesions. A key hallmark is the loss of the epithelial cell adhesion molecule E-cadherin. The microRNA miR-200c is known to play a prominent role in the regulation of EMT, mainly by regulation of the transcription factor ZEB1, which is an essential repressor of E-cadherin.

This project aims to characterize the role of miR-200c in the regulation of the EMT phenotypic shift and more importantly the resistance to MET-TKIs. This is done in a cell model reflecting the clinical situation of erlotinib resistance in NSCLC patients with tumours acquiring amplification of MET.

HCC827-ER cells, a NSCLC cell line resistant to the EGFR TKI erlotinib due to amplification of MET, were treated with increasing doses of the MET TKIs crizotinib or capmatinib to develop resistant cell lines. The sensitivity of the resulting cell lines was investigated by MTS viability assays. The resistant cells presented with characteristics of EMT shown by RT-qPCR and immunofluorescence microscopy analyses of markers of mesenchymal and epithelial phenotypes. Furthermore, hypermethylation of the promoter of miR-200c was evident when analysed by pyrosequencing, and this resulted in decreased expression of miR-200c.

The next step is to evaluate the importance of miR-200c in MET-TKI resistance. This will be done primarily by introduction of the microRNA in the resistant cells, and changes in drug sensitivity and phenotype will be determined.

P09.03   Marie Vognstoft Hjortbak

CARDIOPROTECTIVE EFFECT OF LOCAL AND REMOTE ISCHEMIC CONDITIONING IN COMBINATION WITH MILD HYPOTHERMIA

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Background: Ischemic conditioning and mild hypothermia (MH) are both known to reduce cardiac ischemia-reperfusion (IR) injury. Because

patients with cardiac arrest due to acute myocardial infarction benefit from MH, we aimed to investigate whether the cardioprotective effect of local (IPC) and remote (RIPC) ischemic preconditioning is preserved during MH.

Method: Isolated perfused rat hearts were subjected IR injury and to either IPC or RIPC in combination with normothermia or MH of 34 °C. The study was divided in two experimental series. In series 1, control or IPC protocols were combined with MH, and MH was induced either during the whole ischemic period (MH-I), for the final 20 min of ischemia (MH-I20), during reperfusion (MH-R), or during the total study protocol (MH-T). In series 2, RIPC was combined with MH during the final 20 min of ischemia (MH-I20). The cardioprotective effect was evaluated by hemodynamic recovery and infarct size (IS). To evaluate potential mechanisms, intermediary metabolism was evaluated by microdialysis, glucose oxidation, continuous LDH release, and intracellular pathways.

Results: Both IPC and RIPC reduced IS in normothermia. MH reduced IS in all protocols compaired to normothermia, except when applied during reperfusion alone. The cardioprotective effect of IPC, but not RIPC, was additive to MH. Patterns of LDH release, TCA intermediates, and glucose oxidation during reperfusion differed between treatment groups, indicating different cardioprotective targets for conditioning and MH.

Conclusion: The cardioprotective effect of IPC, but not RIPC, is preserved during MH. Underlying mechanisms may differ between the treatment modalities.

P09.04   Line Bager Andersen

ASSESSMENT AND VALIDATION OF NOVEL IMMUNE SYSTEM BIOMARKER CANDIDATES FOR PROSTATE CANCER USING TISSUE MICROARRAYS

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Background: Prostate cancer (PC) is the most frequent type of non-skin cancer among men in Western countries. Elevated levels of serum prostate specific antigen (PSA) is the most commonly used diagnostic biomarker for PC, but it has no clear association with aggressiveness and/or prognosis.

Aim: PC develops in an immune-competent environment, and the aim of this study is to evaluate the prognostic significance of immune cells as biomarkers.

Methods: In this project, radical prostatectomy (RP) tissue specimens from 900 patients (training cohort 1: n_1 = 500, validation cohort 2: n_2 = 400) treated at AUH (2000-2013) have been collected and will be used to construct two tissue microarrays (TMA). We will use the TMAs for immunohistochemical analysis and validation of potential immune system candidate markers. Subsequently, we will investigate the correlation between key clinical variables and candidate biomarker levels to explore the prognostic potential of the markers. Our statistical analysis will contain Fisher's exact test and/or Chi^2 test to identify differences in the level of each candidate biomarker in different clinical outcomes. Furthermore, we

will investigate time to PSA recurrence/metastastic progression using univariate and multivariate Cox regression analysis and Kaplan-Meier analysis.

Expected results: We expect that our results will contribute to the search for a novel tool to predict the prognosis of prostate cancer in order to help avoid overdiagnosis and overtreatment of many indolent PCs.

P09.05   Trine Vilsbøll Larsen

PD-L1 DNA METHYLATION CORRELATES NEGATIVELY WITH PD-L1 EXPRESSION IN NSCLC

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Introduction: Immunotherapy targeting the PD-L1/PD-1 axis is a relatively new treatment option for some Non-Small Cell Lung Cancer (NSCLC) patients. Currently, immunohistochemistry staining for PD-L1 is the companion diagnostic method for the use of immunotherapy in NSCLC patients. However, this method is inadequate. In this study, the correlation between PD-L1 DNA methylation and PD-L1 expression is examined to explore the possibility of PD-L1 DNA methylation as a new or supporting biomarker for immunotherapy.

Method: 15 NSCLC cell lines, 4 HCC827 erlotinib-resistant cell clones and 2 breast cancer cell lines were investigated. For all cell lines, methylation status of four CpG sites in PD-L1 were examined by bisulfite-pyro-sequencing of extracted DNA. For all cell lines, PD-L1 mRNA expression was examined by quantitative PCR on cDNA synthesized from extracted RNA.

Results: A significant negative correlation was observed for two of the investigated CpG sites (CpG 1; spearman's corr. = -0.5789, p-val. = 0.0075 and CpG 2; spearman's corr. = -0.6647, p-val. = 0.0014). Immunotherapy is less effective in EGFR-mutated or ALK-translocated NSCLC patients. Excluding cell lines with activated EGFR-mutations or ALK-translocation improved the correlation, resulting in a significant negative correlation for three of the four investigated CpG sites (CpG 1; spearman's corr. = -0.6606, p-val. = 0.0438, CpG 2; spearman's corr. = -0.7552, p-val. = 0.0062 and CpG 3; spearman's corr. = -0.7091, p-val. = 0.0182).

Conclusion: PD-L1 DNA methylation correlates negatively with PD-L1 expression. Furthermore, the correlation seems to be mutation dependent.

P09.06   Trine Strandgaard

INVESTIGATION OF THE FIELD EFFECT IN BLADDER CANCER PATIENTS

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Background: Field effect triggers the development of many cancer types and may explain the recurrent nature of bladder cancer (BC). Recent data from BC patients has revealed that tumors developed years apart in the same patient share multiple mutations and that the surrounding normal

appearing urothelial cells contain tumor specific mutations. Exploration of the field effect may heighten our understanding of disease mechanisms and disease development.

Methods: Multiple laser micro-dissected biopsies from tumor and normal appearing urothelium from four patients were studied. Pools of normal and tumor samples were subjected to deep targeted sequencing using NuGEN Ovation® Cancer Panel 2.0 Target Enrichment System and sequenced on the Illumina NextSeq 500 platform. Digital Droplet PCR was used for validation of selected alterations detected in normal and tumor samples.

Results: Deep Targeted Sequencing revealed the presence of low frequency mutations exclusively found in normal samples. The average mean target coverage obtained was 634X (360-1073X). Using MuTect, we identified 8 (2-16) mutations unique for normal samples. Furthermore, 9 (6-13) mutations shared between normal and tumor samples as well as 35(8-75) mutations unique for tumor samples were detected. Normal specific as well as high frequency tumor mutations were validated.

Conclusion: Mutations are present in the normal appearing urothelial cells, indicating the presence of more mutated fields. This may explain the frequent recurrences of BC. The field effect may play a role in tumor initiation, and tumors may hereafter continue to acquire new unique mutations.

P09.07   Maibritt Nørgaard

DEEP SEQUENCING OF CIRCULATING TUMOR DNA FOR PREDICTION AND MONITORING OF ENZALUTAMIDE AND ABIRATERONE TREATMENT RESPONSE IN CASTRATION RESISTANT PROSTATE CANCER

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Metastatic prostate cancer (PC) inevitably progresses to lethal castration resistant prostate cancer (CRPC) despite primary androgen-deprivation therapy. Treatment options for CRPC are limited, and the ideal drug sequencing has not been established. Enzalutamide (enza) and Abiraterone (abi) are routinely used secondary endocrine therapies that each may provide a modest survival benefit, but ~25% of CRPC patients do not respond, and initially responding patients eventually acquire resistance. Resistance is multifactoral and poorly understood, but genomic alterations seem to be commonly involved. Furthermore, preliminary reports suggest that germline and somatic DNA repair gene defects may improve response to enza in CRPC patients. Thus, to guide treatment selection and sequencing for CRPC patients, predictive and monitoring biomarkers are urgently needed.

In this project, we will use low-pass whole genome sequencing and deep targeted sequencing to profile circulating tumor DNA (ctDNA) in longitudinally collected plasma samples from CRPC patients receiving first-line enza or abi. Serially collected plasma samples (pre-treatment, during treatment, and at disease progression) allow us to investigate if ctDNA can be used as a liquid biopsy biomarker to inform on treatment response and resistance.

We expect to identify somatic/germline genomic alterations (incl. copy number alterations) that may be associated with response and resistance to first-line enza or abi. Such markers could be used for clinically relevant patient stratification and thus pave the way for precision medicine in CRPC.

P09.08   Jesper Geert Pedersen

INVESTIGATION OF PLASMA CYTOKINE LEVELS AND CIRCULATING TUMOUR DNA AS POTENTIAL BIOMARKERS FOR DISEASE STATUS IN METASTATIC MELANOMA PATIENTS DURING IMMUNOTHERAPY

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Targeted treatments and immunotherapy have extended the repertoire of treatment strategies and significantly improved treatment of metastatic melanoma. However, treatment resistance and disease progression remain major challenges, making precise monitoring of treatment response crucial for deciding on the best possible treatment strategy. Circulating tumour DNA (ctDNA) in blood samples shows promise as a potential biomarker for monitoring disease status and detecting earlier signs of disease progression in metastatic melanoma patients. However, in some cases, the use of ctDNA monitoring can be challenging. Therefore, it is of high relevance to explore additional approaches to identify other novel biomarkers associated with disease progression.

Here, we present a methodological pilot study using a clinical cohort of patients with metastatic melanoma receiving first-line immunotherapy (n=20) initiated in 2017 at the Department of Oncology, Aarhus University Hospital. Plasma samples were collected prior to treatment initiation with follow-up samples during the first year of treatment.

From a broad 92 immuno-oncology biomarker screen (O-link), we identified a group of cytokines of potential interest, as they correlated with ctDNA changes and are expressed following innate immune sensing of DNA. At this stage, we are evaluating the cytokine profile within each plasma sample for the entire patient group. These data will subsequently be correlated to ctDNA levels.

The findings from this study can provide us with new biomarkers that, either on their own or in combination with ctDNA, may improve monitoring of treatment response and disease status in metastatic melanoma patients.

P09.09   Emma Kirstine Bollmann Laursen

CIRCULAR RNAS IN PROSTATE CANCER AND THEIR POTENTIAL AS CLINICAL BIOMARKERS TO IMPROVE PROSTATE CANCER DIAGNOSIS AND RISK STRATIFICATION FOR MORE INDIVIDUALIZED MANAGEMENT

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Prostate cancer (PC) is the most common cancer among men in DK. Today, the current diagnostic approach is suboptimal, resulting in overtreatment of many indolent PCs and delayed detection of aggressive PCs. Consequently, there is an urgent clinical need for new improved diagnostic and prognostic biomarkers to ensure accurate diagnosis and risk stratification of PC patients. Circular RNAs (circRNAs) are a rising field of study, as they have been implicated in several biological processes and diseases. However, it remains unclear if/how circRNAs influence PC.

The aim of this project is to elucidate the role of circRNAs in PC development and progression, and to develop new minimally invasive diagnostic and prognostic circRNA biomarkers for improved PC detection and risk stratification.

To identify novel circRNA biomarkers, we will use total RNAseq data from fresh frozen tissue samples from 200 PC patients undergoing radical prostatectomy (RP). CircRNAs holding clinical biomarker potential will subsequently be validated in independent patient cohorts and undergo functional investigation in PC cell lines. Moreover, the biomarker potential of identified top candidate circRNAs will be investigated in liquid biopsies (plasma/urine) from large patient cohorts, including men with vs. without PC, recurrent vs. non-recurrent PC after RP, and men undergoing TRUS-biopsy/mpMRI scan due to suspicion of PC. Results of the initial biomarker discovery process will be presented at the meeting.

The development of minimally invasive circRNA biomarkers in PC might significantly improve clinical PC management in the future and decrease adverse side effects caused by the current diagnostic approach.

P10.01 Laura Virginie Toussaint

TEMPORAL LOBE SPARING RADIOTHERAPY FOR COGNITIVE PRESERVATION IN PEDIATRIC BRAIN TUMOR PATIENTS

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Purpose: Reduced radiation exposure to the temporal lobes could be beneficial to preserve cognitive functions in pediatric brain tumor patients. We investigated doses to brain substructures associated with cognition (BSCs) in temporal lobe sparing photon vs. proton therapy of pediatric midline brain tumors and modeled subsequent memory impairments.

Material and Methods: For ten anonymized patients, clinically delivered double scattering proton therapy (DSPT) plans were compared to two temporal lobe sparing strategies (i.e. photon volumetric modulated arc therapy (VMAT) and pencil beam scanning proton therapy (PBS)). Thirty BSCs including temporal lobe substructures (i.e. amygdala, hippocampus, entorhinal cortex) and BSCs outside of this region were delineated. The

fractions of BSCs volume receiving low (V10Gy, V20Gy), intermediate (V30Gy, V40Gy) and high (V50Gy) doses were analyzed for each modality. Two dose-response models of memory function were applied to compare the modalities.

Results: The irradiated volumes of temporal lobe and its substructures were consistently reduced with PBS, e.g. from 41% to 0% for the left hippocampus V10Gy and from 43% to 24% for the left amygdala V40Gy (PBS vs. DSPT). For the BSCs outside of the temporal lobes, the volumes exposed to low doses were in general smaller with PBS, while intermediate and high dose levels to the ventricular substructures were reduced with VMAT. Overall, the reduced doses to the temporal lobes translated into lower estimated risks of memory impairment with the PBS approach.

Conclusion: The irradiated volumes of temporal lobe BSCs were consistently lowest with PBS, predicting better memory outcomes for the patients.

P10.02   Laura Patricia Kaplan

INTER-OBSERVER VARIATIONS IN RADIOTHERAPY PLAN EVALUATION

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Background: The primary objectives of radiotherapy (RT) treatment plans are to maximize target coverage (TC) and minimize doses to organs at risk (OAR). Secondary characteristics of RT plans, such as dose gradient or dose homogeneity, can be quantified but are, in practice, often evaluated qualitatively. Qualitative evaluations can vary between observers. The aim of this study was to compare consistency in qualitative vs. quantitative evaluations of RT plans.

Method: Two planning strategies (S1 & S2) were used for each of 20 head-and-neck cancer pts. Four radiation oncologists performed blinded clinical evaluations of the plans. They chose which plan they preferred for each pt, evaluating TC and OAR doses. They also gave scores for the importance of five different secondary plan characteristics in each choice between two plans. Corresponding quantitative metrics from the literature were calculated. Consistency between the score-metric pairs was evaluated.

Results: All plans complied with critical OAR and TC constraints. In only six cases did all physicians prefer the same plan. For all scores except OAR in S1 plans, a Friedman's ANOVA test showed significant ($p<0.05$) variations between observers. Spearman's ρ for correlations in each score-metric pair (including scores from all physicians) ranged from -0.34 to 0.20 (median -0.07).

Conclusion: There were substantial inter-observer variations in subjective scores. Little to no consistency was seen between qualitative scores and corresponding quantitative metrics. Consistent use of quantitative metrics in addition to subjective plan evaluation should be investigated as a way of mitigating such inconsistencies and variations.

P10.03 Anders Schwartz Vittrup LATE, PERSISTENT, SUBSTANTIAL AND LIKELY TREATMENTRELATED SYMPTOMS (LAPERS): A REPORT FROM THE EMBRACE STUDY

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Background: Incidence methods capturing the first occurrence of an event are often used to summarize late side effects after radiotherapy, but are unable to distinguish transient and persistent symptoms. A method to identify patients with LAte, PERsistent, Substantial and likely treatment related symptoms (LAPERS) is applied on patient reported outcomes (PRO) from the prospective, observational, and longitudinal study on MRI image-guided, adaptive brachytherapy in locally advanced cervical cancer (EMBRACE study).

Materials and Methods: PRO (EORTC QLQ-C30 + CX24) were analyzed in 657 out of 1416 patients who had a valid baseline, 3 months' assessment and at least 3 late follow-ups (6 months and ongoing). A LAPERS event for an individual patient was defined if the median over late follow-ups was "quite a bit" or "very much" (substantial symptoms). For organ-related symptoms (e.g. urinary frequency), baseline morbidity was taken into account by requiring the median to be worse than the minimum of baseline and 3 months scoring (treatment-related). LAPERS was contextualized with crude incidences of substantial symptoms via ratio calculations.

Results: Median follow-up was 42 months (IQR 30-59). LAPERS was ≥10% in 10 out of 31 symptoms (e.g. "swelling in one or both legs"). LAPERS/crude incidence ratios were lower than 0.4 for all symptoms, indicating that less than 40% of patients experiencing substantial symptoms did so persistently. For 7 symptoms (e.g. "blood in stools"), the ratio was lower than 0.1.

Conclusion: When analyzing longitudinal morbidity data, a complementary approach combining incidence methods and LAPERS improves the understanding of burden and duration of toxicity.

P10.04   Nina Jensen   RISK FACTOR ANALYSIS AND DOSE-VOLUME EFFECTS FOR LATE BOWEL MORBIDITY IN LOCALLY ADVANCED CERVICAL CANCER

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Purpose: To identify and quantify risk factors for late bowel morbidity in locally advanced cervical cancer according to treatment-, patient- and disease-related parameters. Furthermore, to investigate if a dose-volume relationship for bowel morbidity exists and can be used in future radio-therapy regarding photons and protons.

Material: The analysis will be based on 1416 patients enrolled from 2008 to 2015 within the international study on MRI-guided Brachytherapy in locally Advanced Cervical cancer (EMBRACE). Risk factors to be investigated in univariate and multivariable analyses include FIGO stage, comorbidity, lymph node involvement, EBRT dose/volume and technique, brachytherapy dose contribution, chemotherapy, prior abdominal surgery.

Results: There are no results in this study yet.

Conclusion: The assumption is that it will be possible to identify independent prognostic factors for late bowel morbidity outcome, including volumetric, dosimetric and clinical risk factors, and to correlate outcome data to dose-volume effects.

P10.05   Raúl Argota Perez ~~CANCELLED~~   ROBUSTNESS OF PROTON RADIOTHERAPY PLANS TOWARDS ANATOMICAL VARIATIONS IN NASOPHARYNGEAL CANCER

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Background: Proton radiotherapy is very sensitive to any variations during the treatment. Setup uncertainties can be accounted for using robust optimization, but anatomical variations are usually not accounted for.

Methods: Five patients with nasopharynx cancer were planned for proton therapy. The plans were made using 3 beam directions. Anatomical changes (weight gain and loss, and nasal cavity filling) were simulated by density overrides in the original CT scans. Setup errors were simulated performing shifts of +/-5 mm in the orthogonal directions. The dose was recalculated with the original plan configurations in each simulated situation, and plan robustness was evaluated comparing tumour coverage (CTV) and doses to organ at risk.

Results: CTV coverage was not affected by the simulated setup errors. For anatomical changes, weight gain and nasal cavity filling deteriorated CTV coverage, although the dose stayed above 95% in all cases. When setup errors and anatomical variations were combined, CTV coverage dropped to unacceptable levels for a subset of patients. Weight loss did not affect CTV coverage, even not when combined with setup errors. The

mean dose to the parotid gland was affected by all the variations, and the largest increases were seen for weight loss and filling of the cavities.

Conclusions: Tumour dose coverage was not compromised by setup errors in nasopharyngeal cancer patients. Weight gain and nasal cavity filling had detrimental effect on target doses, especially in combination with setup errors, reaching unacceptably low levels for several patients. Better robustness methods are needed to account for anatomical variations to minimize the need for plan adaption.

P10.06   Andreas Gravgaard Andersen

EVALUATION OF AN A PRIORI SCATTER CORRECTION ALGORITHM FOR CONE-BEAM CT PROJECTIONS IN PHOTON VS. PROTON THERAPY GANTRIES

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Background and purpose: Cone-beam (CB) computed tomography (CT) imaging may enable image/dose-guided proton therapy, but due to scattering of X-rays in the patient, the CBCTs will contain image artefacts. The aim of this study was to further develop an a priori scatter correction algorithm on CBCT projections to prove its functionality on both photon and proton therapy gantries.

Materials and methods: Scatter corrected CBCTs were derived by reconstructing projection sets, where raw CB projections had been subtracted from the corresponding scatter-inclusive projections that were forward-projected from a conventional planning CT (pCT). CB projections acquired with the On-Board Imager on two different photon therapy gantries and on one proton therapy gantry were investigated. For evaluation, water equivalent path length (WEPL) maps and treatment plans were calculated on different reconstructions of the data sets.

Results: The scatter correction resulted in a mean WEPL difference between -1.5 and 1.5 mm from the rigid registration of the pCT for all gantry types, while the clinical reconstructions had a mean WEPL difference between 2.4 and 7.7 mm for the photon gantries and 1.8 for the proton gantry. Scatter correction of CBCTs from both the photon and proton gantries resulted in significantly higher gamma pass rates and reduced WEPL variation.

Conclusion: An a priori scatter correction algorithm for CB projections improved CBCT image quality and accuracy of dose calculation on both photon- and proton-therapy gantries.

P10.07   Maja Bendtsen Sharma

RADIATION THERAPY OF SINONASAL CARCINOMA: FUNCTIONAL ASSESSMENT OF LATE TOXICITY AND QUALITY OF LIFE

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Objective: We aimed to objectively assess late toxicity and quality of life (QoL) in patients treated with radiation therapy for sinonasal carcinoma.

Materials/methods: Patients who were previously treated with radiation therapy for sinonasal carcinoma were enrolled in this cross-sectional study. Toxicity was assessed by neurocognitive function tests, objective ophthalmological examination, blood samples, synachten test, and Brief Smell Identification Test. QoL was evaluated with four specific questionnaires.

Results: Eighteen patients were enrolled. Compared with normative data, patients evidenced poorer neurocognitive functioning in several cognitive domains, including processing speed ($p<0.05$), verbal learning and memory ($p<0.01$), attention and working memory ($p<0.05$), and verbal fluency ($p<0.01$). Assessment of vision revealed a significant correlation between max radiation dose to the chiasm and grade 3 visual acuity impairment ($p=0.046$). Pituitary gland analysis showed an indication of a relationship between higher doses and more affected hormone levels in all axes, but no significant correlations were found. Olfactory functioning was impaired in 15/18 patients. In the global QoL analyses, the most affected domains were social, emotional, and physical functions. Fifteen out of eighteen participants reported increased anxiety. Anxiety was related to a poorer outcome in the global QoL score ($p=0.029$). The areas that affected the QoL most were lack of smell or taste, thick nasal discharge, need to blow the nose, and blocked nose.

Conclusion: The results of the present study indicate considerable toxicity subsequent to IMRT with a substantial influence on patient QoL.

P10.08   Marie Louise Milo   DBCG COR: THE RISK OF RADIOTHERAPY INDUCED HEART DISEASE IN WOMEN TREATED FOR EARLY STAGE BREAST CANCER

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Introduction: Radiotherapy (RT) is essential in the adjuvant treatment of breast cancer to reduce the risk of recurrence and improve the overall survival. RT may increase the risk of developing a heart disease, and the risk depends on the RT dose to the heart. Due to the anatomical localization of the heart, the ventral part receives a large RT dose.

Aim: The aim of this study is to establish a dose-response relationship linking RT dose to the heart and the risk of radiation induced heart disease based on individual characteristics.

Material and methods: The study is based on data from the Danish Breast Cancer Group (DBCG), a national database that registers breast cancer patients, and the West Danish Heart Database (VDH), which registers all invasive heart procedures in Jutland and Funen. In the DBCG database, 100,685 women have been registered with a diagnosis of breast cancer in the period 1990-2016. Among these women, VDH has registered 4,767 procedures. Since year 2000, the majority of RT treatment plans have been based on CT scans, thus the RT dose to the heart can be evaluated based on individual treatment characteristics. These data make it possible to investigate the localization of heart disease in women treated with and without RT. For those treated with RT, dose corresponding to the heart disease is estimated. A case-control study will be used to establish a dose-response relationship.

Conclusion: The dose-response relationship linking RT dose to the heart and the risk of RT induced heart disease will evaluate the risk of heart disease on an individual basis. The results may contribute to optimal selection of patients to RT, including treatment with protons.

P11.01   Jakob Haldrup Jensen

NOVEL TUMOR SUPPRESSOR FUNCTION AND PROGNOSTIC POTENTIAL OF FRMD6 IN PROSTATE CANCER

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The available tools for prostate cancer (PC) prognosis are suboptimal, and novel biomarkers are urgently needed. Using RNAseq, we identified FRMD6 as a downregulated gene in PC as compared to non-malignant prostate tissue samples, which was validated in two independent radical prostatectomy (RP) patient sets (n=480). Moreover, FRMD6 predicted time to biochemical recurrence independently of routine clinicpathological variables in RP patient set1 (HR: 0.38, [95% CI: 0.16-0.88], p=0.024) and was validated in RP patient set2 (HR: 0.51, [95% CI: 0.32-0.0.82], p=0.005).

Stable PC3 and DU145 knockout (KO) cells were established using CRISPR-Cas9. Both KO cell lines showed increased viability and proliferation in 2D culture, which was reversed by FRMD6 rescue. Likewise, FRMD6 overexpression reduced viability and proliferation in isogenic PC3M and DU145-MN1 cells. Moreover, both 3D spheroids and subcutaneous xenografts of PC3_KO_FRMD6 had higher growth rates than PC3. Finally, preliminary results indicate that orthotropic KO of FRMD6

and PTEN in the prostate of Rosa26 mice accelerated tumor formation as compared to KO of PTEN only.

Gene set enrichment analysis revealed that cMyc signaling was enriched in PC3_KO_FRMD6, and proteomics suggested FRMD6 as an activator of the Hippo pathway. To identify treatments that reverse the oncogenic cMyc signature associated with FRMD6 loss, the connectivity map identified AZD-7762, which reduced cell viability in PC3_KO_FRMD6 as compared to PC3 in a dose-dependent manner.

Together, our results indicate that FRMD6 is a tumor suppressor gene in PC. Further studies are needed to determine the prognostic value of FRMD6 and to validate AZD-7762 in vivo.

P11.02   Margarita Sergeyevna Melnikova

CHARACTERIZATION OF EPITHELIAL CELLS IN COLORECTAL CANCER

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Background: Colorectal cancer (CRC) is the third most common cancer form with metastases being a primary death cause. Tumor metastasizing is promoted by epithelial to mesenchymal transition (EMT). During EMT, epithelial cells undergo phenotypical changes characterized by loss of apicobasal polarity and cell-cell adhesion, while acquiring invasiveness and stromal characteristics. These changes can be visualized using various immunohistochemical (IHC) markers.

Based on gene expression profiling, our group identified different epithelial subtypes of CRC distinguished by expression of cytokeratins (CKs) and EMT markers. Clinically, immunophenotype $CK20^+/CK7^-$ is used for differentiation of CRC metastases from primary adenocarcinomas, and expression of CKs has a prognostic role. Hence, $CK20^-$ and $CK7^+$ tumors have a good prognosis, while patients with $CK8^-$ tumors have a shorter survival compared to patients with $CK8^+$ tumors. Moreover, CK20 expression and CK7 expression are associated with BRAF mutations and MSI (Micro Satellite Instability) status, further highlighting the clinical importance of CKs. In this study, we will characterize epithelial plasticity based on the IHC profiling of CKs and EMT markers.

Methods: Epithelial cells will be stratified into subtypes based on the expression of CK23, CK20, CK8, CK7 and EMT markers (zeb1, β-catenin, E-cadherin, N-cadherin). Quantification of immunoreactivity will be accessed with digital pathology software at the invasive margin and tumor core.

Perspectives: We believe that epithelial subtyping will contribute to our understanding of the pathogenesis of CRC and help to identify new therapeutic targets to improve personalized treatment.

P11.03   Thomas Buus   WHOLE BODY MRI FOR DETECTING ADVANCED BREAST CANCER

T.W. Buus

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Background: More than 400 women are diagnosed with metastatic breast cancer each year. CT is excellent for detecting soft tissue metastases, while MRI is superior for detecting bone metastases. However, at present, no single imaging modality is sufficient for the entire diagnostic workup and follow-up. To accommodate this, patients will often have both CT of the chest abdomen and pelvis (CT CAP) and MRI of the spine and, if metastatic disease is present, the patient will be followed with both imaging modalities during treatment.

Aim: To assess the diagnostic accuracy of whole-body DW-MRI and spectral CT for detecting metastases, as the only diagnostic procedure.

Methods: 182 patients treated for breast cancer suspected of metastatic disease will be recruited from the Dept. of Oncology and Dept. of Surgery, AUH. All patients are scanned with: Whole-body DW-MRI and CT CAP analyzed with and without spectral data. The diagnostic performance of whole-body DW-MRI and spectral CT are compared to contrast enhanced CT.

Results: 50 patients have been included in the study so far. 2 patients had their treatment changed based on the DW-MRI findings. 2 patients had suspicious liver lesions on CT that proved to be cysts based on DW-MRI. 1 patient was false positive for bone metastases on DW-MRI. Analysis of diagnostic performance is pending on inclusion of remaining patients.

Perspectives: A single imaging modality for the entire workup. Possibility of increased sensitivity/specificity of new imaging modalities compared to contrast enhanced CT. No ionizing radiation, contrast agents, blood samples or fasting needed for whole-body DW-MRI.

P11.04   Maria Skydt   NEOADJUVANT SHORT-TERM INTENSIVE CHEMORESECTION VS.
          Lindgren   STANDARD ADJUVANT INTRAVESICAL INSTILLATIONS OF NON-MUSCLE
                         INVASIVE BLADDER CANCER - NICSA

M. Skydt Lindgren

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Aim: To assess the efficacy of a neoadjuvant, short-term, intensive intravesical chemoresection with Mitomycin compared to standard treatment with transurethral resection of the bladder and adjuvant intravesical instillation therapy in patients with non-muscle invasive bladder cancer.

Background: Bladder cancer is the 11th most common cancer in the world and associated with a yearly recurrence rate of 35%. Bladder cancer is, therefore, one of the most costly cancers on a per patient basis due to the costs of operative procedures, follow-up cystoscopies and instillation therapy. Treatment today consists of surgical tumor removal and, in some cases, adjuvant intravesical treatment. Patients affected are often elderly, multimorbid with lower performance status and poor tolerability of

anaesthetics and operative treatments. A more effective strategy with fewer operative procedures is, therefore, urgently needed.

Methods: A randomised controlled trial will include 120 patients with recurrent disease. The control group will receive standard care with surgery and adjuvant treatment, while the intervention group will receive neoadjuvant short-term intensive chemoresection with three instillations with Mitomycin per week for two weeks. Remnant tumor will be evaluated by flexible cystoscopy after three weeks.

Results: The study is ongoing with 65 patients included. The intervention group consists of 31 patients in whom endpoint data has been obtained in 25. 12 patients have complete tumor response.

Conclusion: Positive results would be a leap forward and could result in a more efficient and less aggressive surgical approach in the future treatment of non-muscle invasive bladder cancer.

P11.05   Malene Blond Ipsen   IDENTIFYING MECHANISMS OF PARP INHIBITOR RESISTANCE AND SENSITIVITY IN PROSTATE CANCER BY GENOME WIDE CRISPR-CAS9 SCREENING

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Background: Around 25% of castration resistant prostate cancer (CRPC) patients harbor mutations in DNA repair genes. Evidence suggests that these patients are especially vulnerable to PARP inhibitors (PARPi) due to the concept of synthetic lethality. However, it is not yet established which genomic defects that confer to PARPi sensitivity. Furthermore, several patients develop resistance toward PARPis in spite of initial benefits. Understanding the biological mechanisms of PARPi sensitivity and resistance is crucial in order to predict the patient's treatment benefit.

Methods: To identify genomic perturbations that contribute to PARPi sensitivity or resistance, a genome-wide CRISPR-Cas9 loss-of-function screen was performed in the CRPC cell line C4. Using 77,441 sgRNAs, a total of 19,411 genes were targeted for knockout. Library and Cas9 transduced C4 cells were treated with the PARPi olaparib at IC50 and IC90 concentrations to select for drug resistant mutants. Genes that upon knockout conferred to increased resistance or sensitivity were identified using next generation sequencing.

Results: The screen identified novel genetic perturbations that contribute to PARPi resistance. Knockout of genes involved in single-stranded break repair and the epidermal growth factor receptor pathway led to significant increase in the survival of all olaparib treated replicates compared to non-treated controls.

Conclusion: Through a comprehensive genome-wide CRISPR-Cas9 screen, we identified novel genetic alterations that contribute to PARPi resistance. Results could be useful as predictive biomarkers to help guide treatment of CRPC patients.

P11.06   Signe Neldeborg   EFFECT OF LOW-DOSE CHEMOTHERAPY ON IMMUNE-MEDIATED KILLING OF CANCER CELLS

S. Neldeborg

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Immunotherapy has revolutionized cancer therapy in some cancer forms, such as malignant melanoma and non-small cell lung cancer. However, some tumors lack immune cell infiltration and are therefore not susceptible to immunotherapy.

I want to investigate if low-dose chemotherapy can establish or enhance immune infiltration and immune cell mediated killing of cancer cells in tumors previously non-susceptible to immunotherapy and to explore the underlying mechanisms for this response.

I will use CRISPR technology to create knockout cancer cell lines of chemotherapeutic targets to explore the underlying mechanisms of my hypothesis.

I will profile expression patterns for immune cell attracting and cancer cell revealing genes and up-stream mechanisms for their regulation.

Furthermore, I will investigate how DNA damage and mutational load in cancer cells affect the capability of immune cells to recognize and kill them.

Hopefully, this study will shed light on the cellular mechanisms involved in immune cell recognition and killing of cancer cells and explore new ways to improve and overcome resistance to immunotherapy.

P11.07   Josephine P. Geertsen Keller   TOPOISOMERASE 1 AS A TARGET FOR ANTI-CANCER THERAPY

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Camptothecin (CPT) derivatives that are used in treatment of colon, cervix, lung, and ovarian cancers act by causing accumulation of topoisomerase 1 (TOP1) bound single strand breaks (TOP1cc) in the genome, thereby converting TOP1 into a cell poison. Therefore, the cellular effect of CPT may correlate directly to the enzyme activity. Moreover, TOP1cc are converted to lethal double strand breaks upon collision with replication forks. Hence, CPTs are considered replication dependent drugs and kill rapidly dividing cancer cells. However, tumors are composed of a variety of cells, including slowly dividing "tumor initiating cells" (TIC). It is important to kill all tumorigenic cells to cure cancer. We are investigating the cellular factors that determine drug resistance and side effects of CPTs.

We have investigated the TOP1 activity and CPT sensitivity of sub-populations of colon cancer derived cell lines and shown that CPT resistance of the TIC subpopulation correlates with a reduced TOP1 activity level. We failed to find any such correlation in breast cancer derived cell lines.

To identify new drug targets that will enable eradication of slowly dividing cancer cells, we are setting up a system that will allow us to elucidate the cellular pathways involved in repair of TOP1cc in transcribed genes.

Besides being a target of CPTs, TOP1 has a number of cellular functions. One of those is regulation of G-quadruplex DNA structures, which regulate e.g. expression of proto-oncogenes. Inhibition of TOP1 by CPTs may lead to overexpression of such genes and thereby cause severe side effects. These possibilities are being investigated.

P11.08 Mads Ryø Jochumsen

[82]RUBIDIUM PET/CT - A NEW METHOD FOR TUMOR BLOOD FLOW IMAGING IN PROSTATE CANCER?

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Objectives: The aim of the study was to validate [82]Rubidium ([82]Rb) PET/CT as a method for measuring tumor blood flow (TBF) in prostate cancer (PCa) and to evaluate the potential clinical usefulness of [82]Rb PET/CT in PCa.

Methods: Nine PCa patients underwent static and dynamic [82]Rb PET/CT, which was compared with ^{15}O-water PET/CT with arterial blood sampling.

15 high-risk PCa patients were included in a GCP study and compared to 12 healthy controls. [82]Rb PET standard uptake values (SUV) were measured in the prostate of all participants.

Results: Both dynamic (K1) and static (SUV) [82]Rb TBF correlated strongly with the gold standard method of ^{15}O-water TBF (rho=0.95, p<0.001 and rho=0.86, p=0.003, respectively). [82]Rb TBF correlated with post-prostatectomy Gleason Grade Group (rho=0.70, p=0.03).[82]Rb SUV was significantly higher in prostate tumors than [82]Rb SUV in healthy prostate tissue, with no overlap (p<0.001).

Conclusions: [82]Rb PET/CT prostate TBF correlates strongly with ^{15}O-water PET, the gold standard method of perfusion. [82]Rb PET/CT may have a promising clinical application as [82]Rb prostate uptake was associated with cancer aggressiveness and identified prostate cancer with a 100% accuracy in this pilot study.

P12.01 Kris Chadwick Hede

COMBINED BONE MARROW ASPIRATE AND PLATELET-RICH PLASMA FOR CARTILAGE REPAIR - RESULTS AT TWO-YEAR FOLLOW-UP

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Background: Cell-based cartilage repair treatments are limited due to high costs of cell expansion prior to implantation. The use of autologous bone marrow aspirate concentrate (BMAC) has been proposed as an alternative one-step strategy. Platelet-rich plasma (PRP) is an increasingly popular endogenous source of concentrated growth factors.

Aim: To evaluate the clinical use of combined BMAC and PRP on a collagen I/III scaffold for treating cartilage lesions in the knee.

Material and Methods: Ten patients (Mean age: 29.4 years, range 18-36) suffering from large full-thickness cartilage lesions on patella (n=7) or the femoral condyles (n=3) were treated with BMAC and PRP from January 2015 to December 2016. Bone marrow was aspirated from the iliac crest and was prepared using centrifugation to yield BMAC. PRP was prepared using whole blood. BMAC and PRP was then seeded onto a collagen I/III scaffold and sutured into the debrided defect.

Patients were evaluated by clinical outcome scores (IKDC, KOOS and NRS) pre-operatively, after three months, one and two years and through MRI after one year, evaluated using "magnetic resonance observation of cartilage repair tissue" (MOCART) score (0(worst) - 100(best)).

Results: At one-year follow-up, statistically significant improvements were seen in IKDC, NRS activity, KOOS symptoms, KOOS ADL and KOOS QOL. Mean MOCART was 36.5 after one year. At two-year follow-up, statistically significant improvements were seen in IKDC, NRS rest and NRS activity.

Conclusion: Treatment of cartilage injuries using combined BMAC and PRP resulted in improvements in subjective outcome scores one and two years postoperatively.

P12.02   Caroline Marie Andreasen   RESPONSE TO EARLY-ONSET PAMIDRONATE TREATMENT IN SEVERE CHRONIC NON-BACTERIAL OSTEOMYELITIS:
A RETROSPECTIVE SINGLE CENTER STUDY

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Objectives: Chronic non-bacterial osteomyelitis (CNO) is a sterile inflammatory bone disorder with an unpredictable course of disease. The aim of the present study was to assess clinical and radiological disease activity in children with CNO, including response to early-onset pamidronate treatment in severe CNO.

Methods: We conducted a single center retrospective study of children fulfilling the Bristol Criteria for CNO. At the time of diagnosis, whole body MRI (WBMRI) or local MRI was performed to assess radiological disease activity. Children with multifocal or spinal bone inflammation and clinical disease activity not responding to NSAIDs were categorized as having severe CNO. Clinical disease activity was assessed annually.

Results: Fifty-one children were included. Median follow-up time was 4 (IQR 3-7) years. Children categorized with severe CNO (n=32) were

treated in an early onset two-year pamidronate regimen. In severe CNO, WBMRI was performed at the time of diagnosis, at year one and two in 88%, 84% and 91% of cases, respectively. During the first year, number of bone lesions per patient and spinal bone lesions declined significantly. After one year of treatment, 12/32 children were in clinical remission; 8/12 children experienced clinical relapse. In non-severe CNO (n=19), 10/19 children on medication were in clinical remission after one year and 10/17 children of medication were in clinical remission after two years.

Conclusion: Pamidronate is effective in improving clinical and radiological disease activity in severe CNO, especially after one year of treatment. However, children with continuously active disease refractory after two-year pamidronate treatment were seen.

P12.03 Cecilie Linneberg Matthiesen

EXTRACELLULAR SUPEROXIDE DISMUTASE - ASSOCIATED WITH BONE DEVELOPMENT IN ZEBRAFISH. A ROLE IN HUMAN BIOLOGY?

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Extracellular superoxide dismutase (SOD3) converts extracellular super-oxide (O_2^-) into hydrogen peroxide (H_2O_2), a key mediator of redox signaling. Redox signaling affects diverse biological processes, such as transcription, cell-cell communication, and inflammation. With respect to characterizing the inflammatory response, the zebrafish is a well-established model organism enabling researchers to study single immune cell behavior in vivo, which has supported the development of ground-breaking results highlighting the strong association between ROS and inflammation.

In order to apply the zebrafish model organism for further characterization of the impact of SOD3 on the inflammatory response, we have characterized the protein chemical properties of the zebrafish orthologues, Sod3a and Sod3b. Furthermore, we have studied their expression patterns and found that they likely complement each other as they are expressed in different tissues: sod3a is mainly expressed in tissues associated with the digestive system, whereas sod3b is highly expressed in cartilage and bone, and may be associated with endochondral ossification, as sod3b seems to be co-expressed with collagen10a1a in zebrafish larvae. We are currently investigating the role of SOD3 in bone mineralization in another mammalian system.

Future studies will focus on the inflammatory response using well-established models in zebrafish. We are currently creating knockout sod3a and sod3b zebrafish lines using CRISPR/Cas9 technology. These lines will provide us with a broad range of possible ways to investigate the influence of SOD3 during an inflammatory response.

P12.04   Eva Forsom

ANTIPSYCHOTIC TREATMENT AND THE BONE MINERAL DENSITY OF THE LUMBAR SPINE

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Background: Studies show a correlation between antipsychotic use and lower bone mineral density (BMD), especially among people with schizophrenia. Previous studies examining BMD in patients with schizophrenia and others undergoing antipsychotic treatment have measured BMD using DXA, which yields areal BMD (aBMD). Using QCT, it is possible to measure volumetric BMD (vBMD), which is more sensitive to bone loss. As this is an autopsy-based study, the higher radiation dose of CT compared to DXA is irrelevant.

Aim: To examine if antipsychotic treatment has a negative impact on the bone mineral density of the lumbar spine.

Methods: The material used for cases consists of CT scans of autopsied individuals diagnosed with schizophrenia and/or blood tested positive for antipsychotic medication. CT scans from sex- and age-matched autopsied individuals with no known psychiatric illness and blood negative for antipsychotic medication serve as controls. Scans are analysed with asynchronous QCT, where a Mindways calibration phantom is scanned separately from the autopsy body scans. With Mindways QCT Pro software, vBMD of three consecutive vertebrae is measured. L1-L3 is used, except in cases of vertebral collapse, where T12 or L4 are used instead of the affected vertebra. The results from the case and control groups are compared using a paired t-test.

Results: 41 cases have been analysed so far. Preliminary results are expected in January 2019.

Perspectives: Insight into the potential negative effect of antipsychotic medication on bone health enables the taking of prophylactic measures when starting treatment and provides incentive to develop treatment options that do not affect bone.

P12.05   Morten Aagaard Nielsen

GALECTIN-3 ASSOCIATES WITH OUTCOME IN RHEUMATOID ARTHRITIS

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Background: Galectin-3 (Gal-3) is considered important in inflammation and immune responses. We have previously shown that galectins are capable of binding to receptors of the TNF superfamily, thereby modulating inflammatory signals.

Methods: Gal-3 was measured in plasma samples from newly diagnosed and treatment-naïve RA (eRA) patients at baseline and after 3 months of aggressive treatment (the OPERA trial, n=97) and plasma and synovial fluid samples from chronic RA (cRA) patients (n=17) by ELISA. The 28-joint disease activity score with CRP (DAS28CRP) was used to evaluate treatment outcomes over a 2-year period. Plasma samples from age- and gender-matched healthy controls (HC) (n=48) were included.

Results: Plasma Gal-3 were increased in eRA (mean: 8.1 ng/ml (CI: 7.6-8.6)) compared to HC (mean: 6.4 ng/ml (5.9-6.9)) (p < 0.0001). Gal-3 correlated with DAS28CRP at baseline (ρ = 0.27) (p < 0.05). A decrease in Gal-3 levels from baseline to 3 months was significantly correlated with high disease activity after 2 years of treatment evaluated by DAS28CRP (ρ = 0.23) (p < 0.05). After 3 months of intensive treatment, the plasma levels of Gal-3 were still elevated (mean: 8.3 ng/ml (7.8-8.7)). In cRA, Gal-3 levels in synovial fluid were tripled (mean: 30.9 ng/ml (18.3-43.5)) compared with plasma levels (mean: 9.1 ng/ml (7.8-10.4)) (p< 0.01).

Conclusion: In early RA patients, persistent high plasma levels of Gal-3 during the first 3 months of treatment were associated with lower disease activity after 2 years of treatment. These observations support that Gal-3 is implicated in RA disease pathology and could be a new treatment target.

P12.06   Rasmus Klose-Jensen   DIFFERENCES AND SIMILARITIES OF THE FEMORAL HEAD'S BONE-CARTILAGE UNIT IN PATIENTS WITH OSTEOARTHRITIS AND PATIENTS WITH RHEUMATOID ARTHRITIS

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Despite distinct aetiologies of joint diseases, the osteoarthritic end-stage of primary osteoarthritis (OA) and rheumatoid arthritis (RA) are described using similar radiological features. However, primary and secondary osteoarthritis may be different at the bone-cartilage unit depending on the pathogenesis. Therefore, the main purpose was to investigate the histological differences in the bone-cartilage unit of the hip joint in patients with primary OA and patients with secondary OA due to RA. Femoral heads were obtained during arthroplasty from 12 patients with primary OA and 6 patients with RA. Femoral heads were investigated using stereological methods to provide unbiased quantitative data. The femoral head, articular cartilage (AC), calcified cartilage (CC), sub-chondral bone (SCB) and osteophytes were measuered. Data are presented as Δmean[95%CI], and significance was found using student's t-test. AC was thicker in patients with OA than RA (413[78.9;747]μm, p = 0.029). CC was also thicker in patients with OA than RA (56.4[0.4;113] μm, p = 0.017). No difference was observed in neither femoral head volume (1.2[-3.6;6.1]cm^3, p = 0.598), SCB thickness (-2.5[-212;207]μm, p = 0.980), nor marginal osteophyte area (25.3[-53.6;104]cm^3, p = 0.506). Patients with RA had thinner AC and CC, but they were otherwise not significantly different compared with patients with OA. Thus, the inflammatory joint in RA was associated with a more pronounced loss of cartilage than the degenerative joint disease in primary osteoarthritis. The increased thickness of calcified cartilage in primary osteoarthritis has been attributed to endochondral ossification, which does not seem to be the case in RA.

P12.07 Sebastian Mosegaard

PREOPERATIVE RISK FACTORS FOR LOW PATIENT REPORTED SATISFACTION AFTER CARPAL TUNNEL RELEASE

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Purpose: The purpose of this study was to identify outcome predictors of low patient reported satisfaction following decompression surgery of carpal tunnel syndrome.

Hypothesis: High preoperative Pain Catastrophizing and low preoperative quality of life increases the risk of low patient reported satisfaction after decompression surgery.

Methods: We included 732 hands (468 female, 264 male) from 714 patients with nerve conduction verified carpal tunnel syndrome with a mean age of 58.0 years in a prospective cohort study. We collected preoperative data on distal motor latency, pain catastrophizing, DASH score and Eq5d and 12-month postoperative data on DASH score, Eq5d and patient satisfaction. After exclusion of patients due to missing data (N=92) and bilateral patients (N=18), we were left with 622 hands (405 female, 217 male), which did not change the preoperative mean scores.

Results: We found a statistically significant improvement in preoperative and postoperative measurements of DASH (12.29, p<0.001) and Eq5d (0.14, p<0.001). When using dichotomous patient reported satisfaction as outcome, we found statistically significant increased risk of low satisfaction with higher preoperative pain catastrophizing (p=0.024), lower preoperative Eq5d (p=0.002) and lower preoperative distal motor latency (p=0.027). There was no effect of either age or gender.

Conclusion: Patients improved in DASH and Eq5d from preoperative to 12-month postoperative when analysed as a cohort. Low preoperative quality of life, high pain catastrophizing and low preoperative distal motor latency increase the risk of low patient reported satisfaction following decompression surgery of carpal tunnel syndrome.

P12.08 Laura Houstrup Therkelsen

FEW COMPLICATIONS FOLLOWING PERCUTANEOUS NEEDLE FASCIOTOMY FOR DUPUYTREN CONTRACTURE

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Background: Dupuytren contracture is a progressive flexion contracture of the finger(s), which may lead to disabled hand function. Percutaneous needle fasciotomy (PNF) is a minimal invasive surgical treatment using a fine syringe needle to perforate the Dupuytren chords until the finger can be extended. PNF has slowly become an accepted treatment option in Denmark with more than 1,700 procedures in 2017. However, severe

complications associated with PNF have not yet been investigated. Our aim is to evaluate the safety of PNF for Dupuytren contracture.

Method: This is a single-center register-based follow-up study on all PNF-treated patients in 2007-15 at Silkeborg Regional Hospital. The study population was identified through the Danish National Patient Registry (NPR). Diagnosis codes were used to identify possible severe post-operative complications, such as tendon rupture, nerve damage, infection, amputation and reflex dystrophy for all index treatments. The Danish Drug Statistics Registry was used to identify non-hospital-treated infections. All postoperative complications were verified by review of medical records.

Results: Preliminary results of 2,308 patients with index PNF treatment were identified in NPR. 0.13% (n=3) had flexor tendon rupture. 0.04% (n=1) had digital nerve damage. No amputation or reflex dystrophy was registered. Assessment of infections treated in the primary sector is ongoing, but only 0.04% (n=1) had infection treated in hospital. However, the total infection rate is well below 2.5%, and none of them required surgery.

Conclusion: PNF for Dupuytren contracture appears safe with few severe postoperative complications when an appropriate technique is applied.

P12.09   Jeanette Trøstrup A SHOULDER-CAFÉ INTERVENTION TO REDUCE SHOULDER COMPLAINTS IN EMPLOYEES WITH HIGH MECHANICAL SHOULDER EXPOSURES AND SHOULDER COMPLAINTS: STUDY PROTOCOL

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Background & aim: Shoulder complaints are prevalent and estimated to occur in 16-26% of the general population. In occupations with high mechanical shoulder exposure, shoulder disorders are especially frequent.

In Denmark, citizens with shoulder complaints receive repeated referrals and thus visit several different healthcare providers. This type of health-care usage divides the healthcare, and the course of treatment becomes uncoordinated. Therefore, a new intervention was developed. The intervention comprised of a Shoulder-Café, which unifies the expertise needed to diagnose and treat shoulder complaints.

The aim of the trial is to evaluate the effect of the Shoulder-Café on shoulder complaints compared to Shoulder-Guidance (control intervention).

Methods: Cluster randomization is used. Clusters comprise of companies with employees in service, manufacture and construction. Participants are 120 employees with high occupational mechanical shoulder exposure, who fill in a screening questionnaire and who meet the inclusion criteria

(e.g. have shoulder complaints). The primary outcome is the Oxford Shoulder Score at 6-month follow-up. Intention-to-treat analysis will be performed.

Discussion: Transparency of the trial and the results is improved as the trial is pre-registered at clinicaltrials.gov (ID: NCT03159910). Further more adding to the transparency, the interventions are described based on the TIDieR framework, and a Statistical Analysis Plan will been conducted prior to the analysis.

P12.10   Emil Toft Nielsen   A NOVEL CLINICAL METHOD FOR NON-INVASIVE QUANTIFICATION AND GRADING OF PIVOT-SHIFT TEST

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Background: Anterior cruciate ligament (ACL) injury may be complicated with extrinsic ligament injury, such as injury to the anterolateral ligament (ALL), which may increase rotational instability. The pivot-shift (PS) test dynamically reproduces knee rotational instability, and positive tests correlate with patients' subjective experience of knee stability, reduced sports activity, and risk of early gonarthritis. However, the PS grading is poorly repeatable between clinicians.

Purpose: To develop an objective grading system for the PS test that screened for human errors.

Methods: One examiner graded PS tests performed on eight cadavers exposed to five successive ligament situations: intact, ACL lesion, ACL+ALL lesion, ACL reconstruction, and ACL+ALL reconstruction. Tibial kinematics were assessed using an inertial measurement unit (IMU). An automatic screening algorithm using IMU features approved 95 PS tests (training: n=76, evaluation: n=19). Based on IMU features, four different artificial neural networks (ANNs) were developed and trained to grade individual PS tests using the clinical grades (0,1,2,3) given by the examiner as a gold standard.

Results: Compared to 32 manual screened PS tests, the automatic screening algorithm correctly categorized 97%. The two ANNs that used a combined-average strategy had the best and equal accuracy of 84% for grading the 19 PS tests.

Conclusions: ANNs have a great potential for objective individual grading of PS tests, and further it is a low-cost and user-friendly method. Following ongoing in-vivo testing and calibration, it may be used for clinical individual rotation instability grading in patients with knee injuries.

P13.01 Sara Højslev Avlund

ASSOCIATION OF COMORBIDITY, MEDICATION USAGE AND FAMILY PSYCOPATHOLOGY ON QUALITY OF LIFE IN A COHORT OF ADOLESCENTS REFERRED ON SUSPICION OF AUTISM SPECTRUM DISORDER IN CHILDHOOD

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Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder that often presents early in life. Comorbidity is common in individuals with ASD and complicates diagnostic process, intervention and quality of life (QoL). QoL in individuals with ASD is generally poor on all subdomains compared to both typically developed children and children with other developmental disorders. Studies show that comorbidity along with poor communication skills and behavior problems are associated with low QoL. However, QoL has only been examined in small samples of individuals with ASD. The role of comorbidity, the medication of these co-existing conditions, and the psychopathology in relatives is underexposed and needs attention if we are to improve the wellbeing and the QoL in individuals with ASD. Therefore, we aim to examine the QoL and wellbeing in adolescents with ASD and examine the association with comorbidity, medication usage and family psychopathology.

Methods: A total of 854 preschoolers examined for ASD at Aarhus University Hospital in the period of 2000-2010 are along with their parents invited to participate in a questionnaire survey 8-18 years after initial assessment. Self- and proxy-reports on KIDDSCREEN-27 and SDQ will be used to describe the primary outcome QoL and wellbeing. From the Danish registers, we extract the independent variables: psychiatric comorbidity, medication usage and family psychopathology. Using regression analysis, we test the association between independent variables and outcome while controlling for the effect of IQ, socioeconomic status, type of ASD and current autism severity.

Results: Data collection is ongoing. The first results are expected in the summer of 2019.

P13.02 Janne Tidselbak Larsen

GENETIC RISK FACTORS FOR ANOREXIA NERVOSA

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Eating disorders are psychiatric illnesses characterized by a pathological preoccupation with eating and body image, which have severe personal,

social, and societal consequences. Early detection and intervention increase the likelihood and rates of recovery. The evidence thus far suggests that genes and environment interact to influence eating disorder risk, and it is likely that genetically predisposed individuals are most vulnerable to environmental influences. Identification of high-risk or vulnerable groups may improve detection rates and thereby prognosis.

Eating disorders tend to aggregate in families. For anorexia nervosa, twin studies have estimated the heritability to be 0.48-0.74. Genome-wide association studies have thus far identified one genome-wide significant locus for anorexia nervosa, in a region which has been found to harbor loci associated with type 1 diabetes, rheumatoid arthritis, and other auto-immune phenotypes. Identified genetic correlations include neuroticism, educational attainment, and metabolic markers.

The aim of this proposed study is to investigate potential genetic correlations for anorexia nervosa in a Danish sample using a range of polygenic risk scores, including one-dimensional measures of genetic risk for a given trait. This will be done using genotyped data from the iPSYCH/ANGI-DK cohort of psychiatric cases and random controls. By combing this information with data from nationwide population-based health registers, it is possible to further explore gene-environment interactions and their association with anorexia nervosa.

P13.03   Pernille Kølbæk   CLINICAL VALIDATION OF THE GLASGOW ANTIPSYCHOTIC SIDE- EFFECT SCALE (GASS)

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Background: Antipsychotics are the mainstay in the treatment of psychotic disorders. Treatment with antipsychotics is associated with significant side effects, which may reduce the quality of life and the result in poor treatment adherence. Therefore, regular screening and monitoring of side effects is essential. The UKU side effect rating scale (UKU) is the most comprehensive tool used by health care professionals to assess multi-domain side effects. In order to implement routine side effect screening in real-world settings, a less time-consuming rating scale is needed. The Glasgow Antipsychotic Side Effect Scale (GASS) is a patient self-report scale developed exactly for this purpose. Therefore, the aim of the present study was to perform a clinical validation of the GASS using the UKU assessment as the gold standard reference.

Method: A total of 80 patients will be included in the study. Participants must be ≥18 years old, have a diagnosis of a psychotic disorder, and receive treatment with an antipsychotic drug at the Department for Psychosis, Risskov. Each participant will self-rate his/her side effects on the GASS. Subsequently, a trained rater will conduct the UKU interview and rate the participant's side effects. The scores on the GASS items will be compared with the scores on the corresponding items on the UKU. The statistical analyses will include calculation of specificity, sensitivity, positive predicative value, and negative predictive value of the GASS.

Results: The results will be presented at the PhD Day.

Conclusion: If the results of the validation study are satisfactory, the GASS can be implemented in clinical practice and form the basis for measurement-based care.

P13.04 Katrine Ingeman Beck

DEVELOPMENT OF ASSESSMENT AND TREATMENT OF HEALTH ANXIETY BY PROXY: AN UNRESOLVED CLINICAL PROBLEM

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Context: Health anxiety by proxy refers to excessive parental worries about their child's health and fears that serious illness in the child is being overlooked. Exposure to parental maladaptive illness perception and behavior is suggested as a risk factor for development of health anxiety in young people. Health anxiety by proxy may, therefore, be an important but overlooked treatment target. This study aims to develop and preliminary validate an assessment tool for health anxiety by proxy and develop an internet-based treatment program.

Methods: The development of the assessment tool and the treatment program will be completed in collaboration with patients and clinical and research experts. The specialized assessment tool will be developed from an existing non-validated questionnaire. Subsequently, the validity of the assessment tool will be investigated in a study including 250 parents with different health status. The treatment program's feasibility and preliminary effect will be tested using a single-case design, where target behavior of five patients is measured repeatedly before, during, and after the treatment intervention to compare the patients' results to their own baseline measures.

Results: The development and validation of the assessment tool will be completed in 2018-2020, while development and testing of the new treatment program are expected to be completed in 2019-2021.

Conclusions: This is the first large-scale research project on health anxiety by proxy. The new assessment tool is expected to become an integrated part of the treatment for health anxiety. If the treatment program proves to be feasible, its efficacy will be tested in a randomized controlled trial.

P13.05 Astrid Høeg Tuborgh

ATTACHMENT STYLE AND SYMPTOM REPORTING IN YOUNG PERSONS WITH CONCUSSION

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Background: 5-15 % of people with concussion experience post-concussion symptoms (PCS) more than 3 months post-injury. The etiology of PCS is complex, with interacting biological, psychological, and environmental factors. Attachment style (AS) is grounded in childhood and activated when one is exposed to stressful situations in order to feel

secure. AS may be important to understand how interpersonal processes affect the development of PCS and illness responses.

Aims: In a cohort of 15-30-year-old persons with concussion, we will examine: 1) The distribution of AS according to gender and age, and 2) The associations between AS, illness perception, illness behavior and symptom reporting.

Methods: The project is embedded in an epidemiological study, where 3080 individuals diagnosed with concussion 3 months post-injury received questionnaires on

- General health
- PCS (Rivermead Post-Concussion Symptoms Questionnaire (RPQ))
- AS (Experiences in Close Relationships-Relationship Structure (ECR-RS))
- Illness perception (Brief-Illness Perception Questionnaire (B-IPQ)) and
- Illness behaviour (Behavioural Responses to Illness Questionnaire (BRIQ))

Associations will be explored through linear regression and structural equation models.

Results: 1101 patients responded. Mean age was 21.6 years. Mechanism of injury was primarily fall (36.5%) or blow/jolt to the head (27.7%). Data analyses from the questionnaires are pending and will be presented.

Conclusion: If the assessment of attachment style shows potential for early identification of persons with concussion at risk of a poor prognosis, it may constitute a new avenue for improving treatment strategies.

P13.06   Tina Thorborg   HOW PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS EXPERIENCE
         CANCELLED   FINDING ADEQUATE INFORMATION ABOUT THEIR DISEASE AND LIFE
         OPPORTUNITIES

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Introduction: Patients diagnosed with Amyotrophic lateral sclerosis (ALS) experience a big change in their lives. The disease affects the whole body function and has a big psychological influence. The average survival is 2-4 years from disease onset. However, this survival period may be extended if the ALS patient is offered Home Mechanical Ventilation (HMV). The purpose of this study was to evaluate a decision support tool from a website. Furthermore, we aimed to explore and develop knowledge about the patients' experiences and needs during the decision-making process. Is the decision-making aid helpful when the patients decide whether or not to have HMV?

Methods: Through a qualitative study design and a phenomenological-hermeneutical approach based on the philosopher Paul Ricoeur's interpretation theory, seven semi-structured interviews were collected from ALS patients about their experience with use of the website.

Results: The patients were satisfied with the website and found that it was a good support, although the movies were hard to see. On the other hand,

the movies made it all more real and informed the patients of what would happen in the future if they decided to have HMV. It also showed the reality of challenges individuals often face with the disease. The relatives felt a major responsibility for being a care provider for their spouse.

Perspectives: The new knowledge may be used to further develop and provide targeted help for patients suffering from ALS and their relatives. Patients expressed the need to have contact with a coordinator after being diagnosed with ALS to help navigate the chaos they might be experiencing in their illness pathway.

P13.07   Birgit Refsgaard Iversen   PREVENTATIVE CARE AND HOME TREATMENT IN PATIENTS AT RISK OF HOSPITALISATION DUE TO EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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Background: Exacerbation of chronic obstructive pulmonary disease (COPD) is one of the most common reasons for hospitalization, and the risk of readmission (new admission within 30 days after the last admission) is about 20%. The aim of this study was to examine the effect of being affiliated with a cross-sectorial lung team (CLT) on number of admissions and length of hospitalisations.

Method: The study was designed as a follow-up study. Data on admissions and length of hospitalisation were compared with data from the same sample at the corresponding period from 2013 to 2016. In 2016, patients were affiliated with the CLT for six months (February to August), and 47 patients who had at least one hospitalisation or two medically treated exacerbations of COPD within the last year were included. The CLT consisted of nurses from the hospital and the municipality. Patients were able to phone the CLT day and night. The CLT offered home visits, medical treatment and education.

Results: From 2015 to 2016, the decrease in admissions due to COPD was 12%, and the decrease of hospitalisations due to COPD and comorbidities was 50%. The decrease in the average of length of hospitalisations caused by COPD and COPD-related comorbidities were 10% and 40%, respectively, and 77% of the patients contacted the CLT during February to August 2016. Four of the 11 patients who did not contact the CLT represented 46% of the admissions due to COPD in 2016.

Conclusion: Affiliation to the CLT seems to reduce hospitalisations and length of stay for patients with COPD, but further studies are needed to investigate the effect of the CLT in a larger sample, including e.g. the patients' level of health literacy and the degree of patient involvement.

P13.08   Jose Manuel   "VAPA" - AN INNOVATIVE TELE-REHABILITATION TOOL FOR HOME USE:
           Cerdan de Las   PATIENTS' PERCEPTION AND EXPECTATIONS
           Heras

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Background: Chronic diseases are an economic challenge to society. As part of the solution, telerehabilitation (TR) has been increasingly investigated. In the present study, artificial intelligence, biometric sensor technology, virtual reality and augmented reality (AR) were combined to create a virtual autonomous physiotherapist agent (VAPA) to facilitate TR.

Aim: To study if VAPA is acceptable and effective for patients with Chronic Obstructive Pulmonary Disease (COPD) and Interstitial Pulmonary Fibrosis (IPF); to learn from their perception and wishes for improvement.

Method: 7 patients with COPD and 3 with IPF participated in a focus group interview after ≥ 3 weeks home use of VAPA. The session followed a topic guide divided into 5 themes to explore their experience and perception of the platform and its future versions. Participants reported their views on: "Self experiences" and "Areas for improvement".

Results: 9 patients could see the added value of the TR platform and reported positive points of view. They suggested an easier way to attach the biometric sensor, flexible training appointments in their calendar, a 'back' button, more positive e-learning topics, showcasing success stories of other patients, and a more energetic female 3D agent. The feedback for the achievement reports was positive, while a more robust version of AR hardware was required to feel comfortable.

Conclusion: 9 out of 10 patients with COPD and IPF found value in VAPA. Patient involvement in the development ensures a positive contribution to the design of the envisioned VAPA platform.

P13.09   Christina Bruun   NEUROCOGNITION IN OFFSPRING OF PARENTS WITH SCHIZOPHRENIA
           Knudsen   OR BIPOLAR DISORDER: THE DEVELOPMENT FROM SEVEN TO 11 YEARS
           CANCELLED   OF AGE

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Background: Schizophrenia and bipolar disorder are severe mental disorders associated with neurocognitive deficits that cause lifelong functional disability. Evidence from familial high risk studies shows a broad array of cognitive impairments in children at familial high risk of schizophrenia, and, to a lesser degree, in children at familial high risk of bipolar disorder, which suggests that cognitive deficits are early vulnerability markers for these mental disorders. However, there is currently little research demonstrating whether these cognitive deficits remain stable or deteriorate over time, and only few studies have focused on the early childhood and pre-adolescence.

Aim: To examine the development in neurocognition in children at familial high risk of schizophrenia and bipolar disorder from seven to eleven years of age. Further, to examine the existence of distinct subtypes based on cognitive profiles across the children.

Method: This is a follow-up study. 522 children participated when they were seven years old. A total of 202 children had one or two parents diagnosed with a schizophrenia spectrum psychosis, 120 children had one or two parents diagnosed with bipolar disorder, and 200 children had no parents with neither of the above-mentioned diagnoses. The children's neurocognitive function at seven years of age has been assessed with several instruments that are developed specifically for children and are validated for this age group. The children are currently being assessed with many of the same instruments at 11 years of age.

Perspectives: To use knowledge gained through such studies to guide early interventions and to help design preventive interventions.

P13.10   Cecilie Marie Nielsen

CLINICAL VALIDATION OF PANSS-6 SCHIZOPHRENIA SEVERITY RATINGS AMONG PATIENTS UNDERGOING OUTPATIENT TREATMENT

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Background: In the treatment of schizophrenia, there is a need for rating scales that can be used routinely to monitor the severity of symptoms and to help adjust treatment accordingly. The most widely used schizophrenia rating scale is the 30-item Positive And Negative Syndrome Scale (PANSS-30), which takes approximately an hour to administer. However, this 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 shown promising psychometric properties. To allow for targeted rating of PANSS-6, our group has developed a brief semi-structured interview, SNAPSI.

Objective: The objective of this study is to investigate to which degree PANSS-6 scores rated based on a shorter interview (SNAPSI) correspond to PANSS-6 scores extracted from PANSS-30 ratings obtained using the full structured clinical interview for PANSS (SCI-PANSS).

Methods: A total of 75 patients with a diagnosis of schizophrenia under-going outpatient treatment will be recruited. The participants will be interviewed with both SNAPSI and SCI-PANSS within 24 hours (random order). The interviews will be conducted by two independent interviewers and will be followed by independent PANSS-6 and PANSS-30 ratings.

Statistical analyses: The degree to which PANSS-6 (based on SNAPSI) correspond to PANSS-6 extracted from PANSS-30 will be quantified by computing intraclass correlation coefficients (at the total score and individual item level).

Perspectives: If the results are satisfactory, the perspectives of PANSS-6 include bridging the gap between research and clinical care and enabling measurement-based care of schizophrenia.

P14.01 Samuel Levi Clement Svendsen

A SINGLE GASTRIC K^+LOAD INDUCES ACUTE DIURESIS IN MICE

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Potassium homeostasis depends on the kidney to perfectly match potassium excretion with potassium intake. Recent work by several groups has shed light on the complex physiological elements of this function. One such element is increased urine flow in the distal part of the nephron that amplifies potassium secretion. It remains unclear under which conditions this mechanism is physiologically relevant. By serendipity, we discovered that a single gastric K^+load induces acute diuresis in mice. Here, we hypothesize that the increased diuresis propels enhanced potassium secretion. In this study, we identify where and how an acute potassium load causes increased diuresis.

We used murine in vivo studies and isolated perfused tubules. We saw a two-fold increase in diuresis in mice given 1% K^+solution by gavage, a four-fold increase with 2% K^+solution, but no increase with 2% Na^+solution. Creatinine excretion was not altered. Similarly, NaCl reabsorption in the thick ascending limb was not changed. Intriguingly, when basolateral $[K^+]$ was acutely elevated from 3.5 to 6.0 mM in isolated perfused collecting ducts, the ADH (anti-diuretic hormone)-induced water flux was markedly decreased. This indicates an ADH-antagonizing effect by increases in extracellular potassium. We have thus identified a novel regulatory element facilitating renal potassium excretion.

P14.02 Kristine Fogh Andersen

HEMATURIA AND LONG-TERM RISK OF CHRONIC KIDNEY DISEASE: A DANISH POPULATION-BASED COHORT STUDY

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Background: Hematuria can be a symptom of kidney or urologic disease. However, the cause often remains unknown. Chronic kidney disease (CKD) is an increasing global health problem with a current prevalence of 11%. Early detection and handling of risk factors may prevent development of CKD. Whether hematuria predicts an increased long-term risk of CKD is unknown. Our aim is, therefore, to evaluate the long-term risk of CKD in patients with a first-time hospital diagnosis of hematuria.

Materials and methods: We will conduct a population-based cohort study of patients with a first-time hospital diagnosis of hematuria from 2000 through 2017 using ICD-10 codes. We will obtain data on date of any laboratory-confirmed CKD, death or emigration. Cumulative risk of incident CKD will be assessed in the hematuria and comparison cohorts and compared by hazard ratios computed using Cox regression adjusted for age, sex and chronic diseases.

Results: We expect to include > 130,000 patients nationwide with a hematuria diagnosis. Construction of the dataset is ongoing, and results will be presented at the conference.

Conclusion: We expect to contribute with knowledge about the long-term prognosis in patients with hematuria. By clarifying the prognosis after hematuria and identifying characteristics associated with high risk of CKD, we aim to guide clinicians in the follow-up of hematuria patients to avoid development of CKD.

P14.03   Søren Viborg Vestergaard   VALIDITY OF THE CODING OF NEPHROTIC SYNDROME DIAGNOSES IN DENMARK

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Background: Nephrotic syndrome (NS) is a kidney disorder characterized by heavy proteinuria, hypoalbuminemia, and edema. The Danish National Patient Registry (DNPR) is a potential valuable data source for studying occurrence and prognosis of NS, but the validity of the coding of NS diagnoses in the registry is unknown.

Objectives: We aim to examine the sensitivity, specificity, and predictive values (PPV and NPV) of NS diagnoses in the DNPR, using regional laboratory test results as the reference standard.

Methods: We will identify all patients with a DNPR recorded diagnosis of NS in the Central Denmark Region (population ~ 1.2 million) during 2005-2013. In this population, we will sample all patients with an inpatient or outpatient hospital diagnosis of NS, and all patients with recorded biochemical assessments of proteinuria and plasma albumin during the study period. We consider NS biochemically with concurrently recorded nephrotic range proteinuria and hypoalbuminemia. To estimate the number of persons with true positive and false positive diagnoses, we will identify all patients with a first-time diagnosis of NS in the DNPR and examine whether NS diagnostic criteria were fulfilled based on bio-chemical confirmation of nephrotic range proteinuria and hypo-albuminemia. To estimate true negative and false negative diagnoses, we will screen laboratory data for patients with biochemical confirmation of NS and examine whether NS is recorded in the DNPR. We will compute sensitivity, specificity, PPV, and NPV with corresponding 95% confidence intervals (95% CI) for an estimated 500 patients.

Results and Conclusion: We expect to present preliminary results at PhD Day 2019 at Aarhus University.

P14.04   Marie Houmaa   PRELIMINARY RESULTS FOR THE USE OF NA18F PET/CT IN RENAL
          Vrist   OSTEODYSTROPHIA

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Aim: Implementation of a new method for determination of bone mineral
clearance based on Na18F-PET/CT.

Background: The risk of developing renal osteodystrophy increases when
renal function decreases. Nearly 100 percent of dialysis patients have
bone disease. Renal osteodystrophy is divided into four different types, all
of which require different treatment. The gold standard for diagnosis is
double tetracycline-labeled bone biopsy. The bone biopsy is
cumbersome, expensive and invasive. It is of great interest to develop an
alternative method to diagnose renal osteodystrophy.

Methods: The trial is a pilot study with 20 dialysis patients. All patients
underwent double tetracycline-labeled bone biopsy. The patients under-
went dynamic static Na18F-PET/CT-scan over the cardiac region for 60
min followed by a whole-body scan for 30 min. Venous blood samples
were drawn at -5, 40, 50, 60 and 90 minutes after intravenous injection of
150 MBq Na18F. A 3-tissue compartment model was used to estimate
bone Na18F-clearance (Ki) using PMOD and multi-point Patlak-analysis.

Results: The preliminary results from 9 patients show that the mean value
for Ki by PMOD-analysis in the vertebrae was 0.0414+0.0107 ml/min/cm3.
The corresponding value by multi-point Patlak analysis was
0.0353+0.0099. The values for Ki are in the same range as previously
published data for diverse patient groups. At the PhD Day, we aim to show
the preliminary results from bone biopsies.

Perspectives: The measurement of bone mineral clearance using Na18F-
PET seems feasible, and the clinical value for determination of changes in
Ki after medical intervention will be determined in following studies.

P14.05   Ann Mai   THE EFFECT OF ORALLY ADMINISTRATED NITRATE ON RENAL AND
          Hindkjær   SYSTEMIC HAEMODYNAMICS, WATER AND SALT REGULATION, TUBULAR
          Østergaard   TRANSPORT PROTEINS AND VASOACTIVE HORMONES IN A
                          RANDOMIZED, PLACEBO-CONTROLLED, CROSSOVER STUDY IN HEALTHY
                          SUBJECTS

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Inorganic nitrate reduces blood pressure and improves endothelial
function in both healthy subjects and hypertensive patients.

This effect is thought to be caused through bioconversion to nitric oxide, thus improving risk factors of cardiovascular disease by increasing vasodilatation, salt regulation and vasoactive hormones. The purpose of this study is to investigate the effect of inorganic nitrate on kidney function, hormones and circulation, which is still unknown.

The effect of 4 days of treatment with 24 mmol potassium nitrate capsules on heart rate, blood pressure, vasoactive hormones and urinary excretion of sodium and water will be measured in a randomized, placebo-controlled, double-blinded, crossover study in 20 healthy subjects. Each subject attends 2 examination days at least 4 weeks apart. The examination days are divided into 8 clearance periods of 30 min. each. The first 3 are baseline periods. In period 4, 1L of saline is administered to detect any difference in renal parameters after salt load.

Primary outcomes are changes in renal plasma flow and glomerular fitration rate measured with a double-isotope technique, and systemic haemodynamics are measured by Mobil-O-Graph. Additionally, water and salt balance, vasoactive hormones and tubular transporter proteins (AQP2, ENaC, NKCC2) are measured with well-established assays.

If inorganic nitrate supplementation is found to lower blood pressure in addition to favorable renal effects, it could lead to changes in the general treatment of high blood pressure and cardiovascular disease.

P14.06   Marlene Louise Nielsen

CHARACTERIZATION OF CYST ORIGIN IN ADPKD

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Introduction and Aim: Autosomal dominant polycystic kidney disease (ADPKD) results in progressive cystogenesis. Treatments inhibiting cyst growth in mouse models of the disease have been developed. However, most of these have shown limited effect in humans. Targeting drugs to the renal cysts may provide a way to increase drug concentrations and, thus, efficacy in humans. We hypothesize that, in early stages of the disease, most cysts originate from proximal tubules and that cells lining these cysts express the proximal tubule endocytic receptors megalin and/or cubilin, which may mediate targeted drug uptake to inhibit proliferation of cyst lining cells.

Methods: The segmental origin of cysts lining cells is characterized by immunohistochemistry in kidney tissue obtained from Pkd1$^{RC/RC}$mice at 1 and 6 months of age as well as specimens of nephrectomized kidneys from ADPKD patients. We use antibodies specific to membrane protein markers of the various tubular segments, including: Megalin, Cubilin (Proximal Tubules), Calbindin (Distal Tubules) and AQP2 (Collecting Ducts).

Results: We identified cysts expressing membrane proteins from all parts of the renal tubules, with a superior number of cysts expressing AQP2 or calbindin. Interestingly, markers of the different tubular segments co-localize in some cysts, and partial expression of different markers in distinct parts of the cystic membrane was observed.

Conclusion: Cysts of the proximal tubule origin were identified in both mice and human tissue, but the majority of cysts appeared to originate

from other parts of the nephron and/or express a mix of membrane proteins from different parts of the renal tubular segment.

P14.07   Christian Østergaard Mariager

EX-VIVO INVESTIGATION OF RENAL METABOLIC HETEROGENEITY USING HYPERPOLARIZED ^{13}C-PYRUVATE MRI

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The ability to investigate isolated organs outside the body is becoming increasingly relevant. This is due to several factors, including a need for novel transplantation applications as well as the desire to perform more detailed investigations into metabolism and function. We present an MRI compatible perfusion system that is capable of investigating hemodynamic and metabolic function in ex-vivo porcine models through the use of hyperpolarized and standard MRI.

Whole blood and kidneys are retrieved from healthy female domestic pigs (40 kg BW), followed by the termination of the animal. The kidney is flushed with Ringers acetate (5 °C) and cooled down until the start of the perfusion. The renal artery and ureter is cannulated before connecting the organ to the perfusion system. The organ is perfused using 37 °C whole blood with a flow of 170 mL/min. Glucose, amino acids and insulin are infused continually. Vasodilator is infused to ease the perfusion. Produced urine is collected to avoid contamination of the blood supply. Physio-logical and hemodynamic parameters are monitored throughout the perfusion.

The perfused kidney is placed in a 3.0T MRI scanner with proton and ^{13}C-imaging capability. A carbon-13 dynamic spectro spatial MRI scan following a 9 mL dose of hyperpolarized ^{13}C-pyruvate is performed to map the temporal intra renal metabolic distribution. Preliminary results from these investigations display differences in intra renal heterogeneity. The renal cortex show a predominant lactate production, while alanine production is mostly confined to the renal medullary region. With further analysis, we hope to clarify these observations and investigate the correlation with GFR.

P14.08   Birgith Engelst Grove

TELE FOLLOW-UP USING PATIENT-REPORTED OUTCOMES (PRO) MEASURES IN PATIENTS WITH CHRONIC KIDNEY DISEASE - THE PROKID STUDY: A STUDY PROTOCOL FOR A NON-INFERIORITY RANDOMISED CONTROLLED TRIAL

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Background: Outpatient follow-up in chronic diseases is steadily increasing, but, for stable patients, routinely scheduled visits can turn out to be redundant from both the patient's and the clinician's point of view. Patient-reported outcome measures collected at home (TelePRO) could allow more tailored follow-up of patients based on their individual needs for clinical attention.

Aim: To evaluate the effects on quality of care, use of resources and the patient perception of using TelePRO as the basis for follow-up in patients with chronic kidney disease (CKD).

Method: Newly referred patients diagnosed with CKD will be randomised into:

1) TelePRO-based follow-up without scheduled consultations

2) PRO-based telephone consultations

3) Usual follow-up consultations.

Intervention: A diagnosis-specific electronic questionnaire completed by the patient at home will substitute usual outpatient follow-up visits. The PRO questionnaire will in part be used as a screening tool to identify patients in need of outpatient contact and to identify problem areas. Responses from the questionnaire are processed to a disease-specific algorithm and assigned green, yellow or red status according to patients' needs.

The primary outcome will be loss of renal function measured using estimated glomerular filtration rate (eGFR). The secondary outcomes are 1. Quality of care, 2. Utilisation of resources and 3. Patient perceptions.

Perspectives: If proven efficacious, use of TelePRO may lead to reorganisation of routine clinical practice in nephrology outpatient clinics and may have an impact on other patient groups with chronic conditions attending regular follow-up.

P14.09   Stine Lohmann   EX-VIVO INTRA-ARTERIAL ALLOGENIC MSC THERAPY PRIOR TO TRANSPLANTATION IN A PORCINE DCD MODEL DOES NOT LEAD TO IMPROVED GRAFT FUNCTION

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Introduction: Mesenchymal stromal cells (MSC) may have regenerative effects and be of value for improving renal function after ischemia reperfusion injury in transplantation. So far, MSC have been given intravenously, but intra-arterial ex vivo administration will lead to a more targeted delivery to the kidney. The aim of this study was to clarify, for the

first time, in a porcine donation after circulatory death (DCD) model, whether such treatment can affect early renal function.

Materials and Methods: Female 50 kg pigs were randomized to ex-vivo infusion in the renal artery of 10 million MSC in 50 ml University of Wisconsin (UW®) solution (n=8) or UW® alone (n=8). On day -1, left kidneys underwent 75 mins of warm ischemia. By the end of the 16 hr static cold storage period, MSC were delivered intra-arterial ex-vivo on day 0. After right nephrectomy, the grafts were autotransplanted and animals observed for 14 days.

Results: As intended in this DCD model, renal function was seriously impaired, but with no improvement in the MSC group. Measured glomerular filtration rate (^{51}Cr-EDTA-clearance) at day 14 was similar between the groups (19 versus 24 ml/min/100g, MSC versus Control, p=0.21). Tubular function as evaluated with MAG3 clearance (67 versus 78 ml/min/100g, p=0.49) and urinary NGAL/creatinine (1453 versus 1097 micrg/mmol, p=0.16) as well as peak p-creatinine (1274 versus 1230 µmol/L, p=0.69) were also similar.

Conclusion: Ex-vivo MSC administration before kidney transplantation was successful in distributing the MSC in the kidney. Within 14 days of observation time, MSC do not seem to repair ischemia reperfusion injury.

P14.10   Stine Sundgaard Langaa   DETERMINATION OF RENAL BLOOD FLOW BASED ON PET/CT-RUBIDIUM-82 TECHNOLOGY IN HEALTHY SUBJECTS

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Background: Changes in Renal Blood Flow (RBF) play a patophysiological role in the widespread diseases hypertension and kidney disease. However, RBF determination is difficult in humans. Routine coronary blood flow is assessed with PET/CT and Rubidium-82 (Rb-82).

Aim: Development of a new method for RBF determination based on Rb-82-PET/CT-technology and a 1-tissue compartment model. To include the input function in the model and the kidneys in their entirety in the same field of view (FOV) in order to minimize radiation exposure, we hypothesized that the abdominal aorta (AA) is a valid alternative to the left ventricle (LV), which is routinely used as input function.

Methods: 19 healthy subjects underwent duplicate Rb-82-PET/CT scans in one bed position. The FOV contained the LV, AA and the majority of the kidneys. Volumes of interest were placed in LV, AA and the kidneys. Time activity curves were generated. A 1-tissue compartment model was used to estimate RBF. K1 represents RBF. K1-values derived from LV and AA were compared.

Results: For LV, the mean K1-value was 1.97 ± 0.28 ml/min/g for the right kidney and 1.96 ± 0.30 ml/min/g for the left kidney. For AA, the mean K1-value was 2.41 ± 0.37 ml/min/g for the right kidney and 2.40 ± 0.37 ml/min/g for the left kidney. The intra-assay coefficient of variation was approximately 12% and 11.5% for LV and AA, respectively.

Conclusion: Our preliminary results suggest that RBF determination based on the PET-Rb-82 method is feasible. Physiologically, use of AA as input function seems most valid because of the direct input to the renal arteries and the derived K1 values are significantly higher than K1 values derived from LV.

P15.01 Malene Thygesen

EXPOSURE TO AIR POLLUTION AS A RISK FACTOR FOR THE DEVELOPMENT OF ADHD IN CHILDREN

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Background: It is well documented that exposure to air pollution is associated with adverse health effects and increased mortality. More recently, studies have also found associations between air pollution exposure and cognitive deficits and attention-deficit hyperactivity disorder (ADHD) in children. However, all previous studies had methodological limitations.

Methods: In this nationwide cohort study, we followed all children born in Denmark between 1992 and 2007 for onset of ADHD during 1997-2012. We linked daily concentrations of nitrogen dioxide (NO_2) and fine particulate matter ($PM_{2.5}$) from air-modelling data at a 1 km x 1 km resolution at residences within the first five years of life with population-based data from the Danish registers. We estimated incidence rate ratios (IRRs) with 95% confidence intervals (CI) for ADHD, according to an increase in exposure, adjusting for potential confounders.

Results: Exposure to NO_2 and $PM_{2.5}$ during early life was associated with a significantly increased risk of ADHD: IRR of 1.38 (CI: 1.35 to 1.42) per 10 $\mu g/m^3$ increase in NO_2 and an IRR of 1.51 (CI: 1.40 to 1.62) per 5 $\mu g/m^3$ increase in $PM_{2.5}$. In two-pollutant models, the association between NO_2 and ADHD did not change (IRR 1.35; 95% CI: 1.31 to 1.39), while the association with $PM_{2.5}$ was substantially attenuated (IRR 1.07; 95% CI: 0.98 to 1.16), although in stratified models an elevated association with $PM_{2.5}$ was found in the lowest quintile of NO_2 exposure.

Conclusions: In this large nationwide prospective cohort study, residential air pollution exposure, specifically NO_2, during childhood was associated with the development of ADHD.

P15.02 Daniel Borch   CHANGES IN INTAKE OF DAIRY PRODUCT SUBGROUPS AND TYPE 2
        Ibsen   DIABETES: MODELLING SPECIFIED FOOD SUBSTITUTIONS IN THE DANISH
                       DIET, CANCER AND HEALTH COHORT

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Background: Current dietary recommendations for prevention of type 2
diabetes (T2D) emphasize replacement of whole-fat dairy products with
low-fat dairy products, but few long-term studies have investigated this
directly.

Objective: To investigate the association between increased intake of one
dairy product subgroup at the expense of another during a 5-year period
and the subsequent 10-year risk of developing T2D.

Design: We used the Danish Diet, Cancer and Health cohort including
39,347 men and women with two measurements of diet recorded using a
validated food frequency questionnaire administered in 1993-1997 and
1999-2003. T2D cases were ascertained from the Danish National
Diabetes Register. The substitutions were modelled as 50g/day using the
pseudo observation method.

Results: Data were analysed in three age strata. Participants aged 56-59
years who increased the intake of low-fat yogurt (rate difference (RD)
[95% CI]: -0.05% [-0.10, -0.003]) or whole-fat yogurt (RD [95% CI]: -0.08% [-
0.14, -0.02]) in place of skimmed milk reduced the risk of T2D. Whole-fat
yoghurt in place of semi-skimmed or whole-fat milk was also associated
with a reduced risk. Similar trends were observed for those aged 60-63
years, but not in those aged 64-70 years. Among participants aged 60-63
and 64-70 years, skimmed milk for semi-skimmed milk increased the risk
of T2D (RD [95% CI]: 0.05% [0.02, 0.08] and 0.03% [0.003, 0.07],
respectively).

Conclusions: Our results suggest a reduced risk of T2D when substituting
yogurt for milk products, regardless of fat content, particularly among
those aged 50-59 years and an increased risk when substituting skimmed
milk for semi-skimmed milk among those aged 60-63 and 64-70 years.

P15.03 Jose Omar   FAMILIAL DIABETES STATUS AND THE RISK OF INCIDENT TYPE 2 DIABETES
        Silverman   IN DENMARK
        Retana

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Aim: To quantify the association between familial diabetes status and index individual's risk of developing diabetes and to assess sex differences.

Methods: We performed a register-based follow-up study of all individuals in Denmark aged 30 years or older who did not have diabetes on 1 January 1995 and had available information on parental ID, following them until the end of 2012. Parental and sibling diabetes status (exposures) and index individual incidence of diabetes (outcome) were defined from the Danish National Diabetes Register. We fitted Poisson regression models to estimate age-adjusted incidence rate ratios stratified by sex. We tested interaction terms to determine whether the risk for those with diabetes in both parents and siblings exceeded the contribution from each family member.

Results: We included 1,994,959 individuals who contributed 33,036,441 person-years and identified 60,256 incident diabetes cases. Index individuals who had one parent or full sibling with diabetes had twofold higher risk of diabetes compared to those with no family members with diabetes. Risk estimates were higher in a close to multiplicative pattern when either both parents or the mother and full sibling had diabetes. Risk of diabetes was higher for index individuals who had a full sibling with diabetes compared to those with half siblings with diabetes.

Conclusions: The ability to extract detailed familial diabetes data from population-wide registers offers vast research opportunities and may help to inform strategies for prevention and early detection.

P15.04   Louise Lindholdt   DOES LABOUR MARKET PARTICIPATION AMONG PARENTS AFFECT SELF-RATED HEALTH OF THEIR CHILDREN? A STUDY OF 11,267 ADOLESCENTS AND THEIR PARENTS

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Aim: The aim of this cross-generation study was to investigate whether parents' labour market attachment was associated with self-rated health among adolescents.

Methods: A cohort of Danish adolescents in 9th grade answered a questionnaire about their own self-rated health (SRH) in a newly established youth cohort. One item from SF-36 measured SRH, whereas information on parents' labour market attachment was obtained from registers. The parents were followed in a five-year period before the adolescents completed the questionnaire. Five categories on labour market status were made, and an integration indicator was calculated from an initial sequence analysis to determine how well the parents were integrated in the labour market.

The association between the adolescents' SRH and the parents' labour market attachment was examined by logistic regression. Analyses were performed on 11,267 adolescents and 22,175 parents.

Results: A total of 3,279 adolescents (29.1%) reported low SRH, while 7,988 (70.9%) reported high SRH. The sequence analysis showed that adolescents who reported low SRH had parents who were less integrated in the labour market and had a weaker quality of transitions between the different states compared to the adolescents who reported high SRH. The logistic regression showed that adolescents with parents with weak labour market integration had higher odds for low SRH compared with adolescents with parents with good labour market integration.

Conclusion: The results indicate that unstable labour market attachment among parents affected the perceived health among their adolescent children, indicating a negative effect of labour market marginalisation from generation to generation.

P15.05   Emely Blæhr   SMALL-AREA VARIATION IN SUPPLY OF PSYCHIATRIC CARE: A REGISTER-BASED STUDY

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Background: Variation in the use of health care across small areas defines an important challenge of this century. The causes and consequences of variation are complex and poorly understood, especially in psychiatric disease management.

Purpose/aim: My first study investigates how the supply of psychiatric health and social care, and the compliance of selected clinical guidelines, has varied across regions, municipalities and GPs over the last 10 years.

Materials and methods: Specifically, I will conduct a retrospective register-based study looking at three administrative supplier levels from 2007 to 2017, including five regions, 98 municipalities and 3400 GPs in 2200 practices, to explore the supply of services to Danish mental healthcare users aged 18-65 years with a psychiatric, ICD-10, F-diagnosis. The defined supply will be age, gender and ethnicity standardised.

Discussion and conclusion: As the psychiatric health care sector is currently challenged by need exceeding supply, identification of potential reallocation of resources, from inefficient to efficient practices, has significant policy relevance. Thus, this project will contribute to this identifycation and could inspire future studies in other fields of health care.

P15.06   Mette Hansen Viuff   SEX HORMONE REPLACEMENT THERAPY IN TURNER SYNDROME AND THE IMPACT ON MORBIDITY AND MORTALITY

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Background: In Turner Syndrome (TS), it is recommended to induce puberty around 11-12 years of age by initiating hormone replacement therapy (HRT). However, evidence for the long-term effects on morbidity and mortality is sparse.

Aim: To describe the incidence of cardiovascular and endocrine related morbidity and mortality, and the association with HRT in TS.

Design: Nationwide epidemiological study.

Methods: We identified 1,156 women with Turner Syndrome diagnosed in 1960-2014 using the Danish Cytogenetic Central Registry and linked them with the Danish National Patient Register and the Medication Statistics Register. We used stratified Cox regression to analyze morbidity, mortality and prescriptions, computing proportional hazard ratios (HR).

Results: Women with TS had more than doubled risk of cardiovascular disease, such as arrhythmia, heart failure, hypertension, ischemic heart disease, stroke, and endocrine disease like thyroid disorders, and a 4-fold increase in the risk of diabetes type I and II and osteoporosis. Many TS (17-33% depending on karyotype) never received HRT. Overall mortality in TS is 3-fold increased. Among TS with 45,X receiving HRT, mortality was lower than among HRT non-treated 45,X (HR 5.0 (3.0-8.2) vs. HR 3.0 (1.9-4.5)). We saw a significant reduction in use of antihypertensive medication (HR 0.5 (95% CI 0.4-0.7)), antidiabetics (HR 0.4 (95% CI 0.2-0.9)) and thyroid hormones (HR 0.5 (95% CI 0.3-0.9)) in HRT treated 45,X.

Conclusion: 17-33% of TS women never received HRT. 45,X women that did receive HRT had a lower mortality than those who did not. HRT has a beneficial effect on endocrine conditions, hypertension and stroke.

P15.07   Nanna Weye   ALTERNATIVE METRICS TO QUANTIFY PREMATURE MORTALITY IN MENTAL DISORDERS

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Background: It is widely appreciated that people with mental disorders have higher mortality rates than the general population. While there are several metrics available to quantify premature mortality, the Global Burden of Disease (GBD) study uses Years Life Lost (YLLs). The YLL is a powerful metric within a comparative framework because it only allows individuals to die of one Cause of Death (CoD). As GBD acknowledges only a small number of mental disorders as CoDs, the true impact of mental disorders on premature mortality is underestimated.
Recently, methods have been introduced that compare people with a specific disorder to the general population by estimating Life-Years Lost (LYLs). This metric may be better suited to quantify premature mortality in

those with mental disorder. This paper will compare different measures of premature mortality in mental disorders.

Methods: Using nationwide health registers, we will perform a cohort study of all persons aged 1-94 years living in Denmark in 2000-2015. For GBD mental disorders as a CoD, age- and sex-specific YLLs based on a theoretical minimum risk life table and official year-specific life tables of Denmark are assesed. In addition, we will estimate age- and sex-specific all-cause mortality based on LYLs for all GBD mental disorders. Finally, strengths and limitations of each measure will be discussed.

Perspectives: We hypothesize that newer methods will reveal substantial LYLs related to mental disorders that are not currently captured by GBD methods. If individual level data are available, LYLs are a more precise measure of premature mortality and can provide cause-specific LYLs attributed to all mental disorders.

P15.08   Helle Elisabeth Andersen   ADULT CHILDREN WITH CARE RESPONSIBILITY FOR A PARENT AGED 80+ YEARS LIVING ALONE WITH COMPLEX CARE REQUIREMENTS: A QUALITATIVE STUDY

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Aim: This study explores the phenomenon of 'care responsibility' as experienced and expected by adult children and their parents aged 80+ years in different care settings. What do they perceive as important from a lifeworld perspective in the care pathway from admission to hospital, discharge and home care nursing?

Background: Aging increases the need for health care, so the growth in the number of older persons at very advanced ages puts pressure on health care systems. Older patients aged 80+ years often have complex care requirements, and their adult children are assumed to have caregiving responsibilities, especially if their parent lives alone. Therefore, healthcare professions must find ways of meeting these challenges and understand the needs of adult children of patients aged 80+ and the aged persons themselves.

Method: The study has a descriptive qualitative design with a hermeneutic-phenomenological approach. The sample size will be approximately 10-12 adult children and 10-12 patients depending on when a varied and in-depth description of the phenomenon and pattern recognition appears. Participants with different genders, ages, and occupation will be strategically included and recruited from a geriatric ward in a hospital in the Region of Southern Denmark during 2018.

Ethical considerations: The recommendations of the Declaration of Helsinki, as well as the Ethical guidelines for nursing research in the Nordic countries, will be followed throughout the study. Data Protection Agency: 2015-57-0016.

| P15.09 | Sophie Amalie Glenvad Tind Hamann | ASSOCIATION BETWEEN BMI AMONG SCHOOL CHILDREN AGED 9-17 YEARS AND SOCIO-ECONOMIC STATUS OF THEIR HOUSEHOLD IN LEKHNATH, NEPAL |

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Background: Childhood overweight predicts the risk of adiposity in adulthood, increasing the risk of developing non-communicable diseases. Underweight and stunting are still present in low and middle income countries, causing a double burden of childhood malnutrition. Studies display opposing findings on the association between malnutrition among children and the socio-economic status (SES) of the household in low-income countries. The aim of this study was to determine whether SES of the household is associated with body mass index (BMI) among school children in Nepal.

Methods: A cross-sectional study among school children aged 9-17 years from Lekhnath was performed. 18 schools were selected randomly including children from 4th to 9th grade. SES was measured by a self-administered questionnaire. Weight and height were measured and World Health Organization standard curves for BMI for age and sex were used to categorize nutritional status.

Results: We included 868 (440 girls and 428 boys) with a mean age of 12.6 years equally distributed by sex and age in all groups of SES. Among these, 7% were underweight, 12% were overweight, and 4% were obese. More children being overweight/obese were girls and went to private school. We found 17% stunted. Among these, 10 were overweight/obese. Regression analysis showed no association between SES and overweight/underweight.

Conclusion: The study found that SES is not the determinant factor for BMI as an indicator for malnutrition, neither for overweight nor underweight. Malnutrition is a generalized problem in the society of Lekhnath across SES.

| P15.10 | Sofie Sand Jensen | IN UTERO EXPOSURE TO GLUCOCORTICOIDS AND TIMING OF PUBERTY IN BOYS AND GIRLS: A POPULATION-BASED COHORT STUDY |

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Background: The pubertal age has declined over the past 150 years, but the etiology remains largely unknown. Early pubertal development has been associated with adult diseases, such as obesity, cardiovascular diseases, testicular and breast cancers. Thus, identifying preventable causes is of high public health importance. In utero exposure to exogenous glucocorticoids has been linked to childhood hyperinsulinism, which may increase sex hormone bioavailability, causing earlier pubertal development. The aim of this study is to explore the potential effect of in utero exposure to glucocorticoids on timing of puberty in boys and girls.

Methods: This cohort study will be conducted within the Danish National Birth Cohort on 15,819 out of 22,500 eligible mother-child pairs (70 %). Information on maternal use of glucocorticoids was collected through telephone interviews around gestational weeks 12 and 30, and information on pubertal milestones, such as Tanner Staging, was obtained through half-yearly web-based questionnaires from 11 years of age and throughout puberty. A regression model for normally distributed time-to-event data will be used to obtain mean monthly differences in age at puberty timing between exposure groups taking confounding by indication into account.

Results: Data are currently being prepared for analysis, and results will be presented on PhD Day 2019.

Conclusion: This study will provide valuable knowledge on the potential effect of glucocorticoids use during pregnancy on pubertal development in children. This information is needed when composing guidelines for the use of drugs during pregnancy, especially for women with asthmatic and autoimmune diseases.

P15.11   Tina Kissow Lildal A FEASIBILITY STUDY OF THE NOX T3 HOME SLEEP POLYGRAPHY FOR THE DETECTION OF OBSTRUCTIVE SLEEP DISORDERED BREATHING IN CHILDREN

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Obstructive sleep-disordered breathing (OSDB) is a common condition, affecting both children (1-4%) and adults (5-15%), encompassing sleep fragmentation and oxygen desaturation due to events of partial or complete obstruction of the upper airways during sleep. Polysomnography is the gold standard for diagnosis, but due to high cost and low accessibility in Denmark, the diagnosis is currently based solely on clinical examination, which is of low quality of evidence.

Aim of the study: To conduct a pilot study testing the feasibility of NOX T3 portable home sleep monitoring in young children before conducting a validation study comparing diagnostic accuracy of the NOX T3 for diagnosing OSDB in children to the gold standard in-lab polysomno-graphy (PSG).

Methods: Patients aged 2-10 years referred for evaluation of OSDB at the Department of Otolaryngology, Holstebro, were recruited. Parents were instructed in mounting the NOX T3 device before conducting the sleep monitoring at home and filled out questionnaires reporting their subjective experience with conducting the sleep monitoring.

Results: The final sample consists of 39 participants. Sleep recordings will be evaluated in terms of signal quality and scored both manually according to the American Academy of Sleep Medicine criteria and using the device's autoscore algorithm. The autoscore will be compared to the manual score in terms of Apnea-Hypopnea Index (AHI). Additionally, the parents' reports will be assessed.

P16.01   Lene Wulff   HOSPITAL CONTACTS AND DIAGNOSES FIVE YEARS PRIOR TO HPV
          Krogsgaard   VACCINATION AMONG FEMALES REFERRED FOR SUSPECTED ADVERSE
                            VACCINE EFFECTS: A DANISH NATIONWIDE CASE-CONTROL STUDY

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Background: High health care usage before Human Papilloma Virus (HPV) vaccination might be associated with increased risk of suspected adverse effects. The aim of our study was to investigate hospital contacts and hospital diagnoses five years before HPV vaccination and risk of referral to a specialized hospital-based HPV center for suspected adverse effects.

Methods: The study was a register-based matched case-control study. Cases were females referred to an HPV center. Five controls per case were randomly selected in the source population of Danish HPV vaccinated females. Information on hospital contacts and International Classification of Diseases, 10th version, (IDC-10) diagnoses was obtained from the Danish National Patient Registry. Conditional logistic regression analyses were used to investigate the association between having one or more diagnoses in each specific ICD-10 chapter five years before the HPV vaccination and subsequent referral to an HPV center.

Results: We identified 1,496 cases and 7,480 controls. In total, 80% of the cases versus 65% of the controls had at least one hospital contact prior to HPV vaccination (RR: 1.24 (95% CI: 1.21-1.27)). Cases were more likely to have had a diagnosis in 15 out of 19 ICD-10 chapters before the vaccination, with ORs of ≥1.8 observed for infectious diseases, psychiatric diseases, diseases of the nervous, circulatory, digestive and musculo-skeletal system, unspecific symptoms and unspecific contacts.

Conclusion: Females referred to HPV centers for suspected adverse vaccine effects had a substantially higher number of hospital contacts with various diagnosis before the time of vaccination compared to the source population.

P16.02   Lotte Levison   GUILLAIN-BARRÉ SYNDROME IN DENMARK: VALIDATION OF DIAGNOSTIC
                            CODES AND A POPULATION-BASED NATIONWIDE STUDY OF THE
                            INCIDENCE IN A 30-YEAR PERIOD

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Purpose: To validate the diagnostic codes for Guillain-Barré Syndrome (GBS) in the Danish National Patient Registry (DNPR) using positive predictive value (PPV) as a measure of validity. Secondly, to determine the incidence rate of GBS over a 30-year period in Denmark.

Patients and methods: We used the DNPR to identify all patients diagnosed with a primary GBS diagnosis at a Danish department of neurology between 1987 and 2016. Medical files were reviewed

according to the clinical criteria of the National Institute of Neurological Disorders and Stroke (NINDS) Committee and classified according to the Brighton criteria. The incidence rate was calculated based on data from 1987-2016 and stratified by season, gender and age.

Results: We identified 2,319 patients aged 16 years and above in the DNPR. From a random sample of 573 patients, we retrieved 425 medical files; 356 GBS diagnoses were confirmed. The overall PPV was 83.4% (95% confidence interval (CI): 80.0-87.0). Ninety-nine percent of the confirmed patients also met the Brighton criteria levels 1-3. The crude incidence rate was 1.77 per 100,000 person years (95% CI: 1.70-1.84).

Conclusion: Adult GBS diagnoses in the DNPR have high validity. The DNPR can be used as a data source for epidemiological research on GBS. The Danish GBS incidence rate is similar to GBS incidence rates reported in other European and North American populations.

P16.03 Karen Baden Alstrup

THE DANISH HELICOPTER EMERGENCY MEDICAL SERVICES DATABASE - HIGH QUALITY DATA WITH GREAT POTENTIAL

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Background: The national Danish Helicopter Emergency Medical Services (HEMS) were introduced in 2014 as part of the pre-hospital response, offering advanced patient care on scene and during transportation. Each dispatched mission is entered into a web-based database. Monitoring the quality of critical care has high priority, which underlines the need for research and solid data quality. The aim of this study was to present the design and data quality of the Danish helicopter database.

Method: The study is an observational study including all helicopter dispatches between 1 October 2014 and 30 April 2018. The database layout, data registration, key variables, and data quality in terms of data reliability and internal/external data validity were described.

Results: A total of 13,402 missions were included in the study. The database includes a broad spectrum of mission- and patient-specific data related to the pre-hospital pathway of acutely ill or injured patients in a national coverage. Missing data for the majority of variables is less than 6.5%. The degree of completed report forms has increased over time and reached 99.9% in 2018. Missclassifications were observed for 294 patients, corresponding to 3.7%.

Conclusion: The Helicopter Emergency Medical Services in Denmark are a new and sparsely investigated health care provider. The helicopter database contains nearly all missions dispatched by the five regional Emergency Medical Dispatch Centres. The data quality is generally high, and the database thus creates a solid basis with great potential for future research-based quality improvement.

| P16.04 | Mette Kielsholm Thomsen | CAN WE SCREEN MORE PRECISELY? |

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Introduction: A nationwide colorectal cancer (CRC) screening program was introduced in Denmark in 2014. The screening test searches for invisible yet cancer-revealing blood in participants' stool, and uses a cut-off value of 20 µg of hemoglobin (hgb) per gram feces, to determine risk of cancer and need of further examination. Only 5.2% of participants with a screening result above the cut-off value turn out to have CRC. Thus, many participants unnecessarily go through the colonoscopy procedure, which is unpleasant, expensive and entail a risk of complications. Therefore, the question remains: Can we screen more precisely? Consequently, we aimed to develop a prediction model to assess individual risk of CRC.

Methods: The study is registry-based, including all participants (38,847) in 2014-2015 who had an hgb value above the cut-off and received a colonoscopy. We specified a basic model, including age, gender and hemoglobin, and an elaborated model, which additionally considered measures of comorbidity and socioeconomic position to predict CRC. We compared the two models and evaluated their performance by calibration plots and area under the curve (AUC) for discrimination.

Results: Of the study population, 2,029 had CRC (5.2%). Preliminary results from the basic model (age, gender and hgb) indicate good calibration and discrimination (AUC=75%), with considerable added performance from hgb compared to age and gender only (AUC=65%). Individual risk estimates calculated from this model provide an alternative to the current general hgb cut-off. Using the overall risk of cancer (5.2%) as risk cut-off would mean 25,000 less colonoscopies needed, but conversely 631 missed CRCs.

| P16.05 | Maria Daniella Bergholt | APPROPRIATENESS OF HEALTHCARE, PATIENT OUTCOMES AND EXPERIENCES AMONG PATIENTS IN THE FAROE ISLANDS HOSPITALS BEFORE AND AFTER THEIR FIRST ACCREDITATION |

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Background: Health services worldwide use accreditation as an important element in quality improvement activities. Yet, despite nearly a century with accreditation of hospitals, the evidence base for accreditation is still incomplete.

Objective: The project aims to examine the changes to patient care associated with meeting the accreditation standards.

Design and population: This project is organized as a pre/post study based on medical record audits and questionnaire surveys in all the Faroe Islands hospitals. For the medical record audit, residents will be included if they have been in contact with the hospitals with one of eight selected clinical conditions between 2012 and 2013 before the implementation of accreditation, during 2017 and 2018 after the accreditation. The questionnaire surveys will be conducted in 2016 and in 2018 among hospitalized patients in each of the three hospitals. The study participants will be recruited from surgical and medical wards.

Intervention: The implementation of the Danish Healthcare Quality program including an on-site survey of accreditation.

Outcome measures: Differences in appropriate healthcare (in line with evidence-based clinical guidelines), length of hospital stay, acute readmissions, 30-day all-cause mortality and patient experiences before and after the first accreditation.

P16.06 Nina Mckinnon Edwards

TOTAL HIP ARTHROPLASTY: THE ASSOCIATION BETWEEN SOCIOECONOMIC FACTORS, COMORBIDITIES, POSTOPERATIVE COMPLICATIONS, AND QUALITY OF LIFE

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Background: Total hip arthroplasty (THA) is an effective procedure for reducing pain and improving function and quality of life in patients suffering from disabling diseases in the hip joint. The 5-year survival rate of primary THAs is 95.3%. However, studies have shown that persisting hip-related pain was seen in 28% of patients, and that 7% of patients were dissatisfied one year after primary THA. In addition, THA patients can sustain other adverse outcomes: postoperative venous thromboembolism, serious bleeding, pneumonia, and death. Several patient- and surgery-related risk factors for adverse outcome have been identified. However, knowledge about the effect of socioeconomic factors on adverse THA outcomes remains limited. Socioeconomic status is an economic and sociological combined measure based on income, education and occupation.

Studies:

Study 1: The impact of SES on incidence of THA during 1995-2018

Study 2: Impact of SES on short- and long-term risk of revision of THA, postoperative medical complications and mortality

Study 3: Impact of markers of SES from the self-reported survey "How Are You" on THA outcome.

Study 4: Impact of SES on patient-reported outcomes.

Methods: The Civil Registration System, the Danish Hip Arthroplasty Registry, the Danish National Patient Registry, The Danish National Health Service Prescription Database, the Danish Health Insurance Register, the

Psychiatric Central Research Register, "How Are You" surveys, and some patient-reported outcomes.

Perspectives: By identification of a worse outcome for specific groups of patients, more effective and targeted preventive interventions can be made to further improve the outcome for THA patients.

P16.07 Astrid Julie Bønnelykke

THE MANAGEMENT OF PATIENTS WITH ANAEMIA, THE RISK OF CANCER AND CANCER-RELATED ANAEAMIA SUBTYPES

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Background: Anaemia is a common condition with great prevalence among the elderly and patients with chronic disease. It is important to investigate the underlying aetiology of anaemia, as it is often a symptom of underlying disease and can be an early sign of undiagnosed malignancy. Primary care has a key role in the early diagnosis of cancer, and the accurate diagnosis of anaemia deserves greater clinical attention. However, distinguishing potential malignancy from more common disorders in patients with anaemia is a challenge.

Aim: The overall aim is to improve the diagnostic process in anaemic patients by increasing the alertness of anaemia as a sign of a possible undiagnosed cancer and improving the knowledge of anaemia subtypes.

Methods: The project comprises three individual register-based observational studies. These studies will (i) explore the management of patients with anaemia among general practitioners, (ii) evaluate the risk of cancer in patients with anaemia and compare the cancer risk for selected subtypes of anaemia, and (iii) investigate the prevalence of patients with selected subtypes of anaemia in different types of cancer.

Perspectives: The project will provide new insight into anaemia subtypes and will increase the alertness towards anaemia. This is expected to improve the diagnostic workup of anaemic patients and thereby lead to earlier diagnosis of cancer and improved survival in cancer patients presenting with anaemia. Additionally, the established cohorts will form the basis for future studies of patients with anaemia, such as exploring a variety of diseases related to anaemia, long-term follow-up, side effects of medications and evaluation of cancer recurrence.

P16.08 Sara Koed Badre-Esfahani

HPV VACCINATION IS ASSOCIATED WITH PARTICIPATION IN CERVICAL CANCER SCREENING - A NATIONAL REGISTER-BASED COHORT STUDY

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Introduction: Non-participants in cervical cancer (CCU) screening have a higher mortality than participants. Furthermore, concerns have been raised that human papillomavirus (HPV) vaccination could affect CCU screening non-participation. We aimed to examine the association

between HPV vaccination status and CCU screening participation to target future interventions to high-risk groups.

Methods: In a national register-based cohort study, we included all women born in 1993 (first cohort offered HPV vaccination in Denmark). Primary outcome: Likelihood of non-participation in CCU screening among non-HPV-vaccinated women compared with vaccinated women. Socioeconomic factors were used to adjust for confounding. Simple logistic regression was used to estimate the association between participation in HPV vaccination and screenings. Multiple logistic regression was used to adjust for confounders.

Results: A total of 24,841 women were included in the study population of which 88% were HPV-vaccinated. Among non-HPV-vaccinated women, 53% were non-screened compared with 40% of the vaccinated group. Non-vaccinated women were more likely not to participate in CCU screening than vaccinated women (adj. odds ratio (OR) =1.6 [1.5-1.7]). This association was more outspoken among women from non-western countries (adj. OR=3.8 [3.3-4.2]) than among native Danes.

Conclusion: Non-participation in CCU screening and HPV vaccination may be a matter of general attitude towards health promoting offers. In order to reach non-participants, health promoting initiatives addressing certain groups may be beneficial. Especially, it seems necessary to understand how to target women from foreign countries.

P16.09   Line Stjernholm Tipsmark

ORGANISATION OF EMERGENCY DEPARTMENTS: THE DANISH CASE

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Background: In 2007, a Danish policy recommended reorganisation of emergency medicine. The policy recommendations were, at the time, not evidence based. The aim of this study was to extract any learning from the Danish case by focusing on the relations between evidence, policy and practice 10 years after the policy announcement.

Method: Evidence was identified through a systematic search of the literature on the Danish policy recommendations from January 1st, 2005 to May 13th, 2016. PubMed, CINAHL, Embase, EconLit, and RePEc were searched. Practice was mapped through a survey on emergency department organisational characteristics in Denmark. The data was collected from March 16th to August 28, 2017.

Results: Evidence: From the 28 studies included in the review, there was limited evidence to support the overall objectives of health care. However, 'multidisciplinary team', 'physician in triage', 'senior physician' and 'flow coordinator' were found to improve process quality. Practice: Five out of six recommendations (selected for this article), exceed an implementation

rate of 80%, and the EDs have generally gone through a major change at multiple levels.

Conclusion: We have learned that, even though studies examining the effects of the recommendations now exist, the evidence has low applicability to inform and guide policy-makers. This is due to the narrow outcome measures, study heterogeneity and bias from non-constant settings, where more than one intervention is often tested simultaneously. Furthermore, we have learned that healthcare does not change overnight. A decade has past, and the reorganisation is incomplete, and different organisational models have emerged.

P16.10   Signe Hjuler   A FOLLOW-UP STUDY OF OCCUPATIONAL STYRENE EXPOSURE AND RISK
         Boudigaard   OF SYSTEMIC SCLEROSIS, RHEUMATOID ARTHRITIS, AND OTHER SYSTEMIC
                       AUTOIMMUNE RHEUMATOLOGICAL DISEASES

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Background: Increased risk of autoimmune rheumatological diseases has been suggested following occupational solvent exposure. However, evidence for specific solvents and risk patterns is limited.

Aim: To examine the exposure response relation for systemic sclerosis, rheumatoid arthritis, systemic lupus erythematosus, primary systemic vasculitis and systemic Sjogren's syndrome following occupational styrene exposure.

Methods: We followed 72,467 styrene exposed workers of the Danish reinforced plastics industry in 1977-2012. We modelled styrene exposure from employment history, survey data and historical styrene exposure measurements. We identified cases in a national patient register, and investigated exposure response relations by cumulative styrene exposure for different exposure time windows adjusting for age, decade, educational level and a proxy for tobacco smoking.

Results: During 1,496,053 person-years, we identified 223 women and 453 men diagnosed with an autoimmune rheumatological disease, of which 75% were rheumatoid arthritis. We observed a statistically non-significantly increased risk of systemic sclerosis among women (IRR=2.64; 95% CI 0.53-13.26) and men (IRR=1.84; 95% CI 0.48-7.08). Indications of increased risk were also suggested for primary systemic vasculitis (IRR=2.35; 95 % CI 0.64-8.64) and rheumatoid arthritis (IRR=1.27; 95% CI 0.96-1.67) among men. Analyses of exposure time windows suggest a latency period for rheumatoid arteritis of about 15 years.

Conclusion: This study might indicate that styrene exposure is associated with the occurrence of systemic sclerosis among men and women, and primary systemic vasculitis and rheumatoid arthritis among men.

P17.01 Alexandra Golabek Christiansen

PREVENTION OF DERMATITIS IN EPOXY EXPOSED LAMINATION WORKERS PRODUCING WIND TURBINE BLADES: AN INTERVENTION STUDY USING FLUORESCENCE VISUALIZATION

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Background: The risk of sensitization and contact dermatitis among workers exposed to epoxy resin systems (ERS) is high despite extensive preventive efforts, probably because skin exposure is often left unrecognized. The main objective of this project is to prevent epoxy-related dermatitis and sensitization, caused by working with ERS, by fluorescence visualization of exposure

Methods: In cooperation with global manufacturers of wind turbines, we will randomize 350 lamination workers to either an intervention or a control group and compare the risk of dermatitis and sensitization. Skin exposure will be made visible by a fluorescent tracer added to the ERS. UVA light will illuminate the skin of head, neck, arms and hands, and the fluorescent areas will be recorded by a computer vision system. The intervention group will be shown the fluorescent areas on their skin, while the control group will not. The intervention takes place daily for a period of 1 month, 4 times during the 2-year follow-up period. All participants are patch tested, screened for dermatitis and atopy at start and end of follow-up or at end of employment. We will also assess potential determinants for ERS exposure, including working tasks and procedures.

Perspectives: If exposure visualization reduces the risk of dermatitis and sensitization to epoxy resin systems, this may have significant impact on the health of the many who work with these materials worldwide if such systems can be widely applied. Follow-up studies of persistent exposure to potent skin sensitizers with repeated patch testing have rarely been done, and the study may provide new insights into the epidemiology of allergic dermatitis.

P17.02 Mads Valdemar Anderson

TARGETED GENOME EDITING BY LENTIVIRAL PROTEIN TRANSDUCTION OF CRISPR-ASSOCIATED ENDONUCLEASES

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In the last few years, revolutionizing genome-editing technologies based on the CRISPR/Cas system have been adapted for therapeutic use in humans. Current findings support the use of precise genome surgery for future genetic treatments. In the wake of these discoveries, a new question has arisen: How can we ensure the safety of therapies exploiting delivery of endonucleases to cells? To achieve safe and efficient genetic repair, we recently developed lentivirus-derived nanoparticles (LNPs) as carriers

of endonucleases. Our hypothesis is that the lower nuclease levels and shorter activity obtained through LNP-directed delivery lead to safer genome editing.

In this project, we will develop LNPs as carriers of CRISPR-associated nucleases. We are currently investigating and optimizing strategies for delivery of both the Cas9 endonuclease and the single guide RNA molecule required for tailored genome editing. We focus on editing efficacy and the safety profile of LNP-derived systems compared to conventional CRISPR delivery methods.

P17.03   Randi Istrup   GENOME-WIDE ANALYSIS OF SITE-SPECIFIC HOTSPOTS IN CANCER
          Pedersen
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According to models of known mutational processes, site-specific hotspots of even just a few mutations become unlikely in large cancer genomic datasets. These hotspots may be cancer drivers and selected during cancer development or be a consequence of localized mutational processes. Here, we identify and characterize protein-coding and non-coding site-specific hotspots, using whole genome sequencing data from 2,179 patients from the Pan-Cancer Analysis of Whole Genomes project under ICGC/TCGA. Overall, we identify a total of 726,843 hotspots involving single nucleotide variants (SNVs), deletions and insertions. Only a small fraction of these hotspots overlap protein-coding genes or their regulatory elements. Nevertheless, we see an enrichment of SNV hotspots in protein-coding genes, promoters, 5' untranslated regions, splice-sites and enhancers compared to intergenic regions, which suggests that these hotspots may have a function in cancer development. Analysis of cancer allele fractions across hotspots in some regulatory elements of known cancer genes further support that some of these hotspots may affect cancer development. Among the hotspots in these regions, we point out single cases with additional evidence supporting their potential role in cancer development.

P17.04   Laura Barrett Ryø EXPLORING DOMINANT NEGATIVE DISEASE MECHANISMS IN HEREDITARY ANGIOEDEMA - FROM MAN TO MICE
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Hereditary angioedema (HAE) is a rare autosomal dominant disease characterized by non-predictable episodes of swelling of the deep dermis, submucosal and subcutaneous tissue. HAE is most frequently caused by inherited or de novo mutations in the SERPING1 gene,

encoding the serine protease inhibitor C1 inhibitor (C1INH), resulting in C1INH deficiency. The vast majority of the patients are heterozygotes carrying thus one unaffected allele, which should be expected to produce C1INH protein corresponding to 50% of the normal C1INH level. However, nearly all heterozygous patients present with C1INH plasma levels significantly below the expected 50% of normal, suggestive of the involvement of a dominant negative disease mechanism. Our recent findings have demonstrated that C1INH protein, encoded by a subset of disease-causing SERPING1 variants, induces C1INH aggregate formation leading to intracellular retention of the normal C1INH protein (Haslund, Ryø et al., in press, Journal of Clinical Investigation).

Using two different approaches, we are now working towards creating a mouse model of HAE mimicking the genetic composition in HAE patients. To study aggregate formation in vivo, we aim at utilizing vectors based on adeno-associated virus (AAV) to co-deliver SERPING1 variants to the livers of healthy mice. Moreover, to generate mice that are genetically engineered to carry dominant negative murine SERPING1 variants, we currently investigate aggregate formation among murine C1INH variants and plan on establishing genetically engineered mice by CRISPR/Cas-directed genome editing.

P17.05 Alexander Kristian Damm Grevsen

PLATELET FUNCTION IN PRETERM NEONATES

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Background: Preterm neonates have a higher bleeding tendency than term neonates. A reduced platelet function may be an essential contributor to this clinical challenge.

Aims: 1) To examine the development of platelet function in preterm neonates, 2) to compare platelet function among preterm neonates at term with platelet function in term neonates, and 3) to compare platelet function in peripheral venous and umbilical cord blood.

Methods: Inclusion of 25 preterm neonates at gestational age (GA) 32+0 to 34+0 weeks and 25 term neonates at GA 38+0 to 41+0 weeks is ongoing. Umbilical cord and venous blood is collected at birth and at GA 38+0 to 41+0 weeks in preterm neonates. Platelet function is investigated by analysis of platelet activation employing flow cytometry (Navios), platelet aggregation measured with impedance aggregometry (Rotem® platelet) and platelet count (Sysmex XN-9000™).

Preliminary results: Preterm neonates appear to have increased platelet activation, platelet aggregation and platelet count at term compared with at preterm birth and compared with term neonates. No significant difference was found between umbilical cord and venous blood in regard to platelet activation and platelet count, while platelet aggregation seemed increased in umbilical cord blood compared with venous blood.

Conclusions: In preterm neonates, the platelet function appears increased at term compared with at birth and compared with term neonates. No

substantial difference was found in platelet function in umbilical cord versus venous blood.

P17.06   Cagla Cömert   A CELL MODEL FOR MODELLING DIFFERENT LEVELS OF OXIDATIVE STRESS AND MITOCHONDRIAL DYSFUNCTION

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Besides providing the majority of ATP production in cells, mitochondria are also involved in many other cellular functions and central for cellular stress signaling. Mitochondrial dysfunction induces not only inherited mitochondrial disorders but also contributes to neurodegenerative diseases, cancer, diabetes, and metabolic syndrome.

Mitochondrial oxidative phosphorylation is the major contributor to the production of reactive oxidative species. As a molecular chaperone in the mitochondrial matrix space, the HSP60/HSP10 complex facilitates folding of many mitochondrial proteins and is thus an important factor for many mitochondrial functions. Impairment of the HSP60/HSP10 system causes oxidative stress and mitochondrial dysfunctions. To model different degrees of oxidative stress and mitochondrial dysfunction, we have generated HEK293-Flp-In cells with stable insertion of HSP60 cDNA carrying a dominant negative mutation. The dominant negative HSP60 mutant is incorporated into HSP60/HSP10 complexes and impairs its chaperone activity. Flp-In method provides a feasible way to regulate the expression levels of cDNA inserts. Using this system, different levels of oxidative stress and mitochondrial dysfunction challenges can be generated depending on the induction level of the mutant HSP60 cDNA insert. Here, we describe our system and its possible use in analyses of the effects of oxidative stress, and mitochondrial dysfunction.

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P17.07   Jacob Thyrsted Jensen   GENETIC ENGINEERING IN HUMAN EX VIVO LUNG MODEL

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In a constantly developing era of biomedical research, the need for models that mimic the morphology and physiology of human tissue is high. Using an already existing model of lung epithelium, we have generated a method that combines the novel gene editing strategy using the CRISPR/Cas9 system and the culturing of primary lung tissue cells. This method can be used to elaborate on the role of this natural immune barrier during different types of pulmonary diseases. The human airway epithelium (HAE) air-liquid interface (ALI) model uses primary cells isolated from healthy lung tissue from patients undergoing therapeutic

surgery. Following isolation of the epithelial cells from the pulmonary tissue, cells are dedifferentiated to basal cells. At this stage, we genetically manipulate cells with CRISPR/Cas9 using nucleofection. A guide RNA (gRNA) bound to the Cas9 endonuclease as a ribonucleoprotein (RNP) complex is electroporated into the basal cells followed by single cell sorting. Growing these cells on semipermeable membranes allow us to develop a genetically engineered fully differentiated lung epithelium. With this highly novel genetically engineered tissue model, we are able to investigate the lung physiopathology in a variety of different respiratory diseases, including influenza, cystic fibrosis, pneumonia and lung cancer.

P17.08   Jon Hagen Herskind

THE EFFECT OF LOW FREQUENCY FATIGUE ON DYNAMIC MUSCLE FUNCTION

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Background: Following fatiguing contractions, muscle contractile function is decreased more during low frequency stimulation compared to high frequency stimulation. This low frequency fatigue (LFF) is well established in isometric contraction models, but the effects on dynamic muscle function are less clear. Also, the degree of LFF induced by different contraction modes (concentric, isometric, eccentric) has not been compared.

Purpose: To investigate the effect of LFF induced by different types of fatiguing contractions on dynamic muscle function.

Methods: Wistar rat solues muscles were dissected out and incubated in Krebs-Ringer solution. The force-velocity relationship was assessed by a series of brief contractions elicited at 20 and 80 Hz before and 1 h after fatiguing contractions. Fatiguing protocols consisted of 3 concentric, isometric or eccentric contractions of 5 s duration at 60 Hz. Some experiments used caffeine to assess the importance of calcium release. Force-velocity data were fitted to the Hill equation.

Results: In the fatigued state, maximal force, velocity and power were more severely decreased at 20 Hz compared to 80 Hz of stimulation, regardless of fatiguing protocol. Isometric contractions caused a smaller decrease in maximal power compared to concentric contractions and tended to cause a smaller decrease compared to eccentric contractions. Caffeine alleviated the effects of LFF on all parameters.

Conclusion: LFF can be induced by different types of muscle contraction and affects both maximal force, velocity and power. These effects are mitigated by caffeine, indicating an impaired calcium release in LFF.

P17.09   Emil Aagaard Thomsen   EXPLORING R-CHOP RESISTANCE IN CANCEROUS B-CELLS BY FORWARD GENETIC CRISPR/CAS9-BASED SCREENING OF THE GENOME

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The intrinsic nature of malignancy provides cancer cells with an arsenal of potential mechanisms to develop resistance to immunotherapy and chemotherapy. Drug resistance is a continuous challenge in cancer treatment, and Diffuse Large B-cell Lymphoma (DLBCL), an aggressive B-cell cancer form characterized by extensive clinical and biological heterogeneity, is no exception. Despite good response towards the standard R-CHOP treatment, acquired or inherent drug tolerance often leads to relapsed or refractory disease.

By utilizing the unbiased power of genome-wide lentiviral CRISPR-based genetic screening, we aim at identifying the causative genes behind R-CHOP resistance. In three separate genetic screens, we have identified gene sets linked to resistance of cancerous B-cells to rituximab (R), vincristine (O), and Doxorubicin (H), respectively. Compiling the data sets obtained from these screens, we have identified overlapping genes that may potentially be involved in cross resistance. In addition to overlaps, we found among resistance-related genes a striking prevalence of genes related to B-cell receptor signaling. Using CRISPR-directed knockout, we have validated the impact of some of these genes on the resistance phenotype. The project provides new insight into molecular mechanisms leading to drug tolerance and paves the way for the use of genetic variants as biomarkers toward development of individualized cancer treatments.

P18.01   Anne Beck   FROM WAITING TO PREPARING: A QUALITATIVE FEASIBILITY STUDY OF CANCER PATIENTS' PERSPECTIVES ON PREHABILITATION

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Purpose: The aim of the study was to investigate cancer patients' perspectives on a predefined, home-based, multimodal prehabilitation programme. Knowledge about patients' perspectives on prehabilitation is sparse. A better understanding could contribute to patient-centred prehabilitation programmes that enhance functional capacity and are considered relevant by patients, with a view to improving adherence.

Methods: The feasibility study was developed in accordance with the Complex Interventions Framework. 15 patients with peritoneal carcino-matosis of colorectal or ovarian origin undergoing complete cytoreductive surgery (CRS), with or without hyperthermic intraperitoneal chemotherapy (HIPEC), participated in semi-structured interviews. Malterud's principles of systematic text condensation were used to analyse the data.

Findings: Patients had a positive attitude towards preparation, primarily because of the opportunity to influence own recovery, but also because it could distract their attention from negative thoughts and because they could gain support. However, they would not follow a programme unconditionally, and significant barriers to adherence were identified. These included lack of belief, everyday life, preferences, and restrictions.

Conclusion: Barriers to adherence need to be taken into consideration in the development of future programmes, if they are to be considered relevant by patients and with a view to maximising adherence. The findings also demonstrate the complexity of developing prehabilitation programmes that not only enhance functional capacity, but are also experienced as relevant and that align with patients' everyday lives.

P18.02   Christina Søndergaard Duvald

THE CHINCHILLA AS A NOVEL ANIMAL MODEL OF GESTATIONAL DIABETES

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Background: Gestational diabetes occurs in 5% of all pregnancies. The disease poses important health implications for both mother and child. Several animal models exist in this field, but with significant limitations. Consequently, we want to introduce the pregnant chinchilla as a novel animal model of gestational diabetes. The chinchilla is excelled for various reasons; it gives birth to one or two cubs, is pregnant for 115 days and has a histological similar placenta barrier as compared with humans. Since the chinchilla has never been used in diabetic studies, we aimed to show that it is possible to make it diabetic before making a gestational model.

Methods: Twelve chinchillas were included in the study, six of which received high fructose diet to induce diabetes and six received control diets. Blood glucose was monitored using the Abbott Libre Freestyle glucometer. After 19 weeks, the animals were euthanized, and organs and blood withdrawn for analysis.

Results: The non-fasting plasma glucose levels in chinchillas fed with high fructose diet were 19.3 ± 6.9 mmol/l compared to controls 11.1 ± 2.2 mmol/l, p=0.056. Furthermore, DXA scans showed significant higher body fat percentage among fructose animals, p=0.043, compared to controls. HBA1C was, however, not affected in any of the groups.

Conclusion: We have proven it possible to induce high blood glucose levels in the chinchilla by using high fructose feed. Because of the low sample size, the blood glucose levels were, however, not statistically significant between groups. In spite of this, we are positive that the chinchilla is a promising future animal model of gestational diabetes.

P18.03   Julie Jacoby   FAMILY NURSING - A WAY TO IMPROVE FAMILY FUNCTION AND QUALITY
          Petersen   OF LIFE?

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Background: Patients aged ≥ 70 years who have undergone major abdominal surgery have significantly higher risk of mortality and post-operative complications. Their level of function often decreases during admission, and they find it difficult to regain the ability to manage normal day-to-day tasks.

Aim: To improve the physical and emotional strength related to the course of an illness and increase the quality of life in both patients and their families.

Methods: A prospective, multi-methods, cross-sectorial study in three parts.

1) A total of 16 interviews with previously admitted patients and their families one month post discharge.

2) Two focus group interviews with nurses from the hospital and district nurses from three municipalities.

3) A cross-sectorial feasibility study with Family Strength Oriented Therapeutic Conversations. A total of 60 patients and their families will be randomized to either an intervention group or a control group. The intervention will take place at the Gastro Unit at Hvidovre Hospital, as well as in three municipalities.

Provisional results from sub-study 1 indicate that previously admitted patients still suffer from severe fatigue and reduced psychical function, which has a negative impact on their emotional wellbeing and social lives. Both patients and families experience a gap in the transition between hospital and municipality, which causes uncertainty and worries.

Results from sub-study 2 show that nurses from both sectors request a closer collaboration and more knowledge sharing across sectors to ensure more continuity in care for patients and families. Both sub-studies clearly indicate the relevance of family nursing interventions in a cross-sectorial study.

P18.04   Sigurd Beier Sloth COURSE TO CLINIC TRANSFER BETWEEN SIMULATION-BASED AND OR-
                             BASED SURGICAL TRAINING

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For simulation-based training to be effective, it is a prerequisite that skills acquired in the simulated environment transfer to the operating room (OR). The study aims to investigate surgical trainees' ability to apply the

skills acquired in a simulated training environment in the OR. We want to investigate the transfer possibilities of proficiency-based simulation training in laparoscopy conducted in two different ways: instructor-regulated simulation training (IRST) and self-regulated simulation training (SRST). We include 42 first-year trainees in the specialties Surgery, Urology and Gynaecology in postgraduate training in the North Denmark Region. The trainees will be randomized to either IRST or SRST. Laparoscopic skills are tested before, immediately after, and again six months after the training. Laparoscopic procedures performed by the trainees are video recorded and rated by independent observers blinded to the trainees training status. We use an online platform to collect data on the trainees' involvement in surgical procedures parallel to their allocated training intervention. Questionnaires assessing self-efficacy and educational environment are distributed to the trainees. We conduct a series of semi-structured interviews with informants from the two study groups. Interviews will be thematically analysed to explore different influences contributing to or hindering transfer of training. The study examines surgical education from a clinical and didactic point of view. Knowledge on factors hindering and facilitating transfer of training can help increase the outcome of surgical training, resulting in higher surgical expertise and increased patient safety.

P18.05   Nanna Holt Jessen

INVESTIGATIONS IN THE YEAR PRECEDING A DIAGNOSIS OF AN ABDOMINAL CANCER

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Background: More than 11,500 abdominal cancers are diagnosed each year in Denmark, and abdominal cancers constitute one-third of all cancers. Abdominal symptoms are a common reason for patients to contact primary care, and the symptoms overlap much between different cancer sites. Nevertheless, the positive predictive values of abdominal symptoms are low in general practice. This challenges the diagnostic work-up and increases the risk of unnecessary investigations.

Aim: To explore the healthcare use for different cancer sites in the year preceding a diagnosis of abdominal cancer and to investigate potential overlap in investigations for different cancer sites.

Methods: A national cohort study with consecutive first-time abdominal cancer patients aged ≥ 18 years diagnosed in 2014-2016 was conducted. The cancer patients were identified in the Danish National Cancer Register. Data on prediagnostic investigations were obtained from Danish national registers and linked to sociodemographic variables at Statistics Denmark.

Results: Data are currently being processed. Descriptive statistics are completed in January 2019. Approximately 30,000 patients diagnosed with abdominal cancer will be included. The data output will include

proportions of abdominal investigations during the year preceding a diagnosis of abdominal cancer for selected cancer sites.

Conclusion: The project will provide new insight into the investigations preceding an abdominal cancer diagnosis, including the number of and potential overlap between abdominal cancer sites. The results may help optimise the diagnostic strategies for patients presenting in general practice with abdominal symptoms and may ultimately provide more timely diagnosis.

P18.06   Helene Mathilde   CLINICAL EVALUATION AND TREATMENT OF CHRONIC DIARRHOEA
         Larsen   FOLLOWING CANCER IN THE COLON AND PELVIC ORGANS

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Background: Chronic gastrointestinal symptoms are common among patients surviving treatment for cancer in the bowel or pelvic organs. It is unknown to what degree patients will benefit from evaluation by a gastro-enterologist. The aim of the present study was to present the results of standard clinical evaluation and treatment of chronic diarrhoea among patients surviving cancer in the colon and pelvic organs.

Methods: All patients referred to our department of gastroenterology between May 2016 and June 2018 with chronic diarrhoea after treatment for cancer in the colon or pelvic organs were prospectively evaluated.

Results: In total, 60 patients were included. The patients were treated for cancer in the right colon (n=31), sigmoid colon (n=1), rectum (n=14), anal canal (n=4), cervix uteri (n=5), corpus uteri (n=2), ovary (n=2), and prostate (n=1). The median time from cancer treatment to referral was 5.5 (range 1-36) years. Symptoms mainly included frequent bowel movements (65%), loose stools (87%), urgency for defecation (57%), and faecal incontinence (50%). Bile acid malabsorption was present in 35 patients, and small intestinal bacterial overgrowth was detected in 29. Treatment included bile acid sequestrants (n=35), antibiotics (n=30), loperamide (n=19), and dietary intervention (n=17). Major improvement in bowel symptoms was reported by 19 (32%) patients, while another 24 (40%) reported some improvement.

Conclusion: Most patients with chronic diarrhoea following cancer in the colon or pelvic organs will benefit from expert clinical evaluation and targeted treatment.

P18.07   Rikke Buus Bøje   STRUCTUAL CONTRADICTIONS IN NURSES' COLLABORATION IN
                           TRANSITIONS OF OLDER ADULTS BETWEEN HOSPITAL AND PRIMARY
                           CARE

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Purpose: As a sub-study in a PhD project, the purpose was to identify structural contradictions in nurses' collaboration on older adults' transitions between hospital and primary care.

Background: The PhD study investigates how to develop nurses' collaborative learning across hospital and primary care to lead to changes in clinical practice. The collaboration is challenged by disturbances due to constant changes in tasks, procedures and organization of healthcare, and by complexity in patient trajectories across healthcare sectors. Older adults are particularly vulnerable in transitions due to multi-morbidity and need for transitional care. Knowledge about contradictions in patient transitions can lead to identification of potential areas of learning and development.

Method: The design was focused ethnography. Activity theory (Cultural Historical Activity Theory (CHAT)) was used as a theoretical framework.

Data was obtained from focus groups with nurses (n=6), qualitative interviews with nurse leaders (n=4), medical doctors (n=2), quality advisors (n=2), nurse at a nursing central (n=1), field observations (n=10 days), informal interviews and observations of patient trajectory (n=3).

A deductive data analysis approach was used to identify dilemmas, conflicts, critical conflicts and double binds in order to uncover contradictions and potential areas of development and learning.

Results: The results represent a mapping of contradictions between actors, rules and laws, procedures, division of labor and patients in nurses' collaboration.

Perspectives: The results will be used in the next sub-study as stimuli in an intervention to develop nurses' learning and development.

P18.08   Helle Kristensen   SYSTEMATIC REVIEW OF THE IMPACT OF SOCIOECONOMIC, DEMOGRAPHIC AND RELIGIOUS FACTORS ON QUALITY OF LIFE IN OSTOMIZED COLORECTAL CANCER SURVIVORS

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Background: The formation of a fecal stoma may be necessary to obtain surgical radicality in colorectal cancer (CRC) patients, but it will substantially impact the health-related quality of life (HRQoL) in about 20% of cases. Little is known about patient-related risk factors for reduced HRQoL in ostomates, and we decided to review the literature on this.

Methodology: PubMed, Embase, CINAHL and PsycINFO databases were systematically searched. Two reviewers extracted and quality assessed eligible publications independently. Studies assessing HRQoL with a validated questionnaire at least 6 months after surgery for CRC were

included if statistical analysis was performed on the impact of socioeconomic, demographic and/or religious factors on HRQoL.

Results: Included studies were predominantly small cross-sectional cohorts. Several studies found that HRQoL was lower in women than in men. Age showed equivocal results as some studies found that younger patients had lower HRQoL than older patients, and others found no difference between age groups. Most studies found that socioeconomic factors did not affect HRQoL, while one study found that lower education correlated with reduced HRQoL. How these factors were categorized varied widely.

Conclusions: The impact of socioeconomic, demographic and religious factors on HRQoL in ostomates has only been sporadically investigated in the past. To our knowledge, this is the first review of the literature on this topic. We found greater negative impact of HRQoL in women and in younger individuals, but conclusions regarding other factors were difficult due to varying results and categorization, which impeded comparisons.

P18.09   Ingrid Villadsen   EXPERIENCES OF LIVING WITH END-STAGE RENAL DISEASE PRIOR TO A
          Kristensen   KIDNEY TRANSPLANTATION

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Background: Renal transplantation is a well-established treatment for end-stage renal disease. However, patients experience challenging existential aspects as well as physical complications.

Aim: The aim of this study is to investigate the experiences of patients living with end-stage renal disease prior to a kidney transplantation with a living donor.

Method: The study has a qualitative approach inspired by Ricoeur. Fourteen interviews with patients living with end-stage renal disease are conducted 7-14 days before a planned kidney transplantation with a living donor. Analysis and interpretation are based on Ricoeur's theory of interpretation.

Results: Patients with end-stage renal disease experience living with an invisible condition with no outward signs of their illness. The perceptions of the body are divided into different subjective feelings in accordance with their feelings of illness. At the same time, the patients are objectifying their body in numbers regarding the function of the kidneys. Receiving a kidney from a living donor is perceived as the greatest gift in life, but the patients are simultaneously worrying about the consequences for the donor. Furthermore, the patients are facing the unknown prior to a kidney transplantation, but they still hope to get their life back.

Perspectives: The results increase the insights into individuals' experiences of living with end-stage renal disease. Hereby, the results articulate the need for support from health professionals prior to a kidney transplantation. The interviews are repeated with the same patients approx. six months after the kidney transplantation.

P18.10 Sif Sund Blandfort

CAN SINGLE-BED ROOMS PREVENT DELIRIUM IN GERIATRIC PATIENTS?

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Introduction: Few studies have investigated private rooms and the risk of delirium. In March 2017, our Geriatric Department was moved from old hospital buildings with multiple-bed rooms (old ward) to a new hospital with single-bed rooms (new ward), with no changes regarding uptake area, staff and admission criteria. The aim of the study was to investigate the risk of delirium among patients in single-bed rooms compared to multiple-bed rooms.

Methods: An observational prospective study included 1014 admitted patients (aged ≥75 years) between September 15, 2016 and March 19, 2017 to the old ward and between March 20, 2017 and December 19, 2017 to the new ward. The population included neurological, orthopedic and medical patients admitted to geriatric wards. Exclusion criteria were terminal illness, somnolence and inability to communicate in Danish. Delirium was assessed by by a trained nursing staff every morning and evening using the Confusion Assessment Method (CAM).

Results: At admission, 105 patients had delirium. No significant difference was seen between the old and the new ward. After 12 days, the cumulated incidence of delirium was 16% in the new ward compared to 24% in the old ward ($p<0.02$, Cox regression).

Conclusion: We found evidence that the risk of delirium is reduced in single-bed rooms compared to multiple-bed rooms in geriatric departments.

P19.01 Uwe Martin Pommerich

DEFINING THE MINIMAL CLINICALLY RELEVANT CHANGE OF THE SIX SPOT STEP TEST IN PERSONS WITH MULTIPLE SCLEROSIS

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Background: Multiple sclerosis (MS) is a chronic degenerative disease manifested in the central nervous system (CNS). Progressive heterogenous functional impairment and disability is frequently observed in persons with multiple sclerosis (pwMS) as a result of CNS lesions and demyelination. Walking ability and hand function have previously been identified among the most valuable bodily functions by pwMS, and preservation of both relate to independence and autonomous gainful occupation and improved health-related quality of life. Appropriate tests of walking and arm function are crucial when evaluating and interpreting effects of interventions. Two frequently used tests of walking and arm function are the Six Spot Step Test (SSST) and the Nine-Hole Peg Test (NHPT).

Nonetheless, the minimal important change (MIC) are not known for these two outcomes.

Objective: To establish the minimal important change of the SSST and the NHPT in a sample of Danish pwMS.

Methods: The SSST and the NHPT were performed before and after four weeks of individualised multidisciplinary rehabilitation by 142 pwMS. Responsiveness of the SSST and NHPT will be determined based on anchor- and distribution-based methods. Differences in the responses from baseline to post-intervention on selected items of the Multiple Sclerosis Impact Scale-29 will be used as external criteria to establish the MIC and the smallest real change (SRC) for the tests.

Results: Data analysis is ongoing, and preliminary results will be presented at the Graduate School of Health's PhD Day 2019.

P19.02   Jan Lykke Scheel Thomsen

FIXED MUSCULAR DEFICITS IN MYASTHENIA GRAVIS

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Background: Myasthenia Gravis (MG) is a rare autoimmune, neurological disease caused by autoantibodies directed against components of the neuromuscular junction (NMJ) and complement-mediated destruction of the NJM. MG is hallmarked by muscle weakness and increased muscle fatigability. However, some patients have fixed muscular deficits despite immunosuppressive treatment. The cause remains unsettled; destruction of the neuromuscular junction in combination with atrophy or intra-muscular changes may play a role.

Aim: To examine and characterize fixed muscle weakness in relation to muscular structure as determined by magnetic resonance imaging (MRI).

Methods/Population: Approximately 40 patients with generalized MG and any degree of residual extremity symptoms on knee extensors. Knee extensor strength is measured using Biodex System 3 Dynamometer. True maximal strength will be secured by use of the twitch-stimulation technique. Muscle MRI using T2 and Diffusion Tensor Imaging will be used to determine muscle cross-section area and muscular quality (strength per cross-sectional area).

Expected results: We expect that fixed muscle weakness is caused by muscular atrophy combined with decreased voluntary contraction, but is independent of muscle quality.

P19.03   Charlotte Maria Jensen

EXPERIENCES AND PERSPECTIVES OF GOAL SETTING IN SPINAL CORD INJURY REHABILITATION: SYSTEMATIC REVIEW OF QUALITATIVE STUDIES

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Objective: The aim of this review was to synthesize qualitative research evidence exploring the experiences and perspectives of persons with spinal cord injury (SCI), their relatives and health professionals on goal setting within SCI rehabilitation.

Background: Goal setting is considered an essential part of SCI rehabilitation and has been associated with growing uncertainty regarding its application in clinical practice. It helps to identify the person's needs, values and expectations for the rehabilitation. No previous reviews have explored experiences and perspectives on goal setting in SCI rehabilitation. It is important to gather this knowledge in order to identify gaps in relation to goal setting in research and current clinical practice.

Method: The review was guided by a pre-defined and registered protocol at the International Prospective of Systematic Reviews, PROSPERO database [CRD42018110408]. A systematic search was conducted for original peer-reviewed papers printed in English in the PubMed, Embase, CINAHL and PsycINFO databases from date of conception to September 2018. "Spinal Cord Injury" [AND] "Goal" [AND] "Rehabilitation" were used as key words. Papers were selected by pre-defined inclusion criteria and subsequently critically appraised using the Critical Appraisal Skills Programme (CASP) for qualitative checklist. The analysis was inspired by the inductive qualitative research strategy Interpretive Description.

Result: Out of 426 identified studies, five studies met the inclusion criteria. The analysis is ongoing, and preliminary results will be presented on the PhD Day.

P19.04   Angela Pärn   THE ROLE OF PCSK9 IN BRAIN DEVELOPMENT AND BEHAVIOR

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PCSK9 induces lysosomal degradation of lipoprotein receptors and decreases the uptake of cholesterol-rich LDL particles from the circulation. The main target of PCSK9 is the hepatic LDL receptor, but studies suggest that it also targets related lipoprotein receptors VLDLR and ApoER2. In adults, PCSK9 is produced by the liver, while it is highly and transiently expressed in the developing brain, where its function remains unknown. Notably, the PCSK9 expression pattern here has a significant overlap with VLDLR, ApoER2 and Dab1, which are all components of the Reelin pathway. During development of the brain, Reelin regulates neuronal migration and neurite outgrowth. Impaired signaling of this pathway results in a characteristic phenotype, where neurons fail to organize themselves into distinct layers of the cortical plate.

Our preliminary results from in utero electroporation (IUE) experiments suggest that PCSK9 overexpression arrests neuronal migration, and we speculate that this is caused by degradation of the Reelin signaling receptors VLDLR and ApoER2. In addition, we have data indicating that PCSK9 affects the survival of primary cultures of murine cortical neurons. To further understand the role of PCSK9 in the brain, we have performed behavioral testing using a PCSK9 deficient mouse model. The PCSK9 KO mice have normal memory and spatial learning, but they seem to have a

mild anxiety-like phenotype. In conclusion, the absence of PCSK9 has no major effects on behavior. However, increased levels of PCSK9 affect neuronal survival and migration. Further experiments will show whether high PCSK9 activity during development affects lipoprotein receptor levels and mouse behavior.

P19.05   Morten Riemenschneider   AN OVERLOOKED "WINDOW OF OPPORTUNITY" IN MULTIPLE SCLEROSIS EXERCISE THERAPY - THE MS EARLY EXERCISE STUDY

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Background: Exercise therapy is one of the most promising rehabilitative strategies in multiple sclerosis (MS); a chronic autoimmune disease in the central nervous system. Furthermore, recent research indicates direct disease modifying effects of exercise. Medical disease modifying treatment have shown superior effects of early treatment initiation. However, no studies have reviewed or investigated the impact of timing of exercise therapy initiation with MS.

Aim: To review the existing literature on the timing of exercise therapy initiation, and to outline the design of a randomized intervention study early in the disease course of patients with MS.

Methods: For this topical review, a literature search in the databases Medline and Embase (search terms: "exercise" OR "exercise therapy" AND "multiple sclerosis") was conducted. Pilot studies and studies without sufficient information on disease duration was excluded. Mean (95% CI) disease duration was calculated for the intervention group in each study.

Results: 65 relevant studies were located. Mean (95% CI) disease duration of pwMS in exercise intervention groups ranged from 4.9 (3.5-6.3) years to 16.6 (7.5-25.7) years, clearly showing an uninvestigated "window of opportunity" for exercise therapy early in the disease course of MS.

Discussion: If exercise therapy could serve as a potential disease modifier, and there seems to be consensus on a favorable "window of opportunity" early in the disease course of MS from medical trials, why not initiate exercise therapy early in the disease course as well? Accordingly, the design of a randomized MS exercise study addressing this "window of opportunity" will be presented.

P19.06   Victor Manuel Pando Naude   BRAIN FUNCTIONAL CONNECTIVITY CORRELATES OF MUSIC-INDUCED ANALGESIA IN FIBROMYALGIA

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Listening to self-chosen, pleasant and relaxing music reduces pain in fibromyalgia (FM), a chronic central pain condition characterized by increased sensitivity in skin and musculoskeletal system, which is associated with sleep disorders, stiffness, fatigue, anxiety and depression. We wished to investigate the neural correlates of music-induced analgesia (MIA) in FM patients by means of behavioral measures and resting-state functional magnetic resonance imaging (rs-fMRI). We studied 20 FM patients and 20 matched healthy controls (HC) acquiring rs-fMRI with a 3T MRI scanner, and pain data before and after two 5-min auditory conditions were obtained: music and pink noise (control condition). We performed resting state functional connectivity (rs-FC) seed-based correlation analyses (SCA) using pain-related regions-of-interest (ROIs) to determine the effects before and after the music intervention in FM and HC, and its correlation with pain reports. We found significant baseline differences between FM and HC, showing a disrupted rs-FC of pain-related ROIs in FM. Both groups showed changes in rs-FC in several ROIs after the music condition between different areas, which were left lateralized in FM and right lateralized in HC. FM patients reported MIA that was significantly correlated with rs-FC decrease between the angular gyrus, posterior cingulate cortex and precuneus, and rs-FC increase between amygdala and middle frontal gyrus. MIA in FM correlated with rs-FC changes between important areas of the default mode network (DMN) processing emotion, memory retrieval, and auditory attention. We, therefore, suggest cognitive and emotional modulation of pain in FM after listening to music.

P19.07   Søren Krogh Jensen

THE EFFECTS OF SYSTEMATIC REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION IN REHABILITATION AFTER INCOMPLETE SPINAL CORD INJURY: NEUROMUSCULAR ADAPTATIONS AND RECOVERY OF LOWER LIMB MUSCLE STRENGTH

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A spinal cord injury (SCI) is among the worst survivable catastrophes experienced by a human being. It leads to significant restrictions of opportunities and quality of life. In addition to a reduced ability to move and feel, individuals with SCI often suffer from a wide range of disabling sequelae such as pain, spasticity, autonomic dysfunction and lifestyle diseases. Following incomplete SCI, one of the major goals is regaining the ability to walk. Here, a primary determinant is lower extremity motor function. The technique "repetitive, transcranial magnetic stimulation" (rTMS) may prove successful in improving SCI patients' motor function and gait, while reducing the extent of comorbidities. The method, in which a wire coil is placed on the scalp and a train of magnetic impulses excites a targeted area of the brain, is safe and harmless. The present study explores the potential beneficial effects of rTMS during re-training of leg motor function following SCI and examines the underlying neuromuscular processes. In an RCT interventional study, an active rTMS group (15 SCI patients) will undergo 8 weeks of systematic rTMS in addition to resistance training of the lower limbs, while an SCI control group (n=15) will receive sham rTMS + resistance training in the same period of time. At baseline

and after 8 weeks of training, an extensive test battery will measure adaptive changes in: ambulatory function, muscle function of the lower limbs, neuropathic pain and spasticity. It is hypothesized that the rTMS group will exhibit i) significantly larger gains in motor function and ii) reduced pain sensations and spasticity as compared with the sham group following the intervention.

P19.08   Lotte Hardbo Larsen

UNDERSTANDING THE MECHANISMS OF CRITICAL ILLNESS MYOPATHY BY USE OF A NOVEL ELECTROPHYSIOLOGICAL METHOD - MUSCLE VELOCITY RECOVERY CYCLES (MVRCS)

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Background: Critical illness myopathy (CIM) is characterized by diffuse muscle weakness in critically ill patients and causes delayed recovery and prolonged hospitalisation. Muscle membrane depolarization has been proposed as an underlying mechanism for CIM. Muscle Velocity Recovery Cycles (MVRCs) recordings provide information about muscle membrane properties. We aim to investigate the utility of MVRCs in the early diagnosis of CIM, which may also contribute to a better understanding of the pathophysiology.

Methods: The study will enrol 2 groups of 20 patients aged ≥18 years: 1) patients with sepsis at intensive care units and 2) patients with chronic renal failure and uremia, and 30 sex- and aged-matched healthy controls. All subjects are to undergo neurological examinations, electromyography, nerve conduction studies and MVRCs. Blood tests will be taken in all patients. Patients with sepsis will be examined every week in 3 weeks. The presence of probable CIM will be determined on the 4th examination.

Results: Data will be collected from 1 November 2018 to 31 July 2019. The primary outcomes will be MVRC parameters which will be compared between patients and healthy controls using parametric or non-parametric tests. Furthermore, MVRC parameters will be correlated to blood sample results.

Conclusion: Our study is expected to provide a better understanding of the underlying mechanism of CIM and contribute to the evaluation of MVRCs as a possible future tool for early and more accurate diagnosis of CIM.

P19.09   Mustafa Aykut   CLINICAL VALIDATION OF CRITERIA FOR IDENTIFICATION OF
          Kural   EPILEPTIFORM EEG DISCHARGES IN SENSOR SPACE AND SOURCE SPACE

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Background: Presence of Epileptiform Discharges (ED) in EEG recordings
are highly associated with epilepsy diagnosis. In clinical practice, EDs are
visually identified by experts. The International Federation of Clinical
Neurophysiology (IFCN) suggested 6 criteria in EEG sensor space, so that
presence of at least 4 of them defines a waveform as ED. A novel method
of identifying EDs in sensor space has recently been proposed.

Objectives: To assess inter-rater agreement (IRA) and accuracy of
identifying spikes in sensor space (using the IFCN criteria at different
thresholds) and in source space.

Methods: EEG samples from 100 consecutive patients with epilepsy and
non-epileptic paroxysmal events were reviewed separately in sensor
space and source space in different randomized order by 7 raters, who
scored the presence/absence of each IFCN criterion in sensor space and
presence/absence of EDs in source space. Accuracy was determined for
each rater and for the majority decisions for each sample.

Results: IRA was moderate both in sensor space and in source space
(k: 0.49 - 0.60). In sensor space, highest accuracy (91%) and highest
sensitivity (96%) was achieved using a threshold of 4 criteria. However, this
gave a specificity that was lower than acceptable for EEG (85%). Using a
threshold of 5 criteria in sensor space, a specificity of 96% was achieved at
a sensitivity of 83% and an accuracy of 89%. Results in source space were
identical to using threshold of 5 criteria in sensor space.

Conclusion: Using a threshold of 5 IFCN criteria in sensor space and source
space yields, a high specificity and an acceptable sensitivity for
identifying EDs were achieved.

P19.10   Signe Fruekilde   CONSIDERATIONS WHEN STUDYING NEUROVASCULAR COUPLING IN
                            AWAKE UNANESTHETIZED MICE

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Neuronal activity requires energy and a supply of nutrients, which is met
by an increase in cerebral blood volume (CBV), a phenomenon called
neurovascular coupling. It is hypothesized that faults in this response to
demands is the initiator for various brain diseases, and it is therefore of
great interest to obtain a better understanding of the underlying
mechanisms of neurovascular coupling. With new optical tools, it is
possible to perform precise in vivo measurements of the vascular response
in mice without the masking of anesthesia.

Installing a cranial window over the somatosensory cortex enables
recording the intrinsic signal from hemoglobin and calculating the

increase in blood volume in response to an air-puff stimulation of the whiskers.

The 20 recoding cycles consisting of 8 sec baseline, 2 sec stimulation, and 20 sec post-stimulation, will be averaged to show the CBV changes throughout the 30 second epoch.

Since the mice are fully awake throughout this test, it can be speculated that the mice will "learn" the task and thereby anticipate the air-puffs every 30 sec. If so, the mere anticipation of a stimulus could potentially increase the blood supply to the area.

This study aims to test this with a new stimulation series, where, randomly, 5 of the 20 cycles will not deliver the air-puff stimulation.

Preliminary data indicates that CBV will change even without stimulation. This adds a new variable to consider when working with awake animals. Depending on the scientific question, this anticipation could certainly affect the interpretation of the results of repeated measures. Thus, the study design must be carefully chosen to avoid the anticipation effect.

P20.01   Mathias Alstrup   LYMPHATIC FUNCTION AND MORPHOLOGY IN WOMEN WHO HAVE UNDERGONE BREAST CANCER TREATMENT

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Background: Breast cancer treatment, involving axillary surgery and radiation therapy, can partially obstruct lymph outflow from the arm, chronically raising the lymphatic smooth muscle afterload. This may lead to lymphatic pump failure and could explain features of breast cancer treatment-related lymphedema (BCRL), such as its delayed onset. Studies have shown a change in contractile function of the lymphatic vessels and recognized distinct lymphatic patterns in women diagnosed with BCRL, but no studies have investigated if these changes occur before clinical edema is detectable.

Methods: The morphological state of the lymphatic vessels is described using T2-weighted non-contrast MRI and Near-Infrared Fluorescence (NIRF) imaging. The contractile function of the lymphatic vessels is assessed through NIRF imaging, and the end-points consist of contraction frequency, velocity and pumping pressure. The study population will be 28 breast cancer treated patients. Both the treated and the non-treated arm are examined, and thus the patients serve as their own controls.

Results: Pending.

Perspectives: Studies have shown that if BCRL treatment is implemented before the recognition of clinical BCRL, the incidence of BCRL can be significantly reduced. If changes can be shown in contractile function and/or morphology of the lymphatic vessels in patients destined to develop BCRL, assessment of contractile function and/or the morphological changes can be used as a tool for grading the risk of developing BCRL after treatment. BCRL treatment could be offered to patients at risk of developing BCRL prior to the recognition of clinical edema and could thereby reduce the incidence of BCRL.

P20.02 Aska Drljevic-Nielsen

RESPONSE EVALUATION CRITERIA IN METASTATIC RENAL CELL CARCINOMA: IMPROVED ASSESSMENT OF RESPONSE AND PROGRESSION BY SPECTRAL CT

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The incidence of renal cancer in Denmark is approximatly 900 new cases per year. Untreated, the 5-year survival rate for metastatic renal cancer (mRCC) is 2%. Development of angiogenesis inhibitors (AI) and check-point immunotherapy (CPI) has improved the survival.

Treatment efficacy is evaluated by CT scans using Response Evaluation Criteria in Solid Tumors (RECIST) 1.1. However, RECIST 1.1 only relies on size, which makes it difficult to characterize progression at the right time. Therefore, approximately 50% of the patients are 'lost' to further treatment at the time of progression and die.

Functional parameters from dynamic contrast-enhanced CT (DCE-CT) have shown to correlate with outcome in patient with mRCC treated with AI & CPI, but DCE-CT can only scan over a maximum range of 8 cm and requires a high dose of radiation and constrast media. A new functional imaging modality, spectral CT, has the advantage of being a wholebody scan and does not require more radiation and contrast media than a routine CT.

We aim to evaluate functional imaging parameters using Spectral CT to detect treatment failure earlier, or more accurate, than routine CT in a prospective study in patients with mRCC. Patients are scanned at baseline, after 4 & 11 weeks of treatment and then every 12 weeks. So far, 49 patients have been included. This study has the potential to help us develop a new set of response evaluation criteria for functional imaging,- functional RECIST, which will give a more precise assessment of treatment effect in patients with mRCC treated with AI and CPI.

P20.03 Morten Krogh Herlin

MULTI-OMICS ANALYSIS OF PEDIATRIC ACUTE MYELOID LEUKEMIA, NOT OTHERWISE SPECIFIED BY THE CURRENT WHO CLASSIFICATION

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Acute myeloid leukemia (AML) accounts for 15% of leukemias in children and has a survival rate of 70%. Unfortunately, the high risk of adverse effects hinders further intensification in current treatment protocols. Genetic studies of leukemogenesis are pivotal in the search for new

therapies in order to improve survival and lower toxicity. AML is classified according to WHO by recurrent genetic aberrations of prognostic relevance. However, as the WHO classification is largely based on adult studies, the applicability in childhood AML has been questioned, and the knowledge of molecular genetics in childhood AML remains sparse.

This study aims to investigate the molecular biology of the large heterogeneous group of AML, not otherwise specified (NOS), which includes all patients with none of the recurrent genetic aberrations included in the WHO classification. We will use viable bone marrow (BM) cells from about 50 pediatric patients with AML, NOS, from the Nordic AML biobank in Uppsala and a local biobank at Karolinska Institutet, Stockholm. Extractions of nucleotides and protein are performed using Qiagen AllPrep, and cultures of BM stromal cells are established in order to obtain germline DNA from the samples. Hereafter, we will conduct a multi-level analysis including whole genome sequencing of paired leukemia-normal samples supplied by studies of the methylome, transcriptome and proteome of the leukemia cells.

We believe that the study will provide new insight into the role of molecular genetics in childhood AML development. Ultimately, we hope to find new pathogenic genes and pathways that may serve as potential therapeutic targets in the future.

P20.04 Marianne Agerlund Petersen

15-COLOUR PANEL FOR CHARACTERIZING LEUKEMIC STEM CELLS IN CHILDREN WITH ACUTE MYELOID LEUKAEMIA

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In acute myeloid leukaemia (AML), the leukemic stem cell compartment constitutes a minor fraction of the bulk leukaemia. However, this rare cell subset can have major impact on prognosis, being a source for relapse disease which is associated with a poor prognosis. Leukemic stem cells (LSCs) are predominantly found within the CD34+CD38- cell compartment in bone marrow and differ from normal haematopoietic stem cells by an aberrant immunophenotype. The frequency of aberrant marker positive CD34+CD38- LSCs has been associated with an inferior outcome in adults with AML. Additionally, knowledge on abnormally expressed antigens on cancer stem cells is increasingly relevant due to the continuous expansion of targeted therapies directed against such antigens. Such treatment regimens ideally eradicate malignant stem cells, whilst sparing healthy stem cells needed for reconstitution of bone marrow function.

In this study, we designed a 15-colour panel for detecting multiple aberrant markers simultaneously on leukemic stem cells using flow cytometry in 39 paediatric AML patients. The markers have been selected from prior studies on LSCs in adult AML patients and include the antigens CLEC12A, TIM3, IL1RAP, CD93, CD99, CD25, CD123, CD45RA and Bcl2. We will evaluate the prognostic impact of the LSC frequency and immunophenotype at the time of diagnosis and relapse. By compiling all

markers in one panel, we achieve increased information on this rare cell subset in a single tube. Hereby, we may be able to indicate which markers are less suitable as targets for treatment in paediatric AML patients.

P20.05   Solveig Kärk   MRI WITH DIFFUSION WEIGHTED IMAGING (DWI) FOR FOLLOW-UP OF
           Abildtrup Larsen   PATIENTS TREATED FOR TESTICULAR CANCER STAGE I

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Background: Testicular cancer (TC) affects approx. 1% of Danish men and has a 5-year survival rate of 90-95%. Staging and follow-up involve 5-10 CT scans of each patient, imposing a significant radiation burden. To reduce radiation, we have since 2008 replaced CT thorax-abdomen-pelvis with contrast enhancement with MRI retroperitoneum-pelvis with DWI combined with X-ray or CT thorax for follow-up of TC stage I.

Aim: To retrospectively evaluate the ability of MRI with DWI to detect relapse of TC stage I in the retroperitoneum or pelvis with clinical relapse and time as reference standard.

Method: 565 patients with TC stage I were scanned from Jan 1 2010 to Mar 1 2017 (393 seminomas, 172 non-seminomas, median age 30 years (16-80 years)). All patients were subjected to the same MRI protocol. Pathology attributable to TC in the radiology report was evaluated against confirmed relapse until or at the time of next imaging (or before Mar 1 2017 if no further imaging). Only relapses in the MRI scan field were included in the analysis. 30 MRI scans were negative prior to a relapse and were reexamined.

Preliminary results: We examined 1883 MRI scans with a median of 6 months of follow-up: 1760 scans were true negative, 68 were true positive and 50 were false positive. 5 were false negative: 4 showed minor growth of lymph node (to < 1cm in shortest diameter), and 1 showed a tiny bone metastasis, which was seen on the next MRI. 69 patients with relapse were included in the analysis. The median time of relapse was 9 months after diagnosis.

Conclusion: MRI with DWI can be used as a radiation-free image modality to detect retroperitoneal lymph node metastases in TC stage I.

P20.06   Michael Brun   CAN TEXTURE ANALYSIS HELP DIFFERENTIATE BETWEEN MALIGNANT
           Andersen   AND BENIGN LYMPH NODES IN PATIENTS SUSPECTED OF LUNG CANCER

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Background: In patients with Non-Small-Cell Lung Carcinoma (NSCLC), the lymph node staging in the mediastinum is important due to impact on management and prognosis. Computed tomography texture analysis

(CTTA) is a post-processing technique that can evaluate the heterogeneity of marked regions in images.

Purpose: To evaluate if CTTA can differentiate between malignant and benign lymph nodes in a cohort of patients with suspected lung cancer.

Material and Methods: With tissue sampling as reference standard, 46 lymph nodes from 29 patients were analyzed using CTTA. For each lymph node, CTTA was performed using a research software "TexRAD" by drawing region of interest (ROI) on all available axial contrast enhanced computed tomography (CT) slices covering the entire volume of the lymph node. Lymph node CTTA comprised image filtration-histogram analysis undertaken in two stages: First step comprised an application of a Laplacian of Gaussian filter to highlight fine to coarse textures within the ROI, followed by a quantification of textures via histogram analysis using mean grey-level intensity from the entire volume of the lymph nodes.

Results: CTTA demonstrated a statistically significant difference between the malignant and the benign lymph nodes (p=0,001). By binary logistic regression, we obtained a sensitivity of 53% and a specificity of 97% in the test population. The area under the Receiver Operating Curve was 83.4%, and reproducibility was excellent.

Conclusion: CTTA may be helpful in differentiating between malignant and benign lymph nodes in the mediastinum in patients suspected of lung cancer, with a low intraobserver variance.

P20.07   Astrid Lindman   HIGHLY MOTIVATED, BUT DECEIVED AND EXHAUSTED BY REPEATED, ABRUPT COMPLICATIONS: IMPLICATIONS FOR REHABILITATION WHEN TREATED WITH STEM CELL TRANSPLANTATION

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Objective: To explore patients' experiences and perspectives of their challenges and needs regarding their return to everyday life after allogeneic non-myeloablative haematopoietic stem cell transplantation (NMA-HSCT).

Background: NMA-HSCT can cure patients with malignant blood diseases. However, during the following years, the majority of patients suffer from serious side effects and complications. Hence, it is a major challenge for patients treated with NMA-HSCT to rehabilitate.

Methods: The design was qualitative using the Interpretive Description methodology, and the theoretical framework Symbolic Interactionism inspired the interview guide and analysis. Between April and May 2017, five focus group interviews were conducted with 15 outpatients in a haematological ward in Denmark treated with NMA-HSCT 8-30 months prior to the interviews.

Results: The impaired functioning was the overarching theme and seemed to be the trigger entailing rehabilitation needs related to the following main themes: realising decline, adapting to changes, the

meaning of motivation and reliance on relations. These findings seemed to affect and influence the patients' struggle for a return to an acceptable everyday life.

Conclusion: Based on our findings, a rehabilitation programme should encompass: extensive variation regarding how to address the impaired functioning through individualised approaches, multimodal interventions through several months with varying intensity, an interdisciplinary team approach supporting motivation and visualisation of progress by tangible goal setting, communication regarding hope, extended supportive care for patients living alone and increased adherence through social sessions.

P20.08   Jesper Pedersen   CROSS-MODALITY APPLICABILITY OF RECTAL RADIOTHERAPY DOSE RESPONSE MODELS FROM PHOTONS TO PROTONS

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Background: Proton therapy (PT) is currently being explored to improve normal tissue (NT) sparing beyond what can be achieved with conventional photon-based (PB) therapy. Compared to photons, PT dose distributions have a reduced NT low-to-intermediate 'dose bath' and potentially a different biological effectiveness, questioning the applicability of PB NT complication probability (NTCP) models to PT. The aim of this study was, therefore, to assess the applicability of PB radiotherapy to rectum morbidity outcomes following PT.

Materials and methods: Treatment planning and morbidity data from 1036 prostate cancer patients treated with passive scattering PT and 159 patients treated with conventional 3D conformal four-field photon therapy were analysed. Prospectively scored gastrointestinal morbidity grade >= 2 (subdivided into two groups for protons) was used as endpoint in the analysis, with a total of 155 and 45 events (protons) and 12 events (photons). Rectum dose volume histograms were extracted for all patients and cohorts and were used as input to two different NTCP models.

Results: The predictive power of the PB NTCP models was either highly overestimating or underestimating the clinically observed morbidity when used on the proton cohort, while the single-patient predictions were poor for both cohorts with area under the curve values of ~0.6 for all models and parameter sets.

Conclusion: There were large differences in morbidity prediction between cohorts and modalities, and single-patient morbidity predictions were poor. Mixing of models based on different cohorts might not be optimal when comparing data. NTCP parameters and models should be validated across and within modalities.

| P21.01 | Mathilde Frost Kristensen | PH MEASUREMENTS OF DENTAL BIOFILM UNDER FLOW CONDITIONS - THE IDEA BEHIND THE PROJECT |

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Dental biofilm ferments sucrose into organic acid. If the biofilm is left undisturbed, the resulting pH drops may eventually lead to a cavitated caries lesion requiring operative dental treatment. Researchers from the Department of Dentistry and Oral Health have developed a method that allows for real time monitoring of pH in dental biofilm at the microscale, using a confocal laser scanning microscope (CLSM) and a ratiometric dye (C-SNARF-4). They observed pronounced pH differences within the biofilm. The biofilm exhibited areas with high pH-values (>6) in close proximity to low-pH-areas (<5.5), termed "acidogenic hotspots". These pH differences persisted for several hours, and it may well be that the first caries cavity to form occurs in the enamel under an acidogenic hotspot. Until now, acidogenic hotspots have only been observed under static conditions, which fails to take the flow of saliva into account. The flow of saliva is essential when trying to mimic the environment in the oral cavity. The aim of this project is to investigate if acidogenic hotspots develop under flow conditions. pH in in situ grown biofilms will be monitored in a flow cell with non-filtrated stimulated saliva set to a velocity of 5 mm/min, a saliva film of 70 μm and a temperature set to 35 °C. We hypothesize that acidogenic hotspots will develop, but at a slower speed due to the buffering capacity of saliva, and, furthermore, that the variation in pH between areas will increase with growing biofilm age.

| P21.02 | Arwa Gera | TRANSLATION AND ADAPTATION OF THE DANISH VERSION OF OHIP-14 |

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In Dentistry, Oral Health Related Quality of life (OHRQOL) instruments provide a measure of gains in oral function and psychological well-being. Such subjective measures can be assessed by Oral Health Impact Profile-14 (OHIP-14). However, a translated and validated Danish version is not available. Hence, the OHIP-14 questionnaire cannot be used in Denmark.

Aim: To translate and culturally adapt the OHIP-14 into Danish (OHIP-14-DK).

Materials and methods: Between September and October 2018, the original English version of Oral Health Impact Profile (OHIP-14) was translated into Danish following a standard protocol of cross-cultural adaptation. It included multiple forward and backward translations, comparing translations, and resolving challenges and conceptual equivalences to eventually produce a pre-final version of "OHIP-14-DK".

To assure content validity, OHIP-14-DK was pilot tested on a sample of 32 individuals (24 females: 8 males) aged 15-64 years at Aarhus University, Denmark (10 healthy subjects, 22 orthodontic patients at the Section of

Orthodontics). Each individual was requested to complete the self-administered questionnaire and thereafter be interviewed.

Results: The translations and back translations were very similar. The distribution of responses gave an insight into how people interpreted each item and verified that there were no errors or deviations in the translation. Therefore, no adjustments were needed on the tested version.

Conclusion: The Danish version fits the Danish culture. Validity and reliability of the Danish version is needed.

P21.03   Pankaj Taneja   MODULATION OF EXPERIMENTAL FACIAL PAIN VIA AFFECTIVELY DIFFERENT SOMATOSENSORY STIMULI

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Introduction: Somatosensation is made up of sensory discriminative and affective components. Stimuli may be perceived as unpleasant, pleasant or painful. Activation of C-Tactile afferent nerve fibers, which code for pleasant touch, may possibly provide pain relief, a phenomenon that has never been investigated in facial pain.

Aim: To investigate the modulatory effect of painful, pleasant and unpleasant somatosensory stimuli on experimentally induced facial pain.

Methods: Ten healthy adult female participants attended for 4 sessions, where they received either a local anaesthetic cream (EMLA), placebo cream, naltrexone (opioid antagonist) or placebo tablet (calcium). They were randomised to receive either face skin burning pain (0.1% capsaicin cream) or jaw myalgia pain (infusion of hypertonic saline) in all 4 sessions. The painful region was then stimulated with painful, pleasant, unpleasant and neutral (as a control) thermal and mechanical stimuli.
The pain was recorded prior to and during stimulation.

Preliminary results (n=10): All but one (45.9 °C) active stimuli reduced experimental pain. The greatest reduction in pain was seen during the placebo tablet session utilising all types of thermal stimuli. During the EMLA session, i.e. during reduced peripheral afferent function, the least stimulus-evoked reduction in experimental pain was found. Naltrexone administration, i.e. blockade of endogenous opioids, led to a lesser degree of stimulus-evoked experimental pain reduction than placebo for the majority of mechanical and thermal stimuli.

Conclusion: Both painful, pleasant and unpleasant stimuli reduced experimental pain. The effect was partly blocked by EMLA and naltrexone.

P21.04 Julie Suhr Villefrance **DOES CBCT CHANGE THE CLASSIFICATION OF EXTERNAL CERVICAL RESORPTION COMPARED TO INTRAORAL IMAGING?**

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Objective: To assess the impact of Cone-Beam Computed Tomography (CBCT) on disease severity classification of external cervical resorption (ECR) compared to intraoral images (IO) among observers.

Materials and Methods: 45 teeth (33 patients) with the tentative diagnosis ECR were radiographically examined: first, three intraoral, periapical projections (MOD); second, a CBCT was performed. Resorption severity was scored in the radiographs using Heithersay Classification system (class 1-4 for increasing severity) by three observers. The inter-observer reproducibility was estimated: percentage of observer accordance and weighted kappa statistics in a pairwise design for the two imaging modalities. For each method, the observer's recordings of agreement/disagreement were calculated.

Results: The percentage of accordance among observer pairs were 36-49% for IO and 49-60% for CBCT; and kappa values were 0.30-0.31 for IO and 0.32-0.42 for CBCT. In 40-67% of cases (depending on observer), the classification of severity was identical in both imaging modalities. However, in most cases of disagreement, the severity score was higher in CBCT compared to IO (range 27-58) from the same individual.

Conclusion: There was low reproducibility among observers in assessing the severity of ECR according to the Heithersay Classification system. However, more severe ECRs were observed in CBCT compared to IO of the same patients, which led to a change in the classification system in 27-58% of cases. More research is needed with larger patient samples to assess whether additional information from CBCT may also change the treatment of the patient.

P21.05 Xiaowen Niu **ASSOCIATION BETWEEN RAPID MAXILLARY EXPANSION AND NOCTURNAL ENURESIS IN CHILDREN: A RANDOMIZED CONTROLLED CLINICAL TRIAL**

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Introduction: Nocturnal enuresis (NE) is a multifactorial disease. New treatment options of NE are constantly being investigated, including rapid maxillary expansion (RME).

Objective: The primary objective is to evaluate whether RME could improve breathing, reduce the frequency of NE, and improve the quality of life in children after ruling out a placebo effect. The secondary objective is to investigate whether the effects of RME on nocturnal enuresis are related to the change in morphology of nasal and upper airway.

Method: NE patients aged 6-15 years with posterior cross-bite or narrow palatal will be randomized to receive immediate treatment with RME (group 1) or to have the same treatment delayed for at least 6 weeks

(group 2). The pediatric sleep questionnaires, polysomnographic setup, CBCT will be made at baseline and post-retention. Home record will be obtained at baseline, before active expansion (group 2), after expansion, and after retention.

P21.06   Carolina Bizelli Silveira

STRONTIUM ENHANCES PROLIFERATION AND OSTEOGENIC BEHAVIOR OF BONE MARROW STROMAL CELLS OF DIFFERENT EMBRYONIC ORIGINS IN VITRO

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Objective: Strontium (Sr) enhances osteogenic differentiation and proliferation in populations rich in precursor cells, such as bone marrow stromal cells (BMSCs), which are often used as a cellular source for bone tissue engineering studies. This study investigates the effect of increasing Sr concentrations on the growth and osteogenic behavior of human BMSCs from mesenchymal (i.e. fibula) and ectomesenchymal (i.e. mandible) embryonic origins.

Methods: Fibula and mandible BMSCs were cultured in MEM + 10% FBS without (Ctrl) or with Sr in four concentrations: Sr1, 11.3×10^{-3}mg/L, human seric physiological level; Sr2, 13 mg/L, human seric level after strontium ranelate treatment; Sr3, 130 mg/L, and Sr4, 360 mg/L. Proliferation rate (1, 3, 7 days), osteogenic behavior (alkaline phosphatase - ALP activity, 7 and 14 days; expression of osteogenic genes, ALP, osteopontin - OPN, and osteocalcin - OCN at 7, 14, 21 days), and formation of mineralized nodules (14 and 21 days) of the BMSCs were assessed. Data was compared group- and period-wise using ANOVA tests.

Results: Fibula and mandible BMSCs cultured with Sr4 showed increased proliferation rate, and OCN and OPN gene expression together with more evident formation of mineralized nodules compared with all other Sr concentrations. For both cell populations, Sr4 led to lower ALP activity and ALP gene expression compared to the other Sr concentrations.

Conclusions: BMSCs from the fibula and the mandible responded to Sr4 with increased cellular proliferation and osteogenic behavior in vitro.

P21.07   Stine Julie Hyldal Tingskov

TAMOXIFEN ATTENUATES DEVELOPMENT OF LITHIUM-INDUCED NEPHROGENIC DIABETES INSIPIDUS IN RATS

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Lithium is widely used in treatment of bipolar affective disorders, but often causes nephrogenic diabetes insipidus (NDI), a disorder characterized by severe urinary concentrating defects. Lithium-induced NDI is caused by lithium uptake by collecting duct principal cells and altered expression of aquaporin 2 (AQP2), which are essential for water reabsorption of tubular fluid in the collecting duct. Lithium-induced NDI is also associated with dysregulation of the amiloride-sensitive epithelial sodium channel (ENaC), which is essential for renal sodium reabsorption. Sex hormones have

previously been shown to affect the regulation of AQP2 and sodium transporters, so we tested whether tamoxifen (TAM), a selective estrogen receptor modulator, would attenuate lithium-induced alterations on renal water and salt homeostasis.

Rats were treated for 14 days with lithium and TAM treatment was initiated one week after onset of lithium administration. Lithium treatment resulted in severe polyuria, increased urinary sodium excretion and a significant reduction of AQP2 protein expression as well as a reduction of ENaC at both RNA and protein levels, which was ameliorated by TAM. Consistent with this, TAM attenuated downregulation of AQP2 expression in freshly isolated IMCD tubule suspension prepared from lithium-treated rats.

In conclusion, TAM attenuated dose-dependently the polyuria, impaired urine concentration, downregulated AQP2 protein expression and rescued the adverse effects of the lithium-induced increase in fractional excretion of sodium in rats with lithium-induced NDI. These findings suggest that TAM is likely to be a novel therapeutic option for lithium-induced NDI.

P22.01   Marianne Ørum   DOES COMPREHENSIVE GERIATRIC ASSESSMENT (CGA) IMPROVE THE 90-DAY MORTALITY IN OLDER CANCER PATIENTS?

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Background: The effect of CGA in older cancer patients is a subject of debate in literature.

Purpose: To compare the 90-day mortality in older cancer patients attending CGA prior to initiation of cancer treatment to patients not attending CGA prior to cancer treatment.

Design: Eligible patients were 70+ yrs. referred to the oncology department for treatment of cancer in the lungs, head and neck, upper or lower gastrointestinal tract. As a supplement to the oncology consultation, patients were scheduled for CGA. Death within 90 days was recorded from the medical file.

Results: From January 8th, 2015 to August 31st, 2018, 939 patients were identified. Information on death within 90 day was obtained in 798 patients. Analyses were performed on data from these patients. In total, 481 patients (60%) attended CGA, whereas 317 patients (40%) did not; either due to lack of invitation to CGA (203 patients, 26%) or due to non-response to the invitation (114 patients, 14%). A total of 145 patients (18%) died within 90 days. Hazard Ratio (HR) for death within 90 days was 0.75 among attenders as compared to non-attenders, p= 0.094 (95%CI: 0.54; 1.05). Age and tumor site added statistical significantly to the adjusted model: HR: 0.83, p=0.26 (95%CI: 0.59; 1.16).

Discussion: The present results indicate that CGA may improve the short-term survival in older cancer patients, bearing in mind that we only have follow-up results on 85% of the patients.

If the results are verified in a randomized study, new perspectives in the treatment of older cancer patients may open.

| P22.02 | Pernille Christiansen Skovlund | PATIENT INVOLVEMENT IN THE RESEARCH PROCESS |

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Background: Patient involvement in health research may improve quality and relevance. However, little is known about how and when patients are best involved. In a study investigating the effect of using patient-reported outcomes (PRO) as a dialogue-based tool in oncology consultations, patients and researchers engaged in co-production in the research process. The aim was to gain knowledge and experience with the impact on both process and results.

Methods: A steering group with two patients and six researchers was established in 2017. In the design and management phase, the steering group selected relevant PRO measures and constructed the patient information sheet. In the phase of analysis, the steering group analyzed audiotaped consultations using the VR-CoDES coding system. Disseminating the results of the analysis will be planed in the steering group.

Results: This work demonstrates the contribution and the time consumption of patient involvement in a research project. Patients advocated for PRO measures that enable discussions with both clinicians and relatives in the consultation, which was not considered by the researchers beforehand. The title and wording of the information sheet were adjusted according to the patients' suggestions. Arranging meetings, considerations about the extent of involvement and death of involved patients were challenging elements in the process. The analysis and the dissemination of the results have not yet been performed.

Perspectives: Knowledge and experiences about involving patients in different phases of the research can be applied to other settings and projects, where patients are seen as partners in the research process.

| P22.03 | Rasmus Blechingberg Friis | PROWIDE – PATIENT-REPORTED OUTCOMES USED FOR WEEKLY INTERNET-BASED DETECTION OF PROGRESSIVE DISEASE IN LUNG CANCER: A RANDOMIZED CONTROLLED TRIAL |

R.B. Friis

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Introduction: Progressive advanced lung cancer has poor prognosis. If not recognized in time, the performance status can quickly worsen and make the patient unfit for further anti-neoplastic treatment.

We have initiated a national multicenter randomized trial in Denmark to test if weekly symptom monitoring added to a standard CT-based follow-

up through a Patient Reported Outcome (PRO) application can improve the survival in a Danish population.

Materials & methods: 492 patients with lung cancer will be included in the trial. Patients with advanced lung cancer treated with palliative intent can be included. Other inclusion criteria are performance status ≤ 2, internet connection and non-progressive disease at first CT scan after induction treatment. Maintenance therapy is allowed.

Patients are randomized between PRO monitoring as a supplement to standard CT-based follow-up or standard care. Patients in the PRO arm will weekly fill in a short questionnaire via the internet. A notification will be sent to the clinicians in case of alarming symptoms with the purpose of detecting progressive disease before deterioration of the health status.

Both groups will fill in the EORTC QLQ-C30/LC13, HADS and EQ-5D-5L questionnaires every 2 month.

Results: The study opened for recruitment in September 2018.

The primary endpoint is overall survival. The hypothesis is that the PRO intervention leads to earlier detection and treatment of progressive disease and medical complications, improved performance status, fewer admissions to hospital and better quality of life during follow-up.

P22.04   Kristoffer Brix Olesen   TRANSFERABLE SKILLS IN HEALTH SCIENCES EDUCATION: GLOBAL, LOCAL, AND CLASSROOM DISCOURSES

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The overall purpose of this PhD project is to provide new knowledge and insights that will advance the development of transferable skills among students in the field of health sciences educations, so they can manage and respond flexibly and effectively to changes and demands in the future labour market.

Students need more than discipline-based knowledge and expertise in their major subject area. In recent times, transferable skills have been highlighted as an important curriculum element in health science educations. For example, transferable skills such as problem solving and team collaboration are key components in quality health care and crucial for a safer and more effective health care system.

This PhD project aims to answer two questions: What characterises the global and local discourse on transferable skills in health sciences education? How can we measure students' perception of the transferable skill "collaborative problem solving (CPS)" in health science education?

The project consists of two connected studies. Study 1 is a literature study that aims to examine the characteristics in the international discourse on transferable skills in health sciences education research literature. Study 2 is a validation study that aims to develop and validate a questionnaire to measure collaborative problem solving among students in health science education.

My presentation will focus on study 1, which is conducted as a mixed studies review including a sequential exploratory synthesis.

| P22.05 | Sofia Spampinato | RISK FACTORS FOR BLADDER FISTULA, BLEEDING AND CYSTITIS IN CERVIX CANCER: AN EMBRACE ANALYSIS |

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Purpose: To identify risk factors for bladder fistula, bleeding and cystitis within the prospective, multi-institutional, observational EMBRACE study (an international study on MRI-guided brachytherapy in locally advanced cervical cancer).

Material/Methods: Bladder fistula, bleeding and cystitis (CTCAEv.3) were analysed in Locally Advanced Cervical Cancer (LACC) patients treated with radiochemotherapy and Image-Guided Adaptive Brachytherapy (IGABT). Patient, disease and treatment characteristics were tested as risk factors for grade (G) ≥2 with univariate (UVA) and multivariable (MVA) analyses (Cox proportional hazards) in patients without bladder involvement. UVA and MVA were also performed for G≥3 incidence pooled over the three endpoints. Bladder dose hotspot (D2cm^3) was assessed according to current recommendations.

Results: In 1146 patients, crude incidences for G≥2 fistula, bleeding and cystitis were 0.7%, 2.0% and 7.4%, respectively. Pooled incidence for G≥3 was 1.4%. Mean (SD) bladder D2cm^3 was 75.8±9,7Gy, median follow-up was 35 months, median age was 49 years, and 31% were smokers. Based on MVA analysis, bladder dose was significant ($p<0.05$) for all individual and pooled endpoints. Smoking status was predictive on MVA for bleeding, cystitis and pooled incidence. Risk for cystitis was higher for younger patients on MVA.

Conclusion: In the present study, bladder dose was a dominant risk factor for developing bladder fistula, bleeding or cystitis after IGABT in LACC patients. Limitation of bladder dose could then reduce risk to develop adverse effects. Risk of bleeding and cystitis was higher in smokers. Age was predictor for cystitis, with younger patients at higher risk.

P22.06   Anna Holm   DEVELOPMENT AND TEST OF A COMMUNICATION STRATEGY FOR THE MECHANICALLY VENTILATED INTENSIVE CARE UNIT PATIENT (ICU-COM)

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Background: There has been a shift in paradigm with no-sedation protocols for patients in the intensive care unit, which means that more mechanically ventilated patients are conscious and unable to communicate verbally. This is a challenge in clinical practice and a frustrating experience for patients and nurses. Several studies conclude that key to improving communication is a systematic strategy and a nurse education programme, but none have been developed or tested within the context of no-sedation.

Aim: The purpose is to study the usefulness of a patient-centred communication strategy for mechanically ventilated patients in the intensive care unit (ICU-COM). The strategy will consist of three components for the intensive care nurses: 1) an overall communication strategy, 2) a communication assessment tool and 3) an education programme focusing on augmentative and alternative communication.

Design and methods: The overall frame is Complex Interventions.

Study 1: Descriptive study using the TIDieR template to report the development.

Study 2: Assessment of nurses' perception of ICU-COM. Triangulation study with data from focus group interviews and questionnaires. Qualitative data will be analysed using Ricoeur's theory of interpretation, and quantitative data will be analysed using descriptive statistics.

Study 3: Process evaluation where ICU-COM's feasibility is tested in clinical practice. Observation study with participant observations and informal interviews inspired by Spradley. The combined qualitative data will be analysed using Ricoeur's theory of interpretation.

Preliminary results: The communication strategy and assessment tool has been developed, but it has not yet been tested in clinical practice.

P22.07   Mie Østergaard   ENHANCING INNOVATIVE COMPETENCES IN THE DANISH HEALTH CARE SECTOR - A MIXED METHODS STUDY

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Background: Increased efficiency in healthcare is becoming a necessity, mainly due to external demands on the sector. Healthcare providers must think and act innovatively to accommodate the needs of the sector. Research argues that innovative competences are crucial individual skills in the 21th century. In Denmark, seven core roles of medical doctors are outlined for meeting the external needs of the Danish healthcare sector.

However, as innovative competences are not among these, this may lead to a gap between the education of doctors and the future needs of the sector. Thus, the questions remain: Do doctors need innovative competences to bring the healthcare sector into the future? How may these competences then be enhanced?

Methods/material: A mixed methods research study aiming to explore: 1) What are the needs for innovative competences of medical doctors, and what is done to support these? 2) How can innovative competences of medical doctors be enhanced through healthcare innovation education? Part 1 is a literature review combined with a qualitative study using interviews and participant observation. Based on part 1, new educational elements for healthcare innovation education will be developed.

Part 2 is an intervention study testing if the new educational elements can enhance innovative competences among Danish medical doctors (n ≈ 130).

Perspectives: This research area has several future perspectives. Hopefully, results from the project will provide new knowledge on the individual innovative competences among healthcare professionals and produce elements for optimal education on healthcare innovation, which may possibly lead to cutting-edge healthcare innovations.

P22.08   Jeppe Foged Vigh-Larsen

PERFORMANCE DIFFERENCES BETWEEN ELITE AND SUB-ELITE ICE HOCKEY PLAYERS WITHIN THE BEST AND SECOND BEST DANISH ICE HOCKEY LEAGUE

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The purpose of the present study was to evaluate performance in off-ice and on-ice tests of elite and sub-elite ice hockey players of all playing positions and to test for possible differences related to level and position. Teams from the best and second best Danish ice hockey league were tested during the in-season period. The off-ice tests consisted of measures of weight, height and body composition as well as a vertical jump test. On-ice testing included the submaximal Yo-Yo IR1 test, 5-10-5 Pro Agility test, a straight line sprint test and the maximal Yo-Yo IR1 test. Preliminary results from the currently enrolled 51 elite and 39 sub-elite players showed that elite ice hockey players were heavier (87 vs. 81.9 kg, $p \leq 0.05$) due to more lean body mass (42.4 vs. 39 kg, $p \leq 0.05$) and scored better on the vertical jump test (49.5 vs. 44.7 cm, $p \leq 0.05$), agility test (4.8 vs. 5.0 s, $p \leq 0.05$), sprint test (4.5 vs. 4.7 s, $p \leq 0.05$) as well as the submaximal (77 vs. 89% HR max, $p \leq 0.05$) and maximal Yo-Yo tests (2252 vs. 1657 m, $p \leq 0.05$) than their sub-elite counterparts. As for positional differences, defensemen were taller than forwards (184.7 vs. 181.7 cm, $p \leq 0.05$), whereas no other differences were apparent. These results indicate that elite level ice hockey requires a high level of fitness, both in terms of lean

body mass and power generating capacity on top of a well developed intermittent exercise capacity. In addition, these demands seem to apply for both forwards and defensemen as no significant positional differences were present. Further analyses will establish potential relationships between test performances and final team ranking during the season.

F01.01   Jacob Nicolaisen   MECHANICAL PERFORMANCE AND HEALING PATTERNS OF THE NOVEL SIROLIMUS-ELUTING BIORESORBABLE FANTOM SCAFFOLD IN LONG CORONARY LESIONS

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Background: Implantation of permanent drug-eluting stents (DES) during percutaneous coronary intervention (PCI) is the standard invasive treatment for coronary artery disease. To address long-term risks of stent thrombosis and restenosis, bioresorbable scaffolds (BRS) that completely resorb in 3-4 years were developed. Favorable clinical outcomes and healing patterns were demonstrated for the Fantom BRS (Reva Medical, CA, US) after implantation in short coronary lesions, but data on use in long coronary lesions requiring more than one BRS are lacking. Implantation of serial BRS requires exact end-to-end deployment, but overlap frequently occurs. It is currently unknown how the Fantom BRS performs in serial implantations with overlap.

Methods: The Fantom II Cohort C study is a prospective, proof-of-concept, multicenter study assessing clinical, angiographic, and optical coherence tomography (OCT) outcomes in 50 patients with lesions >20 mm in length, requiring more than one Fantom BRS for full lesion coverage. OCT scans are performed at baseline post-PCI and at 6-month follow-up. Matched scans are analyzed systematically for lumen measurements and healing patterns. The main endpoint is minimal lumen area at 6-month follow-up.

Results: Preliminary results will be presented at PhD Day 2019.

Perspectives: Systematic mechanical and healing results after implantation of serial Fantom BRS may aid proper implantation technique in long lesions. Enrollment is currently ongoing. Complete follow-up is expected in April 2019.

F01.02   Rubina Attar   CLINICALLY MANIFESTED PERIPHERAL ARTERY DISEASE IN PATIENTS WITH
          CANCELLED   ACUTE MYOCARDIAL INFARCTION

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Background: Patients with peripheral artery disease (PAD) are a high-risk population after experiencing a myocardial infarction (MI) with adverse cardiac outcomes. The aim of this study is to describe the characteristics of patients with PAD following MI, analyse 1-year major adverse cardiac events (MACE: all-cause mortality, reinfarction, stroke and heart failure) as

well as to investigate prescriptions of guideline-based medical therapies in a nationwide contemporary MI population.

Methods: All MI patients presenting with a STEMI or NSTEMI between January 1st 2005 and December 31st 2014 with (n=4,213) and without (n=106,763) a concurrent PAD diagnosis were identified and included from the SWEDEHEART registry (prevalence of PAD: 3.8%). Univariable and multivariable Cox proportional hazards and Kaplan-Meier survival models were applied to compare the two populations.

Results: The adjusted results showed an increase in MACE (HR 1.40 95% CI 1.31-1.49), mortality (HR 1.60 95% CI 1.45-1.78), reinfarction (HR 1.49 95% CI 1.33-1.67), stroke (HR 1.32 95% CI 1.09-1.63) and heart failure (HR 1.35 95% CI 1.22-1.48). In the population with PAD, there was a higher prevalence of comorbidities such as diabetes, hypertension, hyperlipidaemia and previous reinfarction. The infarction type, ECG recordings and angiographic findings pointed towards more severe MI. Finally, a lower prevalence of guideline-based medical therapy at discharge (48.3% vs 56.3%) was seen.

Conclusion: Patients with PAD have more severe MI and clinical outcomes. However, despite this, they are less likely to receive guideline- based medical therapy.

F01.03   Kevin Kris Warnakula Olesen

PROGNOSTIC ASSESSMENT OF CORONARY ARTERY DISEASE BY COMPUTED TOMOGRAPHY ANGIOGRAPHY IN DIABETES AND NON-DIABETES PATIENTS: A STUDY FROM THE WESTERN DENMARK CARDIAC COMPUTED TOMOGRAPHY REGISTRY

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Aims: We examined whether severity of coronary artery disease (CAD) measured by coronary computed tomography angiography can be used to predict rates of myocardial infarction (MI) and death in patients with and without diabetes.

Methods: A cohort study of consecutive patients (n=48,731) registered in the Western Denmark Cardiac Computed Tomography Registry in 2008-2016. Patients were stratified by diabetes status and CAD severity (no, non-obstructive, or obstructive). Endpoints were MI and all-cause death. Event rates per 1,000 person-years, unadjusted and adjusted incidence rate ratios (IRR) were computed.

Results: Median follow-up was 3.6 years. Among non-diabetes patients, MI event rates per 1,000 person-years were 1.4 for no CAD, 4.1 for non-obstructive CAD, and 9.0 for obstructive CAD. Among diabetes patients, the corresponding rates were 2.0 for no CAD, 4.8 for non-obstructive CAD, and 12.8 for obstructive CAD. Non-diabetes and diabetes patients without CAD had similar low rates of MI [adjusted IRR 1.36, 95% CI: 0.69-2.71].

Among diabetes patients, the adjusted risk of MI increased with severity of CAD (no CAD: reference; non-obstructive CAD: adjusted IRR 1.72, 95% CI 0.80-3.72; obstructive CAD: adjusted IRR 4.60, 95% CI 2.22-9.51). Diabetes patients had higher death rates than non-diabetes patients, irrespective of CAD severity.

Conclusion: In patients without CAD, diabetes patients have a low risk of MI similar to non-diabetes patients. Furthermore, MI rates increase with CAD severity in both diabetes and non-diabetes patients, with diabetes patients with obstructive CAD having the highest risk of MI.

F01.04   Christian Stæhr Frederiksen

MIGRAINE ASSOCIATED MUTATION IN THE α2 ISOFORM NA+,K+-ATPASE LEADS TO DISTURBANCE IN NEUROVASCULAR COUPLING

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Background: Neurovascular coupling (NVC) was studied in heterozygous mice bearing a mutation (G301R) of the α2 isoform Na+,K+-ATPase (Atp1α2+/G301R), which is known to be associated with familial hemiplegic migraine type 2 in humans. We have previously shown that cerebral arteries from Atp1α2+/G301R mice dilated stronger to increased concentrations of bath K+(8 - 12 mM) than arteries from wild type. This suggests stronger vasodilation to elevation of interstitial K+in vivo, i.e. NVC, in Atp1α2+/G301R mice.

Methods: NVC was assessed in situ in brain slices and in vivo using Laser Speckle Imaging. Membrane potential in vascular smooth muscle cells (VSMC) was measured with conventional sharp electrodes. qPCR analysis and immunohistochemical staining identified mRNA and protein levels of K+inward rectifying 2.1 (Kir2.1) channels in cerebral arteries.

Results: Neuronal excitation in vivo and in situ was associated with exaggerated dilations of cerebral arterioles and thereby hyperperfusion of the cerebral cortex in Atp1α2+/G301R mice. In accordance with exaggerated vasodilation, VSMC from Atp1α2+/G301R mice showed an increased hyperpolarization in response to bath K+elevation. NVC responses were in both groups sensitive to $BaCl_2$, suggesting NVC to be dependent on Kir2.1 channels. Accordingly, increased mRNA and protein levels of Kir2.1 in the arteries from Atp1α2+/G301R mice were found.

Conclusion: Functional experiments suggested NVC disturbances in Atp1α2+/G301R mice. We suggest that increased hyperpolarization, and thereby exaggerated dilation of cerebral arteries from Atp1α2+/G301R mice in response to neuronal activity, is due to increased expression of Kir2.1 channels.

F01.05   Charlotte Brinck   PLASMA LEVELS OF LECTIN PATHWAY PROTEINS HAVE NO PROGNOSTIC
          Holt   VALUE IN SHORT-TERM CARDIAC OUTCOMES AFTER MYOCARDIAL
                            INFARCTION

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Background: The leading worldwide cause of mortality is coronary artery disease, which demonstrates the scientific challenge we are facing in the search for treatment of myocardial infarction (MI). The pathogenesis of MI is a complex process, in which inflammation is accepted as an essential factor. Recently, the association between the lectin pathway of the complement system and ischeamia/reperfusion injury has generated scientific attention, but it requests elucidation in clinical cohorts. We hypothesize that lectin pathway proteins can deteriorate cardiac outcomes after MI. We aim to investigate if physiological variations in the plasma levels of lectin pathway proteins (MBL, M-ficolin, L-ficolin, H-ficolin and sMAC) have an impact on the reperfusion injury in STEMI patients.

Methods: This study includes 74 STEMI patients admitted to the coronary care unit planned for primary PCI. Infarct size and ejection fraction were measured on day 6-9 after the infarct with MRI. A plasma sample was drawn the day after reperfusion. Plasma sC5b-9, MBL, M-ficolin, H-ficolin and CRP were measured with in-house time-resolved immunofluorimetic assay (TRIFMA), and L-ficolin was measured using an enzyme-linked immunosorbent assay.

Preliminary results: In the acute phase, the plasma levels of sMAC and MBL do not appear to be of predictable prognostic value when looking at short-term cardiac outcomes after MI. In correlation analyses, there was no association between plasma levels of sMAC and the cardiac outcomes; ejection fraction (p=0.54) and infarct size (p=0.71). Furthermore, no correlation was found between plasma levels of MBL and ejection fraction (rs=0.95) and infarct size (rs=0.51).

F01.06   Zarmiga   ATRIAL SEPTAL DEFECT - EXERCISE CAPACITY AND PULMONARY
          Karunanithi   HYPERTENSION

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Atrial septal defect (ASD) is a simple congenital heart disease defined as a hole in the atrial wall. For long, it has been assumed that patients with an ASD could be deemed healthy after closure of their defect. However, this turned out not to be the case. In ASD patients with small unclosed defects, we have found a decreased exercise capacity. In addition, ASD patients generally suffer from increased risks of comorbidities and early death, which is most often due to heart failure. It is speculated that this is

secondary to increased pulmonary vascular resistance due to arterial-venous shunting, but the etiology has never been fully studied.

In this PhD study, we examine patients who had closure (by surgery or transcatheter) of their ASD and compare them with healthy controls. We hypothesize that ASD patients suffer from decreased exercise capacity, tachyarrhythmias and decreased myocardial contractility due to increased pulmonary vascular pressures.

A total of 50 persons will be included, 20 catheter closed and 20 surgically closed ASD patients, to determine if method of closure affects the outcomes, and 10 age- and gender-matched controls from the Danish background population. The participants will be studied using echo-cardiography, right heart catheterization with pressure measurements during rest and exercise, cardiopulmonary exercise bicycle test and Holter monitoring.

We aim to clarify the hemodynamic and physiological changes that take place, and thereby shed light on which parameters clinicians should be aware of when dealing with ASD patients. Hopefully, this allows us to optimize the course of the disease, which may not be so simple after all.

F01.07   Anne Brink Behrndtz

TRANSPORT STRATEGY IN PATIENTS WITH LARGE VESSEL OCCLUSION? TRIAGE STROKE: TREATMENT STRATEGY IN ACUTE LARGE VESSEL OCCLUSION: PRIORITIZE IV OR ENDOVASCULAR TREATMENT

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Protocol abstract:

Rationale: The effect of endovascular therapy (EVT) is superior to intra-venous thrombolysis (IVT) in strokes caused by large vessel occlusions (LVO). If a severe stroke with symptoms indicating LVO occurs in the catchment area of a primary stroke center (PSC), there is equipoise about the optimal transport strategy. Should the patient be transported to the PSC for fast IVT (and later possibly transferred to the comprehensive stroke center (CSC) for EVT), or should the PSC be bypassed for faster EVT at the CSC? Observational studies have shown divergent results. Randomized clinical trials are needed to determine the optimal transport strategy.

Aim and hypothesis: We hypothesize that bypassing the PSC will result in better 90-day outcome for patients with suspected LVO.

Methods: TRIAGE-STROKE is a national investigator-driven, multi-centre, randomised single-blinded clinical trial. A simple stroke severity score called PASS (Prehospital Acute Stroke Severity) has been developed. It identifies most patients with LVO in the pre-hospital setting. Patients without a contraindication for IVT are randomized to either transport

directly to a CSC for IVT and EVT or to a PSC for IVT and subsequent transport to a CSC for EVT, if needed.

Results: The primary outcome will be the 90-day modified Rankin Scale score (mRS) for all patients with an ischemic stroke. Secondary outcomes include 90-day mRS for all randomized patients, all patients with ischemic stroke but without LVO, and patients with hemorrhagic stroke.

Discussion: Study results will influence decision-making regarding transport strategy for patients with suspected LVO.

F01.08   Lisa Carlson Hanse

PULMONARY CUSP REPAIR OF CONGENITAL HEART SURGERY: IN VITRO EVALUATION

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Background: Pulmonary valve abnormalities due to congenital cardiac malformations represent a big challenge. Due to the growth of a child, the surgical cornerstones are usually initial repair of the pulmonary valve defect in the infancy period followed by a pulmonary valve replacement later in life. Timing of these surgeries are of outmost importance, as the child is at a risk of pulmonary regurgitation, right ventricular dilation, right ventricular dysfunction, cardiac arrhythmias, heart failure and sudden cardiac death. Our method of cusp repair is designed to bypass the critical phase of timing; thus, the child will grow up with reduced risk of complications in the long term.

Objectives: To investigate the feasibility of repairing the pulmonary valve based on mathematically designed cusps made of autologous pericardium in vitro.

Methods: Eight pulmonary roots explanted from porcine hearts were evaluated in a pulsatile flow loop model at cardiac output of 3 L/min, 4 L/min, 5 L/min and 6 L/min. After testing the native pulmonary root, the native cusps were explanted. Three cusps, designed based on a mathematical model and made of glutaraldehyde treated autologous pericardium, were subsequently implanted. The characterization will be based on geometric data from high-speed camera images, hydrodynamic data from echocardiography and on ventricular and pulmonary artery pressure measurements.

Results: Preliminary results will be presented.

Perspective: With potential promising results, our method of pulmonary cusp repair should be investigated in vivo, which considers the complex interactions seen in the heart.

F01.09 Mikkel Bundgaard Skotting

REGIONAL BRAIN VOLUMES IN NEWBORNS WITH CONGENITAL HEART DEFECTS

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Children with heart defects have a higher risk of cognitive disabilities. The reasons for this are not fully understood. We have previously demonstrated smaller head circumferences at birth in children with heart defects and signs of disrupted fetal brain growth from mid-gestation measured with ultrasound. In the present project, we looked at total and regional brain volumes estimated by magnetic resonance imaging (MRI) to investigate if certain areas of the brain are at particular risk of disrupted growth.

MRI volumetrics of the brain were performed on 20 newborns; 10 with major heart defects (gestational age between 39-54 weeks, mean gestational age 45 weeks + 1 day) and 10 without heart defects (gestational age between 39-52 weeks, mean gestational age 43 weeks + 4 days).
Grey and white matter was differentiated, and the different regions of the brain were isolated. The volume measurements were compared by a multivariate regression.

The brain volumes in children with congenital heart defect were on average 48 ml smaller than in children without heart defects ($P < 0.03$, SE: 20 ml). When separated into white and grey matter, only grey matter was significantly smaller. The volume difference were most profound in the youngest group (gestational age from 38 weeks to 48 weeks). No differences in the ventricles, brainstem and cerebellum were observed.

The brain volume differences observed shortly after birth suggest that the brain affection, which increases the risk of cognitive disabilities, happens during pregnancy. Due to small sample size, the external validity of the results may be low.

F02.01 Kathrine Agergård Kaspersen

USE OF ORAL IRON SUPPLEMENTATION IS NOT ASSOCIATED WITH RISK OF INFECTIONS: RESULTS FROM THE DANISH BLOOD DONOR STUDY (DBDS)

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Background: Blood donors are at increased risk of developing iron deficiency and several studies have recommended iron supplementation for this group.

Aim: The aim of this study was to investigate the effect of oral iron supplementation on the risk of infections among healthy blood donors.

Methods: We included 82,062 participants from the Danish Blood Donor Study, who completed a questionnaire on health-related items including use of oral iron supplementation. Infection outcomes were ascertained by using ICD-10 codes in the Danish National Patient Register and ATC codes in the Danish Prescription Register. Multivariable Cox proportional hazards analysis was used as the statistical model. Risk estimates are presented as crude hazard ratios (HR) with 95% confidence intervals (CI).

Results: During 19,978 person-years of observation, 6,983 donors redeemed at least one prescription of antimicrobials. Similarly, during 19,829 person-years of observation, 240 donors were treated for infection at a hospital. Use of oral iron supplementation was not associated with redeemed prescriptions of antimicrobials in any strata: premenopausal women: HR = 1.00, 95% CI: 0.91 - 1.10, postmenopausal women: HR = 1.07, 95% CI: 0.87 - 1.32, and men: HR = 1.01, 95% CI: 0.84 - 1.21.
In addition, use of oral iron supplementation was not associated with risk of hospital-based treatment for infection.

Conclusion: In a large cohort of blood donors, use of oral iron supplementation was not associated with subsequent short-term risk of infection. These findings are important to help understand the safety of using oral iron supplementation among blood donors and in the general population.

F02.02 Signe Mosegaard

FATTY ACID OXIDATION (FAO) MODULATES INFLAMMATORY RESPONSES; IMPLICATIONS FOR INBORN ERRORS OF FAO AND SEPSIS DEVELOPMENT

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Recent studies have shown that mitochondrial fatty acid oxidation (FAO) is essential for cellular antioxidant and anti-inflammatory function. Mitochondrial FAO is decreased in non-surviving of patients diagnosed with sepsis, characterized by an inflammatory and oxidative stress response. It is also well-documented that patients with genetic FAO disorders (FAOD), in addition to energy deficiency, have increased oxidative stress and inflammation and have a higher risk of dying from multi-organ failure during an infection.

The aim of the present project is to improve diagnosis and treatment of FAOD. This will be obtained by development of a Next Generation Sequencing FAO gene panel, and by investigating treatment options to lower inflammation and oxidative stress in a FAOD patient cell model. As an interdisciplinary and innovative approach, we will use a porcine sepsis

model to investigate temporal changes in FAO as well as pro- and anti-inflammatory markers during the early phase of sepsis, with the aim of identifying a treatment window for boosting FAO and the associated anti-oxidant and anti-inflammatory responses.

The results from the project will reveal new aspects of the interaction between FAO and the inflammatory responses, which may propose new targets for treatment and biomarkers of sepsis development. The genetic panel is key to obtain better and faster diagnostics of FAOD, but it may also be relevant in order to perform association studies that investigate FAO gene variations as predisposing factors for the development of sepsis.

F02.03   Esben Stistrup Lauritzen

CHRONIC METABOLIC EFFECTS OF MELATONIN

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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. Due to treatment of, for example, insomnia, the use of melatonin is increasing rapidly in Denmark with a 100-fold increase from 2007 to 2012 in children and adolescents. Nevertheless, no previous research has assessed changes in insulin sensitivity and insulin secretion after chronic melatonin treatment in patients with T2DM.

Main research questions:

1) Does chronic melatonin treatment change insulin secretion in T2DM patients?

2) Does chronic melatonin treatment change insulin sensitivity in T2DM patients?

Design: A randomized, double-blinded, placebo-controlled, crossover study including 18 participants with T2DM. Participants will be examined on two occasions: 1) after 3 months of daily melatonin treatment before bedtime (10 mg) and 2) after 3 months of daily placebo treatment before bedtime. An intravenous glucose tolerance test and a hyperinsulinemic euglycemic clamp will be performed on study days to assess insulin secretion and insulin sensitivity.

Perspectives: It is highly relevant to evaluate the chronic effects of melatonin on glucose metabolism given the increase in melatonin consumption and the strong association to glucose metabolism.

F02.04   Lene Thorup

VITAMIN D DEFICIENCY IN RHEUMATIC HEART DISEASE PATIENTS AND MATCHED HEALTHY CONTROLS IN NEPAL

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Background: Rheumatic Heart Disease (RHD), the autoimmune response to group A streptococcal infection that destroys the heart valves, affects 33 million people almost exclusively in developing countries. RHD disappeared in industrialized countries before its pathophysiologic mechanisms were fully understood, and a remaining question about RHD is: What makes the host susceptible?

We describe nutritional status in RHD patients with a special focus on vitamin D deficiencies since this has recently been associated with both infectious and autoimmune diseases and regulation of endothelial cell production. Could malnutrition make a person more susceptible to RHD?

Methods: A case-control study of 105 RHD patients and 97 controls selected by echocardiography and matched on sex and age in Nepal. Dried Blood Spots were analysed for s-25(OH)D concentrations and anthropometric measurements performed along with a questionnaire for socioeconomic status (SES) classification.

Preliminary results: Mean age of RHD patients was 31 years (±11) and controls 32 years (±11) with a 4:1 female to male ratio. BMI was significantly lower in RHD patients (22.6; 95% CI, 21.5-23.2) compared with controls (24.2; 95% CI, 23.3-25.1). RHD patients had lower SES ($p=0.001$), with 45% belonging to the poorest class. The first 34 RHD patients have Vitamin D insufficiency, (mean 29.5 nmol/l; 95% CI, 26.8-32.2). Remaining samples are under analysis.

Perspectives: RHD patients are characterized by low s-25(OH)D, BMI and socioeconomic status. Vitamin D deficiency may be a risk factor for disease development and progression and warrants further investigation.

F02.05   Aimi Danielle Munk Hamilton

GROWTH OF UROPATHOGENIC ESCHERICHIA COLI IN HUMAN URINE

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Urinary tract infections (UTIs) are very common and often caused by Escherichia coli. The E. coli that successfully ascends to the kidney and causes pyelonephritis produces different virulence factors, including α-haemolysin (HlyA). Our data from a murine model of pyelonephritis suggest that local growth conditions in the urinary bladder influence the pathogenicity of the bacteria. Preliminary data also show that mice with reduced ability to dilute urine are more susceptible to UTIs. We hypothesised that urine dilution reduces the growth of uropathogenic E. coli.

We used the HlyA-producing E. coli strain ARD6 and a non-HlyA producing strain transfected either with a plasmid containing the full HlyA operon (WAM1824) or with a non-functional HlyA operon (WAM2136). In LB-medium, we found continuous growth for up to 8 hours, whereas there was no detectable growth in HEPES buffered salt solution (HBS). Contrary to HBS, E. coli grew readily in concentrated human urine and dilution of

the urine markedly stagnated the growth. This effect was gradual in the osmotic range of 50-500 mosmol/l, with more than doubling the number of bacteria at 500 mosmol/l compared to 50 mosmol/l after 4 hours. Urea (0-500 mM) did not affect growth, which means that a change in osmolarity cannot explain the difference in growth. We are currently addressing the effect of potential substrate present in urine, including the nitrate donor NH_4^+. We will also test if volume load prevents development of pyelonephritis with uropathogenic E. coli in a murine model. In conclusion, our data show that urine dilution reduces bacterial growth, which may suggest that it could be beneficial to increase volume intake during UTIs.

F02.06   Jacob Rudjord Therkildsen

LACK OF P2X$_7$ RECEPTORS PROTECTS AGAINST RENAL FIBROSIS AFTER PYELONEPHRITIS WITH A-HEMOLYSIN PRODUCING ESCHERICHIA COLI

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Severe urinary tract infections are regularly caused by sub-strains of Escherichia coli secreting the pore-forming virulence factor α-hemolysin (HlyA). Repeated or severe cases of pyelonephritis can cause renal scarring that subsequently can lead to progressive failure. We have previously demonstrated that HlyA releases cellular ATP directly through its membrane pore and that acute HlyA-induced cell damage is completely prevented by blocking ATP-signaling. There is substantial evidence that local ATP signaling and P2X$_7$ receptor activation play a key role in the development of tissue fibrosis. This study investigated the effect of P2X$_7$ receptors on infection-induced renal scarring in a murine model of pyelonephritis.

Pyelonephritis was induced by injecting 100 million HlyA-producing, uropathogenic E. coli into the urinary bladder of Balb/cJ mice. Similar degree of pyelonephritis and mortality was confirmed at day 5 post-infection in P2X$_7^{+/+}$and P2X$_7^{-/-}$ mice. Fibrosis was first observed 2 weeks postinfection, and our data clearly demonstrates that P2X$_7^{-/-}$ mice and mice exposed to the P2X$_7$ antagonist BBG showed markedly less renal fibrosis 14 days postinfection compared to controls (p<0.001). Immunohistochemistry revealed comparable early neutrophil infiltration in the renal cortex from P2X$_7^{+/+}$and P2X$_7^{-/-}$ mice. Interestingly, lack of P2X$_7$ receptors resulted in diminished macrophage infiltration and reduced neutrophil clearance in cortex of P2X$_7^{-/-}$ mice. Hence, this study suggests the P2X$_7$ receptor to be an appealing antifibrotic target following renal infections.

F02.07   Thea Cœcilie Viborg Vestergaard

THE INFLUENCE OF ANTI-TNF-ALPHA TREATMENT ON PLACENTAL FUNCTION AND PREGNANCY OUTCOME IN PATIENTS WITH CHRONIC INFLAMMATORY DISEASE

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More than 50,000 Danish women suffer from inflammatory bowel disease (IBD) or rheumatic disease (RD). IBD/RD often debuts in the years of childbearing age. Biological treatment in the form of anti-Tumor Necrosis Factor Alpha (anti-TNF) is considered safe during the first two trimesters of pregnancy. Anti-TNF treatment inhibits Vascular Endothelial Growth Factor (VEGF) and Placental Growth Factor (PlGF). VEGF and PlGF stimulate both angiogenesis and vasculogenesis during the placentation. Whether anti-TNF inhibits the blood vessel formation during the placentation, thereby obstructing the very key function of the organ, has yet to be investigated. Mothers treated with antiTNF during pregnancy bare smaller children than untreated women, regardless of disease activity.

We aim to investigate the impact of anti-TNF on placental function by three different approaches: clinically, by ultrasound and MRI of fetal growth and blood flow of the placenta; pathohistologically, via assessment of the blood vessel formation of the placenta; and genetically, by gene-expression levels of angiogenesis factors in fetal cells derived from maternal blood.

F02.08 Benjamin Kelly

CANCELLED

MORPHOLOGICAL LYMPHATIC CHANGES IN PATIENTS WITH A UNIVENTRICULAR CIRCULATION

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Background: A number of recent studies have underlined that the changed physiology of the univentricular circulation increases the risk of a number of lymphatic complications, such as protein losing enteropathy, chylothorax, plastic bronchitis and peripheral edema. Furthermore, the physiological changes, including the increased central venous pressure, have been proposed to induce morphological changes to the thoracic duct.

Aim: The current study aimed to examine the morphological characteristics of the thoracic duct of patients with a univentricular circulation.

Materials and Methods: The current study used T2-wighted MRI imaging to visualize the thoracic duct of included patients and controls. Overall, 53 patients with a univentricular circulation and 35 controls were enrolled and examined at two different centers (Aarhus, Denmark and São Paulo, Brazil). Both the straight length of the thoracic duct and the complete length of the thoracic duct were measured and divided to get a relative parameter of the tortuosity of the thoracic duct in the two groups. Additionally, the images were examined for existence of any notable lymphatic malformations or abnormalities.

Perspective: Examination and characterization of possible morphological changes in patients with a univentricular circulation may provide valuable new insight as to how the changed physiology of the univentricular circulation affects the lymphatic system. Thus, a more dilated and tortuous thoracic duct and the existence of more lymphatic abnormalities may provide new insight into to why these patients experience such a large number of complications related to their lymphatic system.

| F02.09 | Laura Boysen Dall | HELMINTH-MEDIATED MODULATION OF INFLAMMATORY RESPONSES IN SYSTEMIC LUPUS ERYTHEMATOSUS |

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Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease caused by complex immunopathological mechanisms. Existing treatment options are suboptimal, and new therapeutic strategies are needed. Therapeutic effect of parasitic worms (helminths) has already been suggested for several autoimmune diseases, and studies in murine models of SLE have shown promising results.

Objective: To evaluate possible immune-modulating effects of helminth products from Ascaris, Trichuris and Oesophagostomum on peripheral blood mononuclear cells (PBMCs) and serum from SLE patients ex vivo.

Methods: We stimulate PBMCs from SLE patients and healthy controls ex vivo with helminth products and, to enhance the pro-inflammatory activity in an SLE-like manner, we further stimulate with TLR-3, TLR-9 and lipopolysaccharide. Furthermore, we stimulate other PBMCs from healthy controls with helminth products and serum from SLE patients. Next, we characterize the inflammatory responses by analyzing the cytokine profile (e.g. CXCL-10, Gal-9, TNF-α, IL-6, IL-10), key lymphocyte subsets (e.g. T-cells memory subsets, T regulatory cell subsets, B regulatory cell subsets), early activation marker status (e.g. CD69), gene expression and specific proteins.

Results: The experiments will be conducted from autumn 2018 to spring 2019. We expect that the helminth products will suppress the pro-inflammatory immune responses in PBMCs and serum from SLE patients ex vivo and induce a regulatory environment.

Perspectives: If this study shows that helminths can reduce inflammation in SLE, this may pave the way for developing novel efficient drugs based on helminth products.

| F03.01 | Mathias Kaas Ollendorff | THE ALZHEIMER'S DISEASE RISK-FACTOR SORLA IS IMPLICATED IN THE AETIOLOGY OF ANXIETY |

CANCELLED

M.K. Ollendorff

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Anxiety disorders are the most prevalent psychiatric disorders and are the cause of significant patient morbidity and socioeconomic cost. We recently found mice lacking the Vps10p-domain receptor SorLA to have reduced anxiety-related behaviour, whereas mice lacking the candidate anxiety gene GDNF showed increased anxiety. However, the implication of SorLA in the aetiology of anxiety is far from clear. To further elucidate SorLA's role in anxiety, we investigated patient samples as well as behavior of transgenic mice. Here we report that anxiety patients show increased SorLA concentration in their serum, a characteristic unique to this psychiatric disorder. Furthermore, we show that SorLA overexpression under the TH promoter results in anxiety-related behaviour in the elevated

plus maze, and that complete loss of SorLA can rescue the anxiety phenotype of GDNF heterozygotes. Taken together, our data supports a role for SorLA in the aetiology of anxiety, and we propose additional research strategies to characterize the implication of SorLA in the neuronal circuitry underlying the disorder.

F03.02   Malene Overby   DISCOVERY OF NOVEL INTERACTING PROTEINS OF THE SORTILIN RECEPTOR - MECHANISTIC INSIGHTS INTO THE REGULATION OF A KEY PROTEIN INVOLVED IN NEUROLOGICAL AND PSYCHIATRIC DISORDERS

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The sortilin receptor stands out as a protein that is increasingly recognized for its involvement in a number of psychiatric and neurological disorders, including depression and Alzheimer's disease. Sortilin is involved in endocytosis, trafficking and sorting of a variety of receptors and ligands, including neurotrophins, which are processes highly coordinated to modify neuronal function and contributing to the mechanisms of synaptic plasticity. However, the signals and proteins involved in organizing and regulating sortilin-mediated targeting of cargo proteins are poorly understood. In preliminary work, we used the yeast two-hybrid system to identify novel interacting proteins of sortilin, which may potentially regulate sortilin-mediated functions. We isolated three interacting proteins, which have previously been associated with mechanisms underlying Alzheimer's disease, thus pointing at sortilin as a potential central mediator of molecular processes controlling Alzheimer's disease pathology. The PhD project is aiming to characterize these newly discovered interactions and their functional impact on sortilin function and on Alzheimer's disease related mechanisms. The project utilizes molecular, biochemical, cellular, proteomics and advanced imaging techniques to characterize these newly discovered interactions with sortilin. Considering the emergence of protein-protein interactions as a promising direction for innovative medicine involving small-molecule inhibitors or stabilizers, the results may have implications for the development of new therapeutic interventions in Alzheimer's disease.

F03.03   Helene Honoré   TRACKING ACTIVITIES OF PATIENTS WITH ACQUIRED BRAIN INJURY WITH ACCELEROMETRY

H. Honoré

Hammel Neurorehabilitation Centre and University Research Clinic & Department of Clinical Medicine, Aarhus University

This presentation covers an integrated PhD plan that span over 4 years and will result in 5 publications. The main idea is to measure physical activity in patients with acquired brain injury using accelerometry.

Data will be collected at Hammel Neurorehabilitation Centre and University Research Clinic and in patients' home environment after discharge.

Factors affecting changes in activity patterns and physical activity of patients with ABI are identified in a systematic literature review. Accelerometer-based data will be analysed using an algorithm to identify a selection of functional parameters essential for independent living, such as walking, sitting and standing, and activity transitions are developed and utilised for the target population. First, the algorithm is validated using video as gold standard. Secondly, it is applied in a large-scale mixed methods rehabilitation study to assess physical activity during the discharge transition phase with consecutive recruitment of up to 300 patients over a period of 1 year. The association between physical activity level and established influential factors from the review is identified, with follow-up after 3 and 12 months. Patients' activity balance is visualised after an observation period of 2 days (also repeated at follow-up), and their experienced activity balance is explored with qualitative in-depth interviews. The association between physical activity level and quality of life and satisfaction of occupation is established with consideration for habitual sedentary lifestyle.

F03.04   James Isaac Lubell

SEEING IS BELIEVING: HOW NEURAL OSCILLATIONS OF THE RETINA AND CORTEX TOGETHER MEDIATE HUMAN VISION

J. Lubell, S. Dalal

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The goal of my project proposal is to establish that retinal function is concurrent and reciprocal with cortical activity. Recent research strongly suggests that the retina itself is more causally active in shaping cortical responses than previously believed. Work by my supervisor, Sarang Dalal, implies that the high-frequency electrical responses to stimuli in the human retina drive and shape corresponding cortical responses. Using neurophysiological imaging and signal processing methods, retinal high-frequency oscillations will be examined in relation to their cortical counterparts. Using a new method called retinocortical coherence in conjunction with conduction timing, Electroretinography (ERG), and Magnetoencephalography (MEG), I will be able to demonstrate how and when cortical oscillatory activity is inherited from the retina. A first experiment will investigate how properties of retinal response are directly evident in cortical responses to the same stimuli. This will be followed by an experiment that will probe the inverse, that is, whether the cortex has a causal influence over retinal functions. A final experiment will limit possible critique by demonstrating that healthy cortical oscillations are necessarily inherited from healthy retinal functions. The end result will be a first for basic research, that is, an accurate account of how the retinal response drives cortical oscillations. Proof positive of a reciprocal relationship will challenge and expand working definitions and models of oscillatory activity in the brain; ultimately showing that neural oscillations of the retina and cortex together mediate human vision.

F03.05   Asbjørn Johan Krom-Thaysen

THE NUCLEAR ANATOMY AND FIBER CONNECTIONS OF THE GÖTTINGEN MINIPIG SEPTUM

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Background: Alzheimer's patients have a well-known degeneration of the forebrain's septal nuclei (SeN) cholinergic neurons. Targetting the cholinergic system by either drugs or neuromodulatory methods is currently used as symptomatic treatment. In the pursuit for effective therapy, large animal models can validate such treatments prior to human trials. Thus, more knowledge of the minipig cholinergic system is needed.

Aim: This study aims to describe in detail the septal anatomy and connectivity in the Göttingen minipig (GM) brain.

Methods: Firstly, 5 GM brains were embedded, sectioned and sliced coronally, horizontally or sagittally. The sections were immunohistochemically stained using anti-ChAT ab and Nissl. Subsequent microscopic analysis elucidated the septal anatomy. Secondly, 6 GMs were sedated, intubated, anaesthetized, and MRI scanned. Using a stereotaxic surgical technique, neuronal tracers were injected in the SeN. A mixture of the anterograde BDA and the retrograde FlouroGold tracers was injected into the GMs' SeN. 4 weeks later, the GMs were euthanized and their brains removed. Afterwards, the distribution of the tracers was visualized and described. Lastly, the tracing study will be compared with MRI derived tractography.

Results: The GM's SeN is bordered laterally by the lateral ventricles, dorsally by corpus callosum, rostrally by the subcallosal gyrus and hippocampal continuation, and ventrally by the n. accumbens, ant. commissure, preoptic area and ant. hypothalamus. The SeN is made of 4 sub-complexes; the lateral, medial, ventral and posterior septal complexes. The septal anatomy and connectivity will be described in detail at PhD Day 2019.

F03.06   Davide Ligato   CAN MUSICAL TRAINING CHANGE HUMAN SENSORY PERCEPTION? A COMPARISON BETWEEN RHYTHMIC SINGERS, CLASSICAL SINGERS, AND NON-SINGERS

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Background and Aims: Humans continuously adjust their own vocal production based on their auditory feedback and making predictions about future states of the system, which facilitates motor preparation and production. After auditory-motor interactions have been sufficiently tuned to generate almost no auditory error, the associations between somatosensory signals become correlated with both the auditory feedback and the corresponding motor commands. Consequently, trained singers rely more on somatosensory feedback and motor predictions, emphasizing the role of body perception in music production. Thus, the aim of the current study was to investigate to what extent musical skill development and accumulated musical training enhance internal body (i.e., interoceptive) awareness, and whether physical fitness is able to influence those responses.

Methods: Three groups of 20 persons - classical singers (CS), rhythmic singers (RS), and non-singers (NS) - underwent a behavioral interoceptive accuracy measure (heartbeat discrimination), Musical Ear Tests (MET), auditory discrimination tests (frequency/rhythm), and tactile sensory thresholds tests. All participants completed an online questionnaire assessing their individual musical and physical training.

Preliminary results: MET analysis with 60 participants (age: 18-60 years, average: 31 years) showed a significant increase in correct responses in both CS and RS compared to NS (ANOVA, $p < 0.05$) for melody tests, while only RS performed significantly better that NS on rhythmic tests (ANOVA, $p < 0.05$). Data on interceptive accuracy are currently being analyzed and will be correlated with both musical and physical training.

F03.07   Rune Rasmussen   DYNAMIC SPEED-DEPENDENT ENCODING OF MOTION DIRECTION IN MOUSE VISUAL CORTEX

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Detecting the direction of motion of an object is essential for our representation of the visual environment. The final steps of this computation, carried out by the visual system, occur in the cerebral cortex. A substantial fraction of neurons in the visual cortex are thus direction tuned, exhibiting the greatest response for a neuron's preferred motion direction and lesser responses for other directions. However, the detailed neural circuit mechanisms that endow cortical neurons with the ability to encode the direction of motion of an object are not fully understood. To address this issue, we used in vivo two-photon calcium imaging to record the activity of thousands of individual neurons in the primary visual cortex (V1) and the extrastriate rostrolateral (RL) and posteromedial (PM) cortical areas in mice. We found that a distinct subpopulation of direction tuned neurons in V1 and RL dynamically shift their preferred motion directions as visual motion speed increases. Such speed-dependent modulation of motion direction preferences were markedly impaired by the ablation of specific direction tuned cells in the retina; were exclusive to neurons in cortical layer 2/3; and specific to cortico-cortical projections from V1 to RL. This work, for the first time, reveals that the preferred motion direction of cortical neurons is not static, but dynamic, depending on the speed of visual motion and governed by bottom-up signals originated in the retina.

F03.08   Bardia   THE OPIOID SYSTEM PLAYS A ROLE IN COGNITIVE PROCESSES AND
          Varastehmoradi   DEPRESSION

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Introduction: The endogenous opioid system is known to modulate emotional and cognitive processing (e.g. perception, attention, memory and learning). Furthermore, it is well established that mood level influences cognitive functions. Thus, negative cognitive affective bias (CAB) is a hallmark of depression, and investigating the pathophysiology underlying this behavior offers a novel approach to depression research and development of novel antidepressants. Importantly, over the last few years, rodent models of CAB have been validated.

Aim: To study the role of kappa opioid receptors (KOR) in CAB.

Methods: Female Sprague Dawley rats in affective bias task (ABT) learnt two independent substrate-reward associations during discrimination learning sessions under vehicle or treatment conditions. Affective bias of corticosterone (CORT) and the KOR agonist U50,488, expressed as % choice bias, was measured during a preference test, where the two previously rewarded substrates were presented together and the rats' preferences tested over 30 trials. Subsequently, we tested the effect of the KOR antagonist, DIPPA, on CORT-induced negative bias in this paradigm.

Results: Both U50,488 and CORT significantly reduced % choice bias in the ABT. Furthermore, DIPPA completely abolished CORT-induced negative affect.

Conclusion: Establishing a role for the KOR in CAB furthers our understanding of the regulation of emotional and cognitive processes by the opioid system. Our data support the notion that the KOR is a therapeutic target for treatment of impaired cognitive function and mood level.

Keywords: cognitive affective bias, opioid system, depression

F03.09 Meet Sanjaykumar Jariwala

DEVELOPING A METHOD TO IDENTIFY THE INPUTS DURING ACTIVATION OF DIFFERENT MEMORY CIRCUITS

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Direct activation of a specific subpopulation of neurons can contribute to behavioral plasticity within the network. However, many techniques prove to activate neural circuits in efficient ways, but setting up an activity-dependent system to genetically map neurons and their connections would represent a significant progress. To achieve this aim, I am developing a technique that can selectively activate the inputs coming from different regions of the brain in an activity-dependent way. I develop this technique working on two different memory circuits: Reward memory and Fear memory. The reward memory circuit was activated by self-administration of cocaine, and fear memory was triggered by classical fear conditioning method. I have used the immediate early gene promoter (IEG) Fos in transgenic mice, which can selectively activate the neurons using Cre-lox recombination. My preliminary data demonstrate proof of concept for this approach by defining the inputs to the ventral tegmental area and the basolateral amygdala. Thus, my novel approach is able to dissect complex brain circuits with unprecedented resolution allowing investigation of neuronal plasticity and wiring in detail.

F04.01   Cœcilie Deisting   INCREASED PLASMA LEVELS OF SOLUBLE T-CELL IMMUNOGLOBULIN AND
Skejø   MUCIN DOMAIN 3 (TIM-3) IN EARLY RHEUMATOID ARTHRITIS CORRELATE
WITH DISEASE ACTIVITY AND PROGRESSION

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Background: Checkpoint inhibitors are important for the outcome in
autoimmune diseases. In this study, we investigated the checkpoint
inhibitor T-cell Immunoglobulin and mucin domain 3 (Tim-3) and its role in
rheumatoid arthritis (RA).

Methods and material: Plasma from early RA (eRA) patients were
analysed by ELISA for soluble Tim-3 (sTim-3) at baseline (n=98), after 3
months (n=96) of treatment and after 12 months of treatment (n=93).
sTim-3 levels in eRA were compared with levels in healthy volunteers (HV)
(n=44). Correlation between sTim-3 and 2 years of clinical data, including
DAS28CRP and Joint Space Narrowing (JSN) etc., were analysed. Plasma
and synovial fluid (SF) from chronic RA patients (cRA) (n=17) were also
analysed. All data are expressed as mean [95%CI].

Results: eRA patients had higher sTim-3 plasma levels (8763 pg/ml,
[7925;9600]) compared with HV (4145 pg/ml, [3537;4754], $p<0.0001$).
sTim-3 in eRA decreased in 3 months (6961 pg/ml, [6315;7607],
$p<0.0001$), and the decrease was inversely correlated with JSN progress
after 24 months of treatment (rho=-0.224, $p<0.05$). In SF, sTim-3 levels
were increased (42922 pg/ml, [31587;54258]) compared with plasma
levels in eRA ($p<0.0001$) and cRA (5557 pg/ml, [4120;6994], $p<0,0001$).

Conclusion: This study shows that plasma levels of sTim-3 are elevated in
eRA and that decrease in plasma levels upon the first 3 months of
treatment correlates with future disease activity and progression in terms
of DAS28CRP and JSN. Levels of sTim-3 are increased in SF, supporting
local production at the major site of pathology.

F04.02   Selim Kilic   A PROSPECTIVE STUDY OF HIGH-RESOLUTION ULTRASOUND IN LOWER
EXTREMITY NERVES IN PATIENTS WITH COMMON FIBULAR COMPRESSION
NEUROPATHY AND IN HEALTHY CONTROLS

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With high-resolution ultrasound (HRUS), it is possible to examine structural
nerve parameters. HRUS has been implemented clinically in the
diagnostic work up of some upper extremity neuropathies, but the benefit
of using HRUS in the diagnosis of lower extremity neuropathies calls for
further elucidation.

The objective of our study is to establish HRUS reference material of lower
extremity nerves and to investigate the intra- and inter-examiner reliability

of those measurements. Furthermore, we aim to examine the usage of HRUS in common fibular compression neuropathies (CFCN) and its correlation with electrophysiological findings.

The study is a prospective controlled single-blinded study. 20 patients with CFCN and 50 controls will be included. Respectively 20 and 10 controls will be re-examined to assess the intra- and inter-rater reliability.

Preliminary results based on 13 controls and 13 patients with CFCN have been gathered at this point. A significant increase in the cross-sectional area (CSA) of the common fibular nerve is found when comparing the symptomatic side in patients to a matched side in controls, and a significant increase is found when comparing the symptomatic side to the asymptomatic side in patients.

In perspective, HRUS measurements of lower extremity nerves may be useful in determining the presence and severity of common fibular compression neuropathy and may thereby serve as a supplementary diagnostic tool in the routine work-up of these diseases. Furthermore, the reference material will lay the basis for further research on high-resolution ultrasound of lower extremity nerves.

F04.03   Sebastian Skejø   PREDICTING THROWING VELOCITY USING ACCELEROMETERS

CANCELLED

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Introduction: A recent study showed that the development of shoulder injuries relates to sudden increases in handball training load. However, due to methodological limitations, handball training load was quantified as playing time instead of a shoulder-specific measure, such as the number and velocity of throws made by a player. The purpose of this project was to develop a predictive model for estimating throwing velocity using only a wrist-mounted accelerometer.

Materials and Methods: We recruited 8 females and 11 males. Participants performed 25 throws of varying type and intensity. During each throw, we recorded position of the hand and ball using 3-D motion capture. We calculated throwing velocity as the slope of the ball's time-position curve at the time of ball release. Simultaneously, an accelerometer measured the acceleration of the wrist. We constructed a linear model with log (Acceleration) as the independent variable and throwing velocity as the dependent variable. To check the model performance, we used leave-one-subject-out cross-validation. Finally, we fitted the model to the complete dataset.

Results: The model performance was satisfying (mean error of the cross-validation = -0.0054 m/s, 95% prediction interval: [-4.4; 4.4] m/s). The final model equation was: Velocity = 6.4*log(Acceleration)-4.9.

Conclusion: The developed predictive model showed satisfying performance in estimating throwing velocity using only a wrist-mounted

accelerometer, but future studies still need to determine how to count the number of throws before the total throwing-related training load can be determined.

F04.04 Andreas Steenholt Niklassen

OLFACTORY TRAINING AND BRAIN PLASTICITY

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The sense of smell is a unique part of the nervous system. It is deeply integrated in the human brain and is strongly connected with emotion, memory, behavior and pleasure. The sense of smell acts as a warning detector saving us from dangers; previously by avoiding the predator at the savanna, and today saving us from spoiled food or fire and gas accidents. The sense of smell is deeply involved in the pleasure of food, and patients with loss of smell sensation (olfactory impairment) lose the pleasure of food, reducing quality of life (QoL).

By this PhD, we wish to revolutionize the QoL for patients with olfactory impairment. By exploiting brain plasticity, the sense of smell is rehabilitated by olfactory training. At the same time, the underlying processes are unraveled using novel and advanced brain imaging methods.

About 20% of the population suffers from olfactory impairment, and 5% has complete loss of olfactory function. Up to 30% of these patients reports severe distress on QoL and depression. However, neural plasticity of the olfactory system enables treatment through repeated stimulation.

The scope of this PhD is to identify the optimal training paradigm as a treatment and improve QoL in patients suffering from olfactory impairment. Simultaneously, we investigate how olfactory training affects the brain by detection of structural changes between primary and secondary olfactory regions in the brain; this new knowledge can help predict the potential and success of rehabilitation training in the future.

F04.05 Simon Meyer Lauritsen

EARLY SEPSIS DETECTION WITH DEEP LEARNING ON EHR EVENT SEQUENCES

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Background: Sepsis is a clinical condition involving an extreme inflammatory response to an infection and is associated with high morbidity and mortality. Without intervention, this response can progress to septic shock, organ failure and death. For every hour that treatment is delayed, the risk of mortality increases. Early identification of sepsis is, therefore, important for a positive outcome.

Methods: We constructed predictive models for sepsis detection and performed a register-based cohort study on patients from four Danish municipalities. We used event sequences of raw electronic health record (EHR) data from 2013 to 2017. In total, we consider 25,622 positive (SIRS

criteria) sequences and 25,622 negative sequences. The number of potential predictor variables in raw EHR data easily exceeds 10,000 and can be challenging for predictive modeling due to this large volume of sparse, heterogeneous events. Traditional approaches have dealt with this complexity by curating a limited number of variables of importance; a labor-intensive process that may discard a vast majority of information. In contrast, we consider a deep learning system constructed as a combination of a convolutional neural network (CNN) and long short-term memory (LSTM) network. Importantly, our system learns representations of the key factors and interactions from the raw event sequence data itself.

Results: Our model predicts sepsis with an AUROC score of 0.8678 at 12 hours before actual treatment was started.

Conclusion: We have presented a novel approach for early detection of sepsis that has more true positives and fewer false negatives than existing alarm systems without introducing domain knowledge into the model.

F04.06   Josefine Slater   STEADY-STATE BONE PHARMACOKINETICS OF RIFAMPICIN COMBINED WITH MOXIFLOXACIN DETERMINED BY MICRODIALYSIS

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Background: Orthopedic implants improve the quality of life for many patients by relieving pain and restoring their ability to move. Unfortunately, some develop an implant-associated infection (IAI), which can be a devastating complication requiring multiple surgeries and prolonged antimicrobial therapy. IAIs are characterized by bacterial biofilm formation, which are complex aggregates of microorganisms exhibiting remarkable resistance to antimicrobials. The antimicrobial agent, rifampicin, displays biofilm degrading properties, and rifampicin-containing combinations have, therefore, become the standard in treatment guidelines for staphylococcal IAIs. However, the optimal dosage and frequency remains undetermined.

Aim: To evaluate bone and soft tissue pharmacokinetics of orally administered Rifampicin combined with Moxifloxacin using microdialysis in a porcine model.

Materials and Methods: 18 pigs will be included in the study and allocated to three study groups (n=6). All pigs will be treated orally until steady state is achieved, receiving either Rifampicin, Moxifloxacin or Rifampicin and Moxifloxacin. The antimicrobial bone concentrations will be determined by microdialysis, a minimally invasive, probe-based method that allows for precise and continuous sampling of unbound water-soluble molecules from the investigated tissue.

Perspective: This study is the first of its kind to assess bone concentrations of Rifampicin and Moxifloxacin by microdialysis. Accordingly, this study has the potential to evaluate existing treatment regimens and

F04.07 Peter Uhrbrand

PROLONGED OPIOID USE: A FREQUENT COMPLICATION AFTER SURGERY?

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Patients are often prescribed morphine or another morphine-like drug (opioids) at hospital discharge after surgery. Patients are then meant to step down the treatment as the postsurgical pain decreases. However, several studies, especially from the United States, have shown that an increasing number of patients continue using opioids even months to years after surgery, hence developing addiction and possible abuse behavior.

This year, the international literature concludes that 'persistent opioid use can be considered one of the most common complications after elective surgery'. Denmark is among those countries with the highest level of consumption per capita. One may, therefore, fear that a large number of the patients undergoing surgery in Denmark (640,344 in 2016) continue using opioids months or years after surgery.

This PhD study encompasses four studies aiming to clarify the extent of the problem after selected surgical procedures and to identify causes and risk factors. In addition, we will propose future preventive actions for clinical practice.

F04.08 Olesya Svystun

IMAGE-STITCHING ARTEFACTS IN CCD-BASED CEPHALOGRAMS AND THEIR ASSOCIATION WITH HEAD MOVEMENT: AN EX VIVO STUDY USING THREE CEPHALOSTATS

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Aim: To assess the presence and severity of image-stitching artefacts (i.e. stitching lines) in cephalograms acquired using CCD-based image sensors and their association with head movement.

Material and Methods: A human skull was mounted on a robot simulating five head movements (antero-posterior translation/lifting/nodding/lateral rotation/tremor), at three distances (0.75/1.5/3 mm). Three cephalostats (OR, D-3, and D-4) were used to acquire skull cephalograms (exposure time 17 seconds) during the predetermined movements (54 images/unit) and no-motion (28 images/unit). A trained observer assessed the presence of image-stitching artefacts, misalignment between the anatomical structure display on each side of the stitching line, and if the image-stitching artefact interfered with orthodontic landmarks.

Results: No image-stitching artefacts were visible in OR images. Image-stitching artefacts were visible in 28 (D-3, 100%) and 2 (D-4, 7%) no-motion images. For D-3, there was a misalignment of anatomical structures over the stitching line in 39% of the no-motion images.

Regarding examinations with movement, 53 (D-3, 98%) and 14 (D-4, 26%) images presented image-stitching artefacts. For D-3, artefacts were associated with a misalignment of anatomical structures in 87% of the cases. For D-4, misalignment of anatomical structures was present in 22% of the cases and were mostly caused by large (3 mm) head movements. Image-stitching artefacts did not interfere with orthodontic landmarks.

Conclusion: The image sensor and head movements have an effect on the presence and severity of image-stitching artefacts in CCD-based cephalograms.

F05.01   Elena Dudukina   VAGINAL BLEEDING IN EARLY PREGNANCY AND RISK OF OCCULT CANCER

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Objective: An association between cancer and the coagulation abnormalities has been established. We investigated whether vaginal bleeding (VB) before the 20th gestational week is associated with occult cancer.

Methods: This cohort study was set in Denmark. We linked data from the Medical Birth Registry, the National Patient Registry, the Danish Cancer Registry, and the Civil Registration System. The VB cohort comprised women with a first-time hospital diagnosis of VB from 1 January 1978 through 30 November 2013. The comparison cohort included women from the general population with a pregnancy ending in a first-time birth or abortion. We followed the VB and comparison cohort from the discharge date after VB or pregnancy end, respectively, until an incident primary cancer, death, emigration, or study end, whichever occurred first. We computed indirectly-standardized incidence ratios (SIRs) of any and site-specific cancers with 95% confidence intervals (CIs).

Results: There were 105,192 women in the VB cohort. Median age at VB was 28.7 years and median follow-up was 17.0 years. During follow-up, 6581 women in the VB cohort had a cancer diagnosis. The SIR for any cancer was 1.0 (95% CI: 0.9-1.0). There was no increased cancer risk in the VB cohort within 6 months (SIR=0.9, 95% CI: 0.7-1.2), 6-12 months (SIR=0.8, 95% CI: 0.6-1.1), or more than 12 months (SIR=1.0, 95% CI: 1.0-1.0) of follow-up. VB was not associated with an increased risk of cancer of the breast (SIR=1.0, 95% CI: 0.9-1.1), uterine cervix (SIR=0.9, 95% CI: 0.8-1.0), ovary (SIR=1.0, 95% CI: 0.9-1.2), or uterus (SIR=0.9, 95% CI: 0.8-1.1).

Conclusion: Vaginal bleeding before the 20th gestational week is not associated with occult cancer.

F05.02   Andreas Ladefoged Ebbehøj   MORBIDITY AND MORTALITY IN PATIENTS WITH PHEOCHROMOCYTOMA: DANISH NATIONAL DATA OVER A PERIOD OF 40 YEARS

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Background: Pheochromocytomas and catecholamine-secreting para-gangliomas (PPGL) are rare catecholamine-producing tumors. Due to the rarity, limited data on prognosis exists. Here, we present national data on morbidity and mortality over a period of 40 years.

Materials and methods: We identified 502 PPGL patients diagnosed while alive in 1977-2016 in Denmark. Each patient was matched on age, sex and year of diagnosis with 100 controls. We used registry data to estimate the Charlson Comorbidity Index (CCI) score. Mortality rate-ratios (MRR) were calculated using Cox regression and adjusted for CCI at time of diagnosis. We performed subgroup analyses on clinical data, which was available for 174 PPGL patients.

Results: 45% of PPGL patients had a comorbidity index of 1 or more compared to 20% of controls (Wilcoxon rank test: p<0.001). Overall MRR for PPGL was 1.9 (CI95 1.7-2.3) compared to controls and 1.7 (CI95 1.5-2.1) when adjusted for CCI. For patients undergoing radical surgery (N=474, 94%), MRR was 1.8 (CI95 1.5-2.2) and 1.4 (CI95 1.2-1.7) when adjusted.

In our subgroup analyses (N=174), we found that patients diagnosed due to secondary hypertension had the highest mortality with a MRR of 4.3 (CI95 2.4-7.9, unadjusted), while patients diagnosed due to symptoms, hereditary PPGL, incidental findings and other reasons had mortality rates closer to the background population.

Conclusion: PPGL patients have a higher mortality compared to the background population, even if undergoing radical surgery and when considering their higher comorbidity index at diagnosis. These results indicate that radical surgery does not completely reverse the harmful effects of PPGL.

F05.03   Casper Gammelmark Muurholm

DOSE-GUIDED MOTION MANAGEMENT DURING LIVER RADIOTHERAPY DELIVERY USING REAL-TIME RECONSTRUCTED TUMOR DOSE-VOLUME HISTOGRAMS

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Background: The radiation dose of radiotherapy is shaped to the target, necessitating motion management which relies on geometrical informa-tion as a surrogate for the absorbed dose. Online, real-time dose recon-struction was recently made possible, allowing intra-treatment quality assurance based on delivered dose. This work presents a new framework that uses real-time dose reconstruction for treatment intervention.

Method: A computer program calculates the motion-including dose distribution and a time-resolved dose-volume histogram, DVH(t), of the tumor dose delivered so far in the treatment. The DVH(t) allows calculation of the minimum dose that has been delivered to 95% of the tumor (D95). The motion-induced reduction in D95 (DD95) is a clinically relevant measure of the tumor dose deficit, which was tested in simulations of 39 fractions of stereotactic body radiotherapy. First, ΔD95 for the full fraction was compared with the treatment planning system (TPS). Next, the time-resolved ΔD95 was used in simulated dose-guided treatments with treatment corrections performed if ΔD95 exceeded either 5% or 10%.

Results: The real-time calculated ΔD95 agreed with the TPS with an RMS error of 2.3%-points. The mean (range) of the final ΔD95 was 5.9%-points (1.0-26.2%-points) without corrections and 3.8%-points (1.0-10.0%-points), and 3.1%-points (0.6-9.5%-points) with dose-guided corrections using 10% and 5% ΔD95 thresholds, respectively. The mean number of corrections per fraction was 0.4 (10% threshold) and 1.1 (5%).

Conclusion: A new method for real-time motion-including dose evaluation was presented and used to simulate dose-guided corrections based on reconstructed tumor dose deficits.

F05.04 Frederikke Schønfeldt Troelsen

COLORECTAL NEOPLASMS IN NEW USERS OF LOW-DOSE ASPIRIN WITH LOWER GASTROINTESTINAL BLEEDING: A DANISH NATIONWIDE MATCHED CROSS-SECTIONAL STUDY

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Introduction: Colorectal cancer (CRC) is one of the most frequently diagnosed cancers. Lower gastrointestinal bleeding (LGIB) following use of low-dose aspirin may promote early detection of CRC and its precursors.

Aim: We examined possible differences in detection of CRC and colorectal polyps among new users and non-users of low-dose aspirin with LGIB.

Methods: For the period 2006-2013, we used Danish health registries to identify all new users of low-dose aspirin with a first-time hospital-based diagnosis of LGIB. Applying same eligibility criteria, we matched each new user with 5 non-users on age and gender at the date of the LGIB. We computed the prevalence and calculated crude and adjusted prevalence ratios (PRs) for colorectal polyps and CRC within 6 months after the LGIB comparing new users with non-users.

Results: We identified 1,038 new users and 5,190 non-users of low-dose aspirin with LGIB. We observed 220 polyps among new users and 950 polyps among non-users during the study period. New users had a slightly higher prevalence of colorectal polyps than non-users [PR = 1.15 (95% CI: 1.01-1.31)]. We observed 53 and 254 CRCs among new users and non-users, respectively. New users and non-users had a similar prevalence of overall CRC [PR = 1.03 (95% CI: 0.77-1.38)]. However, when stratifying on cancer location, we observed a lower prevalence of proximal [PR = 0.71 (95% CI: 0.35-1.43)] and rectal [PR = 0.85 (95% CI: 0.53-1.38)] cancers in new users compared to non-users.

Conclusion: These findings indicate that low-dose aspirin use may promote detection of gastrointestinal polyps in patients with LGIB.

F05.05   Erik Buch Jørgensen

DELIVERED DOSE RECONSTRUCTION BASED ON IN VIVO DOSIMETRY FOR PROSTATE BRACHYTHERAPY

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Purpose: The aim of the project is to investigate the dosimetric effect of positional offsets of the source in prostate BT.

Material and Methods: The actual delivered dose and dose volume histogram (DVH) parameters were reconstructed for 7 fractions of HDR prostate BT. The reconstruction was based on in vivo dosimetry (IVD) and compared to the treatment plans. The treatment plans were performed on MR images taken just before treatment. The IVD was performed using a dosimeter, based on a small luminescence crystal. The crystal was placed inside the prostate in a dedicated needle, and the dose rate was recorded during treatment. The measured dose rate patterns were transformed into positional offsets of the source through an in-house developed optimisation algorithm. The IVD reconstructed source positions were registered to the patient anatomy on the planning MRI and used to reconstruct the delivered DVH parameters. Delivered and planned DVH parameters were compared to investigate the effect of positional changes.

Results: The IVD-measured source positions reflected the uncertainty in the MR reconstruction. The resulting changes in the dose distributions lead to a mean±1SD fractional change of -0.2±0.1Gy in prostate D_{90}, -0.1±0.2Gy in urethra D_{2cm3}, 0.4±2.1% point in rectum $D_{2cm\ 3}$ and 0.1 ± 0.8 Gy in bladder D_{2cm3}. One needle was shifted 4 mm in the cranial direction into the bladder wall, which resulted in a bladder $D_{0.1cm3}$ of 22.8 Gy.

Conclusion: The dosimetric impact of movements and reconstruction uncertainties of the needles were clinically irrelevant, except in one case where the source entered the bladder wall.

F05.06   Simon Grund Sørensen

PREDICTING DNA REPAIR ERROR FROM MUTATIONAL PATTERNS IN WHOLE CANCER GENOMES AND EXOMES

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DNA damages are reversed through various DNA damage responses (DDR). Losing the function of one or more DDR typically causes an accumulation of mutations, leading to cell death or potentially cancer.

As each DDR mechanism repairs certain types of damages, we hypothesize that broken DDR can be identified by looking at patterns of mutations across the whole genome. We have found empirical support for this hypothesis in a pilot study focusing on structural variations across the cancer genome. Identifying DDR errors is a cornerstone in understanding the evolution of cancer, but it also provides therapeutic targets, which can be exploited by existing therapies, such as radiotherapy and systemic antineoplastic drugs.

This study aims to find recurrent patterns of mutations associated with different DDR errors. This is possible through analysis of ~2,600 whole cancer genomes from the PCAWG project and ~30,000 cancer exomes from TCGA, as well as other sources. Each sample will be annotated for DDR errors by searching for knockout mutations in repair genes. Dividing the cancer samples by DDR error makes it possible to search for mutation patterns, such as mutational signatures, structural variants and copy-number changes. Patterns will be stratified through machine learning algorithms, making it possible to detect DDR errors in novel samples. My pilot study has shown that even a subset of the mutational information, the structural variants, enables correct identification of up to ~85% of patients with deficient repair of double strand breaks in the DNA. This can provide a strong tool to support the choice of therapy, as it sensitizes the cancer to cisplatin and PARP inhibitors.

F05.07   Peter Preben
          Eggertsen

MEMANTINE, AN ALZHEIMER'S DRUG, WITH POTENTIAL FOR CANCER THERAPY

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Background: Memantine is a glutamate N-Methyl-D-aspartate (NMDA)-receptor antagonist used to treat Alzheimer's patients. The NMDA signaling pathway seems important in several cancer types. Therefore, memantine might have antineoplastic properties and could be an attractive drug for cancer treatment. The aim of this study is to evaluate the effect of memantine in different types of cancers.

Methods: An in vitro proliferation assay was performed in cervix (SiHa), prostate (DU145), head & neck (FaDu(DD)), and breast (MCF-7) human cancer cell lines. Cells were cultured in Petri dishes and exposed to 100 µM, 200 µM or 500 µM memantine for a duration of 24, 48 or 72 hours. The cells were then fixed in methanol and stained with toluidine blue. Lastly, the Petri dishes were digitalized using a document scanner, and the areas of stained cells were quantified as a measure of the proliferation using the computer software ImageJ.

Results: Memantine significantly inhibited the proliferation of the included cancer cell lines in a dose- and time-dependent manner, except for SiHa, which showed inconsistent results and is not suited for this assay. The results suggest that prostate cancer might be more sensitive to memantine, which is especially apparent after 72 hours of treatment.

Conclusion: The results show that memantine suppress proliferation. The next steps are to explore whether the NMDA receptor is present in these cancer types, and if memantine affects the clonogenic potential. This will be done by using PCR techniques and a clonogenic assay, respectively. If the results are promising, an in vivo experiment with mice will be included.

F05.08   Cathrine Fonnesbech Hjorth

GENETIC VARIATION IN TAXANE METABOLISM AND RISK OF BREAST CANCER RECURRENCE AND MORTALITY: A POPULATION-BASED COHORT STUDY IN DENMARK

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Background: Premenopausal breast cancer patients receive taxane-based chemotherapy as guideline treatment but treatment efficacy varies substantially between patients. Genetic variation in taxane metabolism may modify treatment efficacy - specifically the risk of disease recurrence and mortality.

Objective: To evaluate if women with reduced-function polymorphisms in genes encoding proteins responsible for taxane-metabolism have lower rates of breast cancer recurrence and mortality after taxane-based chemotherapy than their wildtype counterparts.

Methods: We will perform a cohort study nested in the Predictors of Breast Cancer Recurrence (ProBeCaRe) cohort (n=5,959). We have identified 2,635 premenopausal women aged 18-55 years diagnosed with stage I-III breast cancer during 2007-2011 who were candidates for taxane-based chemotherapy. Polymorphisms will be genotyped from archived primary tumors and information on covariates, recurrence and mortality will be assessed by linkage across Danish administrative registries. Patients will be followed from first taxane treatment until recurrence or death, emigration, 10 years, or end of study (25th September 2017). Cumulative incidence (%) and incidence rate per 10,000 person-years of recurrence and mortality according to genotype will be estimated using the Aalen-Johansen estimator. Adjusted hazard ratios and 95% confidence intervals for recurrence and mortality according to genotype will be calculated in Cox regression models.

Perspectives: Findings from this study will offer important insights on the association between genetic variants, treatment efficacy and breast cancer prognosis, and may ultimately aid treatment decision-making.

F06.01 Anna Sandager SUBCLINICAL VAGINAL INFECTIONS AND ADVERSE PREGNANCY
Hansen OUTCOME

CANCELLED

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Aim: We aimed to investigate if a) bacterial vaginosis and b) vaginal
colonization with the Chlamydia-like bacterium, Waddlia chondrophila,
are associated with increased risk of spontaneous abortion or
spontaneous preterm birth.

Background: Bacterial vaginosis (BV) has previously been associated with
preterm birth, but several studies have failed to show this association in
Scandinavian cohorts. Newer molecular methods might give a better
understanding of the believed association in a Danish setting. W. chondro-
phila is an intracellular bacterium of the Chlamydiales class. It has been
associated with abortion in bovines and may be involved in the etiology
of spontaneous abortion in humans.

Materials and methods: An ongoing prospective cohort study including
1400 unselected pregnant women enrolled at 12 weeks of gestation. We
obtained vaginal swabs and vaginal smears from all participants. The
vaginal smears were classified according to the Nugent criteria for BV. The
vaginal swabs will be examined for selected BV associated bacteria using
species-specific quantitative PCR assays. W. chondrophila will be
identified using PCR. Pregnancy outcomes were collected from the
electronic birth files.

Preliminary results: Among the unselected pregnant women, 5%
(57/1148) had BV (Nugent score ≥ 7) and 10% (114/1148) had
intermediate scores (Nugent score 4-6). Within this cohort, 4.6% (56/1218)
gave birth before 37^{+0} weeks of GA. This figure was 2.1% (3/144) among
those with BV and 5.3% (46/871) among women without BV (OR 0.38;
95% CI 0.12-1.24).

Results from PCR analysis for BV associated bacteria and Waddlia
chondrophila are pending and will be presented.

F06.02 Maria THE COST OF TREATED MENTAL DISORDERS: A RECORD-LINKAGE STUDY
Christensen BASED ON DANISH REGISTERS

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Background: Mental disorders are highly prevalent worldwide. The high
prevalence of mental disorders contributes much to societal costs
because of production loss, reduced income taxation, increased public
benefit payments plus direct treatment costs. In 2015, the Danish Health
Authority estimated that direct treatment costs and indirect social costs for
some mental disorders were substantial, but they excluded a wide range
of mental disorders. The results were based only on a yearly average over
a two-year period and did not include the implication of comorbidity
within mental disorders and general medical conditions. Consequently,

there is a significant gap in the literature concerning the societal costs of mental disorders in Denmark, and the true economic costs may be much greater than previously recognized. To guide policy-makers and health planners in the future and to ensure a more equitable distribution of resources, it is important that this topic be examined with modern economic and epidemiological methods.

Purpose: This project seeks to examine the following research questions: What are the aggregate costs for treated mental disorders and associated comorbidity in Denmark? Do these costs vary by number of disorders?

Material and methods: The project will exploit the possibilities of the Danish registers to calculate the costs for the entire population. Regression modelling will be used to compare the costs for exposed and unexposed to mental disorders using a matched cohort study design. The outcomes of interest are the aggregated costs and net costs (incremental costs) per disability-adjusted life year comparing people with and without mental disorders.

F06.03   Tara Ballav Adhikari

COMMUNITY-BASED MANAGEMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN NEPAL: STUDY PROTOCOL FOR A CLUSTER-RANDOMIZED CONTROLLED TRIAL

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Background: Chronic Obstructive Pulmonary Disease (COPD) is the second leading cause of death worldwide and in Nepal. The presence of risk factors like indoor and outdoor air pollution, a high prevalence of smoking and the lack of general awareness of COPD makes it a serious public health concern. According to Global Burden of Disease estimates in 2015, Nepal is among the top four countries in the world with the highest age-standardized Disability Adjusted Life Years (DALYs) rates lost due to COPD. However, no attempt has been made in Nepal to estimate its burden and address the disease at the community level.

Method: The proposed intervention aims to measure the burden of COPD, to assess the magnitude of modifiable risk factors of COPD including tobacco smoking and indoor air pollution, and to spread awareness on the modifiable risk factors led by Female Community Health Volunteers (FCHVs) trained on COPD. An open-label, two-group, community-based, cluster-randomised controlled trial will be implemented in the semi-urban area of Pokhara-Lekhnath Metropolitan city of Nepal. The estimated sample size of the prevalence and intervention study will be 1,508 and 1,302, respectively.

Outcome: Prevalence of COPD and risk factors will be estimated using a population-based survey. Change in lung function (FEV1 and FEV1/FVC) will be measured as the primary outcome, and the change in magnitude of modifiable risk factors will be measured as secondary outcomes.

Perspective: This study will estimate the burden of COPD and generate evidence to mobilise community health workers for COPD prevention and management at the community level in Nepal.

F06.04   Alexandra Lahtinen

DNA METHYLATION IN BLOOD LEUKOCYTES AS PUTATIVE BIOMARKERS FOR INSUFFICIENT SLEEP

A. Lahtinen

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Sufficient sleep is essential for our health. Lack of sleep affects basic physiological processes, including systemic inflammatory reaction, and leads to an increased risk for various psychiatric and somatic disorders. The identification of key players of molecular processes associated with curtailed sleep could improve the assessment and early prevention of the long-term health risks. Though sleep is precisely regulated, the detailed mechanisms of the brain processes during sleep remain unclear. As DNA methylation plays a crucial role in the regulation of cell gene expression, the study of differentially methylated positions (DMPs) might enhance our understanding of the molecular mechanisms underlying insomnia. We performed epigenome-wide association studies for two independent cohorts of males to identify DMPs in whole blood samples of individuals suffering from insufficient sleep or diagnosed with shift-work disorder. Genes corresponding to DMPs common for both cohorts were analyzed by various tools to investigate affected biological pathways in individuals lacking sleep. The data analysis showed that processes related to neuronal plasticity and neurodegeneration were compromised in people lacking sleep, as well as there is an enrichment of genes involved in visual processing and regulation of circadian rhythm. The majority of these DMPs were hypomethylated in cases in both cohorts, as compared to controls, suggesting that insufficient sleep may be associated with loss of DNA methylation. The results give evidence for the importance of the epigenetic regulation in mediating both brain-specific and systemic stress caused by compromised sleep and diurnal rhythm.

F06.05   Charlotte Hansen Gabel

ARE WE CHANGING HEALTH WHILE RE-MODELLING SOCIAL HOUSING ESTATES? AN INTERDISCIPLINARY MULTIPLE SITES FOLLOW-UP STUDY IN DENMARK

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Aim: A global endeavour is to construct high-performance, carbon-neutral and sustainable buildings by creating new or re-modelling the building mass. These will fail if excellent indoor air quality (IAQ) is not accomplished as well as energy targets. People spend nearly 16H in their homes and are thus highly exposed to IAQ. Research has established that poor IAQ affects the occupants' comfort and health. The aim of BE-READY and ReVALUE is to study how different re-modelling scenarios are linked to occupants' health, comfort and IAQ in a holistic approach.

Method: Three sites with rental property blocks from Aarhus and Odense in Denmark, where re-modelling is planned, were included. All measures

were conducted in the occupants' homes before and after re-modelling. A total of 561 interviews were collected before re-modelling; 345 during the heating season and 218 during the non-heating season. A total of 29 anthropological interviews were completed when either heating or non-heating measures were available. Temperature (C°), carbon dioxide (ppm), dampness (absolute and relative humidity) and microbiome (electrostatic dust collector) were measured for 14 days. The survey entailed demographics, health, comfort, IAQ and perception of the home. Anthropological interviews included in-depth conversation about demographics, re-modelling, everyday practices and perception of the home.

Perspective: The interdisciplinary projects seek to advice the industry and policy-makers about building construction, IAQ and health, and to identify and quantify added value from improvements of health to perform as economic arguments to justify more extensive re-modelling of building.

F06.06 Maria Louise Gamborg

CLINICAL DECISION-MAKING IN GERIATRIC EMERGENCY MEDICINE: CURRENT PRACTICE AND TRAINING OBJECTIVES FOR RESIDENTS

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Background: Clinical Decision Making (CDM) refers to the cognitive processes involved in making procedural decisions in the clinical setting. The ability to make clinical decisions in Emergency Departments (ED) is challenged by high levels of uncertainty and task complexity. With a growing group of geriatric patients in emergency medicine, new challenges arise, especially for the many Post-Graduate Year 1 (PGY1) residents in the EDs. PGY1 residents are sparsely trained for and often have little experience with geriatric patients. They may, therefore, risk overlooking the complexities occurring in geriatric medicine (e.g. comorbidities, polypharmacy, etc.), which may increase the risk of errors.

Aim: This project will investigate similarities and discrepancies between residents' and experienced physicians' CDM in geriatric emergency medicine to identify and develop training objectives for PGY1 residents.

Design: The overall design is a mixed methods study. Firstly, we will systematically review the empirical literature on CDM in the ED. Secondly, a Think-Aloud protocol analysis will investigate geriatric encounters in clinical and simulated settings. This investigation will aim to describe the decision-making processes that are currently applied by experienced physicians and PGY1 residents when consulting and treating geriatric patients in the ED. Finally, a Danish nationwide questionnaire study will be conducted focusing on PGY1 residents' training needs. This needs analysis will be supported by expert interviews.

Results: After completion of all three studies, the synthesis of evidence will lead to the development of specific training objectives aiming to improve the ED care for geriatric patients.

| F06.07 | Aamod Dhoj Shrestha | CAN LAY HEALTH WORKERS HELP INCREASE CERVICAL CANCER SCREENING UPTAKE IN NEPAL? |

A.D. Shrestha

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Cervical cancer is the major cause of cancer death among women in Nepal. The International Agency for Research on Cancer (IARC) estimated in 2012 the age standardized incidence rate of cervical cancer to be 19.0 per 100,000 and the age-standardized mortality rate to be 12.0 per 100,000 in Nepal. Cervical cancer screening is one of the most effective tools for early diagnosis and prevention.

The World Health Organization (WHO) and Alliance for Cervical Cancer Prevention (ACCP) recommend that countries, areas, or institutions seeking to initiate or strengthen cervical cancer screening programs should consider introducing or expanding Visual Inspection with Acetic acid (VIA) until more appropriate and affordable HPV-based tests become available. A single-visit approach with VIA and cryotherapy is safe, acceptable, feasible and is a potentially efficient method of cervical-cancer prevention in low-resource settings.

Using data from the World Health Survey 2003, Bruni L et al estimated in 2017 that only 2.8% of Nepalese women aged 25-64 years had participated in cervical cancer screening with Pap smear. There is a need for appropriate, cost-effective and sustainable interventions to increase VIA screening uptake in Nepal. Mobilizing Female Community Health Volunteers (FCHVs) to encourage and educate women to participate in VIA screening through home visits could be an appropriate community-based intervention, which could be tested in a cluster-randomized controlled trial. A community-based, culturally tailored education intervention delivered by non-clinicians, such as FCHVs, can play a key role in increasing the cervical cancer screening uptake in Nepal.

| F06.08 | Karin Rosenkilde Laursen | ACUTE HEALTH EFFECTS OF FINE AND ULTRAFINE PARTICLES IN INDOOR AIR - A HUMAN EXPOSURE STUDY AMONG VULNERABLE POPULATION SUBGROUPS |

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Background: People spend up to 90% of their life indoors, and the way we live and behave in our homes has substantial effects on our health and well-being. However, little is known about acute health risks from indoor air pollution.

Objectives: To examine the association between indoor particulate air pollution from e-cigarettes, candles and cooking, and health and well-being.

Methods: Two separate studies will be conducted. Study A will investigate acute health effects of exposure to particles generated by e-cigarettes among patients suffering from chronic obstructive pulmonary disease. Study B will investigate acute health effects of exposure to particles generated by candles and cooking among asthmatic adolescents. The

exposures are arranged at the climate chamber facilities. For both studies, a randomized, double-blind crossover design is applied. Exposures of interest are fine and ultrafine particles emitted from vape from e-cigarettes, lit candles, and cooking compared to exposure to clean air. The clean air and particle exposure sessions are identical, except for the air quality. Participants are exposed at rest for four hours inside the climate chamber. Selected objective and subjective health outcomes are measured at baseline and at follow-up at predefined time points. Measures include: subjective symptoms, respiratory outcomes, and blood samples. Inflammatory markers in exhaled air are used as the primary outcome in both studies. Data will be analysed using mixed models taking both time and exposure into consideration. Secondary, hypotheses will be analyzed using multivariate analysis of variance for repeated measurements.

CH.01   Kristina Laugesen

CLINICAL INDICATORS OF IATROGENIC ADRENAL INSUFFICIENCY FOLLOWING DISCONTINUATION OF ORAL GLUCOCORTICOID THERAPY: A SELF-CONTROLLED CASE SERIES

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Background: Biochemical adrenal insufficiency induced by glucocorticoid treatment is prevalent, but data on the clinical implications are sparse. We investigated clinical consequences of glucocorticoid-induced adrenal insufficiency after oral glucocorticoid cessation.

Methods: We conducted a population-based self-controlled case series utilizing medical registries. In this design, each individual serves as their own control allowing event rates to be compared as a function of time and treatment. Clinical indicators of adrenal insufficiency were defined as diagnoses of gastrointestinal symptoms, hypotension, cardiovascular collapse, syncope, hyponatremia, and hypoglycaemia. We included 286,680 persons who discontinued long-term oral glucocorticoid treatment. We defined five risk periods and a reference period (before treatment): period 0 (on treatment), withdrawal period (1 month before and after cessation), followed by three consecutive 2-month risk periods after withdrawal (periods 2-4).

Results: Incidence rate ratios comparing the withdrawal period with the reference period were 2.5 [95% confidence interval (CI): 1.4 - 4.3] for hypotension, 1.7 (95% CI: 1.6 - 1.9) for gastrointestinal symptoms, 2.2 (95% CI: 0.7 - 7.3) for hypoglycemia, and 1.5 (95% CI: 1.1 - 2.0) for hyponatremia. During 7 months of follow-up, the rates of hypotension and gastrointestinal symptoms remained elevated.

Conclusion: Oral glucocorticoid withdrawal was associated with adverse outcomes attributable to adrenal insufficiency. Our study underscores the need for future research to establish evidence-based clinical guidance on management of patients who discontinue oral glucocorticoids.

CH.02   Thomas Lassen   EFFECT OF PAROXETINE ON LEFT VENTRICULAR REMODELING IN AN IN VIVO RAT MODEL OF MYOCARDIAL INFARCTION

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Background: Left ventricular (LV) remodeling following a myocardial infarction (MI) involves formation of reactive oxygen species (ROS). Paroxetine, a selective serotonin reuptake inhibitor, acts as antioxidant. We investigated whether paroxetine reduces myocardial ROS formation and LV remodeling following a MI.

Methods: In a total of 32 Wistar rats, MI was induced by a 30-minute ligation of the left anterior descending artery followed by 7 or 28 days reperfusion. During the 28 days of reperfusion, LV remodeling was evaluated by magnetic resonance imaging (MRI) and echocardiography (n=20). The susceptibility to ventricular tachycardia was evaluated prior to sacrifice, and hearts were excised for histological assessment. Myocardial ROS formation was measured after 7 days of reperfusion in separate groups (n=12).

Results: Diastolic LV volume, evaluated by MRI ($417\pm60\mu L$ vs. $511\pm64\mu L$, $p<0.05$) and echocardiography ($515\pm80\mu L$ vs. $596\pm83\mu L$, $p<0.05$) as well as diastolic LV internal diameter evaluated with echocardiography ($7.2\pm0.6mm$ vs. $8.1\pm0.7mm$, $p<0.05$), was lower in the paroxetine group than in controls. Furthermore, myocyte cross sectional area was reduced in the paroxetine group compared with controls ($277\pm26mm^3$ vs $354\pm23mm^3$, $p<0.05$), and ROS formation was reduced in the remote myocardium (0.415 ± 0.19 normalized to controls, $p<0.05$). However, no differences in the presence of fibrosis or myofibroblasts were observed. Finally, paroxetine reduced the susceptibility to ventricular tachycardia (induced in 2/11 vs 6/8 rats, $p<0.05$).

Conclusion: Paroxetine treatment following MI decreases LV remodeling and susceptibility to arrhythmias, probably by reducing ROS formation.

CH.03   Kristian Juul-
         Madsen   CLEARANCE OF EXTRACELLULAR AGGREGATED α-SYN THROUGH COMPLEMENT RECEPTOR 3

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Introduction: Increasing evidence implicates inflammation as a major cause of neuronal loss in many neurodegenerative diseases. Among the most prevalent neurodegenerative diseases is Parkinson's disease (PD). α-Synuclein (α-syn) is a protein closely related to the pathology of PD. The hallmark of PD is the formation of aggregated α-syn into plaques called Lewy bodies. These Lewy bodies are often associated with inflammation of the nerve tissue. Inflammation is caused primarily by microglia cells, which express several β_2 integrins.

Results: This project has identified α-syn as an interaction partner for complement receptor 3 (CR3,$\alpha_M\beta_2$). Cell lines with recombinant expression of $\alpha_M\beta_2$ integrins and primary human monocytes proved able to adhere to surfaces coated with α-syn. Monocytes have been used as a model system for the microglia cells in the brain and showed similar binding to α-syn coated surfaces.

A binding site for α_M I-domain in α-syn has been defined with Surface Plasmon Resonance, constituted by 10 residues (2 - 11) deleted from wild type α-syn. This peptide has been shown to significantly influence the binding of α_MI-domain. Activation of β_2 integrins has been shown to influence the internalization of quantum dots coupled to filament α-syn with imaging flow cytometry. Furthermore, nanoparticle tracking analysis has shown that activation of β_2 integrins can deplete large particles from the medium of the cells.

Conclusion: Integrin $\alpha_M\beta_2$ has proved to be a plausible target for microglia interaction with α-syn. Activation of this integrin could prove to have a protective effect against neurodegeneration by enhancing α-syn clearance.

CH.04   Nanna-Sophie   HOST GENETICS, INNATE IMMUNE RESPONSES, AND CELLULAR DEATH
         Brinck Andersen PATHWAYS IN POLIOMYELITIS PATIENTS

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Background: Poliovirus (PV) is one of the most studied viruses. Despite efforts to understand PV within the host, fundamental questions remain unanswered. These include the mechanisms determining the progression to viremia, the pathogenesis of neuronal infection, and paralysis in only a minority of patients. Because of the rare disease phenotype of paralytic poliomyelitis (PPM), we hypothesize that a genetic aetiology may contribute to the disease course and outcome.

Methods: We used whole-exome sequencing (WES) to investigate the genetic profile of 18 patients with PPM. Functional analysis were performed on peripheral blood mononuclear cells (PBMCs) and monocyte-derived macrophages (MdMs).

Results: We identified rare variants in host genes involved in interferon signalling, viral replication, apoptosis, and autophagy. Upon PV infection of MdMs, we observed a tendency towards increased viral burden in patients compared to controls, suggesting reduced control of PV infection. In MdMs from patients, the IFNb response correlated with the viral burden.

Conclusions: We suggest that genetic variants in innate immune defences and cell death pathways contribute to the clinical presentation of PV

infection. Importantly, this study is the first to uncover the genetic profile in patients with PPM, combined with investigations of immune responses and viral burden in primary cells.

CH.05   Ted Carl Kejlberg   CHANGE IN INTRACEREBRAL MEASURES DURING THE FIRST 24 HOURS
         Andelius   AFTER HYPOXIA-ISCHEMIA IN HYPOTHERMIC AND NORMOTHERMIC
                             NEWBORN PIGLETS

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Background and aim: Hypoxic ischemic encephalopathy (HIE) is a major cause of neurological impairment and death in children. Therapeutic hypothermia (TH) is currently the only treatment for HIE. Brain damage after hypoxia ischemia (HI) is a dynamic process. Therefore, when quantifying damage through MRI (fMRI) and spectroscopy (MRS), timing is of utmost importance. The onset of secondary cell death after HI has not previously been described in detail. The aim of this study was to quantify changes in intracerebral metabolism after HI in hypothermic and normothermic piglets, and healthy controls.

Materials and Methods: 24 piglets (<24 hours old) were anaesthetized. Three devices were installed into the left parasagittal cortex: 1) a probe measuring intracranial pressure, 2) a probe measuring blood flow, temperature, and oxygen tension, and 3) a microdialysis catheter measuring lactate, glucose, glycerol, and pyruvate. HI was induced for 45 minutes. After HI, piglets were randomized to either TH (33.5 °C) or normothermia (38.5 °C). Controls were normothermic. Measurements were acquired hourly for the first 24 hours.

Results: Four animals died due to circulatory failure after the HI insult, resulting in 5 controls, 8 normothermic, and 7 hypothermic piglets. We present preliminary data from microdialysis measures. Secondary cell death was not detectable in lactate measures. However, normothermic piglets showed a secondary increase in glycerol, which peaked at 18 hours and was absent in TH-treated animals.

Conclusion: From these microdialysis data, the optimal time point for MRI/MRS is at the peak of the secondary cell death at approximately 18 hours after HI.

CH.06   Filomena   NEW CHALLENGES FOR ALZHEIMER'S DISEASE THERAPY: INSIGHTS FROM
         Iannuzzi   APP TYR$_{682}$ RESIDUE

F. Iannuzzi

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Alzheimer's disease (AD) is a severe neurodegenerative condition characterized by progressive decline of cognitive and behavioral functions. To date, the diagnosis remains still difficult, and there is no

strategy to prevent or to delay the progression of the neurodegenerative processes.

The major hallmarks of AD are extracellular accumulations of insoluble deposits of amyloid beta (Aβ) peptide generated by sequential proteolytic processing of β-amyloid precursor protein (APP) by β and γ secretase enzymes. These events occur in the acid compartments, such as late endosome and lysosome, and strictly depend on APP endocytosis and trafficking inside neurons. APP neuronal compartmentalization depends on the phosphorylation/dephosphorylation of Tyr_{682} residue located on $_{682}YENPTY_{687}C$- terminal domain of APP.

We previously showed an increase in APP Tyr_{682} phosphorylation levels in neurons from AD patients, and we identified Fyn Tyr kinase as a crucial player in mediating such aberrant APP Tyr_{682} phosphorylation.

Fyn is overexpressed/overactivated in AD neurons and selectively triggers APP Tyr_{682} phosphorylation and promotes amyloidogenic APP cleavage to generate intracellular AICD fragment and extracellular Aβ peptides. Fyn inhibitors, as well as Tyr kinase inhibitors, prevent either APP Tyr_{682} phosphorylation or the extracellular accumulation of Aβ peptides. All together, this evidence points to APP Tyr_{682} residue as a potential target for early AD diagnosis as well as for a promising and more suitable personalized intervention in patients with increased APP Tyr_{682} phosphorylation levels.

CH.07 Anders Kindberg Boysen

CELL-FREE DNA AND HEPATIC ARTERIAL INFUSION OF OXALIPLATIN PLUS SYSTEMIC CAPECITABINE FOR PATIENTS WITH COLORECTAL CANCER LIVER METASTASES

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Background: Hepatic Arterial Infusion (HAI), where the cytotoxic agents are administered intrahepatically, is an experimental treatment option for patients with colorectal cancer liver metastases (CRCLM). We aimed to investigate the level of cell-free DNA (cfDNA) in patients with CRCLM receiving HAI with oxaliplatin and systemic capecitabine.

Methods: Patients were treated according to a single arm phase II study, including patients with CRCLM from November 2004 to May 2010 who were not eligible for any other standard local treatment. Therapy comprised intrahepatic infusion of oxaliplatin 100 mg/m2 every second week with concomitant oral capecitabine 3500 mg/m2 every second week for up to 12 cycles. A pre-treatment plasma sample was used for quantification of cfDNA by a modified fluorescent assay. Survival was analyzed by the Kaplan-Meier method and Cox multiple regression analysis.

Results: Baseline plasma samples were available from 62 patients. The majority of patients were males (61%), the median age was 61.3 years (range 40.8-74.8), and the distribution of colonic/rectal cancers was

68%/32%. The median level of cfDNA was 0.92 ng/µL (95% CI 0.84-1.00). Plasma cfDNA was significantly lower (0.91 ng/µL, 95% CI 0.76-0.98) in patients who achieved an objective response compared to non-responders (1.79 ng/µL, 95% CI 0.99-2.57, p=0.02). Patients with a baseline value of cfDNA above the 75th quartile had a median overall survival of 2.4 years (95% CI 0.7-2.8) compared to 3.9 years (95% CI 2.8-5.9) for patients below the 75th quartile (p=0.02).

Conclusions: Patients with a low baseline level of plasma cfDNA had a favorable outcome from treatment with HAI and capecitabine for CRCLM.

CH.08   Julie Nelly Christensen

MEGALIN REGULATES PROGRESSION-RELATED EVENTS IN MELANOMA CELLS BY CONTROLLING DIFFERENTIATION STAGE AND EMT STATUS

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The molecular changes promoting progression of melanoma cancer to metastatic disease remain poorly understood, and currently no established biomarkers can predict melanoma metastasis at early stages of the disease. The endocytic receptor Megalin is highly expressed in cutaneous melanomas and metastases hereof and frequently expressed in cultured melanoma cell lines. The relationship between Megalin expression and the metastatic potential of melanoma cells is currently being investigated. This is approached in a dual fashion using cell-based model systems:
1) by modulating the Megalin expression in melanoma cells using CRISPR/Cas9 technology, and 2) by stimulating melanoma cells with cytokines, like TGFβ, known to induce epithelial-to-mesenchymal transition (EMT) and promote a more migrative and invasive phenotype. It is hypothesized that Megalin modulates events in melanoma cells, which control their differentiation status, and that modulation of Megalin expression will alter the metastatic potential of melanoma cells. Decreased Megalin expression in our melanoma cell models leads to expressional changes, corresponding to EMT induction, and a less adhesive and more migrative phenotype. The findings point to Megalin as modulator of crucial signaling events in melanoma cells, controlling their differentiation status and their adhesive migrative and invasive abilities, thus promoting a more metastatic phenotype. These discoveries are presently under investigation in primary melanomas, and preliminary findings show loss of Megalin in zonal areas of melanomas reported to have been metastatic.

CH.09   Line Kolding

SSRI EXPOSURE DURING PREGNANCY AND FETAL CARDIAC FUNCTION

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Objectives: Selective Serotonin Reuptake Inhibitors (SSRIs) use during pregnancy has been steadily increasing. Changes in cardiomyocytes and

cardiac function after intrauterine exposure to SSRIs have been shown in animal studies. The objective of this study was to examine the fetal cardiac function in human pregnancies exposed to the SSRI sertraline compared to unexposed pregnancies.

Methods: Fetal echocardiography was performed at gestational week 25/0 - 26/6 in 15 women using sertraline 50-150 mg during pregnancy and 30 healthy controls without any use of medication. The fetal cardiac function was assessed by: annular plane systolic excursion (TAPSE/MAPSE) with 2D M-mode and 4D eSTIC M-mode, E/A index, and Myocardial Performance Index (MPI).

Results: Overall, we found no differences in fetal cardiac function between the sertraline exposed and the unexposed, e.g. MAPSE: 4.03 mm vs. 4.18 mm (p=0.41), MPI: 0.50 vs. 0.49 (p=0.35), respectively. Serum levels of sertraline in exposed participants ranged from 33-266, median 92 nmol/l.

Conclusions: Sertraline, in clinically relevant doses, does not seem to have major impact on fetal cardiac function at mid-gestation.

CH.10   Mai-Britt Hägi-Pedersen

MULTICENTRE RANDOMISED STUDY OF THE EFFECT OF AN EARLY IN-HOME PROGRAMME (PREHOMECARE) FOR PRETERM INFANTS USING VIDEO CONSULTATION AND SMARTPHONE APPLICATIONS COMPARED WITH IN-HOSPITALCONSULTATIONS

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Introduction: Although premature infants and their parents are discharged earlier to inhomecare programmes, how to optimally support parents during this transition remains unknown. The aim of this study is to compare the effects of early inhomecare (PreHomeCare), including video consultations and mobile applications, with those of inhospital consultations.

Method: Parents of premature infants were randomized to either intervention or control group via simple randomization. Families started PreHomeCare when the inclusion criteria were approved. The intervention group received a smartphone application and video system and a babyweight to use under PreHomeCare. The control group included hospital consultations at the hospital. Both groups had planned consultations 2-3 times/week.

Data collection was at inclusion, end of PreHomeCare and one month after discharge, and data were collected from self-reported questionnaires and from hospital records. Primary outcome is proportion of exclusive breastfeeding one month after discharge, secondary outcome are parent/ infant interaction (MABISC) and families' feeling of confidence in caring for their infant (KPCS).

Results: Data collection ended in October 2018. 189 infants were included (88 in intervention group, 101 in control group). Response rates for the intervention/control group were at baseline questionnaire 82%, at discharge 68%, one month after 68%. Preliminary results between intervention and control group show no significant difference on

proportion of exclusive breastfeeding one month after discharge 59%/63%, and on the secondary outcome; MABISC (Mean 10.5, SD 3.1/Mean 11.3, SD 3.4) and KPCS (Mean 42.6, SD 2.4/Mean 41.5 SD, 4.0)

CH.11   Louise Nissen   **EFFECT OF INTRODUCING AN IMAGING BASED RULE OUT STRATEGY FOR CORONARY ARTERY DISEASE IN PATIENTS WITH INTERMEDIATE RISK ON THE UTILIZATION OF INVASIVE CORONARY ANGIOGRAPHY**

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Background: Diagnosing coronary artery disease in patients with atypical symptoms and intermediate risk continues to be clinically challenging and resource demanding. The 2013 ESC guidelines for diagnosing stable coronary artery disease recommend imaging modalities as a first line diagnostic approach. However, specificity of cardiac CT is low, and introduction of cardiac CT as a first line examination has been assumed to substantially increase invasive angiography activity.

Purpose: To investigate whether a change in diagnostic strategy from first line treadmill testing to a primarily cardiac CT-based strategy would lead to an increased utilization of invasive angiography and a consequently lower revascularization rate per invasive angiography.

Methods: We used data from the West of Denmark Heart Database, covering approx. 2.8 mill. inhabitants. All cardiac CT scans performed in the region are reported to this database.

Results: The number of cardiac CT scans almost doubled from 2011 to 2015, while the number of invasive angiographies remained substantially unchanged from 2011 to 2015. The revascularization rate increased from 30% to 35.9%.

Conclusion: For patients with low to intermediate risk of CAD, a strategy of an imaging-based rule-out algorithm can be implemented without an increasing demand for futile invasive angiography.

CH.12   Mathias Johan Holmberg   **GUIDELINE REMOVAL OF ATROPINE AND SURVIVAL AFTER IN-HOSPITAL CARDIAC ARREST**

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Introduction: Atropine was removed from the 2010 ACLS guidelines as routine management of non-shockable cardiac arrest, although the evidence to support or refute the use of atropine is lacking. Whether removing atropine from the guidelines has affected survival remains unknown.

Methods: Using the Get With The Guidelines®-Resuscitation registry, we included adult patients with an index in-hospital cardiac arrest between 2006 and 2015. An interrupted time-series analysis was used to compare survival before (pre-exposure) and after (post-exposure) introduction of the 2010 guidelines. A difference-in-difference approach was used to compare the interrupted time-series results between non-shockable and shockable cohorts to account for guideline changes unrelated to atropine.

Results: We included 20,499 non-shockable and 3,968 shockable cardiac arrests. Patient characteristics were similar between the pre-exposure and post-exposure period. Atropine was used for 8,653 (87%) non-shockable and 680 (35%) shockable cardiac arrests in the pre-exposure period and 3,643 (35%) non-shockable and 320 (16%) shockable cardiac arrests in the post-exposure period. The change over time in survival from the pre-exposure to the post-exposure period was not significantly different for the non-shockable compared to the shockable cohort (risk difference: 2.0% [95%CI: -0.8, 4.8] per year, p = 0.17). Likewise, the immediate change in survival after introducing the guidelines was not different between the cohorts (risk difference: 3.5% [95%CI: -2.6, 9.7], p = 0.26).

Conclusions: The removal of atropine from the 2010 guidelines was not associated with a change in survival.

CH.13   Trine Ørhøj Barkholt   BENCH TESTING OF A DRUG-ELUTING BIORESORBABLE MAGNESIUM SCAFFOLD AND COMPARISON WITH POLYMERIC SCAFFOLDS AND METALLIC DRUG-ELUTING STENTS

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Background: Permanent metallic drug-eluting stents (DES) are the treatment of choice for percutaneous coronary intervention. However, DES treated patients have a late annual incidence of adverse events of a few percent indefinitely. Fully bioresorbable scaffolds (BRS) may reduce this incidence, but early experience has been mixed. Knowing the mechanical properties of each type of BRS is crucial to ensure safe and effective deployment.

Methods: In a systematic bench evaluation, we compared the mechanical properties of the first metallic BRS, Magmaris, with the poly-L-lactic acid (PLLA) BRS, Absorb and DESolve, and with the DES MultiLink 8/Xience Xpedition and Promus Premier.

Results: Acute recoil was largest for the Magmaris and Absorb BRS, but was countered with post-dilatation with balloons 0.5 mm larger than nominal size. The 3.0 mm Magmaris BRS did not fracture after post-dilatation with non-compliant (NC) balloons at diameters up to 4.4 mm. Safe threshold for expansion of a 3.0 mm Absorb BRS was 3.7 mm. For side branch dilatation through stent cells, no fractures were observed with 3.0 mm NC balloons up to nominal pressure. Mini-kissing balloon inflation

with two 3.0 mm NC balloons was performed up to 17 atm without fracture, except for an outlier. Longitudinal strength was similar for Magmaris and Absorb BRS and less than for MultiLink 8 and Promus Premier.

Conclusion: The Magmaris BRS showed improved acute mechanical properties compared with the Absorb BRS, but was not as advantageous as the permanent DES.

CH.14   Jacob Gammelgaard Schultz

TERLIPRESSIN INCREASES SYSTEMIC AND LOWERS PULMONARY ARTERIAL PRESSURE IN EXPERIMENTAL ACUTE PULMONARY EMBOLISM

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Background: Patients suffering from high-risk pulmonary embolism (PE) are challenged by increased pulmonary arterial pressure (mPAP) and systemic hypotension. We aimed to investigate if terlipressin induces systemic vasoconstriction and pulmonary vasodilation in a porcine model of acute PE.

Methods: Three large PEs were administered to 12 pigs (60 kg). Animals then received four increasing concentrations of either terlipressin (n=6) or vehicle (n=6). The effects were evaluated in vivo at baseline, after PE and after each concentration by invasive hemodynamics and blood analysis. Isolated pulmonary arteries were evaluated ex vivo in a myograph.

Results: PE caused a 4-fold increase in pulmonary vascular resistance (PVR) compared to baseline ($p < 0.0001$). Terlipressin caused an increase in mean systemic blood pressure ($+28 \pm 5$ mmHg, $p < 0.0001$) and systemic vascular resistance ($+1320 \pm 143$ dynes, $p < 0.0001$) compared to vehicle. Contrary, terlipressin caused a decrease in mPAP (-6.5 ± 1.8 mmHg, $p = 0.005$) and a trend towards a decrease in PVR (-83 ± 33 dynes, $p = 0.07$). Ex vivo, terlipressin caused relaxation of pulmonary arteries (17 ± 4 %, $p = 0.0007$). Terlipressin caused a decrease in cardiac output (-2.5 ± 0.5 L/min, $p < 0.0001$) and an increase in plasma lactate ($+2.7 \pm 0.2$ mmol/L, $p < 0.0001$), indicating systemic hypoperfusion. S100b, a biomarker of cerebral ischemia, remained unchanged, suggesting preserved cerebral perfusion ($+0.17 \pm 0.11$ µg/l, $p = 0.51$).

Conclusion: Terlipressin caused systemic vasoconstriction and pulmonary vasorelaxation in a porcine model of acute PE. As a net effect, cardiac output declined; this was probably due to a predominant systemic vasoconstrictor effect of terlipressin.

CH.15   Marie Veje Knudsen

FEASIBILITY OF IMPROVING PATIENTS' SELF-MANAGEMENT SKILLS WITHIN A MULTIDISCIPLINARY AND SUPERVISED CARDIAC TELE-REHABILITATION PROGRAMME

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Background: Cardiac rehabilitation (CR) is a crucial element to improve patients' prognoses, self-management and health behaviour after being diagnosed with heart disease. Cardiac telerehabilitation (CTR) may expand access to CR. However, knowledge is needed on whether CTR can improve patients' self-management skills.

Aim: To compare self-management skills in patients completing CTR with patients completing hospital-based CR after end of intervention and at follow-up six months after end of intervention.

Methods: A feasibility study was conducted among patients with ischaemic and heart valve disease referred to CR at Aarhus University Hospital, Denmark. Within a 12-week programme, 25 patients attended home-based CTR and 55 attended hospital-based CR. Self-management was assessed using the 13-item Patient Activation Measure (PAM) concerning knowledge, skills and confidence in self-management, with a higher score indicating a higher level of self-management.

Results: At baseline, the mean PAM score was not significantly different in the two groups (p=0.353). After end of intervention, the mean PAM score improved with 4.5 points (95% CI: 1.6-8.0) among patients in home-based CTR, and with 4.3 points (95% CI: 2.7-5.7) among patients in hospital-based CR. At six-month follow-up, the between-group mean difference in PAM score was 3.6 (95% CI: -2.3-9.4) in favour of the patients participating in CTR.

Conclusion: Patients participating in CTR improved their self-management skills similar to patients participating in hospital-based CR. Thus, home-based CTR and hospital-based CR seemed equally efficient in improving self-management skills among patients with heart disease.

CH.16   Kasper Glerup Lauridsen   RESUSCITATION TEAM CHALLENGES DURING IN-HOSPITAL CARDIAC ARREST: A PROSPECTIVE MULTICENTER STUDY

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Background: Measured quality of cardiopulmonary resuscitation (CPR) is often substandard compared to guideline recommendations during adult in-hospital cardiac arrest.

Aim: To investigate the self-perceived CPR quality, teamwork and communication and to identify the most frequently reported challenges experienced during in-hospital cardiac arrest.

Methods: Prospective multicenter study including self-reported data from resuscitation attempts treated by cardiac arrest teams in 5 Danish hospitals. Following each resuscitation attempt, all cardiac arrest team members were questioned by an online questionnaire.

Results: Of 491 cardiac arrests, the cardiac arrest team was actively involved in 387 cases (79%), and 1,639 responses were collected (response rate: 72%). Overall, 87% agreed or partially agreed that the CPR quality was optimal, 89% agreed or partially agreed that the team work was optimal, and 88% agreed or partially agreed that the communication was optimal. The most frequently reported challenges experienced were: too many health care providers present in the room (26%), health care providers poorly placed relative to each other in the room during CPR (16%), lacking space for resuscitation equipment (16%), problems finding resuscitation equipment (14%), and problems finding the location (5%). Challenges with too many healthcare providers in the room were associated with the amount of non-team members present ($P<0.001$), but not the number of members on the cardiac arrest team ($p=0.70$).

Conclusion: During in-hospital resuscitation, most team members perceive that CPR quality, teamwork, and communication are optimal. However, challenges during CPR are not uncommon.

CH.17   Maria Riedel   A NEW MOUSE MODEL FOR RAPID IDENTIFICATION OF KEY FACTORS DRIVING PROSTATE CANCER PROGRESSION AND INVASIVENESS

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Prostate cancer is among the most frequently diagnosed malignancies and the second leading cause of cancer-related death in men worldwide. Until now, its heterogeneity has been a major challenge in the establishment of good in vivo models for fast validation of potential driver genes.

We successfully introduced a new prostate cancer mouse model based on CRISPR/Cas9 technology, ensuring multiplexed gene editing.

In this model, specific in vivo gene editing is obtained in murine prostate epithelium cells of a transgenic mouse strain, harboring the CRISPR associated protein 9 (Cas9) endonuclease, by transduction with an adeno-associated virus (AAV) carrying multiple single guide RNAs (sgRNA).

Genetically different viral constructs were designed expressing different combinations of sgRNAs targeting Pten, as main driver in prostate cancer, Trp53 and the AP1 transcription factor subunits JunB and c-Fos.

Since viral transduction occurs only in a few cells, edited cell clones can clonally expand, as seen in the human scenario, and simultaneous gene knockouts reflect tumor heterogeneity.

Results were obtained three to nine months post-injection and gave insight in whether or not a gene is crucial for the tumor development in a specific tissue. Histological sections of murine prostates revealed increased proliferation, increased AKT activation as well as invasiveness (after 6 months post-injection) in cells transduced by AAV. Based on this model, gene function, pathway alterations, fundamental characteristics as well as human relevance will furthermore be validated in vitro in JunB and c-Fos KO cell clones and in human biopsy samples.

CH.18   Malou Eva Maria Pinto Barbosa

LONG-TERM FUNCTIONAL OUTCOMES FOLLOWING EARLY SECONDARY REPAIR OF OBSTETRIC ANAL SPHINCTER INJURY AND ITS IMPACT ON QUALITY OF LIFE

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Introduction: A secondary sphincter repair following obstetric sphincter injury may be necessary if the results are unsatisfactory after the primary repair. Traditionally, reconstruction of the anal sphincter has been performed not earlier than three to six months after delivery. The aim of this study was to assess the postoperative complications and the long-term functional outcomes following an early secondary sphincter repair.

Material and method: This is a retrospective cohort study of 51 women who underwent an early secondary sphincter repair following an obstetric anal sphincter injury 3-21 days after delivery from 1991 to 2016 at Aarhus University Hospital. Functional outcome was assessed by a self-reported questionnaire comprising the Wexner Score and the St. Mark's incontinence score. To evaluate impact on quality of life, the symptom specific validated Fecal Incontinence Quality of Life Scale (FIQLS) was used.

Results: 34 women (66.7%) completed the questionnaire. Median age at follow-up was 42.2 years with a median follow-up time of 6.8 years (range 0.8-20.3). No complication was experienced by 44% of the women. The most prevalent complication was a recto-vaginal fistula, which occurred in six women. At follow-up, mean Wexner score was 5.4 (range 0-17). The women reported being fully continent for liquid and solid stools in 59% and 73%, respectively. The overall symptom specific quality of life score was high in all four items of the FIQLS. Women with a Wexner score $\geq$ 9 had a significantly lower quality of life in all domains (p<0.005)

Conclusion: An early repair can be performed within 21 days after delivery with acceptable functional outcomes.

CH.19   Yutao Lu   BLADDER FIBROSIS: EARLY MOLECULAR CHANGES AFTER COMPLETE URETHRAL OBSTRUCTION

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Introduction: Acute complete bladder outlet obstruction (BOO) can be seen in pediatric patients. The aim of this study is to elucidate the molecular changes in the bladder after acute infravesical obstruction.

Materials and Methods: Sixty male and female mice were randomly divided into Control, Sham and BOO groups with 10 mice in each group. Urethral obstruction was achieved by 6-0 suture tying around mid-urethra. In the Sham group, only skin incision was made without further dissection. The bladder tissue was harvested 24 hours after the procedure. Western blot and QPCR analysis were performed for related fibrosis markers. Colonic tissue was analysed to evaluate a possible systemic reaction due to the surgical stress.

Results: Our data indicated upregulation of fibrotic markers (TGF-beta, pSMAD2/3, pSMAD1/5, alpha-SMA) and downregulation of the anti-fibrotic protein (BMP-7) in both BOO male and female mice. Fibronectin protein showed a tendency to increase in BOO male mice, while it was significantly decreased in female BOO mice compared to the Control group. Gender differences concerning histological damage and BMP-7 expression distribution were also observed in the BOO group. In addition, the sham group showed increased bladder weight, TGF-beta expression combined with BMP-7 downregulation compared to the control group. In colonic tissue, TGF-beta and interleukin-1 did not show significant differences between groups.

Conclusion: Acute BOO induces a series of early molecular changes, including a significant fibrotic reaction. The gender differences observed in this study need further investigation. Single skin incision seems to cause molecular changes in the bladder.

CH.20   Thomas Falstie-Jensen   DIAGNOSING CHRONIC PERIPROSTHETIC INFECTION OF THE SHOULDER WITH 18F-FDG PET CT

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Aim: To assess the value of 18F-FDG PET-CT (PET-CT) in diagnosing chronic periprosthetic joint infections (PJI) of failed shoulder arthroplasties.

Background: Chronic PJI can be difficult to diagnose. The role of functional imaging in the preoperative evaluation is not established. Dual-isotope scintigraphy is regarded as gold standard in diagnosing PJI. However, as it is complicated to perform, PET-CT has been suggested as an alternative.

Methods: Two centres participated in this prospective study. Patients referred with a failed shoulder arthroplasty and consenting to a PET-CT were included. Two experienced otho-radionuclear consultants reviewed the scans according to best practice, as no guidelines exist to evaluate PET-CT in failed shoulder arthroplasty. Infection was defined as growth in at least three of five peroperative biopsies. Sensitivity and specificity are presented centre-specific due to differences in the interpretation of PET-CT.

Results: We included 81 patients with both a PET-CT and microbial diagnosis. The most predominant organism isolated was C. Acnes (17 of 20 infections).

At Centre One, 5 scans were true positive, 26 were true negative, 10 were false positive, and 10 were false negative. This corresponds to a sensitivity of 0.33 (95%CI: 0.09-0.57) and a specificity of 0.72 (95%CI: 0.58-0.87).

At Centre Two, zero scans were true positive, 24 scans were true negative, 1 scan was false positive, and 5 scans were false negative. This corresponds to a sensitivity of 0.0 (95%CI: 0.0-0.0) and a specificity of 0.96 (95%CI: 0.88-1.0).

Conclusion: This study suggests that PET-CT has limited usefulness in diagnosing chronic PJI in failed shoulder arthroplasties.

CH.21   Alon Illy Schneider Hait

THE GENETIC BASIS FOR RECURRENT HERPES VIRUS MENINGITIS - A ROLE FOR DEFECTIVE AUTOPHAGY?

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Mollaret's meningitis is a rare disease characterized by recurrent episodes of HSV-2 meningitis reactivation. In this study, we hypothesize that inborn genetic defects in a patient's DNA may contribute to the instillation of the disease. Patients were identified, and blood was collected both for DNA isolation, which was subjected to whole exome sequencing, and for isolation of PBMCs. Patients' PBMCs were stimulated with the nucleic acid analogs poly(dA:dT) and poly(I:C) and infected with 3 MOI of HSV-2. After incubation, total RNA was harvested, and RT-qPCR for antiviral and pro-inflammatory gene expression was performed. Monocyte-derived macrophages from patients were stimulated with dsDNA and infected with HSV-2 and Polio virus (PoV), and cell lysates were subjected to immunoblotting for LC3-I and LC3-II. Conversion of LC3-I to LC3-II represents autophageal flux. No significant impairment in cytokine gene expression was observed. In a subgroup of 7 patients, we have identified a group of gene variations common to the autophagy pathway. A defect in autophagy will show a decreased LC3-I to LC3-II conversion in immunoblotting, such clear features were not observed in any of the patients.
We argue that autophagy will be biologically redundant in circulating macrophages or primary immune cells. Therefore, we continued with

characterization of autophagy in neuronal-like cell lines with or lacking autophagy genes. Autophagy of viral particles was demonstrated in different studies; viral autophagy can be either pro-viral or antiviral. Our study is ongoing, and we believe that we will characterize autophagy in human neural-like cells and shed some light on its involvement in RBLM.

CH.22   Pernille Glahn   CGMP IN HEALTHY ADULTS
         Wernlund

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Background: Some dairy proteins have been ascribed health beneficial effects. One of these, the whey protein, casein glycomacropeptide (CGMP), has shown to possess probiotic and anti-inflammatory effects in animal models of colitis and in cell studies. Bovine CGMP is a small peptide containing 64 amino acid residues. It is cleaved from milk during cheese production. It is rather resistant to acid and to enzymatic degradation and advances fairly unchanged down the gastrointestinal tract to perform its action, probably in the colon. In patients with clinically active distal ulcerative colitis, a pilot study showed that CGMP may have anti-inflammatory effects at the same level as the first choice of medical treatment, mesalazine. In order to further investigate the in vivo effect of CGMP and to shed light on the possible way of action, we designed the present study in healthy subjects.

Methods: We conducted a randomized, double-blinded, placebo-controlled study with an intervention period of four weeks. We included 24 healthy subjects. All participants were included from June 2016 to June 2017 and were assessed at Department of Hepatology and Gastroenterology, Aarhus University Hospital, Denmark. Eligible participants were randomized 1:1 to either intervention or placebo.

Results: C-reactive protein, leukocytes and faecal calprotectin were normal and did not change in any of the groups. The cytokine levels in the blood, the faecal short chain fatty acids and faecal microbiota have not yet been analysed.

CH.23   Tea Lund   IMPROVED METABOLIC LIVER FUNCTION IN PATIENTS WITH CHRONIC
         Laursen   HEPATITIS C AND ADVANCED LIVER DISEASE FOLLOWING SUCCESSFUL
                      SOFOSBUVIR-BASED DIRECT-ACTING ANTIVIRAL THERAPY

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Background: Patients with chronic hepatitis C (CHC) infection are mostly cured by sofosbuvir-based direct-acting antiviral (DAA) therapy. However, the effects on metabolic liver function are unknown. We aimed to

investigate the effects of DAAs on metabolic liver function, macrophage activation, liver stiffness and continuous reaction time (CRT) in CHC patients with advanced liver disease.

Materials and methods: We assessed 71 Danish CHC patients with advanced liver disease before, during, and after 12-24 weeks of sofosbuvir-based DAA therapy. Metabolic liver function was estimated by galactose elimination capacity (GEC), macrophage activation by plasma sCD163 and sMR levels (ELISA), liver stiffness by FibroScan or acoustic radiation force impulse (ARFI)-scans, and reaction time as CRT.

Results: All patients achieved sustained virologic response, except one patient with reinfection. Metabolic liver function improved at follow-up (all: 1.74 vs. 1.98 mmol/min), both in patients with cirrhosis (n=56) and those with advanced liver disease (n=15) (p<0.0005). The sCD163 and sMR levels decreased during the study period (sCD163: 6.9 vs. 3.9; sMR: 0.37 vs. 0.30 mg/L) as did liver stiffness (17.8 vs. 12.1 kPa) (p<0.0001, all). The CRT improved at follow-up (1.86 vs. 2.09, p=0.05). sCD163 levels correlated with GEC and liver stiffness at baseline. However, there were no associations between changes in sCD163 or sMR and changes in GEC or liver stiffness during follow-up.

Conclusion: Successful DAA treatment of CHC proves beneficial in advanced liver disease and leads to improved metabolic liver function and reaction time combined with reduced macrophage activation and liver stiffness.

CH.24   Sanne Marie Thysen   CANCELLED

THE EFFECT OF NEONATAL BCG VACCINATION ON MORTALITY AND PPD RESPONSE IN HOUSEHOLDS WITH AND WITHOUT TUBERCULOSIS CASES

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Background: WHO recommends BCG at birth in countries with high tuberculosis (TB) burden to prevent TB disease. However, BCG vaccination is often delayed. Accumulating evidence shows that BCG, aside from the protection against TB, may have beneficial non-specific effects.

Methods: In the urban Health and Demographic Surveillance System (HDSS) site in Guinea-Bissau, the Bandim Health Project follows children from birth until 3 years of age through 3-monthly household visits. TB cases within the HDSS are registered at first treatment contact.

We excluded children born at the main hospital, where children are vaccinated before discharge. Children entered the analysis when their vaccination card was first inspected after 28 days of life. Using a Cox-proportional hazards model with age as underlying time scale, we assessed the effect of timely BCG (before day 28) on mortality in children aged 0 to 3 years in households with and without TB cases. Children were classified as TB exposed from three months prior to a registration of a TB case in the household and remained exposed throughout follow-up.

Preliminary results and Conclusion: Between October 2003 and September 2017, excluding two periods with randomised trials of preventive TB treatment to children (2005 to 2007, and 2011 to 2013), 24261 children (1392 TB-exposed) were included in the analyses. Timely

BCG was associated with lower mortality among TB non-exposed children (mortality rate ratio (MRR): 0.65 (0.55-0.77)), whereas timely BCG was associated with higher mortality among TB-exposed children (MRR: 2.11 (0.49-9.10). However, we had very few events among TB-exposed children, and the results should be interpreted with caution.

CH.25 David Ricardo Quiroga Martinez

NEURAL RESPONSES TO SURPRISE IN MUSICIANS AND NON-MUSICIANS DURING MUSIC LISTENING

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Surprise is essential for the perception and enjoyment of music. During listening, we constantly create expectations about upcoming musical sounds, which are fulfilled or violated to different degrees, thereby generating neural responses and aesthetic and emotional experiences. In this study, we investigated how musical expertise affects neural responses to musical surprise. Since previous research has mostly compared expected sounds with highly violating sounds, we turned to a computational model to estimate more fine-grained fluctuations in surprise. Moreover, although behavioral research suggests that musicians' expectations reflect more accurately the statistics of musical styles, experimental tasks often require explicit knowledge and stopping the stimuli to produce a response. Consequently, we used magneto-encephalography to continuously track neural responses to subtle fluctuations in surprise during listening to a sequence of melodies. We used the computational estimates to classify single tones in ten categories according to their surprise value. We found that more surprising sounds were significantly associated with larger neural responses in the auditory cortex. However, this association was not different in musicians than non-musicians, suggesting similar musical knowledge. Our results might indicate that musicians and non-musicians are similarly exposed to Western tonal music, which is the style that we modelled. Moreover, the discrepancy with behavioral results raises the possibility that musicians have better explicit knowledge of expectations. Overall, our work supports the use of computational modelling for the continuous measurement of musical surprise.

CH.26 Denise Fabienne Happ

EFFECTS OF PREFRONTAL CORTEX AND NUCLEUS ACCUMBENS LESIONS ON AFFECTIVE BEHAVIOR IN RATS

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Background: Post-stroke depression and anxiety are linked to poorer functional recovery and higher mortality rates. Both diseases are usually undertreated, and many cases may remain undiagnosed. Current animal

models using middle cerebral artery occlusion can induce motor deficits that may interfere with behavioral tests of depression and anxiety. An alternative approach may be to limit stroke lesions to specific brain regions involved in depression and anxiety, while avoiding damage to motor areas.

Objective: Here, we investigated whether unilateral ischemic lesions in the medial prefrontal cortex (mPFC) and nucleus accumbens (NAc) altered depressive- and anxiety-like behavior in male Sprague-Dawley rats.

Methods: Stroke lesions were induced using microinjections of the vasoconstrictor endothelin-1 (ET-1), while control rats received vehicle injections. Behavior was evaluated after 2 and 6 weeks post stroke using standard tests for locomotion (Open Field), cognition (Y-maze), anxiety (Elevated Plus Maze) and depression (Forced Swim Test).

Results: Unilateral ET-1 injections in the mPFC and NAc resulted in replicable and localized lesions. Moreover, rats with mPFC and NAc lesions spent significantly more time in the open arms of the Elevated Plus Maze compared to controls at 2 weeks post stroke, indicating decreased anxiety-like behavior. We found no differences in locomotion, cognition or depressive-like behavior at either time point.

Conclusion: Our results show that unilateral lesions to the mPFC and NAc can affect short-term anxiety-like behavior, but do not produce a reliable and persistent model of post-stroke depression and anxiety in rats.

CH.27   Saida Said   VOLTAGE CLAMP FLUOROMETRY STUDIES OF GAT-1

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The γ-aminobutyric acid (GABA) is the major inhibitory neurotransmitter in the mammalian brain. Synaptic concentration of GABA is regulated by specific high affinity GABA transporters, mainly the GABA transporter subtype 1 (GAT-1) located in the plasma membrane of neurons. The main function of GAT-1 is to remove the released GABA from the synaptic cleft, and thereby it plays a fundamental role in the termination of the GABAergic signaling. The role of the GABAergic system in mental disorders in general and in depression in particular is gaining momentum, thus studies of GAT-1 at the molecular level are highly attractive for understanding how it fulfills its biological role, how it could possibly be targeted better pharmacologically, and how disease-related mutations may manifest themselves in both epilepsy and depression. Translocation of GABA relies on large conformational changes in GAT-1 that expose the central substrate binding site to the cytoplasmic environment. In this study, we combine voltage clamp fluorometry (VCF), fluorescence spectroscopy methods and unnatural amino acid mutagenesis to provide detailed knowledge of how ligand and ion binding control conformational change in GAT-1. For our purpose, we have genetically encoded the small, fluorescent unnatural amino acid ANAP as an environmentally sensitive probe at specific sites into GAT-1 using HEK-T cells and Xenopus oocytes as the expression systems. The current research work provides data on

combining state-of-the-art methods to gain a fundamental understanding of the pharmacological, functional and structural aspects of GAT-1, and thus can provide the basis for developing drugs that target it.

CH.28   Casper Schmidt   IMPULSIVITY AND COMPULSIVITY: THE ROLES OF DOPAMINE AND SEROTONIN IN REWARDS

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Within the neuroscience of addiction, there is lack of evidence both in terms of assessing its mechanisms and treating its different forms. This Cambridge-Aarhus PhD project in its final stage seeks to delineate the relationship between the roles of dopamine and serotonin in rewards, and their roles in the neuropsychological measurements of impulsivity and compulsivity. Although a lot is known about these separate roles, no research has been devoted to the basics of these neurochemical mechanisms when exposed to humans in combination.

The experiments were carried out during 2017 in a between-subjects double-blinded design and contained testing of 127 subjects, including four different arms of approx. 25 healthy volunteers (HV) and a fifth arm of 25 subjects with gambling disorder (GD), a psychiatric patient group with profound deficits in impulsivity and compulsivity. This was done in order to isolate the neural and behavioural correlates of both increasing dopamine and depleting serotonin to investigate:

1) how this affected neural activity in a task-based fMRI experiment on different forms of rewards

2) cognitive components of impulsivity and compulsivity through behavioural testing

3) how these two points relate to a placebo GD group

4) a connectome-based DTI sequence assessing structural neural networks across HV and GD groups.

In conclusion, this project, which is currently underway and finished in its initial stages, holds great promise to infer mechanistically about the neural and behavioural processes associated with dopamine and serotonin, thus providing a novel foundation for future treatment options within the neuroscience of addiction.

CH.29   Maj Ulrichsen   SORTILIN AND SORCS2 IN PERIPHERAL NERVE REGENERATION

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Peripheral nerve fibers are capable of regenerating following peripheral nerve injury, but functional recovery rarely reaches the pre-injury level. Schwann cells support peripheral neurons, and their biology is crucial for neuronal regrowth and remyelination after injury. We have shown that Schwann cells express the sorting receptors sortilin and SorCS2, which are involved in neurotrophin-mediated maintenance, survival and death signaling. Neurotrophin signaling is important for peripheral nerve regeneration, and the present study examines if sortilin or SorCS2 is involved in nerve fiber regrowth and Schwann cell-mediated remyelination via neurotrophin mediated-signaling. Indeed, preliminary in vitro data indicate a reduction in neurotrophin-mediated downstream signaling in the absence of sortilin or SorCS2, and we are examining if this affects Schwann cell proliferation, migration and myelination of axons, which are essentials for peripheral nerve regeneration. A mouse model of regeneration is used to assess if lacking sortilin or SorCS2 affects the number of regenerated nerve fibers and the degree of remyelination in vivo. Functional tests will reveal if sortilin or SorCS2 is important for functional recovery. Furthermore, protein expression analysis of regenerating nerves will unfold the expression pattern of sortilin and SorCS2 and investigate if absence hereof affects overall protein expression. Together, these data will ultimately show if sortilin or SorCS2 is important for proper regeneration of peripheral nerves and will thus increase the knowledge of the underlying mechanism of regeneration. This may clear the way for clinically relevant targets to improve the regeneration of peripheral nerves.

CH.30   Simin Berenji   EVALUATION OF HIGH PRESSURE NEUROLOGICAL SYNDROME (HPNS) IN
         Ardestani   DEEP SEA DIVERS

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Introduction/Background: With the development of the oil and gas industry, the need for offshore commercial underwater work has accelerated. Saturation divers live onboard dive support vessels for a maximum period of 28 days in chambers compressed to a certain storage depth. Divers are transported daily to the depth, 13 meter deeper or shallower than storage depth to carry on their underwater works. When divers perform activities in pressure greater than 150 meter sea water (msw), symptoms of high pressure neurological syndrome (HPNS) might appear. To further improve diving procedures, a tool for monitoring divers' safety and work performances is needed. The aim of this project to validate the current method of HPNS monitoring package (Physiopad, Divetech, Biot, France), which was developed by Technip FMC DSV.

Methods: The Physiopad was operated onboard a Deep Arctic (TechnipFMC Diving Support Vessel) during work scope in Libyan waters

between March and September 2018. The diving work was performed at approx. 190-209 msw. Physiopad package consisted of following tests; Simple math process (MathProc test), Perceptual vigilance task (PPVT), Time estimation task (time wall), Visual analogic scale (VAS), Critical flicker fusion frequency test (CFFF) and Hand dynamometry (Data). The data from 46 divers was collected at three different time points; pre, during and post saturation.

Results: The preliminary analysis shows different HPNS symptoms in divers. However, most of those symptoms disappeared just after 24 hours in saturation. This has confirmed that acclimatization to high pressure of oxygen happens, and divers are able to perform their activities without being at risk.

CH.31   Sandra Sif Gylfadottir

PAINFUL DIABETIC POLYNEUROPATHY IN TYPE 2 DIABETES PATIENTS

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Background and aim: Diabetic polyneuropathy (DPN) is a common complication of diabetes. The prevalence of DPN is around 50%, and 25-50% of patients with DPN suffer from painful symptoms. Painful DPN can be troublesome and greatly affect patients' quality of life. In this study, we aimed to describe a cohort of Danish type 2 diabetes patients in terms of DPN and painful DPN and to examine the relationship between painful DPN and quality of life (QoL) and affective symptoms.

Methods: We invited patients from the nationwide Danish Centre for Strategic Research in Type 2 Diabetes (DD2) cohort to participate in a clinical examination at two centers in Denmark (Aarhus and Odense). The patients completed questionnaires and a clinical examination consisting of a standard neurological examination, nerve conduction studies, skin biopsies, quantitative sensory testing and blood samples.

Results and conclusion: Of the 165 patients included in Aarhus, 24 had no DPN, 28 confirmed DPN without pain and 22 confirmed painful DPN. The remaining 91 were excluded because of subclinical and unconfirmed DPN or other causes of neuropathy and pain.

An age difference was seen between the three groups (no DPN, DPN and painful DPN) driven by the difference between painful DPN and no DPN. The mean age was 58.3 (SD 11.4) years for no DPN, 62.7 (11.3) for DPN and 66.3 (9.8) for painful DPN, p = 0.05. There was no difference in reported QoL and the proportion of patients with sleep impairment and symptoms of depression and anxiety between those with painful DPN, DPN and no DPN.

| CH.32 | Dennis Graversen | QUALITY OF OUT-OF-HOURS TELEPHONE TRIAGE: AQTT - A TOOL ASSESSING COMMUNICATION, PATIENT SAFETY AND EFFICIENCY IN GENERAL PRACTITIONER- AND NURSE-LED TELEPHONE TRIAGE |

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Objective: To develop a valid and reliable assessment tool able to measure quality of communication, patient safety and efficiency in out-of-hours (OOH) telephone triage conducted by both general practitioners (GP) and nurses.

Methods: The Dutch KERNset tool was translated, and input was incorporated from a focus group interview with patients. Face validity, content validity and applicability in OOH telephone triage were secured through a two-round Delphi process with 27 relevant stakeholders. Test-retest and inter-rater reliability was tested in an assessment panel and analysed using $ICC_{agreement}$, Fleiss' kappa and percent agreement.

Results: The 24-item assessment tool (Assessment of Quality in Telephone Triage - AQTT) measured communicative quality, health-related quality and four overall quality aspects. The test-retest reliability of the AQTT was satisfactory. The inter-rater reliability appeared reduced and revealed considerable disagreement among experienced triage professionals. However, in descriptive analyses of percent agreement when differentiating 'poor' from 'sufficient' quality, the agreement was satisfactory.

Conclusion: AQTT seems feasible and clinically relevant for assessing and comparing the quality of GP- and nurse-led OOH telephone triage. However, the reduced inter-rater reliability could reflect that different perceptions of quality of telephone triage exist. AQTT has subsequently been used to assess the quality in 1294 real random patient contacts from Danish OOH telephone triage by GPs, nurses and doctors (i.e. the minority being GPs). Comparative analyses are ongoing and expectantly published by Jan 2019, enabling presentation of comparative results.

| CH.33 | Stine Bak | EFFECTS OF PATERNAL OBESITY ON OFFSPRING AUTISM-LIKE BEHAVIOR |

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The prevalence of autism spectrum disorder (ASD) has increased drastically within the past decades. Epidemiologic studies have linked maternal obesity to the development of ASD, mainly through intrauterine exposures. Recently, paternal BMI has also been implicated as a risk factor for ASD, and epigenetic inheritance (EI) has been suggested as one mode of risk transmission. EI reflects transmission of a phenotype to the next generation that is not carried by the DNA code itself but stems from environmentally driven epigenetic modifications in gametes. Importantly, obesity has been shown to induce epigenetic alterations in spermatozoa.

Thus, the stage for EI as a potential mechanism is set, which is in line with the heritable nature of ASD.

To investigate the effect of paternal obesity on offspring behavior, 5 weeks old C57BL/6J mice were fed either a high-fat diet (HFD) or control diet (n=15) for 10 weeks prior to mating. The sires fed a HFD showed increased body weight and decreased glucose tolerance compared to control fathers. Initially, all offspring were weaned onto a normal chow diet. At 17 weeks of age, half of the offspring were further challenged with a HFD as an additional stressor. When the offspring were 21 weeks old, their behavior was examined in a battery of behavioral tests to assess autism-like behavior such as anxiety level, repetitive behavior and sociability.

The outcomes of the behavioral tests as well as epigenetic changes in paternal spermatozoa are currently being evaluated. Both positive and negative results will provide important information on the developmental effect of paternal obesity on the next generation's health.

CH.34   Anders Damgaard Møller Schlünsen

24-HOUR ACCESS OUTPATIENT CLINIC FOR PATIENTS WITH EXACERBATION OF CHRONIC DISEASE: A BEFORE-AFTER COHORT STUDY OF DIFFERENCES IN ACUTE HEALTHCARE UTILISATION

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Background: We developed a 24-h access outpatient clinic offering 24-h telephone support and triaged access to the hospital for patients with acute exacerbation of four selected chronic diseases. The aim of this study was to conduct a 1-year before-after study of the acute healthcare utilisation in patients offered the 24-h access outpatient clinic intervention.

Methods: The study was conducted as an observational register-based cohort study. Data were extracted 12 months before and 12 months after implementation of the 24-h access intervention. Patients with chronic obstructive pulmonary disease, chronic liver disease, inflammatory bowel disease and heart failure managed in hospital outpatient clinics were enrolled in the study. Differences in healthcare utilisation were analysed for all patients and high-risk patients with at least one acute admission in the year before enrolment.

Results: Length-of-stay remained unchanged for all groups, except for patients with heart failure. Statistically significant reductions in length of stay and acute admissions were observed in all high-risk groups, except for patients with chronic liver disease. A statistically significant reduction in the number of contacts to out-of-hours primary care was seen in patients with chronic obstructive pulmonary disease. Similar patterns were seen in high-risk patients.

Conclusions: The 24-h access outpatient clinic did not increase the use of acute healthcare services in patients with chronic disease. Significant

reductions in hospital utilisation were seen in high-risk patients. These preliminary results should be interpreted with caution due to the observational before-after design of the study.

CH.35 Kristine Jepsen Bennedsgaard

CHRONIC NEUROPATHY AND NEUROPATHIC PAIN FOLLOWING OXALIPLATIN AND DOCETAXEL: A 5-YEAR FOLLOW-UP QUESTIONNAIRE STUDY

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One of the most common and disabling side effects of cancer treatment is chronic chemotherapy-induced polyneuropathy.

Aim: To assess the prevalence of symptoms of polyneuropathy following chemotherapy compared to surgery alone.

Methods: A 5-year follow-up questionnaire was sent to patients treated with adjuvant oxaliplatin or docetaxel for colorectal or breast cancer as part of an ongoing prospective study. An identical questionnaire was sent to patients who had undergone surgery only for colorectal or breast cancer in the same time period. The questionnaire included questions about symptoms of neuropathy, neuropathic pain, anxiety and depression.

Results: A total of 464 patients participated in the study, of which 135 had colorectal cancer (39% received oxaliplatin) and 329 had breast cancer (24% received docetaxel). The preliminary results show that the most common neuropathic symptoms were tingling and numbness. Symptoms of neuropathy were significantly more common following chemotherapy than surgery alone in the colorectal cancer group (P=0.035), and neuropathic pain was more common following chemotherapy in both cancer groups (P=0.001). Symptoms of anxiety and depression were higher in the breast cancer patients treated with docetaxel than those not having chemotherapy (34.2% vs 17.1%; P=0.001). This was not seen in the colorectal cancer group.

Conclusion: The preliminary results show that patients with colorectal cancer treated with oxaliplatin had more severe neuropathic symptoms and neuropathic pain, but no difference was seen in affective symptoms. Patients with breast cancer who received docetaxel were more likely to report affective symptoms than those who received surgery alone.

CH.36 Patricia Alves da Mota

THE CREATIVE BRAIN: A DYNAMIC SYSTEM

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Creativity comes about through the dynamic interplay of multiple brain processes, including attention, mental flexibility and cognitive control. Jazz improvisation is an excellent experimental model for studying creativity, given that jazz musicians have the ability to spontaneously create novel music sequences that are aesthetically and emotionally rewarding. In the present study, we collected task-fMRI for.15 jazz musicians. The participants were asked to perform four different tasks, using a MR-compatible keyboard - melody by heart, play from a score sheet, improvise by melody and freely. In this study, we analysed the static (NBS; timescale of minutes) and dynamic (LEiDA; timescale of seconds) functional connectivity (FC) characterising each of these four complex neural processes. Importantly, we found significant differences between experimental conditions using the dynamic FC approach which were not found using the traditional static approach. These results strongly suggest that creativity is not a static neural process; it is rather the result of inter-actions within a complex and dynamic neural ensemble. The brain as a dynamic system needs to be flexible enough to easily and efficiently segregate and integrate information over different requests and/or timescales. The ability to create something novel requires a higher level of cognitive flexibility, which is often found decreased in neuropsychiatric disorders. Thus, the current study does not only shed new light on brain mechanisms underlying creative processing; the findings could also be key to the development of new treatments for patients in whom these same mechanisms are found disrupted.

CH.37   Anita Tranberg Simonsen   UNRAVELLING CLONAL HETEROGENEITY AT THE STEM CELL LEVEL IN MYELODYSPLASTIC SYNDROME

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Progression from myelodysplastic syndrome (MDS) to secondary AML (sAML) is believed to happen as a result of stepwise accumulation of mutations and clonal selection. However, whether genetic events in immunophenotypically defined immature subsets could drive this progression remains unknown. We aimed to delineate clonal hetero-geneity in stem cells (CD34+CD38-) with an aberrantly expression of the surface receptor CLEC12A from MDS patients who progress to sAML.

Patients and methods: Three MDS/sAML patients were selected based on the presence of CD34+CD38-CLEC12A+ cells at MDS diagnosis. We used fluorescence activated cell sorting, targeted panel sequencing and whole exome sequencing on bulk samples, sorted stem cell subsets and control CD3+ lymphocytes.

Results and perspectives: In two of the three patients, AML-related mutational events emerged in sorted cell fractions (CD34+CD38-CLEC12A+/-) otherwise undetected in diagnostic analyses performed on bulk MDS samples. In pt. 1, genetic aberrations appeared in the CLEC12A-stem cell compartment, and in pt. 2 AML-related events were in the

CELC12A+ stem cell subset. In pt. 3, no additional mutations were identified looking at the stem cell subsets, but information from the variant allele frequencies indicated that the CLEC12A- subset was a mix of normal and malignant stem cells (VAFs ~25%).

From a clinical perspective, as three distinct evolutionary patterns in three individual cases progressing to sAML are identified, the importance of upfront and follow-up knowledge of clonal diversity in distinct cell subsets is very important for designing personalized treatment strategies.

CH.38   Veera Manikandan

COGNITIVE GENETIC ARCHITECTURE OF MAJOR PSYCHIATRIC DISORDERS

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Cognitive deficits occur frequently in psychiatric disorders. Recent genome-wide association studies (GWASs) show that psychiatric disorders are genetically correlated with cognitive traits, such as educational attainment (EA) and intelligence (IQ); while some are positively correlated, e.g. autism and schizophrenia, some are negatively correlated, e.g. ADHD. We conducted a GWAS of ninth level school grades in Danish and math in ~35,000 Danish individuals from the iPSYCH cohort. The heritability of school grades, explained by common genetic variants, was 26%. The genetic correlation with the recent largest (N=>1 million) GWAS on EA was 91%. Polygenic risk scores constructed using SNP effect sizes from EA GWAS predicted school grades with high significance (R2=7.5%, P=0). Next, we conducted GWASs of Danish and math separately. To isolate the trait-specific signals, we used math as a covariate in the Danish GWAS and vice versa. We found significant genetic correlations with psychiatric disorders: (a) schizophrenia and major depression correlated positively with Danish but negatively with math, (a) ADHD correlated negatively with Danish and math, (b) autism and anorexia correlated positively with Danish and math. We replicated these correlations in ~300,000 individuals from the UK Biobank (UKBB): genetic correlations of college completion were similar to that of Danish, and genetic correlations of fluid intelligence were similar to that of math. Using psychiatric polygenic risk scores, we predicted 13 specific cognitive domains in ~4,500 individuals from the Philadelphia neurodevelopmental cohort. In doing so, we mapped cognitive domains specific for six major psychiatric disorders.

CH.39   Sanne Jensen   PEDIATRIC OBSESSIVE-COMPULSIVE DISORDER PATIENTS DIFFER IN LONG-TERM SYMPTOM SEVERITY TRAJECTORIES

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Background: First-line treatment for pediatric obsessive-compulsive disorder (OCD) is cognitive-behavioral therapy (CBT) and/or selective serotonin response inhibitors (SSRIs). Yet, not all patients benefit from the standard treatment, and long-term outcome has only been scarcely studied. Knowledge on individual differences in symptom severity trajectories could aid the personalization of treatment for pediatric OCD.

Method: The study included 269 patients aged 7-17 years from the Nordic Long-term OCD Treatment Study (NORDLOTS). All patients received stepped-care treatment starting with 14 weeks of manualized CBT (Step 1). Non-responders were randomized to either prolonged CBT or SSRIs (Step 2). Symptom severity was assessed with the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) at pre-treatment, mid-treatment, and at the end of Step 1, as well as 6, 12, 24, and 36 months after termination of Step 1. Latent class growth analysis (LCGA) was performed to identify latent classes of symptom severity trajectories from pre-treatment to three years after treatment. Discriminating predictors were investigated with logistic regression comparing the classes on a range of pre-treatment variables.

Results: The LCGA revealed best fit for three trajectory classes with patients presenting as: 1) Early responders, 2) Late responders, and 3) Limited responders. The patients in the three classes differed according to baseline characteristics (analyses are in progress).

Conclusion: Symptom severity trajectories of pediatric OCD patients during and after treatment are heterogeneous. These differences should be considered in the individualization of treatment in this patient group.

CH.40   Lene Haldbo-   NEUROCOGNITIVE DYSFUNCTION AFTER RADIATION THERAPY FOR
         Classen   PRIMARY BRAIN TUMOURS

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Background: The extent of radiation therapy (RT) induced changes in cognitive function is unknown. There is modest knowledge on which parts of the brain we need to spare to prevent cognitive dysfunction. To uncover which cognitive domains is most affected, we compared cognitive functioning in brain tumour patients treated with neurosurgery and RT with brain tumour patients treated with neurosurgery alone.

Methods: A cross-sectional study assessing cognitive function in 110 patients with a primary brain tumour treated at Aarhus University Hospital, Denmark. Two cohorts were established: a cohort of 81 brain tumour patients who had received neurosurgery followed by RT (RT+), and a cohort of 29 brain tumour patients who had only received neurosurgery (RT-). The patients underwent questionnaires and neuropsychological assessment.

Results: Mean age was 53.5 years with an average time since diagnosis of 7.3 years. Compared with normative data, lower average scores were observed for the entire group on domains concerning erbal learning and memory (p<0.001), attention and working memory (p<0.001), processing speed (p<0.001), and executive functioning (p<0.001). Compared to RT- patients, RT+ patients scored lower on domains concerning processing speed (p=0.04) and executive function (p= 0.05) and had higher impairment frequency on verbal fluency (p=0.02), with 16% of patients exceeding 1.5 SD below normative data.

Conclusion: Our results indicate that treatment, including RT, for a primary brain tumour may have negative long-term impact on cognitive function, especially on processing speed and executive function.

CH.41   Maj Haubuf   STORAGE OF URINE SAMPLES FOR DETERMINATION OF PROTHROMBIN
                         FRAGMENT 1 + 2

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Introduction: Determination of prothrombin fragment 1+2 (F1+2) holds the potential for being a marker of thromboembolic risk, e.g. following trauma.

The low molecular weight of F1+2 allows the molecule to be excreted in urine, where it non-invasively can be measured.

The aim was to determine if storage time and/or storage temperature influenced F1+2 values measured in patient urine samples.

Methods: A urine sample from 27 orthopedic patients was collected early morning and analyzed for uF1+2 with ELISA (Enzygnost F1 + 2). The samples were stored at + 4 °C, - 20 °C and - 80 °C for 14 days, 1 month, 3 months, 6 months, or 19 months prior to analysis. Statistical analysis was performed by oneway ANOVA using multiple comparisons testing between the groups.

Results: The three storage temperatures all showed a statistically significant difference over time. At + 4 °C and - 80 °C, a significant difference was found after 6 months. However, at both temperatures, the differences were non-significant when comparing fresh urine with samples stored 19 months. The median differences over time were numerically small, especially for storage at -80°C. Samples stored at + 4 °C showed a tendency to decreasing values when storage time surpassed 1 month. Samples stored at - 20 °C showed some very diverging values, indicating that some samples became unstable after 3 months' storage.

Conclusion: Urine F1+2 showed significant, but numerically small, changes during storage for 19 months. Based on these data, we recommend storage at -20 °C or -80 °C beyond 1 month of storage.

CH.42   Anne Mette Schmidt

COMPARISON OF TWO MULTIDISCIPLINARY REHABILITATION INTERVENTIONS IN PATIENTS WITH CHRONIC LOW BACKPAIN: A RANDOMISED CONTROLLED CLINICAL TRIAL

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Background: Chronic low back pain (CLBP) is a highly prevalent health condition, and the leading cause of years lived with disability. Despite a large body of literature on multidisciplinary biopsychosocial rehabilitation and CLBP, evidence for the benefits of continuous integration of learning into the patient's own environment remains lacking. We, therefore, designed an integrated rehabilitation programme that consists of a participatory biopsychosocial approach encompassing inpatient activities supported by a multidisciplinary team and learning located in the patient's own environment.

Aim: To assess if an integrated multidisciplinary rehabilitation programme is more effective than an existing multidisciplinary rehabilitation programme.

The existing rehabilitation programme is a four-week inpatient programme. The integrated rehabilitation programme consists of: 1) a pre-admission day, 2) two weeks of home-based activities, 3) two-week inpatient, 4) four weeks of home-based activities, 5) two-days

inpatient booster session, 6) six weeks of home-based activities and 7) two-days inpatient booster session.

Materials and methods: A randomised controlled trial on 160 patients with CLBP from Sano. Demographics and patient reported outcome measures (PROM) are collected at baseline and 26-week follow-up. The primary outcome is changes in disability assessed by The Oswestry Disability Index. Secondary outcomes are pain (Numerical Rating Scale), Pain self-efficacy (The Pain Self-Efficacy Questionnaire), Quality of life (EQ-5D) and Depression (Major Depression Inventory).

Results: By August 2018, all patients are included. Data will be available in May 2019.

CH.43 Anne-Birgitte Blavnsfeldt

THE EFFECT OF GLUCOCORTICOIDS ON BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED,CONTROLLED TRIALS

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Background: Glucocorticoids (GC) in the treatment of rheumatoid arthritis (RA) are controversial, in particular their effect on bone. Impairment of bone formation may be counter-balanced by reduced influence from systemic inflammation. This review aims to assess the effect of GCs on bone mineral density (BMD) in RA patients in randomized, placebo-controlled trials.

Methods: We performed a systematic literature search and included studies that used prednisolone or prednisone as intervention and measured BMD at baseline and at least once thereafter. Two authors independently performed reference management, data extraction and risk of bias assessment. Primary endpoint was mean change in BMD from baseline to follow-up.

Results: We identified 7 studies and included previously unpublished data. Standard mean difference (SMD) in change in BMD from 0 to 24 months was–0.02 (95%CI –0.16, 0.12) at the lumbar spine and –0.11 (95% CI –0.25, 0.02) at the hip (both high quality evidence) between patients treated with prednisolone/prednisone or not. Data completeness was low in some studies, concomitant treatment of RA differed between studies, and differences in anti-osteoporotic medication may have influenced the results. However, sensitivity analyses did not alter the estimates.

Conclusion: In patients with early and active RA, we found no difference in change in BMD between patients treated with prednisone/prednisolone versus placebo. This suggests that, at least through 24 months, the suppression of inflammation by glucocorticoids may counterbalance their adverse effects on bone remodeling.

CH.44   Andreas Aalkjær   PREDICTING MECHANICAL RESTRAINT OF PSYCHIATRIC INPATIENTS BY
         Danielsen   APPLYING DATA MINING TECHNIQUES ON ELECTRONIC HEALTH DATA

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Objective: Mechanical restraint (MR) is used to prevent patients with mental disorders from harming themselves or others during inpatient treatment. MR is associated with adverse outcomes and may be avoided via less intrusive preventive interventions. Prevention relies on knowing which patients are at risk of MR. The objective of this study was to investigate whether MR occurring in the first three days following admission could be predicted based on analysis of electronic health data available after only one hour.

Method: The dataset consisted of clinical notes from electronic health records from the Central Denmark Region and data from the Danish health registers on patients admitted to a psychiatric hospital in the period from 2011 to 2015. Supervised machine learning algorithms were trained on a randomly selected subset of the data and validated using an independent test dataset.

Results: A total of 5,050 patients with 8,869 admissions were included in the study. One hundred patients were mechanically restrained in the period between one hour and three days after the admission. A Random Forest algorithm predicted MR with an area under the curve of 0.87 (95% CI 0.79-0.93). At 94% specificity, the sensitivity was 56%. Among the ten strongest predictors, eight were topics identified in the clinical notes.

Conclusions: A machine learning algorithm using data available one hour after admission predicted MR occurring within the following three days with acceptable accuracy. This finding opens for the development of an early warning system that may guide interventions to reduce MR use.

CH.45   Thomas Skovhus   VALIDATION OF THE KING'S BRIEF INTERSTITIAL LUNG DISEASE
         Prior   QUESTIONNAIRE IN DANISH

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Introduction: The King's Brief Interstitial Lung Disease questionnaire (K-BILD) is a validated measure of health-related quality of life in patients with interstitial lung disease. The aim of this study was to validate the Danish version of the K-BILD.

Methods: Patients with idiopathic pulmonary fibrosis (IPF) were recruited. At baseline, the patients completed the K-BILD and the St. Georges Respiratory Questionnaire (SGRQ), and lung function tests were performed. The same questionnaires and Global Rating of Change Scales

were completed 14 days later. Internal consistency, concurrent validity, test-retest reliability and known-group validity were assessed.

Results: At baseline, 150 patients completed the questionnaires, and 139 patients completed the questionnaires after 14 days. The K-BILD had a high internal consistency (Cronbach's α: total 0.92). Concurrent validity of the K-BILD was moderate to strong compared to SGRQ (r_{total}=-0.78) and weak to moderate compared to lung function tests (r_{total}=0.29-0.46). In stable patients, intraclass correlation coefficients (total 0.91) and a Bland Altman plot demonstrated high repeatability, indicating a good reliability of the K-BILD. The questionnaire was also able to discriminate patients with different stages of disease (p<0.002, Δscore > 7.4). These results were equivalent to the original version of K-BILD.

Conclusion: The Danish version of K-BILD is a valid and reliable measure of quality of life in patients with IPF and performs comparably to the original version.

CH.46   Hanan Amadid   ASSOCIATIONS BETWEEN WEEKLY PATTERNS OF OBJECTIVELY MEASURED PHYSICAL ACTIVITY AND INCIDENCE OF CARDIOVASCULAR DISEASE

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Background: The current physical activity (PA) guidelines do not impose any recommendation of regularity of PA throughout the week because research on PA patterns is sparse.

Aim: To identify and describe distinct weekly PA patterns and to examine their association with incident cardiovascular disease (CVD).

Material and methods: 1,355 CVD-free Danish men and women from the population-based ADDITION-PRO study aged 45-79 years. Participants wore a combined heart rate and movement sensor for one week that provided information on PA energy expenditure, time spent in different PA intensities and sedentary time. Data on CVD events and mortality was ascertained from Danish registers. Latent class trajectory modelling was used to derive patterns of PA. The associations between PA patterns and incident CVD were examined by Poisson regression. Models were adjusted for age, sex and overall PA energy expenditure.

Results: Three PA patterns were identified: "regularly inactives" (low PA on all days, n=936), "warriors" (high PA on 3 days and high sedentary time on remaining days, n=122) and "regularly actives" (high PA on all days, n=297). The "regularly inactives" were significantly more often women, older, unemployed and had a relatively unfavourable cardiometabolic risk profile compared to the two more active classes. During an average of 5.4 years of follow-up, 181 CVD events occurred. There was no difference in CVD incidence between the classes (P=0.38).

Conclusions: We found three distinct patterns of weekly PA. However, although the cardiometabolic risk profile differed between the three classes, this did not translate into a difference in CVD incidence.

CH.47 Jeanette Finderup A QUALITATIVE EVALUATION OF A SHARED DECISION-MAKING INTERVENTION FOR DIALYSIS CHOICE

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Background: At Aarhus University Hospital, we have developed an intervention based on shared decision-making for patients facing a choice of dialysis modality. The decision is between haemodialysis and peritoneal dialysis, either performed by patients on their own or with help from a healthcare professional. The intervention consists of three meetings with a dialysis coordinator who introduces a patient decision aid named 'Dialysis Choice' to the patient. The intervention (SDM-DC) has been implemented at four different hospitals in Denmark.

Aim: To evaluate how the SDM-DC intervention influenced patients' experiences of involvement in their choice of dialysis modality and to investigate how and why the intervention works.

Methods: We conducted semi-structured individual interviews with 29 patients using systematic text condensation for data analysis.

Findings: The four main findings were: my own choice; the meetings contributed to the decision process; 'Dialysis Choice' contributed to the decision process; and the decision process was circular and iterative.

Conclusion: The patients experienced the SDM-DC as involving them in their choice of dialysis modality. Due to the circular and iterative properties of the decision-making process, the SDM-DC needs to be adapted to the needs of the individual patients. The active mechanisms of the meetings with the dialysis coordinator were: 1) questions to and from the patient; and 2) the dialysis coordinator's dissemination of exact knowledge about the options. The overview of options and the value clarification in the decision aid particularly contributed to the decision-making process based on informed preferences.

CH.48 Takwa Shaiman Aroankins ALTERATION OF PROTEIN SUMOYLATION IN RENAL EPITHELIAL CELLS BY THE MINERALOCORTICOID HORMONE, ALDOSTERONE

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It is a well-known phenomenon that kidney epithelial cells obtain strong cellular stress from renal or cardiovascular pathophysiological conditions. Oxidative stress in renal cells forces the cells into defence mechanisms, and it is believed that protein SUMOylation is one of them. Small-ubiquitin-related-modifier (SUMO) is a post-translational modification (PTM) of selective lysine (K) residues in target proteins. Five SUMO isoforms (SUMO1-5) are known to be expressed in mammalian cells, which exerts a variety of cellular functions. SUMO1 and SUMO2 are the most

widespread isoforms in mammalian cells, and SUMO4 is a human renal specific isoform. We generated six different renal cell lines; mpkCCD 6xHis-SUMO1-T95K / -SUMO2-T90K, mpkDCT 6xHis-SUMO1-T95K / -SUMO2-T90K, HEK293 10xHis-SUMO4-V55-T91K and 10xHis-SUMO4-V55-T91K-P90Q. The mutant forms allow us to utilize a two-step purification approach by crude protein level, nickel purification and fine peptide level, Lysine-diGlycine (KGG) immunoprecipitation. Following enrichment, SUMOylated peptides were analysed using LC-MS/MS, identified with database search and quantified. Using the outlined approach, we have identified 1428 SUMO1 and 1957 SUMO2 modified sites on proteins in CCD cells and 248 SUMO1 and 258 SUMO2 modified sites in DCT cells. Furthermore, we identified a novel proton and oligopeptide/antibiotic cotransporter protein, SLC15A2, of which SUMOylation is massively altered after aldosterone stimulation. This protein is also yet to be reported to be expressed in DCT or CCD tubule region.

CH.49   Maria Elkjær   COST CONSEQUENCES OF ALTERNATIVE MULTI-PARAMETRIC MAGNETIC RESONANCE IMAGING BASED FOLLOW-UP STRATEGIES IN ACTIVE SURVEILLANCE OF PROSTATE CANCER: A DECISION TREE MODEL STUDY BASED ON MICRO-COSTING

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Background: In active surveillance (AS) of prostate cancer (PCa), multi-parametric MRI (mpMRI) is considered expensive as compared to standard trans-rectal ultrasound (TRUS)-based follow-up. An mpMRI-based follow-up is also still considered experimental.

Objectives: To compare the costs of two alternative AS follow-up strategies based on mpMRI to the costs of standard TRUS-based follow-up.

Design, Setting, and Participants: TA decision tree model was developed, where the standard TRUS-bx-based strategy (TRUS arm) of AS follow-up was compared with a TRUS, mpMRI and on demand in-bore MRI-guided biopsies (odMRGB) (TRUS+MRI arm) and an exclusively mpMRI and odMRGB (MRI arm)-based strategy. Data input were derived from a micro-costing analysis in 78 AS patients, literature searches and national tariffs.

Outcome measurements and statistical analyses: Health care costs, number of biopsies and significant cancers detected were investigated. Probabilistic and one- and two-way sensitivity analysis were performed to assess uncertainty.

Results and limitations: The TRUS+MRI strategy was more expensive (2598€ (95% CI: 2084-3123€) per one year follow-up) and effective (few missed cancers). The MRI strategy cost the same as the TRUS-bx strategy (1872€ (95% CI: 1304-2455€) vs. 1859.4€ (CI95%: 1436-2297€) per year, respectively). The MRI arm missed half as many cancers as the TRUS arm and used only 80.4 biopsies per 100 patients vs. 1200 and 1251.6 biopsies in the TRUS arm and TRUS+MRI arm, respectively.

Conclusion: An mpMRI and odMRGB strategy was not costlier than a TRUS-bx-based strategy but diagnosed more cancers using considerably fewer biopsies.

CH.50   Inge Schjødt   SOCIOECONOMIC STATUS AND RISK OF READMISSION IN PATIENTS WITH HEART FAILURE WITH REDUCED EJECTION FRACTION

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Introduction: Patients with heart failure (HF) have a high risk of readmission. However, the relationship between socioeconomic factors and readmission in these patients is not fully elucidated.

Objective: To study if socioeconomic status (SES) is associated with readmission after a HF diagnosis.

Methods: A nationwide cohort study of 17,122 patients with incident HF with reduced ejection fraction (HFrEF) registered in the Danish Heart Failure Registry between January 2008 and October 2015. Individual-level registered SES was assessed based on four dimensions: cohabitation status, educational level, family income and composite SES. Associations between socioeconomic factors and unplanned all-cause, HF and non-HF readmission within days 1-30, 31-90 and 91-365, and total number of hospital bed-days within 1 year following HF diagnosis was assessed using multivariable regression analysis.

Results: Low income was associated with a higher risk of all-cause (adjusted hazard ratio (aHR) 1.24 CI 95% 1.08-1.43) and non-HF readmission (aHR 1.25; CI 95% 1.12-1.39) within days 31-90. Moreover, low income was associated with a higher risk of all-cause (aHR 1.27 CI 95% 1.14-1.41), HF (aHR 1.26; CI 95% 1.02-1.55) and non-HF readmission (aHR 1.25; CI 95% 1.12-1.39) within days 91-365. Similar patterns were seen for medium income. Patients with low and medium income had a higher relative use of all-cause hospital bed-days. Low income was also associated with a higher relative use of HF hospital bed-days.

Conclusion: Lower income was associated with higher risk of all-cause and non-HF readmission within 1-12 months following HF diagnosis, and with HF readmission within 3-12 months.

CH.51   Michael   HOW DO NOVICE RUNNERS WITH DIFFERENT BODY MASS INDEXES
         Bertelsen   BEGIN A SELF-CHOSEN RUNNING REGIME?

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Background: Overweight and obese novice runners are subjected to a higher load per stride than their normal-weight peers. Do they reduce their running dose accordingly when beginning a self-chosen running regime?

Objectives: To describe and compare the preferred running dose in normal-weight, overweight, and obese novice runners when they commence a self-chosen running regime.

Methods: In this exploratory 7-day prospective cohort study, 914 novice runners were categorized into 1 of 3 exposure groups based on BMI: (1) normal weight (BMI less than 25 kg/m2, n = 405; ref), (2) overweight (BMI of 25 to less than 30 kg/m2, n = 341), and (3) obese (BMI of 30 kg/m2 or greater, n = 168). All runners were equipped with a GPS watch, which provided information about distance, duration, and speed of each running session.

Results: During the first session, overweight runners (difference, -0.5 km/h; 95% CI: -0.8, -0.2 km/h; P<.05) and obese runners (-1.7 km/h; 95% CI: -2.0, -1.4 km/h; P<.05) ran slower than normal-weight runners. Obese runners also ran a shorter distance compared to normal-weight runners (-0.4 km; 95% CI: -0.7, -0.2 km; P<.05). During the first week, overweight runners (-0.5 km/h; 95% CI: -0.7, -0.2 km/h; P<.05) and obese runners (-1.7 km/h; 95% CI: -2.0, -1.4 km/h; P<.05) ran slower than normal-weight runners, while distance and duration were similar.

Conclusion: Overweight and obese runners selected a similar training dose to that of normal-weight runners when starting a self-chosen running regime. This may partly explain the higher running-injury risk among overweight and obese runners compared with normal-weight runners observed in other studies.

CH.52   Nis Brix   MATERNAL PRE-PREGNANCY OBESITY AND TIMING OF PUBERTY IN SONS
                      AND DAUGHTERS: MEDIATION BY CHILDHOOD BMI

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Background: In many countries, an increased prevalence of adult obesity has been observed over the same period as earlier puberty. We aimed to explore the potential effect of maternal pre-pregnancy obesity on the timing of puberty in sons and daughters.

Methods: We studied 15 819 children from the Danish National Birth Cohort. From the age of 11 years, they provided half-yearly information on the pubertal milestones: Tanner stages, voice break, first ejaculation, menarche (the first menstrual bleeding), acne, and axillary hair. We estimated adjusted mean differences in age at reaching the pubertal milestones for maternal pre-pregnancy obesity (body mass index (BMI) $\geq$30 kg/m^2) with normal weight (BMI 18.5 to 24.9 kg/m^2) as the reference. In mediation analysis, we explored whether childhood BMI at 7 years mediated the associations.

Results: Pre-pregnancy obesity was associated with earlier age at attaining most pubertal milestones in sons (e.g., voice break: -2.2 months (95% confidence interval (CI): -3.8, -0.6)) and all pubertal milestones in daughters (e.g., menarche: -3.1 months (95% CI: -4.2, -2.0)). When combining all associations, pre-pregnancy obesity was associated with earlier age at attaining all pubertal milestones in both sons (-1.5 month (95% CI: -2.5, -0.4) and daughters (-3.2 months (95% CI: -4.2, -2.1)). Mediation analyses suggested that changes in childhood BMI mediated the entire association in sons but only partly so in daughters.

Conclusions: Maternal pre-pregnancy obesity may advance the timing of puberty in sons and daughters. This potential advancing effect may potentially be reduced through interventions to prevent childhood obesity.

CH.53   Maria Dietz Toppenberg

EVALUATION OF MOBILE X-RAY WITHIN THE TRIPLE AIM APPROACH

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Background: Mobile X-ray is used where transfer of patients to the radiology department at the hospital may be an obstacle. X-ray examination with mobile X-ray is performed in the patient's own home with transportable equipment. After examination, the images are sent to PACS, the computer system at the hospital, where radiologists evaluate them.

Aim: The overall aim is to evaluate the project 'mobile X-ray' in order to conclude if mobile X-ray improves healthcare for fragile patients.

Method: The overall method used is the Triple Aim Approach. It seeks to optimize health care performance for a specific population, and it contributes to the improvement of the effect of an intervention.

Results and conclusion: No statistical results are available yet, but there have been many organizational challenges due to conducting a randomized trial, which in the first place was a pilot study. The organizational challenges include secretaries, radiologists, radiographs and general practitioners. Common to these healthcare workers is that they all support the conduction of the randomized PhD study, but, at the same time, they have a predetermined opinion on what is best for the individual patient.

Perspectives: The ambition is to contribute to study the effect of mobile X-ray and to create new knowledge about which practice gives the best patient care with the available resources.

CH.54 Andreas Ernst PARENTAL FERTILITY, FERTILITY TREATMENT AND TIMING OF PUBERTY IN SONS AND DAUGHTERS: A NATIONWIDE COHORT STUDY

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Background: The rate of infertile couples and the use of fertility treatment increase, but the impact on reproductive health in the next generation remains unknown.

Methods: This nationwide cohort study of 13,285 children from the Danish National Birth Cohort investigated the associations between parental time-to-pregnancy (TTP), use of fertility treatment to achieve pregnancy and timing of puberty in sons and daughters. Mothers reported TTP and use of fertility treatment, including type of treatment in early pregnancy, and offspring gave information on indicators of pubertal development, such as Tanner stages of genital, breast and pubic hair development, age at menarche and voice break from 11 years of age and every 6 months until full maturation.

Results: Long TTP (TTP>6 months) and use of fertility treatment were associated with slightly earlier mean age of onset for the individual female puberty indicators and slightly later onset for individual male indicators. The difference in overall timing of puberty was -0.40 months (95 % CI: -3.58, 2.78) in girls and 0.43 months (-2.43, 3.28) in boys born by parents with a TTP of 6-12 months receiving fertility treatment when compared to children born by untreated parents (TTP<6 months). We did not observe any patterns with increasing TTP, nor did we detect differences in timing of puberty when comparing children born by IVF or ICSI with children born by less invasive methods (ovarian stimulation or ovulation induction with or without intrauterine insemination).

Conclusion: Parental TTP and fertility treatment seem to play limited or no clinically relevant role for the decline in age at puberty timing observed throughout the last century.

CH.55 Katja Krustrup Pedersen EFFECTS OF DOUBLET STIMULATION ON DYNAMIC MUSCLE CONTRACTILITY IN MUSCLES WITH K⁺-SUPPRESSED EXCITABILITY

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Purpose: Obtaining optimal dynamic muscle contractility demands activation frequencies higher than those needed to produce maximal isometric force. However, high activation frequencies increase cellular efflux of K^+, which impairs muscle excitability. In vivo stimulation frequencies are often low (sub-tetanic) and only contain brief bursts of high frequencies (supra-tetanic) in the form of doublets. We examined how dynamic muscle contractile performance in fast twitch fibers responds to high constant stimulation frequency or doublets, and how this response was modulated by increased extracellular $[K^+]$.

Methods: Dynamic contractions were elicited in isolated rat EDL muscles stimulated either by constant frequency trains of tetanic (150 Hz), by supra-tetanic (300 Hz) frequencies, or by a sub-tetanic frequency (50 Hz) with or without an initiating doublet (300 Hz). Muscles were incubated at 30°C in Krebs Ringer buffer at 4 or 11 mM K^+.

Results: Increasing frequency from 150 Hz to 300 Hz increased maximal power (P_{max}), maximal velocity (V_{max}), and rate of force development (RFD) at 4 mM K^+, but at 11 mM K^+ these increases were attenuated or abolished. When using sub-tetanic frequency trains, addition of a high frequency doublet induced significant increases in maximal force (F_{max}), P_{max}, V_{max} and RFD at both 4 and 11 mM K^+.

Conclusion: These results indicate that the improved contractility achieved with high constant stimulation frequency is strongly attenuated when excitability is suppressed by high extracellular $[K^+]$. However, contractile improvements from doublets initiating a train of sub-tetanic frequency may still be achieved despite a high extracellular $[K^+]$.

CH.56   Elin Rakvaag   EFFECTS OF WHEY PROTEIN AND DIETARY FIBER ON LIPID METABOLISM: A RANDOMIZED, CONTROLLED, DOUBLE-BLIND DIETARY INTERVENTION TRIAL IN SUBJECTS WITH ABDOMINAL OBESITY

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Objective: Elevated lipids, in particular postprandial triglycerides (TG), is a risk factor for cardiovascular events. Acute studies have indicated that both whey protein (WP) and dietary fiber have the potential to improve markers of lipid metabolism. We hypothesized that combining these two dietary components may provide synergistic benefits. Therefore, we aimed to investigate the effects of 12-wk intake of WP and dietary fiber on lipid metabolism.

Methods: We conducted a parallel intervention study, where 65 adults with abdominal obesity were randomized to 1 of 4 isocaloric diets: WP-LoFi (60 g/d WP + 10 g/d fiber), WP-HiFi (60 g/d WP + 30 g/d fiber), MD-HiFi (60 g/d maltodextrin (MD) + 30 g/d fiber), MD-LoFi (60 g/d MD + 10 g/d fiber). Before and after the intervention, we conducted a high-fat meal test and measured the postprandial TG, apolipoprotein B48 (apoB48) and apolipoprotein B100 (apoB100) responses, and fasting levels of TG, apoB48, apoB100, LDL, HDL and total cholesterol.

Results: After 12 weeks, the WP-LoFi group had reduced fasting and postprandial TG levels compared both with baseline and with the other groups. WP-LoFi also had reduced fasting and postprandial apoB48 and

apoB100, reduced total cholesterol, and a small increase in HDL. WP-HiFi had a modest reduction in postprandial TG.

Conclusions: Intake of WP in combination with a low-fiber diet improved markers of lipid metabolism in the fasting and postprandial state in subjects with abdominal obesity. In contrast to our hypothesis, the combination of WP and high fiber did not provide synergistic benefits on markers of lipid metabolism.

CH.57   Per Mose Nielsen   ACUTE KIDNEY INJURY IN DIABETIC RATS LEADING TO FIBROSIS ASSESSED WITH HYPERPOLARIZED 13C MRI

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Background: Diabetes is estimated to affect up to 4.4% in 2030. Diabetes can eventually lead to diabetic nephropathy. This leads to metabolic derangement and eventually kidney fibrosis, which is a major hallmark of end stage renal disease. I have previously successfully evaluated new metabolic and functional imaging biomarkers. However, currently there is no available non-invasive method to quantify renal fibrosis in diabetes. In this study, we wish to develop a protocol to image the metabolic consequences of fibrogenesis and test newly developed fibrosis markers specifically for diabetics.

Methods: Wistar Rats were divided into two groups: a type 1 diabetic group and a control group. Unilateral ischemia was induced in both groups. MR scan sessions were performed after 8 days of reperfusion. The experiments were performed in a 3T clinical MR system. ELISA assays were utilized to measure urinary extracellular matrix (ECM) markers U-TUM8 and U-C4M2.

Results and conclusion: The anaerobic glycolytic flux was highly upregulated in the contralateral (CL) diabetic kidney. In the post ischemic diabetic kidney, this flux was reduced. This might be caused by reduced capability for injury repair. No change in anaerobic glycolytic flux was found in the control group having a normal repair capability. Single kidney GFR was highly upregulated in the CL diabetic kidney, but was reduced in the post ischemic diabetic kidney, which indicates a reduced kidney function. U-TUM8 and U-C4M2 were found to be highly upregulated in the post ischemic diabetic kidney indication fibrogenesis.

CH.58   Charlotte Arp Sørensen   DISPENSING ERRORS IN "SELF-ADMINISTRATION OF MEDICATIONS AT HOSPITAL": A RANDOMISED CONTROLLED TRIAL

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Background: Health care is moving towards systems with more patient involvement, including "self-Administration of medications at hospital" (SAM). Medication errors happen every day and may introduce discomfort and harm to patients, increase costs, length of stay and mortality. The risk of dispensing errors in SAM is unclear.

Purpose: To investigate the number of dispensing errors in SAM as compared to dispensing by nurse.

Materials & Methods: Patients admitted to a cardiology unit were assessed for their ability of SAM. Eligible consenting patients were randomised to self-administration (I, intervention) or dispensing by nurse (C, control). In the I-group, medications brought to hospital were reviewed to match electronic prescriptions. If something was missing or new medications were prescribed, this was provided by the hospital. An updated medication list was printed, and the patient was instructed about SAM by a nurse. The primary outcome was the rate of dispensing errors seen through direct observation of patient or nurse. An opportunity for error (OE) was defined as any medication dispensed and any medication prescribed but not dispensed.

Results: 250 patients were recruited from Aug.17 to Sept.18; 11 were withdrawn as they were discharged prior to observation. For analysis were 1031 OEs (I, 119 patients) and 1024 OEs (C, 120 patients). An error rate of 0.10 (I, 100 errors; CI95%:0.08-0.12) and of 0.13 (C, 132 errors; CI95%: 0.11-0.15) was observed.

Conclusion: The study indicate fewer dispensing errors in SAM. However, the difference was not statistically significant. Letting patients self-administer medications at hospital does not compromise the safety related to dispensing.

CH.59   Martin Lund   QUALITY INDICATORS FOR SCREENING COLONOSCOPIES AND COLONOSCOPIST PERFORMANCE AND THE SUBSEQUENT RISK OF INTERVAL BOWEL CANCER: A SYSTEMATIC REVIEW

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Background: Colorectal cancer is one of the most common cancer diseases. For this reason, bowel cancer screening programs (BCSPs) have been implemented throughout the world. To monitor the performance quality of the screening colonoscopies, a set of colonoscopist dependent quality indicators have been developed. These quality indicators need to be validated against a relevant outcome in order to assess their value.

Objectives: The objective of this systematic review was to assess the association between quality indicators related to the individual colono-scopist's performance and subsequent interval cancers in patients participating in BCSPs.

Review questions: Are the commonly used quality indicators of cecal intubation rate (CIR), adenoma detection rate (ADR), polyp retrieval rate (PRR), withdrawal time (WT), and incomplete adenoma resection (IAR)/incomplete polyp resection (IPR) associated with the outcome of interval cancer? Is it possible to determine cut-off values that are

significantly associated with each of the quality indicators mentioned above and the outcome of interval cancer?

Results and conclusions: CIR, ADR and WT were significantly associated with the outcome of interval cancer, and it was possible to determine cut-off values that were significantly associated with the outcome of interval cancer. It may be recommended in BCSPs to monitor the WT and the CIR to aim for a WT >6 minutes and a CIR ≥90% to minimize the risk of interval cancer. In BCSPs using colonoscopy as their primary screening tool, it may be recommended for the ADR to be at least ≥15%, and better 20-25% or higher, to minimize the risk of interval cancer.

| CH.60 | Anne Ankerstjerne Rasmussen | PATIENT-REPORTED OUTCOMES AND MEDICATION ADHERENCE IN PATIENTS WITH HEART FAILURE |

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Background: Patients with heart failure (HF) have a high risk of adverse outcomes and a poor prognosis. Many predictors of a poor outcome are known. Non-adherence to evidence-based HF medication leads to exacerbation in HF, decline in physical function, readmissions and mortality. Depression has been linked to medication non-adherence. However, the use of self-reported information in patients with HF has not thoroughly been investigated in relation to medication adherence.

Objectives: The aim is to study whether health-related quality of life, anxiety and depression is associated with one- and three-year medication adherence in a Danish cohort of patients with HF.

Methods: Design: cohort study with one- and three-year register-based follow-up. Inclusion: 1,506 patients with a HF diagnosis who answered The DenHeart Questionnaire at discharge from one the five heart centres in Denmark between 2013 and 2104.

Patient-reported outcome (PRO) data include: HeartQoL, the Hospital Anxiety and Depression Scale and EQ-5D. Data is linked to the data sources: The Danish Civil Registration System, the Danish National Patient Register, Statistics Denmark, the Register of Medicinal Product Statistics and medical records.

Perspectives: Medication adherence is associated with survival in patients with HF, and medication adherence is a possible modifiable factor. Knowledge about the association between quality of life, anxiety and depression and medication adherence could help us identify vulnerable patients with HF who could benefit from a closer and more regular contact to the healthcare system. This may enhance their medication adherence and thus improve the survival in these patients.

CH.61   Daniel Gramm   POPULATION RECEPTIVE FIELD MAPPING OF HUMAN V1 REVEALS BIAS-
         Kristensen   FREE DIFFERENCE-OF-GAUSSIANS BANDPASS FILTERS

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Sensory neurons have receptive fields, which are composed of a center and a surround. This center-surround organisation of visual receptive fields has been known since the earliest days of vision science and can be modelled using Difference-of-Gaussians (DoG). In the frequency domain, the DoG acts as a bandpass filter that lets individual neurons of the visual system process specific spatial frequencies. In signal processing, a well-known property of ideal frequency filters is that they are without DC bias. A DC-free filter is characterised by its integral being zero, i.e. the filter amplitude is equally positive and negative. In this context, a DC bias is an undesirable property as it will lower or raise the mean signal between processing stages so that the filtered signal is no longer relatable to the original signal. Ultimately, this means a lower signal to noise ratio. Here, we show that this bias-free state is only achieved under very specific circumstances in the DoG model. Next, we use biophysical modelling of the functional Magnetic Resonance Imaging (fMRI) blood-oxygen-level dependent (BOLD) response in human observers to create voxel-wise population receptive field (pRF) maps using the DoG model. We find that relative estimates of the size and amplitude parameters of the center and surround Gaussian are arranged so that frequency filters without DC bias are approximately achieved across all examined receptive field positions and sizes. In other words, we demonstrate, for the first time in human observers, that the receptive fields in the visual system are naturally organised in a manner that is optimal from a signal processing perspective.

CH.62   Karolina Snopek   THE EFFECTS OF 12 WEEKS OF HIGH INTENSITY RESISTANCE TRAINING IN
         Khan   PATIENTS WITH DIABETIC POLYNEUROPATHY:
                            A RANDOMIZED SINGLE-BLINDED CONTROLLED TRIAL

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Background: Distal sensorimotor polyneuropathy (DSPN) is the most common long-term complication of type 2 diabetes (T2D). At later stages of DSPN, denervation of distal striated muscles may occur, which may lead to atrophy and muscle weakness. In T2D, physical exercise has shown to have great benefits for the prevention and delay of disease progression. However, the role of exercise in DSPN has sparsely been studied, and exercise recommendations remain ambiguous.

Aim: The aim of the study is to investigate the effects of high-intensity resistance training (HIRT) on neuropathic signs and symptoms as well as strength, size and quality of striated muscles in patients with T2D and DSPN.

Method: A pre-test, post-test design is used to measure the effects of 12 weeks of supervised HIRT. In a single-blinded trial, participants are randomly assigned to training or control. Nerve conduction studies and clinical evaluations are used to diagnose and measure symptoms and severity of neuropathy. Isokinetic dynamometry is applied to determine muscle strength of the non-dominant knee, ankle flexors and extensors. Static posturography is assessed by measuring sway on a Tetrax platform. MRI scans of the non-dominant leg are performed to examine the muscle size and muscle quality using T2, Dixon and DTI sequencing.

Results: Until now, we have randomized and examined 38 patients with T2D and DSPN, 27 patients with T2D without DSPN and 27 healthy control subjects.

Conclusion: The results will provide further insight to the field concerning the effect of HIRT in T2D patients with and without DSPN. Further, the results may lead to new and more precise recommendations for exercise in DSPN.

CH.63   Rasmus Wulff   HOW WELL DOES CONTINUOUS PERIPHERAL NERVE BLOCKADE WORK?

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Ultrasound-guided continuous peripheral nerve blockade (cPNB) techniques for alleviating postoperative pain are expert procedures, which are indicated for a limited number of patients. Inserting cPNB catheters may be associated with disadvantages and unacceptably high numbers of failures.

The purpose of this review was to scrutinize the incidence of failures of ultrasound guided nerve catheters in the literature; a discussion of the imitations and the methods employed for evaluation of peripheral nerve catheters. We, therefore, performed a literature search for publications describing ultrasound guided perineural nerve catheter failures either as primary or secondary outcomes. We included 32 studies out of 471 studies and a total of 2679 peripheral nerve catheters.

We found a mean secondary catheter failure rate on 14% [95%CI: 10-17] during a mean observational time of 35 [95%CI: 28-42] hours. No difference in failures between catheters employed for upper or lower extremity surgery was found. Catheters evaluated objectively by image diagnostics had the highest mean failure rate of 19% [95%CI: 9-28], while catheters evaluated by telephone interview, patient charts, pain scores, cumulated opioids or questionnaires had a lower displacement rate of 12% [95%CI: 9-16, p<0.005]. The most plausible explanation is underreporting of catheter failures in outpatients, when evaluation depends on patient-reported proxy markers of catheter failure.

CH.64 Linda Aagaard Rasmussen
~~CANCELLED~~
USE OF GENERAL PRACTICE AND HOSPITAL SERVICES IN THE YEAR PRECEDING A DIAGNOSIS OF CANCER RECURRENCE OR SECOND PRIMARY CANCER: A NATIONWIDE POPULATION-BASED REGISTER STUDY

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Background: The organisation of cancer follow-up programmes are under scrutiny in many countries. In Denmark, general practice is to play a more prominent role in future cancer follow-up. Timely detection of cancer recurrence (CR) and second primary cancer (SPC) are central focus points. However, we need more knowledge on the patient pathway in the period before CR and SPC to ensure well-organised follow-up programmes.

Aim: To describe healthcare utilisation preceding a diagnosis of CR or SPC.

Methods: The study was based on data from patients with primary malignant melanoma and breast, lung, bladder, colorectal, ovarian and endometrial cancers in Denmark in 2008-2016. We estimated the frequency of healthcare use during the 12 months preceding a diagnosis of CR or SPC and compared this to the healthcare use in cancer survivors in remission using a negative binomial regression model and stratifying on healthcare setting and patient factors.

Results: Increasing number of contacts was seen for patients with CR or SPC; from seven months before diagnosis to general practice and from up to 12 months before diagnosis to hospital. The differences were most pronounced in women, younger patients, patients without comorbidity and patients with CR; incidence rate ratios increased from 1.30 (95% CI: 1.18-1.44) at 12 months before diagnosis to 7.95 (95% CI: 7.63-8.28) in the last month.

Conclusion: The results indicate a window of opportunity to provide more timely diagnosis of CR and SPC, from 7 months before in general practice and up to 12 months at hospital. Furthermore, the results emphasise the importance of coordination between general practice and hospital in cancer follow-up.

CH.65 Mia Glerup
LONG-TERM OUTCOME OF TEMPOROMANDIBULAR JOINT ARTHRITIS IN JUVENILE IDIOPATHIC ARTHRITIS

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Background/Purpose: The TMJ-related long-term outcome in JIA remains unknown. The aims of the study were to assess the symptoms, dysfunctions and radiological changes related to TMJ involvement in JIA 17 years after disease onset and compare to healthy controls.

Methods: From a Nordic population-based JIA cohort, 420 patients with disease onset between 1997 and 2000 were eligible. The follow-up visit included demographic data, a standardized clinical examination and a cone-beam computed tomography (CBCT). Two hundred age-matched references were used for comparison. IRB approval was granted.

Results: Out of 420 patients, 265 (63%) were included (mean age 23.5 (±4.2) years). Of the 265 participants completing the clinical orofacial examination, 245 had a full-face CBCT performed.

Orofacial symptoms: In 89/265 (33%) of the participants, jaw or facial pain was reported within the last two weeks. Compared to the controls, the patients with JIA had significantly more frequent orofacial pain (p=0.027). Of the 265 patients, 87 (33%) reported at least one TMJ symptom within the last two weeks.

Orofacial dysfunction: Mean maximal incisal opening was significantly reduced in the JIA group (47.2 mm (±7.7)) when compared to the controls (p<0.001).

Radiologic TMJ appearance: At least one abnormal condyle was found in 150/245 (61%) on CBCT, and 70% had bilateral changes.

Conclusion: This is the first study on the TMJ-related long-term outcome in the biologic era. The patients had more often orofacial pain compared to controls. Maximal incisal opening was significantly lower in the JIA participants. Condyle changes were found in more than half of the patients (61%).

CH.66   Susanna   PALATAL MORPHOLOGY IN UNILATERAL CLEFT LIP AND PALATE
         Botticelli   PATIENTS: IS THERE AN ASSOCIATION WITH CLEFT SIZE OR SURGICAL
                        METHOD APPLIED? A SINGLE CENTRE-CONTROLLED ANALYSIS WITHIN
                        AN RCT

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Aim: To describe palatal dimensions and morphology in UCLP patients randomized for early versus delayed hard palate closure in relation to non-cleft controls.

Setting: Tertiary healthcare. One surgical centre. Age, gender and ethnicity matched controls.

Subjects and Methods: Linear measurements of palatal height and width performed on 116 digital models of UCLP subjects participating in an RCT of primary surgery, with a variation in timing of hard palate closure and compared to a control group. Thereafter, a novel 3D method for analysis of morphological differences was applied and the distances between 3D models visualisized with colour mapping.

Results: UCLP patients presented with a palate higher than the controls at the level of the anterior scar (P=.002), but generally lower in the middle region (P<.001). The group who received hard palate closure presented a flatter palate posteriorly (P=.048). Reduced transversal dimensions were evident in both UCLP groups, but more in the group who received earlier hard palate closure (P= .003 and .031). The morphological analysis in 3D better depicted the anatomical complexity, revealing that, after delayed hard palate closure, the central palate is shallower in the middle and posteriorly. A significant correlation was found between infant cleft size, especially at the anterior level, and palatal height (P=.029; .010).

Conclusions: A UCLP palate significantly differs from a non-cleft control in width and height. Delayed hard palate closure may represent an advantage for the transversal dimension, but a disadvantage for the palatal height. Infant cleft dimensions at birth partially explain differences in palatal height.

CH.67   Stine Derdau   DOES WORKING MEMORY PREDICT MUSICAL COMPETENCE IN
         Sørensen   CHILDREN?

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Measuring melodic and rhythmic abilities is often used as a proxy for general musicality. However, melodic and rhythmic tests often rely on working memory, and the degree to which the test scores relate to the underlying constructs of melodic and rhythmic discrimination ability is

difficult to determine (Harrison et al, 2017). Furthermore, it has been shown that musicians perform better than non-musicians on verbal memory tasks (Talamini et al, 2017). This study investigates the relationships between musical competence, musical training and working memory in children of different ages by determining the strength of the association between the variables. 20,111 children (age range: 5-20 years) participated in the study. We administered the miniMET to assess melodic and rhythmic discrimination, a forward digit span test, and to measure musical engagement, we used the Concurrent Musical Activity questionnaire (Müllensiefen et al, 2015). Relationships between variables were analysed using structural equation modelling. Our preliminary results show that greater working memory capacity increases performance on both musical tasks and that musical training (as well as age) has a positive effect on working memory capacity.

Harrison, P.M., et al (2017). Applying modern psychometric techniques to melodic discrimination testing. Scientific Reports, 7(1), 1-18.

Müllensiefen, D., et al (2015). Investigating the importance of self-theories of intelligence and musicality for students' academic and musical achievement. Frontiers in Psychology, 6(222), 266-14.

Talamini, F., et al (2017). Musicians have better memory than nonmusicians: A meta-analysis. PLoS ONE, 12(10), 1-21.

CH.68   Luca Bordoni   ASSOCIATION BETWEEN MILD HYPONATREMIA WITH SUSTAINED INCREASED INTRACRANIAL PRESSURE IN A NEW ANIMAL MODEL AND ASSESSMENT OF THE EFFECT OF DDAVP DURING SEVERE WATER INTOXICATION

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Introduction: Brain edema has been studied in animals by water intoxication (WI). Classical models of WI use 10-20% body weight (BW) distilled water to induce severe hyponatremia (HN) and elevated intracranial pressure (ICP). Several studies also used desmopressin (dDAVP).

Aims: To establish a mouse model of mild-WI, which enables studies of sustained increased ICP, and to evaluate the effect of dDAVP during WI.

Methods: Six groups of mice (n=6) (B6) were anesthetized (isoflurane). Severe-WI groups (and Shams) received distilled water IP (20% BW), either with or without dDAVP (0.4 µg/kg). In mild-WI, we used 10% BW of a 36.25 mM Na^+ solution. We measured ICP, cerebral perfusion pressure (CPP), mean arterial pressure (MAP), blood gasses and urine production.

Results: In severe-WI groups, a very drastic increase in ICP was observed during severe-WI (ICP = 84.7 ± 12.3 mmHg), which induced brain stem herniation within 25 minutes. CPP was close to zero 26 min after WI. In dDAVP treated animals, time to peak of MAP was significantly shorter (2.9 ± 1.1 min). HN developed 5 min after WI (Na^+: 128±1.4). Surprisingly, urine production stopped regardless of dDAVP (p=0.757).

In mild-WI protocol, no side effects appeared in the measured parameters. HN was chronically mild ($Na^+=130$). ICP was high for the whole experiment (36.1 ± 9.7 for 70 min over 90). CPP experienced a significant drop 26 min after mild-WI, but remained stable afterwards (35.2 ± 8.9 at 60 min.)

Conclusion: dDAVP affected MAP, but not urine production. In mild-WI animals, we observed high ICP, but no side effects. Thus, the new mild-WI model is suitable for experimental studies of sustained cranial hypertension.

CH.69 Anne Vestbjerg Thyø   LONG-TERM SEXUAL DYSFUNCTION AND RISK FACTORS FOR SEXUAL DYSFUNCTION IN DISEASE-FREE FEMALE COLORECTAL CANCER PATIENTS: A POPULATION-BASED STUDY

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Background: Female sexual dysfunction (FSD) after rectal cancer treatment is increasingly addressed. However, most studies include a limited number of patients. FSD is underreported although it is well-recognised that it negatively impacts quality of life.

Aim: The aim of this study was to investigate long-term FSD in female colorectal cancer patients.

Method: Patients treated for colon and rectum cancer in 2001-2014 were identified. Female patients were invited to answer the validated Sexual Vaginal Changes questionnaire. Patients who declared to have been sexually active at time of diagnosis were included. Associations between various aspects of FSD and treatment-related factors were assessed by logistic regression analyses.

Results: 2402 females were included for analysis. Comparing rectal resection to colon resection, no difference in sexual function was found, except an increased OR for sexual inactivity (OR95%CI=1.32 (1.0-1.62). Abdomino-perineal resection with permanent stoma showed higher odds for dyspareunia (OR95%CI=1.97 (1.04-3.70)), reduced vaginal dimension (OR95%CI=2.57 (1.38-4.79)) and overall sexual dysfunction (OR95%CI= 1.98 (1.08-3.64) compared to low-anterior resection without stoma. Lastly, radiotherapy compared to no radiotherapy showed an increased OR ratio for dyspareunia (OR95%CI=1.79 (0.98-3.26)) and overall sexual dysfunction (OR=1.76 (0.98-3.16).

Conclusion: The study implies that pelvic rectal surgery alone is not as damaging on FSD as hypothesised. The main risk factors for FSD were radiotherapy and abdomino-perineal resection. Sexual function must be addressed, especially when treatment involves radiotherapy and/or abdomino-perineal resection.

CH.70   Mette Winther Klinge   **AMBULATORY ASSESSMENT OF GASTROINTESTINAL MOTILITY IN PATIENTS WITH DIABETES**

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Background/aim: Gastrointestinal (GI) symptoms are common in patients with diabetes mellitus (DM). Diabetic gastroparesis has been studied in detail, but data on the rest of the GI tract is scarce. A novel, ambulatory, wireless capsule system, Motilis 3D-Transit System, allows assessment of transit patterns throughout the whole GI tract in one single examination.

Methods: We studied 14 DM patients referred for GI symptoms and 15 healthy controls by means of 3D-Transit.

Results: All subjects were studied without complications. Median transit time through the entire GI tract was 78 hours (range: 26 to 440) in DM patients vs 30 hours (range: 14 to 71) in healthy (p<0.01). Median gastric emptying time was 3.6 hours (range: 0.8 to 43.2) vs 2.4 (range: 0.6 to 3.3) (p<0.01), median small intestinal transit time was 4.9 hours (range: 2.5 to 9.1) vs 4.7 (range: 1.4 to 7.6) (p=0.79), and median colorectal transit time was 60.8 hours (range: 14.6 to 431.4) vs 24.7 (range: 7.2 to 61.2) (p=0.02).

Conclusion: 3D-Transit allows safe, detailed and ambulatory assessment of GI transit in patients with DM. In many patients with DM and GI symptoms, prolonged transit is not restricted to the stomach.

CH.71   Jakob Kirkegård   **IMPACT OF CONCURRENT ACUTE PANCREATITIS ON PANCREATIC CANCER STAGE AND PROGNOSIS: A COHORT STUDY**

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Background: Pancreatic cancer is the 4th leading cause of cancer-related death worldwide. We investigated the association between acute pancreatitis, a potential early symptom, and pancreatic cancer stage and prognosis.

Methods: Using healthcare registries, we identified two cohorts of patients aged >65 years diagnosed with pancreatic cancer in Denmark (2004-2015) and the US (2004-2013). We distinguished between patients with and without a diagnosis of acute pancreatitis up to 90 days before pancreatic cancer, and followed them for up to 3 years from cancer diagnosis to death, loss to follow-up, or 31 December 2017 (31 December 2014 for the US cohort). We computed one-year survival rates with associated 95% confidence intervals (CIs), comparing patients presenting with acute pancreatitis with patients without acute pancreatitis.

Results: We identified 7,354 Danish (1% with acute pancreatitis) and 38,148 US (6% with acute pancreatitis) patients with similar median ages (75 years and 78 years, respectively). In both cohorts, acute pancreatitis patients had less metastatic disease (39% and 35%) than patients without acute pancreatitis (45% and 46%). In Denmark, acute pancreatitis patients had a 1-year survival of 24% (95% CI: 15%-35%) compared with 18% (95% CI: 17%-19%) in patients without acute pancreatitis. In US, these numbers were 23% (95% CI: 22%-25%) and 20% (95% CI: 20%-21%), respectively.

Conclusions: Our findings suggest that acute pancreatitis preceding pancreatic cancer diagnosis is associated with better survival, possibly attributable to earlier detection at a lower tumor stage.

CH.72   Stine Andersen   EFFECTS OF COMBINED ANGIOTENSIN II RECEPTOR ANTAGONISM AND NEPRILYSIN INHIBITION IN EXPERIMENTAL PULMONARY HYPERTENSION AND RIGHT VENTRICULAR FAILURE

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Background: In pulmonary arterial hypertension, increased RAAS activity and reduced production of cGMP contribute to pulmonary vaso-constriction and remodeling and consequently right ventricular (RV) failure. This study evaluates the effects of combined angiotensin II receptor antagonism and neprilysin inhibition by LCZ696 in rats with pulmonary hypertension and RV failure.

Methods: Pulmonary hypertension was induced in rats by combined exposure to the VEGF-receptor antagonist SU5416 and hypoxia (SuHx). To distinguish pulmonary vascular from cardiac effects, isolated RV failure was induced by pulmonary trunk banding (PTB) in another group of rats. In both models, the development of RV dysfunction was verified before randomization to treatment with LCZ696 (60 mg/kg/day) or vehicle for five weeks.

Results: The SuHx and the PTB rats all developed RV failure compared with healthy sham rats. In the SuHx rats, LCZ696 treatment reduced the increase in RV systolic pressure (mean difference: -12±4 mmHg, p<0.01) and the development of RV hypertrophy (RV weight corrected for tibia length) (mean difference: -2.3±0.7 mg/mm, p<0.01) and RV dilatation (RV end diastolic volume) (mean difference: -0.09±0.04 mL, p<0.05) compared with vehicle treatment. LCZ696 also reduced wall thickness of the smaller pulmonary arteries. In the PTB rats, treatment with LCZ696 did not have any effects on RV hypertrophy or function.

Conclusion: LCZ696 reduced RV systolic pressure, hypertrophy and dilatation in rats with pulmonary hypertension. These effects may be

secondary to pulmonary vascular changes, including reduced pulmonary vascular remodeling, as similar effects were not seen in rats with isolated RV failure.

CH.73 Mikkel Giehm-Reese

OUTCOME AFTER CATHETER ABLATION FOR LEFT ATRIAL FLUTTER

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Background: Left atrial flutter (LAFL) has been reported in up to 10% of patients following pulmonary vein isolation or cardiac surgery. LAFL is typically highly symptomatic, responds poorly to medical antiarrhythmic treatment, and is often treated by catheter ablation (CA).

Aim: We aimed to investigate midterm freedom from recurrent arrhythmia after CA for LAFL.

Methods: In the National Danish Ablation Registry, we identified consecutive patients who had undergone CA for LAFL between January 1st, 2014 and April 1st, 2017 at our centre.

Results: A total of 53 patients (median age: 68 years (IQR 60-71) 37 (70%) male) were included. Forty-two patients had previously undergone a left atrial (LA) CA procedure (79%), one patient previously underwent cavo-tricuspid isthmus-block for classic atrial flutter (2%), four patients had prior surgery for congenital heart disease (8%), and six patients (11%) had no previous cardiac intervention. Acute procedural success, defined as non-inducibility of any atrial arrhythmia, was achieved in 45 of 53 patients (85%). During midterm follow-up (mean 20 ± 12 months), 26 patients experienced an episode of recurrent atrial arrhythmia. Median EHRA score was 3 (range: 2-4) before CA and reduced to median 1 (range: 1-3) evaluated at follow-up visits after three and twelve months (both p < 0.001, Wilcoxon rank test).

Conclusion: LAFL is preceded by catheter ablation or cardiac surgery in 89% of patients. Acute procedural success is achieved in the majority of patients, and ablation reduces symptoms effectively. During midterm follow-up, almost half the patients experience recurrent atrial arrhythmia.

CH.74 Elias Didrik Francis Zachariae

CHARACTERIZATION OF EXTRACELLULAR SUPEROXIDE DISMUTASE FROM MENKES DISEASE MACROPHAGES

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Menkes disease (MD) is a rare, lethal multisystemic disorder, arising from mutations in the cellular copper transporter ATP7A. Classical MD patients rarely survive beyond the first years of their life. However, several forms of MD exists, with varying degrees of severity all differing in the number of mutations and the location of these in the ATP7A gene. Most MD patients die within three years of age, normally from infection or vascular

complications. ATP7A is an ATPase and copper-loading chaperone located in the trans-golgi network. ATP7A is responsible for loading copper into copper-containing proteins in the secretory pathway and is thus the copper loading chaperone for extracellular superoxide dismutase (SOD3). SOD3 is an antioxidant enzyme involved in redox signalling, protection against oxidative stress, and immune function. Copper availability has previously been shown to regulate SOD3 expression at the transcriptional level. However, insight into to the process of regulation and its consequences on the level of protein synthesis and folding has yet to be obtained. In the present study, we wish to investigate how copper deficiency affects the protein maturation and expression of SOD3. In order to support this, we characterized SOD3 and its expression in two mutated forms that are perturbed in their copper-binding site. In addition, we investigated the expression and the molecular behaviour of SOD3 in murine macrophages derived from Brindle mice, a strain mutated in the ATP7A gene - thus mimicking MD macrophages. From the present study, we hope to shed light on the role of SOD3 in MD lethality, thereby adding to our knowledge on this rare hereditary disease.

CH.75   Anna Halling Folkmar Andersen

ESTABLISHMENT AND VALIDATION OF A HUMANIZED MOUSE COLONY FOR STUDYING HIV INFECTION AND HUMAN IMMUNE MECHANISMS

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A limitation of investigating human infectious diseases is the inaccessibility of appropriate animal models, which mimic the human immune system. It is especially true for human immune deficiency virus (HIV), which only infects human CD4+ T cells.

We aimed to establish and validate a state-of-the-art humanized mouse susceptible to HIV infection. NOG mice that lack endogenous T, B and NK cells were transplanted with human CD34+ cord blood-derived stem cells. Differentiation of human immune cells were analysed by flow cytometry, where the level of humanization was uniform and correlated with the amount of injected stem cells, indicating a predicable graft success rate. Mice were able to respond in both the human and mouse immune compartment on cellular and cytokine levels to a cGAMP-mediated STING activation, indicating a functional immune system.

Next, mice were exposed through either vaginal (i.vag) or intravenous bolus of the virus isolate RHPA with an empirical low dose. We saw 100% transmission success in 15 i.v. exposed animals and 64% transmission a cohort of 11 i.vag.-exposed mice. We confirmed both integrated HIV DNA in human cells and HIV RNA in plasma by ddPCR. Moreover, we were able to treat the mice with food pellets containing standard of care combination antiretroviral therapy (cART). We are currently pursuing both a prevention and a treatment strategy with a novel long-acting lipid-based cART in this model.

These inaugural results prove that we have a robust mice model with a functional human immune system, susceptible to HIV and responsive to cART. These results will drive future research in anti-HIV strategies.

CH.76   Martin Nors Skov   TELEMETRIC APPROACHES TO ASSESS PROGRESSION OF PERIPHERAL NEUROPATHY

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Peripheral nerve neuropathy (PNN) is a common condition seen in a variety of diseases. PNN may affect both large and small fibers and cause sensory and motor disturbances. The disease may also affect the autonomic nervous system. The autonomic neuropathy is a silent disease, which is not recognized before there are clear manifestations of the disease with gastrointestinal and cardiac disturbances. As of now, how the progression is unfolding in the development of neuropathy is not known. Introduction of novel telemetric devices may become important to reveal this information in animal models.

I have taken the standard setup used in electrophysiology and is in the progress of making it into a small specialized telemetric implant. In combination with Qtrac, a real-time threshold tracking software and a stimulator, the implant can act as a wireless pre-amplification stage. The progress started with finding the parameters for an action potential derived from an artificial stimulation. This is then used for defining the analog filter-amplification input stage of the implant. Due to the sized restricting, different approaches were tried out to maximize the signal-to-noise of the input. A typical approach using a cascaded filter did not work due to the peculiar shape of the signal. A high square signal and 4ms after followed by the low in amplitude action potential. The solution ended up to be a double instrumental amplifier circuit with the latter restricted in one input by a doubled diode limiter circuit. Small adjustment has now been done, and soon quality trails will begin in both human and rats to confirm that the implant is just as good as the regular electrophysiology setup.

CH.77   Jibrin Danladi   THE ROLE OF NEUROGLOBIN AND CYTOGLOBIN IN DENDRITIC SPINE DYNAMICS AND SYNAPTIC PLASTICITY

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Introduction: For the past two decades, a large number of clinical trials for neuroprotectants against stroke and neurodegenerative disorders have yielded mostly disappointing outcomes. The compelling evidence that neuroglobin (Ngb) can act as a neuroprotectant by preserving mito-chondrial function and decreasing oxidative stress under conditions of hypoxia and ischemia has suggested that Ngb may hold potential as a novel therapeutic target for neurological pathologies characterized by neuronal cell death, such as stroke and neurodegenerative disorders.

Material and Method: Adult male mice brains were removed, and Golgi-Cox staining was performed according to standard methods. Brain samples were sliced into 150 μm using a vibratome. Each section was mounted on gelatin-coated glass slides. Z-stacks of dendritic trees (6 neurons per animal) from apical and basal pyramidal neurons from the hippocampus were acquired and 3D reconstructed, and dendritic spine subtypes were identified and quantified using Imaris XT spine classification module.

Results: Dendrite volume in Ngb-ko and Cytoglobin (Cygb)-ko mice were significantly higher compared to wt mice. Spine parameters (number, area, length and spine volume) in Ngb-ko and Cygb-ko mice were significantly higher than wt mice in the apical pyramidal neurons of the hippocampus.

Conclusion: Our results demonstrate that lack of Ngb and Cygb impairs dendrite and spine pruning.

CH.78   Camilla Højland Knudsen

HIPSC-DERIVED OECS FOR SPINAL CORD REPAIR

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Spinal cord repair remains one of the most challenging problems in regenerative medicine, and there is currently no effective cure for spinal cord injury (SCI). Olfactory ensheathing cells (OECs) have shown great promise in promoting axon regeneration in the CNS following nerve damage. However, the availability and immune-compatibility of readily obtainable OECs pose major limitations in the advancement of this exciting field of research, as does the limited knowledge of molecular processes and biomarkers involved in OEC development.

We carried out next generation sequencing (NGS) of the transcriptome of primary OECs to gain insight into the mechanisms of OEC development and identify specific OEC markers. Using NGS analysis, we characterised key transcription factors and signalling pathways relevant to OEC fate specification. We are now using this information to develop novel strategies for directed differentiation of human induced pluripotent stem cells (hiPSCs) into mature OECs. Validation of hiPSCs derived OECs will include RNA and protein expression analysis of common markers and novel markers highlighted in our NGS analysis, along with functional in vitro studies. Finally, we will test the reparative potential of the hiPSC derived OECs in in vivo transplantation studies in rat SCI models.

Producing OECs from hiPSCs would facilitate unlimited expansion of cells whilst simultaneously permitting the creation of cell lines that are immune-compatible to patients. In this manner, generating differentiation protocols that allow the production of highly enriched OECs from hiPSCs will enable us to further investigate the therapeutical potential of OECs in spinal cord repair.

CH.79   Lone Kirkeby   INFLUENCE OF OCCUPATIONAL HAND FORCE REQUIREMENTS ON RETURN TO WORK AFTER TRAPEZIOMETACARPAL TOTAL JOINT ARTHROPLASTY: A ONE-YEAR FOLLOW-UP STUDY

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Background: There are no previously published studies concerning return to work (RTW) after surgery for trapeziometacarpal joint osteoarthritis.

Aim: To determine the prognosis for RTW for patients with trapezio-metacarpal joint osteoarthritis treated with a total joint arthroplasty, hypothesizing that occupational mechanical exposures are negative prognostic factors.

Material & Methods: A prospective follow-up study of 239 consecutive patients aged 39-65 (mean: 55) years who were operated with a trapeziometacarpal total joint arthroplasty in the time period 2003-2015. We obtained information about labour market attachment from the DREAM database and estimates of occupational hand force requirements for individual patients by linking the patients' self-reported job title to a job exposure matrix. We used univariable and multivariable Cox regression models to analyse time until RTW.

Results: Most patients, 122 out of 133 patients (92%) who were active on the labour market before surgery and with stated job title, returned to work within 12 months after surgery, regardless of occupational hand force requirements. Force-demanding work was a predictor of longer sick leave before RTW; for patients with high force-demanding work, the hazard ratio was 0.44 (95% CI 0.27-0.70).

Conclusion: The prognosis after trapeziometacarpal total joint arthroplasty with respect to RTW is generally good. High occupational hand force requirements are associated with prolonged sick leave. Knowledge of the patients' occupational exposures is necessary for conveying realistic expectations regarding the time needed off work postoperatively.

CH.80   Anne Birkeholm Jensen   LEUKOTOXIC ACTIVITY AMONG JP2 AND NON-JP2 GENOTYPES OF AGGREGATIBACTER ACTINOMYCETEMCOMITANS SEROTYPE B

CANCELLED

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Background and Aim: Presence of the JP2 genotype of Aggregatibacter actinomycetemcomitans (Aa) in periodontal pockets is associated with a high risk of development of marginal periodontitis in adolescents. Recently, some non-JP2 genotypes of Aa strains, serotype b were suggested also to have a relatively high leukotoxic potential. The aim of

the present study was to elucidate the leukotoxic potential of Aa strains of JP2 genotype, serotype b compared to the leukotoxic potential of non-JP2 genotypes, serotype b.

Materials and Methods: Forty-nine Aa strains, serotype b (25 JP2 genotypes and 24 non-JP2 genotypes) were analyzed by three different methods, i.e. mRNA expression assay, ELISA, and a cell lysis (lactate dehydrogenase (LDH)) assay, to assess the leukotoxic potential for each of the strains. The expression of the mRNA coding for the production of Leukotoxin (LtxA) was determined by RT-PCR. The amount of produced LtxA was quantified by an ELISA. The LDH assay analyzed the LtxA-mediated killing of a human macrophage cell line.

Results: The group of JP2 genotype strains had a higher leukotoxic potential than the group of non-JP2 genotype strains by use of all three methods (p< 0.05 for all three methods). Five non-JP2 genotype Aa strains showed relatively high leukotoxic activity, which was demonstrated by the LDH assay, but the strains neither produced LtxA nor expressed mRNA coding for the production of LtxA in comparable amounts to the JP2 genotype strains.

Conclusion: By use of three different methods, the results support the notion of the JP2 genotype of Aa, serotype b, as a particularly highly virulent strain compared to the non-JP2 genotype strains of Aa, serotype b.

CH.81   Pernille Byrialsen Elming   COMBING HYPERTHERMIA WITH LOW LET RADIATION IS EQUIVALENT TO HIGH LET RADIATION ALONE

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Purpose: Tumor hypoxia causes resistance to low linear energy transfer (LET) radiation (i.e., photons). An approach is to use high LET radiation (i.e., carbon ions), but this is not so accessible. However, by using additional therapies, it may make tumor response equivalent to that seen with high LET radiation. We investigated this by combining low LET radiation with hyperthermia.

Methods: Mice with a 200 mm^3 tumor on the foot were used. The mice were placed in jigs, and the tumour-bearing leg was immersed in a water bath at 25 °C for radiation alone or with heat at 41-43 °C for 60 minutes. Radiation was applied in the middle of the heating period (simultaneous treatment), or 1 or 4 hours prior to heating (early/late sequential treatment). The endpoint was the TCD50 value (radiation dose causing tumour control in 50% of mice 90 days after treatment), and it was estimated from logit analysis of the radiation dose-response curve.

Results: The TCD50 value for low LET photon irradiation alone was 54 Gy. Previous studies with carbon ions in the same tumor model reported a TCD50 value 1.5 times lower than this. A similar enhancement ratio (ER; ratio of TCD50 values for radiation alone and radiation + modifier) of 1.5 was obtained with a temp. of 41.5 °C when given simultaneously with low LET radiation. For a late sequential radiation and heat treatment, temp. of

42.5 ^{O}C and above were necessary. The effect of using an early sequential approach is pending.

Conclusions: Local tumor control obtained with high LET carbon ions is also possible with low LET photons if combined with hyperthermia. The temp. at which this response is observed is dependent on the radiation and heat sequence.

CH.82   Rikke Smedegaard Rosbjerg

RETURN TO WORK SELF-EFFICACY (RTWSE): VALIDATION OF THE RTWSE QUESTIONNAIRE IN A POPULATION OF CANCER PATIENTS ON SICK LEAVE

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Objective: Return to work self-efficacy (RTWSE) has shown to be an important psychological factor in the return to work process of workers on sick leave due to both psychological and physical disorders. The RTWSE questionnaire has been validated in several countries and in various populations of workers on sick leave. However, the validity of the RTWSE questionnaire has not yet been investigated in a population of cancer patients. Therefore, the aim of the present study is to test the reliability, the validity and the responsiveness of the 19-item RTWSE questionnaire in a population of employees with cancer on sick leave.

Methods: Tests of reliability, validity and responsiveness of the RTWSE-19 questionnaire will be performed on 65 Danish cancer patients with various cancer diagnoses and at different stages of the disease. The participants, who are all on sick leave at baseline, are asked to fill out the RTWSE-19 questionnaire at baseline, at one week follow-up and at three months follow-up. In addition, questionnaires regarding the following secondary variables are also filled out: work ability, general self-efficacy, cancer-related self-efficacy, depression and anxiety. Demographics and illness-related factors are also measured.

Results: Data collection is still ongoing, and results will not be available until spring 2019.

Conclusion: To improve the work ability and the process of return to work for cancer patients, it is necessary to obtain a better understanding of the return to work process of cancer patients. RTWSE may play a key role in that process.

CH.83   Sara Birch   DOES PAIN CATASTROPHIZING PREDICT PHYSICAL FUNCTION AFTER
KNEE ARTHROPLASTY?

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Background: Pain catastrophizing might contribute to acute and long-
term pain after knee arthroplasty (KA), but the association between pain
catastrophizing and physical function is not well studied.

Aim: 1) To examine the association between preoperative pain cata-
strophizing and physical function one year after surgery and 2) to
investigate possible differences in pain, general health and physical
function among two groups of patients with high and low preoperative
pain catastrophizing score.

Methods: A total of 615 patients scheduled for KA were included in this
study between March 2011 and December 2013. The Pain
Catastrophizing Scale (PCS) was completed prior to surgery and Oxford
Knee Score (OKS), Short Form-36 (SF-36) and EuroQol-5D (EQ-5D) were
completed prior to surgery, and 4 and 12 months after the surgery.

Results: Of the 615 patients, 442 underwent Total Knee Arthroplasty (TKA),
and 173 received Unicompartmental Knee Arthroplasty (UKA). Mean age
was 67.3 and 53.2% were females. Patients with PCS>21 have
significantly larger improvement in mean OKS than patients with PCS<11
(3.17 (95%CI: 0.95-5.39)) for TKA and (5.38 (95%CI: 2.24 - 8.52)) for UKA.
Further, patients with preoperative PCS>21 had significantly lower OKS,
SF-36 and EQ-5D and higher pain score than patients with PCS<11, both
preoperatively and 4 and 12 months postoperatively.

Conclusion: The present findings suggest that patients with high levels of
preoperative pain catastrophizing have lower physical function, poorer
general health, and more pain, both before and after KA, which indicates
that interventions designed to reduce pain catastrophizing might have the
potential to further improve the outcome after KA.

CH.84   Anna Sofia   HEART SKILLS - A HEALTH LITERACY PROFILE OF 161 PEOPLE REFERRED
         Elisabeth Aaby   TO MUNICIPAL REHABILITATION

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Background: Health literacy is the skills determining motivation and ability
to access, understand and use information in ways that promote and
maintain good health. Health literacy profiles provide a deep under-
standing of the challenges within a population allowing targeted, context-
sensitive intervention development. Among people referred to a
municipal cardiac rehabilitation programme, this study aims to provide a
health literacy profile characterising clusters with similar health literacy
patterns.

Methods: This study was based on survey data from 161 people referred to cardiac rehabilitation in Randers Municipal Rehabilitation Unit. The survey covered socio-demography, disease course, health status (SF-12) and the nine health literacy aspects in the Health Literacy Questionnaire (HLQ). Hierarchical cluster analysis on the HLQ was performed.

Results: Six clusters were selected as the optimal cluster solution. Each cluster represented a unique health literacy pattern. The two most challenged clusters were cluster E (n=19), characterized by low HLQ scores in navigating the health system as well as engaging actively with and feeling understood by healthcare providers, and cluster F (n=10), characterized by low HLQ scales scores in finding, understanding and evaluating information as well as actively managing their health. Both clusters had distinct socio-demographic and health characteristics.

Perspectives: The health literacy profile has provided a new understanding of the challenges among people referred to Randers Municipal Rehabilitation Unit. Targeted interventions can now be developed.
The specific profile may be generalizable to similar contexts.

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