

# PHD DAY

## HEALTH

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## PROGRAMME & ABSTRACTS

### 27 JANUARY 2017

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# PHD DAY 2017 PROGRAMME

LOCATION: THE LAKESIDE LECTURE THEATRES

27 JANUARY 2017

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- 8.30 **Welcome**  
*Ole Steen Nielsen, Acting Dean, The Faculty of Health, Aarhus University*
- 8.40 **Welcome and today's program**  
*Karthiga Thavachelvam, PhD student, Chairman of the PhD Association, Health, AU*
- 8.45 **Fogh-Nielsen Competition**  
*Chaired by Lise Wogensen Bach, Vice-Dean, Member of the Fogh-Nielsen board and co-chairman  
Rune Dall Jensen, PhD Student, Health, AU*
- 9.30 **Coffee/tea and fruit break**
- 9.45 **"Keep it simple", keynote lecture**  
*Mina J. Bissell, Distinguished Scientist, Biological Systems and Engineering Division, Lawrence Berkeley National Laboratory  
Introduced by Helene Nørrelund, Head of the Graduate School, Health, AU*
- 10.45 **Break**
- 11.15 **Poster presentations**  
*The lakeside Lecture Theatres, the Bartholin Building (build. 1241) and Anatomy (build. 1230)*
- 12.45 **Lunch /poster viewing**  
*The lakeside Lecture Theatres, the Bartholin Building (build. 1241) and Anatomy (build. 1230)*
- 13.30 **Oral presentations**  
*The Lakeside Lecture Theatres and the Bartholin Building (build. 1241)*
- 15.00 **Coffee/tea and cake break**
- 15.15 **"Keep it simple", keynote lecture**  
*Martin Vesterby, MD, Ph.d, Innovation Manager, Department of Clinical Medicine  
Introduced by Helene Nørrelund, Head of the Graduate School, Health, AU*
- 16.15 **Awards, Posters and oral presentations**  
*Professor, Bent Winding Deleuran and PhD Student, Nichlas Riise Jespersen, Chair and Co-chair of the Organizing Committee, PhD Day 2017*
- 16.30 **Closing remarks**  
*Helene Nørrelund, Head of the Graduate School, Health, AU*
- 18.30 **Dinner and awards ceremony for the Fogh-Nielsen Competition**  
*Centralværkstedet*  
**Festive speech**  
*Alexander Fjældstad, PhD Student*

Aarhus University  
Graduate School of Health

**PHD DAY**  
**27 JANUARY 2017**



# Practical Information

- Posters should be hung up between 16:30 and 19:00 on 26 January or between 7:30 and 8:00 on 27 January. All posters must be taken down before 15:15.
- Oral presenters for sessions O1-O5 must meet in the auditorium concerned between 7:30 and 8:00 on 27 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 at Anatomy.

**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 7-22:** Bartholin building, Auditorium 2, 3, 4, Studyroom, Gardenroom, room 130 and halls

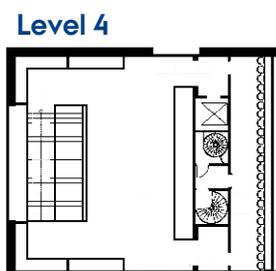
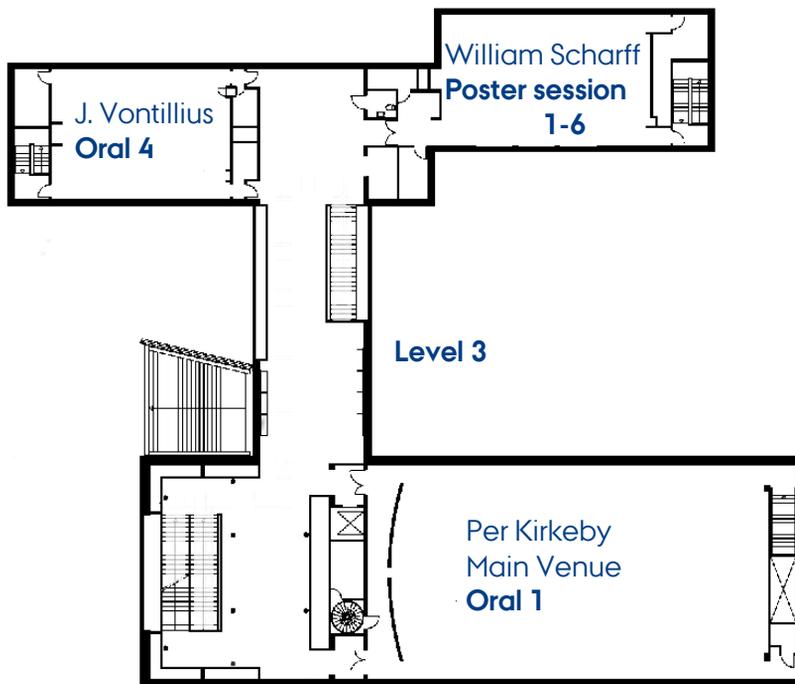
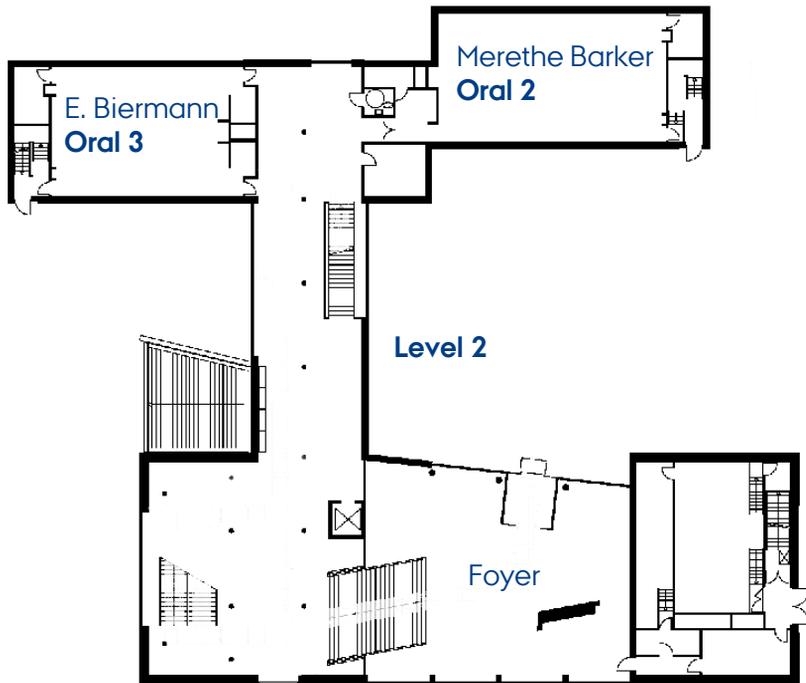
**Poster session 23-30:** Anatomy (building 1230): Hall and Colloquium room 1

## Organizing committee:

- *Bent Deleuran, Professor, Department of Biomedicine, Chairman*
- *Nichlas Riise Jespersen, PhD student, Department of Clinical Medicine, Co-chairman*
- *Anne Louise Hansen, PhD student, Department of Biomedicine*
- *Ebba Nexø, Professor, Department of Clinical Medicine*
- *Helle Møllerup, PhD Administration*
- *Iben B. Pedersen, PhD student, Department of Clinical Medicine*
- *Johan Palmfeldt, Associate professor, Department of Clinical Medicine*
- *Katrine Lehmann, PhD Administration*
- *Mark Denham, Associate professor, DANDRITE - Denham Group*
- *Rasmus Pihl, PhD student, Department of Biomedicine*
- *Rikke Hjortebjerg, PhD student, Department of Clinical Medicine*
- *Rikke Nørregaard, Associate professor, Department of Clinical Medicine*
- *Rune Dall Jensen, PhD student, CESU*
- *Stine Andersen, PhD student, Department of Clinical Medicine*
- *Trine Wigh Arildskov, PhD student, Department of Clinical Medicine*
- *Trine Ørhøj Barkholt, PhD student, Department of Clinical Medicine*
- *Ulla Kampmann Opstrup, Postdoc, Department of Clinical Medicine*

## Social media:

- Facebook: PhD Association Health
- Twitter: #auphd17



**Bartholin Building**

- Oral 5
- Poster session 7-22

**Anatomy**

- Poster session 23-30

# Science - Keep It Simple

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 2017.

You are invited to enjoy five oral and 30 poster sessions as well as the Fogh Nielsen Competition. This year's topic aims to inspire you to present your research in a way that it is easy to understand – *Keep it simple!* This is also the reason why all presentations are mixed, as we emphasize the purpose of being able to deliver a presentation that is understandable for everybody.

This year we have two keynote speakers: Professor Mina Bissell from University of California, Berkeley in USA and innovation manager Martin Vesterby, Aarhus University.

Mina Bissell will engage you all in new ways to understand science. Mina Bissell has won numerous awards for her scientific achievements, but also for her brilliant ability to present her scientific results.

Martin Vesterby is the Innovation Manager at INNO-X Healthcare, Department of Clinical Medicine. He will provide an eye-opener for the value of communicative skills.

By the end of the day we hope that every one of you will be full of new ideas of how to present your scientific results in a way that is easy to understand.

Finally, a warm thank you to everybody who has participated and helped to make the PhD day 2017 a – hopefully – joyful and inspiring event.

Bent Deleuran, Professor  
Chairman of the Organizing Committee  
Health, Aarhus University

Nichlas Riise Jespersen, PhD student  
Co-Chairman of the Organizing Committee  
Health, Aarhus University

Ole Steen Nielsen  
Acting Dean  
Health, Aarhus University

Lise Wogensen Bach  
Vice-dean  
Health, Aarhus University

Helene Nørrelund  
Head of Graduate School  
Health, Aarhus University

# The Keynote Lecture

Mina J. Bissell, Ph.D. Distinguished Scientist



Mina J. Bissell is Distinguished Senior Scientist (the highest academic rank) at the Biological Systems and Engineering Division of Lawrence Berkeley National Laboratory (LBNL), and a Faculty of 4 Graduate Groups in UC, Berkeley.

She is a pioneer in the field of microenvironment and the role of context in gene expression with specific emphasis in breast cancer.

Her research has identified mechanisms that link extracellular matrix (ECM) and organ architecture with regulation of chromatin and gene expression in both normal and malignant cells.

Mina Bissell was the founding director of Cell and Molecular Biology Division, and later the director of all Life Sciences at LBNL. Dr. Bissell earned her Ph.D. in Microbiology & Molecular Genetics from Harvard Medical School and has been elected to most US honorary scientific Academies including NAS, NAM, and American Philosophical Society.

Dr. Bissell is an inspiring mentor, has published more than 400 papers, is one of the most sought after speakers in the field, and has received numerous awards. To name but a few: the Lawrence Award, the American Cancer Society Medal of Honor, the AACR/Pezcollar award, and the inaugural Lifetime Achievement Award from LBNL.

This academic year, she received the Ernst W. Bertner Award from MD Anderson Cancer Center, the Medal of Honor of the Signaling Societies in Germany and the Wilson Medal, the highest award of the American Society of Cell Biology.

Dr. Bissell sits on many National and International scientific boards and has received honorary doctorates from Pierre and Mari Curie, France and Copenhagen University. She continues to engage in full time research as well as other scientific activities.

# The Keynote Lecture

Martin Vesterby, Research Business Manager



Martin Vesterby sold his first ICT-concept (information and communications technology) “NEPO” when he was a medical student. He is cofounder of Visikon - a ICT company that works with animations as an integrated part of communication oriented towards patients. The foundation of the company is the theories Martin developed through his Ph.D. thesis. Visikon is focusing on the empowerment of patients and battling health-illiteracy. While the company received the Danish IT-Innovation price and the Capnova IT-Idea price in 2014 it is most known for the “Safe Delivery App” that helps save lives in Africa and Asia. The app is applauded by healthcare providers and is praised by

Tim Cook from Apple and the Gates Foundation.

At The Department of Health, Aarhus University, Martin functions as Research Business Manager. He is working to connect the foremost researchers from AU with the private and public sectors to increase the value proposition of competencies in academia to the benefit of society.

Martin is a part of the team behind CrowdsWhoCare that is the first crowdfunding- and crowdsourcing-platform of its kind in the healthcare sector. CrowdsWhoCare connects innovation and research projects with individuals and companies who want to support the project with financial resources or expertise. Furthermore, Martin is the Director of Innovation and Research at INNO-X Healthcare, Institute of Clinical Medicine, Aarhus University. INNO-X Healthcare is working with interdisciplinary need driven innovation and research in order to create value and sustainable solutions. The purpose of INNO-X Healthcare is to educate researchers and healthcare providers so they are able to bridge the gap that currently exists between knowledge and value creation in the healthcare area.

Martin spends a majority of his spare time at Stauning Whisky which he cofounded in 2005. Stauning Whisky recently received an investment of more than 100 million DKR and are currently expanding their production so they are able to produce 900.000 liters of whisky a year in 2018.

In 2011, Martin received Reinholdt W. Jorck and Wife’s Foundation Research Prize, administrated by The Confederation of Danish Enterprise (Dansk Erhverv). The foundation emphasized “his exceptional skills as an entrepreneur creating new partnerships between university and industry in ways not previously seen” as a major reason why Martin received the award.

# Student counsellor for PhD students

*Surviving you dissertation*

*From time to time it is more than a book title.*

In the knowledge that studying for a PhD can be an overwhelming challenge, then Health has established a student counsellor for PhD students. What would you answer if I asked:

*Is it difficult to plan your daily work?*

*Are things not working?*

*Is it hard to collaborate with your supervisor?*

*Do you find your situation as a PhD student difficult or unsatisfactory?*

I am always an interested listener. As PhD student counsellor I am a professional interlocutor. Conversations with me are confidential and anonymity is promised. It is not an alternative to the professional research supervision. By means of conversations, the counsellor can help students become aware of what they perceive as difficult and why. This is done in close collaboration with the Secretary of The Graduate School of Health if the process related issues have administrative elements. The intention is to help PhD students gain clarity, come to terms with their situation. It is also to help them to see other opportunities, if they experience personal problems or other difficulties related to the process of working and studying as a PhD student. The counsellor can also assist students to make competent decisions.

**You are always welcome to contact the PhD student counsellor!**

**Sometimes sooner is better than later - no problem is too small for a talk.**

Personal contact: Sanne Angel

phdstudievejleder@sun.au.dk

Phone: 871 67889

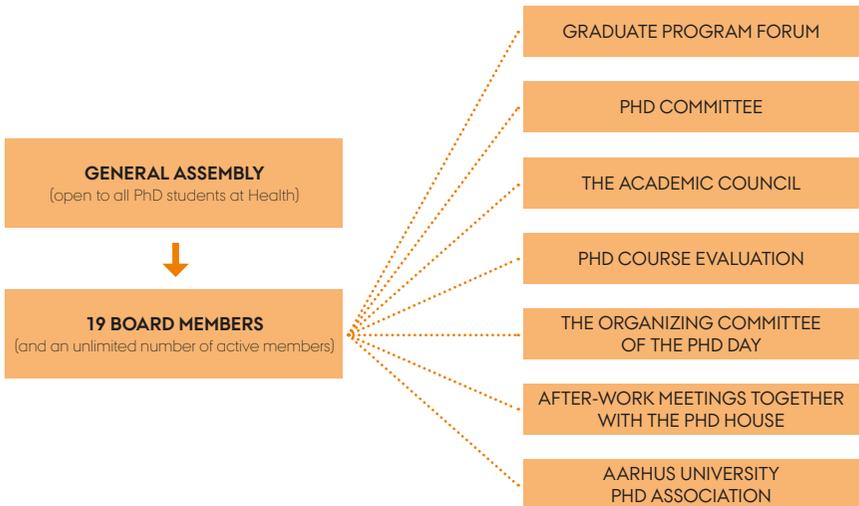


AARHUS UNIVERSITY

# PHD ASSOCIATION HEALTH

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

## ORGANISATION



Working together to improve the education and conditions of  
PhD students at the graduate school of health

Join us on Facebook at: [PhD Association Health](#)  
or check out our webpage: [phdassociation.dk](http://phdassociation.dk)

**ALL PHD STUDENTS CAN JOIN!**

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**Working  
hard  
for you!**

# 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

The Office of International Relations is part of the Dean's Office and located at Nordre Ringgade 1. All students, staff and faculty members are welcome to contact us for information and assistance.



**Anna Kronborg Bell**  
International Coordinator  
Phone: +4540531320  
E-mail: akb@au.dk

**Tanja Hansen**  
International Advisor  
Phone: +4593508108  
E-mail: tanja.hansen@au.dk

## International Academic Staff Services (IAS) at the International Centre

In close collaboration with AU Human Resources, International Academic Staff Services (IAS) helps foreign researchers (incl. PhD students) and their families through the practical challenges tied to living in Denmark. As part of this, the unit operates a help desk and a website [www.ias.au.dk](http://www.ias.au.dk).

IAS provides counsel for international PhD students and their family about issues of relevance, incl. job for the spouse, international schools and nurseries. The unit also provides information about practicalities for PhD students planning a research stay abroad.

Furthermore, IAS assists international staff and PhD students with the paperwork and practical challenges during their stay in Denmark, e.g. health insurance and extension of residence and work permits. The IAS help desk is open Monday, Wednesday & Friday 10am-2pm and Thursday 10am-1pm at the International Centre.

To make the transition to Denmark as easy as possible, IAS encourages new internationals to participate in the AU introductory events. The AU Introduction Day gives a general introduction to AU as an organisation and takes place twice a year. Additionally, twice a month IAS organises Getting Started in Denmark which provides important on-arrival orientation and registration for newly arrived international PhD students and researchers. [www.ias.au.dk/gettingstarted](http://www.ias.au.dk/gettingstarted)

Lastly, IAS helps to arrange social and cultural activities for staff and their families through the University International Club (UIC). [www.au.dk/uic](http://www.au.dk/uic)

## PhD House Activity Group

The PhD House Activity Group is a group of volunteer PhDs and postdocs from all faculties across Aarhus University who organise weekly social events aimed at Danish and international PhDs and postdocs. The group provides a relaxed and fun setting where junior researchers can unwind from long working days and meet their peers from across academic disciplines and cultural backgrounds.

[www.facebook.com/phdhouseau](http://www.facebook.com/phdhouseau)

## The Dale T. Mortensen Building/International Centre

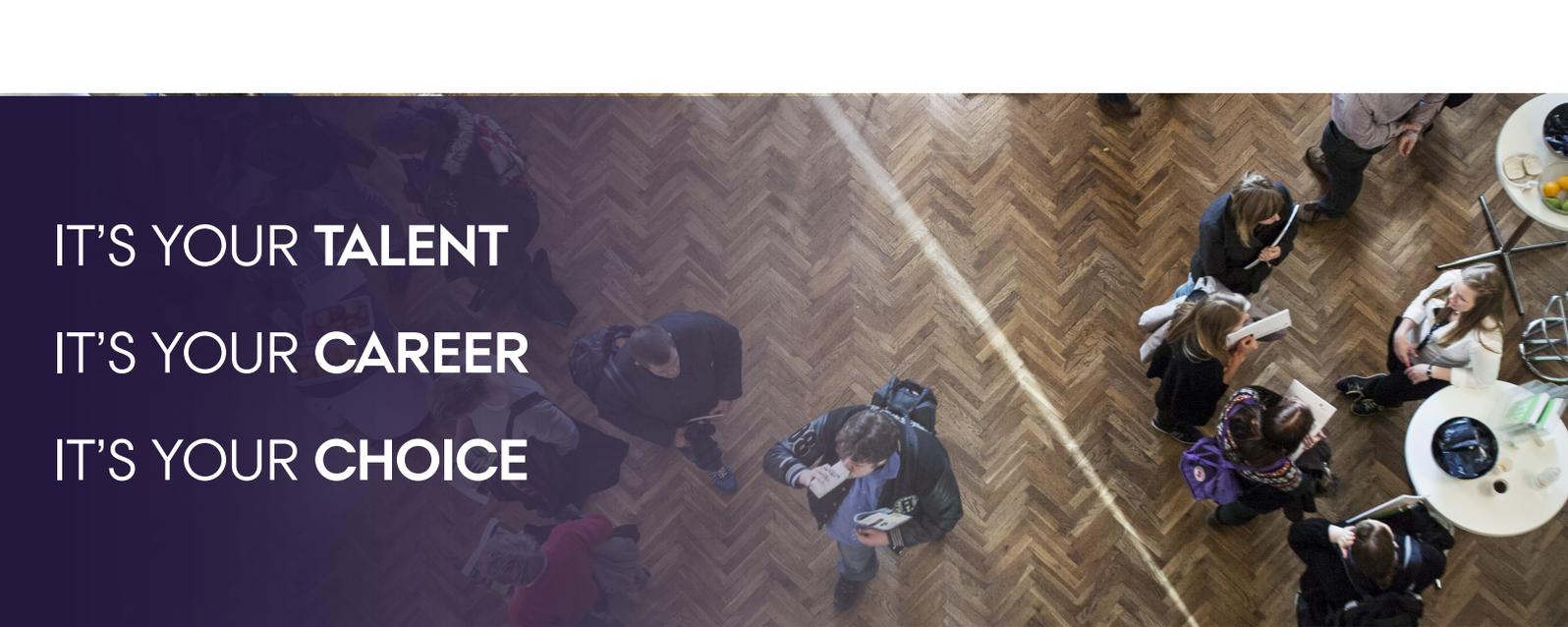
The Dale T. Mortensen Building offers a combination of administrative services, lecture rooms for PhD courses on transversal skills and Dale's Café offering quality coffee, sandwiches and a wide selection of beers. Furthermore, the PhD associations have the possibility to use the facilities in the building for events. IC Dormitory for international PhD students is also part of the Dale T. Mortensen Building.

The Dale T. Mortensen Building is, thus, a focal point for national and international PhD students to meet both professionally and socially. [www.au.dk/ic](http://www.au.dk/ic)

## The International Centre

AU International Centre is located in the Dale T. Mortensen Building (Høegh-Guldbergs Gade 4), which offers administrative services for international students and staff. Among others, it contains IAS and the housing department, which deals with housing matters for international students and staff.





IT'S YOUR TALENT  
IT'S YOUR CAREER  
IT'S YOUR CHOICE

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

**Do you know which specific competences companies are interested in regarding PhD students from Health?**

**Are you aware of your many opportunities?**

## AU CAREER PHD SERVICES

- Individual feedback on career paths, applications and CVs
- Competency mapping
- A mentor from the industry
- Career Talks with a PhD alumni
- Career events
- Information on career opportunities

AU CAREER  
PHD



AARHUS UNIVERSITY

**Vibeke Broe**

PhD Career Consultant

Mobile: 2942 6029

Email: vibr@au.dk

AU Career PhD website: [phd.au.dk/career](https://phd.au.dk/career)



<https://www.facebook.com/AuCareerPhd/>



# AU **LIBRARY** HEALTH SCIENCES

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## THE LIBRARY IS HERE TO HELP

- Information about:
  - Tips and tricks for PubMed, Embase, Scopus, and Cinahl
  - Citation searches in Scopus and Web of Science
  - Alerts from your favourite journals
  - Reference Tools – courses and support for EndNote and RefWorks
  - Bibliometrics and Research Evaluation; e.g. Bibliometric Research Indicator (BFI), Journal Impact Factor, ORCID and H-index
  - Copyright and Open Access
- Support and help for literature search designed for your specific project
- Regular PhD courses 'Literature Search in Medical Databases'

### **AU Library, Health Sciences**

Victor Albeck Building  
Vennelyst Boulevard 4  
DK-8000 Aarhus C  
Tel. +45 8946 2362

[sundhedsvidenskab@statsbiblioteket.dk](mailto:sundhedsvidenskab@statsbiblioteket.dk) [library.au.dk](http://library.au.dk)

### **Opening Hours**

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

# JOINT ACTION: BOOST YOUR RESEARCH CAREER

JOINT ACTION WORKSHOPS INVITE **PHD STUDENTS AND POSTDOCS** TO COME TOGETHER AND DISCUSS TYPICAL CHALLENGES IN THE LIFE OF THE EARLY CAREER RESEARCHER



“WELCOME TO MY WORLD” Exchanging experiences can make you realise that other people are facing similar challenges.

EXPLOIT THE SMARTS OF YOUR COLLEAGUES Learning from others' know-how, you can improve the management of your research career..

## JOIN US FOR OUR NEXT WORKSHOPS

23<sup>rd</sup> February 2017 4:00PM-6:00PM

18<sup>th</sup> May 2017 4:00PM-6:00PM

DALE'S CAFÉ, AU CAMPUS

### PROGRAM

Introduction to the topic (10 min.)

Discussion in small groups (30 min.)

### Social drinks

co-hosted by PhD House Activity Group

Your first beer is on us!

# Do you need **funding** for your research?



- In the Research Support Office **toolbox** you will find tips on how to write an effective grant proposal.
- Our database [www.ResearchFunding.Net](http://www.ResearchFunding.Net) will help you **find funding opportunities**.

# MID1: *1<sup>st</sup> Medical Innovation Day*

6 October 2017

*"Lille Anatomisk Auditorium"*

Aarhus University, Bldg 1231, room 424  
and breakout rooms nearby

You choose a track to provide  
solutions that will improve health

## *A. Challenge Track:*

You solve a defined challenge

from Industry or patient organisations

## *B. Creative Track:*

You propose your idea to investors

*We reward your efforts and ideas with a dinner and  
the opportunity to meet like-minded colleagues  
and start new collaborations*

Registration opens spring 2017. More information to come.

Follow: <http://newsroom.au.dk/en/news/>

# Danish Diabetes Academy 2017

In 2017 the Danish Diabetes Academy is hosting three major PhD courses:

- Basal Metabolism and Molecular Mechanisms in the Metabolic Syndrome  
9-11 May, Nyborg
- Diabetes and Epidemiology  
26-29 June, Nyborg
- Summer School on Diabetes and Metabolism  
28-31 August, Gl. Avernæs

Additionally, the following educational activities are on the drawing board:

- A PhD course in collaboration with Cambridge Metabolic Network  
Primo July, Cambridge
- A diabetes challenge in Toronto between young researchers from Denmark, Joslin Diabetes Center and the Banting and Best Diabetes Center  
19 October, Toronto

Read more on [www.danishdiabetesacademy.dk](http://www.danishdiabetesacademy.dk) or [Facebook](#) and [LinkedIn](#)

The aim of the Danish Diabetes Academy is to define, develop and support talents within diabetes and metabolic research. It is a national initiative - initiated and financed by the Novo Nordisk Foundation, the universities, university hospitals and JDRF - that each year:

- Hosts a number of national and international PhD courses and scientific symposia on different topics within diabetes and metabolism
- Gives young researchers the opportunity to participate in an array of national and international networking activities

## Contact:

Tore Christiansen, Managing Director, Danish Diabetes Academy//[tore.christiansen@rsyd.dk](mailto:tore.christiansen@rsyd.dk)

*"The Danish Diabetes Academy is funded by the Novo Nordisk Foundation and co-funded by the universities in Denmark"*

# PhD Day 2017

## Science – keep it simple

**Can you make your grandmother and fellow scientists pay attention when you describe your research questions? Do they understand the results you try to explain?**

**These questions are in focus during the PhD day 2017.**

The PhD day is an annual event arranged by the PhD Association in collaboration with the Graduate School, Faculty of Health at Aarhus University. The theme of the PhD Day 2017 is: *Science - keep it simple*.

Within this framework, the day offers key lectures and gives PhD and Research Year students an opportunity to present their research through oral or poster presentations, or to co-chair one of the oral sessions.

To *keep it simple* is challenging and also more relevant than ever. You have to simplify your research to get to its core, when you "sell" your ideas to your supervisor, or seek financial support for your studies. Likewise, when you write an abstract, design your poster, and present your results to the outside world, you need to keep it simple in order to keep it interesting and easy to comprehend.

With international and national keynote speakers and all the presentations by the students, the PhD day 2017 will focus not only on the scientific achievements, but also on the way ideas and data are presented.

Sometimes the most complicated thing is to *keep it simple*.

Organizing Committee 2017  
Health, Aarhus University



We welcome  
all our PhD students to the  
PhD Day 2017

**PHD DAY  
2017**



## Session chairmen

Fogh-Nielsen Competition	Lise Wogensen Bach & Rune Dall Jensen (PhD student)
O1	Anders Lade Nielsen, Heidi Theresa Ørum Cueto & Willemijn Comuth (PhD student)
O2	Birgitte Brock, Tue Wenzel Kragstrup & Kirstine Petrea Bak-Fredslund (PhD student)
O3	Hans Erik Bøtker, Mette Richner & Helene Halkjær Jensen (PhD student)
O4	Reimar W. Thomsen, Elise Røge Hedegaard & Esben Næser (PhD student)
O5	Lise Lotte Hansen, Johan Frederik Håkonsen Arendt & Henriette Holm Stabel (PhD student)
P1	Andreas Schröder, Mette Høj Lauridsen (PhD student) & Morten Lykke Olesen (PhD student)
P2	Arne Møller, Zongpei Zhao (PhD student) & Martin Bøhme Rasmussen (PhD student)
P3	Michael J. Mulvany, Andreas Fløe (PhD student) & Rikke Hahn Kofoed (PhD student)
P4	Carmela Matrone, Rune Dall Jensen (PhD student) & Adrian Bauer (PhD student)
P5	Casper Foldager, Vibeke Lynggaard (PhD student) & Arndis Simonsen (PhD student)
P6	Christian Vægter, Michael Schriver (PhD student) & Rasmus Aagaard (PhD student)
P7	Christoffer Laustsen, Jakob Søgaard Juul (PhD student) & Carsten Behr-Rasmussen (PhD student)
P8	Deirdre Cronin Fenton, Søren Nielsen Skov (PhD student) & Kathrine Bang Madsen (PhD student)
P9	Helle Prætorius Øhrwald, Christina Friis Jensen (PhD student) & Esben Søvsø Szocska Hansen (PhD student)
P10	Holger Brüggemann, Pernille Falberg Rønn (PhD student) & Anders Krogh Brøndberg (PhD student)

- P11 Ida Vogel, Sorosh Tabatabaeifar (PhD student) & Casper Larsen (PhD student)
- P12 Jan Alsner, Mia Bendix Rasch (PhD student) & Maria Wielsøe (PhD student)
- P13 Janne Lebeck, Kasper Lisager Jønsson (PhD student) & Vincent Kalumire Cubaka (PhD student)
- P14 Jeppe Prætorius, Anders Laustsen (PhD student) & Susan Larsen (PhD student)
- P15 Lene Seibæk, Thomas Dahl Nielsen (PhD student) & Sara Bisgaard Jensen (PhD student)
- P16 Mai Marie Holm, Rebeka Bodak (PhD student) & Troels Bille Folkmar (PhD student)
- P17 Brian Elmengaard, Charlotte Runge (PhD student) & Hanne Mari Jørgensen (PhD student)
- P18 Marianne Lisby & Joan Fledelius (PhD student)
- P19 Martin R. Jakobsen, Louise Møldrup Nielsen (PhD student) & Martin Christensen (PhD student)
- P20 Martin Thomsen & Lena-Sophie Martis (PhD student)
- P21 Peter Bross, Anna Starnawska & Kousik Sarathy Sridharan (PhD student)
- P22 Rikke Katrine Jentoft Olsen, Dariusz Orłowski & Morten Høggild Pedersen (PhD student)
- P23 Robert Fenton, Iris Brunner & Ellen Marie Høye (PhD student)
- P24 Rubens Spin Neto, Lene Sofie Granfeldt Østgård & Jenny Bertholet (PhD student)
- P25 Sebastian Frische, Priscila Corraini & Mathilde Borg Houlberg Thomsen (PhD student)
- P26 Simon Fristed Eskildsen, Andreas Højlund & Jakob Toftegaard (PhD student)
- P27 Simon Glerup, Bjørn Bay & Jacob Kinggaard Lilja-Fischer (PhD student)
- P28 Ulf Simonsen & Kristian Wemmelund (PhD student)
- P29 Vladimir Matchkov & Jesper Weile (PhD student)
- P30 Yonglun Luo & Henriette Ejlsmark Svensson (PhD student)

## Session overview

### Fogh-Nielsen

Junjing Su. WAVE INTENSITY ANALYSIS PROVIDES NOVEL INSIGHTS INTO PULMONARY HYPERTENSION

Morten Nørgaard Andersen. TUMOR-ASSOCIATED MACROPHAGES IN MULTIPLE MYELOMA: NOVEL TARGETS FOR TAILORED THERAPY

Maria do Nascimento Lopes Primo. MIRNA-382 INDUCTION AS A HALLMARK OF THE CELLULAR ANTIVIRAL RESPONSE

### Oral session 1

Chairmen: Anders Lade Nielsen, Heidi Theresa Ørum Cueto & Willemijn Comuth (PhD student)

O01.01 Casper Kierulf Lassen. THE EFFECT OF UNILATERAL NEPHRECTOMY IN A WARM RENAL ISCHEMIA-REPERFUSION INJURY RAT MODEL

O01.02 (Martin Brandhøj Skov. BALANCING THE SODIUM CURRENT IN MYOTONIA)

O01.03 Dmitrii Kamaev. ROLE OF CHLORIDE IN CONTRACTILITY OF MESENTERIC ARTERIES IN STREPTOZOTOCIN MODEL OF DIABETES

O01.04 Emil Hagen Ernst. A SEARCH FOR MOLECULAR FACTORS RESPONSIBLE FOR HUMAN OOCYTE COMPETENCE

O01.05 Steen Fagerberg. ERYTHROCYTE P2X<sub>1</sub>RECEPTOR EXPRESSION IS CORRELATED TO LOSS OF HEMATOCRIT DURING FIRST HOURS OF BLOOD PATHOGEN-POSITIVE SEPSIS

O01.06 Darshan Kumar. NOGO-A/RTN4A AND NOGO-B/RTN4B ARE SIMULTANEOUSLY EXPRESSED IN EPITHELIAL, FIBROBLAST AND NEURONAL CELLS AND MAINTAIN ER MORPHOLOGY

### Oral session 2

Chairmen: Birgitte Brock, Tue Wenzel Kragstrup & Kirstine Petrea Bak-Fredslund (PhD student)

O02.01 Marie Maagaard Sørensen. DOES THE FUNCTIONAL CAPACITY DEPEND ON THE SIZE OF THE SHUNT? A PROSPECTIVE, COHORT STUDY OF ADULTS WITH SMALL, UNREPAIRED VENTRICULAR SEPTAL DEFECTS

O02.02 Line Staun. ACCUMULATION OF FLUORIDE IN BIOFILM SOLIDS AFTER RINSING WITH 1,500 OR 5,000 PPM FLUORIDE

O02.03 Morten Krogh Christiansen. CORONARY PLAQUE BURDEN AND ADVERSE PLAQUE CHARACTERISTICS ARE INCREASED IN HEALTHY RELATIVES OF PATIENTS WITH EARLY-ONSET CORONARY ARTERY DISEASE

O02.04 Mads Riiskjær. PELVIC PAIN AND QUALITY OF LIFE BEFORE AND AFTER LAPAROSCOPIC BOWEL RESECTION FOR RECTO-SIGMOID ENDOMETRIOSIS: A PROSPECTIVE, OBSERVATIONAL STUDY

- O02.05 Linda Skibsted Kornerup. TISSUE DISTRIBUTION OF ORAL VITAMIN B12 IS INFLUENCED BY B12 STATUS AND B12 FORM. AN EXPERIMENTAL STUDY IN RATS
- O02.06 Ninna Cathrine Schmidt Voss. ARTERIES FROM HUMAN COLON CANCER HAVE ENHANCED ENDOTHELIAL FUNCTION COMPARED WITH CONTROL ARTERIES

### Oral session 3

Chairmen: Hans Erik Bøtker, Mette Richner & Helene Halkjær Jensen (PhD student)

- O03.01 Pia Kjær Kristensen. SOCIOECONOMIC INEQUALITY IN PATIENT OUTCOME AMONG HIP FRACTURE PATIENTS: A POPULATION-BASED COHORT STUDY
- O03.02 Lene Duez. MAGNETOENCEPHALOGRAPHY AND EEG SOURCE LOCALIZATIONS' IMPACT ON THE DECISION-MAKING BY THE DANISH EPILEPSY SURGERY TEAM
- O03.03 Rikke Hjortebjerg. IGFBP-4 FRAGMENTS PROVIDE INCREMENTAL PROGNOSTIC INFORMATION ON CARDIOVASCULAR EVENTS AND MORTALITY IN PATIENTS WITH ST-ELEVATION MYOCARDIAL INFARCTION
- O03.04 Kira Vibe Jespersen. THE EFFECT OF MUSIC ON INSOMNIA: A RANDOMIZED CONTROLLED TRIAL
- O03.05 Hugo Angleys. THE EFFECTS OF CAPILLARY TRANSIT TIME HETEROGENEITY (CTH) ON THE BOLD SIGNAL
- O03.06 Steffen Leth. COMBINED EFFECT OF VACC-4X, RECOMBINANT HUMAN GRANULOCYTE MACROPHAGE COLONY-STIMULATING FACTOR VACCINATION, AND ROMIDEPSIN ON THE HIV-1 RESERVOIR (REDUC): A SINGLE-ARM, PHASE 1B/2A TRIAL

### Oral session 4

Chairmen: Reimar W. Thomsen, Elise Røge Hedegaard & Esben Næser (PhD student)

- O04.01 Johanne Liv Agger. IMIPRAMINE VERSUS PLACEBO FOR MULTI-ORGAN BODILY DISTRESS SYNDROME: A DOUBLE-BLIND, RANDOMIZED TRIAL
- O04.02 Emil Christensen. LIQUID BIOPSY ANALYSIS OF ACTIVATING FGFR3 AND PIK3CA MUTATIONS FOR MONITORING DISEASE AGGRESSIVENESS IN BLADDER CANCER
- O04.03 Sanne Shiroma Harsløf. THE EFFECT OF ANCHORING DEVICE ON MESH SHRINKAGE DEPENDS ON TYPE OF MESH: AN EXPERIMENTAL LONG-TERM STUDY IN SHEEP
- O04.04 Morten Møbjerg Callesen. A INDUCIBLE TRANSGENIC INTESTINAL CANCER MODEL
- O04.05 Malene Juul Rasmussen. NON-CODING CANCER DRIVER CANDIDATES IDENTIFIED WITH A SAMPLE- AND POSITION-SPECIFIC MODEL OF THE SOMATIC MUTATION RATE
- O04.06 Oscar Casares Magaz. SPATIAL RECTAL DOSE/VOLUME METRICS PREDICT PATIENT-REPORTED GASTRO-INTESTINAL SYMPTOMS AFTER RADIOTHERAPY FOR PROSTATE CANCER

## Oral session 5

Chairmen: Lise Lotte Hansen, Johan Frederik Håkonsen Arendt & Henriette Holm Stabel (PhD student)

- O05.01 Rasmus Cleemann. AUGMENTATION OF REVISION IMPLANT FIXATION WITH COMBINATION OF ALLOGRAFT, BMP-2 AND LOCAL OR SYSTEMIC BISPHOSPHONATE
- O05.02 Lone Dragnes Brix. PAIN IS THE MAIN REASON FOR UNSCHEDULED HEALTHCARE CONTACTS AFTER OUTPATIENT SURGERY
- O05.03 Sigrún Alba Jóhannesdóttir. PARTNER BEREAVEMENT AND RISK OF HERPES ZOSTER: RESULTS FROM TWO POPULATION-BASED CASE-CONTROL STUDIES IN DENMARK AND THE UNITED KINGDOM
- O05.04 Chalotte Willemann Stecher. THE MALI SCHISTOSOMIASIS MORBIDITY STUDY - MASCHISMO
- O05.05 Malene Beck. NEUROLOGICAL PATIENTS' EXPERIENCES OF EATING IN THE HOSPITAL: A PHENOMENOLOGICAL-HERMENEUTIC STUDY
- O05.06 Tove Lise Nielsen. CLIENT-CENTRED IN-HOME OCCUPATIONAL THERAPY IMPROVES OLDER ADULTS' OCCUPATIONAL PERFORMANCE: RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

## Poster session 1

Chairmen: Andreas Schröder, Mette Høj Lauridsen (PhD student) & Morten Lykke Olesen (PhD student)

- P01.01 Estefano Pinilla. TRANSGLUTAMINASES AS PHARMACOLOGICAL TARGETS IN VASCULAR DYSFUNCTION
- P01.02 Patricia Alves da Mota. THE NEURAL SIGNATURES OF CREATIVITY IN JAZZ IMPROVISATION
- P01.03 Signe Toft Andersen. AGREEMENT BETWEEN CLINICAL SCORES OF DIABETIC NEUROPATHY AND NERVE CONDUCTION STUDIES IN ELDERLY TYPE 2 DIABETIC PATIENTS - A CROSS SECTIONAL STUDY
- P01.04 Line Stensig Lynggaard. NOR-GRASPALL 2008: SINGLE-ARM PHARMACOKINETIC/PHARMACODYNAMIC AND SAFETY STUDY OF ERYASPASE (GRASPA®) FOR PATIENTS WITH HYPERSENSITIVITY TO PEG-ASPARAGINASE, DIAGNOSED WITH PH(-) ACUTE LYMPHOBLASTIC LEUKEMIA
- P01.05 Jens Hartlev. DONOR AND RECIPIENT SITE PAIN AFTER LATERAL ALVEOLAR BONE AUGMENTATION
- P01.06 Kathrine Hald. LONG-TERM FOLLOW-UP ON A SOCIALLY DIFFERENTIATED CARDIAC REHABILITATION INTERVENTION
- P01.07 Charlotte Slagelse Jensen-Haarup. USE OF ANGIOTENSIN-CONVERTING ENZYME INHIBITORS AND ANGIOTENSIN-RECEPTOR BLOCKERS AND THE RISK OF ACUTE KIDNEY INJURY AFTER COLORECTAL CANCER SURGERY: A POPULATION-BASED COHORT STUDY

- P01.08 Bo Langhoff Hønge. THE CHALLENGE OF DISCRIMINATION BETWEEN HIV-1, HIV-2 AND HIV-1/2 DUAL INFECTIONS
- P01.09 Helene Mathilde Larsen. LONG-TERM BOWEL DYSFUNCTION IN PATIENTS TREATED FOR CANCER IN CECUM AND THE ASCENDING COLON
- P01.10 Niels Lyhne Christensen. FACTORS RELATING TO EARLY DEATH IN DANISH LUNG CANCER PATIENTS (LCP)

## Poster session 2

Chairmen: Arne Møller, Zongpei Zhao (PhD student) & Martin Bøhme Rasmussen (PhD student)

- P02.01 Stine Høgsholt. DISEASE-SPECIFIC HOSPITALIZATIONS AMONG SURVIVORS OF WILMS TUMOR: A NORDIC POPULATION-BASED COHORT STUDY
- P02.02 Ole Adrian Heggli. ARE WE DOING THE SAME? A DUAL-EEG TAPPING STUDY
- P02.03 Caroline Mejdahl. EPILEPSY SELF-MANAGEMENT BY USE OF PATIENT-REPORTED OUTCOMES AND PATIENT-INITIATED FOLLOW-UP - A QUALITATIVE OBSERVATIONAL STUDY
- P02.04 Anita Tønder Nielsen. SEVERE MENTAL ILLNESS, DIABETES MELLITUS AND RISK OF DIABETIC COMPLICATIONS; CARDIOVASCULAR MORBIDITIES
- P02.05 Jesper Damsgaard. EARLY ADMINISTRATION OF LATENCY REVERSING THERAPY AND BROADLY NEUTRALIZING ANTIBODIES TO LIMIT THE ESTABLISHMENT OF THE HIV-1 RESERVOIR DURING INITIATION OF ANTIRETROVIRAL TREATMENT - A RANDOMIZED CONTROLLED TRIAL
- P02.06 Thorkil Anker-Møller. EVIDENCE FOR THE USE OF TRANEXAMIC ACID IN SUBARACHNOID HAEMORRHAGE AND SUBDURAL HAEMORRHAGE - A SYSTEMATIC REVIEW
- P02.07 Emil Rindom. EFFECT OF LOW-INTENSITY BLOOD FLOW RESTRICTED EXERCISE ON PROTECTION OF MUSCLE HEALTH AND VITAL ORGANS IN HEALTHY SUBJECTS AND PATIENTS WITH AMI
- P02.08 Rajath Pillai. PAIN, UNPLEASANTNESS AND QUALITY OF LIFE RELATED TO OROFACIAL NERVE DAMAGE
- P02.09 Ninna Rasmussen. MONOSOMAL AND COMPLEX KARYOTYPE IN CHILDHOOD AML
- P02.10 Peter Andersen. OPEN VERSUS LAPAROSCOPIC RECTAL CANCER RESECTION AND RISK OF SUBSEQUENT INCISIONAL HERNIA REPAIR AND PARACOLOSTOMY HERNIA REPAIR: A NATIONWIDE POPULATION-BASED COHORT STUDY

### Poster session 3

Chairmen: Michael J. Mulvany, Andreas Fløe (PhD student) & Rikke Hahn Kofoed (PhD student)

- P03.01 Nina Jensen. BOWEL MORBIDITY AFTER RADIOCHEMOTHERAPY IN CERVICAL CANCER: PHYSICIAN- AND PATIENT-REPORTED OUTCOME FROM THE EMBRACE STUDY
- P03.02 Suzi Ross. PREDICTING THE AUDITORY CONSEQUENCES OF ACTION IN EXPERT MUSICIANS
- P03.03 Mette Schou Mikkelsen. HYPERTHERM INTRAPERITONEAL CHEMOTHERAPY (HIPEC) USED IN TREATMENT OF ADVANCED OVARIAN CANCER
- P03.04 Sara Bønløkke Simonsen. HPV AND BREAST CANCER - IS THERE AN AETIOLOGICAL CONNECTION?
- P03.05 Rasmus Wulff. ADDITION OF PERINEURAL DEXAMETHASONE TO BUPIVACAINE-EPINEPHRINE SCIATIC NERVE BLOCK FOR POSTOPERATIVE ANALGESIA AFTER MAJOR FOOT AND ANKLE SURGERY: A RANDOMISED, CONTROLLED, DOUBLE-BLIND STUDY
- P03.06 Charlotte Stephansen. ELECTRO-CRT - LEFT VENTRICULAR LEAD IMPLANT AND OPTIMIZATION GUIDED BY ELECTROCARDIOGRAPHY IN CARDIAC RESYNCHRONIZATION THERAPY: A DOUBLE-BLINDED, RANDOMIZED, CONTROLLED, CLINICAL TRIAL
- P03.07 Anne Bo. EARLY ONSET TYPE 2 DIABETES. CLINICAL CHARACTERISTICS OF NEWLY DIAGNOSED TYPE 2 DIABETES PATIENTS AGED UNDER AND ABOVE 45 YEARS: RESULTS FROM THE DD2 STUDY, DENMARK
- P03.08 Casper Kruse. DIAGNOSTIC VALIDITY OF PERIAPICAL RADIOGRAPHS AND CONE BEAM CT IN RELATION TO TEETH ASSESSED AS FAILURES SIX YEARS AFTER SURGICAL ENDODONTIC RETREATMENT: A HISTOLOGICAL STUDY
- P03.09 Kasper Bonnesen. PREHOSPITAL TRIAGE OF PATIENTS DIAGNOSED WITH PERFORATED PEPTIC ULCER AND PEPTIC ULCER BLEEDING
- P03.10 (Jesper Falkesgaard Højen. THE BROAD ROLE OF ANTI-IL-1R3 MONOCLONAL ANTIBODIES FOR TREATING CANCER AND IL-1 FAMILY-MEDIATED INFLAMMATION)

### Poster session 4

Chairmen: Carmela Matrone, Rune Dall Jensen (PhD student) & Adrian Bauer (PhD student)

- P04.01 Claus Kjær Pedersen. DIAGNOSES AND MORTALITY IN EMS-CALLERS SUFFERING CHEST PAIN
- P04.02 Katrine Munk Begtrup. DOES RADIOOTHERAPY AFFECT COAGULATION?
- P04.03 Trine Block Mattesen. TUMOR MICROENVIRONMENT SUBTYPING BY DNA METHYLATION BIOMARKERS FACILITATES PERSONALIZED TREATMENT OF COLORECTAL CANCER PATIENTS

- P04.04 Rasha Hyder. NEURAL FOUNDATIONS OF LANGUAGE PROCESSING DEFICITS IN PARKINSON'S DISEASES AND THEIR MODULATION WITH DEEP BRAIN STN STIMULATION: NEURO-MAGNETIC INVESTIGATIONS
- P04.05 Berit Bargum Booth. CERVICAL DYSPLASIA - HOW CAN WE IMPROVE THE DIAGNOSTICS?
- P04.06 Birgit Rasmussen. MEANINGFUL LIVING ENGAGING IN PHYSICAL ACTIVITIES; EXPERIENCES OF OLDER PEOPLE AFTER HIP FRACTURE
- P04.07 Millicent Addai Boateng. INTEGRATED COMMUNITY CASE MANAGEMENT OF MALARIA (ICMCM); A GATEWAY TO HEALTH LITERACY IN GHANA
- P04.08 Lasse Bjerg Hansen. CLUSTERING OF MICROVASCULAR COMPLICATIONS IN TYPE 1 DIABETES
- P04.09 Susanna Botticelli. A NOVEL STANDARDIZED 3D ANALYSIS TO ASSESS CLEFT SIZE BASED ON DIGITAL MODELS OF UNILATERAL CLEFT LIP AND PALATE PATIENTS
- P04.10 Anni Winckelmann. ROMIDEPSIN-INDUCED HIV-1 VIREMIA DURING SUPPRESSIVE ART IS OLIGOCLONAL AND CONTAINS LIMITED DELETERIOUS MUTATIONS

## Poster session 5

Chairmen: Casper Foldager, Vibeke Lynggaard (PhD student) & Arndis Simonsen (PhD student)

- P05.01 Marie Vognstoft Hjortbak. MODULATION OF ISCHEMIC CONDITIONING OF THE HEART - INFLUENCE OF HYPOTHERMIA, AEROBIC CAPACITY AND OXYGEN TREATMENT
- P05.02 Jeanett Lykke Møller Nielsen. TOXICITY AFTER HIGH DOSE METHOTREXATE TREATMENT IN PAEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKAEMIA - CAN WE INDIVIDUALIZE THE TREATMENT?
- P05.03 Sarah Fogh. ETHYLMALONYL-COA DECARBOXYLASE (ECHDC1); A NOVEL PLAYER IN ETHYLMALONIC ACIDURIA
- P05.04 Andreas Engel Krag. DOES REMOTE ISCHEMIC PRECONDITIONING INCREASE FIBRINOLYSIS IN HEAD AND NECK CANCER SURGERY? PRELIMINARY RESULTS FROM A RANDOMIZED CONTROLLED TRIAL
- P05.05 Sandra Sif Gylfadottir. THE PREVALENCE OF PAINFUL DIABETIC POLYNEUROPATHY IN NON-SELECTED TYPE 2 DIABETES PATIENTS IN DENMARK
- P05.06 Rune Lykke. INCIDENCE OF PELVIC ORGAN PROLAPSE REPAIR SUBSEQUENT TO HYSTERECTOMY: A COMPARISON BETWEEN RADICAL HYSTERECTOMY AND TOTAL ABDOMINAL HYSTERECTOMY
- P05.07 Markku Hakala. TWINFILIN REGULATES LAMELLIPODIAL DYNAMICS DURING CELL MIGRATION - THE ROLE OF PROTEIN-MEMBRANE INTERACTION
- P05.08 Line Thorndal Moll. BRIEF VS. MULTIDISCIPLINARY INTERVENTION IN NECK/SHOULDER PATIENTS ON SICK LEAVE: RESULTS ON RETURN-TO-WORK

- P05.09 Yasser Haddadi. COMPARISON OF CONVENTIONAL IMPRESSION TECHNIQUE AND INTRAORAL SCAN; EVALUATION OF TREATMENT DISCOMFORT AND TIME CONSUMPTION. AN IN VIVO, RANDOMISED SPLIT-MOUTH STUDY
- P05.10 Jacob Lynge Callesen. HOW DOES PROGRESSIVE RESISTANCE TRAINING AND BALANCE TRAINING AFFECT GAIT AND FATIGUE IN PATIENTS WITH MULTIPLE SCLEROSIS?

## Poster session 6

Chairmen: Christian Vægter, Michael Schriver (PhD student) & Rasmus Aagaard (PhD student)

- P06.01 Leila Louise Benhassen. CHARACTERIZATION OF VALVE-SPARING AORTIC ROOT REPAIR WITH DIFFERENT SUBVALVULAR ANNULOPLASTIES: A CLINICAL EXPERIMENTAL STUDY
- P06.02 Martin Fogtmann Berthelsen. THE CRISPR-CAS9 MINIPIG - A TRANSGENIC PIG TO PRODUCE SPECIFIC GENOME EDITING IN SELECTED TISSUES
- P06.03 Alexander Gramm Kristensen. UNDERSTANDING UNDERLYING MECHANISMS OF DIABETIC POLYNEUROPATHY
- P06.04 Abdelhakim Salem. HISTAMINE METABOLISM AND TRANSPORT ARE DERANGED IN HUMAN KERATINOCYTES IN ORAL LICHEN PLANUS
- P06.05 Louise Bang Grode. PREVALENCE, INCIDENCE AND COMORBIDITIES OF CELIAC DISEASE IN DENMARK; A NATIONWIDE POPULATION-BASED STUDY FROM 1977 TO 2014
- P06.06 Sidsel Boie. COCHRANE REVIEW: DISCONTINUATION OF INTRAVENOUS OXYTOCIN IN THE ACTIVE PHASE OF INDUCED LABOUR
- P06.07 Ellen Hollands Steffensen. PREADMISSION ANTIDEPRESSANT USE AND BLADDER CANCER: A POPULATION-BASED COHORT STUDY OF STAGE AT DIAGNOSIS, TIME TO SURGERY, AND SURGICAL OUTCOMES
- P06.08 Anna Bystrup Jacobsen. REPRODUCIBILITY AND DIAGNOSTIC UTILITY OF A NOVEL MUNE METHOD IN ALS: MSCAN MUNE
- P06.09 Stine Bak. MOLECULAR DETAILS OF OBESITY INDUCED BY MATERNAL LOW-GRADE CHRONIC INFLAMMATION
- P06.10 Kamilla Pedersen. EXPLORING THE IMPACT OF TEACHING FORMATS ON PATIENT-CENTEREDNESS IN MEDICAL STUDENTS

## Poster session 7

Chairmen: Christoffer Laustsen, Jakob Søgaard Juul (PhD student) & Carsten Behr-Rasmussen (PhD student)

- P07.01 Louise Devantier. THE BALANCE ORGAN IS STIMULATED DURING MRI SCANS

- P07.02      Gitte Boier Tygesen. DEVELOPMENT AND EVALUATION OF A PATIENT SAFETY MODEL TARGETING SEVERE CLINICAL DETERIORATION AND SAFETY AWARENESS IN THE EMERGENCY DEPARTMENT
- P07.03      Lise Brogaard Roed Jensen. LIVE TEAMS IN OBSTETRIC EMERGENCY SITUATIONS
- P07.04      Thomas Skjærlund Grønnebæk. EFFECT OF LOW LOAD BLOOD FLOW RESTRICTED RESISTANCE EXERCISE ON MUSCLE MITOCHONDRIAL BIOGENESIS
- P07.05      Carina Bagge. THE RISK OF DEMENTIA IN ADULTS WITH CONGENITAL HEART DISEASE: A NATIONWIDE COHORT STUDY
- P07.06      Anders Sjørlev Schmidt. CARDIOVERSION EFFICACY USING PULSED BIPHASIC OR BIPHASIC TRUNCATED EXPONENTIAL WAVEFORMS: A RANDOMIZED CLINICAL TRIAL
- P07.07      Casper Schmidt. IMPULSIVITY AND COMPULSIVITY: THE ROLES OF DOPAMINE AND SEROTONIN IN REWARDS
- P07.08      Anders Kindberg Boysen. SURVIVAL AFTER RESECTION OF COLORECTAL CANCER WITH SYNCHRONOUS METASTASES - A DANISH POPULATION-BASED HISTORICAL COHORT STUDY
- P07.09      Linn Håkonsen Arendt. MATERNAL DIABETES MELLITUS AND GENITAL MALFORMATIONS IN SONS: A REGISTRY-BASED STUDY IN DENMARK AND SWEDEN
- P07.10      Frederik Ahlers. DO INFECTIONS CAUSE EPILEPSY? A NATIONWIDE, REGISTER- BASED COHORT STUDY

## Poster session 8

Chairmen: Deirdre Cronin Fenton, Søren Nielsen Skov (PhD student) & Kathrine Bang Madsen (PhD student)

- P08.01      Iben Bach Pedersen. CORNEAL LENTICULE TRANSPLANTATION FOR CORRECTING MODERATE TO SEVERE HYPEROPIA
- P08.02      Gitte Øskov Skajaa. INSULIN SENSITIVITY IN WOMEN AROUND PARTURITION AND 6 MONTHS POST PARTUM
- P08.03      Søren Christiansen. TIMING OF RENAL REPLACEMENT THERAPY AND LONG-TERM RISK OF DEATH AND CHRONIC KIDNEY DISEASE IN INTENSIVE CARE PATIENTS WITH ACUTE KIDNEY INJURY
- P08.04      Anuj Pareek. ULTRASONOGRAPHIC ASSESSMENT OF INTERSTITIAL LUNG FLUID LEVELS DURING POSTNATAL LUNG TRANSITION: A COMPARISON BETWEEN CAESAREAN SECTION AND VAGINAL DELIVERY
- P08.05      Wenqian Gu. EXPLORE THE EFFECTS OF THE ANTI-DIABETIC DRUG, ISOSTEVIOL, ON ALPHA- AND BETA-CELLS DURING GLUCOTOXICITY, LIPOTOXICITY AND AMINOACIDOTOXICITY INDUCED CONDITIONS
- P08.06      Marcell Juan Tjørnild. MITRAL LEAFLET AUGMENTATION AND RECONSTRUCTION USING PORCINE EXTRACELLULAR MATRIX: FUNCTIONAL AND BIOMECHANICAL ASPECTS

- P08.07 Nina Stockfleth Buch. NEUROMAS AS THE CAUSE OF NEUROPATHIC PAIN IN PATIENTS WITH PERIPHERAL NERVE INJURIES AND AMPUTATIONS?
- P08.08 Ann-Katrine Jakobsen. TARGETING REPAIR PROTEINS IN CANCER TREATMENT
- P08.09 Camma Damsted. PROJECTRUN21: RUNNING SCHEDULES FOR HALF-MARATHON - ARE THEY SAFE OR INJURIOUS?
- P08.10 Sebastian Møller. ACCIDENTAL DEATHS IN PEOPLE WITH EPILEPSY: A REGISTER-BASED COHORT STUDY

## Poster session 9

Chairmen: Helle Prætorius Øhrwald, Christina Friis Jensen (PhD student) & Esben Søvsø Szocska Hansen (PhD student)

- P09.01 Ann Mai Hindkjær Østergaard. THE EFFECT OF ORALLY ADMINISTERED NITRATE ON RENAL AND SYSTEMIC HAEMODYNAMICS, WATER AND SALT REGULATION, TUBULAR TRANSPORT PROTEINS AND VASOACTIVE HORMONES IN A RANDOMIZED, PLACEBO CONTROLLED, CROSSED OVER STUDY IN HEALTHY SUBJECTS
- P09.02 Liv Marit Valen Schougaard. EFFECT OF PATIENT-INITIATED VERSUS FIXED-INTERVAL TELEPRO-BASED OUTPATIENT FOLLOW-UP: STUDY PROTOCOL FOR A PRAGMATIC RANDOMISED CONTROLLED STUDY
- P09.03 Klaus Ulrik Koch. INFLUENCE OF VASOPRESSORS ON BRAIN OXYGENATION AND MICROCIRCULATION
- P09.04 Stine Andersen. ASSESSMENT OF FIBROSIS AND THE EFFECTS OF PIRFENIDONE IN EXPERIMENTAL RIGHT HEART FAILURE
- P09.05 Rasmus Fuglsang Nielsen. DIETARY FIBER AND WHEY PROTEIN: THE EFFECT ON RISK MARKERS OF THE METABOLIC SYNDROME IN ABDOMINALLY OBESE SUBJECTS - A 12-WEEK PARALLEL, DOUBLE-BLINDED INTERVENTION STUDY
- P09.06 Lea Lykke Lauridsen. GESTATIONAL DISEASES AND ONSET OF PUBERTY IN OFFSPRING
- P09.07 Katrine Andersen. EPILEPSY AND SCHIZOPHRENIA HAVE INCREASED RISK OF PREMATURE MORTALITY: A NATION-WIDE COHORT STUDY
- P09.08 Anne Sofie Dam Laursen. SUBSTITUTIONS OF DAIRY PRODUCT INTAKE AND RISK OF STROKE - A DANISH COHORT STUDY
- P09.09 Mette Wulf Christensen. IS POOR OVARIAN RESPONSE IN FERTILITY TREATMENT ASSOCIATED WITH AN ACCELERATED GENERAL SOMATIC AGEING?
- P09.10 Sofie Gottschalk Højfeldt. HLA-DQA2 INVOLVED IN ALLERGIC REACTIONS TO PEG-ASPARAGINASE - A GENOME WIDE ASSOCIATION STUDY ON THE NOPHO ALL 2008 PROTOCOL

## Poster session 10

Chairmen: Holger Brüggemann, Pernille Falberg Rønn (PhD student) & Anders Krogh Brøndberg (PhD student)

- P10.01      Andreas Nygaard Jørgensen. USING URINARY EXCRETION OF NGAL AS BIOMARKER TO EVALUATE 155 MMOLAR CHLORIDE INFUSION VERSUS 98 MMOLAR CHLORIDE IN PATIENTS UNDERGOING PRIMARY UNCEMENTED HIP REPLACEMENT SHOWED NO EVIDENCE OF CHLORIDE NEPHROTOXICITY
- P10.02      Georgios Katzilieris Petras. SENSING OF HSV-1 AND CELL RECRUITMENT AT THE SITE OF INFECTION IN THE CNS
- P10.03      Camilla Kjersgaard. LIFESTYLE DURING PREGNANCY AND RISK OF CRYPTORCHIDISM IN SONS
- P10.04      Mai-Britt Worm Ørntoft. COMPREHENSIVE ANALYSIS OF 13 DIFFERENT METHODS FOR BISULFITE CONVERSION OF CIRCULATING CELL-FREE DNA
- P10.05      Lene Holst Pedersen. EARLY GERIATRIC FOLLOW-UP AFTER DISCHARGE REDUCES READMISSIONS AMONG PATIENTS DISCHARGED TO NURSING HOMES
- P10.06      Søren Bruno Elmgreen. RESTORING LOCOMOTION IN SPINAL CORD INJURY: A RANDOMIZED CONTROLLED TRIAL OF THE LION PROCEDURE
- P10.07      Jacob Gammelgaard Schultz. A NOVEL MODEL OF ACUTE PULMONARY EMBOLISM IN PIGS
- P10.08      Amr Abou Elezz. ALL FILAMENTS ARE EQUAL, BUT SOME FILAMENTS ARE MORE EQUAL THAN OTHERS
- P10.09      Christine Ladegaard Geyti. MENTAL HEALTH ASSESSMENT IN HEALTH CHECK CAN IMPROVE RECOGNITION OF UNACKNOWLEDGED POOR MENTAL HEALTH: A LARGE-SCALE COHORT STUDY
- P10.10      Per Mose Nielsen. RENAL ISCHEMIA/REPERFUSION NECROSIS MONITORING WITH HYPERPOLARIZED FUMARATE

## Poster session 11

Chairmen: Ida Vogel, Sorosh Tabatabaeifar (PhD student) & Casper Larsen (PhD student)

- P11.01      Marianne Bjerre. MOLECULAR ANALYSES OF CIRCULATING TUMOR DNA FOR DEVELOPMENT OF NOVEL DIAGNOSTIC AND PROGNOSTIC BIOMARKERS FOR PROSTATE CANCER
- P11.02      Line Amalie Aarestrup Hellelose. ACCIDENTAL DEATHS AMONG PERSONS WITH SCHIZOPHRENIA
- P11.03      Steffen Nielsen. RADIOBIOLOGY IN PROTON THERAPY

- P11.04 Lene Margrethe Ring Madsen. BONE TURN-OVER IN ROUX-EN-Y GASTRIC BYPASS OPERATED TYPE 2 DIABETIC PATIENTS COMPARED TO NON-OPERATED TYPE 2 DIABETIC CONTROLS: A 6-YEAR FOLLOW-UP STUDY
- P11.05 Alice Knudsen. DISTURBANCE OF MUCOSAL INTEGRITY - A NEW MEANS TO SENSE INFECTION AND INSTIGATE ANTIVIRAL DEFENSE
- P11.06 Takwa Shairman Aroankins. IDENTIFICATION OF SUMOYLATED PROTEINS IN KIDNEY EPITHELIAL CELLS
- P11.07 Kathrine Stokholm. PRE- AND POST-SYNAPTIC DOPAMINERGIC ALTERATIONS IN AN ALPHA SYNU-CLEIN RAT MODEL OF PARKINSON'S DISEASE
- P11.08 Johanne Marie Holst. SEARCH FOR AND CHARACTERIZATION OF POSSIBLE MOLECULAR RELATIONSHIPS BETWEEN LYMPHO- AND MYELO-PROLIFERATIVE NEOPLASMS OCCURRING IN THE SAME HOST
- P11.09 Mette Habekost. STUDY OF APP INTRACELLULAR DOMAIN USING CELLS FROM A NEW PORCINE MODEL OF ALZHEIMER'S DISEASE
- P11.10 Ina Qvist. PERSON CHARACTERISTICS AND EXPERIENCES ASSOCIATED WITH ADHERENCE TO PHARMACOLOGICAL TREATMENT AMONG 65-74 YEAR-OLD MEN IN CARDIOVASCULAR SCREENING STUDIES

## Poster session 12

Chairmen: Jan Alsner, Mia Bendix Rasch (PhD student) & Maria Wielsøe (PhD student)

- P12.01 Martin Lund. QUALITY INDICATORS FOR SCREENING COLONOSCOPIES AND THE RISK OF INTERVAL CANCER ASSESSING THE PERFORMANCE OF COLONOSCOPISTS: A SYSTEMATIC REVIEW
- P12.02 Michael Christensen. METFORMIN INCREASES RENAL MEDULLARY PARTIAL OXYGEN TENSION
- P12.03 Iben Lyskjær. PREDICTION OF THERAPY RESPONSE IN COLORECTAL CANCER TREATMENT USING CIRCULATING TUMOR DNA
- P12.04 Rasmus Kold-Christensen. MONITORING REACTIVE METABOLITES BY ELISA
- P12.05 Maria Celeste Fasano. NEURAL CHANGES AFTER MULTIMODAL LEARNING IN PIANISTS - AN FMRI STUDY
- P12.06 Anna Halling Folkmar Andersen. A NOVEL DRUG DELIVERY PLATFORM EXHIBITS ENHANCED LYMPHOID LOCALIZATION AND POTENTLY DELIVERS ANTIRETROVIRAL THERAPY
- P12.07 Charlotte Nygaard. PRIMARY HEALTHCARE USE IN THE YEARS PRECEDING PRIMARY INTRACRANIAL TUMOUR DIAGNOSIS - A NATIONWIDE REGISTER STUDY
- P12.08 Helle Gotfred-Rasmussen. SLEEPING SICKNESS: ELUCIDATING MECHANISMS FOR PARASITE RESISTANCE

P12.09 Anne Ankerstjerne Rasmussen. PATIENT-REPORTED OUTCOMES IN PATIENTS SUFFERING FROM HEART FAILURE: PREDICTORS OF ADVERSE OUTCOMES?

### Poster session 13

Chairmen: Janne Lebeck, Kasper Lisager Jønsson (PhD student) & Vincent Kalumire Cubaka (PhD student)

- P13.01 Sheyanth Mohanakumar. THE MORPHOLOGY AND FUNCTION OF THE LYMPHATIC CIRCULATION IN FONTAN OPERATED PATIENTS
- P13.02 Anne Gedebjerg. MANNAN-BINDING LECTIN AND RISK OF COMPLICATIONS IN PATIENT WITH TYPE 2 DIABETES
- P13.03 Safa Therwani. THE EFFECT OF VASOPRESSIN ANTAGONISM ON RENAL HANDLING OF WATER AND SODIUM AND CENTRAL AND BRACHIAL BLOOD PRESSURE DURING INHIBITION OF THE NITRIC OXIDE SYSTEM IN HEALTHY SUBJECTS: A DOSE-RESPONSE STUDY
- P13.04 Marie Toft-Petersen. THE HUMAN MYELOID INHIBITORY C-TYPE LECTIN-LIKE RECEPTOR AIDS IN DISCRIMINATION OF BASOPHILS IN PERIPHERAL BLOOD
- P13.05 Anders Valdemar Edhager. MYOCARDIAL PROTEOME DURING METABOLIC SYNDROME AND TYPE 2 DIABETES IN ZUCKER DIABETIC FATTY RATS
- P13.06 Anne Louise Svenningsen. SORTILIN IN MICROGLIA REACTIVITY
- P13.07 Denise Happ. INVESTIGATING THE INTERACTION BETWEEN NICOTINIC RECEPTORS AND SEROTONERGIC SIGNALING IN DEPRESSION: IMPLICATIONS FOR ANTIDEPRESSANT NON-RESPONDERS
- P13.08 Sashia Pernille Bak-Nielsen. KERATOCONUS
- P13.09 Anne-Louise Kristine Moltke. THE ECONOMIC ASPECT OF PHOTODYNAMIC DIAGNOSTICS IN ADDITION TO WHITE-LIGHT FLEXIBLE CYSTOSCOPY AFTER TRANSURETHRAL RESECTION OF THE BLADDER
- P13.10 Madalina Carter-Timofte. IDENTIFYING NOVEL INNATE IMMUNODEFICIENCIES IN PATIENTS WITH VARICELLA ZOSTER VIRUS CNS INFECTION

### Poster session 14

Chairmen: Jeppe Prætorius, Anders Laustsen (PhD student) & Susan Larsen (PhD student)

- P14.01 Jens Sundbøll. POSITIVE PREDICTIVE VALUE OF CARDIOVASCULAR DIAGNOSES IN THE DANISH NATIONAL PATIENT REGISTRY: A VALIDATION STUDY
- P14.02 Diana Hedevang Christensen. USING ICD-10 DISCHARGE DIAGNOSES AND PRESCRIPTION DATA TO IDENTIFY DIABETIC POLYNEUROPATHY AND DIABETIC FOOT ULCERS IN DANISH REGISTRIES

- P14.03 Malene Söth-Hansen. OCCURRENCE OF DELAYED DIAGNOSIS OF CLINICALLY RELEVANT ALARMS BY REMOTE MONITORING IN ICD SYSTEMS WITH DIFFERENT AUTOMATIC TRANSMISSION FREQUENCIES
- P14.04 Sara Konstantin Nissen. MUTATIONS IN INNATE IMMUNE SENSING PATHWAYS COULD CONTRIBUTE TO THE HIV ELITE CONTROLLER PHENOTYPE
- P14.05 Ditte Drejer. COMPARISON OF WHITE LIGHT, PHOTODYNAMIC DIAGNOSIS, AND NARROW-BAND IMAGING IN DETECTION OF CARCINOMA IN SITU (CIS) OR FLAT DYSPLASIA AT TRANSURETHRAL RESECTION OF THE BLADDER: THE DABLACA-8 STUDY
- P14.06 Michael Roost Clausen. PROGNOSTIC RELEVANCE OF PRE-THERAPEUTIC ANEMIA IN DIFFUSE LARGE B-CELL LYMPHOMA. DANISH MULTI REGISTRY DATA ON 3522 PATIENTS TREATED WITH CURATIVE INTENT IN THE PERIOD FROM 2000 TO 2012
- P14.07 Ann Bjørnshave. WHEY PROTEINS CONSUMED AS A PRE-MEAL - COMPARISON OF METABOLIC PARAMETERS IN SUBJECTS WITH AND WITHOUT TYPE 2 DIABETES
- P14.08 (Visse Theresia Skov Moestrup. THE EFFECT OF 'X' TO DECREASE A-BETA IN ALZHEIMER'S DISEASE)
- P14.09 Trine Korsgaard. NEPHROTIC SYNDROME IN DANISH CHILDREN
- P14.10 Sophie-Charlott Seidenfaden. POTENTIAL OF NOVEL BIOMARKERS IN PREHOSPITAL MANAGEMENT OF TRAUMATIC BRAIN INJURY: THE PRE-TBI STUDY

## Poster session 15

Chairmen: Lene Seibæk, Thomas Dahl Nielsen (PhD student) & Sara Bisgaard Jensen (PhD student)

- P15.01 Oliver Pedersen. PLATELET TURNOVER AND AGGREGATION IN PATIENTS WITH ESSENTIEL THROMBOCYTOSE
- P15.02 Farhad Waziri. HEMODYNAMIC CHARACTERISTICS OF CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION PATIENTS DURING EXERCISE
- P15.03 Gitte Vrelits Sørensen. LONG-TERM DISEASE-SPECIFIC HOSPITALIZATION IN SURVIVORS OF CHILDHOOD LEUKEMIA IN THE "ADULT LIFE AFTER CHILDHOOD CANCER IN SCANDINAVIA" (ALICCS) COHORT
- P15.04 Mridul Johari. NOVEL GENETIC RISK LOCI ASSOCIATED WITH SPORADIC INCLUSION BODY MYOSITIS
- P15.05 Rasmus Pihl. COMPLEMENT FACTOR D EXISTS AS A PROENZYME IN THE CIRCULATION AND IS ACTIVATED BY MASP-3
- P15.06 Agnes Hauschultz Witt. MUSCLE MEMBRANE PROPERTIES IN A PATIENT WITH SPINAL CORD INJURY
- P15.07 Mary Nguyen Nielsen. CAUSES OF DEATH IN DANISH MEN WITH PROSTATE CANCER
- P15.08 Brigitta Villumsen. DOES HOME-BASED EXERCISE MAKE A DIFFERENCE?

- P15.09 Christoffer Krogager. EVALUATION OF INTER-ARM BLOOD PRESSURE DIFFERENCES USING THE MICROLIFE WATCHBP OFFICE IN A CLINICAL SETTING
- P15.10 Fernando Exposto. PHENOTYPIC AND GENOTYPIC CHARACTERIZATION OF A TENSION-TYPE HEADACHE POPULATION

## Poster session 16

Chairmen: Mai Marie Holm, Rebeka Bodak (PhD student) & Troels Bille Folkmar (PhD student)

- P16.01 Anne Staub Rasmussen. OBSTETRIC AND NON-OBSTETRIC SURGERY DURING PREGNANCY: A 20-YEAR DANISH POPULATION-BASED PREVALENCE STUDY
- P16.02 Nichlas Riise Jespersen. IS PROTECTION AGAINST MYOCARDIAL ISCHEMIA-REPERFUSION INJURY AT ONSET DIABETES DEPENDENT ON MITOCHONDRIAL FUNCTION?
- P16.03 Charlotte Madsen. UPFRONT RITUXIMAB MAINTENANCE AFTER INDUCTION THERAPY IMPROVES OUTCOME AND REDUCES THE RISK OF HISTOLOGICAL TRANSFORMATION IN PATIENTS WITH FOLLICULAR LYMPHOMA: REAL- WORLD DATA FROM A DANISH POPULATION-BASED COHORT
- P16.04 Mikkel Bo Brent. ADDITIVE EFFECT OF GH AND PTH IN PREVENTION OF DISUSE OSTEOPENIA IN RATS
- P16.05 Anna Sofia Elisabeth Aaby. HEART SKILLS - IMPROVING CARDIAC REHABILITATION SERVICES THROUGH CO-CREATION: A PHD PROTOCOL ON SYSTEMATIC DEVELOPMENT OF A HEALTH LITERACY INTERVENTION
- P16.06 Anne Maj van der Velden. NEURAL MECHANISMS AND PREDICTORS OF TREATMENT RESPONSE TO MINDFULNESS-BASED COGNITIVE THERAPY IN THE TREATMENT OF RECURRENT MAJOR DEPRESSIVE DISORDER: A STUDY PROTOCOL
- P16.07 Anne-Mette Oxvig. A BETTER UNDERSTANDING OF METHYLGLYOXAL-DERIVED PATHOPHYSIOLOGICAL CHANGES
- P16.08 Trine Line Hauge Okholm. THE LANDSCAPE OF CIRC RNAs IN BLADDER CANCER AND THEIR BIOMARKER POTENTIAL
- P16.09 Line Khalidan Vibholm. TLR9 AGONIST TREATMENT HAS A DUAL ROLE IN HIV-ERADICATION BY ENHANCING ACTIVATION OF CYTOTOXIC NK CELLS AND INDUCING PLASMA HIV-1 RNA IN VIVO
- P16.10 Camilla Christensen. DYNAMIC REMODELLING OF THE RIGHT VENTRICULAR MYOCARDIUM THROUGH THE CARDIAC CYCLE

## Poster session 17

Chairmen: Brian Elmengaard, Charlotte Runge (PhD student) & Hanne Mari Jørgensen (PhD student)

- P17.01 Mads Bengtsen. IN VIVO METABOLIC RESPONSES IN SKELETAL MUSCLE TO INSULIN, HYPOGLYCEMIA AND ADRENALINE

- P17.02 Kristine Jepsen Bennedsgaard. CHRONIC NEUROPATHIC PAIN FOLLOWING OXALIPLATIN AND DOCETAXEL: A 5-YEAR FOLLOW-UP QUESTIONNAIRE STUDY
- P17.03 Mette-Lise Simonsen. THE IMPORTANCE OF AN ACUTE BLOOD SCREENING FOR DRUGS IN POISONED PATIENTS WITH ALTERED MENTAL STATUS
- P17.04 Marie Weinreich Petersen. FUNCTIONAL SOMATIC SYNDROMES IN THE GENERAL DANISH POPULATION: A STUDY PROTOCOL
- P17.05 Kristian Nørgaard Larsen. THE EFFECTS OF LETTING AGENTS CHOOSE PERFORMANCE INDICATORS IN HEALTHCARE
- P17.06 Bodil Gade Hornstrup. OBSTRUCTIVE SLEEP APNEA AND BLOOD PRESSURE IN HYPERTENSIVE PATIENTS WITH CKD2 AND HEALTHY SUBJECTS
- P17.07 Anita Tranberg Simonsen. WHOLE GENOME AMPLIFICATION AND EXOME SEQUENCING AT THE SINGLE CELL LEVEL - A WAY TO ADDRESS CLONAL HETEROGENEITY ON VERY SPARSE MATERIAL
- P17.08 Stine Thyssen. THE LINK BETWEEN PROTEIN OXIDATION AND AGING
- P17.09 Stefanie Luecke. INNATE DNA RECOGNITION BY CGAS IS DEPENDENT ON THE LENGTH OF DNA
- P17.10 Camilla Bang. RAPID USE OF HIGH-SENSITIVE CARDIAC TROPONIN I FOR RULING-IN AND RULING-OUT OF ACUTE MYOCARDIAL INFARCTION - THE RACING-MI STUDY

## Poster session 18

Chairmen: Marianne Lisby & Joan Fledelius (PhD student)

- P18.01 Ida Jakobsen. VALIDATION OF THE FEAR OF CANCER RECURRENCE INVENTORY (FCRI) IN A DANISH POPULATION OF COLORECTAL CANCER PATIENTS
- P18.02 Viktoria Papp. A POPULATION-BASED EPIDEMIOLOGICAL AND SEROLOGICAL STUDY OF THE NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOSD)
- P18.03 Per Høgh Poulsen. CHILDHOOD SOCIOECONOMIC POSITION AND HOW IT RELATES TO MENTAL HEALTH AND OBESITY IN ADOLESCENCE AND EARLY ADULTHOOD
- P18.04 Trine Ørhøj Barkholt. BALLOON CATHETER TIP DAMAGE: A CLINICAL AND BENCH STUDY
- P18.05 Stine Overvad Fredslund. ADJUVANT TREATMENT OF BREAST CANCER RELATED TO CARDIOTOXICITY AND DYSFUNCTIONAL ENDOTHELIUM: THE ABCDE STUDY
- P18.06 Camilla Hansen. CERTIFIED BASIC LIFE SUPPORT INSTRUCTORS ASSESS CARDIOPULMONARY RESUSCITATION SKILLS POORLY
- P18.07 Karthiga Thavachelvam. RECOMBINANT PROTEINS OF THE OAS FAMILY RESTRAIN HIV INFECTION BY ALTERING THE CCR5 RECEPTOR
- P18.08 Katrine Hygum. DIABETES MELLITUS IS A STATE OF LOW BONE TURNOVER - A META-ANALYSIS

- P18.09 Trine Wigh Arildskov. THE RELATIONSHIP BETWEEN ADHD TRAITS AND DAILY FUNCTIONING & QUALITY OF LIFE IN CHILDREN FROM THE GENERAL POPULATION
- P18.10 Rasmus Espersen. SKELETAL EFFECTS OF ROUX-EN-Y GASTRIC BYPASS IN OBESE TYPE 2 DIABETES PATIENTS MEASURED BY DXA AND HR-PQCT: A 6-YEAR FOLLOW-UP STUDY

## Poster session 19

Chairmen: Martin R Jakobsen, Louise Møldrup Nielsen (PhD student) & Martin Christensen (PhD student)

- P19.01 Morten Fenger-Grøn. MENTAL DISTRESS AND THE PROGNOSIS OF MYOCARDIAL INFARCTION - SPOUSAL BEREAVEMENT AS A NATURAL EXPERIMENT
- P19.02 Ditte H. Jensen. NATION-WIDE INTERNET-DELIVERED TREATMENT FOR PATIENTS SUFFERING FROM HEALTH ANXIETY: A PILOT FEASIBILITY STUDY
- P19.03 Christelle Gansonre. TASK-FREE EEG PARADIGM FOR REGISTERING MULTIPLE LEVELS OF LANGUAGE PROCESSING IN THE BRAIN
- P19.04 Troels Munch. IMPACT OF PRE-ADMISSION OPIOID TREATMENT ON ONE-YEAR MORTALITY FOLLOWING NON-SURGICAL INTENSIVE CARE ADMISSION
- P19.05 Rasmus Stilling Tougaard. ACUTE AFTERLOAD-IMPOSED SHIFT IN PORCINE CARDIAC ENERGETICS IMAGED BY HYPERPOLARIZED [1-<sup>13</sup>C]PYRUVATE
- P19.06 Giacomo Frattari. ELIMINATION OF THE ACTIVE HIV RESERVOIR: ENHANCEMENT OF NK CELL-MEDIATED ADCC ACTIVITY BY TOLL-LIKE RECEPTOR 9 STIMULATION
- P19.07 Johanne Bach Andersen. STABILITY OF EGFR MUTATIONS IN WHOLE BLOOD AND PLASMA IN PATIENTS WITH NSCLC
- P19.08 Mona Sharghbin. COMPARISON OF AORTIC VALVE REPAIR TECHNIQUES WITH DIFFERENT SUBVALVULAR ANNULOPLASTIES - AN IN VITRO EVALUATION
- P19.09 Astrid Johannesson Hjelholt. GROWTH HORMONE INDUCES LIPOLYSIS IN HEALTHY, OBESE SUBJECTS
- P19.10 Anne Louise Hansen. ENDOGENOUSLY FORMED NITRO-FATTY ACIDS DAMPEN HSV-2 INDUCED INFLAMMATION

## Poster session 20

Chairmen: Martin Thomsen & Lena-Sophie Martis (PhD student)

- P20.01 Alon Schneider Hait. IDENTIFICATION OF NOVEL INNATE IMMUNODEFICIENCIES IN PATIENTS WITH HERPES ENCEPHALITIS
- P20.02 Yulia Olsen. AIRBORNE ALTERNARIA AND CLADOSPORIUM FUNGAL SPORES: EFFECT ON ASTHMA SOURCES IN DENMARK

- P20.03 Maria-Louise Røn Kobberø. INFILTRATING THE STRONGHOLD OF HIV-1 DURING SUPPRESSIVE ART: VIROLOGICAL AND IMMUNOLOGICAL EFFECTS OF TLR9-TARGETED IMMUNOTHERAPY IN LYMPH NODES
- P20.04 Mille Thastum. LONG-TERM IMPROVEMENTS IN SYMPTOMS, ILLNESS PERCEPTIONS AND ILLNESS BEHAVIOUR IN YOUNG PEOPLE AFTER A BRIEF INTERVENTION FOR PERSISTENT POST-CONCUSSION SYMPTOMS: AN UNCONTROLLED STUDY
- P20.05 Thea Pinholt Lillethorup. MULTI-NEUROTRANSMITTER DEFICITS IN A MINIPIG MODEL OF PARKINSON'S DISEASE
- P20.06 Pernille Gabel. TARGETED INFORMATION DESIGNED TO REACH EVERYONE? DEVELOPMENT OF A DECISION AID IN THE COLORECTAL CANCER SCREENING PROGRAMME
- P20.07 Kasper Adelborg. RISK OF STROKE IN PATIENTS WITH HEART FAILURE: A POPULATION-BASED 30-YEAR COHORT STUDY
- P20.08 Simon Haugaard. THE LECTIN PATHWAY IN POST CARDIAC ARREST PATIENTS
- P20.09 Sigrid Salling Árnadóttir. CHARACTERIZATION OF GENETIC INTRA-TUMOR HETEROGENEITY OF COLORECTAL CANCER AND MATCHING ORGANOID
- P20.10 Martin Lund. CAN INBORN ERRORS OF METABOLISM BE CORRECTED WITH MONOTHERAPY?

## Poster session 21

Chairmen: Peter Bross, Anna Starnawska & Kousik Sarathy Sridharan (PhD student)

- P21.01 Jens Bay Vegger. BOTULINUM TOXIN INDUCED DISUSE OSTEOPENIA DOES NOT DIFFER BETWEEN SKELETALLY MATURE YOUNG AND AGED FEMALE C57BL/6 MICE
- P21.02 Julie Brogaard Larsen. THE INFLUENCE OF HEPARIN ON THE LECTIN PATHWAY IN PULMONARY CANCER PATIENTS
- P21.03 Nis Brix. SMOKING AND USE OF NICOTINE REPLACEMENTS DURING PREGNANCY IN RELATION TO PUBERTAL DEVELOPMENT IN SONS AND DAUGHTERS
- P21.04 Dmitri Zintchouk. EFFECT OF COMPREHENSIVE GERIATRIC CARE ON HEALTHCARE UTILIZATION, QUALITY OF LIFE AND MORTALITY IN ELDERLY REFERRED TO A REHABILITATION UNIT
- P21.05 Veera Manikandan. GENOME WIDE ASSOCIATION STUDY OF DYSLEXIA IN DANISH POPULATION
- P21.06 Allan Hansen. IN VIVO IMAGING OF NEUROMELANIN IN PARKINSON'S DISEASE USING <sup>18</sup>F-AV-1451 PET
- P21.07 Mathis Rasmussen. ESTABLISHMENT OF A HL-1 CELL BIOASSAY TO EVALUATE THE PROTECTIVE CAPACITY OF EXOSOMES AGAINST SIMULATED ISCHEMIA-REPERFUSION INJURY

- P21.08 (Samuel Joseph Windross. IDENTIFICATION OF EARLY EVENTS IN IMMUNE SIGNALING STIMULATED BY FOREIGN DNA)
- P21.09 Marie Veje Knudsen. RETURNING TO DAILY LIVING FOLLOWING CARDIAC TELE-REHABILITATION; AN ANALYSIS OF PATIENT NARRATIVES
- P21.10 Andreas Holmgaard. INTRAOCULAR GENE EDITING IN MICE FOLLOWING SUBRETINAL INJECTION OF CRISPR/CAS9 EXPRESSING LENTIVIRAL PARTICLES

## Poster session 22

Chairmen: Rikke Katrine Jentoft Olsen, Dariusz Orłowski & Morten Høgild Pedersen (PhD student)

- P22.01 Marlene Christina Nielsen. DEVELOPING QPCR ASSAYS FOR MEASURING CD163 SPLICE VARIANTS
- P22.02 Morten Kelder Skouboe. STING LIGANDS IMPROVE THE SURVIVAL OF HERPES SIMPLEX VIRUS TYPE 2 INFECTION IN VIVO
- P22.03 Andreas Lodberg. ACTIVIN DECOY RECEPTOR (IIA) AMELIORATES IMMOBILIZATION INDUCED LOSS OF BONE IN MICE AND IN THE CORTICAL BONE; DOES SO PREFERENTIALLY BY PERIOSTEAL AND NOT ENDOSTEAL BONE FORMATION
- P22.04 Bente Toft. BEING A LARGE BODY IN ACTIVITY: EXPERIENCES OF LIFESTYLE CHANGE DURING 18 MONTHS
- P22.05 Alexander D'Amore. TRANEXAMIC ACID FOR BLOOD LOSS, NEED OF TRANSFUSION AND COAGULATION IN CHILDREN WHO UNDERGO CRANIO-FACIAL SURGERY: THE TACTIC TRIAL
- P22.06 Rune Bæksager Nielsen. ALZHEIMER'S DISEASE IS LINKED TO CORTICAL MICROVASCULAR DYSFUNCTION: AN MRI PERFUSION STUDY
- P22.07 Signe Voigt Lauridsen. HAEMOSTATIC FUNCTION IN PATIENTS AFTER ACUTE SPONTANEOUS INTERCEREBRAL HEMORRHAGE
- P22.08 Sarah Christine Christensen. (ABSTRACT TITLE)
- P22.09 Elias Didrik Francis Zachariae. REGULATION OF EXTRACELLULAR ANTIOXIDANT CAPACITY BY STRUCTURE HETEROGENEITY
- P22.10 Tommy Kragh Bechsgaard. GEOMETRIC COMPARISON OF REPAIR PROCEDURES FOR THE AORTIC ROOT, AN IN VIVO EXPERIMENT

## Poster session 23

Chairmen: Robert Fenton, Iris Brunner & Ellen Marie Høye (PhD student)

- P23.01 Filip Carl Arne Eckerström. LONG-TERM MORPHOLOGICAL CHANGES OF THE RIGHT VENTRICLE IN ADULTS OPERATED FOR VENTRICULAR SEPTAL DEFECTS
- P23.02 Anne Mette Fløe Hvass. SYSTEMATIC SCREENING OF MIGRANTS IN DENMARK: A CROSS-SECTIONAL STUDY OF INFECTIOUS DISEASES IN A POPULATION OF NEWLY ARRIVED REFUGEES

- P23.03 Marzieh Katibeh. MODELLING AND EVALUATION OF A COMMUNITY-ORIENTED HEALTH-BASED SCREENING AND PROMOTION PROGRAMME FOR IMPROVING EYE HEALTH IN IRAN
- P23.04 Vibeke Bay Sørensen. THE EFFECT OF ISCHEMIC REMOTE PERCONDITIONING ON INFARCT VOLUME EVALUATED BY MRI AND HISTOLOGY
- P23.05 Niels Dalsgaard Nielsen. IS LUMBOSACRAL PLEXUS BLOCK AN EFFECTIVE AND SAFE ALTERNATIVE AS SURGICAL ANESTHESIA FOR TOTAL HIP REPLACEMENT?
- P23.06 Mie Mathiasen. ASSISTED REPRODUCTIVE TECHNIQUES (ART) AND THE POSSIBLE EFFECT IN THE PROGRESSION OF ENDOMETRIOSIS SYMPTOMS
- P23.07 Peter Sieljacks. LOW-LOAD BLOOD FLOW RESTRICTED EXERCISE AS A GENTLE TRAINING ALTERNATIVE TO HEAVY RESISTANCE TRAINING IN PATIENTS WITH RHEUMATOID ARTHRITIS
- P23.08 Rasmus Hansen Olesen. INSULIN RESISTANCE AND INFLAMMATION IN THE DORSOLATERAL PREFRONTAL CORTEX
- P23.09 Louise Nissen. DAN-NICAD: DANISH STUDY OF NON-INVASIVE TESTING IN CORONARY ARTERY DISEASE: STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL
- P23.10 Christian Philip Rønn. FUNCTIONAL STUDY OF SELECTED ATP1A3 DISEASE-CAUSING MUTATIONS

## Poster session 24

Chairmen: Rubens Spin Neto, Lene Sofie Granfeldt Østgård & Jenny Bertholet (PhD student)

- P24.01 Tua Gyldenholm. HISTONE-DNA COMPLEXES AND THROMBIN GENERATION AFTER INTRACRANIAL HAEMORRHAGE
- P24.02 Charlotte Ibsen. DEVELOPMENT OF A PATIENT-REPORTED OUTCOME INSTRUMENT FOR PATIENTS WITH LUMBAR RADICULAR PAIN
- P24.03 Peter Lund Ovesen. THE ROLE OF SORCS1 IN GABAERGIC SIGNALLING IN THE BRAIN
- P24.04 Charlotte Bodin. INCIDENCE AND PREGNANCY OUTCOME OF PRENATALLY DIAGNOSED SPINA BIFIDA IN DENMARK
- P24.05 Bente Kjær Lyngsøe. MATERNAL DEPRESSION AND OFFSPRING ATTENDANCE IN ROUTINE HEALTH CARE
- P24.06 Simon Skov. METAL WEAR AND CORROSION AFTER GROWTH ROD INSTRUMENTATION (GR) IN CHILDREN WITH SEVERE EARLY ONSET SCOLIOSIS
- P24.07 Andrey Chuhutin. PRECISION AND ACCURACY OF DIFFUSION KURTOSIS ESTIMATION AND THE INFLUENCE OF B-VALUE SELECTION
- P24.08 Mette Holm Hjorth. METAL-ON-METAL HIP RESURFACING ARTHROPLASTY: ANTERO-LATERAL VERSUS POSTERIOR SURGICAL APPROACH: A 2-YEAR RANDOMIZED RADIOSTEREOMETRIC AND DUAL X-RAY ABSORPTIOMETRY STUDY OF 49 PATIENTS

- P24.09 Didde Haslund. UNRAVELING THE MOLECULAR DISEASE MECHANISMS IN HEREDITARY ANGIOEDEMA BY ESTABLISHMENT OF A NEW CELLULAR SCREENING SYSTEM
- P24.10 Ana Carlota Gonzalez-Ebsen. ANALYSIS OF THE METABOLIC STATE IN CULTURED FIBROBLASTS FROM PATIENTS WITH MULTIPLE ACYL-COA DEHYDROGENATION DEFICIENCY (MADD), A MONOGENIC MITOCHONDRIAL DISORDER

## Poster session 25

Chairmen: Sebastian Frische, Priscila Corraini & Mathilde Borg Houlberg Thomsen (PhD student)

- P25.01 Mads Christian Larsen. ONCE VERSUS TWICE DAILY ASPIRIN TREATMENT IN PATIENTS WITH ESSENTIAL THROMBOCYTOSIS
- P25.02 Niels Sanderhoff Degn. CAN SORCS2 MODULATE BDNF SIGNALING AND DISEASE PROGRESSION IN HUNTINGTONS DISEASE?
- P25.03 Line Stjernholm Tipsmark. ORGANISATIONAL DESIGN OF EMERGENCY CARE: POLICY EVALUATION
- P25.04 Johan Fredrik Borg. REGULATED EXPRESSION OF THE NA/K-ATPASE IN COLONIC EPITHELIUM BY BILE ACIDS
- P25.05 Linda Aagaard Rasmussen. THE PATIENT PATHWAY FOR RECURRENT AND NEW PRIMARY CANCER: INVESTIGATING THE ROLE OF GENERAL PRACTICE
- P25.06 Karoline Knudsen. GASTROINTESTINAL FUNCTION IN PARKINSON'S DISEASE
- P25.07 Anne Højager Nielsen. CONSOLATION OR CONFRONTATION WHEN CO-AUTHORING A DIARY IN THE ICU
- P25.08 Jonathan Yde. AQUAPORIN WATER CHANNEL-EXPRESSION IS ALTERED IN RAT MODEL OF CHRONIC DIARRHOEA DUE TO BILE ACID MALABSORPTION
- P25.09 Lone Kirkeby. DO HIGH OCCUPATIONAL MECHANICAL EXPOSURES INFLUENCE THE RISK OF FAILURE OF TRAPEZIOMETACARPAL JOINT ARTHROPLASTY?
- P25.10 Steffan Tábori Jensen. FUNCTION, HEALTH STATUS AND SATISFACTION AFTER SURGERY WITH THA FOLLOWING FEMORAL NECK FRACTURE OR OSTEOARTHRITIS

## Poster session 26

Chairmen: Simon Fristed Eskildsen, Andreas Højlund & Jakob Toftegaard (PhD student)

- P26.01 Kailash Rani Kumar. EVALUATION OF BLOOD FILTRATION MEMBRANES FOR MULTIPLEXED POINT-OF-CARE DIAGNOSTIC DEVICES
- P26.02 Zenthuja Sivalingam. THE PREDICTIVE ROLE OF NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (NGAL) IN PATIENTS WITH STABLE CORONARY ARTERY DISEASE
- P26.03 Anders Kristensen. EFFECTS OF CALCIUM ON THE FORCE-VELOCITY RELATIONSHIP IN ISOLATED RAT SOLEUS MUSCLES

- P26.04      Cecilie Siggaard. TRANSANAL COLONIC IRRIGATION IS EFFECTIVE IN FUNCTIONAL FECAL INCONTINENCE
- P26.05      Gunhild Mo Hansen. CONSTRAINT-INDUCED MOVEMENT THERAPY (CIMT) AND SHOULDER FUNCTION
- P26.06      Marie-Louise Ladegaard Baun. ACCESS TO FAST TRANSVAGINAL ULTRASOUND THROUGH GENERAL PRACTICE FOR EARLIER DIAGNOSIS OF OVARIAN CANCER
- P26.07      Sidsel Hastrup. CENTRALIZATION AND SPECIALIZATION OF ACUTE STROKE TREATMENT
- P26.08      Gudrun Winther. EFFECT OF PERINATAL OBESITY AND EXERCISE ON OFFSPRING METABOLISM AND MENTAL HEALTH
- P26.09      Thomas Kristoffersen. LEPTIN POTENTIATES THE PRO-INFLAMMATORY EFFECT OF PSORIASIS-RELATED CYTOKINES IN THE DERMAL FIBROBLAST POSSIBLY LINKING PSORIASIS TO OBESITY
- P26.10      Kaj Verner Døssing. THE ACCURACY OF ULTRASOUND AS A SCREENING MODALITY ON SUSPICION OF EXTREMITY FRACTURE IN ADULTS

## Poster session 27

Chairmen: Simon Glerup, Bjørn Bay & Jacob Kinggaard Lilja-Fischer (PhD student)

- P27.01      Karen Rokkedal Lausch. BEHIND CANDIDAEMIA: DESCRIBING A HIGH INCIDENCE NATIONWIDE SETTING
- P27.02      Simon Skouboe. MOTION INCLUDING REAL-TIME DOSE RECONSTRUCTION FOR CALYPSO PATIENTS IN RADIOTHERAPY
- P27.03      Hanne Mørkenborg Bove. PROVIDING NURSING CARE TO PATIENTS SUFFERING FROM HARMFUL ALCOHOL CONSUMPTION OR ALCOHOL DEPENDENCY IN SOMATIC ACUTE ADMISSION UNITS: A PHENOMENOLOGICAL STUDY IN AN ACUTE ADMISSION UNIT AT AARHUS UNIVERSITY HOSPITAL
- P27.04      Lasse Reimer. INTERFERON INDUCIBLE PKR KINASE PHOSPHORYLATE SERINE129 ON ALPHA-SYNUCLEIN CAUSES ALPHA-SYNUCLEIN AGGREGATION-DEPENDENT CELL DEATH IN AN OLIGODENDROGLIAL CELL MODEL OF MULTIPLE SYSTEM ATROPHY
- P27.05      Mette Winther Andersen. GASTROINTESTINAL MOTILITY IN DIABETES PATIENTS
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- P27.07      Morten Stokholm. NEUROINFLAMMATION IN PREDIAGNOSTIC PARKINSON'S DISEASE: A MULTI-TRACER PET STUDY
- P27.08      Marlene Beyer Eg. CHILD ABUSE IN THE NORTHWESTERN PART OF DENMARK - A 12-YEAR RETROSPECTIVE STUDY

P27.09 Thomas Falstie-Jensen. CAN LOW-GRADE INFECTIONS OF SHOULDER ARTROPLASTIES BE DIAGNOSED BEFORE REVISION?

## Poster session 28

Chairmen: Ulf Simonsen & Kristian Wemmelund (PhD student)

P28.01 Dennis Graversen. DEVELOPMENT OF A VALID AND RELIABLE QUALITY MEASUREMENT TOOL FOR GENERAL PRACTITIONER AND NURSE LED TELEPHONE TRIAGE IN OUT-OF-HOURS CARE

P28.02 Mathias Rædkjær. COMORBIDITY AFFECTS DISEASE-SPECIFIC MORTALITY IN SARCOMA PATIENTS: A NATIONWIDE, POPULATION-BASED STUDY

P28.03 Sofie Eg Jørgensen. GENETIC DETERMINANTS UNDERLYING SEVERE INFLUENZA INFECTION

P28.04 Randi Steensgaard. HOW DIRECT INVOLVEMENT OF NURSES IN RESEARCH CAN SUPPORT PATIENT PARTICIPATION IN REHABILITATION

P28.05 Julie Nelly Christensen. IDENTIFICATION OF MELANOMA-SPECIFIC REFERENCE GENES FOR QUANTITATIVE GENE EXPRESSION STUDIES

P28.06 Mette Saksø. DOSE-ESCALATED RADIOTHERAPY GUIDED BY FUNCTIONAL IMAGING FOR PATIENTS WITH HYPOXIC HEAD AND NECK SQUAMOUS CELL CARCINOMA

P28.07 Maj Ulrichsen. SORTILINS AND NEUROTROPHIN SIGNALING IN SCHWANN CELLS

P28.08 Lisbet Grønbaek. FAMILIAL ACCUMULATION OF AUTOIMMUNE HEPATITIS AND EXTRAHEPATIC AUTOIMMUNE DISEASES: A NATIONWIDE, REGISTRY-BASED COHORT STUDY

## Poster session 29

Chairmen: Vladimir Matchkov & Jesper Weile (PhD student)

P29.01 Anne Bendix Andersen. THE INFLUENCE OF A POLICY DOCUMENT IN THE PRACTICE OF INTERSECTORIAL COLLABORATION IN DANISH HEALTHCARE: A CRITICAL DISCOURSE ANALYSIS

P29.02 Vibe Bolvig Hyldegård. SOCIOECONOMIC INEQUALITY IN THE PROVISION OF BEST CLINICAL PRACTICE IN THE TREATMENT OF STROKE PATIENTS

P29.03 Sarunas Dikinis. SIMVASTATIN IMPACT ON LIVER REGENERATION IN HEALTHY RATS FOLLOWING LIVER RESECTION

P29.04 Mats Bue. BONE AND SUBCUTANEOUS TISSUE PHARMACOKINETICS OF VANCOMYCIN IN TOTAL KNEE REPLACEMENT PATIENTS

P29.05 Caroline Marie Andreasen. RESPONSE TO PAMIDRONATE TREATMENT ASSESSED BY WHOLE BODY MAGNETIC RESONANCE IMAGING IN PAEDIATRIC CHRONIC NON-BACTERIAL OSTEOMYELITIS

- P29.06 Rikke Smedegaard Rosbjerg. RETURN TO WORK SELF-EFFICACY (RTW-SE) AND ACTUAL RETURN TO WORK IN A DANISH POPULATION OF CANCER SURVIVORS
- P29.07 Jakob Wetche. EFFECT OF ACUTE STRESS ON HPA AXIS ACTIVATION, GENE EXPRESSION AND BEHAVIOR IN A MOUSE MODEL POSSESSING AF GENETIC SUSCEPTIBILITY TO MENTAL ILLNESS
- P29.08 Sara Buskbjerg Jager. THE FORGOTTEN CELL TYPE: SATELLITE GLIAL CELLS

## Poster session 30

Chairmen: Yonglun Luo & Henriette Ejlsmark Svensson (PhD student)

- P30.01 Mette Tranberg Nielsen. ACCURACY OF HRHPV TESTING IN SELF-COLLECTED CERVICOVAGINAL AND URINE SAMPLES
- P30.02 Rikke Madsen. EXPERIENCES OF PATIENTS AND SIGNIFICANT OTHERS CONCERNING TRANSITIONS DURING THE COURSE OF INCURABLE CANCER
- P30.03 Morten Overgaard. PSEUDO-OBSERVATIONS AND THE CHALLENGE OF VARIANCE ESTIMATION
- P30.04 Peter Lykke Eriksen. MAPPING OF METABOLIC LIVER FUNCTIONS IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE
- P30.05 Zhijia Wang. DEFINING ROLES OF BOTH CDK12/CYCK AND CDK13/CYCK TRANSCRIPTION ELONGATION KINASES IN THE CONTROL OF GENE EXPRESSION, PRE-MRNA PROCESSING AND CANCER
- P30.06 Berit Dalsgaard Nielsen. ATTENUATION OF FLUORINE-18-FLUORODEOXYGLUCOSE UPTAKE IN LARGE-VESSEL GIANT CELL ARTERITIS AFTER SHORT-TERM, HIGH-DOSE STEROID TREATMENT: A DIAGNOSTIC WINDOW OF OPPORTUNITY
- P30.07 Anne-Birgitte Blavnsfeldt. LOW-DOSE PREDNISONE OR PREDNISOLONE DOES NOT AFFECT BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED, CONTROLLED STUDIES
- P30.08 Rola Ismail. IMAGING BIOMARKERS IN SUBJECTS WITH ALZHEIMER'S DISEASE AND SUBJECTS AT RISK OF ALZHEIMER'S DISEASE: A STUDY OF THE TEMPORAL AND SPATIAL RELATIONSHIPS BETWEEN NEUROINFLAMMATION, BETA-AMYLOID AND TAU AGGREGATION IN SUBJECTS AT RISK OF ALZHEIMER'S DISEASE

## PhD student chairmen

- CH.01 Willemijn Comuth. STABILITY OF DABIGATRAN-SPIKED PLASMA AFTER STORAGE AT -80°C
- CH.02 Kirstine Petrea Bak-Fredslund. IMPACT OF RECONSTRUCTION ALGORITHMS ON FUNCTIONAL 2-[<sup>18</sup>F]FLUORO-2-DEOXY-*D*-GALACTOSE PET/CT OF HUMAN LIVER
- CH.03 Helene Halkjær Jensen. HOST CELL STRUCTURE, POLARITY AND PROTEIN ORGANIZATION DURING INFECTION WITH TWO PATHOGENIC ESCHERICHIA COLI STRAINS
- CH.04 Morten Højild Pedersen. SUBSTRATE METABOLISM DURING FASTING IN OBESE HUMAN SUBJECTS: IMPACT OF GH BLOCKADE
- CH.05 Henriette Holm Stabel. RUPTURE OF A NON-TRAUMATIC ANTERIOR COMMUNICATING ARTERY ANEURYSM: DOES LOCATION OF ANEURYSM PREDICT FUNCTIONAL INDEPENDENCE AFTER NEUROREHABILITATION?
- CH.06 Mette Høj Lauridsen. 2ND TRIMESTER HEAD SIZE IN FETUSES WITH CONGENITAL HEART DISEASE: A COHORT STUDY
- CH.07 Morten Lykke Olesen. PLATELET-RICH PLASMA LEADS TO NEW MATRIX FORMATION AROUND ARTICULAR CARTILAGE CHIPS EMBEDDED IN FIBRIN GLUE IN VITRO
- CH.08 Martin Bøhme Rasmussen. ROUTINE USE OF POINT-OF-CARE TROPONIN T MEASUREMENT FOR PREHOSPITAL DIAGNOSIS AND RISK-STRATIFICATION IN PATIENTS SUSPECTED OF ACUTE MYOCARDIAL INFARCTION
- CH.09 Zongpei Zhao. INSIGHTS INTO THE STRUCTURAL BIOLOGY OF A NEURAL PROTEIN COMPLEX INVOLVED IN NEURODEGENERATION
- CH.10 Andreas Fløe. TUBERCULOSIS-SPECIFIC CD8 CELLS AND ACTIVE AND LATENT TUBERCULOSIS
- CH.11 Rikke Hahn Kofoed. A NEW POSSIBLE PATHWAY FOR TREATMENT OF PARKINSON'S DISEASE
- CH.12 Adrian Bauer. ARE REDUCED HEPARIN LEVELS DURING MINIMAL INVASIVE EXTRACORPOREAL (MIECC) SAFE? SAFETY OF A NEW ANTICOAGULATION STRATEGY
- CH.13 Rune Dall Jensen. EXPLORING THE DEVELOPMENT OF TALENT IN SURGERY - A STUDY ACROSS THE PERFORMANCE DOMAINS OF SURGERY AND SPORTS
- CH.14 Vibeke Lynggaard. PATIENT EDUCATION: LEARNING AND COPING STRATEGIES IMPROVE THE ADHERENCE IN CARDIAC REHABILITATION (LC-REHAB) – A RANDOMISED CONTROLLED TRIAL
- CH.15 Ardis Simonsen. AUTOMATIC ACTION IMITATION IN SCHIZOPHRENIA
- CH.16 Michael Schriver. UNDERSTANDING AND MEASURING THE QUALITY OF EXTERNAL SUPERVISION OF RWANDAN PRIMARY HEALTHCARE PROVIDERS

- CH.17 Rasmus Aagaard. ECHOCARDIOGRAPHY DURING RESUSCITATION: A PARADOX OF RIGHT VENTRICULAR DILATATION IN CARDIAC ARREST CAUSED BY HYPOVOLEMIA AND HYPERKALEMIA - A RANDOMIZED PORCINE STUDY
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- CH.19 Carsten Behr-Rasmussen. MAGNETIC RESONANCE IMAGING OF THE INTRALUMINAL THROMBUS IN ABDOMINAL AORTIC ANEURYSMS - A QUANTITATIVE AND QUALITATIVE EVALUATION AND CORRELATION TO GROWTH RATE
- CH.20 Kathrine Bang Madsen. DISCORDANCE BETWEEN PARENT-REPORTED BEHAVIOUR AND ADHD-DIAGNOSIS IN THEIR CHILDREN
- CH.21 Søren Nielsen Skov. NOVEL REMODELING MITRAL ANNULOPLASTY RING THAT PRESERVES AXIAL DYNAMICS OF THE NATIVE MITRAL ANNULUS
- CH.22 Christina Friis Jensen. HYPOTHERMIA AND RESPIRATORY DISTRESS SYNDROME IN VERY PRETERM INFANTS
- CH.23 Esben Søvsø Szocska Hansen. IMAGING PORCINE CARDIAC SUBSTRATE SELECTION MODULATIONS BY GIK INTERVENTION: A HYPERPOLARIZED [ $^{13}\text{C}$ ]PYRUVATE STUDY
- CH.24 Pernille Falberg Rønn. OBESITY-ASSOCIATED RISK OF CARDIOVASCULAR DISEASE AND THE INFLUENCE OF ETHNICITY: A COMPARATIVE STUDY IN INUIT AND EUROPEANS
- CH.25 Anders Krogh Brøndberg. NATIONWIDE EXPERIENCE OF CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA CAUSED BY RYR2 MUTATIONS
- CH.26 Casper Larsen. STRUCTURAL CHARACTERISATION OF COBALAMIN UPTAKE AND TRANSPORT: THE CUBILIN-AMNIONLESS INTERACTION
- CH.27 Sorosh Tabatabaeifar. MEDIAN NERVE AFFECTION DURING SEASONAL REPETITIVE WORK WITH MODERATE FORCE
- CH.28 Mia Bendix Rasch. VITAMIN D TREATMENT INCREASES T CELLS PROGRAMMED DEATH RECEPTOR-1 EXPRESSION IN CROHN'S DISEASE
- CH.29 Maria Wielsøe. SERUM LEVELS OF ENVIRONMENTAL POLLUTANTS ARE ASSOCIATED WITH BREAST CANCER RISK
- CH.30 Vincent Kalumire Cubaka. UNDERSTANDING AND MEASURING PATIENT-PROVIDER COMMUNICATION IN PRIMARY HEALTH CARE SETTINGS IN RWANDA
- CH.31 Kasper Lisager Jønsson. IFI16 PLAYS A DUAL ROLE IN THE CGAS-STING PATHWAY BY PROMOTING BOTH PRODUCTION AND FUNCTION OF CGAMP
- CH.32 Susan Larsen. SHORT UNPLANNED ADMISSIONS IN HAEMATOLOGY
- CH.33 Anders Laustsen. VERSATILE PLATFORM FOR INVESTIGATING PLASMACYTOID DENDRITIC CELL DEVELOPMENT AND FUNCTION

- CH.34 Thomas Dahl Nielsen. ULTRASOUND GUIDED OBTURATOR NERVE BLOCK - INVESTIGATING THE PROXIMAL SPREAD AND INVOLVEMENT OF THE HIP ARTICULAR BRANCHES
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- CH.41 Jesper Weile. THE USE OF ULTRASOUND IN TRAUMA IN DENMARK
- CH.42 Louise Møldrup Nielsen. EFFECTIVENESS OF ASSESSMENT OF FUNCTIONAL ABILITY AND FOLLOW-UP AT HOME FOR ELDERLY MEDICAL PATIENTS
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- CH.52 Jacob Kinggaard Lilja-Fischer. RADIOSENSITIVITY IN OROPHARYNGEAL CANCER PATIENT-DERIVED XENOGRAFTS
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- CH.54 Christian Andreas Hvid. CONE BEAM CT-BASED APPROACH TO ADAPTIVE RADIOTHERAPY IN HEAD AND NECK CANCER
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## Abstracts

Fogh-  
Nielsen      Junjing Su

WAVE INTENSITY ANALYSIS PROVIDES NOVEL INSIGHTS INTO  
PULMONARY HYPERTENSION

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**Introduction:** Pulmonary hypertension (PH) is a severe disease with a 5-year survival of 50% with current treatment. Therefore, novel approaches to study the pulmonary hemodynamics are required. The aim was to assess arterial wave propagation in the pulmonary artery and explore the clinical usefulness of wave intensity analysis (WIA) in PH.

**Methods:** Right heart catheterisation was performed using a pressure and Doppler flow sensor tipped catheter to obtain simultaneous pressure and flow velocity measurements in the pulmonary artery in 10 control subjects, 11 pulmonary arterial hypertension (PAH) patients and 10 chronic thromboembolic pulmonary hypertension (CTEPH) patients. WIA was applied to the acquired data.

**Results:** Wave speed, a marker of arterial stiffness, was significantly greater in PH patients compared to controls and was significantly correlated to the severity of PH. Wave reflection index (WRI) in PH patients (25.1 % [17.4 - 29.6 %] in PAH and 30.2 % [11.8 - 35.5 %] in CTEPH) was significantly greater compared to controls (3.93 % [3.38 - 6.78 %]), indicating vascular impedance mismatch. Patients with mild and severe PH had similar WRI. The forward wave to right ventricular (RV) energy ratio was greater in CTEPH than PAH indicating differences in RV function and the ratio revealed significant discriminatory capacity to differentiate CTEPH from PAH (AUROC = 0.87).

**Conclusion:** Wave reflection in the pulmonary artery was increased in PH and is unrelated to severity. Increased wave reflection could be an early indicator of pulmonary vascular disease. Furthermore, forward wave to RV energy ratio may be an additional tool to distinguish between the PAH and CTEPH.

Fogh- Morten Nørgaard TUMOR-ASSOCIATED MACROPHAGES IN MULTIPLE MYELOMA:  
Nielsen Andersen NOVEL TARGETS FOR TAILORED THERAPY

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Background: Infiltration by tumor-associated macrophages (TAMs) is associated to poor outcome in most human malignancies. TAMs induce therapy-resistance, immunosuppression, and promote metastasis. These effects may be due to over-activation of the transcription factor STAT3. In multiple myeloma (MM), however, the role of TAMs is less defined. The aim of the present study was to characterize TAMs in MM, and to develop a STAT3-inhibitory drug that can be targeted to TAMs.

Methods: We enrolled patients with the benign state MGUS (n=32), with MM (n=45), and healthy donors (HD, n=8). Bone marrow RNA was isolated, and RT-qPCR was done using a LightCycler 480. Immunohistochemistry (IHC) was done on the BenchMark XT platform. Liposomes containing a STAT3-inhibitor were produced using a NanoAssemblr.

Results: Bone marrow expression of the TAM marker CD163 was strongly increased in both MGUS and MM: mRNA: 4- and 5-fold vs. HD, P<0.001, IHC: positive area: HD=4.5%, MGUS=8.7%, and MM=7.0% (P=0.02). A subset of patients had markedly increased STAT3 activation, which was positively correlated with higher CD163 expression (P<0.0001).

We developed a liposome-based STAT3-inhibitory drug that can be targeted to CD163<sup>pos</sup> cells. The targeted drug effectively inhibited STAT3-activation in CD163<sup>pos</sup> monocytes, with no off-target effect in CD163<sup>neg</sup> lymphocytes. Further, in cultured macrophages, the effect of the drug increased with higher CD163 expression.

Conclusion: The myeloma bone marrow is rich in CD163<sup>pos</sup>TAMs. We have developed a CD163-targeted STAT3-inhibitor, which may represent a novel treatment paradigm in a subset of MM patients. Studies in murine cancer models are warranted.

Fogh-  
Nielsen  
Maria do  
Nascimento  
Lopes Primo

## MIRNA-382 INDUCTION AS A HALLMARK OF THE CELLULAR ANTIVIRAL RESPONSE

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Emerging evidence suggests that virus infection is accompanied by a cellular miRNA response with potential implication for triggering and regulating innate immunity. Here, we conduct a miRNA profile study in differentiated monocytic THP1 cells stimulated with foreign dsDNA to elucidate the roles of miRNAs during regulation of the innate immune response. Together with in silico studies to further search for candidate miRNAs targeting cytosolic protein sensors, we identify miRNA-382 and miRNA-3135b as regulators of infection by HSV and potentially other DNA or RNA viruses in THP1 cells. Studies of miRNA overexpression validate posttranscriptional regulation of STING and MAVS, which are key players in the DNA and RNA sensing pathways. Moreover, transient expression of miRNAs-382 and -3135b results in decreased levels of interferon expression in THP1 cells, sensitizing these cells to a viral infection. Interestingly, miRNA-382 and -3135b expression patterns are also affected in primary macrophages after stimulation with dsDNA and Poly I:C. Additional experiments performed in primary macrophages indicate that miRNA-3135b is induced by IRF3 pathway, while miRNA-382 is induced by the STAT1/STAT2 pathway, supporting previous findings in THP1 cells. While inhibition of endogenous miRNA-382 leads to increased levels of interferon to prevent a viral infection, similar effect is not observed for inhibition of endogenous miRNA-3135b. These findings indicate that induction of miRNA-382 by the DNA and RNA sensing pathways triggers a feedback mechanism to reduce interferon expression and regulate the innate immune response to viral infection.

- O01.01 Casper Kierulf Lassen THE EFFECT OF UNILATERAL NEPHRECTOMY IN A WARM RENAL ISCHEMIA-REPERFUSION INJURY RAT MODEL
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- Background: Ischemia-reperfusion injury is the leading cause of acute kidney injury following renal transplantation and septic and hypovolemic shock. In experimental studies, the removal of a single kidney (unilateral nephrectomy, UNx) protects against ischemia-reperfusion injury (IRI) in the remaining kidney. The mechanisms underlying this protection remain to be elucidated. A pilot study was conducted in order to confirm the renoprotective effect in our setup. Subsequently, a full scale study was planned and carried out.
- Method: Wistar rats were randomized to either UNx or sham UNx either one week or immediately prior to 37 minutes of unilateral renal artery clamping (n = 3-4 in each of the 4 groups). Animals were terminated 24 hours after reperfusion. Blood and renal cortical tissue were harvested. The mRNA levels of inflammatory and oxidative stress markers were evaluated by qPCR.
- Results: Unilateral nephrectomy markedly reduced the inflammatory and oxidative stress response in the postischemic kidney. This was demonstrated by lower cortical TNF- $\alpha$ , IL-1 $\beta$  and MCP-1 and HO-1 expression levels in the nephrectomized groups compared with the sham UNx groups.
- Conclusion: Unilateral nephrectomy attenuates the acute inflammatory and oxidative stress response associated with IRI in a rat model. This effect was demonstrated in both pilot studies. To investigate the acute effects of nephrectomy, this was chosen for the full scale study. MRI technique is used to investigate postischemic renal blood perfusion and oxygenation, and microarray for gene expression analysis to explore renoprotective pathways evoked by unilateral nephrectomy. Results are expected before the 27th of January 2017.

- O01.02 Martin Brandhøj Skov Cancellation BALANCING THE SODIUM CURRENT IN MYOTONIA
- M. Skov, F.V. de Paoli, O.B. Nielsen, T.H. Pedersen*

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Skeletal muscle is responsible for movement of the skeleton, allowing us to walk, run and interact with our surroundings. Activation of skeletal muscle is achieved by the motor nerves via chemical synapses, in which

chemical signals are translated into electrical waves on the muscle fibre. The ability of the muscle fibre to generate and propagate these electrical waves is referred to as excitability. A number of diseases where muscle excitability is affected are known, and they may originate from mutations in a number of different ion channels involved in the activation of skeletal muscle. Most commonly mutations are found in Na<sup>+</sup> or Cl<sup>-</sup> channels, affecting the channels in a way that results in hyperexcitable muscle fibres. In this state, the muscle fibre responds excessively to stimulation from the motor nerve, resulting in prolonged, sometimes even spontaneous, contraction, known clinically as myotonia. In our research, we have investigated the effect of extracellular Mg<sup>2+</sup> and Ca<sup>2+</sup> on myotonia. The investigations were performed in isolated rat and human muscle pharmacologically treated to induce myotonia, and in a patient suffering from the disorder. In all cases, it was shown that elevating Mg<sup>2+</sup> and Ca<sup>2+</sup> concentration reduced myotonia markedly, and in the patient all symptoms were abolished. It has been shown that the extracellular Mg<sup>2+</sup> and Ca<sup>2+</sup> concentration modulates the sodium current in the nerve and muscle tissue by influencing the voltage sensitivity of the Na<sup>+</sup> channels. In addition, we used mathematical modelling to show that small changes in the extracellular Mg<sup>2+</sup> and Ca<sup>2+</sup> concentration may impact the sodium current sufficiently to provide a possible explanation for the observed results.

001.03 Dmitrii Kamaev ROLE OF CHLORIDE IN CONTRACTILITY OF MESENTERIC ARTERIES IN STREPTOZOTOCIN MODEL OF DIABETES

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Vascular pathology is one of the chronic complications associated with diabetes mellitus although the mechanism behind it is debated. In our study, we attempted to investigate the contribution of chloride ions to functional changes in arteries from diabetic rats.

A model of type 1 diabetes was obtained by a single injection of streptozotocin. Concentration response curves to noradrenaline of small mesenteric arteries from STZ-treated and control rats were compared under normal and chloride-free conditions in an isometric myograph. The results of force measurement are expressed as wall tension in H/m.

Arteries from diabetic rats had higher maximum contraction to noradrenaline in PSS (control  $4.00 \pm 0.17$  n=9, diabetic arteries  $5.43 \pm 0.22$  n=9,  $P < 0.05$ ). After substitution of chloride in extracellular solution, no difference in maximum contraction to noradrenaline between groups was seen. Substitution of chloride in extracellular solution resulted in decrease of maximum contraction to norepinephrine for diabetic and control arteries (control arteries in PSS  $4 \pm 0.17$ , after chloride substitution  $3.13 \pm 0.2$  n=9,  $P < 0.05$ ; diabetic arteries in PSS  $5.43 \pm 0.22$ , after chloride substitution  $3.69 \pm 0.18$  n=9,  $P < 0.05$ ). These findings are in accordance

with the increased expression of the calcium-activated chloride channel protein TMEM16A in arteries of STZ-treated animals. Calcium-activated

chloride channels are hypothesized to be important for vascular contractility by amplifying agonist-induced influx of calcium.

We suggest possible association between an increased role of chloride in contractile process of diabetic arteries and TMEM16A protein expression.

O01.04 Emil Hagen Ernst A SEARCH FOR MOLECULAR FACTORS RESPONSIBLE FOR HUMAN OOCYTE COMPETENCE

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The ability to reproduce is a major determinant of quality of life. Assisted reproductive technologies has existed since the early 1980s, and fertility treatment is now involved in approximately 15% of all children born in western countries. Even so, our knowledge on the basal molecular mechanisms responsible for correct oocyte maturation is sparse. With the goal of optimizing current infertility treatment, we wanted to identify molecular factors responsible for normal oocyte competence.

We procured normal human ovarian tissue, laser-micro-dissected oocytes and somatic supportive cells from all pre-ovulatory stages. We RNA sequenced samples to gain global expression profiles. Using bioinformatic tools and enrichment analysis, we interrogated selected protein-, and non-protein-coding transcripts and their relation to signalling pathways for each cell type and stage.

We found "HIPPO signalling" and "Regulation of eIF4 and p70S6K signalling" to be highly enriched during oocyte activation. In the somatic granulosa cells, we found high expression of the ROS scavengers; PRDX5, and TXN2 as well as molecular pathways "CREB Signalling", and "Androgen Signalling". Further, we identified a large number of known epigenetic modifiers of the lnc-RNA class not previously associated with reproductive biology.

We characterised the global expression profile in ovarian cells responsible for normal human fertility. These results may aid us in understanding the molecular regulation in normal oocyte development.

This will help us understand and potentially treat abnormal oocyte development causing endocrine dysfunction and female infertility as seen in Polycystic Ovary Syndrome.

O01.05 Steen Fagerberg ERYTHROCYTE P2X<sub>1</sub>RECEPTOR EXPRESSION IS CORRELATED TO LOSS OF HEMATOCRIT DURING FIRST HOURS OF BLOOD PATHOGEN-POSITIVE SEPSIS

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P2X receptors have recently been suggested to amplify the cytolytic effect of pore forming bacterial toxins on both red blood cells and monocytes. P2X expression shows variation throughout the population, with a minor fraction being functional knock out and the rest having genetic variations within the P2X receptor system. Here we investigate the correlation between P2X receptor abundance on the blood cell membrane surface, and the protection of blood cells during the first stages of sepsis, between ER and ICU admission.

Patients admitted to the ICU with sepsis were grouped into being either blood pathogen-positive or blood pathogen-negative. Blood samples drawn at ICU admission were analyzed for P2X<sub>1</sub> and P2X<sub>7</sub> receptor abundance by immunohistochemistry and flow cytometry. Patient data, clinical outcomes and blood logs were obtained from patient charts in the REDCap database project.

Here we find a strong inverse correlation between P2X<sub>1</sub> receptor expression and the time-adjusted change in hematocrit and hemoglobin levels between ER and ICU in blood pathogen-positive sepsis ( $\Delta$ Hct/hour or  $\Delta$ Hbg/hour). This correlation was not found in patients diagnosed with blood pathogen-negative sepsis. Patients with high amounts of P2X<sub>1</sub> expression were more likely to decrease their hematocrit during the observed period. This correlation was strengthened when looking at hemolysin-producing bacteria only.

Blockage of P2X<sub>1</sub> may improve the cellular defense against bacterial pore formers. This supports previous findings, suggesting that P2X activation amplifies the harm done by bacterial pore formers, and provides new knowledge of interest to future therapeutics in initial stages of sepsis.

O01.06 Darshan Kumar NOGO-A/RTN4A AND NOGO-B/RTN4B ARE SIMULTANEOUSLY EXPRESSED IN EPITHELIAL, FIBROBLAST AND NEURONAL CELLS AND MAINTAIN ER MORPHOLOGY

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Reticulons (RTNs) are a large family of membrane-associated proteins with various functions. NOGO-A/RTN4A has a well-known function in limiting neurite outgrowth and restricting the plasticity of the mammalian central nervous system. On the other hand, Reticulon 4 proteins have been shown to be involved in forming and maintaining endoplasmic reticulum (ER) tubules. Using comparative transcriptome analysis and qPCR, we show here that NOGO-B/RTN4B and NOGO-A/RTN4A are simultaneously expressed in cultured epithelial, fibroblast and neuronal cells. Electron tomography combined with immunolabelling reveal that both isoforms localize preferably to curved membranes on ER tubules and sheet edges. Morphological analysis of cells with manipulated levels of NOGO-B/RTN4B revealed that it is required for maintenance of normal ER shape; over-expression changes the sheet/tubule balance strongly towards tubules and causes the deformation of the cell shape, while depletion of the protein induces formation of large peripheral ER sheets.

O02.01 Marie Maagaard Sørensen DOES THE FUNCTIONAL CAPACITY DEPEND ON THE SIZE OF THE SHUNT? A PROSPECTIVE, COHORT STUDY OF ADULTS WITH SMALL, UNREPAIRED VENTRICULAR SEPTAL DEFECTS

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Objectives: Small ventricular septal defects (VSDs) are considered to have great prognosis and most remain unrepaired. However, we have recently demonstrated lower functional capacity in patients with small, open VSDs compared with healthy peers. With MRI scans, we determined whether functional capacity was correlated to the size of the shunt.

Methods: We included patients with small, unrepaired VSDs and healthy adults, all between 18 and 40 years of age. Functional capacity was previously determined using an incremental bicycle test, establishing

peak oxygen. MRI scans were performed using a 1.5 tesla Philips scanner. With ECG-triggered flow measurements, cardiac output from the pulmonary trunk and ascending aorta, as well as vessel diameters, was calculated.

Results: In total, 29 patients with open VSDs (26.5±6 years) and 25 controls (26.9±5 years) completed both studies. Previously found peak oxygen uptake was nearly 20% lower in patients compared with controls (p=0.002). All patients had shunt ratios below 1.5, confirming their small VSD. When shunt size was correlated to the functional capacity, a negative correlation was found; r=-0.44 (p=0.020). Compared with controls, patients had increased pulmonary retrograde flow, but similar aortic flow. Pulmonary diameter was also increased in patients; 30.3±4mm, compared with controls; 28.2±3 (p=0.041), whereas aortic dimensions were comparable.

Conclusion: Our results demonstrate that - although small - unrepaired VSDs demonstrate reduced functional capacity that can be negatively correlated to the size of the shunt. MRI further revealed pulmonary regurgitation that could potentially be a consequence of the small, open VSD.

O02.02 Line Staun

ACCUMULATION OF FLUORIDE IN BIOFILM SOLIDS AFTER RINSING WITH 1,500 OR 5,000 PPM FLUORIDE

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Daily use of fluoride (F) toothpaste leads to elevated F levels in the oral fluids. The background level of F depends on the concentration of F in the toothpaste and is probably a crucial factor in caries control. In the oral cavity, F accumulates mainly in the dental biofilm solids. The effect of changing the F concentration in toothpaste on F accumulation in the biofilm is not known. The aim of this randomized double-blind crossover study was to examine the concentration of F in young undisturbed biofilm of 12 participants after mouth rinsing for 7 days (3 times/day) with either 0, 1,500 or 5,000 ppm NaF rinses. Each biofilm accumulation phase was preceded by a 14-day non-F toothpaste wash-in period. Following each phase, biofilm was harvested approximately 10 h after the last rinse (baseline) and 10, 30 and 60 minutes after rinsing. Samples were analyzed using an F electrode adapted for microanalyses. Results demonstrated a statistically significant increase in the accumulation of F in the biofilm solids both when using the 1,500 ppm ( $\Delta AUC_{total}$ : 1,154  $\mu\text{mol/g}$ , CI = (743.5; 1,564.4)) and the 5,000 ppm ( $\Delta AUC_{total}$ : 1,477  $\mu\text{mol/g}$ , CI = (1,066; 1,887)) F rinse compared to the control (0 ppm F). Interestingly, when increasing the F concentration from 1,500 ppm to 5,000 ppm the F accumulation in the biofilm solids barely changed ( $\Delta AUC_{total}$ : 323  $\mu\text{mol/g}$ , CI = (-88; 733)). Further studies are needed to explore this phenomenon since the current argument for using high-

fluoride toothpaste (5,000 ppm) relies on the presumption that there is a much greater accumulation of fluoride in the dental biofilm than when using regular toothpaste (1,500 ppm F).

O02.03 Morten Krogh  
Christiansen

CORONARY PLAQUE BURDEN AND ADVERSE PLAQUE CHARACTERISTICS ARE INCREASED IN HEALTHY RELATIVES OF PATIENTS WITH EARLY-ONSET CORONARY ARTERY DISEASE

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**Objectives:** We aimed to characterize and quantify subclinical atherosclerosis by coronary computed tomography angiography (CTA) in 1st degree relatives of patients with a family history of early-onset coronary artery disease (CAD).

**Background:** A strong family history of CAD is an important risk factor for adverse cardiovascular events. Whether predisposed individuals suffer an increased burden of coronary atherosclerosis and adverse plaque features is not known.

**Methods:** We included 88 healthy middle-aged 1st degree relatives from 59 families with early-onset CAD. Participants were matched by age and sex with 88 control patients with atypical angina or non-anginal chest pain, and no family history of CAD, referred for coronary CTA. A blinded analysis of plaque burden and composition was performed by semi-automated plaque quantification software. The relative difference of the median volume or the odds ratio (OR) was compared between groups using a mixed model.

**Results:** First-degree relatives had a higher total plaque volume than controls (relative difference [95% confidence interval (CI)]: 5.8 [2.8-11.9]). The relative difference (95% CI) of total calcified plaque (CP), total non-calcified plaque (NCP), and total low-density NCP (LD-NCP) were 2.6 (1.5-4.5), 5.8 (2.9-12.0), and 3.6 (2.1-6.1), respectively. The adjusted OR (95% CI) of any positive remodeling plaque or any LD-NCP plaque were 4.2 (1.2-14) and 4.2 (1.9-9.5), respectively.

**Conclusions:** Healthy 1st degree relatives of patients with early-onset CAD have an increased coronary plaque burden compared with symptomatic patients. The plaques display characteristics associated with myocardial ischemia and adverse coronary events.

O02.04 Mads Riiskjær PELVIC PAIN AND QUALITY OF LIFE BEFORE AND AFTER LAPAROSCOPIC BOWEL RESECTION FOR RECTO-SIGMOID ENDOMETRIOSIS: A PROSPECTIVE, OBSERVATIONAL STUDY

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Objective: To assess pelvic pain and quality of life before and after laparoscopic bowel resection for recto-sigmoid endometriosis.

Design: Prospectively collected data regarding pelvic pain and quality of life in bowel endometriosis patients.

Setting: Tertiary endometriosis referral unit, Aarhus University Hospital.

Sample: 155 patients who underwent laparoscopic bowel resection for endometriosis.

Methods: Questionnaires for pain (NRS) and quality of life (RAND SF-36) were answered before and after surgery. Data on analgesic and hormone treatment was collected.

Main outcome measures: Pre- and post-operative pelvic pain and quality of life scores were compared, and risk factors for improvement/worsening were identified.

Results: A total of 96.7% of the women completed the 1-year follow-up. A significant decrease ( $p=0.0001$ ) was observed on all pelvic pain parameters. Most profound was the decrease in dyschezia. A significant improvement on all quality of life scores was observed ( $p=0.0001$ ). A surgical complication did not have a negative impact on outcome 1 year after surgery. The post-operative outcome was not related to the type of surgery.

Conclusions: A significant and clinically relevant improvement in pelvic pain and quality of life 1 year after laparoscopic bowel resection for endometriosis was found. We strongly recommend surgery for recto-sigmoid endometriosis unresponsive to conservative treatment.

O02.05 Linda Skibsted  
Kornerup TISSUE DISTRIBUTION OF ORAL VITAMIN B12 IS INFLUENCED BY B12 STATUS AND B12 FORM. AN EXPERIMENTAL STUDY IN RATS

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Introduction: Hydroxocobalamin (HOCbl) is the dominating Cbl form in food, whereas cyanocobalamin (CNCbl) is common in vitamin pills and oral supplements. This study compares single dose absorption and distribution of oral HO[<sup>57</sup>Co]Cbl and CN[<sup>57</sup>Co]Cbl in Cbl-deficient and normal rats.

Materials and methods: Male Wistar rats (7 weeks) were fed a 14-day

diet with (n = 15) or without (n = 15) Cbl. We compared the uptakes of HO[<sup>57</sup>Co]Cbl (free or bound to bovine transcobalamin) and free CN[<sup>57</sup>Co]Cbl administered by gastric gavage (n = 5 in each diet group). Rats were sacrificed after 24 hours. Blood, liver, kidney, brain, heart, spleen, intestines, skeletal muscle, 24-hour urine and faeces were collected, and the content of [<sup>57</sup>Co]Cbl was measured. Endogenous Cbl in tissues and plasma was analysed by routine methods.

Results: Mean endogenous plasma-Cbl was 7-fold lower in deficient vs. normal rats (190 vs. 1330 pmol/L, p < 0.0001). Cbl depletion increased endogenous Cbl ratios (tissue/plasma =  $k_{in}/k_{out}$ ) in all organs, except for the kidney where the ratio decreased considerably. Twenty-four-hour accumulation of labelled Cbl showed: HOCbl > CNCbl (liver) and CNCbl > HOCbl (brain, muscle and plasma).

Conclusions: The Cbl status of rats and the administered Cbl form influence 24-hour Cbl accumulation in tissues and plasma.

O02.06 Ninna Cathrine Schmidt Voss ARTERIES FROM HUMAN COLON CANCER HAVE ENHANCED ENDOTHELIAL FUNCTION COMPARED WITH CONTROL ARTERIES

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Background: Blood supply to cancer tissue is typically insufficient to maintain normal nutrient and O<sub>2</sub> levels in the tissue and eliminate waste products from cell metabolism. Multiple studies have investigated the mechanisms involved in tumor vascularization. However, our understanding of the functional differences between cancer-affected and normal arteries remains limited.

Methods: Human biopsies of primary colon carcinomas and normal colon tissue were obtained from surgical operations. Small arteries were dissected from fresh biopsies of colon cancer and matched with normal colon and mounted in wire myographs for studies of vasoconstriction, relaxation and thickness of arterial tunica media.

Results: Vasocontractile responses to noradrenaline, arginine vasopressin, and depolarization with elevated extracellular [K<sup>+</sup>] were similar in arteries from colon cancer and normal colon. In contrast, the vasocontractile responses to endothelin-1 and thromboxane analog U46619 were reduced. Endothelium-dependent vasorelaxation to acetylcholine was enhanced in colon cancer compared with control arteries. The vasorelaxant and vasocontractile differences between cancer-affected and normal arteries were attenuated following endothelial NO synthesis inhibition with L-NAME. We found no difference in the relaxant response to the NO donors S-nitroso-N-

acetylpenicillamine, sodium nitroprussid and spermine NONOate or in the thickness of the arterial tunica media.

Conclusion: We demonstrate that colon cancer arteries differ functionally from equivalent normal arteries. Endothelium-dependent vasorelaxation and attenuation of vasoconstriction are increased in colon cancer arteries due to enhanced NO-dependent signaling.

O03.01 Pia Kjær  
Kristensen

#### SOCIOECONOMIC INEQUALITY IN PATIENT OUTCOME AMONG HIP FRACTURE PATIENTS: A POPULATION-BASED COHORT STUDY

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Socioeconomic status influences the risk of hip fractures, but we do not know to which extent low socioeconomic status will have an impact on mortality. Furthermore, little is known about intermediate factors, eg, potential socioeconomic related differences in care. We, therefore, examined the association between socioeconomic status and 30-day mortality, acute readmission, quality of care, time to surgery and length of stay. We conducted a population-based cohort study using prospectively collected data from the Danish Multidisciplinary Hip Fracture Registry. We identified 25,354 patients  $\geq 65$  years admitted with a hip fracture between 2010 and 2013. From Statistics Denmark, we assessed data on socioeconomic status including highest obtained education, family mean income, cohabiting status and ethnicity. We performed multilevel regression analysis, controlling for potential confounders. Patients with highest education had lower 30-day mortality compared to patients with low education (7.3% vs 10.0% adjusted odds ratio (OR) = 0.74 (95% confidence interval (CI) (0.63-0.88)). Highest level of family income was also associated with lower 30-day mortality (11.9% vs 13.0% adjusted OR = 0.77, 95% CI 0.69-0.85). Cohabiting status and ethnicity were not associated with 30-day mortality in the adjusted analysis. Patients with both high education and high income had lower risk of acute readmission (14.5% vs 16.9% adjusted OR = 0.94, 95% CI 0.91-0.97). The higher mortality among low socioeconomic patients seems not to be explained by differences in hip fracture care as we found no differences in quality of care, time to surgery or length of stay for low versus high socioeconomic groups.

MAGNETOENCEPHALOGRAPHY AND EEG SOURCE LOCALIZATIONS  
IMPACT ON THE DECISION-MAKING BY THE DANISH EPILEPSY SURGERY  
TEAM

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**Objective:** This prospective ongoing study investigates the impact of magnetoencephalography (MEG) and EEG source localization, as a non-invasive tool to guide the multidisciplinary epilepsy surgery team.

**Methods:** MEG (306 sensors) and EEG (75 channels) were recorded, and source localization using CURRY Neuromag software was done in 62 consecutive patients with refractory focal epilepsy referred for epilepsy surgery. All patients underwent conventional non-invasive presurgical evaluation. The Danish epilepsy surgery team evaluated the patients, first blinded and two weeks later unblinded to MEG. At both sessions, the multidisciplinary team determined the presumed localisation of the epileptogenic zone and decided on surgical or additional presurgical plans. The impact of MEG was divided into predefined categories.

**Results:** MEG and EEG source localization changed the epilepsy surgery team's decision in 39% of the patients. In total, 10% of the patients changed from operation not possible to implantation of intracranial electrodes. Three % changed from operation not possible to operation. Eight % changed from implantation of intracranial electrodes to operation. Two % changed from implantation of intracranial electrodes to operation not possible, and in 16% the implantation strategy changed. MEG alone detected the epileptic activity and changed the decision of the epilepsy surgery team in 10% of the patients. EEG alone changed the decision of the epilepsy surgery team in three % of the patients.

**Conclusion:** MEG and EEG source localization makes epilepsy surgery possible in patients where conventional non-invasive presurgical evaluation did not localize the epileptogenic zone.

O03.03 Rikke Hjortebjerg IGFBP-4 FRAGMENTS PROVIDE INCREMENTAL PROGNOSTIC INFORMATION ON CARDIOVASCULAR EVENTS AND MORTALITY IN PATIENTS WITH ST-ELEVATION MYOCARDIAL INFARCTION

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Background: The enzyme PAPP-A is involved in the development of atherosclerosis. PAPP-A stimulates local IGF-1 action within the plaque through cleavage of IGF binding protein 4 (IGFBP-4). We hypothesized that PAPP-A activity can be assessed by measuring the two IGFBP-4 fragments in plasma. Thus, we developed novel immunoassays for the IGFBP-4 fragments and investigated if they were useful as biomarkers in patients with ST-elevation myocardial infarction (STEMI).

Methods: We included 656 patients with STEMI treated with PCI from September 2006 to December 2008. To determine the two IGFBP-4 fragments created by PAPP-A cleavage, we developed and validated immunoassays for N-terminal (NT) and C-terminal (CT) IGFBP-4. Primary end-point was 5-year cardiovascular mortality. The prognostic potential was compared to a clinical prediction model with 15 traditional risk factors.

Results: During follow-up, 69 patients died from cardiovascular causes. Both IGFBP-4 fragments were associated with cardiovascular mortality ( $p < 0.001$ ). After multivariate adjustments, NT- and CT-IGFBP-4 fragment levels remained associated with cardiovascular mortality with hazard ratios (HR) (95% confidence interval (CI)) per doubling in protein concentration of 2.54 (1.59;4.07) ( $p < 0.001$ ) and 2.07 (1.41;3.04) ( $p < 0.001$ ), respectively. Incorporation of the IGFBP-4 fragments into the clinical prediction model improved the performance of the model, which became more accurate than the clinical model alone.

Conclusion: Circulating IGFBP-4 fragment levels are associated with increased risk of cardiovascular mortality in patients with STEMI and may serve as clinically relevant and pathogenically involved biomarkers.

O03.04 Kira Vibe  
Jespersen

#### THE EFFECT OF MUSIC ON INSOMNIA: A RANDOMIZED CONTROLLED TRIAL

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Insomnia is highly prevalent in modern society. Around one third of the general population experience insomnia symptoms such as difficulties falling asleep or maintaining sleep, and around 6% fit the criteria for an insomnia diagnosis. Music has been suggested as a candidate for a non-pharmaceutical, low-cost and flexible sleep aid, and surveys find that many people use music as a self-help strategy to improve sleep. In a recent Cochrane review, we found a positive effect of music on sleep quality, but the quality of the evidence was not sufficiently high, and no studies included objective measures of sleep.

In the present study, we conducted a randomized controlled trial with three parallel groups: music, audiobook (active control) and no intervention (passive control). In total, 45 adults with insomnia were included in the study and randomized to one of the three groups. Participants in the music group were given the choice among four types of slow music (classical, new-age, jazz or ambient). They were asked to listen to the music for 60 minutes at bedtime for three weeks. The same procedure was used for the audiobook group. Sleep was measured before and after the intervention period using ambulant polysomnography and actigraphy as objective measures and standardized questionnaires as subjective measures.

The data collection is finished, and data are currently being prepared for analysis. Preliminary results may be presented.

O03.05 Hugo Angleys

#### THE EFFECTS OF CAPILLARY TRANSIT TIME HETEROGENEITY (CTH) ON THE BOLD SIGNAL

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Objectives: In the brain, the MR signal increases with neural activity owing to changes in blood oxygenation. This blood oxygenation level dependant (BOLD) signal is the basis of functional MRI studies done to map patterns of activation in the working human brain.

This signal shows interesting and robust transients, which depend on the physiological condition, and suggest an interesting interplay of

physiological parameters regulating blood oxygenation. Capillary transit time heterogeneity (CTH) has been shown to have an important effect on blood oxygenation, but the influence of this parameter on the BOLD signal has not been assessed yet. Here, we examine whether dynamic changes in CTH can better predict BOLD response and explain signal transients, which remain poorly understood, even after almost 25 years of research.

Methods: We develop a three compartment (haemoglobin, plasma, tissue) model to predict dynamic changes in blood oxygenation and in the BOLD signal. The model incorporates the effects of dynamic changes in CTH.

Results: We applied our model to predict the BOLD signal during brain activation under different conditions, such as hypercapnia, hyperoxia, and caffeine uptake, where the physiology, and hence the BOLD response, is altered. Our model predictions show good agreement with experimental measurements of BOLD signal under these conditions. In particular, signal transients are consistently reproduced only when CTH is included in the model.

Conclusion: Including dynamic changes in CTH provides a way to accurately predict the BOLD signal under a wide range of physiological conditions, based on realistic physiological mechanisms.

O03.06 Steffen Leth

COMBINED EFFECT OF VACC-4X, RECOMBINANT HUMAN GRANULOCYTE MACROPHAGE COLONY-STIMULATING FACTOR VACCINATION, AND ROMIDEPSIN ON THE HIV-1 RESERVOIR (REDUC): A SINGLE-ARM, PHASE 1B/2A TRIAL

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Background: Immune priming prior to reversal of HIV-1 latency might form part of a functional HIV-1 cure. We tested this concept in vivo in a single-arm trial enrolling HIV-1 infected adults on antiretroviral treatment.

Methods: Participants received six therapeutic HIV-1 immunizations with Vacc-4x/rhuGM-CSF prior to receiving romidepsin once weekly for 3 weeks. This was followed by analytic treatment interruption (ATI). Co-primary endpoints were copies of HIV-1 DNA (total and integrated) per

$10^6$ CD4+ T cells and infectious units per million (IUPM) resting CD4+ T cells determined by viral outgrowth.

Findings: Seventeen of 20 enrolled participants completed study therapy. Following romidepsin administration, HIV-1 transcription increased significantly and 8/17 participants had  $\geq 1$  quantifiable plasma HIV-1 RNA measurement (range: 21-619 copies/mL). Total HIV-1 DNA declined from baseline to 6 weeks after romidepsin treatment (mean reduction 39.7%, 95% CI: -59.7--11.5,  $p=0.012$ ), and a similar trend was observed for integrated HIV-1 DNA (mean reduction 19.2%, 95% CI: -38.61-6.31,  $p=0.123$ ). IUPM was measurable at baseline and at  $\geq 1$  point following study therapy in 6/17 participants. Among the 6 evaluable participants, the mean reduction in IUPM was 38% (95% CI: -67.0--8.0,  $p=0.019$ ). Median time to viral rebound during ATI was 14 days ([IQR]: 7-21 days). Of 141 adverse events, 95% were grade 1 and 5% were grade 2-3.

Conclusion: In this first reported dual intervention trial designed to target the HIV reservoir, we observed a significant reduction in the size of the latent HIV-1 reservoir. Our findings may serve as a foundation for the optimization of HIV-1 curative strategies.

O04.01 Johanne Liv Agger

IMIPRAMINE VERSUS PLACEBO FOR MULTI-ORGAN BODILY DISTRESS SYNDROME: A DOUBLE-BLIND, RANDOMIZED TRIAL

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Background: Bodily Distress Syndrome (BDS) is a unifying diagnosis encompassing the somatoform disorders and functional somatic syndromes (FSS). Multi-organ BDS is one of the five sub-syndromes of BDS, characterized by multiple persistent bodily symptoms from several organ systems not attributable to well-defined disease. The condition inflicts severe suffering and represents a substantial socioeconomic burden to society. Pharmacological treatment is sparsely investigated, with most trials focusing on single FSS such as fibromyalgia and irritable bowel syndrome. The tricyclic antidepressant imipramine (IM) is an easily available treatment option. We hypothesized that IM improves patients' perception of overall health as well as physical, mental and social functioning.

Methods: In a randomized, double-blind trial, we recruited consecutively referred patients with multiple functional somatic symptoms. Patients who fulfilled the diagnostic criteria for multi-organ BDS were randomly assigned to either 10 weeks of 25-75 mg IM or placebo. Primary outcome was patient-rated improvement measured by Clinical Global Improvement Scale after 10 weeks. Secondary outcomes were physical,

mental and social functioning measured by scales from the SF-36. ClinicalTrials.gov NCT01518634.

Findings: In total, 125 patients received at least one dose of study drug; 65 were allocated to IM and 60 to placebo. In total, 15 terminated the treatment prematurely; 7 because of adverse events. Preliminary results are promising. The final analyses will be completed by the end of 2016.

Perspectives: IM may have the potential of improving overall health as well as physical, mental and social functioning in patients with multi-organ BDS.

O04.02 Emil Christensen LIQUID BIOPSY ANALYSIS OF ACTIVATING FGFR3 AND PIK3CA MUTATIONS FOR MONITORING DISEASE AGGRESSIVENESS IN BLADDER CANCER

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Background: Surveillance for disease progression in patients with bladder cancer is important for early diagnosis and optimal therapeutic treatment.

Objective: To develop sensitive urine- and plasma-based assays for disease surveillance for patients with activating FGFR3 and PIK3CA tumour mutations.

Methods and participants: Highly sensitive and specific digital droplet PCR (ddPCR) assays were developed, and tumour DNA from two patient cohorts was screened for activating FGFR3 and PIK3CA mutations. Cohort 1 included 363 patients diagnosed with non-muscle invasive bladder cancer (NMIBC). Cohort 2 included 468 patients with bladder cancer undergoing radical cystectomy. Urine supernatants (cohort 1: n=216, cohort 2: n=27) and plasma samples (cohort 1: n=39, cohort 2: n=27) from patients harbouring activating mutations were subsequently screened using ddPCR assays.

Results: In total, 36% of the patients in cohort 1 (129/363) and 11% of the patients in cohort 2 (44/403) harboured at least one activating mutation in FGFR3 or PIK3CA in their tumour DNA. Screening of DNA from urine supernatants from cohort 1 using ddPCR assays showed that high levels of tumour DNA were significantly associated with later disease

progression in (NMIBC) ( $p=0.0033$ ). Furthermore, high levels of tumour DNA in urine supernatants and plasma samples were associated with disease recurrence following cystectomy in cohort 2 ( $p=0.068$  and  $p=0.0164$ , respectively).

Conclusions: Increased levels of FGFR3 and PIK3CA mutated DNA in urine and plasma may be indicative of later progression and metastasis in bladder cancer.

O04.03 Sanne Shiroma  
Harsløf THE EFFECT OF ANCHORING DEVICE ON MESH SHRINKAGE DEPENDS ON TYPE OF MESH: AN EXPERIMENTAL LONG-TERM STUDY IN SHEEP

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Background: The choice of mesh and anchoring device in laparoscopic ventral hernia repair is controversial. Clinically important long-term properties of mesh and anchoring device such as mesh shrinkage have been sparsely investigated. Furthermore, the effect of various anchoring devices on mesh properties has never been examined.

Methods: In 20 sheep, using laparoscopy, we inserted three Physiomesht<sup>TM</sup> (light-weight mesh) and three Ventralight<sup>TM</sup> ST (medium-weight mesh), anchored with ProTack<sup>TM</sup>, Securestrap<sup>TM</sup> or Glubran<sup>TM</sup>, respectively. After 6 and 12 months, 10 sheep at each time-point, we euthanized the sheep, harvested the meshes with fascia, and measured the exact size and area of the mesh, expressing mesh shrinkage as a percentage of the initial area.

Results: The shrinkage of Physiomesht<sup>TM</sup> was 35.7%, 23.8% and 17.7% when anchored with Protack<sup>TM</sup>, Glubran<sup>TM</sup> or Securestrap<sup>TM</sup>, respectively. Shrinkage with Protack<sup>TM</sup> was significantly higher than with either Glubran<sup>TM</sup> or Securestrap<sup>TM</sup>, respectively ( $p$  The shrinkage of Ventralight<sup>TM</sup> ST was 19.3%, 22.2% and 19.6% when anchored with Protack<sup>TM</sup>, Glubran<sup>TM</sup> and Securestrap<sup>TM</sup>, respectively ( $p>0.05$  for all pairwise

comparisons). Overall shrinkage of Physiomesht<sup>TM</sup> anchored with Protack<sup>TM</sup> was significantly higher for all comparisons ( $p<0.01$ ).

Conclusion: Our results suggest that mesh shrinkage in sheep takes place within 6 months after implantation. A significant interaction between mesh and type of anchoring indicates that shrinkage depends on both mesh properties and anchoring device. The results of the current study imply that the combined effect of mesh and anchoring device on shrinkage should be evaluated in future studies.

O04.04 Morten Møbjerg  
Callesen

#### A INDUCIBLE TRANSGENIC INTESTINAL CANCER MODEL

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Objective: To develop an inducible transgenic (TG) intestinal cancer pig model.

Background: Pig models, compared to rodent models, bring novel possibilities for cancer research due to their physical and genetic similarities with humans.

Design: TG minipigs were generated using somatic cell nuclear transfer by hand-made cloning. The TG pigs encode two cassettes: 1) an Flp-recombinase inducible oncogene cassette containing KRAS-G12D, cMYC and Simian Vacuolating Virus 40 large TAG, and 2) a 4-hydroxytamoxifen (4-OHT) inducible Flp-recombinase activator cassette controlled by the intestinal epithelium specific Villin promoter. Expression from the oncogene cassette was furthermore governed by an rTR-KRAB-mediated repressor and TET-responsive elements capable of inhibiting the oncogenes upon doxycycline administration.

Results: Thirteen viable transgenic minipigs were born containing a single integrated oncogene cassette and six-nine activator cassettes. The ability of 4-OHT to activate the oncogene cassette was confirmed in vitro using TG colonic organoids and ex vivo using intestinal biopsies. The oncogene cassette was also successfully activated in vivo and two months after peroral treatment with 400 mg tamoxifen over 2x5 days, a duodenal neuroendocrine carcinoma with lymph node metastasis was detected. Molecular analysis of the carcinoma and metastasis confirmed activation of the oncogene cassette and above endogenous levels of KRAS and cMYC. No tumour formation was observed in untreated TG pigs.

Conclusion: We have generated the world's first inducible oncopig model of intestinal cancer. The model is capable for forming metastatic disease already two months after induction.

O04.05 Malene Juul  
Rasmussen

#### NON-CODING CANCER DRIVER CANDIDATES IDENTIFIED WITH A SAMPLE- AND POSITION-SPECIFIC MODEL OF THE SOMATIC MUTATION RATE

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Non-coding mutations may drive cancer development and can be studied systematically with the advent of cancer whole-genomes. Distinguishing non-coding driver and passenger mutations is challenging as the mutation rate varies and their impact generally is unknown. Driver detection methods addressing these issues are needed.

We developed ncdDetect, a statistically-founded method for non-coding cancer driver detection, and applied it to 505 pan-cancer whole-genomes. The method captures sample-specific mutational signatures and long-range variation in the mutation rate. We systematically assessed three scoring-schemes on protein-coding genes and found known cancer-drivers top-ranked.

We screened promoters, untranslated regions (UTRs), and splice-sites of protein-coding genes, which identified 216 non-coding driver-candidates using the preferred conservation-based scoring-scheme. These included previously characterized non-coding drivers, such as the TERT and WDR74 promoters. To gain further evidence for individual candidates, we correlated presence of non-coding mutations with gene expression as well as patient survival.

We found that STK11 splice site-mutations in lung adenocarcinoma are associated with decreased gene-expression and a tendency for decreased survival. Furthermore, promoter and coding mutations to a base-excision-repair gene (SMUG1) correlate with a C-to-T mutational signature, as does expression in the extended sample set.

In conclusion, we find that a rich model of mutational heterogeneity facilitates statistical identification of non-coding driver candidates, some of which may be of clinical relevance.

O04.06 Oscar Casares  
Magaz

SPATIAL RECTAL DOSE/VOLUME METRICS PREDICT PATIENT-REPORTED GASTRO-INTESTINAL SYMPTOMS AFTER RADIOTHERAPY FOR PROSTATE CANCER

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Background and purpose: To explore associations between spatial rectal dose/volume metrics and patient-reported gastro-intestinal (GI) symptoms after radiotherapy (RT) for localized prostate cancer, and to compare these with dose-surface/dose-volume histogram (DSH/DVH) metrics.

Materials and methods: Dose distributions and seven GI symptom scores (defecation urgency/emptying difficulties/fecal leakage;  $\geq$ moderate severity; median time to follow-up: 3.6y) were extracted for 212 patients treated with image-guided RT in 2005-2007. In total, 530 potential predictors assessed from 2D rectal dose maps and DSHs/DVHs were subject to 50-times iterated five-fold cross-validated univariate and multivariate logistic regression analysis (UVA, MVA) in 70% of the data. The most frequently selected MVA models were investigated in the complete data (performance: area under the receiving-operating characteristics curve, AUC).

Results: Dose map based models had higher AUCs than DSH/DVH-based models (mean $\pm$ SD over all symptoms: AUC: 0.63 $\pm$ 0.04 vs. 0.58 $\pm$ 0.04), with statistical significance ( $p \leq 0.05$ ) for seven vs. four symptoms. Symptoms were mostly explained by doses of 55-75Gy at the central/upper region of the maps. The models for defecation urgency and emptying difficulties had the strongest associations (AUC: 0.66-0.68,  $p < 0.001$ ).

Conclusions: The high-dose region primarily explained the occurrence of the investigated GI symptoms with the overall strongest associations for spatial metrics describing the lateral extent of high doses.

O05.01 Rasmus  
Cleemann

AUGMENTATION OF REVISION IMPLANT FIXATION WITH COMBINATION OF ALLOGRAFT, BMP-2 AND LOCAL OR SYSTEMIC BISPHOSPHONATE

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Introduction: Bone stock can be poor and have diminished healing potential in revision settings. Clinically, bone chips (allograft) improve longevity, and experimentally we previously showed that adding bisphosphonate (BP) to allograft improved revision fixation. We hypothesize that fixation of revision implants, can be further improved by adding bone anabolic Bone Morphogenetic Protein 2 (BMP-2) to local or systemic BP.

Methods: Two groups, with 12 canines each, underwent a surgical protocol bilaterally in the medial femur condyles to establish a revision cavity. After 8 weeks, a revision procedure with impacted allograft was

performed. One group received BP Zolendronate locally soaked in allograft (t=0), the other by systemic administration (t=10 days). Half of each group's implants were coated with 5 µg of BMP-2. After an additional 28 days, implants were harvested with biomechanical and histomorphometric evaluation.

Results: Adding BMP-2 to local BP did not improve fixation: mean diff Strength [95% CI] = 0.3 MPa [-1.0; 1.5]. No difference was seen in volume of retained allograft between groups (p=0.31). Adding BMP-2 to systemic BP also did not improve fixation: mean diff Strength [95% CI] = 0.4 MPa [-2.1; 2.9], with a 56% reduction in volume of allograft with BMP-2 (p=0.002).

Discussion: We did not show benefit of adding BMP-2 to BP (neither local nor systemic) to further increase fixation of revision implants by retention and incorporation of allograft. Dose and time effects may be important in the clinical setting, but the lack of improvement shown here suggests that the addition of BMP-2 with local or systemic bisphosphonate in human patients may not improve fixation.

#### O05.02 Lone Dragnes Brix PAIN IS THE MAIN REASON FOR UNSCHEDULED HEALTHCARE CONTACTS AFTER OUTPATIENT SURGERY

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Background: Outpatient surgery has obvious advantages and is safe and convenient for patients. Little is, however, known about how well patients cope after discharge, e.g. with postoperative pain. We hypothesised that 10% of outpatients would have pain-related unscheduled contact with healthcare services, and that the incidence would differ depending on the type of surgical procedure.

Methods: In this prospective observational study, an electronic questionnaire concerning unscheduled contact with healthcare services was sent 1 and 8 weeks after surgery to 905 patients who had undergone one of five common outpatient surgeries (knee or shoulder arthroscopy, surgical correction of hallux valgus, laparoscopic cholecystectomy, or laparoscopic gynaecological procedures).

Results: Data from 732 patients (81%) were available for analysis. Within the first 8 weeks after surgery, 150 patients (20.5%) reported a total of 247 pain-related unscheduled contacts with healthcare professionals. Risk factors were female gender, unemployment, and laparoscopic cholecystectomy as surgical procedure. The most frequent healthcare

contact was in the first postoperative week with the GP (46.4%), and the most frequent outcome was further information and guidance (41.2%).

Conclusions: Pain-related unscheduled contacts for outpatients are frequent and differ depending on the type of the surgical procedure. These findings should be considered when planning postoperative monitoring and support as well as when developing postoperative patient education programs. The number of unscheduled contacts with healthcare services may represent an indicator of outcome quality in outpatient surgery.

O05.03 Sigrún Alba  
Jóhannesdóttir

PARTNER BEREAVEMENT AND RISK OF HERPES ZOSTER: RESULTS FROM TWO POPULATION-BASED CASE-CONTROL STUDIES IN DENMARK AND THE UNITED KINGDOM

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Background: Psychological stress is commonly thought to increase the risk of herpes zoster by causing immunosuppression. However, research on the topic is sparse and inconsistent. We conducted two parallel case-control studies of the association between partner bereavement and risk of zoster using electronic healthcare data covering the entire Danish population and general practices in the UK Clinical Practice Research Datalink.

Methods: We included patients with a zoster diagnosis from primary care or hospital diagnosis of zoster in 1997-2013 in Denmark (n=295,833) and 2000-2013 in the UK (n=150,207). We matched up to four controls to each case by age, sex, and general practice (UK only) using risk-set sampling. The date of diagnosis was the index date for cases and their controls. We computed adjusted odds ratios with 99% confidence intervals for previous bereavement among cases vs. controls using conditional logistic regression with results from the two settings pooled using random-effects meta-analysis.

Results: Overall, the adjusted odds ratios for the association between partner bereavement and zoster were 1.08 (1.06-1.10) in Denmark and 1.01 (0.98-1.05) in the UK. The pooled estimates were 0.83 (0.57-1.21), 0.90 (0.57-1.44), 1.15 (0.92-1.44), 1.12 (0.99-1.25), 1.05 (0.88-1.26), 1.06

(0.97-1.15), and 1.04 (0.97-1.12) for bereavement within 0-7 days, 8-14 days, 15-30 days, 31-90 days, 91-365 days, 366-1095 days, and >1095 days before the index date, respectively.

Conclusions: We found no consistent evidence of an increased risk of zoster following partner death. Initial fluctuations in estimates may be explained by delayed healthcare contact due to the loss.

O05.04 Charlotte  
Willemann  
Stecher

#### THE MALI SCHISTOSOMIASIS MORBIDITY STUDY - MASCHISMO

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Elimination and transmission interruption of schistosomiasis is an out-spoken 2025 WHO goal. Symptoms of *S. haematobium* are frequently ignored due to the subtle nature of symptoms, but in endemic areas impact on socio-economic and general health is massive. Genital involvement is present leading to reproductive and sexually related illness and increased risk of HIV transmission. Organomegaly is prevalent, and growth-retardation and anemia are prominent problems. Despite efficient national prevention programs focusing on medicinal mass-drug treatment with praziquantel in sub-Saharan Africa, prevalence of schistosomiasis has shown to rebound to pre-interventional levels within a few years if treatment is not regularly repeated.

The MaSchisMo study was conducted in Mali as a clinical randomized trial to compare two different treatment strategies in terms of re-infection rates, cure rates and grade of general morbidity and to provide insight into the inflammatory processes of the multiple manifestations of *Schistosoma haematobium* infection.

Results: The study demonstrates organomegaly, anemia and growth retardation caused by *S. haematobium*. No long-term benefit of a second dose of praziquantel was demonstrated. The study discusses hitherto used strategies of parasite elimination and points out gaps of unexplored possibilities for future control and treatment of schistosomiasis in sub-Saharan Africa.

O05.05 Malene Beck NEUROLOGICAL PATIENTS' EXPERIENCES OF EATING IN THE HOSPITAL: A PHENOMENOLOGICAL-HERMENEUTIC STUDY

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Background: Many neurological patients experience eating difficulties during mealtimes. Consequently, they often refrain from eating in public places to avoid potentially awkward situations. Eating is an essential part of life, providing patients with comfort during their hospitalization. Therefore, attention should be paid to neurological patients who encounter eating difficulties to foster a positive mealtime experience.

Aim: To investigate what neurological patients experience when participating in mealtimes during hospitalization.

Method: Ten semi-structured interviews with neurological patients were conducted and recorded. After transcription, the text was analyzed and interpreted comprising three methodological steps inspired by the French philosopher, Paul Ricouer.

Findings: Three themes were identified through data analysis and interpretation: 1) The missing feeling of homeliness 2) The battle between socialization versus isolation 3) The loss of time, rhythm and presence.

Conclusion: To the neurological patients, mealtimes are not only a manageable task, but also part of the existential care that leads to a positive experience. Aesthetic elements were shown to have the potential of making the patients feel comfortable and homely when hospitalized. This was important since our study also identified that the patients were longing for homeliness when participating in mealtimes during hospitalization.

O05.06 Tove Lise Nielsen CLIENT-CENTRED IN-HOME OCCUPATIONAL THERAPY IMPROVES OLDER ADULTS' OCCUPATIONAL PERFORMANCE: RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

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Background: To improve home-dwelling older adults' functioning in daily occupations, occupational therapists in Danish municipalities provide in-home rehabilitation. By law, rehabilitation goals should be decided through shared decision-making. At local policy-level, however, the usual practice is in some cases standardized to target problems within self-care and domestic chores only, thus restricting older adults'

occupational choices. This trial aims to evaluate the effect of intensive, in-home client-centred occupational therapy (ICC-OT) with shared decision-making on older adults' occupational performance.

Method: A randomised, assessor-blinded controlled trial among 119 older adults (60+) referred to home care. The control group received the usual practice of home-care, physiotherapy, assistive devices, and up to 3 weeks of standardized in-home rehabilitation when meeting certain criteria. The intervention group received the usual practice of home-care, physiotherapy, and assistive devices when meeting certain criteria, plus 11 weeks of in-home ICC-OT addressing client-chosen occupational goals. Occupational performance was measured on the Canadian Occupational Performance Measure (COPM) at baseline and at 3 and 6 months.

Results: Initial results show that the intervention group improved significantly more on occupational performance after 3 months than the usual-care group: COPM difference 1.26 points, p 0.001.

Conclusion: ICC-OT effectively outperforms usual care in improving older adults' occupational performance. This may benefit individual older adults and support a change in local policies towards offering a broader range of occupational choices in home rehabilitation.

P01.01 Estefano Pinilla TRANSGLUTAMINASES AS PHARMACOLOGICAL TARGETS IN VASCULAR DYSFUNCTION

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Background and hypothesis: Tissue transglutaminase (TG2), a multi-functional and ubiquitously expressed member of the transglutaminase family of enzymes, has been associated with both arterial remodeling in hypertension and increment of vessel stiffness related to ageing. Moreover, high levels of extracellular glucose in diabetes have been shown to upregulate TG2 activity, playing an important role in endothelial dysfunction. Recently, we found that pharmacological inhibition of TG2 leads to vasodilatation through opening of voltage-gated potassium channels in the smooth muscle. Therefore, the hypothesis of my project is that TG2 inhibition will prevent vascular dysfunction in diabetes by activation of potassium channels and improved endothelium-dependent vasodilatation.

Methods: Diabetic (db/db) and control mice are used for: isometric and isobaric myograph experiments to assess microvascular function, simultaneous nitric oxide and tension measurements, patch-clamp studies in isolated cells and 'in situ' to register potassium currents, measurements of blood pressure and vessel stiffness in vivo using

doppler imaging, immunoblotting and quantitative RT-PCR to assess the differential expression of TG2.

Preliminary results: In small mesenteric arteries of Wistar rats mounted in isometric myographs, the TG2 specific inhibitor LDN-27219 induced an endothelium-dependent vasodilation sensitive to the inhibition of endothelial NO synthase (eNOS). Furthermore, LDN-27219 potentiates both the acetylcholine-mediated vasodilatation and the smooth muscle sensibility to NO. This 'in vitro' potentiation seems to increase with the age of the animal.

- P01.02 Patricia Alves da Mota THE NEURAL SIGNATURES OF CREATIVITY IN JAZZ IMPROVISATION  
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Current literature in music improvisation includes nine neuroimaging studies, from which only two were conducted on a population of jazz musicians. The lack of fundamental convergence across these studies is far from optimal for a comprehensive understanding of the neural mechanisms underlying musical improvisation. In this study, we aim to explore music improvisation in jazz by combining different already validated experimental designs in order to characterise the neural signatures of memory retrieval, improvisation modes, reading score and free improvisation.

We hypothesise that the neural mechanisms underlying the unique capabilities of jazz musicians to improvise are shaped by distinct and robust structural and functional neural signatures, involving systems linked to memory, language, emotion and motor, which are fundamentally connected to creative processing.

Ultimately, the combination of structural and functional neuroimaging data with connectomics and whole-brain computational models of continuous listening to music will help to shed new light into the neural mechanisms underlying jazz improvisation.

- P01.03 Signe Toft Andersen AGREEMENT BETWEEN CLINICAL SCORES OF DIABETIC NEUROPATHY AND NERVE CONDUCTION STUDIES IN ELDERLY TYPE 2 DIABETIC PATIENTS - A CROSS SECTIONAL STUDY

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Background: To determine the agreement between clinical scores of diabetic polyneuropathy (DN); Michigan Neuropathy Screening Instrument (MNSI) and the Toronto Clinical Scoring System (TCSS), and nerve conduction studies (NCS) in elderly patients with type 2 diabetes. Methods: In total, 169 participants underwent NCS and examination using MNSI and TCSS. MNSI was considered abnormal if either the questionnaire score was  $\geq 4$  or/and the examination score was  $\geq 2.5$ . TCSS was considered abnormal with a score of  $\geq 5$ . Prevalence of DN and joint prevalence of DN from MNSI, TCSS and NCS was calculated. Kappa coefficients of the agreements were computed. For MNSI and TCSS, the sensitivity, specificity, positive and negative predictive values against NCS were calculated. Odds ratios for DN from MNSI and TCSS were computed.

Results: In total, 108 (64%) men, mean age 70 years (SD:6.5), mean diabetes duration 12 years (SD:1.9). In total, 44 (26%) had DN based on NCS. MNSI and TCSS were abnormal in 33 (20%) and 39 (23%) respectively. The kappa coefficient of MNSI against NCS was 0.27, odds ratio of 4.3 (CI:1.9;9.5) for DN when MNSI positive. Sensitivity 39% (CI:24;55), specificity 87% (CI:80;93), positive predictive value 52% (CI:34;69) and a negative predictive value 80% (CI:72;87). The kappa coefficient of TCSS against NCS was 0.23, the odds ratio for DN was 2.9 (CI:1.4;6.3). Sensitivity 39% (CI:24;55), specificity 82% (CI:75;89), positive predictive value 44% (CI:28;60) and negative predictive value 79% (CI:71;86). The kappa coefficient of MNSI against TCSS was 0.60.

Conclusion: There was only a moderate agreement between MNSI, TCSS and NCS. Yet, MNSI and TCSS seem useful for ruling out DN in the elderly. The agreement between MNSI and TCSS was good.

P01.04 Line Stensig  
Lynggaard

NOR-GRASPALL 2008: SINGLE-ARM PHARMACOKINETIC/ PHARMACODYNAMIC AND SAFETY STUDY OF ERYASPASE (GRASPA®) FOR PATIENTS WITH HYPERSENSITIVITY TO PEG-ASPARAGINASE, DIAGNOSED WITH PH(-) ACUTE LYMPHOBLASTIC LEUKEMIA

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Pegylated-asparaginase (PEG-ASP) is a very important part of the treatment of childhood acute lymphoblastic leukaemia (ALL). Unfortunately, 13% of patients develops allergy, and further treatment is impossible. Furthermore, 6% of patients have developed antibodies (silent inactivation) and have no effect of the PEG-ASP treatment. Truncated asparaginase therapy is associated with inferior event-free survival outcomes, in particular CNS relapse. Eryaspase is a new formulation of asparaginase encapsulated in erythrocytes. The

erythrocyte membrane protects asparaginase against fast degradation and elimination processes. The encapsulation eliminates the direct

somatic contact, and it is hypothesized that this provides the potential to prolong the activity of the enzyme and reduce toxicities.

The aim of this study is to evaluate the biological activity, tolerability and toxicity of eryaspase given in combination with multi-agent chemotherapy according to the NOPHO ALL2008 protocol in patients with allergic reactions or silent inactivation. Furthermore, we will evaluate how eryaspase affects the level of maintenance metabolites from the maintenance therapy with 6-mercaptopurine.

This is a prospective single-arm, multicenter, multinational study. In total, 30 patients (aged 1-45 years) will be included in the project; they will receive 1-7 doses of eryaspase, which will replace the remaining PEG-ASP doses. All samples will be collected prospectively, but the analyses will be done retrospectively. Matched controls for comparison will be found.

The NOR-GRASPALL 2008 study is expected to start inclusion in January 2017.

P01.05 Jens Hartlev

DONOR AND RECIPIENT SITE PAIN AFTER LATERAL ALVEOLAR BONE AUGMENTATION

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Background: Previous studies have indicated that lateral alveolar ridge augmentation by an autogenous bone graft harvested from an intraoral donor site may be associated with severe patient discomfort. Clinical studies in other fields of surgery have included the use of a platelet concentrate during the surgical intervention to reduce post-operative pain.

Aim: The purpose of this study was to evaluate the postoperative pain at the recipient and donor site after lateral alveolar ridge augmentation by using an autogenous mandibular ramus bone graft covered by 1) a platelet rich fibrin (PRF) membrane (test group) or 2) a resorbable collagen barrier membrane (control group).

Materials and methods: A total of 27 consecutively treated patients (12 females, 15 males) were included at random (block randomization) within the test (n=14) and the control (n=13) group. After the bone block augmentation, all patients were handed a systematic questionnaire after thorough information and instruction. The questionnaire included pain evaluation at the donor and recipient site 1-8 hours and 1-7 days postoperatively. Furthermore, the patients were asked if they would recommend a friend to undergo the same treatment. Patients could

choose between the answers "yes", "do not know" and "no". Subjective neurosensory disturbances were also registered.

Results and conclusions: Data collection is ongoing. Preliminary results and conclusions will be presented.

P01.06 Kathrine Hald

#### LONG-TERM FOLLOW-UP ON A SOCIALLY DIFFERENTIATED CARDIAC REHABILITATION INTERVENTION

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Background: Cardiac rehabilitation has a positive influence on cardiovascular risk factors. It reduces disabilities, increases the quality of life and lowers the likelihood of re-infarctions and mortality. However, socially vulnerable patients do not achieve the same effect. A research project performed at Aarhus University Hospital from 2000 to 2004 offered an expanded rehabilitation intervention to socially vulnerable patients. One-year follow-up showed significant improvements concerning medicine compliance, lipid profile, blood pressure and BMI when compared to socially vulnerable patients who received standard rehabilitation.

Aim: The aim of the PhD project is to perform a long-term follow-up and examine the effect of the socially differentiated intervention. The outcomes that we wish to evaluate are the patients' adherence to secondary prevention, their use of health and social services, and their morbidity and mortality at two, five, seven and ten years after the intervention.

Methods: The PhD project uses quantitative register-based data and quantitative data from questionnaires.

Expected results: The hypothesis is that socially vulnerable patients who received the expanded rehabilitation intervention will show significant improvements concerning the outcomes of interest when compared to socially vulnerable patients who received standard cardiac rehabilitation.

Perspectives: It is estimated that the PhD project can support the development of new clinical guidelines and disease management programs regarding cardiac rehabilitation.

- P01.07 Charlotte Slagelse Jensen-Haarup
- USE OF ANGIOTENSIN-CONVERTING ENZYME INHIBITORS AND ANGIOTENSIN-RECEPTOR BLOCKERS AND THE RISK OF ACUTE KIDNEY INJURY AFTER COLORECTAL CANCER SURGERY: A POPULATION-BASED COHORT STUDY
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- Background and aim: Angiotensin-converting enzyme inhibitors (ACE-Is) and angiotensin-receptor blockers (ARBs) are commonly used drugs with potential nephrotoxicity. Acute kidney injury (AKI), defined as a sudden decline in the kidneys excretory function, is a common post-surgical complication. We examined whether preadmission use of ACE-Is and/or ARBs impacts the risk of acute kidney injury (AKI) after colorectal cancer (CRC) surgery.
- Methods: We identified all patients undergoing surgery for CRC from 2005 to 2011 in Northern Denmark using the Danish Colorectal Cancer Group Database. Patients were characterized as current users, former users and non-users of ACE-Is and/or ARBs. We identified AKI, using creatinine within 7 days after surgery. We computed cumulative AKI risk (95% CI) for the 3 groups of patients, and included death as a competing risk. Hazard ratios (HRs) were computed using Cox proportional hazards regression analysis, controlling for potential confounders and stratified by subgroups.
- Results: In total, 6,755 patients were included; 20.3% were ACE-Is and/or ARBs users, 6.1% were former users and 73.6% were non-users. The overall cumulative 7-day post-surgical risk of AKI was 28.5 % (26.1-30.9 %) for current users, 26.0 % (21.9-30.3 %) for former users, and 19.2 % (18.1-20.3 %) for non-users. The adjusted HRs were 1.10 (0.95-1.28) for current users and 1.02 (0.82-1.26) for former users, compared with never users. The stratified analyses revealed similar estimates across subgroups.
- Conclusion: One in five CRC surgery patients in the study is under treatment with ACE/ARB. The increased risk of AKI observed in users of ACE-Is and/or ARBs could be partly explained by confounding.
- P01.08 Bo Langhoff Hønge
- THE CHALLENGE OF DISCRIMINATION BETWEEN HIV-1, HIV-2 AND HIV-1/2 DUAL INFECTIONS
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Background: It is important to discriminate between HIV types, as HIV-2 is intrinsically resistant to non-nucleoside reverse transcriptase inhibitors (NNRTIs). However, correct discrimination may be difficult because of cross-reacting antibodies and because many HIV-2 infected patients do not have detectable HIV-2 RNA plasma levels.

Methods: Samples from ART naïve HIV infected patients from the Bissau HIV Cohort in Guinea-Bissau were selected for the study. The two tests INNO-LIA HIV-1/2 Score and ImmunoComb HIV 12 Bispot were performed on all samples. HIV-1 and HIV-2 RNA and DNA were measured using Abbott m2000 system and an in-house method, respectively.

Results: INNO-LIA categorized samples as 122 HIV-1 positive, 69 HIV-2 positive and 48 HIV-1/2 dually positive. According to ImmunoComb, 122 were HIV-1, 49 HIV-2 and 68 HIV-1/2 dually infected. There was disagreement in 22 samples, of which 20 were typed HIV-2 infected by INNO-LIA but HIV-1/2 dually infected by ImmunoComb. None of these 20 samples had detectable HIV-1 RNA or DNA, and 10 (50.0%) had detectable HIV-2 RNA levels. These results are in accordance with the HIV-2 typing called by INNO-LIA but not with dual infection as called by ImmunoComb, as undetectable HIV-1 RNA in untreated dual infected patients is unlikely.

In two other samples discordantly typed HIV-1 and HIV-1/2 dually infected, HIV-1 RNA was detected, whereas HIV-2 RNA was not. Thus, final type determination could not be concluded.

Conclusions: Both assays have been used as gold standards for HIV type discrimination in several studies. However, ImmunoComb overestimated the number of HIV-1/2 in dually infected samples.

P01.09 Helene Mathilde Larsen LONG-TERM BOWEL DYSFUNCTION IN PATIENTS TREATED FOR CANCER IN CECUM AND THE ASCENDING COLON

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Aim: This study investigates the long-term bowel dysfunction after right-

sided hemicolectomy among patients curatively operated for cancer in the cecum and the ascending colon, by comparing right-sided hemicolectomy patients to polypectomy patients.

Method: A questionnaire containing several bowel function scores, including the Bristol stool scale, was sent to all colon cancer patients treated with a right-sided hemicolectomy or local excision between May 2001 and March 2015 (n = 6603). The results from the questionnaire were compared to data on tumour stage and localisation, treatment, and co-morbidity from the National Colorectal Cancer database.

Results: In total, 4104 patients agreed to participate, corresponding to a response rate of 62%. Of those, 507 (15.4%) right-sided hemicolectomy patients had Bristol stool scores of 6 or 7, and thus diarrhoea. In comparison, only 7.7% of the polypectomy patients had diarrhoea (P = 0.001). Analyses of the influence of sex, age, time since surgery, and adjuvant chemotherapy will be presented. The impact of diarrhoea on quality of life will be examined as well.

Conclusion: Right-sided hemicolectomy is associated with diarrhoea. Investigations of the aetiology of the diarrhoea must be initiated along with intervention studies. Thereby, the quality of life in this patient group can be improved.

P01.10 Niels Lyhne  
Christensen

FACTORS RELATING TO EARLY DEATH IN DANISH LUNG CANCER PATIENTS (LCP)

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Introduction: The Danish cancer registries have a high degree of completeness and cover almost all patients, thus allowing for high-quality register-based research.

Methodology: Through two case/control studies (I and II) and one cohort study (III), the aim is to identify factors both clinical, patient-related, and tumor-specific factors, which could be associated with disease relapse and mortality. All studies are retrospective.

Data sources: The Danish Lung Cancer Register, the Danish National Patient Register, Statistics Denmark, and patient medical records.

Study I:

Cases: Stage I LCP who die within one year after diagnosis.

Controls: Stage I LCP, who survive more than one year.

Both groups are treated with curative intent.

Matching criteria: Sex, age, and treatment modality.

Variables tested: Way of diagnosis, smoking, alcohol abuse, co-morbidity

(incl. psychiatric) and adherence to the follow-up program. In patients with relapse or a cancer specific mortality, PET signal ( $SUV_{max}$ ) and lympho-vascular invasion will be tested as predictive variables.

Study II:

Cases: Stage I LCP in good condition, who do not receive treatment with curative intent.

Controls: Age, gender and performance status matched stage I LCP who receive treatment with curative intent.

Variables tested: Co-morbidity, patient choice, socioeconomic status, and region of residence.

Study III: Stage IIIa patients who have undergone curative treatment are included from three centers, where the clinical practice regarding cerebral imaging differs. The aim is to assess differences in incidence of brain metastases development depending on center. Moreover, we will evaluate the follow-up program.

P02.01 Stine Høgsholt DISEASE-SPECIFIC HOSPITALIZATIONS AMONG SURVIVORS OF WILMS TUMOR: A NORDIC POPULATION-BASED COHORT STUDY

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Background and aim: With five-years survival in Wilms tumor exceeding 90%, focus is now increasingly on morbidity and especially late onset diseases. The objective of this study is to investigate the spectrum and frequency of late sequelae in survivors of Wilms tumor.

Methods: This study is part of the Nordic collaboration Adult Life after Childhood Cancer in Scandinavia (ALiCCS). From the cancer registries, we identified all five-year survivors of Wilms tumor. We randomly sampled an age- and sex-matched comparison group from the general population. Study subjects were followed for recurrent disease-specific hospitalizations in the national hospital registries. We computed overall and organ system specific standardized hospitalization rate ratios (RRs).

Results: Our study population included 913 survivors of Wilms tumor of which 17% were older than 40 years at the end of follow-up. Survivors of Wilms tumor had increased rate of disease-specific hospitalizations (RR 1.8). They had an increased rate of hospitalization within all organ systems, e.g. kidney and urinary tract diseases (RR 2.5; 95% confidence interval (CI) 2.1-3.0), cardiovascular disease (RR 2.2; 95% CI 1.7-2.9), and gastrointestinal disease (RR 1.4; 95% CI 1.2-1.7). Among specific disease entities, some of the highest rates were seen for chronic renal failure (RR

46; 95% CI 25-88), cardiomyopathy (RR 19; 95% 8.6-41) and paralytic ileus (RR 27; 95% CI 20-38).

Conclusions: Survivors of Wilms tumor had an increased risk of a wide range of diseases, with the highest risks of disease in organs with close anatomical relation to the kidneys.

P02.02 Ole Adrian Heggli ARE WE DOING THE SAME? A DUAL-EEG TAPPING STUDY

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Humans are highly adept at coordinating movements with one another, an ability that is strikingly apparent when performing music. In order to successfully play music together, we have to mutually predict and adapt to the other's actions on a millisecond timescale. To uncover the mechanisms that facilitate this type of synchronization, we are undertaking a dual-EEG joint finger tapping study. Previous research points to two types of strategies when two participants are tapping together, with the purpose of maintaining a beat and synchronizing to the auditory feedback from the other person or a metronome. In some studies, a leader-follower strategy is reported, where the leader is the least adaptive tapper. Other studies reports mutual adaptation. In this strategy, one can observe the two tappers constantly updating their predictions on a tap-by-tap basis, leading to their intertap interval oscillating in opposite directions for each tap. A previous dual-EEG study was able to categorize leaders by differences in frontal alpha oscillations. In our study, we aim to explore the effect of having a shared predictive model of the interaction. By using polyrhythms we are able to induce different rhythmic context models in a pair, while retaining identical motor output. We hypothesize that the lack of a shared rhythmic context model will impair the predictive nature of coordination, thus leading to a worse interaction in terms of synchronization. In addition, we expect to see higher occurrences of leading/following, rather than mutual adaptation, in the case of a conflicting rhythmic context model.

P02.03 Caroline Mejdahl EPILEPSY SELF-MANAGEMENT BY USE OF PATIENT-REPORTED OUTCOMES AND PATIENT-INITIATED FOLLOW-UP - A QUALITATIVE OBSERVATIONAL STUDY

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Background and aim: A web-based system combining patient-reported outcomes (PROs) and patient-initiated follow-up (PIFU) has recently been implemented at three neurological departments in Central

Denmark Region. Potentially, this system can result in the patients becoming more involved in their own care pathway, by which their self-management may improve. In our study, we aim to explore the patients' experiences of the system and the system's potential to facilitate self-management support.

**Methodology:** We designed this interpretive description study with participant observations, semi-structured interviews and document analysis. We let critical realism constitute the epistemological position. The target group for participation is patients with epilepsy in the neurological departments using the PRO system.

**Preliminary results:** In our preliminary analysis, we found rudiments of PROs and PIFU leading to patient education, patient-centred communication and an additional focus on psychosocial problems. However, the very application of the system in the outpatient clinics and the patients' attitudes seem to be substantial and crucial barriers for the system to facilitate self-management support.

**Conclusion:** The use of patient-reported outcomes and patient-initiated follow-up may support patients' self-management by a) supporting patient education, b) impelling patient-centred communication in the consultations and c) enhancing the focus on psychosocial problems. Yet, applying PROs and PIFU into clinical practice does not automatically involve the patients and support their self-management. We suggest supplementary clinical initiatives to strengthen the patient-involving benefits.

P02.04 Anita Tønder  
Nielsen

SEVERE MENTAL ILLNESS, DIABETES MELLITUS AND RISK OF DIABETIC COMPLICATIONS; CARDIOVASCULAR MORBIDITIES

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**Background:** Individuals with Severe Mental Illness (SMI), including schizophrenia and bipolar disorder, experience two- to three-fold higher mortality rates than the general population, which corresponds to a gap of 15-20 years in life expectancy. Diseases and medical conditions (natural death) is suggested to explain 2/3 of this excess mortality, and suboptimal treatment may be a contributing factor. Individuals with SMI and diabetes mellitus have a three- to four-fold higher risk of death than

the general population, which may be explained by suboptimal treatment of diabetes mellitus. Hence, we aim to examine if individuals with SMI experience suboptimal treatment of diabetes compared to individuals with diabetes mellitus only.

Methods: We will perform a cohort study and use national population-based registers to identify and follow individuals with SMI, diabetes mellitus and examine their level of cardiovascular morbidity. As cardiovascular morbidities are diabetic complications, they will constitute a proxy for suboptimal treatment of diabetes. We will perform survival analysis using Cox Regression and take gender, calendar time and age into account.

Perspectives: We expect the results will show that individuals with SMI and diabetes mellitus will have higher rates of cardiovascular morbidity, and hence more diabetic complications, than individuals with diabetes mellitus only. These results will then reflect that individuals with SMI experience suboptimal treatment of diabetes mellitus and hence explain why individuals with SMI and diabetes mellitus have a three- to four-fold higher risk of death than the general population.

P02.05 Jesper  
Damsgaard

EARLY ADMINISTRATION OF LATENCY REVERSING THERAPY AND BROADLY NEUTRALIZING ANTIBODIES TO LIMIT THE ESTABLISHMENT OF THE HIV-1 RESERVOIR DURING INITIATION OF ANTIRETROVIRAL TREATMENT - A RANDOMIZED CONTROLLED TRIAL

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Background: Antiretroviral therapy (ART) suppresses productive HIV-1 infection, but is not curative. HIV-1 primarily persists as integrated proviral DNA within memory CD4+ T cells. The basis for this latent HIV-1 reservoir is thought to be established during the earliest stages of infection.

The 'kick-and-kill' strategy is one way to attack the HIV-1 reservoir, which involves three steps: 1. Shutting down the virus spread and thus preventing de novo infection (by ART), 2. Activation of HIV-1 expression in latently infected cells and thus unveiling HIV-1 to the immune system (e.g. using latency reversing agents [LRA]), 3. Eliminating the HIV-1 transcribing cells (e.g. using immunotherapy).

Romidepsin, a potent LRA, significantly increases HIV-1 replication. However, the size of the HIV-1 reservoir is not reduced by romidepsin alone, which indicates that additional interventions are needed to effectively kill HIV-1 infected cells. 3BNC117 is one of the most potent broadly neutralizing antibodies (bNAbs) cloned to date. bNAbs accelerate clearance of cell-free virus, induce antibody dependent

cytotoxicity to kill infected cells, and produce immune complexes that activate antigen presenting cells.

Models suggest that interventions aimed at diminishing the HIV-1 reservoir will have the most pronounced effect at ART initiation.

Design: An investigator-initiated open-label randomized controlled international multicenter interventional phase IIa trial (eCLEAR) conducted among ART naïve HIV-1 infected patients randomized 1:1:1:1 to either:

- A) ART
- B) ART + romidepsin
- C) ART + 3BNC117
- D) ART + romidepsin + 3BNC117

Results and conclusion: Trial starts ultimo 2016.

P02.06 Thorkil Anker-Møller

EVIDENCE FOR THE USE OF TRANEXAMIC ACID IN SUBARACHNOID HAEMORRHAGE AND SUBDURAL HAEMORRHAGE - A SYSTEMATIC REVIEW

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Background: Subarachnoid- and subdural haemorrhages have a high mortality rate and leave many of the survivors disabled, despite neuro-surgical intervention. There is a high risk of re-bleeding after the initial haemorrhage, and this is a key detrimental factor. Antifibrinolytic treatment, such as tranexamic acid, has been suggested in an effort to prevent re-bleeding, but there is no international consensus on the use of tranexamic acid, and guidelines vary among countries.

Method: We will perform a systematic review of the evidence for the use of tranexamic acid in patients with subarachnoid- and subdural haemorrhage by searching EMBASE, MEDLINE, Scopus and Web of Science for relevant literature.

Results: Results from the systematic review will be presented.

Conclusion: The review provides a systematic summary of present knowledge and supports further clinical research to clarify the evidence for the use of tranexamic acid in patients with subarachnoid- and subdural haemorrhage.

P02.07 Emil Rindom

EFFECT OF LOW-INTENSITY BLOOD FLOW RESTRICTED EXERCISE ON PROTECTION OF MUSCLE HEALTH AND VITAL ORGANS IN HEALTHY SUBJECTS AND PATIENTS WITH AMI

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Pharmaceutical intervention in patients with chronic ischemic heart failure as a consequence of acute myocardial infarction (AMI) is associated with immense socioeconomic consequences and numerous side effects. Therefore, alternative strategies of treatment are warranted. In this regard, physical activity constitutes a potent mean to attenuate disease-related muscle wasting and protecting cardiac function. To achieve maximum effects, physical activity must be practiced at a high intensity, which conflicts with the tolerability in many heart patients. Recent findings suggest that low-intensity blood flow restricted exercise (BFRE) or occlusion per se (remote ischemic preconditioning (RIC)), can constitute a mechanically gentle, yet potent means to; (1) attenuate disease related muscle wasting and; (2) exert protective effects against heart failure. Therefore, BFRE and RIC seem to possess great potential for patients characterized with chronic ischemic heart failure and disease-related muscle wasting, but this has yet to be investigated.

To assess effects of BFRE vs. traditional resistance exercise on acute anabolic signalling and skeletal muscle hypertrophy, muscle biopsies will be sampled from healthy subjects and heart failure patients in a randomized controlled study. This allows for evaluation of mechanosensitive intramyocellular signalling responses, highlighting differences between exercise modes. Furthermore, to assess cardio-protective effects of RIC vs. BFRE vs. traditional resistance exercise, blood samples will be drawn and used in a Langendorff rodent heart model during simulated AMI, which allows for comparison of exercise modes on infarction size following AMI.

P02.08 Rajath Pillai

PAIN, UNPLEASANTNESS AND QUALITY OF LIFE RELATED TO OROFACIAL NERVE DAMAGE

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Background: Damage to the Trigeminal nerve (TN) may result in chronic pain and unpleasant phenomena. This pain condition can be debilitating and may adversely affect a person's quality of life.

Aim: 1) To evaluate the sensory function in patients with TN damage with and without pain and in healthy participants with experimentally

modulated sensitivity; 2) To improve the characterization of perceived pain, primary and secondary unpleasantness related to experimental and clinical changes in sensory function; 3) To investigate the association between parameters of sensory function, pain and unpleasantness scores and measures of psychosocial function as well as oral health

related quality of life (OHRqoL) in TN damage patients and in healthy participants.

Methods: All participants will undergo quantitative sensory testing for assessment of sensory function, pain-specific blink reflex for TN transmission, and questionnaires for pain, unpleasantness and OHRqoL. In 20 healthy adult participants, these tests will be performed before and after experimental modulation of sensitivity on their cheek. In 40 TN damage patients and 40 age- and gender-matched controls, these tests

will be similarly performed and data analysed within and between the groups.

Perspectives: We expect that the findings from this study will provide new knowledge on mechanisms behind neuropathic pain and unpleasantness in patients with damage to the TN. Also, the understanding of the impact on such patients' psychosocial status and quality of life will be improved for the benefit of future medico-legal evaluations.

P02.09 Ninna Rasmussen MONOSOMAL AND COMPLEX KARYOTYPE IN CHILDHOOD AML

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No studies have up until today investigated occurrence, genetic characteristics and prognostic impact of monosomal and complex karyotype in children with acute myeloid leukemia (AML) at diagnosis. Our aim was to study these genetic variations on children in a large unselected cohort. Monosomal karyotype was defined as two or more distinct autosomal chromosome monosomies (excluding loss of X and Y) or one single autosomal monosomy in association with at least one structural chromosomal aberration and in the absence of core-binding factor translocation. Complex karyotype was defined as at least three unrelated cytogenetic aberrations in the absence of recurrent genetic abnormalities of AML as defined by the WHO. From the Nordic Society for Pediatric Hematology and Oncology (NOPHO) database, 800 patients with complete karyotype were included. Of these, 91 (11%) had a complex karyotype with no monosomal karyotype and 41 (5%) patients had monosomal karyotype.

Unadjusted 5-year overall survival showed no significant differences on monosomal and complex karyotype in comparison with patients presenting neither monosomal nor complex karyotype (non-complex, non-monosomal vs complex, non-monosomal, 0.66 vs 0.58, p 0.11; non-complex, non-monosomal vs monosomal, 0.66 vs 0.64, p 0.22; complex, non-monosomal vs monosomal, 0.58 vs 0.64, p 0.68). Monosomal karyotype indicated a lower unadjusted 5-year event-free survival compared to patients without either monosomal or complex karyotype (0.35 vs 0.48, p 0.04). Especially refractory disease was associated with monosomal karyotype. Analyses are still ongoing, and adjusted results have not been fully evaluated yet.

P02.10 Peter Andersen OPEN VERSUS LAPAROSCOPIC RECTAL CANCER RESECTION AND RISK OF SUBSEQUENT INCISIONAL HERNIA REPAIR AND PARACOLOSTOMY HERNIA REPAIR: A NATIONWIDE POPULATION-BASED COHORT STUDY

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Objective: To investigate the risk of incisional hernia repair (IHR) and paracolostomy hernia repair (PHR) following open and laparoscopic rectal cancer resection with curative intent.

Background: IHR and PHR following open and laparoscopic rectal cancer resection have only been sparingly evaluated.

Methods: Patients who underwent rectal cancer resection were identified in the database of the Danish Colorectal Cancer Group. To identify IHR and PHR following rectal cancer resection, we linked data to the Danish Ventral Hernia Database (DVHD). The absolute risk of IHR and PHR was estimated as cumulative incidence proportions, treating death as competing risk. We used Cox proportional-hazard regression analysis with multivariable adjustment to compute hazard ratios (HR) comparing open and laparoscopic approach.

Results: The 5-year risk of IHR was 4.1% (95% CI: 3.5%-4.9%) among patients undergoing open resection (n=3,090) and 3.2% (95%CI: 2.5%-3.9%) among those undergoing laparoscopic resection (n=3,099). Laparoscopic rectal resection was not associated with lower risk of IHR (adjusted HR=0.94, 95% CI: 0.67-1.31, P = 0.709). A total of 2,577 patients had a colostomy at rectal cancer resection, and the 5-year risk of PHR was 2.1% (95%CI: 1.4%-3.0%) after open surgery compared with 6.7% (95%CI: 5.1%-8.5%) after laparoscopic surgery. Laparoscopic surgery was

associated with increased risk of PHR (adjusted HR= 2.56, 95%CI: 1.53-4.29, P < 0.001).

Conclusion: We observed no association between surgical approach of rectal cancer resection and subsequent IHR. Laparoscopic surgery was associated with increased risk of PHR.

P03.01 Nina Jensen

#### BOWEL MORBIDITY AFTER RADIOCHEMOTHERAPY IN CERVICAL CANCER: PHYSICIAN- AND PATIENT-REPORTED OUTCOME FROM THE EMBRACE STUDY

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Purpose: Provide a descriptive overview of the prospectively collected physician (CTCAE) and patient reported outcome (PRO) on bowel morbidity within the multicenter EMBRACE study, and to jointly evaluate the development symptoms.

Material: The analysis was based on 1419 patients enrolled from 2008 to 2015. Treatment consisted of radiochemotherapy with prescribed doses of 45-50 Gy in 1.8-2.0 Gy fractions. Morbidity was assessed at baseline, every 3 months (1<sup>st</sup> year), every 6 months (2<sup>nd</sup> and 3<sup>rd</sup> year) and yearly thereafter. Bowel endpoints evaluated were diarrhea, flatulence, incontinence and stenosis/fistulas grade 0-5. The related PRO was reported as; "a little", "quite a bit" and "very much".

Results: Baseline morbidity and follow-up information was available for 1176 patients (PRO 942), median follow-up of 27 months. The prevalence rates at 5 years for diarrhea were 24% for G<sub>≥</sub>1 and 4% for G<sub>≥</sub>2 (CTCAE). According to PRO, any patient-reported diarrhea was 35% and 3% for "very much". Both reached a plateau at a certain level. Incontinence occurred in 9% as G<sub>≥</sub>1 and 2% as G<sub>≥</sub>2. For PRO, any patient-reported difficulty in controlling bowel was 29% and 3% for "very much", both with increasing prevalence. Bowel stenosis and fistulas G<sub>≥</sub>2 were present in 16 and 6 patients, respectively.

Conclusion: Within the EMBRACE study, bowel morbidity is overall frequently reported. However, severe morbidity is limited. The results indicate that patients report higher burden of bowel symptoms. However, no direct correlation is possible between both assessment methods. In

the future, a practical way of interpreting the complementary information from PRO regarding morbidity will be investigated.

P03.02 Suzi Ross

### PREDICTING THE AUDITORY CONSEQUENCES OF ACTION IN EXPERT MUSICIANS

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The extensive expertise musicians gain in pairing goal-directed actions with specific auditory consequences over a lifetime of practice on their instrument make them the ideal model for studying coupling between perception and action. The aim of this study is to use electroencephalography to investigate prediction mechanisms in expert musicians. We will compare event-related potential (ERP) responses to manipulated auditory feedback during piano performance to determine whether musicians can accurately predict the pitch of the sounds they produce. Expert pianists will play short sequences on the piano and auditory feedback will either be correct, or manipulated to sound at an incorrect pitch. ERP responses and implicit behavioural measures (key press speed and onset times) will be recorded. We expect increased ERP attenuation for correct versus manipulated pitches. We additionally expect key press speed and onset to be significantly slower in response to manipulated versus correct pitches. Expected results would indicate that musicians can accurately predict the pitch resulting from well-learned goal-directed actions.

P03.03 Mette Schou Mikkelsen

### HYPERTHERM INTRAPERITONEAL CHEMOTHERAPY (HIPEC) USED IN TREATMENT OF ADVANCED OVARIAN CANCER

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Introduction: Five-year survival of advanced ovarian cancer with peritoneal carcinomatosis is around 14% - 23%. The mainstay of ovarian cancer treatment is surgery combined with adjuvant systemic chemotherapy, but even though no visible disease is left behind after surgery, risk of recurrence is high. Hypertherm intraperitoneal chemotherapy (HIPEC) consists of intra-operative perfusion of the abdominal cavity with a heated solution with a cytotoxic agent. Addition of HIPEC to surgery improves survival in some peritoneal surface malignancies.

Aims:

- 1) To evaluate feasibility and safety of surgery combined with HIPEC in treatment of advanced ovarian cancer
- 2) To determine the pharmacokinetic profile of carboplatin used for HIPEC in dose 800 mg/m<sup>2</sup>, including minimal required perfusion time.

Materials and methods:

- 1) In a pilot study, 15 patients with advanced ovarian cancer will be offered HIPEC with carboplatin in 90 minutes as supplement to surgery. Endpoints are haematological toxicity, postoperative complications, and 30-day mortality.
- 2) The pharmacokinetic profile of carboplatin used for HIPEC in dose 800 mg/m<sup>2</sup> will be evaluated by use of repetitive measurements of carboplatin concentrations over time in plasma and perfusate (the heated chemosolution) in 20 patients. The area under plasma and perfusate concentration time curve of carboplatin will be measured as well as the elimination half-life of carboplatin in perfusate.

Perspectives: After examining feasibility, safety and pharmacokinetics of carboplatin used for HIPEC, we intend to evaluate the benefit of HIPEC in advanced ovarian cancer in a randomized design.

P03.04 Sara Bønløkke  
Simonsen

HPV AND BREAST CANCER - IS THERE AN AETIOLOGICAL CONNECTION?

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Objectives: Breast cancer (BC) is the most common cancer among women, accounting for 1,700,000 cases and 521,900 deaths worldwide every year. A previous study has found an increased risk of BC among women with prior cervical dysplasia. By including only severe cervical neoplasms, this study aimed to describe the possible difference in the prevalence of human papillomavirus (HPV) in BC tissue from women with and without prior cervical neoplasia.

Methods: This case control study identified 200 women diagnosed with BC (1998-2012) at Aarhus University Hospital or Copenhagen University Hospital Herlev, both in Denmark. Cases were 100 women with cervical intraepithelial neoplasia grade 3 or worse prior to their BC diagnosis. Controls were 100 women without prior cervical dysplasia and with two recent cervical smears negative for dysplasia. The participating

pathology departments performed HPV testing and genotyping of breast and cervical tissue using the SPF10 PCR-DEIA-LiPA25 (DDL Diagnostic Laboratory, The Netherlands) and a Taqman based in-house real-time PCR.

Results: Analysis is ongoing. Results will be revealed at PhD Day 2017.

Conclusion: Knowledge of an association between HPV and BC may pave the way for preventive strategies. Possible areas of future research include whether a prevalence of HPV corresponds to causality between HPV and BC and how HPV is transmitted from the anogenital region to the breast. If causality is established, we would expect a decrease in BC incidence following the implementation of HPV vaccination.

Furthermore, current recommendations on HPV vaccination may be extended to also include women previously treated for HPV-related diseases.

P03.05 Rasmus Wulff

ADDITION OF PERINEURAL DEXAMETHASONE TO BUPIVACAINE-EPINEPHRINE SCIATIC NERVE BLOCK FOR POSTOPERATIVE ANALGESIA AFTER MAJOR FOOT AND ANKLE SURGERY: A RANDOMISED, CONTROLLED, DOUBLE-BLIND STUDY

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Sciatic nerve block (SCb) along with saphenous nerve block (SNb) provides effective analgesia after major foot surgery. Perineural local anaesthetics (LA) with added dexamethasone (DEX) consistently prolongs block duration for other types of nerve blockade. However, the effect on duration by addition of DEX to LA for popliteal SCb needs further investigation. We estimated postoperative duration of analgesia in patients undergoing major foot surgery randomized to popliteal SCb with either DEX or saline (SAL) added to LA.

Methods: In total, 56 patients scheduled for surgery had preoperative SNb and were randomly assigned to a SCb of 18 mL 0.5% bupivacaine with 1:200.000 epinephrine added either 2 mL of 0.4% DEX (intervention) or 2 mL 0.9% SAL (controls). Primary outcome was time (minutes) until return of sensation and motor function.

Results: Mean time until return of normal sensory and motor functions was 1557.4 ± 349.3 min vs. 945.4 ± 214.1 min in the DEX group and SAL groups, respectively (p<0.0001). Time until first opioid request (2060 ±

669.2 min vs.  $897 \pm 386.5$  minutes,  $p < 0.001$ ) as well as total opioid (oral morphine) administered 0-48 hours ( $57.0 \pm 31.8$  mg vs.  $27.3 \pm 28.5$  mg,  $p < 0.005$ ) differed significantly between the two groups. All components of the primary endpoint (time until first sensation, first movement, full sensation and full movement) differed significantly between the two groups. Pain-free sleep during the first night was significantly more frequent in the DEX group.

Conclusions: Addition of DEX to 0.5% Bupivacaine-Epinephrine significantly prolongs duration of SCb as well as reduces and postpones opioid consumption in patients scheduled for major foot surgery.

P03.06 Charlotte Stephansen

ELECTRO-CRT - LEFT VENTRICULAR LEAD IMPLANT AND OPTIMIZATION GUIDED BY ELECTROCARDIOGRAPHY IN CARDIAC RESYNCHRONIZATION THERAPY: A DOUBLE-BLINDED, RANDOMIZED, CONTROLLED, CLINICAL TRIAL

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Background: Cardiac resynchronization therapy (CRT) is an established treatment in heart failure patients with a QRS-width  $> 120$  ms in whom a biventricular pacemaker is implanted to achieve faster contraction of the myocardium. Despite convincing effect of CRT, 30-40% of patients do not benefit from the treatment. A potentially correctable cause for non-

response to CRT is non-optimal left ventricular (LV) lead positioning in myocardial scar tissue with impaired electrical activation.

Aim: To investigate if excess increase in left ventricular ejection fraction (LVEF) can be achieved by implantation of the LV lead guided by electrophysiology as compared with implantation guided by imaging.

Methods: In total, 122 patients will be enrolled in this double-blinded, randomized clinical trial. Echocardiography is performed to assess LVEF. The extent of myocardial scar tissue is determined by myocardial scintigraphy, and venous anatomy is assessed by cardiac CT. The patients are randomly assigned to either

- Placement of the LV lead guided by cardiac CT and electrophysiology during implantation to identify the segment of the myocardium with the latest electrical activation followed by individual pacemaker programming (intervention group) or

- Placement of the LV lead guided by three imaging modalities: echocardiography (to identify the latest mechanical activation), cardiac CT and myocardial scintigraphy (to avoid scar tissue) (control group).

Echocardiography and myocardial scintigraphy are repeated after 6

months to assess changes in LVEF (primary endpoint) and myocardial perfusion.

We expect an increase in LVEF of 12% in the intervention group and an increase of 8% in the control group.

P03.07 Anne Bo

EARLY ONSET TYPE 2 DIABETES. CLINICAL CHARACTERISTICS OF NEWLY DIAGNOSED TYPE 2 DIABETES PATIENTS AGED UNDER AND ABOVE 45 YEARS: RESULTS FROM THE DD2 STUDY, DENMARK

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Background: The incidence of type 2 diabetes (T2D) in young adults is increasing. Early onset (EO) T2D patients have a high risk of complications. This is due to a long disease duration and may be accelerated by a high prevalence of cardiovascular (CV) risk factors. Gaps in the knowledge about disease profiles of EO patients could lead to delayed and deficient health care and prevention.

Aim: To compare clinical characteristics, health behaviour, complications, and treatment between newly diagnosed EO T2D

patients ( $\leq$  45 years at diagnosis) and later onset (LO) patients ( $>$ 45 years).

Methods: A cross-sectional study of 4,853 newly diagnosed T2D patients enrolled between 2010 and 2014 in the DD2-cohort (Danish Centre for Strategic Research in Type 2 Diabetes). Prevalence ratios with 95% confidence intervals were calculated using Poisson-regression analysis.

Results: EO (n=490, 10.1%) patients had a high prevalence of several CV risk factors. When comparing EO with LO patients, EO patients had a higher prevalence of poor glycemic control, obesity, dyslipidemia, and hospital diagnosed retinopathy. Use of insulin was more prevalent among EO than LO patients. Use of antihypertensive, hypolipidemic, and anticoagulant medication was less frequent among EO than LO patients.

Conclusion: Newly diagnosed EO patients had a poorer glycemic control and higher prevalence of CV risk factors than LO patients. T2D in young age is a growing public health problem, and specific attention is needed to target this young and vulnerable patient group.

P03.08 Casper Kruse DIAGNOSTIC VALIDITY OF PERIAPICAL RADIOGRAPHS AND CONE BEAM CT IN RELATION TO TEETH ASSESSED AS FAILURES SIX YEARS AFTER SURGICAL ENDODONTIC RETREATMENT: A HISTOLOGICAL STUDY

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Introduction: Traditionally, healing after surgical endodontic retreatment (SER) is assessed on 2D periapical radiographs (PR). During recent years, the use of 3D Cone Beam CT (CBCT) has increased within dentistry. In general, CBCT detects more periapical lesions, but basic research on the true status of these lesions is still missing.

Aim: Assessment of diagnostic validity of PR and CBCT in relation to unhealed cases after SER using histology as reference.

Methods: Patient records from 149 patients (165 teeth) receiving SER in 2004-10 were screened. Of these, 41 patients (46 teeth) were excluded from recall due to death, tooth loss or re-surgery. In total, 108 patients (119 teeth) were recalled for clinical examination, PR and CBCT. Patients lost after recall were 18 (19 teeth) refusing participation and 16 (17 teeth) not responding to the invitation. Seventy-four patients (83 teeth) participated in the follow-up examination. Three observers assessed clinical and radiographic status as successful or not. A new SER was offered to all unsuccessful cases with an expected favourable prognosis for tooth survival both regarding periapical health and clinical function; 21 persons (21 teeth) of which 19 patients (19 teeth) accepted. During the new surgery, biopsy was performed and histopathology used for diagnosis.

Results: Histopathologic diagnosis revealed that 42% (teeth=8) had no inflammation, 16% (teeth=3) had light inflammation, and 42% (teeth=8) had moderate to intense inflammation.

Conclusion: Of the retreated teeth, 42% had no periapical inflammatory lesion and hence no benefit from the new SER procedure.

P03.09 Kasper Bonnesen PREHOSPITAL TRIAGE OF PATIENTS DIAGNOSED WITH PERFORATED PEPTIC ULCER AND PEPTIC ULCER BLEEDING

*K. Bonnesen*

Research & Development: Prehospital Emergency Medical Services, Central Denmark Region

Introduction: Perforated peptic ulcer (PPU) and peptic ulcer bleeding (PUB) are serious conditions associated with high mortality. All prehospital 1-1-2 calls are triaged by dispatch personnel according to five levels of emergency (A-E). We hypothesized that 1-1-2 calls from patients later diagnosed with PPU and PUB are undertriaged compared to other conditions, such as respiratory failure, stroke, cardiac chest pain, cardiac arrest and trauma.

Materials and methods: 1-1-2 calls in Central Denmark Region from 1 October 2011 to 31 December 2015 (n≈76.000) are examined. Data are merged with in-hospital information on diagnosis and Charlson Comorbidity Index scores from the Danish National Patient Register. Vital status is obtained from the Danish Civil Registration System. PPU and PUB are defined according to the Danish Clinical Register of Emergency Surgery.

Preliminary results: Compared to patients with PPU and PUB, the odds ratios (OR) of receiving the highest level of response (i.e. A-response) were as follows: respiratory failure: 1.24 (p=0.08); stroke: 3.60 (p=0.001); cardiac chest pain: 7.27 (p=0.001); cardiac arrest: 7.19 (p=0.001) and trauma: 0.92 (p=0.52).

Discussion and conclusion: Patients with PPU and PUB were less likely to receive an A-response compared to the other five diagnoses mentioned above. The 30-day mortality of PPU, PUB and these diagnoses will be explored in a time-to-event analysis adjusting for relevant confounders, such as age and comorbidity. This will reveal whether patients with PPU and PUB are undertriaged at the level of dispatch.

P03.10 Jesper  
Falkesgaard  
Højten

THE BROAD ROLE OF ANTI-IL-1R3 MONOCLONAL ANTIBODIES FOR  
TREATING CANCER AND IL-1 FAMILY-MEDIATED INFLAMMATION

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Cancellation

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IL-1R3 is the co-receptor required for signaling of IL-1a, IL-1b, IL-33 and IL-36a, b and y. The naturally occurring IL-1 receptor antagonist (anakinra) is used to block IL-1b and IL-1a, and clinical trials have demonstrated a reduction in progression to multiple myeloma and increased overall survival in stage IV pancreatic cancer using anakinra. However, blocking IL-1R3 would reduce not only IL-1b and IL-1a but also IL-33 and IL-36a, b and y.

In the present studies, monoclonal humanized anti-IL-1R3 antibodies were studied in mixed leukocyte reactions (MLR), in peripheral mononuclear cells (PBMC) stimulated with LPS, heat-killed *Candida albicans* or anti-CD3/antiCD28 as well as in THP-1 cells, an AML-derived cell line.

Collectively, these studies indicate that antibody blockade of IL-1R3 is effective in reducing cytokines from primary cells using in-vitro models of organ rejection, infection and immunostimulation. In THP-1 cells, the reduction in inflammasome-dependent IL-1b suggests that anti-IL-1R3 can be used to treat acute myeloid leukemia or progression to multiple myeloma. Since anti-IL-1R3 inhibits the signaling through IL-1R1, both IL-1a and IL-1b are targeted by this antibody, thus suggesting a future role for this anti-body in not only AML, but also in other cancer types dominated by IL-1 mediated inflammation, such as metastatic colorectal and pancreatic cancer.

P04.01 Claus Kjær  
Pedersen

#### DIAGNOSES AND MORTALITY IN EMS-CALLERS SUFFERING CHEST PAIN

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Background: Chest pain might indicate life-threatening conditions, e.g. acute coronary syndrome (ACS) and acute myocardial infarction (AMI), but also a range of other low-risk conditions. In Denmark, ambulance dispatch is criteria-based. The aim of this study was to investigate the proportion of patients assigned the dispatch criteria "Chest pain - suspected heart disease" subsequently diagnosed with ACS or AMI and the associated mortality.

Method: Population-based follow-up study of patients calling 112 in the Central Denmark Region from 1 October 2011 to 31 December 2014. Diagnoses according to the 10th version of the International Classification of Disease (ICD-10) were retrieved from the Danish National Patient Registry. Vital status from the Danish Civil Registration System was retrieved using a censor date of 26 November 2015. Long-term mortality was compared using Cox proportional hazards regression.

Results: Of the total 75,696 112-calls, 8,555 patients suffered from chest pain. ACS was confirmed in 11% (n=949), including AMI in 8% (n=700). The 30-day mortality was 1.7% (95% CI: 1.4 - 2.0) in patients not diagnosed with ACS and 2.2% (95% CI: 1.5 - 3.4) in patients diagnosed with ACS. Long-term mortality was higher in patients diagnosed with ACS with a HR of 1.24 (95% CI: 1.04 - 1.5) compared to patients not diagnosed with ACS.

Conclusion: In patients calling 112 due to chest pain, only 11% was diagnosed with ACS and 8% with AMI. Mortality in these patients is slightly higher when a diagnosis of ACS is confirmed.

- P04.02 Katrine Munk Begtrup
- DOES RADIOTHERAPY AFFECT COAGULATION?
- K.M. Begtrup<sup>1</sup>, J.A. Højbjerg<sup>1</sup>, B. Offersen<sup>2</sup>, A.M. Hvas<sup>1</sup>*
- Cancellation
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- Background: Cancer is associated with an increased risk of thromboembolic disease, and the risk is further increased by chemotherapy. Thromboembolic disease adds substantially to morbidity and mortality in cancer patients. Yet, only sparse knowledge exists about the influence of radiotherapy on coagulation and the risk of thromboembolic disease.
- Aim: To investigate coagulation during radiotherapy subsequent to local excision and chemotherapy in breast cancer patients with lymph node metastasis.
- Methods: In total, 40 women receiving adjuvant radiation therapy will be included. They will receive either 50 Gy administered by 25 radiation therapies or 40 Gy administered by 15 radiation therapies. Blood samples will be obtained before and immediately after the first, the middle and the last radiation therapy. Platelet aggregation will be measured with a Multiplate® Analyzer. Thrombin generation will be measured with a calibrated automated thrombogram.
- Preliminary results: Preliminary results on 25 women have been measured. Platelet aggregation showed a statistically significant increase during the first radiation therapy after addition of two out of four agonists. No other differences in platelet aggregation were found comparing results obtained before and after radiation therapy, respectively. Platelet aggregation did not show a substantial change in any of the agonists from the first to the final radiation therapy. Thrombin generation measured during radiotherapy will be ready for presentation.
- Conclusion: Overall, radiation therapy did not influence platelet aggregation. The present study will establish if radiotherapy affects thrombin generation as a measurement for the secondary hemostasis.
- P04.03 Trine Block Mattesen
- TUMOR MICROENVIRONMENT SUBTYPING BY DNA METHYLATION BIOMARKERS FACILITATES PERSONALIZED TREATMENT OF COLORECTAL CANCER PATIENTS
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- Recent molecular characterization of colorectal cancer (CRC) has established that the tumor microenvironment (TME) plays an underappreciated role in disease progression. This encourages the

development of novel TME classification systems that may guide clinical treatment decisions. By RNA sequencing and histological analysis of >300 CRCs, we recently identified three major TME subtypes each characterized by a unique cellular composition of non-cancer immune and stromal cells. Very notably, the content and interactions between stromal and immune cells were main determinants of patient prognosis within each TME subtype. The clinical utilization of this knowledge, however, require the establishment and validation of a simplified and cost-efficient biomarker panel for TME subtyping that can be applied to formalin fixed and paraffin embedded tissue rather than fresh frozen tissue (typically not available in the clinic). Here we establish such a biomarker panel for TME subtyping and prediction of patient prognosis by developing cell type specific DNA methylation biomarkers that evaluate the cellular composition of the TME. We exploit that each cell type in the TME has unique and robust DNA methylation patterns that can be evaluated by quantitative methylation-specific PCR. We have established preliminary proof for our strategy by stratifying CRC patients into prognostic classes upon quantifying only B-lymphocytes and fibroblasts within the TME. With these promising results, we foresee that we will be able to successfully expand our cell type specific DNA methylation biomarker panel and by validation confirm the promising prognostic potential of stratifying patients into TME subtypes.

P04.04 Rasha Hyder

NEURAL FOUNDATIONS OF LANGUAGE PROCESSING DEFICITS IN PARKINSON'S DISEASES AND THEIR MODULATION WITH DEEP BRAIN STN STIMULATION: NEURO-MAGNETIC INVESTIGATIONS

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Parkinson's disease (PD) is a neurodegenerative disorder characterised by motor symptoms such as tremors, postural instability, rigidity and bradykinesia. Sub-thalamic nucleus Deep Brain Stimulation (STN-DBS) has become an established therapeutic option for advanced PD with motor deficits that are refractory to medical treatment. STN-DBS improves cardinal motor symptoms of PD and allows a significant reduction of anti-Parkinson drug treatment. Although beneficial effects of STN-DBS on motor symptoms are well established, the effects on cognition and language are still controversial, and the mechanisms of action remain to be elucidated. The impact of DBS on language performance is of increasing interest with many reports of negative outcomes resulting from DBS.

In this PhD project, we aim to investigate the neural foundations of language processing deficits in Parkinson's diseased patients and their modulation with deep brain STN stimulation. For this purpose, we intend to examine two PD subgroups: with and without STN-DBS and to compare these with a group of age-matched healthy volunteers. In the

first phase of this project, we will test two language paradigms on a group of healthy young volunteers to choose the best design for our language protocol. We will record brain activity using combined magnetoencephalography (MEG) and electroencephalography (EEG). Individual MRIs of participants' brains will be used for E/MEG analysis. The results of this project will help to extend our knowledge of the effective mechanisms of STN-DBS, increase our understanding of both PD generally and DBS treatment specifically on language functions, and optimize DBS treatment options.

P04.05 Berit Bargum  
Booth

CERVICAL DYSPLASIA - HOW CAN WE IMPROVE THE DIAGNOSTICS?

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Background and objective: Before cervical cancer 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.

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

Methods: In a randomized clinical trial, 3500 women referred with cervical dysplasia will randomly be assigned examination with or without this new technology at the Department of Gynecology and Obstetrics, at the regional hospitals in Randers and Horsens, respectively. All women will have 4 biopsies taken, in line 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 we gain in sensitivity by using the new DSI colposcopy?
- If the biopsies correlate to the diagnosis in the conisation material?
- If there are any differences in the biopsies taken by the nurses, residents or consultants?

Perspectives: With improved diagnostics of cervical dysplasia, we aim to avoid under- and over-treatment, side effects and thereby, in the worst case, development of undiagnosed cervical cancer.

P04.06 Birgit Rasmussen MEANINGFUL LIVING ENGAGING IN PHYSICAL ACTIVITIES;  
EXPERIENCES OF OLDER PEOPLE AFTER HIP FRACTURE

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Background: The number of hip fractures (HF) is predicted to rise from 1.6 million in 2000 to 6.26 million in 2050. After HF, older people are evidenced to have a sedentary life. Studies testify that older people have challenges related to being active in everyday life, such as pain, dependency and fear of falling. For the individual, these challenges may impact the perception of meaningfulness when engaging in activities after HF. However, the meaning older people ascribe to being active when living with a HF needs further investigation.

Aim: To explore and describe the experiences of meaningful physical activity in older people during the first 18 months after HF. Three sub-studies will be conducted. Study one considers experiences of facilitators and barriers; study two focuses on the meaning of body, time, space, human relations, mood and identity, and study three considers consistency and change across time.

Method: Theoretically, the study is inspired from an existential theory of mobility and dwelling. The approach is phenomenological-hermeneutic. Data will be collected through individual interviews. A conceptual-driven coding will inspire the initial interpretation and gradually be replaced by a new understanding during the inductive process. Steps will include obtaining an overall picture of each interview; delineating, condensing and interpreting meaning units; determining themes from clusters of meaning; and validating the themes by quotes.

Perspective: Results from this study will contribute to development of interventions to support older people in being active after HF, designed with the meaningfulness for the older people it may concern in mind.

P04.07 Millicent Addai Boateng INTEGRATED COMMUNITY CASE MANAGEMENT OF MALARIA (iCCMm); A GATEWAY TO HEALTH LITERACY IN GHANA

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Background: iCCMm is one among several malaria control programs in Ghana. Despite success with the program, malaria accounts for 29.5% of child mortality in the country. Lower health literacy could be a contributing factor because it is known to result in acute clinical outcomes.

Objective: To analyse the impact of iCCMm with increased focus on health literacy of caregivers with children under 5 on malaria morbidity and its associated costs.

Methodology: We will adopt a multistage stratified random sampling method in selection of caregivers to be enrolled in the study. The study sites include Ejisu-Juaben, one of the pioneer districts, where iCCMm was introduced, and Kwabre East, which is currently not involved in the programme and will serve as control district. The proposed study has been divided into four sub-studies. In study 1, a baseline survey in both districts will compare the health literacy levels, use of health care and costs among users and non-users of iCCMm. In study 2 (qualitative), we will focus on group discussions and in-depth interviews with some caregivers and other stakeholders to assess the perceptions that guide the choice of use or non-use of iCCMm. Study 3 will be a follow-up survey after rolling out a health literacy intervention to assess its impact on health literacy levels, use of health care and costs. In study 4, the cost effectiveness of the intervention will be analysed. The expected sample size will be around 1270.

Findings: No results yet, but we expect to find a positive effect of the intervention on health literacy and the other health outcomes.

P04.08 Lasse Bjerg Hansen CLUSTERING OF MICROVASCULAR COMPLICATIONS IN TYPE 1 DIABETES

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Aim: We will describe the association pattern between all three microvascular complications in type 1 diabetic patients accounting for interaction.

Material and methods: We conducted a cross-sectional study of type 1 diabetic patients attending the Steno Diabetes Center. Patients attended the clinic between 2001 and 2013. Information from yearly structured

clinical check-ups of complication status was used to create a dataset characterizing the presence of microvascular diabetic complications on 30 September 2013. We calculated the prevalence of neuropathy (biothesiometry >25 mV), retinopathy (retinopathy  $\geq$  grade two) and nephropathy (micro- or macro- albuminuria) and each combination of complications. Association was described by log-linear analysis and logistic regression adjusted for potential confounders.

Results: In total, 1895 patients (1039 male, mean age: 53 years [41;64 years], median HbA1c: 63 mmol/mol [56;71 mmol/mol], median duration of diabetes: 24.2 years [14.3;37.2]) fulfilled the inclusion criteria; 34.8% had micro- or macro-albuminuria, 36.5% had signs of neuropathy and 59.1% had retinopathy, respectively. By using log-linear analysis, we found two-way interaction for all three complication pairs, but we did not observe any three-way interaction. Common OR, calculated by logistic regression, between complication pairs were: nephropathy ~ neuropathy 1.33 [1.03; 1.72], nephropathy ~ retinopathy 2.71 [2.06; 3.57] and retinopathy ~ neuropathy 1.50 [1.12; 2.02].

Conclusion: Clustering occurs at both extremes of the three-dimensional distribution of complications. There is an association between all complication pairs but no sign of interaction.

P04.09 Susanna Botticelli A NOVEL STANDARDIZED 3D ANALYSIS TO ASSESS CLEFT SIZE BASED ON DIGITAL MODELS OF UNILATERAL CLEFT LIP AND PALATE PATIENTS

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Aims: To develop a 3D analysis to measure cleft size on digital models of unilateral cleft lip and palate patients (UCLP) and to examine validity and intra-examiner reproducibility.

Materials: In total, 31 infant casts (mean age: 1.1 months) of UCLP subjects were digitized. The virtual models were analyzed with two types of software for 3D measurements and modeling (Mimics 18.0 and 3-matic 10.0, Materialise, Belgium). Anatomical and geometrical landmarks and a coordinate system were defined. Cleft size was measured linearly and as an area, and the ratio between cleft area and total palatal surface was calculated (Infant Cleft Severity Ratio). The error of the method was assessed. To determine validity, the areas measured digitally on 10 models were compared with silicone membranes adapted to the palatal surface on the plaster casts and analyzed by optic microscopy.

Results: Bland Altman plots revealed minor systematic bias for anterior cleft width (0.2 mm) and arch length (0.2 mm). The technical error of the method (TEM) was 0.1 mm for linear measurements and 10mm<sup>2</sup> for area measurements. Test-retest reliability for ratio measurements was 0.99. Differences for area measurements performed on digital and plaster models were no more than 2%.

Conclusions: Laser-scanned digital infant models offer the potential for a complete 3D analysis of cleft size and morphology. Our analysis revealed to be accurate and reproducible. Calculation of a 3D Infant Cleft Severity Ratio, to describe the relative dimension of the defect at birth with respect to the maxilla, may have an important diagnostic value when planning surgical closure and also a prognostic value when predicting maxillary growth.

P04.10   Anni  
          Winckelmann

ROMIDEPSIN-INDUCED HIV-1 VIREMIA DURING SUPPRESSIVE ART IS OLIGOCLONAL AND CONTAINS LIMITED DELETERIOUS MUTATIONS

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HIV integrates into the genome of CD4+ T cells and establishes a latent infection that is not eliminated by antiretroviral therapy (ART). The administration of latency reversing agents (LRAs) may facilitate the clearance of replication-competent HIV-1. The aim is, through transcription of latent HIV, to facilitate immune- or virus-mediated killing of latently infected cells. The administration of the LRA romidepsin once weekly for 3 weeks to individuals on ART revealed increases of cell-associated (CA) and plasma HIV RNA in 5 of 6 participants, following the romidepsin infusions. To determine the origin of this romidepsin-induced viremia, we sequenced and compared HIV DNA and CA RNA from circulating CD4+ T cells to plasma HIV RNA sequences obtained during romidepsin therapy. In all three participants with available plasma samples, we identified plasma HIV RNA sequences that were identical to DNA and/or CA RNA sequences from peripheral blood CD4+ T cells. In 2 participants, we identified several expansions of identical plasma HIV-1 RNA sequences, corresponding to 62% and 100% of the total plasma RNA sequences, respectively. Plasma HIV RNA had very low amounts of defective viruses compared to CA RNA (OR 20.85, p<0.001) and to DNA (OR 7.07, p=0.011) during romidepsin therapy. This indicates that romidepsin induced transcription from circulating proviruses contributed to the induced viremia. The oligoclonal pattern of viremia and low

amounts of defective plasma HIV RNA sequences indicate that the romidepsin-induced viremia arises from intact proviruses with highly similar or identical genetic backgrounds. These findings may inform future trials employing LRAs.

P05.01 Marie Vognstoft  
Hjortbak MODULATION OF ISCHEMIC CONDITIONING OF THE HEART -  
INFLUENCE OF HYPOTHERMIA, AEROBIC CAPACITY AND OXYGEN  
TREATMENT

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Background: The main predictor of mortality and morbidity after myocardial infarction (MI) is infarct size (IS). This PhD project aims to investigate several cardioprotective strategies to limit IS and thereby improve the outcome of patients suffering from ischemic heart disease.

Ischemic conditioning consists of brief non-lethal episodes of ischemia and reperfusion applied before a prolonged period of ischemia. Ischemic conditioning can be performed locally on the heart (IPC) or as remote ischemic conditioning (RIC), where the stimulus is applied to either the arm or the leg. Both IPC and RIC have been shown to reduce IS after MI.

The mechanisms underlying conditioning remain incompletely understood, and interactions with other treatment regimes are not clarified. In this project, ischemic conditioning will be combined with three other cardioprotective strategies: mild hypothermia (34 °C), aerobic condition and oxygen treatment. The project is divided into three studies:

Study I will investigate the effect of combining mild hypothermia with IPC and RIC in terms of optimal timing and mechanistic responses.

Study II will characterise the effect of aerobic capacity on myocardial IR and the interaction with IPC and RIC.

Study III will evaluate the effect of oxygen supplementation on infarct size and the interaction with RIC.

Methods: The studies will be carried out in two different animal models of myocardial ischemia and reperfusion: an isolated heart model and an in vivo model of regional no flow ischemia.

The main endpoint is final IS. Secondary endpoints are hemodynamic recovery and mechanistic changes.

P05.02 Jeanett Lykke  
Møller Nielsen TOXICITY AFTER HIGH DOSE METHOTREXATE TREATMENT IN  
PAEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKAEMIA - CAN  
WE INDIVIDUALIZE THE TREATMENT?

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In the treatment of paediatric acute lymphoblastic leukaemia (ALL), the children receive 8 rounds of high dose methotrexate. Folic acid rescue treatment is administered according to the pace of which the patient excretes MTX. This treatment is an essential way of decreasing the likelihood of severe toxicity due to the chemotherapy. Patients with a fast excretion receive fewer folic acid doses. It is unknown whether this leads to a higher degree of haematologic toxicity and a higher tendency for infections, and it has never been documented if this subgroup of ALL patients could possibly benefit from extra doses of folic acid.

The aim of the present study is to assess whether patients with a fast MTX excretion experience toxicities to a degree more severe than patients with a slightly slower drug excretion, and if such toxicities result in suspension of the chemotherapy regime.

Data on all paediatric ALL patients treated in Aarhus according to the NOPHO2008 protocol is extracted from the Danish HDM database. Patients with a fast MTX excretion are identified, and their level of haematologic toxicity and the occurrence of infections are evaluated in comparison to patients with a slightly slower excretion. It is also evaluated whether toxic effects from the methotrexate result in suspension of the Purinethol treatments.

In other international protocols, patients experiencing severe side effects from the MTX treatments are treated with extra folic acid or receive a lower MTX dosage. This study can possibly clarify whether patients with a fast drug excretion could benefit from extra doses of folic acid and whether this should be implemented in future Nordic protocols.

P05.03 Sarah Fogh ETHYLMALONYL-COA DECARBOXYLASE (ECHDC1); A NOVEL PLAYER IN  
ETHYLMALONIC ACIDURIA

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Background: Short-chain acyl-CoA dehydrogenase (SCAD) is located in the mitochondria, where it is involved in ATP production from short-chain fatty acids by initiating beta-oxidation of these. The clinical picture of SCAD deficiency (SCADD) is very diverse, spanning from developmental delay to myopathy. There are numerous variants, off which c.625G>A

(p.Gly209Ser) has been detected in both symptomatic and asymptomatic individuals; c.625G>A is a susceptibility variant, which depends on external genetic/environmental factors for disease manifestation.

Symptomatic individuals accumulate butyryl-CoA, which is converted to ethylmalonic aciduria (EMA). EMA excreted in the urine is used as a diagnostic marker. But, EMA is not only a diagnostic marker; it also potentially elevates reactive oxygen species (ROS) production to harmful levels.

In 2011, a novel co-player to SCAD was identified, ethylmalonyl-CoA decarboxylase (ECHDC1). ECHDC1 is an enzyme, which prevents the buildup of EMA and thereby potentially lowers ROS levels.

Methods: We investigated the link between ECHDC1 and SCAD by two different approaches: 1) We sequenced the ECHDC1 gene of 80 patients, where high EMA could not be explained by the SCAD genotype alone and 2) Knockdown of ECHDC1 by shRNA in fibroblast, either wild type, heterozygous or homozygous for the common c.625G>A variation.

Results and conclusion: We identified seven patients with likely pathogenic ECHDC1 gene variants. Knockdown of ECHDC1 revealed a synergistic effect between ECHDC1 level and SCAD genotype on EMA level. ECHDC1 is likely to play a role in some patients, where EMA levels cannot be explained by SCADD, supporting SCADD as a multifactorial disease.

P05.04    Andreas Engel  
              Krag            DOES REMOTE ISCHEMIC PRECONDITIONING INCREASE FIBRINOLYSIS IN HEAD AND NECK CANCER SURGERY? PRELIMINARY RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

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Background: Cancer induces abnormal coagulation and fibrinolysis, leading to an increased risk of thrombosis. Large head and neck tumors are primarily treated by surgical resection and reconstruction of the defect with transfer of the patient's own tissue. Thrombosis in the transferred tissue or the patient's circulation is a major complication to head and neck cancer surgery.

Aim: The aim of the trial is to investigate if remote ischemic preconditioning (RIPC) increases fibrinolysis in head and neck cancer patients undergoing surgery.

Methods and materials: The effect of RIPC on fibrinolysis during head and neck cancer surgery is investigated in an ongoing randomized controlled trial. Sixty patients will be randomized 1:1 to RIPC or sham. RIPC is carried out perioperatively by four 5-minute periods of upper extremity ischemia induced with an inflatable tourniquet, with each period separated by five minutes of reperfusion. Blood samples are collected during a 24-hour period covering the preoperative, perioperative, and postoperative phase. Clot lysis assay, tissue plasminogen activator (tPA), and plasminogen activator inhibitor-1 (PAI-1) will be measured.

Results: Twenty-six patients have been included in the trial. Preliminary results show that RIPC increases tPA and reduces PAI-1 in the postoperative period.

Conclusion: These preliminary results indicate that RIPC increases endogenous fibrinolysis in head and neck cancer patients undergoing surgery. Increased fibrinolysis may reduce the postoperative thrombosis risk. Hence, the chance of successful cancer surgery is improved.

P05.05 Sandra Sif  
Gylfadottir

THE PREVALENCE OF PAINFUL DIABETIC POLYNEUROPATHY IN NON-SELECTED TYPE 2 DIABETES PATIENTS IN DENMARK

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Background: Diabetic polyneuropathy (DPN) is the most common long-term complication of diabetes, with an estimated prevalence of 25-50% in Europe. The prevalence of painful DPN is estimated to be 3-25%, but many studies are small and not population-based. Furthermore, most studies have used different populations (both type 1 and 2 diabetes) and different diagnostic criteria and methods to determine the prevalence. In this study, we will determine the prevalence of painful DPN in non-selected type 2 diabetes patients. We hypothesize that the prevalence of DPN is 35%, and that 50% of these patients will have painful DPN.

Materials and methods: This is a population-based study of diabetes patients recruited from the nationwide Danish Centre for Strategic Research in Type 2 Diabetes (DD2) Cohort. The patients will be screened for symptoms of peripheral neuropathy and neuropathic pain using the Michigan Neuropathy Screening instrument (MNSI), numeric rating scale (NRS), ranging from 0-10, and the Douleur Neuropathique 4 (DN4) questionnaire. A stratified random sample of patients will be drawn, and we will examine 450 patients with symptomatic neuropathy and 150 asymptomatic patients. This will allow us to validate the questionnaire

and estimate the prevalence of painful DPN in the whole sample of 7-8,000 patients.

Perspectives: This study will determine the prevalence of painful DPN in Danish type 2 diabetes patients. Other components of this study will hopefully contribute to the identification of risk factors and, ultimately, to prevent or delay the development of painful DPN.

P05.06 Rune Lykke

#### INCIDENCE OF PELVIC ORGAN PROLAPSE REPAIR SUBSEQUENT TO HYSTERECTOMY: A COMPARISON BETWEEN RADICAL HYSTERECTOMY AND TOTAL ABDOMINAL HYSTERECTOMY

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Introduction: The aim of this study was to compare the incidence of subsequent pelvic organ prolapse (POP) repair in women subjected to radical hysterectomy versus that in women subjected to total abdominal hysterectomy.

Methods: From the Danish National Patient Registry, we collected data on all radical hysterectomies, all total abdominal hysterectomies, and all POP operations performed in Denmark from 1 January 1977 to 31 December 2009. We excluded patients with prior POP repair and patients with POP diagnoses or concomitant POP repair at hysterectomy. We analyzed the incidence of POP surgery by Kaplan-Meier curves and Hazard Ratio (HR).

Results: In all, 5,279 women underwent radical hysterectomy, and 63 of these underwent subsequent POP surgery. In the same period, 149,920 women underwent total abdominal hysterectomy, and 6,107 of these had a POP operation subsequent to the hysterectomy. The cumulative incidence of POP surgery was significantly lower for radical hysterectomy than for abdominal hysterectomy, 3.4% and 9.5%, at the end of the study period, yielding a crude HR of 0.36 and an adjusted HR of 0.40 in favor of the radical hysterectomy. The distribution of POP operations in the defined compartments was the same for the two types of hysterectomy.

Conclusion: This study found a significantly lower incidence of subsequent POP operations among women subjected to radical hysterectomy than in women subjected to total abdominal hysterectomy.

P05.07 Markku Hakala TWINFILIN REGULATES LAMELLIPODIAL DYNAMICS DURING CELL MIGRATION - THE ROLE OF PROTEIN-MEMBRANE INTERACTION

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The assembly of actin filaments towards plasma membrane generates protrusions, such as filopodia and lamellipodia, which are essential for cell migration. Especially lamellipodia are protruding and retracting synchronously, and thus actin filament assembly and disassembly must be regulated by several actin-binding proteins.

Twinfilin (TWF) sequesters actin monomers and caps actin filament barbed ends with its two ADF-H domains, which leads to decreased rate of filament elongation. It also binds heterodimeric capping protein (CP) via its C-terminal tail region. Here, we have revealed that TWF regulates lamellipodia dynamics. Knockout of TWF in mouse melanoma cells leads to decreased amount of lamellipodial retractions, as well as thicker and wider lamellipodia in general. This indicates that activities of TWF are tightly regulated during protrusions and retractions of lamellipodia.

Binding to phosphoinositol-(4,5)-biphosphate (PIP<sub>2</sub>) inhibits the ability of TWF to interact with actin. In this study, by revealing the exact binding mechanism between TWF and PIP<sub>2</sub> using combined biochemical and molecular dynamics simulation methods, we have been able to explain why PIP<sub>2</sub> can regulate TWF. Additionally, we found that CP and PIP<sub>2</sub> share the binding interface in C-terminal tail of TWF, suggesting that PIP<sub>2</sub> regulates also TWF-CP interaction.

Since both TWF and PIP<sub>2</sub> localize to regions of high actin turnover, such as lamellipodia, it would be essential to study the role of this interaction also in cells. Our model of interaction, as well as the mapped binding sites for PIP<sub>2</sub>-rich membranes in TWF, is able to facilitate these studies.

P05.08 Line Thorndal Moll BRIEF VS. MULTIDISCIPLINARY INTERVENTION IN NECK/SHOULDER PATIENTS ON SICK LEAVE: RESULTS ON RETURN-TO-WORK

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Objective: Neck pain is a common cause of sick leave and disability, being the 4th most common reason for years lived with disability. Studies

have shown effect of both multidisciplinary and brief rehabilitation programmes regarding return-to-work (RTW) rates. It remains unknown, however, which rehabilitation programme is the more effective. Our aim is to estimate the effect on RTW comparing brief with multidisciplinary intervention.

Methods: A randomized controlled trial design was chosen. From May 2009 to January 2014, patients on sick leave due to neck/shoulder pain (aged 18-60 years, sick leave 4-16 weeks) were enrolled in a trial comparing multidisciplinary with brief intervention. Brief intervention comprised examination and advice by a rheumatologist and a physiotherapist. This treatment was also offered to patients in the multidisciplinary intervention group. However, an additional focus on RTW was added by assigning the patients with a case manager with whom they made individual return-to-work plans. The case manager coordinated contacts with the patient, the workplace, the municipality job service and the rest of the multidisciplinary team. Team participants included a rheumatologist, a physiotherapist, a specialist of clinical social medicine, a social worker, an occupational therapist and, in relevant cases, a psychologist. Follow-up data consists of register information on RTW. The latter is supplied by a national Danish database registering social transfer benefits on a weekly basis. RTW status at 52 weeks of followup is estimated using Chi-squared test.

Results: Results on RTW will be presented at the PhD Day.

Conclusion: The conclusion will be presented at the PhD Day.

P05.09 Yasser Haddadi COMPARISON OF CONVENTIONAL IMPRESSION TECHNIQUE AND INTRAORAL SCAN; EVALUATION OF TREATMENT DISCOMFORT AND TIME CONSUMPTION. AN IN VIVO, RANDOMISED SPLIT-MOUTH STUDY

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Objective: Compare patient discomfort and clinical time-consumption associated with conventional impression technique and intraoral scan taken as part of routine prosthetic treatment.

Background: Digital dentistry is a rapidly growing field with intraoral scanners being the gateway to a fully digital workflow. However, for intraoral scanners to become a broadly utilised tool in general dental practice, high-quality research must demonstrate not only sufficient accuracy but also patient acceptance and clinical time efficiency comparable to that of conventional impression technique.

Materials and methods: Nineteen patients fitting a split-mouth design received two full ceramic crowns. One impression was taken in a full-arch tray with addition-cured silicone using heavy-body/light-body technique. The other impression was an intraoral scan with Trios 3

(3Shape, Denmark). Total time for both methods was registered. After both impressions had been taken, patients were asked to rate the discomfort on a VAS.

Results: Mean total impression/scan time was 5:11 ± 1:05 for the intraoral scan and 18:39 ± 6:22 for the conventional impression method ( $p < 0.0001$ ).

Mean VAS score indicating discomfort associated with impression/scan was 6.2 ± 4.7 for the intraoral scan and 59.8 ± 32.3 for the conventional impression method ( $p < 0.0001$ ).

Conclusion: Intraoral scans are less time-consuming and cause less discomfort to patients than conventional impression technique.

P05.10 Jacob Lynge  
Callesen

HOW DOES PROGRESSIVE RESISTANCE TRAINING AND BALANCE TRAINING AFFECT GAIT AND FATIGUE IN PATIENTS WITH MULTIPLE SCLEROSIS?

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Introduction: Multiple sclerosis (MS) is characterized by a demyelination that results in reduced conductivity in the somatosensory nervous system, decreased strength, vestibular alteration, and severe fatigue. Progressive resistance training (PRT) has proven to be a promising intervention showing a positive effect on muscle strength. Another promising intervention is task specific training of motor function that is frequently used in neurorehabilitation, which, in this study, will be termed Balance and Motor Control Training (BMCT). Interestingly, the principles of BMCT do fundamentally contrast the principles of PRT in terms of variation in movement pattern, loading and repetitions. Consequently, knowledge of any diverse effect would be of clinical relevance.

Aim: To compare the effects of PRT or BMCT on gait, balance and fatigue in persons with MS.

Method: A three-armed multi-center, single-blinded cluster-randomized controlled trial with two intervention groups (1. PRT of the lower extremities and 2. BMCT that challenges gait function) and a control group that receives usual care while on a waitlist followed by PRT + BMCT. Interventions are run for ten weeks with two sessions per week in groups of 3-6 participants. Number of participants is 30 per intervention; 90 in total. Primary outcome measures of gait function are Timed 25 Foot Walk (T25FW) and Six Spot Step Test (SSST). Secondary outcomes are fatigue, self-perceived gait function, temporospatial gait characteristics, balance and strength. Inclusion: EDSS 2-6, SSST > 8.5 sec and T25FW > 5 sec.

Exclusion: Recent attacks and ongoing intensive rehabilitation.

Analysis: ANOVA and unpaired analysis of changes between groups.

P06.01

Leila Louise  
Benhassen

CHARACTERIZATION OF VALVE-SPARING AORTIC ROOT REPAIR WITH DIFFERENT SUBVALVULAR ANNULOPLASTIES: A CLINICAL EXPERIMENTAL STUDY

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Background: Aortic valve replacement has been the treatment of choice for patients with severe aortic insufficiency. Valve sparing aortic root repair has become an advantageous alternative to avoid the adverse effects of prosthetic valve replacement. New evidence suggests that adding a subvalvular annuloplasty provides a better repair, but no standardisation or comparison has yet been made for the different types of annuloplasty approaches.

Aim: The aim is to compare different types of annuloplasties in a porcine experimental in vivo model after performing aortic root repair. We will be testing different annuloplasties to evaluate support, stabilization and stress distribution exerted on the native aortic root by adding: a) Suture annuloplasty, b) Conventional Dacron-ring, c) New semiflexible ring and d) Double subvalvular and supra-annular external ring annuloplasty.

Material and methods: A 80 kg porcine model will be used. A force transducer will be inserted in the aortic root to assess stress distribution, and piezoelectric crystals will be used to assess the geometrical changes of the aortic root. 2D echocardiography will be used for evaluation of valve performance. Furthermore, we will perform MRI postoperatively to evaluate aortic root dynamics and perform a stress-strain analysis.

Results: Pending.

Discussion: From this study, a comprehensive description and a new understanding of the biomechanical effects of an added suture or ring annuloplasty will be obtained. This is highly relevant in the emerging field of aortic root repair, and this might lead to optimization of surgical procedures applied to the aortic root in relevant patient groups.

P06.02 Martin Fogtmann THE CRISPR-CAS9 MINIPIG - A TRANSGENIC PIG TO PRODUCE SPECIFIC  
Berthelsen GENOME EDITING IN SELECTED TISSUES

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We have produced a transgenic minipig expressing Cas9 under a ubiquitous promoter that will reduce the cost and time to develop new pig models with unique gene alterations substantially. This was carried out by inserting a transposon harboring the CRISPR-Cas9 gene into the genome of minipig fibroblasts. Fibroblasts containing few copies of the Cas9 transgene were selected and used for cloning by somatic cell nuclear transfer, which gave rise to seven founder pigs. The genetic design has been validated in vitro in fibroblasts isolated from the Cas9 minipigs. Sequencing of DNA from fibroblasts transfected with guide RNAs against TP53 and PTEN revealed knockout of the genes. Moreover, transfection with guide RNA against KRAS in combination with a homology directed repair templated revealed the desired G12D point-mutation leading to constitutive activation of KRAS.

IVIS scanning and IHC staining of tissues biopsies from one of the founder pigs verified transgene expression in major organs, including heart, lung, liver, colon, and prostate. The transgene expression varied from 25 to 100 percent positive cells among different organs and cell types.

A virus-based technology will be implemented for the delivery of guide RNAs to induce gene alterations in vivo. A pilot study in Danish Landrace pigs has validated that our adeno-associated virus particles indeed are capable of infecting the lung epithelium of pigs. The porcine Cas9 model is currently being validated in vivo by induction of lung cancer through mutation of TP53, PTEN, and KRAS. It is expected that a few cells will be mutated in all three genes and that these will clonally expand to develop adenomas in the lung.

P06.03 Alexander UNDERSTANDING UNDERLYING MECHANISMS OF DIABETIC  
Gramm POLYNEUROPATHY  
Kristensen

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Background: Diabetic polyneuropathy (DPN) develops in over half of diabetic patients and constitutes a serious issue in the treatment of diabetes. The mechanisms leading to DPN are at present poorly understood. Early detection and understanding of the underlying mechanisms of DPN are not always possible with conventional electrophysiological methods.

Materials and methods: In this study, we will investigate the presence of early motor involvement using a novel motor unit number estimation (MUNE) test, the so-called CMAP Scan MUNE, and correlate MUNE values to Nerve Excitability Testing (NET) parameters. NET applies various kinds of conditioning stimuli to a peripheral nerve, and the results can show the function of the axonal ion channels. We will study a large cohort of over 100 diabetic patients and use various methods to grade the severity of diabetic neuropathy, including CMAP scan MUNE, and correlate the dysfunction of specific ion channels with the severity of DPN. NET parameters will also be investigated in a study with induced hyperglycaemia in patients and controls, while in another study NET parameters will be correlated to large nerve fibre changes in skin biopsy.

Perspectives: This PhD project will be conducted as a part of the International Diabetic Neuropathy Consortium (IDNC), which aims to address the pertinent questions related to DPN with international collaboration. We expect our results to improve our understanding of underlying pathophysiological mechanisms of DPN and open new areas of research.

P06.04 Abdelhakim Salem

HISTAMINE METABOLISM AND TRANSPORT ARE DERANGED IN HUMAN KERATINOCYTES IN ORAL LICHEN PLANUS

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Background: Recent reports indicated that non-immune cells can produce low concentrations of histamine. This observation, together with the discovery of the histamine H4 receptor (H4R), has added additional layers of complexity to our understanding of histamine signalling. Human oral keratinocytes (HOKs) possess a uniform H4R-pattern, which is deranged in oral lichen planus (OLP).

Objectives: To investigate histamine metabolism and transport in HOKs of healthy controls and OLP patients.

Methods: Tissue sections and cultured primary HOKs were studied using immunostaining, quantitative real-time polymerase chain reaction and confocal microscopy. Histamine levels were analyzed using high-performance liquid chromatography.

Results: L-histidine decarboxylase (HDC) and organic cation transporter-3 (OCT3) were increased at mRNA and protein levels in OLP. In contrast, histamine N-methyltransferase (HNMT) was decreased in OLP.

OCT1/OCT2 and diamine oxidase (DAO) were not detectable in HOKs. Stimulation with lipopolysaccharide (LPS) or interferon-gamma upregulated the HDC-gene transcript in HOKs, whereas high histamine concentration and tumor necrosis factor- $\alpha$  downregulated it. LPS induced dose-dependent release of low histamine in HOKs, while high histamine concentration downregulated their epithelial adhesion proteins.

Conclusions: HOKs are histamine-producing cells. They release histamine via OCT3 channels in concentrations too low to activate the classical low-affinity H1R and H2R, but high enough to stimulate the high-affinity H4R in autocrine and paracrine modes. The substantially deranged histamine metabolism and transport in OLP could contribute to disease pathogenesis and perpetuation.

P06.05 Louise Bang  
Grode

PREVALENCE, INCIDENCE AND COMORBIDITIES OF CELIAC DISEASE IN DENMARK; A NATIONWIDE POPULATION-BASED STUDY FROM 1977 TO 2014

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Background: Celiac disease (CD) is an autoimmune disease with a permanent gluten-sensitive enteropathy. Previous studies reported an increasing incidence and prevalence of diagnosed CD, but these studies were mostly restricted to specific age groups, limited time-periods or small geographic areas. The aim of this study was to examine the prevalence, incidence and comorbidities of CD in Denmark according to age, sex and calendar year.

Methods: A nationwide population-based cohort study identifying all patients registered with a diagnosis of CD in the Danish National Patient Register from 1977-2014. Incident cases were defined as patients with a new diagnosis of CD from 1980 onwards, using the period 1977-1979 as a "wash-out" period. Comorbidity was defined by the Charlson Comorbidity Index.

Results: We identified 9835 patients with CD (64% female). The mean age at diagnosis was 34.2 years (SD 24.8). The prevalence in 2004 and 2014 was 60 and 140 per 100,000 person-years, respectively. From 1980 to 1984, the incidence rate was 1.6, which increased to 12.8 per 100,000

person-years in 2010-2014. The most common comorbidities at the time of diagnosis in the age groups were: (i) age <20: diabetes (10%); (ii) age 20-59: chronic pulmonary disease (7%); (iii) age 60-79: any tumor (13%); (iv): age >79: cerebrovascular disease (23%). In total, 27% of the patients had at least one comorbidity when diagnosed.

Conclusion: From 2004 to 2014, the prevalence of CD has more than doubled in Denmark, and 27% of the patients are dealing with at least one comorbidity when diagnosed. A description of the patterns of CD can be a step towards understanding the public health impact of the disease.

P06.06 Sidsel Boie

#### COCHRANE REVIEW: DISCONTINUATION OF INTRAVENOUS OXYTOCIN IN THE ACTIVE PHASE OF INDUCED LABOUR

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Oxytocin is a powerful drug enhancing uterine contractions during labour. The potential side effects and risks for both mother and child are well-established. Labouring women should only be stimulated with oxytocin when necessary. The aim of this Cochrane review is to assess whether discontinuation of intravenous oxytocin infusion used for induction of labour, once active labour is established, will improve maternal and neonatal outcomes. Important outcomes are caesarean section and neonatal ashyxia. We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (search performed on 10 August 2016), Scopus, ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) (search performed on 26 August 2016) for randomised control trials (RCTs) comparing continuous intravenous oxytocin infusion with discontinued administration of oxytocin for induction of labour. Two review authors independently assessed trials for inclusion and risk of bias. Two review authors independently extracted data. In total, 1376 studies were screened on title and abstract for eligibility; 10 studies were retrieved for full text assessment. We included 9 RCTs in the metaanalysis involving 787 participants. Preliminary data demonstrate a significant decrease in caesarean section rate among women for whom oxytocin was discontinued when the active phase of labour was established (OR 0.58, 95% CI 0.44, 0.77).

P06.07 Ellen Hollands Steffensen PREADMISSION ANTIDEPRESSANT USE AND BLADDER CANCER: A POPULATION-BASED COHORT STUDY OF STAGE AT DIAGNOSIS, TIME TO SURGERY, AND SURGICAL OUTCOMES

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Background: A history of psychiatric disease has been associated with worse survival after cancer. Differences in stage at diagnosis or treatment may explain this. In bladder cancer patients, we examined associations between prior antidepressant use and stage of cancer at diagnosis, rate of surgery, and surgical outcomes.

Methods: This register-based cohort study included all bladder cancer patients in Denmark in 2005-2015. We defined exposure as redemption of two or more antidepressant prescriptions before cancer diagnosis. We used logistic regression to compare stage at diagnosis and Cox regression to estimate hazard ratios for outcomes. Results were adjusted for age, sex, comorbidity, and marital status.

Results: Among 10,427 patients with bladder cancer, 10% used antidepressants. At diagnosis, 51% of users and 52% of non-users had muscle-invasive disease. The adjusted odds ratio for invasiveness was 0.86 (95% confidence interval (CI): 0.74-0.99). Fewer users had surgery within one year (20% vs. 34%, adjusted hazard ratio (aHR): 0.75 (95% CI: 0.60-0.94)).

Of 2532 patients undergoing surgery, 6% were users. The cumulative incidence of 30-day readmission was 41% for users and 33% for non-users (aHR: 1.31 (95% CI: 1.01-1.71)). Users also had higher incidence of 90-day reoperation (44% vs. 38%, aHR: 1.18 (95% CI: 0.93-1.51)). We found comparable 1-year mortality risks among users (15%) and non-users (14%) (aHR: 0.94 (95% CI: 0.61-1.43)).

Conclusion: Prior antidepressant use in bladder cancer patients was associated with less advanced stage at diagnosis and lower rate of surgery. After surgery, users had higher rates of readmission and reoperation, but not increased 1-year mortality.

P06.08 Anna Bystrup Jacobsen REPRODUCIBILITY AND DIAGNOSTIC UTILITY OF A NOVEL MUNE METHOD IN ALS: MSCAN MUNE

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**Background:** Motor unit number estimation (MUNE) methods have proven to be useful in diagnosis and follow-up of diseases with loss of motor units, particularly Amyotrophic Lateral Sclerosis (ALS). However, current methods are largely based on subjective decisions during the analysis. The objective of this study was to examine the inter- and intra-rater reproducibility of a new MUNE method, MScan MUNE (MScan) and to compare it with two traditional MUNE methods; Multiple point stimulation MUNE (MPS) and Motor Unit Number Index (MUNIX).

**Methods:** Twenty-two patients with ALS and 20 sex- and age-matched healthy controls were included prospectively. Examinations with MPS, MUNIX, and MScan were performed twice each by two blinded physicians. Reproducibility of MUNE values was assessed by coefficient of variation (CV) and intra class correlation coefficient (ICC).

**Results:** The results for MScan were significantly more reproducible than for MPS or MUNIX, both between and within operators. The mean CV for MScan (12.3%) was significantly lower than for MPS (24.7%) or for MUNIX (21.5%). All three methods had ICCs of > 0.94.

**Conclusion:** MScan provided more consistent MUNE values than MPS or MUNIX. This promising new method may, therefore, improve the diagnostics and follow-up of ALS and other neuromuscular disorders.

P06.09 Stine Bak

#### MOLECULAR DETAILS OF OBESITY INDUCED BY MATERNAL LOW-GRADE CHRONIC INFLAMMATION

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Obesity arises from a complex interplay between biology, behavior, and environmental factors affecting energy balance. It is now evident that also parental lifestyle exerts an important influence; maternal obesity has been shown to predispose to the development of metabolic syndrome and obesity in the next generation.

Obesity is strongly associated with a subclinical state of low-grade chronic inflammation. This inflammatory state plays a pivotal role in the development of insulin resistance and could mediate the detrimental effects of maternal obesity on metabolic imprinting in the offspring. Recently, our research group developed a novel and unique mouse model, where the low-grade chronic inflammation is mimicked by a continuous low-dose delivery of an immunostimulatory substance. Offspring exposed to this inflammatory state in utero developed obesity, hyperphagia and impaired capacity to cope with a post-natal high-fat

diet (HFD) challenge; a phenotype similar to offspring born by mice with HFD-induced obesity.

As an ongoing study, we investigate whether the two similar phenotypes have identical molecular background by comparing epigenetic markers and gene expression in adipose tissue. For the epigenetic analysis, we have performed methylation DNA immunoprecipitation followed by next generation sequencing. Furthermore, RNA-sequencing will be performed to identify differentially expressed genes. If identical molecular changes are identified in offspring exposed to maternal low-grade chronic inflammation and offspring born by mice with HFD-induced obesity, it indicates that the low-grade chronic inflammation is a key regulator in developmental origins of metabolic diseases.

P06.10 Kamilla Pedersen EXPLORING THE IMPACT OF TEACHING FORMATS ON PATIENT-CENTEREDNESS IN MEDICAL STUDENTS

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Introduction: A patient-centred approach is essential to psychiatric diagnosis and treatment. Little is known about the influence of various teaching formats on preparing medical students for interpersonal competences in their clerkships.

The objective of this study was to explore the impact of a video-based teaching format on medical students' patient-centred awareness in their clerkships.

Method: Context was the four-week psychiatric clerkship for 4<sup>th</sup> year medical students at Aarhus University. A video portraying real patients was designed to be used in a preparatory lecture on diagnostic interviewing skills. After the clerkship, eight rich pictures interviews were conducted with students. The interviews explored the students' experience with the diagnostic interview situations in their clerkship. The recorded and transcribed data was subject to thematic content analysis. Emerging themes were analyzed according to classical anthropological liminal theory.

Findings: Results demonstrated that the impact of the video cases depended on the subsequent teaching format in the clerkship. In situations where the students were actively engaged in the patient interview, the students expressed reflections on a patient perspective regarding a variety of biopsychosocial issues. In contrast, when the students were passively observing a doctor interviewing a patient, the focus turned to the doctor's performance and how to mimic the verbal

and nonverbal interviewing skills. Student engagement in learning seems highly influential on whether students adopt a patient-centered awareness or self-centered focus.

P07.01 Louise Devantier THE BALANCE ORGAN IS STIMULATED DURING MRI SCANS

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Introduction: Studies have shown that a strong magnetic field can stimulate the balance organ. Functional Magnetic resonance imaging (fMRI) is increasingly used to visualize brain activity induced by different types of stimuli. We aim to validate functional MRI as an imaging technique by studying how the balance organ is affected by the magnetic field of the MRI scanner.

Method:

Population: 3 healthy volunteers

Eye movements were registered with videonystagmography:

- Outside a 3T MRI scanner,
- Head first inside the 3T MRI scanner
- Legs first into the 3T MRI scanner (to study the importance of the magnetic field polarity).

Results: None of the subjects had nystagmus outside the MRI scanner. All subjects developed a persisting nystagmus inside the MRI scanner. The direction of nystagmus was dependent on the magnetic field polarity.

Conclusion: The magnetic field of the MRI scanner affected the balance organ and elicited a strong and persistent nystagmus in all subjects. The magnetic field evoked nystagmus depends on the polarity of the magnetic field. The significance of this for functional MRI remains unresolved.

P07.02 Gitte Boier  
Tygesen

DEVELOPMENT AND EVALUATION OF A PATIENT SAFETY MODEL  
TARGETING SEVERE CLINICAL DETERIORATION AND SAFETY  
AWARENESS IN THE EMERGENCY DEPARTMENT

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Despite systems for early detection of critical illness, 12% of patients in an emergency department deteriorate with increased risk of dying. Cincinnati Children's Hospital has introduced a patient safety model complementing the early warning system with systematic evaluation of patients' or relatives' concerns, staff's concerns and clinical gaze, high risk medicine and communication. Additionally, the model consists of formalized organizational processes targeting a systematic review of patients at risk and early treatment efforts. American studies indicate that the model can result in a significant reduction of serious adverse events and increase staff awareness of patient safety. The model is designed for children and has yet to be evaluated in a controlled study. The aim of the present study is to develop and evaluate the effect of a patient safety model inspired by the Cincinnati model, adjusted to the Danish healthcare system and targeting adult patients in the acute care setting.

The present PhD project is based on:

1. A systematic literature review to identify risk factors that should be included in a patient safety model targeting severe clinical deterioration
2. Development and pilot test of a Danish patient safety model
3. A controlled intervention study testing the effect of the model.

The intervention will be carried out at the emergency and intensive care departments at the regional hospitals of Horsens and Viborg with the hospitals in Randers and Herning as control departments.

A positive outcome of the study is expected to increase patient safety by reducing the number of patients with serious deterioration, reducing the number of serious adverse events and increase staff safety awareness.

P07.03 Lise Brogaard  
Roed Jensen

LIVE TEAMS IN OBSTETRIC EMERGENCY SITUATIONS

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Background: In obstetric emergency situations, inadequate non-technical skills (NTS) are the leading causes of substandard care.

Aim: To describe how the NTS and the clinical performance are related among teams in obstetric emergency situations.

Methods:

1. Inclusion of the teams: Obstetric emergency teams were included in two Danish hospitals: Aarhus University Hospital, Skejby, and Horsens Regional Hospital. Emergency teams were automatically recorded in the delivery rooms. The emergency situations included were: post-partum hemorrhage, assisted vaginal delivery, shoulder dystocia, emergency caesarean section, and twin deliveries.

2. Development of assessment tools to rate clinical performance: Assessment tools will be developed for each emergency situation and will be based on an international Delphi process. Test for validity and reliability will be performed in simulated as well as in live obstetric emergency situations.

3. Assessment of clinical performance: After pilot-testing the tools, the assessment of the video recordings will be performed.

4. Assessment of non-technical skills: Video recording of teams will be rated by the validated list: Assessment of Obstetric Team Performance, AOTP<sup>4</sup>. Furthermore, important observations will be coded.

5. Explore the association between clinical performance and NTS: Results from step 3 and 4 will be explored.

Discussion: The overall inclusion was 269/456 (59%). Main reason for not eligible teams was missing consent. We expect that this study will add to the knowledge of NTS and the effect on clinical performance in obstetric emergency situations.

P07.04 Thomas Skjærlund Grønnebæk

EFFECT OF LOW LOAD BLOOD FLOW RESTRICTED RESISTANCE EXERCISE ON MUSCLE MITOCHONDRIAL BIOGENESIS

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Introduction: From a clinical perspective, it is of interest to investigate

whether differentiated resistance exercise regimens can exert dual effect on muscle mitochondrial and contractile properties.

Low load blood flow restricted resistance exercise (BFRE) has recently emerged as an efficacious strategy to augment contractile properties. However, the effect of BFRE on mitochondrial biogenesis and function (MBF) is yet to be investigated. Exercise induced mitochondrial biogenesis has traditionally been achieved through prolonged continuous or intermittent bouts of submaximal contractions (endurance exercise). BFRE introduces endurance exercise-like stress (e.g. decreased intramuscular oxygen tension), which may augment MBF compared to traditional resistance training (TRT).

Aim: This study aims to investigate the effect of single treatment and repeated BFRE versus TRT on MBF.

Methods: In total, 36 healthy, male, subjects are randomised to 6 weeks of BFRE, TRT, or non-exercise control. Biopsies are harvested pre and post intervention and at multiple time points during recovery from single bout exercise. During the intervention, deuterium oxide is orally administered, which allows for in vivo measurements of mitochondrial biogenesis. Mitochondrial respiratory capacity is measured in permeabilised myofibers by high-resolution respirometry. Markers of mitochondrial capacity and signalling are measured by western blotting and PCR.

Context: This study forms part of an interdisciplinary research initiative investigating conditioning effects of ischaemia and exercise on vital organs. The study involves Department of Cardiology, INANO, CFIN, Department of Biomedicine and Section for Sport Science, Department of Public Health.

P07.05 Carina Bagge

THE RISK OF DEMENTIA IN ADULTS WITH CONGENITAL HEART DISEASE: A NATIONWIDE COHORT STUDY

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Background: There is increasing recognition of neurologic complications associated with congenital heart disease (CHD) during childhood and early adult life. We aimed to examine the risk of dementia of CHD adults with that of the general population.

Methods and results: This Danish population-based cohort study used medical registries covering all national hospitals to identify CHD patients diagnosed between 1963 and 1982, who were alive at age 30 years. They were followed until diagnosis of dementia, death, emigration, or end of study (December 2012). For each CHD adult, 10 members from the general population were identified utilizing the Danish Civil Registration System, matched on sex and birth year. We computed cumulative incidences and hazard ratios (HRs) of dementia adjusted for gender and birth year.

The CHD cohort consisted of 10,632 patients (46% male). The cumulative incidence of dementia was 4% by age 80 years in the CHD cohort. The overall HR of dementia in CHD adults relative to the comparison cohort was 1.6 (95% CI: 1.3-2.0) and did not vary according to gender (male 1.6; 95% CI: 1.1-2.3, and female 1.7; 95% CI: 1.3-2.2). The HR in subjects without extracardiac defects was 1.4 (95% CI: 1.1-1.8). The HR for subjects with mild CHD was 1.6 (95% CI: 1.2-2.2), while it was 1.2 (95% CI: 0.7-2.1) and 2.0 (95% CI: 1.1-1.3) for moderate and severe CHD, respectively. The HR for early onset dementia (<65 years of age) was 2.6 (95% CI: 1.8-3.8) and 1.3 (95% CI: 1.0-1.8) for late onset.

Conclusion: The risk of dementia was increased in CHD adults compared with the general population. Dementia may become an important aspect of adult CHD care in the decades to come.

P07.06 Anders Sjørølev  
Schmidt

CARDIOVERSION EFFICACY USING PULSED BIPHASIC OR BIPHASIC TRUNCATED EXPONENTIAL WAVEFORMS: A RANDOMIZED CLINICAL TRIAL

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Background: Several different defibrillators are currently used for cardioversion and defibrillation of cardiac arrhythmias. The efficacy of a novel pulsed biphasic (PB) waveform, which is in clinical use, has not been compared to other biphasic waveforms. Accordingly, this study aims to compare the efficacy and safety of PB shocks with biphasic truncated exponential (BTE) shocks in patients undergoing elective cardioversion of atrial fibrillation or atrial flutter.

Methods: This prospective, randomized study included patients admitted for elective direct current cardioversion. Patients were randomized to

receive cardioversion using either PB or BTE shocks. We used escalating shocks until sinus rhythm was obtained or to a maximum of four shocks. Patients randomized to PB shocks received 90 J, 120 J, 150 J, 200 J, and patients randomized to BTE shocks received 100 J, 150 J, 200 J, 250 J, as recommended by the manufacturers.

Results: In total, 69 patients (51%) received PB shocks, and 65 patients (49%) received BTE shocks. Successful cardioversion, defined as sinus rhythm four hours after cardioversion, was achieved in 43 patients (62%) using PB shocks and in 56 patients (86%) using BTE shocks; ratio 1.4 (95% confidence interval: 1.1-1.7),  $p=0.002$ ). There was no difference in safety between waveforms, i.e. myocardial injury judged by changes in high-sensitive troponin I levels; ratio 1.1 (95% confidence interval: 1.0-1.3),  $p=0.15$ .

Conclusions: Cardioversion using a BTE waveform was more effective when compared with a PB waveform. There was no difference in safety between the two waveforms, as judged by changes in troponin I levels.

P07.07 Casper Schmidt IMPULSIVITY AND COMPULSIVITY: THE ROLES OF DOPAMINE AND SEROTONIN IN REWARDS

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Within addiction research, there exists a lack of knowledge in terms of both assessment and treatment options. This PhD project seeks to delineate the relationship between the roles of dopamine and serotonin in rewards, and between dopaminergic and serotonergic roles in the neuropsychological measurements of impulsivity and compulsivity, correspondingly.

The background for the project lies in the large body of existing evidence on the roles of dopamine and serotonin, and the impulsive and compulsive behaviours that can follow. Within these roles, dopamine has been proposed as an active cause of impulsivity, whereas serotonin is thought to be linked to compulsivity. Although a lot is known about these roles, no research has been devoted to the basics of these neurochemical mechanisms when exposed to humans in combination.

The experiments will be between-subjects double-blinded designs and will contain testing of four arms of 25 healthy volunteers (HV) and a fifth arm of 25 pathological gamblers (PG), a patient group with profound deficits in impulsivity and compulsivity. This will be done to isolate the neural and behavioural correlates of both increasing dopamine and depleting serotonin to investigate:

- 1) how this affects neural activity in a task-based fMRI experiment
- 2) cognitive components of impulsivity and compulsivity through

behavioural testing

3) how these two points relate to a placebo group of PG.

In conclusion, this project holds great promise to delineate this relationship on a general premise in the case of understanding deeper the neural and behavioural processes associated with dopamine and serotonin, but also specifically for knowledge about PG.

P07.08 Anders Kindberg SURVIVAL AFTER RESECTION OF COLORECTAL CANCER WITH  
Boysen SYNCHRONOUS METASTASES - A DANISH POPULATION-BASED  
HISTORICAL COHORT STUDY

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Background: Conflicting data exist on the optimal treatment for resectable synchronous metastatic disease in liver and/or lungs in patients with colorectal cancer (CRC). We examined the long-term survival of a large national cohort of patients resected for CRC and timing of treatment for synchronous metastasectomies.

Methods: From 2000 to 2013, we included all patients from the Danish Cancer Registry and the Danish National Patient Registry recorded with CRC surgery for adenocarcinoma. We also obtained data from the Danish National Patient Registry for patients operated for liver and/or lung metastases synchronously (<90 days) from the date of CRC surgery.

Results: A total of 35,993 patients had surgery for colon (n=24,206) or rectal cancer (n=11,787) (46.4% females (n=16,711) and 53.6% males (n=19,282)).

In total 2,625 patients (7.3%) were surgically treated for metastatic disease with liver and/or lung surgery, with 682 patients (1.9%) operated for synchronous metastases. In total, 117 patients (17%) had liver surgery prior to CRC surgery, while 106 patients (16%) were operated for lung metastases before resection of the primary. In total, 459 patients (67%) were treated with first resection of the primary and subsequent metastasectomy

The 1- and 5-year overall survival for the entire cohort of patients operated for CRC were 84.1% (83.8%-84.5%) and 56.7% (56.1%-57.2%), respectively. For the subset of patients undergoing synchronous metastasectomy, the 1- and 5-year survival were 88.0% (85.3%-90.2%) and 41.4% (36.9%-45.9%).

Conclusion: We found a 5-year survival of 41.4 % in patients treated for synchronous metastatic disease with liver and/or lung surgery.

P07.09 Linn Håkonsen  
Arendt

MATERNAL DIABETES MELLITUS AND GENITAL MALFORMATIONS IN SONS: A REGISTRY-BASED STUDY IN DENMARK AND SWEDEN

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Background: Maternal diabetes mellitus is associated with an overall increased risk of congenital malformations. However, studies on the genital anomalies cryptorchidism and hypospadias in boys are inconclusive and possible causal mechanisms are poorly understood.

Methods: In a register-based study of all singleton boys born alive in Denmark (1978-2012) and Sweden (1987-2012), we studied the association between maternal diabetes and the risk of genital anomalies according to type and severity of diabetes.

Results: The study population consisted of 2,416,248 singleton live-born boys; 1,073,026 born in Denmark and 1,343,222 born in Sweden. We observed an association between pre-gestational type 1 diabetes and hypospadias (hazard ratio (HR): 1.80; 95% confidence interval: 1.45; 2.24) and cryptorchidism (HR: 1.44; 95% CI: 1.22; 1.69). The same tendency was seen for type 2 diabetes. The risks were higher for boys of mothers with pre-gestational diabetic complication than for boys of mothers without diabetic complications. Finally, we found no association with gestational diabetes when adjusting for body mass index.

Conclusions: Maternal pre-gestational diabetes was associated with an increased risk of genital anomalies in boys, and the risk was highest among boys of mothers with diabetic complications. These results suggest that poor glycemic control, as indicated by diabetic complications, may interfere with fetal genital development in the critical early period of organogenesis. Given the widespread occurrence of diabetes, the results are of public health importance, and women with diabetes should be made aware of this risk in order to optimize glycemic control.

P07.10 Frederik Ahlers

DO INFECTIONS CAUSE EPILEPSY? A NATIONWIDE, REGISTER-BASED COHORT STUDY

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Background: The causes of epilepsy are not yet fully understood, but certain infectious diseases have been shown to increase the risk of epilepsy. Epilepsy is known to have a high degree of psychiatric comorbidity, and it has previously been shown that infections increase the risk of psychiatric disorders. We, therefore, study the association between infections and epilepsy.

Aim: To investigate whether infectious diseases increase the risk of subsequent epilepsy.

Design: This is a nationwide prospective cohort study including all persons born since 1935, who were alive in Denmark from 1977. Using national health registers, all persons will be individually followed from 1 January 1977, or the day they were born, until one of the following end points: epilepsy diagnosis, death, emigration, disappearance, or 31 December 2015, whichever comes first. We expect to include around 5.5 million persons in the cohort, including at least 1-1.5 million persons with hospital contacts for infection and approximately 40-45,000 with an epilepsy diagnosis.

Methods: The Danish Civil Registration System provides information about date of birth, emigration, disappearance and death. The Danish National Patient Register provides data on hospital contacts, including diagnoses. The outcome measure will be the incidence rate of epilepsy, which will be compared between different exposure groups, adjusting for potential confounders. The following exposure variables will be studied: total number of admissions with infections, number of different types of infection, time since last infection, total number of days hospitalized with infection, organ of infection, and microbiological type.

P08.01 Iben Bach  
Pedersen

CORNEAL LENTICULE TRANSPLANTATION FOR CORRECTING  
MODERATE TO SEVERE HYPEROPIA

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Background: Femtosecond laser technology has made it possible to perform high precision surgery in the corneal tissue. A stromal lenticule can be cut and removed through a small incision to reduce the corneal curvature and thereby correct myopia. It has been speculated if the extracted lenticule can be used to treat hyperopia by implanting the lenticule in a stromal pocket, called endokeratophakia. Only few cases and animal studies of endokeratophakia have been reported worldwide. It seems that the effect of the lenticule implantation is reduced due to a bulging of the corneal posterior surface. However, it has not yet been examined how the incision depth affects the anterior and posterior

corneal curvature.

Aim: To analyze anterior and posterior corneal curvature changes after endokeratophakia performed in various stromal depths.

Methods: Human donor corneas deemed unsuitable for therapeutic use are pairwise mounted on artificial anterior chambers. A stromal lenticule is cut in with femtosecond laser in one of the mounted corneas and removed through a 2.5 mm incision. In the recipient cornea, a stromal pocket with a 2.7 mm incision is created. The stromal lenticule is transferred into the stromal pocket of the recipient cornea. Lenticule implantations are performed with various lenticule thickness and incision depths from 110  $\mu\text{m}$  to 160  $\mu\text{m}$ . Postoperative changes in corneal curvature and the lenticule position are evaluated. Preliminary results will be presented at the PhD Day.

Perspectives: It is essential to understand the front and back corneal curvature changes before we can consider endokeratophakia as a potential technique for correcting moderate to severe hyperopia.

P08.02    Gitte Øskov  
              Skajaa

INSULIN SENSITIVITY IN WOMEN AROUND PARTURITION AND 6 MONTHS POST PARTUM

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Aim: We aim to identify the rapid changes in insulin sensitivity around parturition and the following 6 months post partum in women with GDM. Such knowledge would be clinically useful and markedly improve insulin treatment before and after parturition and serve to identify the best possible timing of testing women with GDM for the development of post partum T2DM.

Design: A hyperinsulinaemic euglycaemic clamp is performed in women before, immediately after delivery and 6 months post partum. We are comparing 20 women with gestational diabetes in late pregnancy, day 15 post partum and 6 months post partum with 20 control women matched on gestational age and BMI.

Methods: The hyperinsulinaemic euglycaemic clamp technique is widely accepted as the "gold standard" method for directly determining metabolic insulin sensitivity in humans. To obtain a measure for both insulin secretion (beta-cell function) and insulin sensitivity during the same test, we perform an intravenous glucose tolerance test (IVGTT) followed by a hyperinsulinaemic euglycaemic clamp, also called the Botnia clamp.

Perspectives: Diabetes during pregnancy is a common condition with important implications for pregnancy outcome and long-term morbidity for mother and offspring. Accordingly tailoring the best treatment is

expected to have beneficial consequences both for the pregnant women and the future generation.

P08.03 Søren  
Christiansen

#### TIMING OF RENAL REPLACEMENT THERAPY AND LONG-TERM RISK OF DEATH AND CHRONIC KIDNEY DISEASE IN INTENSIVE CARE PATIENTS WITH ACUTE KIDNEY INJURY

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Background: The optimal time to initiate renal replacement therapy (RRT) in intensive care unit (ICU) patients with acute kidney injury (AKI) is unclear. We examined the impact of early RRT on risk of chronic kidney disease (CKD), end-stage renal disease (ESRD) and death in a cohort study with long-term follow-up.

Methods: All adult patients receiving RRT at the ICU at Aarhus University Hospital, Skejby, Denmark from 2005 to 2015 were included. Data were obtained from an Electronic Health Record and population-based registries. Early and late initiation of RRT was defined as Kidney Disease Improving Global Outcomes AKI stage 2 or below and stage 3, respectively, and 1:1 propensity score matched. The cumulative risk of CKD (eGFR<59 ml/min/ 1.73 m<sup>2</sup>), ESRD and death was assessed in patients with early and late RRT and compared by Cox regression.

Results: We identified 1213 patients receiving RRT. Among those were RRT initiated early and late in 621 and 592 patients, respectively. The 5-year risk of CKD was 38.6% (95% CI, 28.2%-49.1%) in the early group and 44.7% (95% CI, 33.5%-55.9%) in the late group, corresponding to a hazard ratio (HR) of 0.79 (95% CI, 0.46-1.37) in early compared to late. The 5-year risk of ESRD in the early group was 13.0% (95% CI, 7.8%-18.1%) and 14.5% (95% CI, 9.0%-20.0%) in the late group, corresponding to a HR of 0.91 (95% CI, 0.50-1.67). The 5-year mortality was 69.8% (95% CI, 64.9%-74.6%) in the early group and 67.4% (95% CI, 62.2%-72.5%) in the late group, corresponding to a HR of 1.10 (95% CI, 0.88-1.36).

Conclusion: Early initiation of RRT was associated with an imprecisely lowered risk of CKD, but no difference was observed in mortality and risk of ESRD.

P08.04 Anuj Pareek

#### ULTRASONOGRAPHIC ASSESSMENT OF INTERSTITIAL LUNG FLUID LEVELS DURING POSTNATAL LUNG TRANSITION: A COMPARISON BETWEEN CAESAREAN SECTION AND VAGINAL DELIVERY

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Background: Delayed lung fluid clearance during postnatal lung transition may result in respiratory distress and hospitalization to the NICU. Respiratory distress due to increased lung fluid levels is more common in infants delivered by caesarean section compared to vaginal delivery. Consequently, birth by caesarean section is associated with a higher admittance rate to the NICU. Hospitalization is based primarily on indirect evidence of increased lung fluid levels such as poor vital signs and abnormal breathing sounds. Currently, no clinical tool exists for direct assessment of interstitial lung fluid levels in the neonate. Ultrasonographic occurrence of B-lines has been proven to be a valuable marker of interstitial lung fluid levels in adult patients. We, therefore, hypothesize that interstitial lung fluid levels can be quantified by counting B-lines in the neonate.

Aim: To count ultrasonographic B-lines in neonates immediately after birth and compare results between caesarean section and vaginal delivery. In addition, we wish to investigate if a higher count of B-lines is associated with a higher rate of subsequent admittance to the NICU.

Methods: We record lung ultrasound scans of neonates with a gestational age of  $\geq 36$  weeks at three separate time points after birth; within 1 hour of delivery, 2 hours after delivery, and 3 hours after delivery. We aim to include 100 neonates delivered by caesarean section and 100 delivered vaginally. The B-lines in each ultrasound scan are quantified by two independent raters blinded to all patient data.

Perspectives: Ultrasound might be useful in early prediction of delayed neonatal lung transition requiring admittance to the NICU.

P08.05 Wenqian Gu  
Cancellation

EXPLORE THE EFFECTS OF THE ANTI-DIABETIC DRUG, ISOSTEVIOL, ON ALPHA- AND BETA - CELLS DURING GLUCOTOXICITY, LIPOTOXICITY AND AMINOACIDOTOXICITY INDUCED CONDITIONS

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Long-term complications of T2D have caused a striking increase in morbidity and mortality, especially for cardiovascular (CV) diseases in the past decades. Therefore, it is crucial to identify effective substances that are anti-hyperglycemic and counteract CV risk factors, e.g. dyslipidemia and hypertension. Numerous studies indicate that the bioactive compound, Isosteviol (IS), possesses anti-diabetic effects. Long-term treatment with IS improves glucose homeostasis and insulin sensitivity, lowers plasma triglycerides and increases HDL-cholesterol, which can reduce adiposity and positively influence the gene expression

profile of key insulin regulatory genes. Hence, IS shows great pharmaceutical potential to treat diabetes and has potential as a future drug. This project aims to investigate whether IS is able to counteract and improve cell survival and decrease cell apoptosis after chronic exposure to excessive glucose, fatty acid and amino acid as well as mitigate insulin resistance in skeletal muscle and liver cells.

P08.06 Marcell Juan  
Tjørnild

#### MITRAL LEAFLET AUGMENTATION AND RECONSTRUCTION USING PORCINE EXTRACELLULAR MATRIX: FUNCTIONAL AND BIOMECHANICAL ASPECTS

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**Objectives:** Mitral valve reconstructive surgery often involves leaflet extension, use of patches, or extensive surgery on both leaflets. For extension and reconstruction, a new generation of decellularized porcine small intestinal submucosa extracellular matrix (CorMatrix®) has been developed. It can adapt to the high-pressure system of the left side of the heart. The aim of this study is to conduct an integrated in-vivo experimental evaluation of mitral valve posterior leaflet extension, total reconstruction of the posterior leaflet, and total mitral valve reconstruction. Furthermore, the aim is to describe the recellularization and decomposition rate of the CorMatrix® over time.

**Materials and methods:** An open chest porcine model will be used. The three intervention groups defined above will be tested against a control group with native valve preservation in an acute 80 kg (n=32) and chronic 60 kg (n=24) porcine model. In the acute model, sonomicrometry crystals will be used for 3D geometry, while dedicated force transducers will measure forces. 3D echocardiography will be used to assess valve competence and leaflet motion. The chronic model is a six- and nine-month survival model with histological, immunohistochemical, 3D echocardiography and cardiovascular MRI analysis of valve function.

**Results:** Pending.

**Discussion and perspectives:** With this study, the hope is to expand the current knowledge of mitral leaflet augmentation and reconstruction using porcine extracellular matrix. The perspective is to gain more treatment options for mitral valve surgery with a new material that can be recellularized with the patient's own cells.

- P08.07 Nina Stockfleth Buch NEUROMAS AS THE CAUSE OF NEUROPATHIC PAIN IN PATIENTS WITH PERIPHERAL NERVE INJURIES AND AMPUTATIONS?
- N.S. Buch, E. Qerama, N.B. Finnerup, L. Nikolajsen*
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- Introduction: Neuropathic pain is pain caused by a lesion or disease of the somatosensory nervous system, and is common after e.g. trauma, surgery, amputation and chronic conditions such as diabetes. Neuropathic pain is a major socioeconomic burden and is responsible for chronic pain in up to 10% of the general population.
- Aim and hypothesis: Our aim is to examine whether neuropathic pain following trauma, surgery and amputation is maintained by peripheral input or autonomous central generators. Our hypothesis is that the pain is driven by input from the periphery.
- Methods: Study 1: "Identification of neuromas"; 80 patients with amputations or peripheral nerve injury will be assessed with pain questionnaires, and undergo a clinical examination with quantitative sensory testing (QST) followed by ultrasound examination in order to identify neuromas. The primary outcome is the proportion of patients with neuromas among those with and without neuropathic pain. Study 2: "Infiltration of neuromas with local anesthetics"; 24 patients with both neuropathic pain and ultrasound verified neuromas will receive an injection with a local anesthetic/saline water near the neuroma in a double-blinded crossover fashion. Primary outcomes are measurement of spontaneous and evoked pain scores after infiltration.
- Perspectives: The studies will help identify possible peripheral generators of neuropathic pain, and an increased understanding of these will hopefully lead to improved treatment.
- P08.08 Ann-Katrine Jakobsen TARGETING REPAIR PROTEINS IN CANCER TREATMENT
- A.K. Jakobsen<sup>1,3</sup>, M. Stougaard<sup>1</sup>, L. Bjergbæk<sup>2</sup>, L.B. Madsen<sup>1</sup>, T. Steiniche<sup>1,3</sup>*
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- Drugs from the camptothecin (CPT) family are today used in cancer treatment with a moderate response. CPT drugs inhibit the enzyme topoisomerase 1 (TOP1), but this effect has been discovered to be counteracted by the enzymatic activity of the protein tyrosyl-DNA phosphodiesterase 1 (TDP1). We have, in a small pilot study, found TDP1 to be upregulated in tumor tissue compared to normal tissue in lung cancer patients. This raises the hypothesis that cancer treatment with CPT drugs will be more effective if combined with inhibition of TDP1.

In this PhD study, we have validated assays for measuring TDP1 and TOP1 activity, protein level, and mRNA level in fresh frozen tissue sections, and we are now measuring these values in paired tumor and non-tumor tissue from a cohort of 150 lung cancer patients to confirm the relevance of TDP1 as a target in cancer treatment.

Another part of the study takes into account that if combined inhibition of TOP1 and TDP1 should be possible, a drug inhibiting TDP1 must be developed. Therefore, we are collaborating with a group in Spain with expertise in designing small inhibitory molecules. We are testing the small molecules designed to inhibit TDP1 for their inhibitory effect against TDP1 in purified TDP1 enzyme and human cell extract. So far, we have found several candidates highly effective in inhibiting TDP1.

In parallel with the above mentioned studies, we investigate proteins involved in repair of DNA damages occurring when TOP1 is being inhibited by CPT drugs and not repaired by TDP1. This is being investigated by combining knockdown of different repair proteins in human cells to search for new candidates for cancer treatment.

P08.09 Camma Damsted PROJECTRUN21: RUNNING SCHEDULES FOR HALF-MARATHON - ARE THEY SAFE OR INJURIOUS?

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Introduction: Since 2000, the number of half-marathon (HM) events and its attractiveness has been steeply growing. Training for HM has in general a positive impact on the health, but the risk of sustaining a running-related overuse injury (RRI) is high. Therefore, it is important that the available running schedules are of highest quality with a custom-fit content tailored to the runners' needs for adjustments of training loads. Unfortunately, knowledge for designing such schedules does not exist.

Aim: To investigate the injury risk for runners with different running profiles and different demographics when following the same running schedule for HM. Further, to identify changes in running participation, which are associated with the risk of RRI.

Methods: A 14-week prospective cohort study with four sub-cohorts based on different running schedules for HM. Runners included: 805. Running data was collected objectively by smart-phone or GPS-watch. Injury data was gathered using the questionnaire developed by the Oslo Sports Trauma Research Center. RRI was defined as "Running-related (training or competition) musculoskeletal pain in the lower limbs that causes a restriction on or stoppage of running (distance, speed, duration,

or training) for at least 7 days or 3 consecutive scheduled training sessions, or that requires the runner to consult a physician or other health professional".

Perspectives: The results can directly be implemented into practice in order to design runner-specific running schedules for HM with minimal injury risk. This will hopefully increase the number of HM-finishers, and their ability to continue a more active and healthier lifestyle.

P08.10 Sebastian Møller ACCIDENTAL DEATHS IN PEOPLE WITH EPILEPSY: A REGISTER-BASED COHORT STUDY

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Background: Epilepsy is associated with increased premature mortality. We investigated the risk of premature mortality from accidents in people with epilepsy (PWE) compared to the general population.

Methods: We created cohort of 3,431,393 people born in Denmark between 1960 and 2011 who were alive in 1980 and residing in Denmark. The follow-up period was from 1980 to 2011, and people were followed until death, emigration or end of follow-up (31 December 2011). Poisson regression was used to calculate mortality rate ratios (MRRs) adjusted for gender, age and calendar period.

Results: After 1,052,536 years of follow-up in PWE, 438 had died from an accident. In PWE, the mortality rate from accidents was almost 3 times higher compared to people without epilepsy (MRR: 2.92 (95% CI: 2.65-3.22)). The mortality was particularly high during the 1<sup>st</sup> year after diagnosis (MRR: 6.28 (95% CI: 4.77-8.28)). Psychiatric comorbidity was highly associated with the risk of accidents. In PWE the MRR was 20.85 (95% CI: 18.07-24.05) for co-occurring substance or alcohol misuse and 6.90 (95% CI: 6.03-7.90) for other psychiatric diagnoses compared to people with no epilepsy and psychiatric diagnoses.

Conclusion: The mortality from accidents is significantly increased in PWE, especially shortly after the diagnosis and in people with comorbid psychiatric disease. Increasing the information and the attention to these high risk groups may help reduce the mortality associated with epilepsy.

P09.01 Ann Mai Hindkjær THE EFFECT OF ORALLY ADMINSTRATED NITRATE ON RENAL AND  
Østergaard SYSTEMIC HAEMODYNAMICS, WATER AND SALT REGULATION, TUBULAR  
TRANSPORT PROTEINS AND VASOACTIVE HORMONES IN A  
RANDOMIZED, PLACEBO CONTROLLED, CROSSED OVER 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, saltregulation 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 four 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 2x2 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 and in period 4 1L of saline is administered to detect any difference in renal parameters after saltload.

Primary outcome are changes in renal plasma flow determined by renografi. Glomerular filtration rate is measured with constant infusion 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.

P09.02 Liv Marit Valen EFFECT OF PATIENT-INITIATED VERSUS FIXED-INTERVAL TELEPRO-  
Schougaard BASED OUTPATIENT FOLLOW-UP: STUDY PROTOCOL FOR A  
PRAGMATIC RANDOMISED CONTROLLED STUDY

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Background: The traditional system of routine outpatient follow-up of chronic disease in secondary care may involve a waste of resources if

patients are well. The use of patient-reported outcomes (PRO) could support more flexible, cost-saving follow-up activities. AmbuFlex is a PRO system used in outpatient follow-up in the Central Denmark Region. PRO questionnaires are sent to patients at fixed intervals. The clinicians use the PRO data to decide whether a patient needs a visit or not (standard telePRO). PRO may make patients become more involved in their own care pathway, which may improve their self-management. Better self-management may also be achieved by letting patients initiate contact. The aim of this study is to obtain data on the effects of patient-initiated follow-up (open access telePRO) on resource utilisation, quality of care, and the patient perspective.

Methods: The study is a pragmatic 2-arm randomized controlled trial. Participants are randomly assigned to one of two follow-up methods: a) standard telePRO; or b) open Access telePRO. Participants are epilepsy outpatients aged  $\geq 15$  years, referred to standard telePRO, and web-respondents recruited from the epilepsy clinic at Aarhus University Hospital. The number of contacts will be used as the primary outcome measure. Secondary outcome measures include well-being, general health, number of seizures, treatment side effects, mortality, health literacy, and self-efficacy. Data will be collected at baseline and 18 month after randomisation. Inclusion of patients started in January 2016.

Results: By July 2016, a total of 591 patients have been included; 346 in the open access arm and 245 in the standard arm.

P09.03 Klaus Ulrik Koch INFLUENCE OF VASOPRESSORS ON BRAIN OXYGENATION AND MICROCIRCULATION

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Background: Vasopressors are used to increase the blood pressure to maintain an adequate cerebral perfusion during anesthesia and surgery. Either beta agonist vasopressors as ephedrine or alfa agonist vasopressors like phenylephrine are used to raise the blood pressure during induction of anesthesia. However, the effects on brain oxygenation and micirculation are unknown. We, therefore, compared the effects of ephedrine and phenylephrine on brain oxygenation and microcirculation on patients undergoing surgery for cerebral tumors.

Aim and hypothesis: The objective of the study is to examine whether the choice of vasopressor treatment during anesthesia influences brain oxygenation and microcirculation. We hypothesize that the use of

phenylephrine is associated with a reduction in brain oxygenation and microcirculation by altering the capillary transit time heterogeneity and decreasing the oxygen extraction fraction compared to ephedrine.

Methods: The study is an investigator-initiated, single-center, double-blinded randomized study. Patients with brain tumors and scheduled for craniotomy are randomized to receive either ephedrine or phenylephrine infusion during general anesthesia prior to examination with either MRI or PET/CT. In both studies, 20-30 patient will be examined.

Conclusion: The possible dissimilar effects of alfa agonists and beta agonists on cerebral oxygenation may be caused by different influences on cerebral blood flow or alternated capillary transit time heterogeneity. The study is ongoing, and no results are available at present.

P09.04 Stine Andersen ASSESSMENT OF FIBROSIS AND THE EFFECTS OF PIRFENIDONE IN EXPERIMENTAL RIGHT HEART FAILURE

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Background: Fibrosis is increasingly recognized as a major pathophysiological factor in the development of right heart failure. In a pulmonary trunk banding (PTB) model of pressure overload induced right ventricular (RV) failure, we aimed to quantify RV fibrosis and evaluate the effects of treatment with the antifibrotic agent pirfenidone.

Methods and results: Male Wistar rats were randomized to PTB or sham operation (sham, n=11). One week after the procedure, RV function was assessed by echocardiography, and PTB rats were randomized to vehicle (PTB, n=11) or pirfenidone treatment (PTB+pirf, n=10). Sham operated rats received vehicle treatment. After six weeks of treatment, hemodynamics was evaluated by echocardiography, magnetic resonance imaging and pressure-volume measurements, and the hearts were excised for evaluation of RV fibrosis by stereology and molecular analyses.

Banding of the pulmonary trunk induced RV failure verified by the presence of RV dysfunction (cardiac output: PTB vs sham 0.057 L/min [0.052;0.063] vs 0.133 L/min [0.124;0.143], p<0.001) and RV hypertrophy (RV weight adjusted for tibia length: PTB vs sham 12.0 mg/mm [11.1;13.1] vs 5.4 mg/mm [5.1;5.7], p<0.001). Treatment with pirfenidone

did not reduce the degree of RV hypertrophy or improve cardiac output compared to vehicle treatment.

Conclusions: In our PTB model of pressure overload induced RV failure, treatment with pirfenidone did not affect RV hypertrophy or function. These are preliminary results, and further analyses of RV tissue are required to assess the development of fibrosis in the pressure overloaded RV and evaluate the effects of pirfenidone on this development.

- P09.05 Rasmus Fuglsang  
Nielsen DIETARY FIBER AND WHEY PROTEIN: THE EFFECT ON RISK MARKERS OF THE METABOLIC SYNDROME IN ABDOMINALLY OBESE SUBJECTS - A 12-WEEK PARALLEL, DOUBLE-BLINDED INTERVENTION STUDY

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Background: Since the 1980s, obesity has more than doubled worldwide, leading to an increased prevalence of metabolic syndrome (MeS), which is defined by a cluster of risk factors associated with an increased risk of type 2 diabetes (T2D) and cardiovascular disease (CVD). Studies indicate that dietary fibers as well as whey protein may have preventive potential against MeS. However, findings have been inconsistent.

Objective: To examine the individual and additive effects of a 12-week dietary intervention with dietary fibers from wheat and whey protein on MeS risk markers in subjects with abdominal obesity. Primary outcome is change in postprandial lipaemia. Secondary outcomes are insulin sensitivity, p-incretins, p-lipids, satiety measures, 24 h blood pressure, augmentation index, waist and hip circumference, energy expenditure and body composition.

Methods: The trial is a randomized, double-blinded, parallel interventional study. Eighty abdominally obese subjects are randomized to one of four intervention groups: 1) Low protein/Low fiber, 2) Low protein/High fiber, 3) High protein/Low fiber or 4) High protein/High fiber. The 12-week intervention period is preceded by a 7-day run-in. Bread and cereals of high/low fiber content are incorporated into the habitual diet of the subject. Whey protein (high/low) is supplemented twice daily. Pre- and post-intervention data as described are ultimately analyzed and compared.

Perspectives: Implementation of dietary fibers and whey protein in the daily diet is a potentially simple and cost-efficient means to prevent T2D and CVD. Consequently, the findings from the present study will be of marked interest in preventive health care.

P09.06 Lea Lykke  
Lauridsen

#### GESTATIONAL DISEASES AND ONSET OF PUBERTY IN OFFSPRING

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Secular trends in pubertal maturation have been observed throughout the world. In many countries, including Denmark, the age at menarche has fallen rapidly since the late 19th century. Only few etiological factors of altered pubertal timing have consistently been reported. This project will be among the first to investigate whether gestational diseases are important factors in accelerating the age at which children enter puberty. Diabetes mellitus, thyroid diseases and pre-eclampsia are all diseases that affect the hormonal balance of the body. However, it is not clear whether such imbalance, during a period of time where the hormonal and reproductive organs in the fetus are developed, may have a programming effect on the child's pubertal development later in life.

In this project, we will 1) investigate the possible effect of diabetes mellitus, thyroid diseases and pre-eclampsia during pregnancy on the onset of pubertal development in offspring, 2) investigate whether diabetes mellitus, thyroid diseases and pre-eclampsia during pregnancy increase the risk of precocious puberty in sons and daughters, 3) validate the accuracy of the self-reported pubertal stage in the PredicPub Cohort (a sub-cohort of the Danish National Birth Cohort) compared to clinical examinations.

Until now, most etiological studies on onset of puberty have been limited by recall bias, a large number of missing data and low statistical power. By using large cohorts with prospectively collected data on both the children's fetal exposures and on puberty onset, as well as registry based information, we are able to gain new and important knowledge on the causes of changes in the timing of puberty onset.

P09.07 Katrine Andersen EPILEPSY AND SCHIZOPHRENIA HAVE INCREASED RISK OF PREMATURE MORTALITY: A NATION-WIDE COHORT STUDY

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Purpose: Persons with epilepsy have excess premature mortality, in particular with comorbid psychiatric disorders. We assessed the overall mortality for people with epilepsy and schizophrenia in absolute and relative measures.

Methods: We identified 1,620,377 persons born in Denmark between 1960 and 1987, who were alive and residing in Denmark by their 25<sup>th</sup> birthday. Participants were followed from their 25<sup>th</sup> birthday to death, emigration, or 31 December 2012. Diagnoses of epilepsy, schizophrenia, or both epilepsy and schizophrenia prior to their 25<sup>th</sup> birthday were determined. The primary outcome was overall mortality. We conducted sub-analyses with stratification by sex, a stricter definition of schizophrenia, and with follow-up from participants' 20<sup>th</sup> and 30<sup>th</sup> birthday.

Results: Total follow-up time was 24,167,574 person years; median 15 years. Adjusted mortality rate ratios (aMRR) for epilepsy and schizophrenia compared with a reference group without these disorders were; epilepsy aMRR 4.4 (95% CI, 4.1-4.7), schizophrenia aMRR 6.6 (95% CI, 6.1-7.1), and epilepsy and schizophrenia aMRR 12.8 (95% CI, 9.1-18.1). Sub-analyses did not modify the estimates. Estimated cumulative mortality at the age of 50 were; without epilepsy and schizophrenia 3.1% (95% CI, 3.0-3.1%), with epilepsy 10.3% (95% CI, 9.3-11.3%), with schizophrenia 16.7% (95% CI, 15.4-18.2%), and with both epilepsy and schizophrenia 27.2% (95% CI, 15.7-40.1%).

Interpretation: The combination of epilepsy and schizophrenia was associated with a high mortality in both relative and absolute terms. Identifying and treating schizophrenia and epilepsy among persons with comorbid disorders should be a priority.

P09.08 Anne Sofie Dam Laursen SUBSTITUTIONS OF DAIRY PRODUCT INTAKE AND RISK OF STROKE - A DANISH COHORT STUDY

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Low-fat dairy products are part of the dietary guidelines. However, evidence regarding dairy product intake and risk of stroke is inconclusive. We, therefore, investigated the associations for substitutions between subgroups of dairy products and risk of stroke.

We recruited 57,053 Danish men and women aged 50-64 years. After excluding participants with prevalent stroke or missing data, 55,211 were left for analysis. At baseline, the participants reported their habitual dietary intake in a validated 192-item semi-quantitative food frequency questionnaire. Strokes were identified in national registers and validated by review of each medical record. The associations were analyzed using Cox proportional hazards regression.

During a median follow-up of 13.4 years, we identified 2,272 strokes, of which 1,870 were ischemic and 389 were hemorrhagic. Substitution of semi-skimmed fermented milk for whole-fat fermented milk was associated with a higher rate of ischemic stroke (hazard ratio (HR)=1.23 (95% confidence interval (CI): 1.02-1.49) per 1 serving/day substituted), and substitutions of whole-fat fermented milk for low-fat milk, whole-fat milk or buttermilk were associated with a lower rate (low-fat milk: HR=0.84 (95% CI: 0.72-0.97), whole-fat milk: HR=0.83 (95% CI: 0.71-0.97) and buttermilk: HR=0.82 (95% CI: 0.68-0.97) per 1 serving/day substituted). We observed no associations for substitutions between dairy product subgroups and risk of hemorrhagic stroke.

Our results suggest that intake of whole-fat fermented milk as a substitution for semi-skimmed fermented milk, buttermilk or milk, regardless of fat content, is associated with a lower rate of ischemic stroke.

P09.09 Mette Wulf  
Christensen

IS POOR OVARIAN RESPONSE IN FERTILITY TREATMENT ASSOCIATED WITH AN ACCELERATED GENERAL SOMATIC AGEING?

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Introduction: A reduced ovarian reserve in younger women results in early ovarian ageing, reduced fertility and early menopause (EM). Women at risk of EM may be revealed at the fertility clinics when only few oocytes are harvested despite high doses of FSH. This is termed poor ovarian response (POR). Early menopause is associated with increased early incidence of cardiovascular diseases and a shorter survival. We hypothesize that the increased morbidity and mortality associated with EM represent a general ageing starting before menopause, e.g. POR in young women may be a marker of an accelerated somatic ageing.

Aim: To investigate the association of early somatic ageing and POR in young women.

Material and methods: A prospective cohort study of 50 women with POR and 50 women with normal ovarian response as reference group. The level of low-grade inflammation, the prevalence of cardiovascular risk indicators, telomere shortening and methylation in lymphocytes are evaluated as biochemical and genetic indicators of accelerated somatic ageing. Further, the association of POR and early somatic ageing is evaluated in a historical cohort study based on information from the National IVF Registry and the National Patient Registry.

Perspectives: The study will provide new information on the biological changes associated to early ovarian ageing and will demonstrate if the somatic ageing process associated to early menopause is present even before menopause occurs.

P09.10 Sofie Gottschalk Højfeldt HLA-DQA2 INVOLVED IN ALLERGIC REACTIONS TO PEG-ASPARAGINASE - A GENOME WIDE ASSOCIATION STUDY ON THE NOPHO ALL 2008 PROTOCOL

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Pegylated asparaginase (PEG-asp) is an essential part of the treatment of acute lymphoblastic leukemia (ALL) in children. However, 13% of the patients experience an allergic reaction to the drug and must truncate their treatment. Previous studies have shown that patients with these allergic reactions have no enzyme activity.

The aim of this study was to investigate if a genetic predisposition exists to the development of allergic reactions to PEG-asp. A genome wide association study (GWAS) was performed in order to determine the genetic differences between those with an allergic reaction to PEG-asp and those without.

In total, 1288 children treated according to the NOPHO ALL-2008 protocol were eligible for inclusion; 178 children were registered with an allergic reaction to PEG-asp. In order to support the phenotype, asparaginase enzyme measurement without any activity was used as an inclusion criterion in the case group. Data on enzyme measurements was available on 66 cases. In total, 53 cases and 670 controls met the inclusion criteria for the GWAS and passed the quality control. Germline DNA was genotyped on Omni2.5exome-8-v2.1 BeadChip arrays.

The preliminary results show a tendency towards a genetic difference between cases and controls, but while working with the data, new ideas and possibilities have emerged. The HLA-DQA2 variant rs9275599 showed strong association with allergic reactions to PEG-asp ( $P=6.9e-6$ ;  $OR=2.9$ ), but not on a genome wide significance level.

This is, to our knowledge, the first GWAS on PEG-asp allergy that takes enzyme activity into account in the phenotype description. This could be essential since clinical presentations of the allergic reactions are so diverse.



encephalitis (HSE). Although macrophages of the CNS, microglia, detect the virus and initiate immune mechanisms, it still remains unclear which cells first sense the virus in the CNS, and which molecular pathways are activated in order to prime the recruitment of microglia to the site of infection in order to eliminate the infection. To address these questions, we hypothesize that neurons, astrocytes and/or microglia first detect HSV-1 and initiate innate immune responses leading to the production of one or more chemokines, which in turn attract resident microglia and infiltrating monocytes/ microglia to the infected site. In this project, cornea scarification will be performed to simulate an in vivo mouse model of HSE. To identify which chemokine is responsible for the migration of microglia, we will test chemokine- and chemokine receptor-deficient mouse strains and generate knockout cell types of the chemokine of interest. In addition, we will isolate primary microglia, astrocytes and/or neurons from various PRR-deficient newborn mice to investigate which signaling pathways of the innate immune system lead to the production of the chemokine of interest. These approaches will allow us to delineate the key elements of cellular crosstalk and molecular mechanisms behind HSV-1 sensing in the CNS and the recruitment of microglia in order to gain a clearer understanding of the immune responses during the early stages of HSE.

P10.03 Camilla  
Kjersgaard

LIFESTYLE DURING PREGNANCY AND RISK OF CRYPTORCHIDISM IN SONS

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Background: Cryptorchidism (undescended testis) is one of the most common congenital malformation worldwide. Studies have suggested that smoking, overweight, caffeine and alcohol consumption during pregnancy may be possible risk factors for the malformation. However, previous studies are small, inconsistent or, for some exposures, non-existing.

Aim: We aim to explore the associations between prenatal exposure to maternal lifestyle factors and the risk of having a son with cryptorchidism.

Materials and methods: We will use data from the Danish National Birth Cohort and the Aarhus Birth Cohort with approximately 90,000 mother-son pairs. Data will be linked to several Danish health registers and Cox proportional hazards models will be carried out to assess these associations.

Results: Data currently undergo cleaning, and the analytic strategy is planned. We expect to present the results at the PhD Day 2017.

Perspectives: This study will be the largest of its kind and will hopefully add important knowledge to the existing literature. The malformation is suspected to increase risk of infertility and testicular cancer and by identifying risk factors for cryptorchidism; one could potentially increase the long-term health of younger men.

P10.04 Mai-Britt Worm  
Ørntoft COMPREHENSIVE ANALYSIS OF 13 DIFFERENT METHODS FOR BISULFITE  
CONVERSION OF CIRCULATING CELL-FREE DNA

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Both healthy and pathologically altered cells in the body release DNA by apoptosis/necrosis into the bloodstream, referred to as circulating cell-free DNA (cfDNA). cfDNA "real-time" biomarkers are becoming popular in disease screening, diagnostics, and surveillance through "minimally-invasive liquid biopsies" (i.e. blood samples). Subsequent evaluation of pathological cfDNA traits could address increased DNA quantity, chromosomal alterations, mutations, and epigenetic changes. Among the latter, DNA methylation is a promising marker of disease, particularly cancer, as aberrant methylation is known to arise early in pathogenesis.

A significant challenge for the clinical utilization of cfDNA as a biomarker is the small size of cfDNA (~167 bp) and the very limited amount present in blood samples, compared to traditional biomarkers. This has required establishment of alternative, more efficient strategies for cfDNA purification and application of ultrasensitive detection methods, such as digital droplet PCR. However, few efforts have focused on ensuring high recovery and high efficiency during the bisulphite conversion of cfDNA required for application of methylation-based biomarkers.

To identify the most suited method for bisulfite conversion of cfDNA, we directly compared 13 different methods. We found clear differences in performance, primarily in terms of cfDNA loss, but also in conversion efficiency upon analysis of both genomic and cfDNA-sized DNA. Collectively, our comprehensive comparison reveals the methods best suited for cfDNA methylation biomarker pipelines.

P10.05 Lene Holst  
Pedersen EARLY GERIATRIC FOLLOW-UP AFTER DISCHARGE REDUCES  
READMISSIONS AMONG PATIENTS DISCHARGED TO NURSING HOMES

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Objectives: To examine if early geriatric follow-up after discharge reduces readmissions in patients discharged to nursing homes.

Method: The present study is a subgroup analysis of a quasi-randomised controlled trial. The analysis includes permanent nursing home residents and patients discharged to a short stay in a nursing home.

Patients were 75 years or older and admitted to the emergency department (ED) with one of following diagnoses: pneumonia, COPD, dehydration, delirium, constipation, anaemia, heart failure, urinary tract infection or other infections.

Both patients in the control and intervention groups received comprehensive geriatric assessment before being discharged or transferred to a geriatric ward. The intervention comprised a visit by a nurse and a doctor from the geriatric department on the first working day after discharge. In addition, the patients could to contact the team on specific days.

Results: From 1 June 2014 to 31 August 2016, 703 patients were discharged to nursing homes. Baseline characteristics did not differ between the two groups, except for more women in the control group. The readmission rate was significantly reduced in the intervention group (13%) compared to the control group (22%),  $p=0.004$ .

The hazard ratio (HR) was adjusted for age, sex, comorbidity, admission diagnosis, and walking ability. The intervention group had a lower risk of readmissions (HR=0.57 (95% CI: 0.39-0.81)).

None of the adjustment variables were independent risk factors.

Conclusion: Early geriatric follow-up after discharge reduces readmissions among patients discharged to a nursing home.

P10.06 Søren Bruno  
Elmgreen

RESTORING LOCOMOTION IN SPINAL CORD INJURY: A RANDOMIZED CONTROLLED TRIAL OF THE LION PROCEDURE

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Possover and co-workers pioneered a minimally invasive and fully reversible laparoscopic implantation technique allowing for precise placement of electrodes for continuous low-frequency stimulation of pelvic nerves to control micturition. Unexpectedly, Possover made the clinical observation that four patients with chronic traumatic spinal cord

injury (SCI) regained significant sensory and motor function following this laparoscopic implantation of neuroprosthesis (LION).

Our aim is, therefore, to conduct a prospective randomized active-controlled trial with elaborate neurophysiological and clinical assessment at baseline and 12-month follow-up to evaluate the effects of the LION procedure in subjects with traumatic SCI.

Primary endpoint of the study is change in study participants' ability to ambulate assessed by the Walking Index for SCI (WISCI) and the 10 meter walk test. Secondary endpoints include changes in independence assessed by the Spinal Cord Independence Measure (SCIM), changes in objective neurophysiological measures of motor, sensory, and autonomic functioning, and changes in pain and quality of life assessed by validated clinimetric scales.

Having shown promising results, the LION procedure could be a game changer in the rehabilitation of SCI improving both motor and sensory functioning in subjects who have otherwise exhausted their possibilities for further progress; ultimately, the LION procedure could help reduce the burden of long-term complications after SCI.

P10.07 Jacob  
Gammelgaard  
Schultz

#### A NOVEL MODEL OF ACUTE PULMONARY EMBOLISM IN PIGS

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Background: Acute pulmonary embolism is a common disease with a high mortality. A cornerstone in the treatment is thrombolytic therapy. However, one third of patients have contraindications due to increased risk of major bleeding. Catheter directed embolectomy has shown promise as a new approach to effective thrombus removal without the risks of standard treatment. However, an experimental model of acute pulmonary embolism enabling controlled evaluations of novel catheter directed therapies is lacking. Therefore, we aimed to develop and characterize a model of acute pulmonary embolism in pigs.

Materials and methods: 8 Danish Landrace pigs were anaesthetized and ventilated by a mechanical ventilator. Two preformed autologous blood clots were administered consecutively in the lungs via a large catheter inserted in the right external jugular vein. The hemodynamic and biochemical effects were evaluated by repeated invasive pressure measurements, Magnetic Resonance Imaging (MRI) and blood analysis.

Results: We created large centrally located autologous pulmonary embolisms visualized by MRI. After the first embolism, pigs showed signs of right ventricular strain with increased pulmonary artery pressure (PAP)

with no change in heart rate or blood pressure. After the second embolism, right ventricular function further deteriorated evident by a further increase in PAP and an increase in heart rate. Systolic blood pressure, however, remained unchanged. Further data on the hemodynamic and biochemical response are yet to be analyzed and will be presented at PhD Day.

Conclusion: We succeeded in creating a model of large centrally located autologous pulmonary embolisms in pigs.

P10.08 Amr Abou Elezz ALL FILAMENTS ARE EQUAL, BUT SOME FILAMENTS ARE MORE EQUAL THAN OTHERS

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The axon initial segment (AIS) is the site of action potential initiation and plays an important role in regulating neuronal excitability. In addition, the AIS is important for establishing and maintaining neuronal polarity. AIS functions are largely the result of a unique structural and cytoskeletal arrangement that remains poorly understood. This study investigates the AIS actin cytoskeleton.

We found a distinct population of stable, tropomyosin-decorated actin filaments in the mature AIS that is essential for overall AIS integrity. Specifically targeting this population of filaments led to the loss of sodium channel clustering, a loss of the accumulation of AIS structural proteins ankyrinG and neurofascin-186, as well as a loss of polarity and redistribution of somatodendritic proteins. These data shed new light on AIS structure and function and may help to identify new targets for treating neuronal excitability disorders.

P10.09 Christine Ladegaard Geyti MENTAL HEALTH ASSESSMENT IN HEALTH CHECK CAN IMPROVE RECOGNITION OF UNACKNOWLEDGED POOR MENTAL HEALTH: A LARGE-SCALE COHORT STUDY

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Introduction: Poor mental health (MH) is a growing public health concern with human, social, and economic costs. Early recognition of poor MH allows prevention, but is still not systematic delivered in primary care. This

study evaluated the use of MH assessment in general health check.

Aim: Investigate association between MH, physical health, and socio-demography in persons participating in health check Examine level of MH care among persons recognized with poor MH.

Method: A cohort study with 9767 randomly selected 30-49-year-olds invited to health check; 4871 (50%) participated and reported on MH; 49% were men. Data were obtained from questionnaires and national registers. Poor MH defined from SF-12 as mental health component score <35.76. MH care defined as at least one of the following within 12 months prior to date of participation: psychotropic medication, psychological therapy, psychometric test used by GP and/or contact to psychiatrist.

Results: Poor MH was reported by 7% of the men and 11% of the women. Low education (24 vs. 13%) and living alone (32 vs. 20%) were more commonly associated with poor MH than with better MH. Persons with poor MH were more likely to smoke (29%) than persons with better MH (17%). One out of eight (12%) with poor MH and 7% with better MH were burdened by more than 3 chronic diseases. Fifty-five % of participants with poor MH did not receive MH care.

Conclusion: Health checks that include MH assessment can improve recognition of persons with poor MH. People with poor MH identified at health check are more disadvantaged regarding physical health and socioeconomic status. More than half of persons with poor MH did not receive MH care.

P10.10 Per Mose Nielsen RENAL ISCHEMIA/REPERFUSION NECROSIS MONITORING WITH HYPERPOLARIZED FUMARATE

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Synopsis: Renal ischemia/reperfusion injury is a leading cause of acute kidney injury in several disease states; there is a current lack of precise methods to directly assess kidney injury. In the present study, we investigated the in situ conversion of hyperpolarised <sup>13</sup>C-fumarate to <sup>13</sup>C-malate in a unilateral ischemia/reperfusion model. The MR detectable <sup>13</sup>C from fumarate loses signal within minutes. This means that a turnover of fumarate-to malate is only seen if plasma membrane and mitochondrial membranes are disrupted under necrotic conditions. We saw a strong binary [1,4-<sup>13</sup>C<sub>2</sub>]malate signal in the postischemic kidney and a strong binary [1,4-<sup>13</sup>C<sub>2</sub>]fumarate signal in the healthy contralateral kidney. This was correlated with histological examinations indication

renal tubular necrosis. Furthermore, the ischemia/reperfusion injury also led to fumarase release to urine and blood, which was detectable with standard colorimetric fumarase assay. Together, this might give rise to a new biomarker of necrosis. General necrosis can be detected using a fumarase assay on blood and/or urine. The necrotic tissue can then be localized using the more sensitive hyperpolarized  $^{13}\text{C}$ -fumarate.

P11.01 Marianne Bjerre MOLECULAR ANALYSES OF CIRCULATING TUMOR DNA FOR DEVELOPMENT OF NOVEL DIAGNOSTIC AND PROGNOSTIC BIOMARKERS FOR PROSTATE CANCER

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Overdiagnosis and overtreatment of prostate cancer (PC) is today a major challenge, and there is an urgent need for novel diagnostic and prognostic molecular biomarkers for PC. Tumors shed DNA into the blood, known as circulating tumor DNA (ctDNA), and cancer-specific DNA methylation aberrations have shown particularly promising biomarker potential for PC. Here, we hypothesize that ctDNA represents a clinically relevant liquid tumor biopsy for PC and thus could be a novel source for discovery of new minimally-invasive diagnostic and prognostic biomarkers. The aim of this project is to identify and validate novel diagnostic and prognostic DNA methylation biomarker candidates in blood (plasma). We used the Marmal-Aid public database, which contains DNA methylome data from > 10.000 tissue samples, to identify novel PC-specific candidate methylation markers based on 5031 samples (males only). We selected 11 marker candidates displaying a very high sensitivity and specificity for PC, all being significantly hypermethylated in PC tissue as compared with non-malignant prostate tissue, other cancer tissues and normal blood cells. The diagnostic and prognostic potential of the top candidate markers will be assessed using methylation-specific digital droplet PCR in plasma samples from large patient cohorts, including men with vs. without PC, recurrent vs. non-recurrent PC after radical prostatectomy, and localized vs. metastatic PC. At the end of the study, we hope to have identified a novel set of diagnostic and prognostic ctDNA-based biomarker candidates in plasma, which in the future may be used to improve the accuracy of PC diagnosis and/or help guide treatment decisions.

P11.02 Line Amalie  
Aarestrup  
Hellemose

## ACCIDENTAL DEATHS AMONG PERSONS WITH SCHIZOPHRENIA

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Objectives: Persons with schizophrenia have a 20-year shorter life expectancy than the background population. Little is known about deaths caused by accidents among persons with schizophrenia, but it is plausible, that accidents contribute substantial to the shorter life expectancy.

We aimed to investigate the rates of accidental death among persons with schizophrenia, and compare them with those of the background population.

Methods: We conducted a national register-based cohort study of all persons born between 1955 and 2011. Death caused by accidents was compared between persons with schizophrenia to those without. The main outcome measure was hazard ratios (HRs); deaths from accidental cause. The cohort included 2,703,307 persons representing 56,845,085 person-years at risk.

Results: In total, there were 12,425 accidental deaths in the population, including 312 accidental deaths among persons with schizophrenia. Women with schizophrenia had a higher HR (10,47; 95% CI=8,07-13,58) than the background population. Men with schizophrenia had higher HR (8,33; 95% CI=7,44-9,33) as well. After adjusting for substance abuse, we found lower HRs for both women (HR=3,22; 95% CI=2,46-4,20) and men (HR=3,23 ; 95% CI=2,87-3,63).

Conclusions: Schizophrenia is a strong independent risk factor for deaths caused by accidents. Substance abuse is a substantial part of the association.

P11.03 Steffen Nielsen

## RADIOBIOLOGY IN PROTON THERAPY

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Background: Radiotherapy using external proton beams provides a more precise in depth dose distribution compared to conventional photon beams. It is well established that the extent of adverse effects following conventional radiotherapy vary significantly between patients due to genetic differences. There has only been limited focus on radiobiology and patient specific radiation sensitivity in proton therapy.

The primary objective was to identify differences in gene expression

patterns specific to radiation type and position in the beam. The secondary objective was to determine whether a 9-gene predictive test for risk of developing radiation-induced fibrosis following conventional radiotherapy can be applied for proton therapy.

Methods: The study includes 30 primary fibroblast cell lines, which were exposed to different proton irradiation conditions or Co-60 reference irradiation. For each treatment condition, fibroblasts were given 3 fractions of 3.5 GyE. Total RNA was extracted from cell lysates, and qPCR was performed to establish gene expression levels.

Results and conclusion: Induced expression levels of genes, such as CXCL12, FAP, IL8 and VEGF-A, were shown to depend on radiation type and position in the proton beam. The most substantial differences were observed in fibroblasts exposed to proton irradiation and positioned at the distal end of the beam. The differences in gene expression levels between radioresistant and radiosensitive fibroblasts were the same in all treatment groups, suggesting the test might be used to identify radioresistant patients in proton therapy.

- P11.04 Lene Margrethe Ring Madsen BONE TURN-OVER IN ROUX-EN-Y GASTRIC BYPASS OPERATED TYPE 2 DIABETIC PATIENTS COMPARED TO NON-OPERATED TYPE 2 DIABETIC CONTROLS: A 6-YEAR FOLLOW-UP STUDY

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Introduction: Roux-en-Y gastric bypass is a highly effective treatment of severe obesity leading to both sustained weight loss as well as improvements in obesity-related comorbidities such as T2DM, hypertension, female infertility, and sleep apnea. The procedure involves the creation of a small gastric pouch that is anastomosed directly to the proximal jejunum, thus bypassing the greater part of the stomach and the duodenum. This leads to restricted food uptake and results in weight loss, but also malabsorption of B12, magnesium, phosphate, iron, calcium, vitamin D and other fat-soluble vitamins, some of which are important nutrients for bone metabolism.

Thus, we speculated that bone turn-over and bone health in the long term could be influenced in these patients, ultimately leading to increased risk of osteoporosis and fractures.

Methods: We conducted a clinical trial including 99 Roux-en-Y gastric bypass operated type 2 diabetic patients and 49 non-operated type 2 diabetic controls matched on age, gender and current body mass index. We evaluated markers of bone and calcium metabolism and anthropometric measures. Furthermore, we gathered information on

weight history, family history of osteoporosis, intake of dairy products and medication including calcium and vitamin D supplementation, exercise, menstrual status, and smoking habits from the participants.

Results: Baseline characteristics and results will be presented at PhD Day 2017.

Conclusion: Although overall metabolic consequences of Roux-en-Y gastric bypass are favorable, the effect of Roux-en-Y gastric bypass on bone metabolism may potentially be harmful. Data from the study will be presented at PhD Day 2017.

P11.05 Alice Knudsen DISTURBANCE OF MUCOSAL INTEGRITY - A NEW MEANS TO SENSE INFECTION AND INSTIGATE ANTIVIRAL DEFENSE

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Early activation of defense against infections is essential for clearance of infections and prevention of disease. Type I interferon (IFN)s are produced early after viral infections, and potently stimulate antiviral defense. However, it is now also emerging that type I IFNs contribute significantly to pathology, and there is an increasing interest in early antiviral mechanisms that act independently of this class of cytokines. The host laboratory recently identified a novel IFN-independent type of immune sensing of virus infections at mucosal surfaces. In this project, we will dissect the molecular mechanism through which this pathway is activated and will further explore the spectrum of antiviral activities that are activated following viral disturbance of mucosal integrity. To address the questions raised in the project, we will use a series of systems and technologies, including mouse models of mucosal virus infections, in vitro air-liquid interphase cell cultures of epithelial cells, CRISPR/Cas9-mediated genome editing, RNA sequencing, protein assay and confocal laser scanning microscopy. The project will lead to a mechanistic understanding of a novel principle in early pre-IFN antiviral immunity and will also provide new insight into how this system effectuates antiviral activity.

P11.06 Takwa Shaiman Aroankins IDENTIFICATION OF SUMOYLATED PROTEINS IN KIDNEY EPITHELIAL CELLS

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SUMO (small-ubiquitin-related-modifier) is a post-translational modification (PTM) of selective lysine (K) residues in target proteins. Three SUMO proteins (SUMO1-3) are expressed in mammalian cells, which exert a variety of functions to their target proteins e.g. SUMO

modifications appear to crosstalk with the ubiquitin proteasomal system, with some poly-SUMOylated proteins targeted by ubiquitin ligases and proteasomal degradation. Despite becoming increasingly recognized as an essential PTM, no previous studies have investigated the role of SUMO for protein function within kidney epithelial cells. To examine this, we generated four novel kidney cell lines, based on mouse distal convoluted tubule (mpkDCT) or cortical collecting duct (mpkCCD) cells, with stable expression of mutant forms of SUMO1 or SUMO2, where the preceding C-terminal Gly-Gly (diGly) residue of SUMO is replaced with a lysine and an N-terminal 6xHis-tag (CCD-/DCT-6xHisSUMO1<sup>KGG</sup> and CCD-/DCT-6xHisSUMO2<sup>KGG</sup>). This approach allowed two-step purification of in vivo SUMOylated proteins by Nickel-purification followed by peptide level enrichment using an antibody targeting KGG residues remaining on SUMOylated peptides following Lys-C digestion. Following enrichment, SUMOylated peptides were identified using LC-MS/MS. Using this approach, we have identified 1224 SUMO1 and 548 SUMO2 modified sites on proteins in CCD cells and 263 SUMO1 and 66 SUMO2 modified sites in DCT cells. Current investigations are utilizing a similar approach to determine how various hormones modulate the landscape of SUMOylated proteins.

P11.07 Kathrine  
Stokholm

PRE- AND POST-SYNAPTIC DOPAMINERGIC ALTERATIONS IN AN ALPHA  
SYNU-CLEIN RAT MODEL OF PARKINSON'S DISEASE

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Aim: Parkinson's disease (PD) is characterised by progressive degeneration of dopaminergic neurons in the substantia nigra (SN) and loss of striatal dopaminergic terminals. The protein alpha-synuclein (asyn) is implicated in PD pathogenesis, but its role in the early disease stages remains to be elucidated. The aim is to characterize changes in the dopamine system in a rat model of PD induced by asyn overexpression, shown previously to exhibit synaptic deficits in the absence of cell death.

Methods: Rats were injected with recombinant adeno-associated virus pseudotype 2/6 encoding human wild-type asyn or enhanced green fluorescent protein (eGFP) in the right SN. Motor performance was assessed with cylinder test ten weeks after the injections. At twelve weeks, rats were decapitated, and autoradiography was performed on

the brain tissue with the following tracers: [3H]-DTBZ, a tracer of the vesicular monoamine transporter 2 (VMAT2); [3H]-GBR12935, a tracer of the dopamine transporter (DAT); and [3H]-Raclopride, a tracer of dopamine 2/3 (D2/3) receptors.

Results: The asyn rats exhibited motor defects absent in the GFP group. Tracer binding in the asyn animals significantly declined with DTBZ and GBR12935 and increased with raclopride in the ipsilateral vs. contralateral striatum compared to the GFP group.

Conclusion: Reduced VMAT2 and DAT and increased D2 receptor expression together with asyn deposition and motor impairments replicates the pathology observed in PD patients. These changes in the absence of cell death makes this asyn model relevant to study treatments in early PD, when there is a greater chance to modify the disease course.

P11.08 Johanne Marie Holst

SEARCH FOR AND CHARACTERIZATION OF POSSIBLE MOLECULAR RELATIONSHIPS BETWEEN LYMPHO- AND MYELO-PROLIFERATIVE NEOPLASMS OCCURRING IN THE SAME HOST

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Traditionally, lympho- and myelo-proliferative disorders have been regarded as having different pathogenetic mechanisms, leading to distinct therapeutic approaches. Recent studies have reported an increased risk of developing other types of malignancies in patients with chronic myeloproliferative neoplasms (MPN) (Frederiksen et al., Blood, 2011).

We hypothesize that patients with MPN are at increased risk of developing lymphoid neoplasms and that there exists a pathogenetic link between lymphoproliferative disorders and MPN.

Patients with both MPN and lymphoproliferative disorders from 1990 to 2015 were identified through the Danish Pathology Register. Patients are included on the basis of written descriptions of the diagnostic lymphoma and MPN biopsies to determine coexisting malignancies. In order to avoid therapy-related causes of development of MPN, a requirement for study inclusion was a primarily diagnosis with MPN and subsequently the lymphoproliferative disease.

Diagnostic lymphoma and MPN tissue specimens from 169 patients are under collection. All specimens are revised according to the 2008 edition of the WHO classification of Hematopoietic Tumors. The cohort includes a broad spectrum of lymphoproliferative diseases, from different

aggressive B-cell lymphomas to peripheral T-cell lymphomas and

chronic lymphocytic leukemia.

Establishment of this unique series of tissue specimens from patients with co-existing myelo- and lympho-proliferative diseases will allow us to proceed with genomic analyses in the search of defining driving mutations and will potentially lead to novel therapeutic approaches at both myeloid and lymphoid level.

P11.09 Mette Habekost STUDY OF APP INTRACELLULAR DOMAIN USING CELLS FROM A NEW PORCINE MODEL OF ALZHEIMER'S DISEASE

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Objectives: APP Intracellular Domain (AICD) implicated in gene regulation is difficult to study, as it is rapidly degraded and poorly detectable in cells and tissues. However, AICD is easily detectable in fibroblasts from a new porcine model of Alzheimer's Disease (AD).

Methods: Fibroblasts from non- and double-transgenic porcine fibroblasts carrying the APP<sup>sw</sup> and PSEN1 M146I mutations (both associated with early onset familial AD) were cultured with or without alpha-, beta- and gamma-secretase inhibitors to determine whether AICD produced from alpha-gamma and beta-gamma cleavage behave differently. Using western blotting, the levels of AICD were determined in whole-cell lysates and in nuclear and cytosolic fractions.

Results: Western blot analysis showed that AICD production was remarkably increased in fibroblasts from transgenic pigs compared to controls. Our preliminary nuclear enrichment experiments indicated that AICD is translocated to the nucleus, and we predict that it originates from the beta-gamma cleavage. Next, it would be interesting to study AICD mechanisms in a neuronal in vitro model generated from these animals.

Conclusions: We believe that transgenic pigs might be a valuable tool to further analyse the role played by AICD fragment in APP functions opening new perspectives in the comprehension of the mechanisms leading to AD.

P11.10 Ina Qvist PERSON CHARACTERISTICS AND EXPERIENCES ASSOCIATED WITH ADHERENCE TO PHARMACOLOGICAL TREATMENT AMONG 65-74 YEAR-OLD MEN IN CARDIOVASCULAR SCREENING STUDIES

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Background: Cardiovascular disease (CVD) can be prevented with blood pressure and cholesterol-lowering drugs. From the literature, we know that only 30-50% of heart medications are taken as prescribed. These conditions increase patients' morbidity, hospitalizations and mortality, which increases the overall cost of health care and impairs patients' quality of life. In a screening program for CVD, the effect will be eroded if a major proportion of the participants do not adhere to the recommended treatment. This is an area that suffers from lack research. Additionally, we need to explore if screening participants' health literacy and attitude to preventive medication can be a factor for adherence.

Aim: This study investigates personal characteristics, experience with pharmacological treatment and perception of own health as predictors of non-adherence to health counseling for participant in a screening program for CVD.

Methods: Participants from a cardiovascular screening program for men aged 65-74 years were interviewed before screening and will be interviewed one year after. All interviews will be audio-recorded and transcribed verbatim for Thematic Analysis. A register study will examine the extent of redemption of prescriptions during five years after screening and identify characteristics of adherence. A randomized study will clarify whether a phone call from a health care person four months after screening increases adherence.

Expected results: The study provides important scientific insight into the extent of adherence and person characteristics for non-adherence with pharmacological treatment. The new knowledge may be useful for special measures targeting this group.

P12.01 Martin Lund

QUALITY INDICATORS FOR SCREENING COLONOSCOPIES AND THE RISK OF INTERVAL CANCER ASSESSING THE PERFORMANCE OF COLONOSCOPISTS: A SYSTEMATIC REVIEW

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Purpose: To assess the strength of association between quality indicators related to the individual colonoscopist and subsequent interval cancer in patients participating in bowel cancer screening programs.

1. Are the commonly used quality indicators cecal intubation rate, adenoma detection rate, polyp recovery, withdrawal time, and incomplete adenoma resection/incomplete polyp resection associated with the outcome interval cancer?

2. Is it possible to find cut-off values, which are significantly associated with each of the quality indicators and the outcome interval cancer?

Methods: The method is to synthesize the evidence on the association between quality indicators, screening colonoscopists and the outcome interval cancer. A meta-analysis will combine the findings from the primary studies into a single overall summary estimate on each of the quality indicators related to the screening colonoscopists and the outcome interval cancer. Effect sizes will be expressed as relative risks for categorical data and weighted mean differences for continuous data and their 95% CI's will be calculated. A random effects model will be used, and heterogeneity will be assessed statistically using the standard Chi-square test.

Conclusion: The meta-analysis will give information about which quality indicators are the most relevant to use. In this way, it will be possible to monitor the quality of the screening colonoscopies and to set standards, which should be met in order to justify the level of quality in a bowel cancer screening program.

P12.02 Michael Christensen

METFORMIN INCREASES RENAL MEDULLARY PARTIAL OXYGEN TENSION

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Background: The type-2 diabetes drug metformin has shown protective effects in several renal diseases, including diabetic nephropathy, which is considered the most lethal complication of diabetes. The development of hypoxia in the kidney is suggested to be an important driving force of the development of diabetic nephropathy. We, therefore, want to investigate how metformin affects the oxygenation levels and mitochondrial function in the diabetic kidney.

Methods: Sprague Dawley rats were injected with streptozotocin (STZ) (50 mg/kg) and treated with metformin (250 mg/kg) in the drinking water. Four weeks later, the animals were anesthetized, placed on a

heating pad and tracheotomized. A catheter was placed in the left femoral vein for infusion of Ringer solution, and the left femoral artery was catheterized for blood pressure measurements and blood sampling. Catheters were placed in the left ureter as well as bladder for collection of urine. Furthermore, mitochondria was isolated from the kidney, and mitochondrial oxygen consumption was analyzed.

Important findings: The diabetic animals showed increased glomerular filtration rate (GFR), which was not affected by metformin treatment. The partial pressure of oxygen (PO<sub>2</sub>) was decreased both in the outer medulla and in cortex in the diabetic animals. Metformin treatment elevated PO<sub>2</sub> in the outer medulla both in the control animals and in the diabetic animals. Mitochondrial respiration data suggested an inhibition of mitochondrial uncoupling proteins (UCP).

Conclusion: Metformin increases PO<sub>2</sub> in the outer medulla both in control and diabetic animals; this could in part be mediated by inhibition of UCPs.

P12.03 Iben Lyskjær

PREDICTION OF THERAPY RESPONSE IN COLORECTAL CANCER TREATMENT USING CIRCULATING TUMOR DNA

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Recently, it has become increasingly clear that tumor evolution and tumor heterogeneity have to be implemented in the way we view, study, and treat cancer. So, it is necessary to monitor evolution longitudinally through the disease course and to adapt treatment as the tumor evolves.

This project aims to show the clinical benefits of monitoring tumor burden and evolution using circulating tumor DNA (ctDNA) from plasma of colorectal cancer (CRC) patients. We further aim to identify tumor specific mutations associated with drug resistance and to develop a clinically applicable approach to monitor tumor burden and evolution.

Blood and tumor samples have been collected from two cohorts of metastatic CRC patients (n =36) administrated 1<sup>st</sup> line treatment with either of the two main stay drugs: irinotecan or oxaliplatin. Biopsies have been collected from resected tumors, and blood samples drawn prior to drug treatment, day 1, 2 and 7 during the first 2-4 cycles and then every 14 days for the first 12 cycles.

Tumor evolution is studied by mutational profiling of tumor and plasma

ctDNA using ultra-deep targeted sequencing. This technology adds molecular barcodes to each original DNA fragment present in the plasma sample, consequently increasing the sensitivity to  $>1:10^4$  and allowing faithful distinguishing of sequencing errors from low frequency tumor subclones.

This project is expected to significantly increase our knowledge of how ongoing cancer evolution impacts the clinical management of CRC. Ultimately, continuous monitoring of tumor evolution will lead to better treatment of the individual patient since treatment can be altered in response to acquisition of new mutations.

P12.04 Rasmus Kold-Christensen

#### MONITORING REACTIVE METABOLITES BY ELISA

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Small endogenous metabolites are problematic to detect and quantify using conventional antibody based ELISAs, which is the routine method used in many biochemical laboratories. Furthermore, if the metabolite is reactive or unstable, quantitative ELISA is generally not even an option. Reliable quantification of reactive metabolites usually requires the use of a derivatization reagent followed by more advanced instrumental detection, such as chromatography and mass spectrometry. However, these techniques are not suitable for high-throughput screenings and often require expensive specialized equipment to be carried out. We have developed a simple, robust, and specific reaction-based capture ELISA (ReactELISA) that allows us to detect and quantify small reactive metabolites by ELISA. ReactELISA exploits the intrinsic chemical reactivity of the small metabolites using a bifunctional chemically synthesized probe with a capture group and a biotin affinity tag. A chemoselective reaction between the capture group and the metabolite in a complex matrix generates a stable adduct, and using the biotin affinity tag this adduct can be trapped and purified using streptavidin-coated microtiter plates. The adduct is then assayed by ELISA using an adduct-specific recombinant antibody.

Two bifunctional probes have currently been developed; one for the toxic dicarbonyl metabolite methylglyoxal, an unavoidable by-product of glycolysis, and one for the neuroprotective ketone body acetoacetate, a desired product of lipo-oxidative metabolism.

P12.05 Maria Celeste Fasano

#### NEURAL CHANGES AFTER MULTIMODAL LEARNING IN PIANISTS - AN FMRI STUDY

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Human behavior is inherently multimodal: we use different brain systems cooperatively combining multimodal input for a multimodal output. This is evident when pianists listen to music they know well and exhibit spontaneous activity in motor and premotor cortices. This link is well explained by the mirror neuron system. Here we investigated the interaction between multimodality of learning and mirror neuron system using ISC in a naturalistic setting. We presented 10 highly skilled pianists with audio, video and audio-video recordings of a sonata by D. Scarlatti (initially unfamiliar to all pianists) in three phases. During phase 1, each pianist was measured with functional magnetic resonance imaging while being presented with the recordings. In phase 2, pianists learned at home to play the sonata by heart for 4 weeks. Phase 3 was a repetition of phase 1. We examined the similarity between pianists' brain activity during stimulus presentation before and after learning by means of inter-subject correlation (ISC) analysis. We found that when presented with the audio-video recording after learning the pianists showed an increased synchronization in activating visual, auditory and motor areas. For the audio-only recording, after learning visual cortices become synchronized. Our study provides new information regarding inter-subject brain synchronization in response to natural stimulus before and after learning it. For the first time, we follow the neural formation of auditory-motor learning of a naturalistic music stimulus exploring and attesting the multimodality associated to this process.

P12.06 Anna Halling  
Folkmar  
Andersen  
Cancellation

A NOVEL DRUG DELIVERY PLATFORM EXHIBITS ENHANCED LYMPHOID LOCALIZATION AND POTENTLY DELIVERS ANTIRETROVIRAL THERAPY

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Background: Even on antiretroviral treatment, human immunodeficiency virus (HIV) replication persists in lymphoid tissues due to poor drug penetration to these organs, and treatment is complicated by short and un-identical half-lives of the antiviral drugs.

Methods: We used novel RAFT polymerization techniques to develop a new drug delivery strategy based on an albumin-polymer drug (APD) platform for the release of nucleotide-reverse transcriptase inhibitors (NRTIs), which inhibit the life cycle of HIV. To evaluate the potency of the platform, we employed a single-round replication HIV infection reporter

cell line, TZM-bl, which expresses luciferase upon HIV infection. We also utilized fluorescent versions of the APD to confirm cytosolic delivery by confocal microscopy and lymphatic tissue targeting in mice.

Results: In cell lines, we found that APDs with NRTIs potently inhibited viral infection (IC<sub>50</sub>=21 nM) (using equivalent drug content). Furthermore, we provide in vivo evidence that albumin conjugates with synthetic polymers accumulate in lymphoid tissues and have extended blood residence time compared to polymers without albumin (680 min vs. 320 min).

Perspectives: Our results show that the platform is responsible for delivery of high payloads therapeutic drug ratios to cells with increased circulation time in mice. With this work, we propose a possible strategy to achieve some highly desired abilities of antiretroviral treatment. We envision that the outcome of our approach will greatly improve drug delivery options for antiretroviral treatment. Moreover, we suggest that this drug delivery platform can have multiple applications for treatment of other infections besides HIV.

P12.07 Charlotte Nygaard

#### PRIMARY HEALTHCARE USE IN THE YEARS PRECEDING PRIMARY INTRACRANIAL TUMOUR DIAGNOSIS - A NATIONWIDE REGISTER STUDY

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Background: Knowledge of the pre-diagnostic healthcare use in primary intracranial tumour patients is sparse.

Aim: Describe the diagnostic activity in Danish primary healthcare two years prior to diagnosis of primary intracranial tumours in adults compared to a cancer-free reference group for both benign and malignant tumours.

Material and methods: The study includes all patients diagnosed with a first time primary intracranial tumour from 1 January 2004 to 31 December 2014, who were 30-90 years of age and with no prior cancer diagnosis (except non-melanoma skin cancer). For each case, ten references were identified. Differences in the frequency and timing of primary health care use (i.e. general practitioner (GP) and other private healthcare providers) are analysed by odds ratios (ORs) and monthly incidence rate ratios (IRRs).

Results: We identified 10,440 cases and 104,400 age- and sex-matched controls. Preliminary results show that both men and women with benign tumours had significantly more GP consultations than their references

during two years prior diagnosis, with an adjusted IRR two months prior to diagnosis of 1.82 (95%CI 1.69;1.96) and 1.72 (95%CI 1.63;1.81), respectively. Preliminary analyses show that both men and women with malignant tumours had significantly more GP consultations than their references from eight and nine months prior to diagnosis, respectively.

Conclusion: Preliminary results indicate that the increased primary health care use is seen within relatively close proximity to diagnosis for patients with malignant tumours, whereas patients with benign tumours have increased use of primary health care two years prior to diagnosis.

P12.08 Helle Gotfred-Rasmussen

SLEEPING SICKNESS: ELUCIDATING MECHANISMS FOR PARASITE RESISTANCE

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Sleeping Sickness or Human African Trypanosomiasis (HAT) is a lethal disease affecting more than 0.5 mio people in sub-Saharan Africa countries. Treating HAT is possible, but the best outcome for the patient is if HAT is diagnosed and treated in the early phase, while drugs used in later stage of HAT have more severe side effects.

One of two parasites causing HAT is *Trypanosoma brucei rhodesiense* (T. b. r.). T. b. r. escapes the immune response by changing its surface proteins with time, but being hemoauxotroph T. b. r. relies on the human host for heme. In the lysis of erythrocytes, hemoglobin (Hb) is released to the bloodstream, where it is bound to haptoglobin (Hp) or the structural similar protein: Haptoglobin related protein (Hpr), and both complexes can be endocytosed by T. b. r. When T. b. r. takes up the Hb-Hpr, it also takes up the Apolipoprotein L1 (Apo L1); Apo L1 will incorporate itself into the membrane of the lysosome, causing the lysosome to swell and finally burst and kill the parasite. To counteract this, T. b. r. expresses the Serum resistance associated (SRA) glycoprotein, which neutralizes the deadly effect of Apo L1.

The project will try to elucidate the structure of SRA and characterize its interaction with Apo L1 using X-ray crystallography and various biochemical techniques. Insights into the function of SRA and its ability to inhibit Apo L1 will provide a platform for development of new drugs for treating T. b. r. infections.

P12.09 Anne  
Ankerstjerne  
Rasmussen

## PATIENT-REPORTED OUTCOMES IN PATIENTS SUFFERING FROM HEART FAILURE: PREDICTORS OF ADVERSE OUTCOMES?

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Background: In Denmark, approximately 100,000 individuals suffer from heart failure (HF). HF is a serious condition with frequent contacts to the healthcare system and high mortality. Objective risk factors are established, while a substantial need remains for clarifying the prognostic significance of self-reported information. Patient-reported outcomes (PRO) measure patient's subjective assessment of health status, quantify patient's perspective on the disease, symptoms and impact on every day life. We propose a project that gives us opportunity to evaluate PRO at discharge and follow patients over time.

Objective: To study whether PRO predict one-year readmission, cardiac events and mortality in patients suffering from HF. To study the role of medical adherence as a possible intermediary factor in the association between PRO and one-year readmission, cardiac events and mortality in patients suffering from HF.

Methods:

Design: Cohort study with one-year register-based follow-up.

Inclusion: In total, 1,514 patients with a HF diagnosis who answered the DenHeart Questionnaire at discharge from one of the five heart centres in Denmark in 2013-2014.

The questionnaire data is linked to the following data sources: the Danish Civil Registration System, the Danish National Patient Registry, the Drug Statistics Register, the Danish Register of Causes of Death and medical records.

Perspectives: The perspective of this study is from PRO to identify a particularly vulnerable group of patients with HF who could benefit from a closer and more regular contact to the healthcare system. This could potentially avoid readmissions and improve the prognosis and quality of life.

P13.01 Sheyanth Mohanakumar THE MORPHOLOGY AND FUNCTION OF THE LYMPHATIC CIRCULATION IN FONTAN OPERATED PATIENTS

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Background: The lymphatics regulate the interstitial fluid by removing excessive fluid. It represents an extremely important step in the prevention of edema. The Fontan procedure has revolutionized the treatment of univentricular hearts. However, it is associated with severe complications such as protein-losing enteropathy (PLE) and peripheral edema that may involve the lymphatic circulation.

Hypothesis: Patients with a univentricular circulation have a reduced functionality of the lymphatic vasculature, which predisposes them to developing complications such as edema and PLE.

Methods: The functional state of lymphatics is investigated using near infrared fluorescence imaging, NIRF. The anatomy is described using non-contrast MRI, and the capillary filtration is measured using plethysmography. The study population is 10 patients with Fontan circulation operated at Aarhus University Hospital. Exclusion criteria is BMI > 30 and age < 18 years. The Fontan group will be compared with an age-, gender- and weight-matched control group (n=10) of healthy volunteers.

Results: Preliminary data (n=7) show that Fontan patients with clinical edema have a vast abnormal network of lymphatic collateralization. We also find a dilated thoracic duct with an abnormal course compared to normal. Lymphatic function in the Fontan group using NIRF shows a contraction frequency: 0.8(0.2) min<sup>-1</sup>, propulsion velocity: 2,4(0.4) cm/s and a pumping pressure: 53(4.4) mmHg. No significant difference is seen for these parameters between Fontan patients and controls.

Conclusion: The results indicate that lymphatics in some Fontan patients are abnormal with respect to morphology, while function seems not to be altered.

P13.02 Anne Gedebjerg MANNAN-BINDING LECTIN AND RISK OF COMPLICATIONS IN PATIENT WITH TYPE 2 DIABETES

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Medicine, Aarhus University, Aarhus, Denmark, <sup>4</sup>Department of Clinical Medicine, Aarhus University

Background: A better understanding of underlying biological mechanisms and risk prediction for microvascular and macrovascular complications and infections in Type 2 diabetes (T2D) is needed. Mannan-binding lectin (MBL) is a multifunctional protein involved in innate immunity that may affect susceptibility to infections and microvascular and macrovascular complications in T2D.

Aim: To investigate the link between MBL and T2D complications.

Materials and methods: We will conduct a nationwide cohort study of prospectively enrolled newly diagnosed T2D patients throughout Denmark, drawing on the unique cohort and biobank established by the Danish Centre for Strategic Research in Type 2 Diabetes (DD2) and on nationwide hospital, prescription, and laboratory databases. We will measure MBL in ~7,500 DD2 patients and follow them for development of myocardial infarction, stroke, nephropathy, antibiotic use, infections requiring hospitalization, and all-cause mortality. We will describe baseline cohort characteristics and calculate incidence rates of the outcomes under study and hazard ratios with 95% CIs using Cox proportional hazards regression analyses. We will examine the biological interaction of CRP and MBL by examining outcome rates and adjusted hazard ratios in patients with MBL elevation, CRP elevation, and both MBL and CRP elevation versus patients with neither factors elevated. We will investigate the influence of blood glucose, immune-modulatory diabetes medications, and MBL genotype according to polymorphisms in the MBL2 gene.

Perspectives: The proposed study may clarify whether MBL is a crucial link in the development of microvascular and macrovascular complications and infections in T2D.

P13.03 Safa Therwani

THE EFFECT OF VASOPRESSIN ANTAGONISM ON RENAL HANDLING OF WATER AND SODIUM AND CENTRAL AND BRACHIAL BLOOD PRESSURE DURING INHIBITION OF THE NITRIC OXIDE SYSTEM IN HEALTHY SUBJECTS: A DOSE-RESPONSE STUDY

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Background: Nitric Oxide (NO) has an effect on renal water and sodium excretion, but the effect is unknown in the principal cells of the nephron. In a dose-response study, we measured the effect of tolvaptan on renal handling of water and sodium and systemic hemodynamics during baseline and NO-inhibition with L-NMMA.

Methods: In a randomized, placebo-controlled double-blind, cross-over

study, 15 healthy subjects received tolvaptan 15, 30 and 45 mg or placebo.

L-NMMA was given as a bolus followed by continuous infusion during 60 minutes. We measured GFR, urine output (UO), free water clearance ( $C_{H_2O}$ ), fractional excretion of sodium ( $FE_{Na}$ ), urinary aquaporin-2 excretion (u-AQP2), urinary excretion of the  $\gamma$ -fragment of the epithelial sodium channel (u-ENaCy), plasma vasopressin (p-AVP), and central blood pressure (cBP).

Results: During baseline, tolvaptan increased UO and  $C_{H_2O}$ , whereas GFR and  $FE_{Na}$  were unchanged. P-AVP increased three fold. After NO inhibition, UO and  $C_{H_2O}$  decreased, but to a lesser extent during tolvaptan.  $FE_{Na}$  decreased only after placebo. U-AQP2 decreased to the same extent during all tolvaptan doses. U-ENaCy decreased only after placebo. Central BP increased after NO-inhibition.

Conclusion: During baseline conditions, tolvaptan increased renal water excretion in a dose dependent way. NO-inhibition antagonized the increases in renal water and sodium excretion by tolvaptan. The lack of decrease in u-AQP2 by tolvaptan could be due to a counteracting effect of elevated p-AVP.

P13.04 Marie Toft-Petersen

#### THE HUMAN MYELOID INHIBITORY C-TYPE LECTIN-LIKE RECEPTOR AID IN DISCRIMINATION OF BASOPHILS IN PERIPHERAL BLOOD

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Introduction: Immunophenotyping of basophilic granulocytes is based on a characteristic CD45dim/SSC low profile and a number of surface markers with the combination of CD123+/HLA-DR- being widely used (Chirumbolo, 2011). In peripheral blood (PB), the human Myeloid Inhibitory C-type lectin-like receptor (hMICL) (also named CLEC12A or CLL-1) is predominantly expressed on monocytes and granulocytes. In acute myeloid leukemia (AML), a 6-color multicolor flow cytometry (FCM) based assay including hMICL proved valuable in minimal residual disease detection (Roug, 2014). We find the same FCM panel useful in discriminating basophils in PB as being CD45low/SSClow/CD14-/CD123+/hMICL+/CD34-/CD117-.

Results: We studied PB from 20 diagnostic stable phase chronic myeloid leukemia (CML) samples and 8 normal controls. By FCM, the median percentage of basophils from CML patients was 2.3 (range 0.5-10.1%). The equivalent percentage was 0.7 (range 0.5-1.0%) in normal PB. For

the CML samples, the basophilic percentages correlated with the manual differential blood counts ( $r=0.69$ ;  $p=0.0007$ ).

Fluorescent activated cell sorting and subsequent Giemsa stained cytopsin preparations morphologically confirmed the CD45<sup>low</sup>/SSC<sup>low</sup>/CD14<sup>-</sup>/hM1CL<sup>+</sup>/CD123<sup>+</sup> cell subset to be highly enriched for basophilic granulocytes ( $n=1$ ).

Perspectives: The combination of hM1CL and CD123 is a promising marker of basophilic granulocytes. The FCM based assay is easily applicable and consists of surface markers widely used in the diagnostics of myeloid disorders. Importantly, awareness of the basophilic population is crucial when using hM1CL and/or CD123 as a marker of minimal residual disease, especially in CD34<sup>-</sup>/CD117<sup>-</sup> AML.

P13.05 Anders Valdemar Edhager MYOCARDIAL PROTEOME DURING METABOLIC SYNDROME AND TYPE 2 DIABETES IN ZUCKER DIABETIC FATTY RATS

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Approximately 5% of the world's population is suffering from type 2 diabetes mellitus (T2DM). T2DM is highly linked to cardiovascular disease (CVD), and an increasing prevalence of T2DM within the population will lead to higher occurrence of CVD deaths. This increase in T2DM will in the future have a great impact on society's health and economy.

The aim of the project is to apply advanced protein analysis by mass spectrometry to map protein perturbations of rat heart tissue in order to gain insight of the underlying molecular mechanisms linking metabolic diseases to CVD.

Zucker Diabetic Fatty (ZDF) rats (fa/fa) and their age-matched lean controls (fa/+) were studied at stage 6, 12, and 24 weeks, which corresponds to a pre-diabetic state, onset of, and late type 2 diabetes, respectively ( $n=3$  in each group). ZDF rats were sacrificed, the heart removed, and the tissue proteins were subjected to mass spectrometry analysis.

At each of the three stages, roughly 50 proteins were found significantly altered compared to age-matched controls. They comprise proteins involved in the mitochondrial energy machinery, such as the fatty acid oxidation, Krebs cycle and electron transport chain. The results show progressive changes of the central energy metabolism of the heart, which can have severe consequences for the heart function.

P13.06 Anne Louise  
Svenningsen

#### SORTILIN IN MICROGLIA REACTIVITY

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Neuropathic pain is a serious neurological disease estimated to affect around 8% of the Western population. It can be caused by either direct injuries to the peripheral nervous system (e.g. surgery) or indirect injuries (e.g. diabetes or cancer). Unfortunately, patients very often do not respond to, experience severe side effects or become resistant to the treatment. Hence, there is an enormous unmet need to develop more targeted therapeutic treatments.

Neuroinflammation is a major contributing factor in the development and maintenance of neuropathic pain. It is well known that activation of microglia is essential in the spinal neuroinflammatory process underlying development of neuropathic pain after a peripheral nerve injury (PNI). Unpublished data from Sortilin deficient mice shows that lack of the neuronal receptor Sortilin decreases development of neuropathic pain after PNI. As Sortilin is reported to influence the inflammatory response in macrophages and T-cells, we speculate that Sortilin has a similar role in microglia. Therefore, the aim of this project is to understand how Sortilin influences the spinal microglial response following PNI.

This project is divided into two parts: 1) The in vitro part focuses on investigating primary microglia cultures from wild type and Sortilin deficient mice by comparing profiles of released cytokines following an injury mimicking stimulation, 2) The in vivo part compares cytokine expressions in spinal cord lysates after PNI.

We hope that this study will improve the understanding of the microglial response in the central nervous system after PNI and contribute to development of better and more targeted treatments of neuropathic pain.

P13.07 Denise Happ

#### INVESTIGATING THE INTERACTION BETWEEN NICOTINIC RECEPTORS AND SEROTONERGIC SIGNALING IN DEPRESSION: IMPLICATIONS FOR ANTIDEPRESSANT NON-RESPONDERS

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Depression is a serious mental health problem affecting the lives of many individuals. A common treatment strategy is to increase extracellular serotonin concentrations, e.g. by using selective serotonin reuptake inhibitors (SSRIs). However, the therapeutic response can take several weeks, and many patients fail to show a substantial clinical response.

Recent literature has indicated an interaction between serotonergic signaling systems and nicotinic acetylcholine receptors (nAChRs) in depression. Modulation of nAChR activity can have antidepressant-like effects and potentiate the effect of SSRIs. However, it is still under discussion whether these effects are due to activation, desensitization or inhibition of nAChRs.

This project will systematically investigate the interaction between nAChRs, specifically the  $\alpha 7$  subtype, and the serotonergic system in greater detail both in vivo and in vitro using a multidisciplinary approach. By combining pharmacology, neurochemistry and advanced imaging technologies, the functional interactions between nicotinic and serotonergic neurotransmission will be investigated in two rat models of depression (Flinders Sensitive Line and Wistar Kyoto). Further, to demonstrate loss and gain of function in vivo, we will use DREADD technology ("designer receptors exclusively activated by designer drugs") to activate and/or silence activity of relevant receptors in freely behaving animals.

These studies will provide a better understanding of the interaction between the nicotinic and serotonergic systems that may have important clinical implications regarding the treatment of depression, especially in patients with reduced responses to SSRIs.

P13.08 Sashia Pernille  
Bak-Nielsen

KERATOCONUS

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Background: Keratoconus is a bilateral corneal disease, which causes corneal thinning and ectasia and thereby compromised vision. The disease develops during adolescence and progresses for 10-20 years. Ten percent of affected subjects have family members with keratoconus, but no specific gene has been identified. It is estimated that the prevalence currently is 86 per 100,000 individuals in Denmark.

Purpose: The purpose of this study is to characterise the Danish population of keratoconus patients with respect to socio-economic and general health aspects, such as prevalence of other diseases, particularly inflammatory diseases, use of health benefits, life expectancy, cause of

death, level of education, employment status and level of personal income.

Method: The study is registry-based. The population consists of all patients registered with the ICD-10 diagnosis "H18.6 Keratoconus" in the Danish National Patient Registry from 1977 to 2015, and 10 controls per case, matched on age and sex, not having keratoconus at the time of diagnosis of their matched case. Data are retrieved from several different registries, including CPR registry, the Danish National Patient Registry and Statistics Denmark. Multivariate logistic regression will be performed to test if keratoconus patients differ from non-keratoconus subjects.

Preliminary results: Basic characteristics of the Danish keratoconus population, such as number of patients, age and gender distribution, will be presented at the PhD Day 2017.

Perspectives: The unique Danish registries will enable us to learn more about the health-related and socio-economic aspects of this relatively uncommon eye disease from a relative large number of patients.

P13.09 Anne-Louise  
Kristine Moltke

#### THE ECONOMIC ASPECT OF PHOTODYNAMIC DIAGNOSTICS IN ADDITION TO WHITE-LIGHT FLEXIBLE CYSTOSCOPY AFTER TRANSURETHRAL RESECTION OF THE BLADDER

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Objectives: Non-muscle-invasive-bladder-cancer is one of the most costly cancers per patient. Patients are regularly examined at the outpatient clinic with a white light (WL) flexible cystoscopy as the gold standard.

This study investigates the economic aspect of photodynamic diagnostic (PDD) in addition to WL flexible cystoscopy after a transurethral resection of the bladder (TURB).

Materials and methods: 187 patients were enrolled at three Danish urological departments during the period from February to September 2016. Four months before, each patient had been diagnosed with either pTa low grade or pTa high grade after a TURB. Patients were randomized to a normal WL cystoscopy (N=95) or to a cystoscopy with PDD (N=92). The same urologist performed all cystoscopies.

The costs of cystoscopies and TURB are estimated with a bottom-up technique and include lifetime, sterilization and repair of equipment as well as the expenditure of time and all utensils.

Results: Tumor recurrences that needed a TURB were found in 32.6% and 16.3% of WL and PDD patients, respectively ( $p < 0.01$ ). Whereas

recurrence that was treatable at the outpatient clinic was found in 31.6% and 47.8% of WL and PDD patients, respectively ( $p < 0.05$ ). No difference in total number of patients with recurrence was observed ( $p = 0.991$ ).

Mean cost per PDD patient was DKK 6,849, whereas mean cost per WL patient was DKK 3,437. Thus, a mean reduction of 0.51 TURBs per patient would have to be found in order to compensate the costs of PDD used during the first cystoscopy after the TURB.

Conclusion: The results suggest that PDD initially augments both costs and effectiveness. Longer follow-up is needed for further conclusions.

P13.10 Madalina Carter-Timofte IDENTIFYING NOVEL INNATE IMMUNODEFICIENCIES IN PATIENTS WITH VARICELLA ZOSTER VIRUS CNS INFECTION

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Varicella zoster virus (VZV) is a highly contagious virus and the causative agent of the childhood disease, chicken pox. Re-activation of the virus causes the aggressive disease shingles, with some patients developing rare but serious complications of the central nervous system (CNS). We hypothesize that the differential susceptibility to viral CNS infection can be explained by host genetics, in particular mutations found in genes encoding innate immune molecules involved in viral recognition and anti-viral type I interferon (IFN) production. The project aims to identify and functionally characterize novel single gene inborn errors of immunity. To achieve this, our study will take a reverse approach to studying VZV pathogenesis. Initially, we will carry out whole exome sequencing (WES) of patients with a history VZV CNS infection to identify host gene variations in immune cells. We will functionally characterize identified mutations for associations with altered anti-viral response in patient cells. Finally, we will aim to identify the molecular basis for altered function by flow cytometry analysis of patient leukocyte function.

P14.01 Jens Sundbøll POSITIVE PREDICTIVE VALUE OF CARDIOVASCULAR DIAGNOSES IN THE DANISH NATIONAL PATIENT REGISTRY: A VALIDATION STUDY

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Background: The majority of cardiovascular diagnoses in the Danish National Patient Registry (DNPR) remain to be validated despite extensive use in epidemiological research.

Methods: Using medical record review as the reference standard, we examined the PPV of cardiovascular diagnoses in the DNPR between 2010 and 2012. For each diagnosis, we randomly selected up to 100 patients from one university hospital and two regional hospitals in the Central Denmark Region. We computed the PPVs as the proportion of confirmed diagnoses.

Results: A total of 2153 medical records (97% of the total sample) were reviewed. The PPVs ranged from 64% to 100% with a mean PPV of 88%. The PPVs were  $\geq 90\%$  for first-time myocardial infarction, stent thrombosis, stable angina pectoris, hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, takotsubo cardiomyopathy, arterial hypertension, atrial fibrillation/flutter, cardiac arrest, mitral valve insufficiency/stenosis, aortic valve insufficiency/stenosis, pericarditis, hypercholesterolemia, aortic dissection, aneurysm/dilatation, and arterial claudication. Apart from myocarditis (PPV: 64%) the remaining diagnoses had PPVs between 80% and 90% (recurrent myocardial infarction, unstable angina pectoris, pulmonary hypertension, bradycardia, ventricular tachycardia/fibrillation, endocarditis, cardiac tumours, first-time venous thromboembolism) and 70%-80% (first-time and recurrent admission for heart failure, dilated cardiomyopathy, restrictive cardiomyopathy, recurrent venous thromboembolism).

Conclusions: The validity of cardiovascular diagnoses in the DNPR is overall high and sufficient for use in research since 2010.

P14.02 Diana Hedevang Christensen USING ICD-10 DISCHARGE DIAGNOSES AND PRESCRIPTION DATA TO IDENTIFY DIABETIC POLYNEUROPATHY AND DIABETIC FOOT ULCERS IN DANISH REGISTRIES

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Background: Diabetic polyneuropathy (DN) is a common diabetic complication associated with major morbidity (including diabetic foot ulcers, DFU), mortality and health care costs. Our understanding of risk factors and exact mechanisms behind DN in patients with type 2 diabetes (T2D) is lacking, thus hampering prevention and disease-modifying treatment of this serious complication. The use of medical

registries and administrative databases offers an important and cost-effective resource to study DN. However, prior knowledge about the validity of the diagnosis codes is a prerequisite.

Aim: To determine the most valid ways of identifying DN and DFU in Danish registries.

Methods: Based on hospital contact diagnoses (e.g. T2D, polyneuropathy and ulcer) and prescription medication codes (e.g. neuropathic pain medication), we have defined 3 algorithms to identify T2D patients with DN, painful DN (pDN) or DFU. Within each of these 3 groups, we will randomly select 100 patients from the Central Denmark Region, 2009-2015. Using the unique CPR number, we will identify each patient's medical record. A predefined checklist of symptoms, signs and diagnostic test results described in the medical record will serve as gold standard. Positive predictive values (PPVs) will be calculated as the proportion of DN/pDN//DFU patients that can be confirmed by medical record review. Post-hoc analyses will be performed in order to identify the algorithms with the highest PPVs.

Perspectives: The final algorithms will offer endless possibilities for comprehensive investigation of DN and DFU in Danish registries, including studies of risk and prognostic factors as well as pharmaco-epidemiological studies.

P14.03 Malene Söth-Hansen

OCCURRENCE OF DELAYED DIAGNOSIS OF CLINICALLY RELEVANT ALARMS BY REMOTE MONITORING IN ICD SYSTEMS WITH DIFFERENT AUTOMATIC TRANSMISSION FREQUENCIES

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Background: Device-based remote monitoring (RM) of Implantable Cardiac Defibrillator (ICD) has been linked to improved clinical outcomes compared with in-clinical follow-up. RM enables automatic transmission of ICD status data, along with alarms upon detection of technical or clinical problems. However, the interval of the automatic ICD status transmission differs between different ICD manufacturers' devices.

Aim: This study investigates whether ICDs with daily automatic status transmission reduce the incidence of delayed diagnosis of clinically relevant alarms compared to less frequent transmission.

Method: This retrospective study includes all ICD alarms sent between September 2014 and 2016 to Aarhus University Hospital. Patients without RM or without wireless transmission are excluded. Date of alarm, transmission and recognition, alarmtype and clinical consequence are collected from the RM record. The primary outcome is occurrence of

delayed diagnosis of a clinical relevant alarm, defined as a timeline of more than 24 hours between alarm detection and alarm recognition by staff. Secondary outcome is time spent on each alarm by the staff measured through a two- week period. Baseline patient data are obtained from the Danish National ICD Registry, the Danish National Patient Registry and the Electronic Patient Journal.

Results: Around 2500 patients will be included, and we expect 20% of these to have had an ICD alarm within the study period.

Conclusions: Data collection is ongoing.

Funding: Department of Cardiology, Aarhus University Hospital, Skejby.

P14.04 Sara Konstantin  
Nissen

MUTATIONS IN INNATE IMMUNE SENSING PATHWAYS COULD  
CONTRIBUTE TO THE HIV ELITE CONTROLLER PHENOTYPE

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Objectives: HIV infection leads to viremia and CD4 T cell depletion within few years without treatment. HIV Elite Controllers (ECs) and Long-term Nonprogressors (LTNPs) constitute less than 1% of all HIV infected individuals. ECs and LTNPs are able to control virus and have a normal CD4 number without treatment for decades contrary to normal HIV Non-controllers (NCs). By finding and functionally understanding mutations and alterations in immune responses from ECs/LTNPs, we will increase understanding of HIV pathogenesis and pave the way for future treatment options.

Methods: We have performed whole exome sequencing (WES) on 11 ECs and LTNPs in order to identify mutations responsible for their advantageous course of disease/infection. We are examining the functional consequence of interesting variants in their exomes by stimulation of patient PBMCs with innate immune sensor agonists followed by mRNA and protein expression measurements. The relevant mutations will be verified by sanger sequencing, and protein expression will be investigated by Western blot.

Results: We have identified several different mutations in genes encoding molecules of the innate immune system. Our preliminary data show that ECs/LTNPs with mutations in DNA-sensing pathways have a lower induction of IFN $\beta$  and CXCL10 mRNA after DNA transfection.

Conclusions: Data suggest that innate immune defects in ECs and LTNPs may result in a decreased immune activation and slower disease progression compared to NCs.

COMPARISON OF WHITE LIGHT, PHOTODYNAMIC DIAGNOSIS, AND NARROW-BAND IMAGING IN DETECTION OF CARCINOMA IN SITU (CIS) OR FLAT DYSPLASIA AT TRANSURETHRAL RESECTION OF THE BLADDER: THE DABLACA-8 STUDY

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Photodynamic diagnosis (PDD) and narrow band imaging (NBI) are two different modalities used to improve detection of tumors, carcinoma in situ (CIS) and flat dysplasia compared to white light (WL) cystoscopy.

Objectives: To compare findings in NBI to findings in WL and PDD in a high-risk patient population.

Method and materials: In total, 171 patients were included in the study from four different urological departments in Denmark and Norway. Patients were scheduled for a PDD-guided transurethral tumor resection or cystoscopy-guided biopsy in accordance with Danish guidelines, on the suspicion of primary or concomitant CIS. All patients were examined with WL cystoscopy followed by both NBI and PDD before biopsy.

Measurements: Sensitivity, specificity and positive predictive value regarding identification of pathology were compared between modalities on patient- and biopsy-level.

Results: A total of 136 patients were biopsied due to findings with suspicion of CIS in at least one modality (482 biopsies/3.5 biopsies per patient). Analysis at patient level showed that NBI and PDD had a significantly higher sensitivity regarding identification of CIS and dysplasia compared to WL (NBI: 95.7%, PDD: 95.7% vs. WL: 65.2%) ( $p < 0.05$ ). Specificity was not significantly different between the three methods (NBI: 52.0%, PDD: 48.0% and WL: 56.8%). When analyzed per biopsy, NBI and PDD had a significantly higher sensitivity than WL (NBI: 72.7% and PDD: 78.2% vs. WL: 52.7%  $p < 0.05$ ), whereas the positive predictive values were not significantly different (NBI: 23.7%, PDD: 22.2% and WL: 19.0%).

Conclusion: NBI was found to be a valid alternative to PDD regarding diagnosis of CIS and flat dysplasia.

P14.06 Michael Roost  
Clausen

PROGNOSTIC RELEVANCE OF PRE-THERAPEUTIC ANEMIA IN DIFFUSE LARGE B-CELL LYMPHOMA. DANISH MULTI REGISTRY DATA ON 3522 PATIENTS TREATED WITH CURATIVE INTENT IN THE PERIOD FROM 2000 TO 2012

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Prognosis in diffuse large B-cell lymphoma (DLBCL) is still based on the International Prognostic Index (IPI). The National Comprehensive Cancer Network IPI (NCCN-IPI) adds to the IPI factors more refined age and lactate dehydrogenase (LDH) strata and weighs extranodal disease according to site of involvement. In Denmark, the completeness of population-based health care parameters is high. For lymphoma, a disease-specific national database (LYFO) has been established since 1982.

The aims of the present study were (i) to validate the NCCN-IPI; and (ii) to analyze, in a multivariate model, whether information on pre-therapeutic hemoglobin level improved the ability of the NCCN-IPI to predict outcome.

Inclusion criteria were: 'de novo' DLBCL and anthracycline containing front line therapy.

Overall survival according to NCCN-IPI, rituximab treatment and pre-therapeutic hemoglobin level was described using Kaplan-Meier estimates. Univariate and multivariate analyses were performed using Cox proportional hazard model including NCCN-IPI group, hemoglobin level and treatment cohort (w/wo rituximab) as covariates with mutual adjustment.

Median age was 65 years (IQR: 56-73), 56% of patients were men and 46% had pretherapeutic anemia. NCCN-IPI risk groups were: low 13%, low-intermediate 40%, high-intermediate 35% and high 12%.

Patients with anemia had a HR of 2.3 (95%CI: 2.1-2.6). After adjusting for NCCN-IPI factors, the HR remained significant 1.5 (95%CI: 1.3-1.7). In this population-based study, NCCN-IPI was confirmed as an effective risk classifier. The presence of pretherapeutic anemia added independent prognostic information to the NCCN-IPI.

P14.07 Ann Bjørnshave WHEY PROTEINS CONSUMED AS A PRE-MEAL - COMPARISON OF METABOLIC PARAMETERS IN SUBJECTS WITH AND WITHOUT TYPE 2 DIABETES

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Objective: Meal timing crucially influences the action of nutrients and may be a simple way to modify postprandial metabolic responses. Whey proteins (WP) are potent insulinotropic secretagogues, both in healthy and subjects with type 2 diabetes (T2D). We want to determine if a pre-meal of WP influences the responses of triglycerides (TG) and chylomicrons (ApoB-48) more pronounced in subjects with T2D than without T2D, and compare the impact of WP ingested as a pre-meal and as part of the main meal.

Methods: We conducted two acute, parallel, randomized, cross-over trials with two arms. Two groups of each 12 subjects with and without T2D matched for BMI, age and gender completed the study. At the test day, fasting data were collected (blood, urine and anthropometric measurements). A 200 ml pre-meal containing 20 g WP was served at -15 min or as a part of the fat-rich breakfast (main meal) served at 0 min. The subjects were observed for 360 min after the second meal.

Results: We found a significant stimulating effect on insulin (0min:  $P=0.002$ ) and glucagon responses (0min:  $P=0.039$ , 15min:  $P=0.011$ ) of WP taken as a pre-meal in both groups. Furthermore, the responses of the incretin hormone gastric inhibitory polypeptide (GIP) (0min:  $P<0.0001$ , 15min:  $P=0.006$ ) were larger after a pre-meal of WP. Interestingly, we observed no difference over time between the two groups of responses of TG or ApoB-48.

Conclusion: WP as a pre-meal differentially influences hormone and lipid metabolism, i.e. triggers significantly larger responses of insulin, glucagon and GIP compared to WP as part of the main meal, while WP did not influence TG or ApoB-48 responses in subjects with T2D and without T2D.

P14.08 Visse Theresia Skov Moestrup  
Cancellation THE EFFECT OF 'X' TO DECREASE A-BETA IN ALZHEIMER'S DISEASE  
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Alzheimer's disease (AD) is the most common cause of dementia; it is characterized by progressive neurodegeneration, caused by cell shrinking, loss of synapses, and neuronal death. One of the main contributors to these neuronal changes is the accumulation of beta

amyloid ( $A\beta_{42}$ ), a protein highly associated with AD.

In this study, we will investigate a compound ('X') for its ability to decrease the amount of  $A\beta_{42}$ . Our collaborator at Shanghai Advanced Research Institute (SARI) has previously shown promising effect of 'X'.

To further build on this research, we will test 'X' in the APP/PS1 mouse model. This is to investigate the effect of 'X' on  $A\beta_{42}$  accumulations, and the memory deficits described in this mouse model.

Furthermore, we will test the effect of 'X' in organotypic hippocampal slice cultures. We wish to investigate the effect of 'X' in tissue from healthy rats and mice, as well as in adult APP/PS1 mice. The effect of 'X' will be evaluated through comparison to a battery of already existing  $A\beta$  treatments.

Finally, we will radioactively label 'X' and through PET scanings in pigs evaluate the ability of 'X' to cross the blood brain barrier (BBB) and thereby enter the brain. This test is highly relevant in the future work of generating a functional human pharmaceutical.

We expect to show a potent effect of 'X' in decreasing the level of  $A\beta$  in both organotypic slice cultures and the APP/PS1 model, as well as to improve the memory deficits seen in these mice. Finally, we expect to show the ability of 'X' to cross the BBB in pigs.

P14.09 Trine Korsgaard NEPHROTIC SYNDROME IN DANISH CHILDREN

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Purpose: Nephrotic syndrome (NS) is defined by edema, hypoalbuminemia and proteinuria. The prognosis and long-term outcome of the disease is still incompletely understood, which is why we established a database containing clinical information on children with NS to study these questions.

Method: The cohort of patients enrolled in this study was identified by search on ICD-10 codes associated with nephrotic syndrome/proteinuria admitted to all paediatric departments in the Central Denmark Region and the North Denmark Region between January 1998 and January 2016. Data were obtained from medical journals and were collected in Research Electronic Data Capture (RedCap).

Results: A total of 283 paediatric patients were identified by the ICD-10 codes; 162 patients meet the inclusion criteria. On 27 October, complete data of 115 patients were available. The incidence of NS was 1.3/100,000; 74% (85/115) patients were classified as steroid sensitive (SSNS) and 26% (30/115) as steroid resistant (SRNS). Biopsy findings in

SRNS patients showed minimal change NS in 50% (15/30) of the patients; 13% (4/30) with focal segmental glomerulosclerosis, 10% (3/30) with membranoproliferative glomerulonephritis, and 27% (8/30) with IgA-nephritis. Four of the patients with SRNS developed end stage renal disease (ESRD).

Conclusion: The study is the first to present clinical data from a well-defined cohort of children with NS. Our preliminary analysis indicates that the incidence of SRNS is higher in the studied population compared to the literature, but further data collection and analysis are still ongoing.

P14.10 Sophie-Charlott Seidenfaden POTENTIAL OF NOVEL BIOMARKERS IN PREHOSPITAL MANAGEMENT OF TRAUMATIC BRAIN INJURY: THE PRE-TBI STUDY

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Background: Traumatic brain injury (TBI) is the leading cause of death and disability among young adults worldwide. Difficulties in the clinical assessment and triage of TBI patients in the prehospital phase result in numerous precautionary hospital admissions of mild TBI patients and treatment delay due mis-triage of moderate and severe TBI patients. Early knowledge on biomarker values is suggested to be key to improvement of patient outcome as it may guide the clinical decision-making.

Aim: To investigate the potential of early biomarker measurements in prehospital management of TBI patients.

Methods: Three prospective, observational studies were designed to investigate ROC characteristics of S100B, GFAP and NSE in relation to clinically relevant endpoints. In total, 690 adult patients suffering mild, moderate and severe TBI in the Central Denmark Region will be included, and repeated biomarker measurements will be performed in the ambulance and during admission.

Study I: Diagnostic Potential of S100B and GFAP in Prehospital Rule-Out of Intracranial Lesions in Patients suffering Mild TBI.

Study II: S100B and GFAP in Prehospital Prediction of Need for Neuro-surgical Observation or Intervention in Patients suffering Moderate TBI.

Study III: Prognostic Potential of S100B, GFAP and NSE in Patients suffering Severe TBI.

Perspectives: To underline the potential of prehospital biomarker measurements for effective rule-out of low-risk patients and rule-in of high-risk patients in order to minimize treatment delay, secure optimal resource consumption and streamline patient courses for patients

suffering neurotrauma. Ultimately, we aim to elucidate the need for development of a point-of-care analysis.

P15.01 Oliver Pedersen PLATELET TURNOVER AND AGGREGATION IN PATIENTS WITH ESSENTIAL THROMBOCYTOSE

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Background: Essential thrombocytosis (ET) patients are characterized by increased platelet count and provide a biological model of platelet aggregation and accelerated turnover. ET patients have increased risk of thromboembolic events, partly explained by platelet count. Increased proportion of immature platelets may also be important. Aggregation analyzed by Multiplate<sup>®</sup> is dependent on platelet count, but flow cytometry can evaluate aggregation potential of each platelet independently of count.

Aims: Investigate associations between platelet count, platelet turnover and platelet aggregation in patients with ET.

Methods: In 24 ET patients, platelet aggregation was measured by whole blood impedance aggregometry using Multiplate<sup>®</sup>. Arachidonic acid (AA), thrombinreceptor-activating-peptide (TRAP) and ADP were agonists. Platelet surface expression of P-selectin, CD63 and fibrinogen were measured with flow cytometry after activation with the same agonists. Immature platelet count was used as marker of turnover.

Results: Significant correlation was found between platelet count and aggregation whether induced by AA ( $r=.43$   $P=.04$ ), TRAP ( $r=.46$   $P=.03$ ) or ADP ( $r=.60$   $P=.003$ ). Expression of fibrinogen, CD63 and P-selectin when induced by AA and ADP were significantly increased in patients compared with healthy individuals (all  $P$ -values  $<.03$ ). Immature platelet count was significantly higher in patients compared to healthy individuals (median 12.4 [IQR 9.8-19.0] vs median 6.9 [IQR 5.5-10.3]  $P<.0001$ ).

Conclusion: ET patients have increased aggregation potential. This is likely explained by platelet count and accelerated platelet turnover resulting in a high proportion of haemostatically reactive platelets.

P15.02 Farhad Waziri HEMODYNAMIC CHARACTERISTICS OF CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION PATIENTS DURING EXERCISE

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Introduction: Chronic thromboembolic pulmonary hypertension (CTEPH) can cause severe right ventricular dysfunction, which can lead to death. Correctly diagnosing CTEPH is of major importance, as CTEPH is potentially curable by surgery (pulmonary thromboendarterectomy, PTE). The traditional work-up for operation includes invasive measurements of the pulmonary hemodynamics with Swan-Ganz catheter at rest. However, pulmonary pressure rises during activity, which loads the right ventricle even more.

Hypothesis: The pulmonary hemodynamic response to exercise will reveal the true severity of CTEPH and reveal patients with borderline CTEPH, who could benefit from PTE.

Aim: Our aim is to examine cardiopulmonary hemodynamics in CTEPH patients at rest and during activity, and to assess the right ventricular remodeling with echocardiography.

Methods and results: We will examine 20 CTEPH patients before PTE, and 3 and 12 months after. Right ventricular structure and function will be evaluated using 2D and 3D echocardiography at rest and at semi-supine exercise test. Invasive hemodynamics is measured at rest and during exercise test using a Swan-Ganz catheter. The study is still ongoing. Presently we have baseline data for 20 patients prior to operation, 15 patients at 3-month follow-up and 4 patients at 12-month follow-up.

The data is currently being analyzed, and the final results will be presented at the PhD Day.

Perspectives: A better understanding of the morphological changes in right ventricular structure and hemodynamics following PTE.

P15.03 Gitte Vrelits Sørensen LONG-TERM DISEASE-SPECIFIC HOSPITALIZATION IN SURVIVORS OF CHILDHOOD LEUKEMIA IN THE "ADULT LIFE AFTER CHILDHOOD CANCER IN SCANDINAVIA" (ALICCS) COHORT

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**Background:** With a growing population of childhood leukemia survivors, characterization of long-term health consequences has become increasingly important. We aim to give a comprehensive description of the somatic disease-specific hospitalization with results reported separately for acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML) and chronic myeloid leukemia (CML) survivors.

**Methods:** The cohort is part of the Adult Life after Childhood Cancer in Scandinavia (ALiCCS) study comprising 32,791 patients diagnosed with cancer before age 20 years from 1960 through 2008 in Denmark, Sweden, Iceland or Finland. Five population comparisons matched to each childhood cancer patient served as the comparison cohort. A total of 4,153 five-year survivors of childhood leukemia were followed-up for hospitalizations in the national hospital registries, and disease-specific hospitalization rates in survivors and comparisons were used to calculate standardized hospitalization rate ratios (RRs) and absolute excess risks (AERs) per 100 person-years.

**Results:** After a median follow-up of 11 years, 37% of the survivors had had at least one hospitalization for a somatic disease. Survivors of CML (n=97) had the highest RR for any hospitalization (4.3; 95%CI: 3.5-5.2), followed by AML (n=396) (3.0; 95%CI: 2.7-3.4) and ALL (n=3,477) (2.0; 95%CI: 1.9-2.1). AERs were 10 (95%CI: 7.5-13), 5.7 (95%CI: 4.8-6.5) and 2.7 (95%CI: 2.5-2.9) for CML, AML and ALL survivors, respectively.

**Conclusion:** Survivors of ALL, AML and CML had an increased risk of hospitalization for somatic diseases.

P15.04 Mridul Johari

NOVEL GENETIC RISK LOCI ASSOCIATED WITH SPORADIC INCLUSION BODY MYOSITIS

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Sporadic Inclusion Body Myositis (sIBM) is the most frequent disabling muscle disease of the elderly people with an onset after 45 years of age. It is a slowly progressive muscle disorder, characterized by the coexistence of both degenerative muscle pathology and inflammatory changes of unknown etiology. One hypothesis favoring the genetic background of sIBM suggests that post-translationally modified proteins

accumulated in the aging muscle fibers may elicit a T-cell inflammatory reaction as the result of defects in several different susceptibility genes, making sIBM a complex multifactorial disease. By whole exome sequencing (WES) followed by association analysis, we have found five SNPs in three novel genes that have an observed considerably higher frequency in 30 Finnish sIBM patients compared to the control population. These variants could individually or in combination be associated with higher susceptibility for the disease.

P15.05 Rasmus Pihl

#### COMPLEMENT FACTOR D EXISTS AS A PROENZYME IN THE CIRCULATION AND IS ACTIVATED BY MASP-3

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The complement system is an important part of the innate immune system. It is centered around a cascade of proteases that ultimately lead to clearance of pathogens and cell debris, inflammation, and bridges innate and adaptive immunity.

The effector functions of the complement system must be tightly controlled to avoid damaging the host itself, as seen in several autoimmune diseases. One element of regulation is that many complement proteases are synthesized as inactive zymogens that only become activated upon recognition of foreign molecular patterns.

The proteolytic cascade of complement activation can be initiated by three pathways, but regardless of the initiation route the alternative pathway (AP) is key for amplifying the response. Complement factor D (FD) is traditionally viewed as the first-acting protease of the AP and was believed to be synthesized as an active enzyme. However, recent evidence suggests that FD is synthesized as an inactive proenzyme (proFD) that is quickly converted to FD after secretion.

By using isoelectric focusing blots, which enable analytical separation of proFD and FD from blood samples, we show that proFD exists in the circulation of healthy blood donors. Furthermore, we confirm that the enzyme MASP-3 is important for the conversion of proFD into FD, as recently suggested in the literature. This is highlighted by the fact that proFD is the predominant form found in serum from patients that lack active MASP-3. Lastly, we show that the AP activity can be rescued in MASP3<sup>-/-</sup> mice, which have an inherently low AP activity due to the absence of active FD, by injecting recombinant MASP-3.

P15.06 Agnes Hauschultz MUSCLE MEMBRANE PROPERTIES IN A PATIENT WITH SPINAL CORD  
Witt INJURY

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Introduction: The peripheral nervous system should be left intact after a spinal cord injury (SCI). However, recent studies have shown spontaneous activity, a sign of denervation, on electromyography (EMG) of muscles below level of injury. To better understand the pathophysiology of the spontaneous activity after SCI, we asked if muscles with spontaneous activity in SCI patients show the same findings in muscle membrane properties as we find in the denervated muscles.

Methods: To answer this question, we examined a 25-year old man with SCI three weeks post injury with nerve conduction studies (NCS) and EMG. We recorded the muscle membrane properties using muscle velocity recovery cycle (MVRC) from the tibial anterior muscle in the SCI patient, 17 patients suffering from drop foot due to neurogenic diseases and 13 controls. We compared the obtained MVRC variable, relative refractory period (RRP) of the SCI patient and the two groups.

Results: We found no spontaneous activity in the tibial anterior muscle and normal NCS of the common peroneal nerve of the SCI patient. There was an increased RRP of 5.20 ms in the SCI patient as compared to the controls (mean RRP 3.70 ms range: 3.02 ms - 4.42 ms). RRP was also increased in neurogenic patients (mean RRF: 6.37 ms range 3.14 ms - 13.77 ms).

Discussion: The SCI patient had normal nerve conduction, but we found no spontaneous activity. The changes in muscle membrane properties of the SCI patient may indicate a depolarized muscle membrane potential. These changes did resemble those of neurogenic muscles. However, further examinations with EMG and MVRC on patients with SCI must be done before we can make further conclusions.

P15.07 Mary Nguyen CAUSES OF DEATH IN DANISH MEN WITH PROSTATE CANCER  
Nielsen

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Background: Prostate cancer (PC) is a major disease that affects men's health worldwide. It remains unclear whether PC should be considered

as a leading cause of death in men or, in contrast, whether we have moved into an era where PC is now a non-lethal disease that men live with rather than die of, as has been suggested in the literature. Currently, the number of deaths due to PC is approximately 1,250 deaths per year in Denmark.

**Aim:** We investigated cause of death in a nationwide cohort of Danish men diagnosed with incident PC in the 5-year period from February 2010 to October 2015.

**Methods:** Death cases were identified from the Danish Prostate Cancer Database (DAPROCA data), which is a nationwide clinical database that prospectively collects data on all incident PC patients in Denmark since February 2010. In the period from February 2010 to November 2014, over 17,000 Danish men were registered with newly diagnosed PC. From this cohort, and within the same calendar period, a total of 1588 deaths occurred. Cause of death was then assessed by blinded medical chart review.

**Results:** Medical charts available for review n=722 (%); PC specific death n=337 (47%); Other specified cancer death n=95 (13%); Cardiovascular disease death n=115 (16%); Other causes (e.g. infection) n=114 (16%); Unknown n=61 (1%).

**Discussion and conclusion:** Prostate cancer remains a leading cause of death in men diagnosed with PC, accounting for nearly half of all deaths (47%). Future investigations will include an analysis of the validity of data in the Danish Register of Causes of Death against the results from the blinded medical chart review, and an analysis of prostate cancer-specific mortality.

P15.08 Brigitta Villumsen DOES HOME-BASED EXERCISE MAKE A DIFFERENCE?

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**Introduction:** Decreased quality of life (QoL), fatigue, metabolic and cardiovascular complications are common side effects of androgen deprivation therapy (ADT) in prostate cancer patients. To overcome these side effects, 150 min. of cardio and resistance exercise per week is recommended.

**Objective:** To examine the effectiveness of a 12-week home-based exercise program using the interactive video gaming console Xbox 360 Kinect and free weights in prostate cancer patients receiving ADT.

**Methods:** Randomized trial with two groups: a) intervention group (n=23)

and b) control group (n=23).

Physical tests: 6-minute walk test, leg extensor power, bioelectrical impedance analysis.

Questionnaires: EORTC QLQ-C 30, Functional Assessment of Cancer Therapy-Prostate (FACT-P), Functional Assessment of Chronic Illness therapy - Fatigue (FACIT-F).

Blood samples: Cholesterol, triglyceride, glucose, insulin sensitivity, adiponectin, Insulin-like Growth Factor-1 (IGF-I) and Insulin-like Growth Factor Binding Protein (IGF-BP).

Tests are done at baseline, at 12 week and at 24-26 weeks.

Results: Baseline results show non-compliance to the exercise recommendation; the incidence of metabolic syndrome is 74%. QoL scores are decreased, which is consistent with findings in other studies, whereas fatigue is seen to a lesser extent. No serious adverse event has been reported.

Two participants have dropped out of the control group due to high motivation for exercising along with allocation to usual care.

Conclusion: Unsupervised home-based exercise using an interactive video gaming console is a safe, motivating and innovative approach to promote lifestyle changes in prostate cancer patients undergoing ADT.

P15.09 Christoffer  
Krogager

EVALUATION OF INTER-ARM BLOOD PRESSURE DIFFERENCES USING  
THE MICROLIFE WATCHBP OFFICE IN A CLINICAL SETTING

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Objective: The aim of this study was to evaluate the usefulness of Micro-life WatchBP Office and the effect of increasing the number of measurements in the clinical evaluation of systolic inter-arm difference (IAD).

Method: Office blood pressure (BP) was measured simultaneously on both arms in 339 patients (85% diabetic) using the Microlife WatchBP Office, a fully automatic, oscillometric device. The included patients were all scheduled for ambulatory blood pressure measurement (ABPM) at the outpatient clinic of endocrinology at Silkeborg Regional Hospital, Denmark. Two successive sets of three individual measurements were made. A statistical analysis of variance was performed on the measurements.

Results: In the first set of measurements, the mean IAD was -0.3 mm Hg

and the prevalence of IAD  $\geq 10$  mm Hg was 9.1%. Only 7.6% of the patients with an IAD  $< 10$  mm Hg in the first set of measurements had an IAD  $\geq 10$  mm Hg in the second set of measurements. The 95% limits of agreement (LoA) for the mean IAD for a single set of three measurements was  $\pm 13.16$  mm Hg. The probability of detecting an IAD  $> 10$  mm Hg only increased slightly with an increasing number of measurements.

Conclusion: A single set of triplicate measurements using Microlife WatchBP is an acceptable method for evaluating IAD since more measurements do little to improve the probability of detecting an IAD  $> 10$  mm Hg due to high intra-individual variation.

P15.10 Fernando Exposto PHENOTYPIC AND GENOTYPIC CHARACTERIZATION OF A TENSION-TYPE HEADACHE POPULATION

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Background: Tension-type headache (TTH) is the most common type of headache and is the second most prevalent disorder in the world. Despite this, it remains poorly understood, deficiently managed, and no improvement in treatment has been achieved in the past decades. A pathophysiology-based approach to diagnosis is needed to achieve better treatment outcomes.

Aims: This proposal primarily aims to re-classify TTH patients through phenotype and genotype analysis, so that the pathophysiology behind its variable clinical presentations can be better understood. A further aim is to identify the reason why pericranial tenderness is present in some but not all TTH patients.

Methods: We plan to include 72 patients with the diagnosis of TTH according to the International Classification for Headache Disorders (ICHD-3) and 36 healthy controls. Participant evaluations will occur at baseline and 1 month and 2 months after baseline. Phenotypical characteristics will be assessed through quantitative sensory testing (QST), conditioned pain modulation (CPM), analysis of autonomic nervous system (ANS) parameters and immunohistochemistry analysis of NO, TNF- $\alpha$ , IL-1, IL-6 and  $\beta 2$  and  $\beta 3$  adrenergic receptors from muscle fibers taken from the temporalis muscle through microbiopsies. The genotyping will be done by assessing the COMT haplotypes and DRD3 polymorphisms.

Future perspectives: This project will shed light on the underlying pain

mechanisms of TTH and may help define a new classification of TTH patients that would better express the underlying pathophysiology. In consequence, a new rationale for treatment other than the one used now would develop.

P16.01 Anne Staub  
Rasmussen

OBSTETRIC AND NON-OBSTETRIC SURGERY DURING PREGNANCY: A 20-YEAR DANISH POPULATION-BASED PREVALENCE STUDY

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Objective: Population-based studies evaluating the use of obstetric and non-obstetric surgery during pregnancy are sparse. The aim of this study was to describe the prevalence of surgery during pregnancy in Denmark in 1996-2015 to clarify any change in prevalence of surgical procedures over the years, and to evaluate changes in prevalence of non-obstetric surgery in each trimester.

Materials and methods: We included all pregnancies in Denmark in 1996-2015. The outcome was surgery during pregnancy categorised as obstetric surgery or non-obstetric surgery. Surgical groups were tabulated by calendar year period, and prevalence of each type of surgery was calculated. Finally, we calculated prevalence of non-obstetric surgeries by trimester and year.

Results: The study included 1,687,176 pregnancies of which 311,896 (18.5%) received a total of 340,811 surgical procedures. The prevalence of obstetric surgery during pregnancy more than doubled during the study period. The prevalence of non-obstetric surgery remained stable during the period. Throughout the study period most non-obstetric procedures were conducted in the 1<sup>st</sup> trimester of pregnancy. Surgery on female reproductive organs, however, became more evenly distributed over the trimesters during the study period.

Conclusion: During the study period, the prevalence of obstetric procedures during pregnancy doubled. This was mainly due to a more than doubled prevalence in the conduction of caesarean sections. The main part of non-obstetric surgical procedures was conducted in the 1<sup>st</sup> trimester.

P16.02    Nichlas Riise  
              Jespersen

IS PROTECTION AGAINST MYOCARDIAL ISCHEMIA-REPERFUSION  
INJURY AT ONSET DIABETES DEPENDENT ON MITOCHONDRIAL  
FUNCTION?

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Background: In type 2 diabetic patients, the outcome following an acute  
myocardial infarction is worsened compared to non-diabetic patients.  
Resistance to ischemia is determined by the stage of diabetes with  
protection at onset diabetes and increased damage in late diabetes.  
The underlying mechanism is unknown but may be due to differences in  
the ability to protect post-ischemic mitochondrial function.

Objective: We will determine if cardioprotection induced by onset  
diabetes is through preservation of post-ischemic mitochondrial OXPHOS  
capacity.

Methods: Experiments are performed using Zucker diabetic fatty rats and  
age-matched non-diabetic controls at ages 6, 12 and 24 weeks,  
corresponding to pre-diabetes, onset diabetes and late type 2 diabetes.  
Isolated rat hearts will be divided into three groups: (I) Sham hearts  
without ischemia, (II) ischemic controls without treatment and (III)  
ischemic hearts treated with Dimethyl Malonate 10 min. prior to  
ischemia. All hearts will be exposed to 40 min. of global no-flow  
ischemia followed by 30 min. of reperfusion. Following reperfusion, the  
left ventricle is rapidly cooled. Cardiac fibers are isolated and  
permeabilized for measurement of mitochondrial respiration by high-  
resolution respirometry.

Results: Study experiments on diabetic rats have been conducted, and  
data is being analyzed. No preliminary data is yet available.

Conclusion: This study will improve our understanding of the metabolic  
changes in diabetes and how they influence the sensitivity against  
ischemia and reperfusion injury in diabetic hearts.

P16.03    Charlotte Madsen UPFRONT RITUXIMAB MAINTENANCE AFTER INDUCTION THERAPY  
              IMPROVES OUTCOME AND REDUCES THE RISK OF HISTOLOGICAL  
              TRANSFORMATION IN PATIENTS WITH FOLLICULAR LYMPHOMA: REAL-  
              WORLD DATA FROM A DANISH POPULATION-BASED COHORT

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Introduction: Follicular Lymphoma (FL) is an incurable condition with an indolent clinical course, recurrent relapses and, in some cases, transformation to an aggressive histology (HT). During the last decade, maintenance with Rituximab (RM) after initial immunochemotherapy has been introduced. In this population-based study, we investigated the effect of upfront RM on survival probability and rates of progression and HT in FL patients.

Patients and methods: Patients diagnosed with FL in Denmark in 2000-2015 were identified through the National Danish Pathology Registry and cross-linked with the Danish Lymphoma Registry (LYFO). Pathology reports were reviewed, and patients with HT identified. Patient characteristics were compared using Fisher's exact or Student's t test. All time-related end-points, i.e. overall survival (OS), progression-free survival (PFS) and time to transformation (TTT), were estimated by Kaplan-Meier analysis and compared using the log-rank test. Factors of clinical relevance were tested in a multivariate analysis.

Results: Of 722 patients completing induction treatment, 364 patients were consolidated with RM, while 358 were not. As compared to no-RM patients, those consolidated with RM had a significantly improved 5-year OS (83% vs. 90%;  $p=0.003$ ) and PFS (63% vs. 72%;  $p<0.001$ ) at univariate level and confirmed in a multivariate analysis. Similarly, the rate of HT was reduced in RM treated patients (10% vs. 6%;  $p=0.067$ ), and the mean TTT was prolonged (1.8 yrs vs. 2.7 yrs;  $p=0.052$ ).

Conclusions: Upfront consolidation with RM in patients with FL results in improved OS and PFS. Furthermore, after RM, HT seems to occur less frequently, and the event is postponed.

P16.04 Mikkel Bo Brent ADDITIVE EFFECT OF GH AND PTH IN PREVENTION OF DISUSE OSTEOPENIA IN RATS

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Immobilization is known to cause a low bone mineral density (osteopenia) due to decreased osteoblastic bone formation and increased osteoclastic bone resorption. Growth hormone (GH) and intermittent parathyroid hormone 1-34 (PTH) are both potent bone anabolic agents. The aim of the present study was to investigate whether GH and PTH, alone or in combination, could prevent osteopenia due to immobilization. Immobilization was achieved by injecting 4IU Botox (BTX) into the right hind limb musculature. Seventy-two 14-week-old female Wistar rats were randomized into 6 groups: 1. Baseline; 2. Control (Ctrl); 3. BTX; 4. BTX + GH; 5. BTX + PTH; 6. BTX + PTH + GH. PTH (60  $\mu\text{g}/\text{kg}$ ) and GH (5  $\text{mg}/\text{kg}$ ) were administered s.c. 5 days/week twice daily. The animals were sacrificed after 6 weeks. Femur and tibia were removed, and bone properties were evaluated with DEXA,  $\mu\text{CT}$ , dyn. bone histomorphometry, and mechanical testing. BTX resulted in

significantly lower femoral trabecular bone volumen/tissue volumen BV/TV (-39%), lower cortical thickness (Ct.Th) (-9%), and lower femoral areal bone mineral density (aBMD) (-13%) compared with Ctrl. BTX + GH resulted in no significant changes in femoral BV/TV, Ct.Th, and aBMD compared to BTX. BTX + PTH increased femoral trabecular BV/TV (+18%) and femoral aBMD (+10%). BTX + PTH + GH increased femoral trabecular BV/TV (+50%), increased Ct.Th (+7%), and femoral aBMD (+15%). In conclusion, BTX-induced immobilization led to lower BV/TV, Ct.Th, and aBMD. In general, GH and PTH alone did not fully revert the BTX-induced osteopenia. However, in combination, GH and PTH completely prevented osteopenia.

P16.05 Anna Sofia HEART SKILLS - IMPROVING CARDIAC REHABILITATION SERVICES  
Elisabeth Aaby THROUGH CO-CREATION: A PHD PROTOCOL ON SYSTEMATIC  
DEVELOPMENT OF A HEALTH LITERACY INTERVENTION

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Background: Health literacy (HL) is people's knowledge, motivation and competences to access, understand, appraise and apply health information. Cardiac rehabilitation (CR) is a crucial part of cardiovascular disease care. Successful CR depends on differentiated services based on self-care competences. HL seems to encompass skills needed for self-care, and system responsiveness to HL challenges may constitute important requisites for successful CR.

Aim: To explore HL challenges in patients with cardiovascular disease, and use a participatory strategy to model and pilot a system-level intervention aimed at mitigating the effect of low HL in a community-based CR programme.

Methods: The project is carried out in three phases:

1. Needs assessment: a mixed-method study using the Health Literacy Questionnaire (HLQ), disease and sociodemographic data and qualitative interviews to develop HL vignettes.
2. Intervention development: a co-creational process involving clinicians, administrators, patients and collaborators.
3. Intervention piloting: small-scale cycles testing feasibility and effect.

The setting is the rehabilitation unit of Randers Municipality, which receives patients referred to CR in continuation of a hospital admission.

To ensure applicability, the project is organised with an advisory board of clinicians, researchers and lay people and with patients as part of the research team.

Perspectives: The needs assessment provides a comprehensive HL profile on which the intervention can be based. The co-creative development process ensures local ownership and acceptability, and the piloting allows adjustment of the intervention before future large-scale implementation.

- P16.06 Anne Maj van der Velden NEURAL MECHANISMS AND PREDICTORS OF TREATMENT RESPONSE TO MINDFULNESS-BASED COGNITIVE THERAPY IN THE TREATMENT OF RECURRENT MAJOR DEPRESSIVE DISORDER: A STUDY PROTOCOL

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Mindfulness-Based Cognitive Therapy (MBCT) is an effective prophylactic treatment for prevention of relapse risk amongst individuals with a history of recurrent MDD. However, only about half experience sustained remission following MBCT. To improve clinical outcomes, we need to identify early markers that can be used to predict which individuals will demonstrate long-term benefit from treatment and identify key mechanisms of change. There is currently a paucity of studies looking at the neural mechanisms of MBCT in the treatment of recurrent MDD and neural predictors of treatment response. The default-mode network (DMN) has received much attention in the context of the clinical neuroscience of depression, and abnormal intrinsic and extrinsic connectivity in DMN has been suggested as a marker of rumination and vulnerability to depression. Using resting-state functional connectivity MRI and diffusion tensor imaging, we shall examine the structural connectivity and functional connectivity in the DMN in individuals with a history of recurrent MDD at baseline and following MBCT treatment. The study will i) compare fully or partially remitted individuals with a history of three or more episodes of depression (N=60) and healthy matched controls (N=30) at baseline to explore whether DMN hyperconnectivity will mark vulnerability to relapse, and ii) subsequently randomize participants with recurrent MDD to MBCT (N=30) in addition to treatment as usual (TAU) or TAU (N=30) to investigate whether MBCT treatment can alter connectivity patterns associated with increased risk of relapse. Clinical status and symptom severity will be measured before and after treatment and at 6- and 12-month follow-up.

- P16.07 Anne-Mette Oxvig A BETTER UNDERSTANDING OF METHYLGLYOXAL-DERIVED PATHOPHYSIOLOGICAL CHANGES

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Methylglyoxal is a metabolite formed as a byproduct in the glycolysis. Being highly reactive, methylglyoxal reacts with amino acids, arginines and lysines, forming protein modifications known as advanced glycation end-products. These post-translational modifications cause alterations of the native protein structure, which consequently may disrupt the function of the protein. Even though these protein modifications are generally accepted to be implicated in a range of age- and diabetes-related pathologies, such as endothelial dysfunction, only little is known about which proteins get modified *in vivo* and how the modifications lead to age-related diseases. To elucidate this, we have developed a methylglyoxal-analogue probe (AlkMG), which binds proteins equally to endogenous methylglyoxal. Hereby, using AlkMG, we are able to isolate and identify proteins targeted by methylglyoxal in living cells. In this context, we hypothesize that the most reactive protein targets to methylglyoxal are also the proteins most likely to lead to disease progression or biological aging. Hence, a large-scale proteomic study in HeLa cells with mass spectrometric identification of AlkMG-target proteins has been performed. Several hundred proteins were found to be modified by AlkMG, including various glycolytic enzymes, ribosomal proteins and histones. Further studies of these proteins will reveal which impact these methylglyoxal modifications have on the pathophysiological changes during aging.

P16.08 Trine Line Hauge Okholm THE LANDSCAPE OF CIRC RNAS IN BLADDER CANCER AND THEIR BIOMARKER POTENTIAL

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Circular RNAs (circRNAs) have recently been discovered to be abundant in mammalian cells. They are expressed in a tissue, cell type and developmental stage specific manner and have been associated with diseases, including cancer. Due to their circular structure, they are not degraded by exonuclease, which make them more stable than linear transcripts.

Here we study circRNAs in bladder cancer (BC), which is the 9<sup>th</sup> leading cause of cancer. Survival rate highly depends on the stage of the cancer at diagnosis, implicating the need for early-stage BC biomarkers. As circRNAs have recently been reported in human blood, these stable, highly specific, and easily accessible circular transcripts may represent a new class of biomarkers.

Using bioinformatic approaches, we identify and characterize the expression of circRNAs in a big cohort of early-stage BC samples (n=457) and explore their prognostic/diagnostic biomarker potential. We found multiple circular transcripts that are significantly differentially expressed

between different BC stages and some that correlate with progression status independently of their linear counterpart (e.g. circHIPK3, circPTK2 and circEXOC6B). Furthermore, we describe the biology of the circRNAs and their expression in cell lines and across tissues. We are currently validating promising circRNA candidates in the laboratory and setting up experiments to test the presence of circRNAs in human urine samples. Candidates that are excreted to urine and differentially expressed between BC stages and/or correlated with cancer progression would be promising non-invasive biomarkers.

P16.09 Line Khalidan  
Vibholm TLR9 AGONIST TREATMENT HAS A DUAL ROLE IN HIV-ERADICATION BY ENHANCING ACTIVATION OF CYTOTOXIC NK CELLS AND INDUCING PLASMA HIV-1 RNA IN VIVO

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In HIV-1 infected individuals on antiretroviral therapy (ART), HIV-1 persists in a silent state in the latently infected memory CD4<sup>+</sup>T cells. This provirus is not amenable to immune-mediated or pharmacological eradication. A proposed path for curative HIV-1 eradication is treatment with latency reversing agents (LRA), designed to reactivate transcriptionally silent HIV-1 in vivo. Such interventions, however, only lead to modest reductions in the size of the latent reservoir, possibly due to insufficient immune-mediated elimination of infected cells.

We hypothesized that a novel toll-like receptor 9 (TLR9) agonist, MGN1703, could function as both an enhancer of antiviral immunity and an LRA in vivo. We designed a single-arm phase 1b/2a clinical trial, where fifteen virologically suppressed HIV-1 infected individuals on ART received 60 mg of MGN1703 (s.c.) twice weekly for 4 consecutive weeks. Plasmacytoid dendritic cells (pDCs) express TLR9. Accordingly, we observed pronounced activation of pDCs and elevated levels of plasma interferon- $\alpha$ 2 ( $p < 0.0001$ ). Furthermore, proportions of activated cytotoxic NK cells ( $p < 0.0001$ ) and CD8<sup>+</sup>T cells ( $p = 0.032$ ) were expanded. MGN1703 treatment also demonstrated efficient LRA properties; in 6 of 15 participants, plasma HIV-1 RNA spiked up to levels  $> 1500$  copies/mL during the study. Consistent with our hypothesis, these data indicate that TLR9 stimulation by MGN1703 has a dual role in HIV-1 eradication therapy: reactivating latent HIV-1 and enhancing antiviral immunity.

P16.10 Camilla Christensen

DYNAMIC REMODELLING OF THE RIGHT VENTRICULAR MYOCARDIUM THROUGH THE CARDIAC CYCLE

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Background: Congenital heart disease will, in the majority of cases, be of great challenge to the right ventricle. Dysfunction is likely to occur, and both systolic and diastolic dysfunction has a great impact on the short- and long- term outcome. To promote the understanding of right ventricular dysfunction and failure, a detailed knowledge of the myocardial structure is needed, but no studies have investigated the three-dimensional rearrangement of the cardiomyocytes through the cardiac cycle in the normal right ventricle. This lack of knowledge constitutes a significant hole in the understanding of right ventricular cardiodynamics. Using diffusion tensor magnetic resonance imaging, we investigate the dynamic changes in the right ventricular myocardial morphology through the cardiac cycle in normal porcine hearts.

Methods: In total, 14 female domestic 20 kg pigs were included. Using conventional cardiac MRI, ventricular volumes and overall anatomy were determined. Subsequently, the hearts were excised and then randomized to fixation in either the diastolic or the systolic state; 7 in each group. In order to assess the changes in the right ventricular myocardial morphology from diastole to systole, diffusion tensor magnetic resonance imaging was used.

Results: Results are pending. The final results will be presented at the PhD Day.

P17.01 Mads Bengtzen

IN VIVO METABOLIC RESPONSES IN SKELETAL MUSCLE TO INSULIN, HYPOGLYCEMIA AND ADRENALINE

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Hypothesis: Insulin increases oxidative glucose metabolism and bicarbonate spikes. Hypoglycemia induces anaerobic metabolism and lactate spikes. Adrenaline induces anaerobic metabolism (1-3). Type 1 diabetics will maintain oxidative glucose metabolism during hypoglycemia and fail to activate lipolysis (4).

Background: Hypoglycemia is a limiting factor for optimal glycemic management of diabetes. It causes recurrent morbidity in most people with type 1 diabetes and can be fatal. Episodes of hypoglycemia impair the physiologically protective mechanism in subsequent episodes of hypoglycaemia, which is known as hypoglycemia-associated autonomic failure. Dynamic nuclear polarization (DNP)/MR-

hyperpolarization is a newly developed MRI technology. DNP allows rapid and highly sensitive in vivo detection of pre-polarized <sup>13</sup>C compounds (bioprobes) with a signal enhancement of more than 10,000. Pyruvate is a key molecule that is critical for numerous aspects of eukaryotic and human metabolism. In striated and cardiac muscle, pyruvate metabolism is highly regulated by insulin and other hormones and substrates.

Method: With the new DNP technology, we will study the effects of insulin, hypoglycemia and adrenaline on pyruvate, lactate etc. kinetics in skeletal muscle in a rodent clamp model (1-3). In addition, we will perform a clinical human study designed to test whether type 1 diabetic patients have defective glucometabolic and lipometabolic responses to hypoglycemia compared to non-diabetics (4).

Perspectives: Validate/implement DNP in animal studies. A better understanding of pyruvate can result in enhanced human health. Improving our knowledge of hypoglycemia will gain important knowledge that may help prevent hypoglycaemia in the future.

P17.02 Kristine Jepsen  
Bennedsgaard

CHRONIC NEUROPATHIC PAIN FOLLOWING OXALIPLATIN AND DOCETAXEL: A 5-YEAR FOLLOW-UP QUESTIONNAIRE STUDY

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Background: A growing number of patients survive cancer due to improved treatment and detection. Adjuvant chemotherapy with docetaxel and oxaliplatin increases the survival in patients with high-risk breast cancer and colorectal cancer, respectively. However, neurotoxicity is a common complication. A previous questionnaire study indicates that approx. 40% of patients develop neuropathy, and 30% experience pain one year after chemotherapy, but pain characteristics are poorly described. This questionnaire study is a 5-year follow-up of symptoms in patients treated with adjuvant chemotherapy for either high-risk breast cancer or colorectal cancer. The study will examine the development of neuropathy in the two groups of patients and characterize their pain.

Methods: In the period 2011-12, 100 patients with high-risk breast cancer and 74 patients with high-risk colorectal cancer answered a questionnaire before, during and one year after receiving adjuvant chemotherapy. A 5-year follow-up with the same questionnaire will be performed in survivors.

Results: In the group with breast cancer, six patients have died and one has moved abroad. In the group with colorectal cancer, 18 patients have

died since 2012. Of survivors, 86% in the breast cancer group and 93% in the colorectal cancer group answered the questionnaire. The analysis of the questionnaires is ongoing, and results will be ready in 2017.

Perspective: This study will document the development of neuropathy and pain and describe the characteristics of pain 5 years after chemotherapy in two groups of cancer patients. The study will also elucidate the impact of pain and neuropathy on the patients' quality of life, depression and anxiety.

P17.03 Mette-Lise  
Simonsen

#### THE IMPORTANCE OF AN ACUTE BLOOD SCREENING FOR DRUGS IN POISONED PATIENTS WITH ALTERED MENTAL STATUS

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Drug poisoned patients with altered mental status are most often treated on presumption, as current drug screenings are not useful in acute cases. Urine screenings as a "rapid test" are not accurate enough. With blood screenings, it can take up to 48 hours before a result for what the patient has taken is available. This often implies that patients are being overtreated and admitted to the hospital when it is not needed. At the Department of Forensic Medicine, Aarhus University, a new analysis method makes it possible to perform a blood screening for several hundred drugs in three hours.

The aim of this study is to evaluate if an acute blood screening for drugs can improve the treatment of poisoned patients with altered mental status, so that observation level and treatment matches the patient's needs. Thereby we can avoid undertreatment and over treatment of these patients and ultimately help utilize the hospital resources in the best possible way.

When examining the effect of the new analysis method in drug poisoned patients with altered mental status, we will be using the same method as in the pilot project where we examined the effect in conscious patients. When the patients for the study are admitted to the emergency department, a blood sample will be taken and later analysed if the patient has given consent. When the results are available, each of five physicians will retrospectively evaluate the patients during the first 24 hours and choose observation level and treatment, with and without the screening result.

According to the Danish Register of Causes of Death over 200 patients die each year due to poisoning. We also hope that this new analysis method can help reduce this number.

P17.04 Marie Weinreich Petersen FUNCTIONAL SOMATIC SYNDROMES IN THE GENERAL DANISH POPULATION: A STUDY PROTOCOL

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Background: Functional somatic syndromes (FSS) are characterised by patterns of persistent physical symptoms for which adequate examination does not reveal any specified pathology. FSS can be very disabling for the patients and costly for the society. The occurrence of the various FSS in the general population is not clear, and the criteria for the different syndromes have typically been reached through expert consensus based on data from highly selected patient groups. Epidemiological studies have shown that several syndromes can be classified in clusters with substantial overlap. A new empirically derived diagnostic category, bodily distress syndrome, may be more appropriate to delimit the syndromes.

Aim: To establish prevalence, sociodemographic characteristics, and mutual overlap of irritable bowel syndrome, fibromyalgia syndrome, chronic fatigue syndrome, whiplash associated disorder, multiple chemical sensitivity, and bodily distress disorder in the general Danish population.

Method: This study is part of a large-scale epidemiological study, the Danish Study of Functional Disorders (DanFunD). During DanFunD, a total of 7493 individuals from the general Danish population answered screening questionnaires about physical symptoms, life style, and wellbeing. Validated diagnostic algorithms will be used to assign diagnoses. Prevalence of each syndrome will be estimated with logistic regression. Sociodemographic characteristics will be explored with descriptive statistics.

Perspectives: Knowledge from this study will optimize future assessment and diagnosing of FSS.

P17.05 Kristian Nørgaard Larsen THE EFFECTS OF LETTING AGENTS CHOOSE PERFORMANCE INDICATORS IN HEALTHCARE

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Objective: We analyse an initiative trial launched in early 2014 by the Central Denmark Region delegating the responsibility for selecting performance indicators, formerly held by the principal, to healthcare

agents (i.e. healthcare professionals). The aim of our study was to investigate if this delegation of authority has led to increased performance of the agents before and after the new trial takes place.

Data: In this longitudinal study, we utilized data from the Danish National Patient Register and the Danish health economic DRG database. Data were collected from nine departments subject to delegation-based hospital governance. These departments chose a total of 91 different agent-selected performance indicators and 16 performance indicators chosen by the principal. The performance indicators are available from before (2012-2013) and after (2014-2016) the initiation of the trial. Indicators are reported monthly.

Methods: Our theoretical frame builds upon delegation theory. Delegation of authority has been proposed as a solution to solve information asymmetry between principal and agent. The performance indicators are investigated in an interrupted time series study (ITS). Furthermore, we apply the principal-selected indicators as non-equivalent dependent variables to strengthen the statistical design of our study.

Results: With respect to long-term effect, our study results show a significant, expected increase in the performance over time in 28 of the 91 agent-selected indicators and a non-significant expected change in 14 out of the 16 principal-selected indicators. The results are characterised by variation, and the preliminary evidence is mixed.

P17.06 Bodil Gade  
Hornstrup

#### OBSTRUCTIVE SLEEP APNEA AND BLOOD PRESSURE IN HYPERTENSIVE PATIENTS WITH CKD2 AND HEALTHY SUBJECTS

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Background: Nocturnal blood pressure (BP) is an important prognostic factor in the risk evaluation of cardiovascular disease in hypertensive patients. Many patients with chronic kidney disease (CKD) suffer from high nocturnal BP and non-dipping. This may be related to the presence of obstructive sleep apnea (OSA).

Methods: Invitation to participate was sent to 238 hypertensive subjects with CKD2 and 300 healthy subjects. In total, 95 hypertensive subjects responded and 76 were included, and 116 healthy subjects responded and 54 were included. All participants underwent 24h conventional and central BP monitoring, blood samples, and cardiorespiratory monitoring (Apnea Hypopnea Index, AHI).

Results: OSA was diagnosed in 31.6% of the hypertensive subjects with CKD2 and in 24.1% of the healthy subjects. This difference was not significant, but significantly more hypertensive subjects suffered from moderate to severe OSA (AHI>15). Hypertensive subjects were

significantly older, more obese and had lower nocturnal BP dipping than healthy subjects. The hypertensive subjects had higher blood levels of triglycerides, lower levels of HDL and LDL, and lower eGFR. Only 13 (17%) of the subjects diagnosed with hypertension prior to participation had normal 24 h BP.

Conclusion: OSA was diagnosed in a larger part than expected among both hypertensive and healthy subjects. Selection bias could explain this. Subjects with hypertension had less nocturnal dip in BP than healthy subjects. This may be related to comorbidity in the form of moderate to severe OSA. Only 17% of the subjects with known hypertension were normotensive. A reason for this can be unawareness of the importance of well-treated hypertension.

P17.07 Anita Tranberg  
Simonsen

WHOLE GENOME AMPLIFICATION AND EXOME SEQUENCING AT THE SINGLE CELL LEVEL - A WAY TO ADDRESS CLONAL HETEROGENEITY ON VERY SPARSE MATERIAL

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Single cell resolution in combination with next generation sequencing (NGS) would be the ultimate feat for characterization of subclonal contribution to leukemogenesis. Unfortunately, allelic dropout generally occurs with high frequency when performing whole genome amplification (WGA) and sequencing of single cells.

We aim to determine the cell number threshold by conventional laboratory analyses, and to elucidate what resolution to expect from whole exome sequencing (WES) at relatively low coverage.

Methods: 6 single cells and triplets of 2, 5 and 10 cells from the OCI-AML3 cell line extracted manually by micromanipulation along with serial dilutions to approximately 25 and 50 cells were used. Microsatellite genotyping analysis encompassing 21 short tandem repeat loci, fragment analysis of NPM1W288fs mutation and qPCR of the DNMT3AR882C mutation were performed after WGA. For exome sequencing, 5-, 25- and 50-cell assays were manually prepared.

Results: Microsatellite genotyping of single cells showed recurrent allele dropout compared to 2, 5 and 10 cells, etc. Detection of DNMT3AR882C mutation was consistent from 2 cells and up. From exome sequencing, a mean of  $9.4 \times 10^7$  reads was achieved with 99.3% of the sequences mapped to human reference genome GRCh37. Somatic NPM1 W288fs and somatic DNMT3AR882C were detected in all sequenced subsets with 16 of 44 to 19 of 43 reads, respectively, and mean allele frequency

of 41.5% (25.9-75%) and 44.5% (31.3-57.1%).

Conclusion: By choosing a very low number of cells from a well-characterized leukemia cell line, we have simulated genomic profiling of a small subpopulation; this will contribute to a more detailed picture of the cell biology.

P17.08 Stine Thyssen THE LINK BETWEEN PROTEIN OXIDATION AND AGING

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Aging is closely linked to various changes within cells, and an important factor is the level of intracellular oxidative stress. The increase in oxidative stress seen during aging is mainly due to a decrease in the ability for cells to convert oxygen to ATP. Instead, oxygen can be converted into reactive oxygen species (ROS). The highly reactive ROS can oxidize a wide range of biomolecules including proteins. Oxidation of proteins is essential for regulation of their activity and is, therefore, an important factor in cell signaling. It is reasonable to believe that the increase in ROS may introduce protein oxidation and change cell signaling with age.

The role of protein oxidation in aging and cell signaling is still not fully understood. This is partly due to the complexity of oxidation products and the instability of these oxidative modifications, which make them difficult to study. We are investigating which proteins are particularly prone to oxidation, and whether these oxidations may have a biological effect on aging and age-related diseases. Due to the instability of the oxidative modifications, we use different in-house synthesized chemical probes to trap these modifications. By coupling a fluorophore to the probe, we can visualize the oxidized proteins on a SDS-PAGE gel. For a large-scale proteomics study, we are currently developing and optimizing a protocol to capture oxidized proteins by affinity chromatography. For analysis and identification of target proteins and specific oxidation sites, we are using high resolution mass spectrometry. Eventually, we hope to obtain results that can give us a better understanding of the relationship between protein oxidation and aging.

P17.09 Stefanie Luecke INNATE DNA RECOGNITION BY CGAS IS DEPENDENT ON THE LENGTH OF DNA

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Recently, a number of pattern recognition receptors have been discovered that sense cytosolic DNA as a potent pathogen-associated molecular pattern. The DNA sensor cGAS (cyclic GMP-AMP synthase) is essential for the induction of an antiviral defense against many human pathogens, such as the DNA viruses and bacteria. Upon DNA sensing, cGAS produces the secondary messenger cGAMP, which activates the downstream signaling pathway via the signaling adaptor STING. Aberrant sensing of cellular nucleic acids causes severe autoimmune symptoms. Clearly defining the molecular characteristics of DNA that allow for self-from-non-self recognition by DNA sensors is essential for the understanding and treatment of these diseases.

We show that long DNA induces a stronger interferon response than short DNA when transfected into human macrophage-like cells in a cGAS-STING dependent manner. This is only seen when using low DNA concentrations similar to those present during infection. Differences in transfection efficiency or differences in degradation by the cytosolic exonuclease TREX are not responsible for the length dependency.

Importantly, recombinant human cGAS produces cGAMP in a DNA length-dependent manner in vitro, indicating that the length-dependent DNA recognition is based on intrinsic properties of cGAS and not mediated by cellular co-factors. We hypothesize that this is based on oligomerization of cGAS on DNA and will test this with cross-linking experiments. The relevance of the length dependency will be confirmed in the context of infection, by analyzing the size distribution of cytosolic DNA and cGAS-bound DNA during infection with capillary gel electrophoresis.

P17.10 Camilla Bang

RAPID USE OF HIGH-SENSITIVE CARDIAC TROPONIN I FOR RULING-IN AND RULING-OUT OF ACUTE MYOCARDIAL INFARCTION - THE RACING-MI STUDY

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Background: Early rule-in or rule-out of myocardial infarction (MI) is essential in patients presenting to the Emergency Department (ED) with chest pain. Recently, the European Society of Cardiology (ESC) has suggested an accelerated 0h/1h algorithm to rule-in or rule-out MI as a valid alternative to the standard 0h/3h approach. So far, no 0h/1h algorithm has been derived or validated using Siemens Advia Centaur high sensitive cardiac troponin I (hs-cTnI) Assay. Moreover, it is unknown

if MI can be ruled-out by measuring hs-cTn already at 30 minutes (0h/30m) after presentation to the ED. This study aims to investigate if Siemens Advia Centaur hs-cTn Assay can rule-in or rule-out MI when using a 0h/30m and a 0h/1h algorithm.

Methods: This is a prospective, observational study of 1 600 patients presenting to the ED with chest pain. Hs-cTnI will be measured at presentation (0 hour) and after 30m, 1h and 3h. Final treatment will depend on hs-cTnI after 0h and 3h, equivalent to clinical practice. For the first 800 patients, the measurements will be used to derive the 0h/1h- and 0h/30m algorithms for the Siemens Advia Centaur hs-cTnI Assay. For the next 800 patients, the algorithms will be validated. A 30-day follow-up of major adverse cardiac events will be retrieved from the Danish National Patient Register.

Results: Results are pending.

Perspectives: If the 0h/1h-algorithm can rule-in or rule-out MI, this study can contribute to the global implementation of the algorithm. Furthermore, hs-cTn testing after 30m may allow for even faster diagnosis. Early rule-in or rule-out of MI means less time to relevant treatment, improved patient outcome and increased bed availability in the ED.

P18.01 Ida Jakobsen

VALIDATION OF THE FEAR OF CANCER RECURRENCE INVENTORY (FCRI) IN A DANISH POPULATION OF COLORECTAL CANCER PATIENTS

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Background: Fear of cancer recurrence (FCR) is a frequent late effect from cancer. Consequences from FCR are impaired quality of life, change in health behaviour, psychological distress and increased perceived symptom burden. The Fear of Cancer Recurrence Inventory (FCRI) is a multidimensional measure for FCR. It has shown strong psychometric properties in the English and French versions. The Danish version of the FCRI has not been validated prior to this study.

Aim: To assess the psychometric properties of the FCRI in a Danish population of colorectal cancer (CRC) patients.

Methods: The psychometric properties of the FCRI were assessed in patients with primary non-advanced CRC from four surgical departments. Patients were asked to complete questionnaires immediately before a planned CT scan, and eight and ten weeks after. Clinical FCR was defined using a cut-off value of 16 at the FCRI severity sub-scale. The psychometric properties of the FCRI were assessed by responsiveness, test-retest reliability, discriminant and convergent validity.

Results: Among 122 invited, 69 patients (57%) responded to the questionnaire, of whom 20 (29%) reported clinical FCR. The FCRI showed good responsiveness, test-retest reliability (intraclass correlation= 0.84) and high agreement (dif= -2.23, 95% CI: -6.15; 1.74). As hypothesised, the FCRI identified significant age differences in FCR. We found a positive correlation between the FCRI score and a measure for worry traits ( $r=0.49$ ,  $p<0.00$ ), thus an acceptable convergent validity.

Conclusion: The Danish version of the FCRI is a reliable and responsive measure for FCR in CRC patients, and it shows acceptable discriminant and convergent validity.

P18.02 Viktoria Papp

#### A POPULATION-BASED EPIDEMIOLOGICAL AND SEROLOGICAL STUDY OF THE NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOSD)

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This collaboration study between the universities of Aarhus, Copenhagen and Southern Denmark consists of a complex national/international epidemiology study and an experimental part, which explores novel diagnostic assays and investigates the antibody-mediated pathogenesis of neuromyelitis optica spectrum disorder (NMO/NMOSD).

Aim: The project is designed to explore the population-based epidemiology of NMO/NMOSD, which is still poorly characterized. We will provide the first epidemiological and serological comparison of two European populations (DK vs. HU), which differ from each other regarding MS epidemiology. We wish to validate different criteria of NMO/NMOSD, which may contribute to precise diagnosis. We will use a cell-based assay for antibodies against myelin oligodendrocyte glycoprotein (MOG) and new methods (TRIFMA, flowcytometry) for testing anti-aquaporin 4 (AQP4) antibodies.

Data sources: Danish National Patient Register, Danish MS Register, laboratories providing anti-AQP4 test.

Results: For a year, 627 Danish patients have been re-evaluated; 25 NMO/NMOSD cases have been recognised based on the 2006, 2008 criteria, and 29 cases have been selected based on the 2015 criteria. This number may be increased when the antibody analyses are to be performed. We have found 4 patients who fulfilled only the IPND 2015 for seronegative NMOSD and were only identified in relation to the study.

Perspectives: NMO/NMOSD epidemiology and serological status will be explored. This will facilitate better differentiation between MS and

NMO/NMOSD and assist the choice of correct treatment for both patient populations. A better understanding of disease development, treatment and prognosis can be achieved.

P18.03 Per Høgh Poulsen CHILDHOOD SOCIOECONOMIC POSITION AND HOW IT RELATES TO MENTAL HEALTH AND OBESITY IN ADOLESCENCE AND EARLY ADULTHOOD

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Introduction: According to the OECD, Denmark has one of the lowest Gini coefficients in the world. However, it appears that the gap between rich and poor is increasing and leads to negative public health effects. Danish adolescents from lower affluence families tend to have poorer health and well-being compared to adolescents from higher affluent families. Low level of socioeconomic position (SEP) during childhood has previously been linked to poor future health outcomes. However, there has been an increasing demand for research, which addresses and explores the pathways and mechanisms by which low SEP in childhood exerts its long-term effects on future health.

The aim of the study is to examine how socioeconomic position during early and late childhood relates to mental health and obesity in adolescence and early adulthood.

Methods: A prospective cohort study using data from the project Vestliv, which is an ongoing survey following a complete regional cohort of young people born in 1989 and resident in the former county of Ringkøbing (N=3681). The main outcome variables are mental health measured by the CES-D and obesity defined by Body Mass Index. Exposure variables of interest: SEP based on yearly household income and parental education level, both derived from Statistics Denmark, and parents' labor market participation derived from the DREAM database.

We use regression analyses to estimate the association between the outcome and exposure variables. To deal with repeated measures within persons over time, we use multi-level analyses. All analyses are stratified by gender.

P18.04 Trine Ørhøj  
Barkholt BALLOON CATHETER TIP DAMAGE: A CLINICAL AND BENCH STUDY

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Background: Damage of the distal tip of percutaneous angioplasty balloons can occur after crossing through a stent to a side branch. Balloon tip damage may prevent passage of the balloon between the struts of a stent and may lead to stent distortion.

Aims: To determine frequency and severity of balloon tip damage clinically. In a bench test, we wished to compare the susceptibility to distal tip distortion and the tip dimensions of different balloons.

Methods: Balloon catheters used to cross through a stent to a side branch were collected. Catheter tip damage was evaluated by microscopic examination. Damage was graded and compared to the ease of side branch access. In a bench study, the force required to compress catheter tips of 0.5 mm was measured. Measurements of balloon tips were taken and compared for 2.5 mm and 3.5 mm diameter balloon catheters.

Results: A total of 50 patients and 110 catheters were included. After exclusion, 95 balloon catheters were available for analysis. Eight different devices were used. Catheter tip damage occurred in 67 (71%) balloons. In the bench compression test, the Flexx2 (Medinol) balloon tip required more force for 0.5 mm compression compared to other balloon tips and showed no damage. There was no difference in tip dimension of 2.5 mm and 3.5 mm balloons.

Conclusions: Balloon tip damage is common after side branch crossing. As the distal diameter of a 2.5 mm balloon tip is not different from a 3.5 mm tip, it may be unnecessary to choose a smaller diameter balloon to cross. Changing balloon catheter to one with an undamaged tip, changing wire position for better access and post-dilatation are possible solutions for better side branch access.

P18.05 Stine Overvad  
Fredslund

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

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Background: With increasing number of breast cancer survivors, long-term consequences of curative cancer treatment should be studied.

Several cytotoxic regimens are related to endothelial cell damage and

vascular toxicity. Endothelial dysfunction is implicated in the pathogenesis of all known cardiovascular diseases (CVD) and is closely related to the metabolic syndrome. Both CVD and diabetes contribute importantly to the mortality among breast cancer patients.

Methods and materials: We study the changes in endothelial function and metabolic parameters in breast cancer patients before and after receiving chemotherapy. For comparison, we examine healthy age-matched controls. Participants are characterized by age, smoking status, concurrent medication, BMI, body composition, blood pressure, metabolic parameters, endothelial function, and for patient's tumor characteristics and anticancer treatment. We strive to follow minimum 35 patients from before start of treatment to one year after ended treatment.

Results: Until now, 46 patients are enrolled. Of these, 34 have been followed since prior to start of chemotherapy. So far, we see a clear trend towards worsening of the metabolic parameters. In addition, a tendency towards increased blood flow after chemotherapy is seen.

Conclusion: The results imply that cytotoxic therapy worsens metabolic parameters. The changes in flow could indicate that the endothelium is inflamed, possibly on the way to being dysfunctional. More results are needed.

The next step will be to evaluate how strict metabolic control will affect the prognosis. Our results may be applicable to other cancer types.

P18.06 Camilla Hansen CERTIFIED BASIC LIFE SUPPORT INSTRUCTORS ASSESS  
CARDIOPULMONARY RESUSCITATION SKILLS POORLY

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Introduction: During basic life support (BLS) training, instructors assess learners' CPR skills to ensure high-quality standards. The aim of this study was to investigate certified BLS instructors' assessment of chest compressions and rescue breaths.

Methods: Data were collected at BLS courses for medical students at Aarhus University, Denmark. In pairs, certified BLS instructors evaluated each learner in an end-of-course test. Instructors' assessments were compared with data from the resuscitation manikin. Correct chest compressions were defined as  $30 \pm 2$  compressions at a depth of 50-60mm and rate of 100-120  $\text{min}^{-1}$ . Correct rescue breaths were defined as  $\geq 50\%$  efficient breaths with visible, but not excessive, manikin's chest

raise (for instructors) or a volume of 500-600 mL (manikin data).

Results: We included data from 90 end-of-course assessments done by 16 instructor pairs. Instructors identified correct chest compressions with a sensitivity of 0.96 (95% confidence interval (CI 95%) 0.79-1) and a specificity of 0.05 (CI 95% 0.01-0.14), and correct rescue breaths with a sensitivity of 1 (CI 95% 0.40-1) and a specificity of 0.07 (CI 95% 0.03-0.15). Instructors mistakenly failed one learner due to inadequate compression depth, while passing 53 (59%) learners with inadequate compression depth based on manikin data. Instructors correctly failed 6 (7%) learners due to inadequate rescue breaths. However, 80 (89%) inadequate rescue breath performances were not identified.

Conclusions: Certified BLS instructors assess performance of chest compression depth and rescue breaths poorly. This emphasizes the need for further education of instructors in undertaking CPR assessment.

P18.07 Karthiga  
Thavachelvam

#### RECOMBINANT PROTEINS OF THE OAS FAMILY RESTRAIN HIV INFECTION BY ALTERING THE CCR5 RECEPTOR

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The 2'-5' oligoadenylate synthetases (OAS) proteins are interferon-induced genes producing 2'-5A that activate the RNase L within infected cells. However, recent evidence indicates several RNaseL independent pathways for OAS proteins.

In this project, recombinant OAS1 and -3 as well as OASL(1-350) were purified in-house. Cellular uptake of recombinant OAS (rOAS) supplemented to culture media was validated by western blotting, and demonstrated significant intracellular protein levels were present for 2-72 hours. Next, rOAS-treated cells were challenged with a variety of replication competent HIV strains, and viral replication was assessed during a 5-day infection. Several members of the OAS family exerted potent antiviral activity against HIV strains that utilized the CCR5 for viral entry, whereas no antiviral activity was observed for HIV strains that used CXCR4 for viral entry. In addition, clinically selected HIV transmitted founder strains, which only exhibit CCR5-tropism, were completely blocked for infection of CD4+ T cells and macrophages by rOAS treatment. Importantly, infection with a clinical HIV strain, which is resistant to the antiretroviral drug MVC (CCR5 inhibitor), was also inhibited by OAS treatment. Analyses were eventually able to demonstrate that CCR5 surface expression was reduced upon rOAS treatment, which proposes a possible explanation for the antiviral

functionality.

In conclusion, our findings demonstrate an unknown antiviral mechanism of OAS, which has a tremendous impact on HIV CCR5-tropic strains to establish infection. Hence, we believe OAS products have a favourable future as vaginal ring microbicides that effectively block HIV transmission.

P18.08    Katrine Hygum    DIABETES MELLITUS IS A STATE OF LOW BONE TURNOVER - A META-ANALYSIS

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Background: Patients with diabetes mellitus types 1 and 2 are more susceptible to fractures than their healthy peers. The reason for this yet defies solution. Current evidence indicates an altered bone turnover in patients with diabetes, which can be evaluated by measuring bone turnover markers in serum.

Aim: To investigate differences in bone turnover between patients with diabetes and controls by conducting a systematic review and a meta-analysis.

Methods: A literature search was performed using the databases Medline at Pubmed and Embase employing specified free text search terms. Studies were eligible for inclusion if they investigated bone turnover markers in patients with diabetes compared with controls.

Results: A total of 2881 papers were identified of which 66 studies were included in the meta-analysis. Serum levels of the bone resorption marker C-terminal cross-linked telopeptide and the bone formation markers osteocalcin and procollagen type 1 amino terminal propeptide were lower in patients with diabetes compared with controls. Serum levels of sclerostin were significantly higher in patients with type 2 diabetes and in patients with type 1 diabetes compared with controls, and serum levels of osteoprotegerin were increased in patients with diabetes compared with controls.

Conclusions: Markers of both bone formation and bone resorption are decreased in patients with diabetes. This suggests that diabetes mellitus is a state of low bone turnover, which may lead to altered bone quality and hence more fragile bone. Altered levels of sclerostin and osteoprotegerin may be responsible for this.

P18.09 Trine Wigh  
Arildskov

THE RELATIONSHIP BETWEEN ADHD TRAITS AND DAILY FUNCTIONING & QUALITY OF LIFE IN CHILDREN FROM THE GENERAL POPULATION

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Background: Studies suggest that the categorical either-or definition of ADHD (disorder vs. no disorder) in the diagnostic manual may be suboptimal and that ADHD is better conceptualized as a dimension: a continuum ranging from the complete absence of symptoms to severe ADHD symptoms. That is, ADHD traits are natural aspects of human behavior, and we all have varying degrees of hyperactivity, impulsivity and inattention. However, it remains unknown to what extent varying degree of ADHD traits relates to daily functioning and well-being.

Objective: To assess the relationship between ADHD traits and daily functioning & quality of life in schoolchildren.

Methods: Parents of children in 1st, 2nd and 3rd grade (about 7-9 years) are invited to participate in an online survey through "Forældreintra" - a web-based intranet for communication between schools and home. Parents are asked to fill in a range of questionnaires assessing ADHD traits, impairment in daily functioning, strengths and difficulties, and quality of life using the ADHD rating scale, the Weiss Functional Impairment Rating Scale, the Strengths and Difficulties Questionnaire, and the Pediatric Quality of Life Inventory. Moreover, the parents provide information regarding their socio-economic status (e.g. income, education, occupation).

Results: The survey is currently being carried out at schools in the Aarhus area, and about 300 parents have participated so far. Preliminary results are expected to be available in January 2017.

Perspectives: The study will generate important findings regarding the distribution and consequences of ADHD traits, thereby having implications on how to conceptualize ADHD in the future.

P18.10 Rasmus Espersen

SKELETAL EFFECTS OF ROUX-EN-Y GASTRIC BYPASS IN OBESE TYPE 2 DIABETES PATIENTS MEASURED BY DXA AND HR-PQCT: A 6-YEAR FOLLOW-UP STUDY

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Introduction: Roux-en-Y gastric bypass (RYGB) is a highly effective treatment of severe obesity, leading to sustained weight loss as well as improvements in obesity-related comorbidities. The procedure creates a small gastric pouch and bypasses the greater part of the stomach and the duodenum. This leads to restricted food intake and malabsorption of important nutrients for bone metabolism like calcium and vitamin D. Furthermore, large weight loss also causes bone loss by skeletal unloading.

Dual-energy X-ray absorptiometry (DXA) is the common approach to evaluate bone health. However, this method has a limited accuracy in obese patients. As a result, high resolution peripheral quantitative computed tomography (HR-pQCT) is emerging as a supplement to DXA. This method distinguishes between cortical and trabecular bone as it reveals the microarchitecture of the bone, and it estimates the strength of the bone by finite element analysis. We hypothesize that RYGB operated type 2 diabetes patients have impaired bone health compared to non-operated type 2 diabetes patients.

Methods: We conducted a clinical trial including 98 RYGB operated and 49 non-operated patients with type 2 diabetes matched on age, gender and current body mass index. We performed DXA, including vertebral fracture assessment, on lumbar spine, femoral neck and radius and HR-pQCT, including finite element analyses, on radius and tibia. These were supplemented by blood samples and questionnaires regarding skeletal health.

Results: Baseline data and results will be presented at PhD Day 2017.

Conclusion: A conclusion will be presented at PhD Day 2017.

P19.01 Morten Fenger-Grøn MENTAL DISTRESS AND THE PROGNOSIS OF MYOCARDIAL INFARCTION - SPOUSAL BEREAVEMENT AS A NATURAL EXPERIMENT

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Background: Mental distress is common after myocardial infarction (MI) and associated with a 2-3 fold higher mortality, but it remains unclear whether it is a causal factor or merely a marker of MI severity. Spousal bereavement is a major life event causing numerous mental reactions and can be assumed independent of MI severity. Thus, it may resemble a

natural experiment which is well suited to study the causal effect of mental distress on MI prognosis.

Material and methods: Using Danish nationwide registers, we identified all patients surviving the day of their first MI from 1984 through 2013. The cohort was followed for up to 2 years ending in December 2013, and members were linked to spouse's death date. Mortality was analysed using Poisson regression with bereavement as a time dependent exposure and adjustment for calendar period, time since MI, sex, age, cohabitation status and Charlson indexed diseases before the MI date.

Results: In total, 219,039 incident MI patients were identified of whom 63,882 died within 2 years of follow-up. Loss of a partner was experienced by 4,460 of whom 570 died. MI patients experiencing spousal bereavement had a more than 50% increased mortality in the first month after bereavement (MRR and 95% CI: 1.51 [1.29-1.77]). Mortality remained significantly increased for the remainder of the first year after bereavement, but to a more modest extent (MRR and 95% CI: 1.14 [1.08-1.21]). The association between bereavement and mortality appeared strongest for men and for MI patients experiencing the least expected losses.

Conclusion: Spousal bereavement after MI was associated with a significantly increased mortality, particularly on the short term and among males.

P19.02 Ditte H. Jensen NATION-WIDE INTERNET-DELIVERED TREATMENT FOR PATIENTS SUFFERING FROM HEALTH ANXIETY: A PILOT FEASIBILITY STUDY

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Background: Few available treatment options exist for patients suffering from health anxiety, or hypochondriasis. It is a disabling disorder characterized by preoccupation with fear of having a serious illness that persists despite medical reassurance. Health anxiety is costly in terms of patients' use of health care services. Currently, few treatment options and geographical distance hinder many patients from seeking specialized treatment. Therefore, easily accessible, specialized treatment is urgently needed for this debilitating illness.

Objectives: To develop and test the feasibility of a new internet-delivered 'Acceptance and Commitment Therapy' (iACT) treatment program for health anxiety prior to conducting a larger randomized, controlled trial.

Methods: Fifteen patients with HA recruited nation-wide received 7 sessions of iACT containing psychoeducation, exercises and therapist

support. Self-report questionnaires were obtained at baseline, at end of treatment and at 3-month follow-up. The primary outcome measured health anxiety (Whiteley-7), and secondary outcomes measured depression and anxiety (SCL-92) and quality of life (WHO-5).

Results: Paired t-tests showed significant changes on all variables, both at end of treatment and 3-month follow-up. Symptoms of health anxiety decreased 31.9 points at 3-month follow-up (95% CI 12.8 to 51.0,  $t(12) = 3.64$ ,  $p = 0.003$ ); a reduction of 41%. Depression decreased 56%, anxiety decreased 55% and quality of life increased 56% at 3-month follow-up.

Conclusion: iACT may be a feasible treatment for HA and may broaden the availability and accessibility of specialized treatment.

P19.03 Christelle  
Gansonre

#### TASK-FREE EEG PARADIGM FOR REGISTERING MULTIPLE LEVELS OF LANGUAGE PROCESSING IN THE BRAIN

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Previous research has shown that the brain exhibits specific neural signatures of auditory stimulus processing in passive listening conditions, such as the P1-N1-P2 complex for basic sound processing or the P300 deflection in response to unexpected surprising sounds.

Building on these previous findings, we present an unattended paradigm simultaneously assessing acoustic, phonological, lexical levels of spoken language processing and attention modulation. Healthy participants were instructed to ignore the sequence of speech and non-speech sounds they were presented with and to concentrate on watching a silent video while their brain activity was recorded using a 75-channel EEG setup.

Our results show that infrequent sounds elicited a clear P1-N1-P2 complex showing the integrity of sound processing functions in the auditory cortex. We found an enhanced negativity, index of automatic lexical processing, in response to real words compared to native-like meaningless words, likely reflecting automatic activation of word memory traces. The level of phonological processing was indexed by differential responses to speech stimuli and acoustical similar non-speech stimuli and by an early ERP difference between native and non-native spoken stimuli. Finally, a large P300-like positivity at 300 ms after the onset of novel sounds reflected automatic auditory attention reorientation.

In sum, we present a technique which can test sound and language processing at multiple levels of complexity in a single passive EEG

experiment. This paradigm may potentially be useful in clinical settings, especially when assessing the neurocognitive status of uncooperative/unresponsive individuals.

P19.04 Troels Munch

#### IMPACT OF PRE-ADMISSION OPIOID TREATMENT ON ONE-YEAR MORTALITY FOLLOWING NON-SURGICAL INTENSIVE CARE ADMISSION

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Background: Preadmission opioid use may worsen prognosis following intensive care unit (ICU) admission.

Objectives: To examine the impact of pre-admission opioid use on one-year mortality following non-surgical ICU admission.

Methods: Using Danish registries, this cohort study included all non-surgical patients admitted to an ICU in 2005-2014. Patients were grouped based on the timing of last redeemed opioid prescription prior to admission: current users (0-30 days prior), recent users (31-365 days prior), former users (365+ days prior), or non-users. Outcome was all-cause mortality at 0-30 days and 31-365 days following ICU admission. Mortality was estimated using the Kaplan-Meier method, and crude and adjusted hazard ratios (HR) with 95% confidence intervals (CI) were estimated by Cox regression. Adjusted models included age, gender, socioeconomic factors, co-medication, and comorbidity.

Results: In total, 118,388 non-surgical ICU patients were included; 15% were current opioid users, 15% recent users, 30% former users, and 40% non-users. The 30-day mortality was 34% for current users, 27% for recent users, 23% for former users, and 19% for non-users. After confounder adjustment, current users remained at elevated risk: HR = 1.20, 95% CI: 1.16-1.25. No association remained for recent or former users. A similar pattern was evident for 31-365 day mortality: 24% among current users, 19% among recent users, 13% among former users, and 10% among non-users. During 31-365 days, current users and recent users remained at elevated risk of mortality (HR = 1.47, 95% CI: 1.39-1.55 and HR = 1.20, 95% CI: 1.13-1.27, respectively).

Conclusion: Current use of opioids is associated with increased mortality during the first year following ICU admission.

P19.05 Rasmus Stilling ACUTE AFTERLOAD-IMPOSED SHIFT IN PORCINE CARDIAC ENERGETICS  
Tougaard IMAGED BY HYPERPOLARIZED [1-<sup>13</sup>C]PYRUVATE

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Background: Deranged metabolism is now being seen as a key causal factor in several heart diseases, primarily heart failure. This topic has garnered much interest in recent years owing to the belief that metabolically targeted treatments could potentially better the prognosis for heart failure patients, who remain in poor health despite recent advancements. Animal studies and clinical trials on metabolism have so far displayed immense heterogeneity, and some of the results have been conflicting. This is in part due to methodological challenges with invasive methods altering metabolism and imaging technology merely measuring uptake of tracer. These challenges can possibly be overcome by the novel technique hyperpolarized MR.

Methods: In total, 5 pigs were scanned with hyperpolarized [1-<sup>13</sup>C]-Pyruvate cardiac MR at baseline, given a sugar bolus in the stomach and scanned again 1 hour later, then infused intravenously with angiotensin II to elevate afterload for 30 minutes and scanned for a final time.

Results: Blood pressures were significantly elevated and Ejection Fraction had decreased at final time point, at which point lactate/alanine- and bicarbonate/alanine-ratios were both significantly increased. No effect of sugar bolus was seen with hyperpolarized [1-<sup>13</sup>C]Pyruvate MR in spite of both blood sugar and insulin levels increasing throughout the study.

Conclusions: Acute elevation of afterload in an in vivo porcine model produced measurable increases in both anaerobic and aerobic cardiac metabolic pathways. This entails exciting future prospects for monitoring a cardiac energetic response to afterload-reducing treatment by way of hyperpolarized MR.

P19.06 Giacomo Frattari ELIMINATION OF THE ACTIVE HIV RESERVOIR: ENHANCEMENT OF NK  
CELL-MEDIATED ADCC ACTIVITY BY TOLL-LIKE RECEPTOR 9  
STIMULATION

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Background: NK cell-mediated immunity is important for controlling HIV replication and for preventing disease progression. More specifically,

Antibody-Dependent Cell Cytotoxicity (ADCC) plays a central role in the NK cell mediated killing of HIV infected cells. However, two barriers associated with chronic HIV infection and ART still preclude effective ADCC mediated clearance: 1) the generalized impairment of NK cell functions and 2) the low abundance of HIV-specific neutralizing antibodies. These limitations may be overcome by combination immunotherapy with MGN1703, a TLR-9 agonist, and two HIV-specific broadly neutralizing antibodies (bNAbs), 3BNC117 and 10-1074.

Methods: In this study, we will isolate PBMCs from HIV-infected donors on ART and stimulate them with MGN1703 ex vivo. We will then isolate the stimulated NK cells and test their HIV-specific ADCC activity when 3BNC117 and 10-1074 are added. Moreover, NK cells will be analyzed by flow cytometry for MGN1703-induced immunomodulatory effects.

Hypothesis: The anticipated outcome is that MGN1703 stimulation will trigger NK cells to enhance Granzyme B delivery and that this improvement in ADCC is facilitated by the presence of bNAbs such as 3BNC117 and 10-1074.

Significance: The significance of this research year project is the detailed characterization of the interplay between two different clinical approaches for enhancing HIV immunity via ADCC: monoclonal broadly neutralizing antibodies and immunomodulation via TLR9 stimulation.

P19.07    Johanne Bach  
              Andersen    STABILITY OF EGFR MUTATIONS IN WHOLE BLOOD AND PLASMA IN PATIENTS WITH NSCLC

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Objectives: The cobas<sup>®</sup> EGFR Mutation Test v2 for detection of epidermal growth factor receptor (EGFR) mutations in blood samples can be used to obtain circulating tumor DNA in the clinic. Knowledge of the EGFR mutation status in non-small cell lung cancer (NSCLC) patients is essential to designing optimal, individualised treatment. But implementing blood-based analyses to detect cancer-specific mutations demands standardized preanalytical conditions. However, research in this field is rare and inadequate. The aim of this project is to establish the stability of the EGFR mutations under various preanalytical conditions. We test if prolonged storage before DNA extraction will influence the stability of the EGFR mutations.

Design and methods: In this study, we used blood samples from patients with advanced NSCLC. The mutation status and amount of mutated DNA was demonstrated using the cobas<sup>®</sup> EGFR Mutation Test v2. We tested if EGFR mutations are stable in whole blood stored at 32°C for 8 hours. We

also tested if EGFR mutations are stable in plasma stored at 32°C, 2-8°C, -20°C and at -80°C at various time periods.

Results: All data are generated and are currently being processed.

Perspectives: Establishing stability of the EGFR mutations at various storage conditions ascertains the robustness of the analysis and makes it more suitable for the clinic. Our results will generate more knowledge on correct specimen handling and enhance the use of liquid biopsies.

P19.08 Mona Sharghbin COMPARISON OF AORTIC VALVE REPAIR TECHNIQUES WITH DIFFERENT SUBVALVULAR ANNULOPLASTIES - AN IN VITRO EVALUATION

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Background: Traditionally, severe aortic insufficiency has been treated with aortic valve replacement. Aortic valve sparing repair has become an advantageous alternative to avoid the adverse effects of valve replacement. Increasing evidence shows that an annuloplasty is needed in aortic valve sparing repair techniques. However, the biomechanical characteristics of these annuloplasties have not yet been examined. The aim of the study is to characterize and compare two types of annuloplasties in vitro.

Methods: Eighteen aortic roots from 80 kg pigs were randomized to three groups: 1) native valve with suture-annuloplasty, 2) native valve with Dacron ring, and 3) native valve as reference. A force transducer was attached to the aortic root annulus before mounting the root into the in vitro model. The transducer consists of strain gauges allowing individual force measurements of annulus geometry. The resultant flow was recorded by an ultrasonic flow meter, and the ventricular and aortic pressures were recorded using micro-tip pressure catheters. High-speed imaging and echocardiography allowed evaluation of leaflet motion, valve dynamics, and opening and closing velocities. Data analysis will be performed by comparing these parameters between the groups.

Results: Pending.

Conclusion: A comprehensive description of aortic valve sparing repair with supporting annuloplasties will be obtained. With a new understanding of the biomechanical and hemodynamic effects of an added suture or ring annuloplasty, we expect this study to provide important information leading to optimized surgical procedures in the relevant patient groups.

- P19.09 Astrid Johannesson Hjelholt GROWTH HORMONE INDUCES LIPOLYSIS IN HEALTHY, OBESE SUBJECTS  
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- Introduction: It is well known that growth hormone (GH) induces lipolysis, but the molecular mechanisms remain uncertain. Recent studies indicate that GH suppresses the expression of genes encoding insulin-dependent signaling proteins involved in anti-lipolysis.
- The aim of this study was to examine signaling pathways for lipolysis, insulin and GH in vivo in consecutive human adipose tissue biopsies following an intravenous GH bolus.
- Methods: Nine healthy, obese males were studied twice, randomly receiving either GH (intervention day) or pegvisomant, which blocks the actions of GH (control day). The study day included four biopsies from subcutaneous adipose tissue, blood samples and indirect calorimetry.
- Signaling proteins and expression of gene targets will be analyzed in the biopsies by western blotting and real time qPCR.
- Preliminary results: Serum levels of free fatty acids (FFA) were significantly higher on the intervention day compared to the control day. A distinct temporal pattern of serum FFA levels was seen after GH exposure characterized by a lag phase of approximately 60 minutes prior to an increase, which peaks after about 180 minutes. The respiratory exchange ratio (RER) was significantly lower after GH exposure, indicating a higher utilization of fat.
- Discussion: Preliminary results from the present study show that GH induces lipolysis, release of FFA and fat utilization in healthy, obese subjects. The distinct temporal pattern of serum FFA levels seen after GH exposure indicates that assessment of the effects of GH on adipose tissue lipolysis in vivo necessitates multiple fat biopsies in a prolonged period following GH exposure.
- P19.10 Anne Louise Hansen ENDOGENOUSLY FORMED NITRO-FATTY ACIDS DAMPEN HSV-2 INDUCED INFLAMMATION  
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Herpes Simplex Virus type 2 (HSV-2) is one of the most common sexually transmitted infections. The infection is lifelong with recurrent outbreaks of genital blisters and ulceration. The HSV-2 infection leads to initiation of anti-viral and inflammatory responses. It is essential to regulate the inflammation to prevent tissue damage and development of severe symptoms.

Nitro-fatty acids (NFA) are formed naturally by a non-enzymatic addition of NO or NO<sub>2</sub> to unsaturated fatty acids and can be measured by mass spectrometry. The electrophilic NFAs have previously been reported to reduce inflammation through post-translational modifications of regulatory proteins.

We hypothesize that NFAs are formed during HSV-2 infection and that NFAs can dampen the viral-induced inflammation.

Here, we demonstrate, for the first time, that a certain NFA, NO<sub>2</sub>cLA, is endogenously formed during HSV-2 infection in vivo. NO<sub>2</sub>cLA formation was also found in vitro when media was supplemented with cLA. The formation was dependent on inducible nitric oxide synthase (iNOS) shown by the absence of NO<sub>2</sub>cLA release in CRISPR/Cas9 deficient iNOS murine macrophages. iNOS, expressing CD11b+Ly6C+ cells, was present at the site of infection in vivo; these cells can hence be accountable for the NO<sub>2</sub>cLA formation. The NO<sub>2</sub>cLA displayed anti-inflammatory actions by attenuating type I interferon production and by reducing pro-inflammatory cytokines like MCP-1 and IL-6.

Overall, our findings demonstrate, for the first time, endogenously NO<sub>2</sub>cLA formation during viral infection, and the NO<sub>2</sub>cLA displayed anti-inflammatory properties. Thus, NO<sub>2</sub>cLA can provide novel strategies for damping of destructive inflammatory responses.

P20.01 Alon Schneider  
Hait IDENTIFICATION OF NOVEL INNATE IMMUNODEFICIENCIES IN PATIENTS WITH HERPES ENCEPHALITIS

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Introduction: Worldwide, HSE is the most common form of sporadic viral encephalitis. Previous work in the field of herpes virus pathogenesis using DNA sequencing of clinical HSV-1 isolates supported the idea of gene variations in host factors-encoded pattern recognition receptors, which contribute to susceptibility of some individuals to HSV-1 CNS invasion and infection progressing to HSE.

Objectives: In this study, we hypothesize that differential susceptibility to viral CNS infections is explained by host genetics, and in particular mutations found in gene encoding innate immune molecules involved in type-I interferon production. In the study, we wish to identify and

functionally characterize novel single gene inborn errors of immunity associated with increased susceptibility to herpes simplex virus infections of the central nervous system (CNS).

Methods: We have identified and treated 35 cases of HSE during the past five years. From these patients, genomic DNA was isolated and subjected to WES. In order to identify novel innate immune point mutations, we will short-list genes based on known to be involved in the recognition/signaling pathways activated by HSV. We will confirm the relation between the mutations found by the patients' cells stimulation for PRR and cytokine receptors. To further characterize the relevant immune-associated mutations, we will clone and express the wild-type and mutant molecule in a cell line with no endogenous expression of the relevant protein using CRISPR/Cas9 technology.

P20.02 Yulia Olsen

AIRBORNE ALTERNARIA AND CLADOSPORIUM FUNGAL SPORES: EFFECT ON ASTHMA SOURCES IN DENMARK

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Background: Alternaria and Cladosporium are ubiquitous in the air and important aeroallergens (1; 2). However, little is known about their sources and their effect on asthma. There is a link between Alternaria concentration and the density of agricultural areas (3;4), but the sources of Cladosporium are still to be identified.

Aim: To establish the most relevant local sources of Cladosporium and Alternaria in Denmark with a specific attention to crop harvesting and its effect on asthma exacerbations.

Hypotheses: a) Increase in daily fungal spore counts and harvesting periods are associated with asthma exacerbations; b) Higher loads of Alternaria are found in western vs. eastern Denmark; c) The major portion of airborne Cladosporium is emitted from sources other than grain crops.

Methods and plans: Two epidemiological studies (time-series and case-crossover designs) based on health registers and daily spore concentrations. Obtaining data on spore air concentrations through microscopic analysis of archived samples. Identification of airborne Cladosporium source areas by use of back trajectories. Evaluation of Cladosporium vs. Alternaria colonization by field measurements during grain crops harvesting.

References:

Gravesen S. 1979. Allergy 34:135-54 Horner WE, Helbling A, Salvaggio JE, et al. 1995. Clinical Microbiology Reviews 8:161-79 Skjøth CA, Damialis A, Belmonte J, et al. 2016. Aerobiologia 32:3-22 Skjøth CA, Sommer J, Frederiksen L, et al. 2012. Atmos. Chem. Phys. 12:11107-23

P20.03 Maria-Louise Røn Kobbere INFILTRATING THE STRONGHOLD OF HIV-1 DURING SUPPRESSIVE ART: VIROLOGICAL AND IMMUNOLOGICAL EFFECTS OF TLR9-TARGETED IMMUNOTHERAPY IN LYMPH NODES

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Background: Antiretroviral therapy (ART) for HIV-1 infection efficiently suppresses viral replication to below detection levels. However, latent HIV-1 DNA persists within cells despite therapy. Particularly lymph nodes (LN) are known to constitute a major HIV-1 reservoir during ART. A suggested approach to eradicate this reservoir is to stimulate latently infected cells to resume transcriptional activity, hereby making the cells susceptible to immune mediated killing. Yet sufficient killing to completely eradicate all latent HIV-1 is unlikely without concomitant enhancement of the patients' antiviral immune response. MGN1703 is a novel toll-like receptor 9 (TLR9) agonist, which induces HIV-1 transcriptional activity and enhances cellular antiviral immunity in HIV-1 infected individuals in vivo.

Hypothesis: We hypothesize that TLR9 agonist treatment with MGN1703 reduces the levels of HIV-1 DNA in LN of HIV-1 infected individuals. Additionally, we will characterize the immunological effects of MGN1703 in LN.

Design and methods: This project is a subset analysis in a single-arm phase 1b/2a clinical trial, where HIV-1 infected individuals on ART receive MGN1703 for 24 weeks. At baseline and during the last week of dosing, LNs will be excised and analyzed by in situ hybridization and immunohistochemistry to quantify induced changes in HIV-1 DNA and RNA and markers of immune activation.

Anticipated outcomes: Our results will contribute to the understanding of HIV-1 persistence in LN. Furthermore, the study will provide new insights to the effects of TLR9 agonist treatment in an HIV-1 cure context.

P20.04 Mille Thastum LONG-TERM IMPROVEMENTS IN SYMPTOMS, ILLNESS PERCEPTIONS AND ILLNESS BEHAVIOUR IN YOUNG PEOPLE AFTER A BRIEF INTERVENTION FOR PERSISTENT POST-CONCUSSION SYMPTOMS: AN UNCONTROLLED STUDY

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Background: About 5-15 % of patients with concussion experience impairing post-concussion symptoms (PCS) for longer than 3 months post-injury. Existing literature suggests that negative illness perceptions and maladaptive illness behaviours may be involved in symptom maintenance. Currently, no evidence-based intervention is available.

Aim: To explore the overall outcome of a brief behavioural intervention in young patients (15-30 years) with PCS 3-6 months after concussion.

Methods: Thirty-two patients received an 8-week interdisciplinary intervention based on principles from cognitive-behavioural therapy and gradual return to activities. Self-report measures were completed pre-intervention, post-intervention (N=23), and 3 months (N=20) and 12 months (N=26) post-intervention. Change after intervention was measured by the Rivermead Post-concussional Symptoms Questionnaire (RPQ) (primary outcome), the Behavioural Response to Illness Questionnaire (BRIQ), and the Brief Illness Perception Questionnaire (B-IPQ). Data was analysed using an unadjusted mixed model.

Results: Mean age was 23.3 years, and 81 % were women. Patients showed a reduction in PCS from 35.2 points pre-intervention to 25.6 points post-intervention ( $d=9.6$  (95% CI: 13.9 - 5.2),  $p=0.000$ ,  $ES = 1.04$ ), and a reduction in negative illness perceptions ( $p=0.000$ ) and maladaptive illness behaviour ( $p<0.05$ ). Improvements were maintained at 3- and 12-month follow-up.

Conclusion: Based on uncontrolled data, the new intervention was associated with significant symptom reduction and more adaptive illness cognitions and behaviours. It may have the potential to prevent chronification of PCS. An RCT is currently performed.

P20.05 Thea Pinholt  
Lillethorup

MULTI-NEUROTRANSMITTER DEFICITS IN A MINIPIG MODEL OF PARKINSON'S DISEASE

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Aim: Both aging and Parkinson's disease (PD) are characterized by progressive decreases in activity of the ubiquitin proteasome system (UPS). In PD, this is thought to contribute to widespread cell death and protein aggregation (Lewy bodies). Here, we induced long-term inhibition of the UPS in minipigs and used positron emission tomography (PET) to evaluate its effect on multiple monoaminergic systems.

Methods: Adult minipigs were implanted with an intracerebroventricular catheter connected to an injection port. Low doses of lactacystin (UPS inhibitor) were injected weekly. PET scans were performed with [<sup>11</sup>C]DTBZ (tracer of the vesicular monoamine transporter 2), [<sup>11</sup>C]Yohimbine (tracer of the α2-adrenoceptor) and [<sup>11</sup>C]DASB (tracer of the serotonin transporter) at baseline and 3 and 6 months following the start of injections. The animals were longitudinally monitored for motor deficits.

Results: By 6 months, lactacystin administration induced a decrease in [<sup>11</sup>C]DTBZ and [<sup>11</sup>C]DASB binding in striatal regions compared to baseline, consistent with loss of dopaminergic and serotonergic brainstem neurons. An increased volume of distribution of [<sup>11</sup>C]Yohimbine was detected in thalamic and cortical regions, likely reflecting upregulation of the receptors in response to loss of pontine adrenergic cell bodies. Moreover, impairments in motor performance were observed.

Conclusion: The imaging evidence of loss of multiple neuronal brainstem populations are consistent with Braak's pathology staging of PD, which suggests a caudo-rostral gradient of deficits with serotonin and noradrenaline nuclei affected early in PD. Prolonged UPS inhibition may provide a new, progressive model of PD.

P20.06 Pernille Gabel

TARGETED INFORMATION DESIGNED TO REACH EVERYONE?  
DEVELOPMENT OF A DECISION AID IN THE COLORECTAL CANCER  
SCREENING PROGRAMME

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Introduction: The participation rate in colorectal cancer screening is lower among lower educational attainment citizens. Information materials are often long and difficult to read, while decision aids targeted at lower educational attainment citizens with higher readability are shown to increase knowledge in these citizens. However, some citizens like a clear recommendation from authorities, while others want thorough and detailed information about the choice they are facing. Hence targeted decision aids need to be differentiated to reach everyone.

The aim of this study is to develop a decision aid targeted at lower educational attainment citizens based on the different information needs of this population; hereby aiming to increase citizen involvement in colorectal cancer screening decisions.

Methods: The decision aid will be web-based and interactive. Development will be made according to the International Patient

Decision Aids Standard instrument as well as previous experiences of lower educational attainment citizens' information needs.

Both citizens with lower educational attainment and medical experts will contribute to the development of the decision aid through expert panels, focus group interviews, peer review and user testing. In this way, the decision aid should reach as many citizens as possible in information level, availability, readability and usability.

Results: The decision aid is developed throughout 2016, and hence results and conclusions will be presentable in January 2017.

Discussion: A differentiated decision aid may be necessary to reach citizens in their own context and hence help citizens make the right decisions for themselves.

P20.07 Kasper Adelborg RISK OF STROKE IN PATIENTS WITH HEART FAILURE: A POPULATION-BASED 30-YEAR COHORT STUDY

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Background: The long-term risk of specific stroke subtypes among heart failure patients is largely unknown.

Objective: We examined short-term and long-term risk of ischemic stroke, intracerebral hemorrhage (ICH), and subarachnoid hemorrhage (SAH) in heart failure patients and in a general population comparison cohort.

Methods: In this nationwide cohort study (1980–2012), we used Danish population-based medical registries to identify and follow (1) all patients hospitalized for the first time with heart failure and (2) a birth year-, sex-, and calendar year-matched general population comparison cohort. Age-, sex-, and comorbidity-adjusted stroke rate ratios (aSRRs) were computed based on Cox regression analysis.

Results: Overall, 289,353 patients with heart failure and 1,446,765 individuals from the general population were included in the analysis. One- and 5-year risks among heart failure patients were 1.4% and 3.9% for ischemic stroke, 0.2% and 0.5% for ICH, and 0.03% and 0.07% for SAH. The 30-day aSRR was increased markedly for ischemic stroke [5.08, 95% confidence interval (CI), 4.58-5.63] and was also elevated for ICH (2.13, 95% CI, 1.53-2.97) and SAH (3.52, 95% CI, 1.54-8.08). Between 31 days and 30 years, risk of all stroke subtypes remained positively associated with heart failure (1.5- to 2.1-fold for ischemic stroke, 1.4- to 1.8-fold for ICH, and 1.1- to 1.7-fold for SAH) in comparison with the general population cohort.

Conclusions: Heart failure was associated with increased short-term and long-term risk of all stroke subtypes, suggesting that heart failure is a potent and persistent risk factor for ischemic stroke, ICH, and SAH.

P20.08 Simon Haugaard THE LECTIN PATHWAY IN POST CARDIAC ARREST PATIENTS

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Background: Out-of-hospital cardiac arrest strikes more than 3500 Danish citizens every year and is associated with a severe prognosis. Recent studies suggest that complement system proteins might influence injury after out-of-hospital cardiac arrest.

Aim: The aim was to investigate levels of lectin pathway proteins in patients resuscitated after out-of-hospital cardiac arrest compared with healthy individuals.

Method: We included 82 comatose patients resuscitated after out-of-hospital cardiac arrest. Upon admission, treatment with targeted temperature management at  $33 \pm 1$  °C was initiated. Blood samples were obtained 22 hours after the target temperature was reached. Data from a cohort of 82 gender matched healthy individuals (blood donors) was used for comparison. Levels of the lectin pathway proteins (mannan-binding lectin (MBL), M-ficolin, H-ficolin, collectin liver 1 (CL-L1), MBL-associated serine protease 1 (MASP-1), MASP-2, MASP-3 and MBL-associated protein of 44 kDa (MAp44)) were analyzed using time-resolved immunofluorometric assays (TRIFMA®).

Results: Higher levels in cardiac arrest patients compared with healthy individuals were found for CL-L1, MASP-1, MASP-2 and MAp44. Lower levels were found for M-ficolin, and no differences in levels were found for MBL, H-ficolin and MASP-3.

Conclusion: Out-of-hospital cardiac arrest patients had higher levels of CL-L1, MASP-1 and MASP-2 compared with healthy individuals, which may indicate that cardiac arrest induces increased activation in the complement system. Further studies will be made to examine whether lectin pathway proteins is associated with mortality in post cardiac arrest patients.

P20.09 Sigríð Salling  
Árnadóttir

CHARACTERIZATION OF GENETIC INTRA-TUMOR HETEROGENEITY OF  
COLORECTAL CANCER AND MATCHING ORGANOID

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In recent years, it has become evident that intra-tumor heterogeneity (ITH) of solid tumors, such as colorectal cancer (CRC), complicates development of efficient therapy strategies. A minor clone of the tumor might have the ability for treatment resistance and hence the ability for re-establishing the tumor. Organoid cultures derived from the patient's tumors can be used for ex vivo drug screening prior to treatment of the patient. But this approach is only efficient if the organoids represent the heterogeneity of the tumor. In this study, we aim to characterize the genetic ITH of CRC and see how well it is reflected in matching organoid cultures. For this, we have collected three spatially distinct biopsies per tumor from five CRC patients. Each biopsy was divided in two; one half of the biopsy was fresh frozen for DNA purification, while the other half was grown as organoid culture. Whole exome sequencing was performed using next generation sequencing. Each tumor contained multiple mutations that were common for all biopsies and present in the organoids as well, representing a major clone or a common ancestral branch. Private mutations observed in a single area of the tumor were often matched in the organoids originating from the same area. Nevertheless, both primary tumor biopsies and organoids contained a few mutations that were only observed in the respective sample. In one case, the clone that seeded seven lymph node metastases clearly originated from a single area of the tumor. Our data indicates that the major clone(s) are present in all samples, while the minor clones are localized to certain areas, and that the organoid cultures reflect this heterogeneity.

P20.10 Martin Lund

CAN INBORN ERRORS OF METABOLISM BE CORRECTED WITH  
MONOTHERAPY?

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In this study, we argue that development of monotherapy for many inborn errors of metabolism (IEM) is often a flawed approach.

For the question posed in the above title, the answer for most of the several thousand monogenetic inborn metabolic disorders is no. When routine genetic surgery becomes available, then fully corrective

treatment of IEM will be possible. Until that time, new therapies for the different disorders have to be developed on a piecemeal basis. Apart from diet/supplement interventions, the approach so far has been to focus on monotherapy. In some cases, such as for example enzyme replacement for lysosomal disorders, this has proven effective.

But for most IEM, there is no treatment available. This unmet need should not be left unaddressed, considering the many children that are diagnosed via screening programs each year.

Bezafibrate has been proposed as a drug candidate for the relatively common long-chain fatty acid oxidation disorders, but has proven disappointing. We show that the long known ability of fibrates to boost fatty acid oxidation is also associated with an increase in the production of reactive oxygen species and increased vulnerability to metabolic stress induced cell death in patient cells. Fibrates activate a broad spectrum of signaling pathways, amongst which several lead to an overall increased mitochondrial activity. For patients that have dysfunctional mitochondria, this could potentially be dangerous. Our data indicate that in order for patients to benefit fully from compounds that boost deficient enzymatic systems, it is probably necessary in most cases to protect the cellular compartment associated with the disorder.

P21.01 Jens Bay Vegger BOTULINUM TOXIN INDUCED DISUSE OSTEOGENESIS DOES NOT DIFFER BETWEEN SKELETALLY MATURE YOUNG AND AGED FEMALE C57BL/6 MICE

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Introduction: Osteopenia and osteoporosis are foremost phenomena in the fully grown skeleton. However, it is unknown whether disuse osteopenia and osteoporosis in skeletally mature, but growing, mice resembles that of fully grown mice.

Materials and methods: In total, 24 16-week-old (young) and 18 44-week-old (aged) female C57BL/6 mice were investigated; 12 young and 9 aged mice were injected with botulinum toxin in one hind limb, while the remaining mice served as controls. The mice were euthanized after three weeks of disuse. The distal femoral metaphysis and epiphysis were  $\mu$ CT scanned. Bone strength was determined by mechanically testing the femoral mid-diaphysis and neck.

Results: At the distal femoral metaphysis, the loss of trabecular bone volume fraction (BV/TV) was not different between the young and aged mice ( $-49.4 \pm 3.4\%$  vs.  $-46.6 \pm 7.5\%$ , N.S.). However, at the distal femoral epiphysis, the aged mice lost more BV/TV than the young mice ( $-57.1 \pm 1.8\%$  vs.  $-60.5 \pm 3.0\%$ ,  $p < 0.01$ ). Thinning of the trabeculae were more pronounced in the aged mice than in the young mice at both the distal femoral metaphysis ( $-35.5 \pm 2.4\%$  vs.  $-42.3 \pm 4.2\%$ ,  $p < 0.001$ ) and

epiphysis ( $-44.2 \pm 1.7\%$  vs.  $-51.6 \pm 2.9\%$ ,  $p < 0.001$ ). Furthermore, the aged mice lost more bone strength at the femoral mid-diaphysis ( $-27.7 \pm 2.6\%$  vs.  $-39.9 \pm 4.1\%$ ,  $p < 0.001$ ), but not at the femoral neck ( $-60.4 \pm 3.6\%$  vs.  $-60.4 \pm 3.6\%$ ).  
-the aged mice lost more BV/TV than the young

Discussion: In general, the bone loss following botulinum toxin induced disuse does not differ substantially between young and aged mice. Therefore, the loss of bone in young mice resembles that of aged mice, even though they are not fully grown.

P21.02 Julie Brogaard  
Larsen

#### THE INFLUENCE OF HEPARIN ON THE LECTIN PATHWAY IN PULMONARY CANCER PATIENTS

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Background: The lectin pathway of the complement system is activated in some cancer types. The lectin pathway activates coagulation in vitro, but its contribution to the thrombosis risk in cancer is unresolved. Heparin inhibits complement activation in vitro. This opens new perspectives for its role in complement-mediated conditions. However, the effect of heparin on the complement system in vivo has not been investigated.

Aims: To investigate 1) changes in lectin pathway proteins during surgery, 2) the influence of low molecular weight heparin (LMWH) treatment on the lectin pathway and 3) correlations between the lectin pathway and coagulation in lung cancer patients undergoing minimal invasive surgery.

Methods and materials: Patients with lung cancer eligible for thoracoscopic surgery were randomised to LMWH from 1 day prior to surgery until discharge (n=31) or no anticoagulant (n=30). Blood was drawn before the first LMWH dose, perioperatively and on the 1st postoperative day. Lectin pathway proteins were measured with time-resolved immunofluorometric assay. Coagulation was assessed with thrombelastometry (TE), thrombin generation, plasma fibrinogen and fibrin d-dimer.

Results: In total, 8 of 9 lectin pathway proteins decreased significantly during surgery. There was no difference between the LMWH and control group. A statistically significant, but weak, correlation between M-ficolin and fibrinogen, d-dimer and TE clotting time was found perioperatively.

Conclusion: Surgery influences lectin pathway proteins, but LMWH in

prophylactic doses does not influence the lectin pathway in vivo. There was no consistent correlation between the lectin pathway and coagulation in these patients.

P21.03 Nis Brix

#### SMOKING AND USE OF NICOTINE REPLACEMENTS DURING PREGNANCY IN RELATION TO PUBERTAL DEVELOPMENT IN SONS AND DAUGHTERS

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**Introduction:** Smoking and use of nicotine replacements are widespread during pregnancy. Smoking during pregnancy is associated with earlier age of menarche in daughters. However, data on other pubertal milestones are sparse in girls and hardly non-existing in boys, and no studies have investigated the potential effect of nicotine replacements on pubertal development. We aim to investigate whether smoking and use of nicotine replacements during pregnancy are associated with pubertal development in sons and daughters.

**Methods:** This cohort study is based on the Danish National Birth Cohort (DNBC) and its Puberty Cohort. The latter holds information on 22,500 Danish children who have been invited since August 2012 to give half-yearly information on pubertal development through web-based questionnaires. Information on smoking and nicotine replacements was collected during telephone interviews in pregnancy.

**Results:** Currently, data undergo cleaning and analysis. Results will be presented in January 2017.

**Conclusion:** We expect to add considerably to the literature on smoking and use of nicotine replacements during pregnancy. Early puberty is a marker, and potentially an intermediate factor, of a number of serious adult diseases. Identifying preventable causes of early puberty may help reduce the burden of these diseases.

P21.04 Dmitri Zintchouk

#### EFFECT OF COMPREHENSIVE GERIATRIC CARE ON HEALTHCARE UTILIZATION, QUALITY OF LIFE AND MORTALITY IN ELDERLY REFERRED TO A REHABILITATION UNIT

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Objective: Elderly with multiple illnesses represent the fastest growing sector of society and make increasing demands on all sectors of the healthcare system. The aim of this study was to investigate the effect of CGC in elderly referred to a community care rehabilitation unit.

Materials and methods: The study was a randomized controlled trial. Settings: two rehabilitation units in Aarhus Municipality, Denmark. Inclusion: elderly aged 65 and older admitted from home or hospital. Exclusion: assessment by a geriatrician during the past month or receiving palliative care. Intervention by a geriatrician at the rehabilitation unit: medical history, physical examination, blood tests, medication adjustment, treatment including intravenous antibiotics and blood transfusions. Control: patients received standard care with GPs as back-up. Outcomes: unplanned hospital contacts (primary outcome), GP contacts, ADL, quality of life and mortality within 90 days after arrival to rehabilitation.

Results: In total, 370 persons were randomized (184 controls/186 interventions). Mean age was 77.8±7.9/78.3±8.3 years. No difference was found between the groups at baseline or in mortality (15/17 death). In the intervention group, we found a significant reduction in total number of contacts to GPs (C:2873/I:1948) and a significant improvement in quality of life by Depression List (C:46%/I:57%); OR=1.57(1.03-2.38).

Conclusion: CGC in elderly referred to a community rehabilitation unit reduces utilization of the GPs' services and improves elderly's quality of life during the 90-day follow-up period. Analyses of specified GP contacts, unplanned hospital contacts and other outcomes are ongoing.

P21.05 Veera  
Manikandan

GENOME WIDE ASSOCIATION STUDY OF DYSLEXIA IN DANISH POPULATION

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Background: Developmental dyslexia is a common childhood disorder with a prevalence of 5-10% among school-aged children. A large-scale twin study has shown that dyslexia is highly heritable (~50%), which supports that genetic risk factors contribute to the disorder.

Aims: To perform a genome-wide association study (GWAS) of dyslexia in the Danish population.

Methods: The Danish samples from the iPSYCH consortium will be used. The study samples include 28,000 controls and 1,387 cases with a diagnosis of developmental dyslexia (ICD-10 code F81). The cases and controls have been identified based on register information. The DNA of the identified samples was extracted from dried blood spots stored in the Danish New-born Screening Biobank and genotyped using the PsychChip (~0.5 million markers). The GWAS will be performed using logistic regression and relevant principal components as covariates in order to adjust for the population stratification. The genetic correlation between dyslexia and other childhood psychiatric disorders (attention deficit hyperactivity disorder, autism spectrum disorder) as well as educational attainment, reading and learning traits will be estimated using the linkage disequilibrium (LD) score regression method. Specific enrichment of pathways or tissue-specific genes will be analyzed using tools such as MAGMA, Haploreg, etc. The gene expressions in brain tissues will be imputed from the genotypes using predixcan/metaxcan software to identify differentially expressed genes.

Perspectives: The present study will be the largest GWAS of dyslexia done so far. The results of the study will help us identify the genes involved in the pathophysiology of dyslexia.

P21.06 Allan Hansen

IN VIVO IMAGING OF NEUROMELANIN IN PARKINSON'S DISEASE USING 18F-AV-1451 PET

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Objectives: To examine the PET tracer 18F-AV-1451's off-target neuromelanin binding ability as a tool to show substantia nigra depigmentation in in vivo Parkinson's disease.

Background: The radiotracer 18F-AV-1451 (previously known as 18F-T807) primarily binds to paired helical filaments of tau protein, but it has also been shown to bind to neuromelanin in the midbrain. It may, therefore, be a measure of the pigmented dopaminergic neurons in the substantia nigra. Neuromelanin in the substantia nigra has long been known to increase with age, but to decrease in Parkinson's disease. We investigated the utility of 18F-AV-1451 PET to visualize the concentration of nigral neuromelanin in Parkinson's disease.

Methods: In total, 17 patients with idiopathic Parkinson's disease and 16 age- and sex-matched control subjects had 18F-AV-1451 PET on a Siemens High-Resolution Research Tomograph.

Results: Visually, many Parkinson's disease patients showed apparent

decreased 18F-AV-1451 signal in the midbrain. On average, patients showed a 30% mean decrease in total nigral 18F-AV-1451 volume of distribution compared with controls ( $p=0.004$ ), but a large overlap of individual ranges was seen. We found no significant correlation between symptom dominant side and contralateral nigral volume of distribution. Also, there was no correlation between nigral 18F-AV-1451 volume of distribution and age or time since diagnosis.

Conclusion: The 18F-AV-1451 PET may be the first radiotracer to reflect the loss of pigmented neurons in the substantia nigra of parkinsonian patients. Large within-group variance prevents immediate clinical utility.

P21.07 Mathis Rasmussen ESTABLISHMENT OF A HL-1 CELL BIOASSAY TO EVALUATE THE PROTECTIVE CAPACITY OF EXOSOMES AGAINST SIMULATED ISCHEMIA-REPERFUSION INJURY

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Background: Ischemia/reperfusion injury (I/RI) occurs to the myocardium when coronary circulation is reestablished after acute myocardial infarction. Remote ischemic conditioning (RIC) is an easy-performed treatment that can attenuate I/RI. RIC is performed by inflating a cuff on the upper arm, causing four 5-minute periods of global ischemia of the arm. Exosomes are physiological circulating vesicles that are thought to be involved in the signaling of RIC.

Aim: The aim of the study is to establish a bioassay using the HL-1 cell to evaluate the protective capacity of exosomes against I/RI.

Method: Cultured HL-1 cells are subjected to 5 hours of simulated ischemia followed by 2 hours of simulated reperfusion. Exosomes will be added prior, during or after the simulated ischemia, and the extent of cell death will be measured using a PI/Hoechst stain.

Results: Data will be collected during the next months, and results will be presented at the poster presentation.

Perspectives: The study will provide further knowledge about the signaling of RIC. The study may provide bioassay that can be used to screen a variety of different types of exosomes from different patient types and animal models.

- P21.08 Samuel Joseph Windross  
Cancellation

IDENTIFICATION OF EARLY EVENTS IN IMMUNE SIGNALING STIMULATED BY FOREIGN DNA

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The recently discovered cGAS-STING (stimulator of interferon genes) pathway, and the role it plays in sensing of DNA viruses, has resulted in an explosion in innate immune signaling research. However, many aspects of this pathway have yet to be defined. For instance, how viral entry and capsid release could interact with the DNA sensing pathway, and whether DNA detection primes STING for activation in the endoplasmic reticulum are two questions that remain unanswered. In this PhD project, we will first focus on how STING form becomes covalent dimers on the surface endoplasmic reticulum (ER), which is an essential step in the signaling pathway. Previous work in the lab has shown that DNA stimulation induces a covalent STING dimer. To further explore this, we will initially generate THP1-derived cells (macrophage like cell line) stably expressing STING mutants in the individual and combinations of the 9 cysteins in the protein. The cells will then be screened to determine the position of disulfide bond formation. Secondly, we will use high-resolution microscopy and live cell imaging to determine spatial and temporal aspects of DNA detection in the cytosol. We hope to define how events such as virus entry and capsid release prime the detection of viral nucleic acids through direct/indirect interaction with DNA sensors like cGAS and IFI16. This research aims to identify novel mechanisms in the early events in the DNA-activated antiviral pathway, which is essential for successful clearance of infection with DNA viruses.

- P21.09 Marie Veje Knudsen

RETURNING TO DAILY LIVING FOLLOWING CARDIAC TELE-REHABILITATION; AN ANALYSIS OF PATIENT NARRATIVES

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Background: Telemedicine has been introduced in cardiac rehabilitation to improve participation rates with some success. To further optimise the potential of telemedicine, insight is needed into its use and results among patients in cardiac rehabilitation.

Aim: To improve the knowledge of the patients' understanding of cardiac tele-rehabilitation.

Methods: A phenomenological-hermeneutic study was conducted among patients after completing cardiac tele-rehabilitation. The

interviews were analysed using the interpretation theory by Ricoeur. Through three levels of textual analysis, a deeper insight into the patients' understanding of tele-rehabilitation and its impact on daily life was obtained.

Results: The patients' understanding of the rehabilitation recommendations mirrored to a great extent their previous life. In the seven narratives, two narratives showed to be polar opposites regarding the understanding of tele-rehabilitation: One narrative focused on physical exercise, while the other focused on getting through rehabilitation as easy as possible. Paradoxically, the patient who focused on physical exercise and tried to comply with the recommendations did not feel adequate, whereas the other who was not engaged in the recommendations had a positive understanding of himself.

Conclusion: The narratives only partially reflected the rehabilitation recommendations, which may call for a clarification of the expectations between patients and healthcare professionals as well as more attention to the patients' expectations. Furthermore, it is necessary to increase the understanding of cardiac tele-rehabilitation as a whole with both physical exercise and permanent lifestyle changes.

P21.10 Andreas  
Holmgaard

INTRAOcular GENE EDITING IN MICE FOLLOWING SUBRETINAL  
INJECTION OF CRISPR/CAS9 EXPRESSING LENTIVIRAL PARTICLES

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Programmable nucleases are powerful tools in gene editing studies allowing site-specific genome engineering. We will use the CRISPR/Cas9 system for intraocular gene editing of the vascular endothelial growth factor (VEGF) gene. Over-expression of VEGF in RPE cells cause serious eye diseases resulting in vision loss. We have designed 6 pairs of 'guide strands' and cloned them into a lentivirus (LV)-CRISPR/Cas vector. Following LV-transduction of retinal cells, including RPE cells, specific cutting in the VEGF gene was demonstrated. Next, we assessed the possibility to use the LV-CRISPR/Cas vector for intraocular editing following subretinal injections in mice. We observe rapid and persistent expression of the GFP-marker simulations expressed from the LV-CRISPR/Cas vector, suggesting efficient delivery and expression of the CRISPR/Cas expression cassette. Ocular gene editing is assessed in RPE cells isolated from injected eyes using FACS and the TIDE analysis. The investigation also includes off-target analysis provided by gDNA sequencing of predicted off-target sites.

P22.01 Marlene Christina Nielsen DEVELOPING QPCR ASSAYS FOR MEASURING CD163 SPLICE VARIANTS

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Background: The receptor CD163 is expressed by human monocytes and macrophages, and a soluble form of the receptor (sCD163) is present in plasma. sCD163 is a biomarker for a number of diseases, including acute and chronic liver inflammation. However, this marker is unable to distinguish between acute and chronic illnesses. CD163 exists in three splice variants, and our hypothesis is that the expression levels of these splice variants differ in patients with acute inflammation compared to patients with chronic inflammation. Therefore, the first aim of this study was to develop qPCR assays which specifically measure the expression level of each of the three splice variants.

Methods: Based on known CD163 cDNA sequencing data, a set of specific DNA primers was designed for each splice variant. The specificity of each primer set was tested using qPCR on material purified from cultured human macrophages. The resulting qPCR products were run on an agarose gel, purified, and sequenced. Furthermore, the assays were tested on full blood from twenty patients.

Results: Based on sequencing results, each of the specific primer sets gives rise to a qPCR product matching of the CD163 splice variant they were designed to be specific for. In addition, preliminary results show that all three CD163 splice variants are present in full blood samples and that the expression levels and ratios between the variants differ between patients.

Discussion: Our results indicate that the qPCR assays we have designed are able to measure the expression level of each of the CD163 splice variants specifically in human full blood samples. Future experiments will address optimization and validation of the assays.

P22.02 Morten Kelder Skouboe STING LIGANDS IMPROVE THE SURVIVAL OF HERPES SIMPLEX VIRUS TYPE 2 INFECTION IN VIVO

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During a viral infection, one of the first innate immune responses is the production of interferon (IFN), which promotes antiviral responses, interferes with virus replication and modulates innate and adaptive immune responses. Viral DNA sensing occurs in the cytosol, where the cyclic-GMP-AMP-synthase (cGAS) produces 2'3'-cGAMP, which activates the Stimulator of Interferon Genes (STING) and in turn the transcription of IFN- $\beta$ . The STING-ligand DMXAA has previously been investigated for

anti-cancer effects, but its antiviral potential has not yet been investigated in vivo. The next generation of drugs with similar pharmacodynamics is the cyclic dinucleotides, of which we screened a panel and found 2'3'-cGAM(PS)<sub>2</sub>(Rp/Sp) to be a potent stimulator of STING.

By use of both wild type and cGAS<sup>-/-</sup> mice, we demonstrate how DMXAA and 2'3'-cGAM(PS)<sub>2</sub>(Rp/Sp) can act as potent antivirals during a herpes simplex type 2 (HSV-2) infection of the vagina. Both compounds bypass cGAS by interacting directly with STING to mount a large type I IFN-response both in vivo and in human HaCat cell lines. In vivo, this markedly decreases the virus load and greatly improves on the survival of infected mice. Taken together, our results indicate that STING could be a potential antiviral drug target, revealing a new way to enhance the innate immune response instead of targeting the virus itself directly.

P22.03 Andreas Lodberg ACTIVIN DECOY RECEPTOR (IIA) AMELIORATES IMMOBILIZATION INDUCED LOSS OF BONE IN MICE AND IN THE CORTICAL BONE; DOES SO PREFERENTIALLY BY PERIOSTEAL AND NOT ENDOSTEAL BONE FORMATION

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Attention to Activin Decoy Receptors (ADeR) has increased in recent years. None of the studies investigating ADeRs have focused on the bone loss induced by unloading, which is driven by different mechanisms than the bone loss associated with menopause.

We investigated whether RAP-011 (an Activin ReceptorIIA Decoy) could ameliorate bone loss in a model of unloading caused by Botulinum Toxin A (BTX).

Sixteen-week-old C57BL/6 mice were divided into five groups: Baseline (n=10), Control (n=12), RAP-011 (n=12), BTX (n=12), and BTX+RAP-011 (n=12). Immobilization was induced by injecting 2 IU/100 g BTX in the right hind limb musculature. The mice were euthanized after 21 days. The femur was analyzed by DXA,  $\mu$ CT of the cortex, mechanical testing, and dynamic histomorphometry. The proximal tibia was analyzed by  $\mu$ CT.

At the proximal tibial metaphysis, we found increases in BV/TV when comparing Control vs. RAP-011 (28%) and BTX vs. BTX+RAP-011 (62%). At the mid-femur, the 3 point bending test displayed increases of 20% (Control vs. RAP-011) and 12% (BTX vs BTX+RAP-011). Cortical dynamic histomorphometry of the femur showed increases in periosteal MS/BS

(110%), MAR (170%), and BFR/BS (192%) when comparing Control vs. RAP-011. There was an increase in periosteal Alz.S/BS by 65% (Control vs. RAP-011) and 82% (BTX vs. BTX+RAP-011). RAP-011 did not influence the dynamic histomorphometry of the endocortical surface.

In conclusion, RAP-011 may be used to increase bone strength and bone microstructural parameters. Notably, RAP-011 had a profound impact on the histomorphometry of the periosteal surface while no effect was detected at the endosteal surface.

P22.04 Bente Toft

#### BEING A LARGE BODY IN ACTIVITY: EXPERIENCES OF LIFESTYLE CHANGE DURING 18 MONTHS

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Background: Severely obese persons are physically, mentally and socially affected by their body size. Movement is, therefore, a challenge that is often avoided. Being severely obese may entail living involuntarily in a large body, not feeling at home in the present situation and wanting to change. Lifestyle interventions may be instrumental to achieving such change, relieving suffering and improving wellbeing. In-depth knowledge of severely obese experiences of facilitators and barriers to physical activity are lacking. The aim of this study is to explore and describe adults' lived experiences of being physically active when living with a large body.

Design and methods: Qualitative study based on individual interviews (n=48) were conducted at the start of a lifestyle intervention, after 6 months and after 18 months. Gender-specific focus group interviews (n=4) were conducted. Eight male and 8 female patients admitted to Danish public hospitals were included by the criteria: age  $\geq 18$  y and BMI  $\geq 40$  kg/m<sup>2</sup>. Using Heidegger and Gadamer's hermeneutic philosophy of understanding, the subjects' understanding is elicited through language and interpretation of the data describing the participants' lifeworlds. An initial concept-driven coding of findings is conducted and followed by a data-driven five-step procedure of interpretation focusing on meaning. Categories and sub-categories are developed, illustrated, contextualized and described.

Perspective: The findings of this study will enhance our current understanding of how to address PA in the everyday life of people living with severe obesity, and the results may inform future interventions.

P22.05 Alexander D'Amore

TRANEXAMIC ACID FOR BLOOD LOSS, NEED OF TRANSFUSION AND COAGULATION IN CHILDREN WHO UNDERGO CRANIO-FACIAL SURGERY: THE TACTIC TRIAL

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Background: Craniosynostosis (CS) is a condition where the cranial sutures ossify prematurely. To avoid brain damage, CS needs to be surgically corrected within the first years of life. This intervention is associated with substantial blood loss, which can exceed the child's total blood volume. The aim of this study is to establish whether tranexamic acid (TXA) can reduce blood loss in these children.

Methods: At present, a cohort of 15 out of 30 children has been double-blindly randomized to receive either TXA or placebo (NaCl) during and 8 hours after surgery. The pre- and post-operative blood loss as well as the sum of transfused red cell volumes will be evaluated. The coagulation will be investigated by rotating thromboelastometry both during and after surgery.

Results: If the null-hypothesis of the study, i.e. no difference between TXA and placebo, will be rejected in favour of TXA, a new standard of care for bleeding prophylaxis during CS surgery will be introduced. As a novel contribution, our study will provide extensive knowledge on how TXA influences coagulation parameters over time in the pediatric setting.

Conclusion: The TACTIC trial is among the first randomized studies in CS children to investigate the effect of TXA on blood loss when administered during and after surgery. Simultaneously, we analyze how TXA influences haemostasis over time. If evidently in favour of TXA, the results of our study contribute to a new evidence-based clinical approach in paediatric CS surgery.

P22.06 Rune Bæksager Nielsen

ALZHEIMER'S DISEASE IS LINKED TO CORTICAL MICROVASCULAR DYSFUNCTION: AN MRI PERFUSION STUDY

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Alzheimer's disease (AD) is associated with changes in cerebral capillary morphology and function, which likely increases capillary transit time heterogeneity (CTH) of blood, in principle, limiting oxygen delivery. We examined whether cortical microvascular hemodynamics is consistent with tissue hypoxia in AD and whether they correlate with cognitive performance and cortical thinning. In total, 32 AD patients underwent cognitive testing and MRI at baseline and after 6 months. We measured cortical thickness, microvascular cerebral blood volume (CBV), cerebral blood flow (CBF), mean transit time (MTT) and CTH. Further, we estimated the oxygen tension ( $P_tO_2$ ) that would result if the minimum oxygen requirement of resting brain tissue was met by this hemodynamics. Correlation was assessed with linear regression within an atrophic cortical region (AC). Post hoc, correlation models were applied all across cortex. False discovery rate (FDR) correction was applied at  $\alpha=0.05$ . At baseline, poor cognitive performance and regional cortical thinning correlated with lower CBF and CBV, with higher MTT and CTH and with low  $P_tO_2$  within AC. The correlation between hemodynamics and cognitive performance extended into cuneus and precuneus, while for  $P_tO_2$ , correlations were observed widespread across cortex. Cognitive decline over time was associated with increasing whole brain relative transit time heterogeneity ( $RTH=CTH/MTT$ ). We localized this correlation to the left posterior cingulum, precuneus and cuneus. Our results confirm the involvement of microvascular pathology in AD and suggest that deteriorating microvascular hemodynamics may cause hypoxia, which is known to precipitate amyloid retention.

P22.07 Signe Voigt Lauridsen

HAEMOSTATIC FUNCTION IN PATIENTS AFTER ACUTE SPONTANEOUS INTERCEREBRAL HEMORRHAGE

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In Denmark, 1,500 patients suffer a spontaneous intracerebral haemorrhage (ICH) annually. Treatment options are few. New laboratory tests provide opportunities to investigate changes following ICH.

We aimed to describe global haemostatic function in ICH patients at admission and compare this with healthy individuals. Secondly, we aimed to analyse haemostatic changes during 24 hours after symptom

onset. Our hypothesis was that ICH patients had a systemic activated coagulation at admission compared to healthy individuals.

Blood samples were collected at admission and 24 hours after symptom onset. ROTEM<sup>®</sup> analyses were performed according to the manufacturer's instructions. Trombin generation were quantified by Calibrated Automated Thrombogram<sup>®</sup>. Data on healthy individuals were from the Department of Clinical Biochemistry, Aarhus University Hospital.

We enrolled 41 ICH patients. At admission, ICH patients showed increased clot stability compared with healthy individuals indicated by increased maximum clot firmness in EXTEM ( $p < 0.0001$ ), INTEM ( $p < 0.0001$ ) and FIBTEM ( $p < 0.0001$ ). Compared with healthy individuals, thrombin generation results demonstrated a higher endogenous trombin potential ( $p = 0.001$ ) and maximum generated trombin (peak) ( $p < 0.0001$ ) at admission.

Thrombin generation results within 24 hours after symptom onset showed a decrease in endogeneous trombin potential ( $p = 0.01$ ) and maximum generated trombin (peak) ( $p = 0.01$ ).

Thromboelastometri and thrombin generation indicated a subtle systemic activated coagulation in ICH patients in the acute phase at admission compared to healthy individuals. Total amount of trombin-generating capacity decreased significantly within 24 hours from admission.

P22.08 Sarah Christine Christensen

ABSTRACT TITLE

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Due to its low permeability and efflux transport system, the blood-brain barrier (BBB) poses a great challenge to systemically administrated immunotherapies for brain diseases. Consequently, only 0.1-0.2% of the systemically injected antibody will enter the brain under normal physiological conditions. Thus, it is important to develop new strategies in order to improve drug delivery to the brain and thereby increase the efficacy of immunotherapies.

Today, one of the most promising strategies is to target the endogenous transport system in brain endothelial cells (BEC), which constitute the morphological basis of the BBB. In line with this strategy, we are going to investigate the expression levels, intracellular localization, and trafficking routes of Basigin, CD320, CD98hc, and Glut1 in primary porcine and rat BEC. These transmembrane proteins have been reported to have high transcript levels in mouse BEC and could therefore be promising targets.

The studies will be performed by using in vitro blood-brain barrier models and immunofluorescence techniques evaluated by spinning disk

confocal microscopy, live cell imaging, and a high content imaging system.

Since the internalization routes of these receptors and transporters are not well described in BEC, our investigation of the trafficking routes in these cells may reveal new target candidates for improved antibody delivery across the BBB. Based on these findings, we seek to generate a bispecific antibody construct with improved BBB penetration, which ultimately can be used for human immunotherapy.

- P22.09 Elias Didrik REGULATION OF EXTRACELLULAR ANTIOXIDANT CAPACITY BY Francis Zachariae STRUCTURE HETEROGENEITY

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An elevated level of reactive oxygen species (ROS) are known to be associated with disease, but research within the last decades has shown that the physiological levels of ROS are important signalling molecules in biological systems. It is, therefore, important to understand how the level of these molecules is regulated. The protein extracellular superoxide dismutase (SOD3) is a copper and zinc-containing enzyme responsible for scavenging of (ROS) in the extracellular space. Previous studies have shown that SOD3 exists as two folding variants characterized by heterogenous disulphide bridge patterns that result in an active (aSOD3) and an inactive (iSOD3) protein. During this PhD project, we aim to determine the factors that govern the heterogenic folding of SOD3 at a cellular level. To fulfil this aim, we will establish a number of mutant SOD3 species that can provide us with information on chaperones involved in the folding process. Furthermore, mutating the metal binding residues in SOD3 as well as perturbation of copper and zinc transport and availability will provide information on the roles of the metal ligands of SOD3 in the folding mechanism. Moreover, we will investigate if the oxygen tension can affect folding of the protein since disulphide formation is affected by the redox conditions. In conclusion, our studies will provide a deeper understanding of how cells can regulate the level of ROS and consequently use these unorthodox molecules in cellular signalling.

- P22.10 Tommy Kragh Bechsgaard GEOMETRIC COMPARISON OF REPAIR PROCEDURES FOR THE AORTIC ROOT, AN IN VIVO EXPERIMENT

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Introduction: Patients with aortic regurgitation secondary to ascending aortic dilation or aneurism can be treated with valve sparing techniques, such as the David reimplantation or the Yacoub remodeling technique. To assess the geometrical changes caused by these repair procedures, sonomicrometry equipment were used in an in vivo porcine model.

Materials and methods: In an acute setting, 21 pigs were randomized into three groups: (1) repair with the Yacoub procedure, (2) repair with the David procedure, and a (3) native group. In each experiment, 11 sonomicrometry crystals were implanted; three in the annulus at each cusp nadir, one at each commissural point, one at the nodulus arantii on each cusp, and two references in the apex of the heart and the aortic arch. Three planes were created from the crystals: the annulus plane, the cusp plane and the commissural plane. To estimate the plane lumina, a circle was fitted to the three crystals in each plane.

Results: Data from 10 heart cycles from each experiment were used to calculate the mean and the standard deviation from all groups. Data are reported as mean $\pm$ SD. At the annular level, the circle radii found were: 11.30 $\pm$ 0.01mm in the David group, 12.10 $\pm$ 0.30mm in the Yacoub group, and 14.08 $\pm$ 0.01mm in the native group, respectively.

Discussion: The preliminary data support the hypothesis that the David procedure is the most confined of the two repair procedures under investigation, while the Yacoub procedure leaves the aortic root closer to normal regarding annular measurements and physiological behavior.

P23.01 Filip Carl Arne Eckerström

LONG-TERM MORPHOLOGICAL CHANGES OF THE RIGHT VENTRICLE IN ADULTS OPERATED FOR VENTRICULAR SEPTAL DEFECTS

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Background: Ventricular septal defects (VSD) successfully closed in the first years of life are considered to have great prognoses, with little or no follow-up in the adult patients. Nevertheless, 20 years following surgical repair, adults were recently found with decreased functional capacity and disrupted force-frequency relationship during exercise. A possible link to ventricular morphological alteration remains to be investigated. Therefore, a Magnetic Resonance Imaging (MRI) study was performed on VSD patients 20 years following surgical repair in order to evaluate biventricular morphology and function.

Methods: Adult patients and healthy, age- and gender-matched controls underwent cine MRI for the evaluation of the biventricular volumes and ejection fraction. The MRI measurements were analysed post hoc in a

blinded fashion by one main investigator.

Results: In total, 20 adult VSD patients ( $22.4 \pm 2.2$  years) and 20 healthy controls ( $23.1 \pm 2.1$  years) were included. At surgery, patients' mean age was  $2.1 \pm 1.4$  years. Right ventricular (RV) end-systolic volume index was larger in patients ( $20.2 \pm 3.8 \text{ ml/m}^2$ ) compared with controls ( $17.4 \pm 3.9 \text{ ml/m}^2$ ),  $p=0.032$ . The RV end-diastolic volume index was also larger in patients ( $53.4 \pm 8.5 \text{ ml/m}^2$ ) compared with controls ( $46.5 \pm 9.8 \text{ ml/m}^2$ ),  $p=0.023$ . Furthermore, an increased stroke index was seen in VSD patients;  $33.2 \pm 5.6 \text{ ml/m}^2$  (controls:  $29.0 \pm 7.1 \text{ ml/m}^2$ ,  $p=0.046$ ). Left ventricular measurements displayed no differences between groups.

Conclusion: We demonstrate altered RV morphology 20 years following surgical VSD repair. These findings may explain some of the mechanisms behind the exercise limitations previously found in adulthood.

P23.02 Anne Mette Fløe Hvass SYSTEMATIC SCREENING OF MIGRANTS IN DENMARK: A CROSS-SECTIONAL STUDY OF INFECTIOUS DISEASES IN A POPULATION OF NEWLY ARRIVED REFUGEES

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Background: The worldwide estimate of migrants in 2010 was 214 million of international migrants. The estimate for 2050 is 400 million. The most vulnerable group of migrants are the refugees, and Denmark currently experiences refugees arriving in increasing numbers. The majority of migrants come from countries with higher prevalence of infectious diseases.

Material and methods: We here present preliminary results from an ongoing Danish study performed in the city of Aarhus. All refugees who have been granted a residence permit are offered a health assessment. A history is taken, including the family background, education, medical history, self-rated health, a physical examination and a general blood sample screening, including parameters on hepatitis, HIV, TB (interferon gamma release assays (IGRA)), diabetes, and thyroid disease. A report with suggestions for an individual health plan is sent to the family doctor and the patient's social worker.

Results: Currently, approx. 50% of the refugees who have been offered the screening have participated. From October 2014 to March 2016, we have screened 452 refugees; 69/452 (15%) had a positive IGRA test (TB). The patients with a positive IGRA had a median age of 35.5 years [7;74 years]; 64% were male, and 36% were female.

Conclusions: Our study shows that infectious diseases among refugees is prevalent and needs to be taken seriously. A large proportion of the IGRA positives are from Syria. To care for the refugees and to stop the

spread of infectious diseases, it is important to find these infections early after arrival and start treatment.

P23.03 Marzieh Katibeh MODELLING AND EVALUATION OF A COMMUNITY-ORIENTED HEALTH-BASED SCREENING AND PROMOTION PROGRAMME FOR IMPROVING EYE HEALTH IN IRAN

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Ninety percent of people with blindness or visual impairment live in low and middle income countries (LMICs), where they do not have access to proper eye care services or enough information. With great number of mobile phone users and availability of health-related applications, mobile health (mHealth) can offer a unique avenue for delivering health interventions to populations. In this project, as the first community trial in the field of eye health in Iran, we are going to develop an mHealth tool and train primary health care (PHC) workers to use the tool, enabling the PHC workers and community members to have interaction through this technology for early detection of common blinding eye disorders.

In collaboration with local and international experts, the best possible content and the most relevant target group are identified. We will then evaluate the tool through an extended study of 3750 urban and rural community members. The eye care needs will be identified, and we will randomly implement the mHealth intervention in some areas and compare to other areas without the intervention. Those who need more specific services will be referred to equipped eye hospitals.

We will compare different areas to evaluate eye care utilization, the efficacy and acceptability of the tool. If the tool is proven to be successful, we will try to introduce it to the local health authorities and advocate for implementing it in a broader scale. We also hope that the project will enhance scientific exchange with Iran, which is in line with the new diplomatic developments between Denmark and Iran. The experience and evidence may also be beneficial for other LMICs.

P23.04 Vibeke Bay Sørensen THE EFFECT OF ISCHEMIC REMOTE PERCONDITIONING ON INFARCT VOLUME EVALUATED BY MRI AND HISTOLOGY

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Stroke is a leading cause of death and disability. Ischemic conditioning has shown promising results by reducing infarct sizes for blood clots in both heart and brain, in animal as well as clinical studies. During ischemic conditioning, short periods of controlled undamaging hypoxia are induced; this creates protection against subsequent prolonged ischemia.

This study aimed to evaluate the protective effect of ischemic remote preconditioning on the infarct volume in rats subjected to a middle cerebral artery occlusion (MCAO).

A 60-minute MCAO was performed in a control (n=9) and a preconditioned (n=8) group followed by 24 hours of reperfusion before euthanasia by perfusion fixation. Remote preconditioning consisted of 4 cycles of 5 minutes hind leg occlusion followed by 5 minutes of reperfusion, performed 10 minutes after MCAO initiation. The fixed brains were subjected to ex-vivo high-field MRI and histology (hematoxylin) to assess infarct volumes. Two MRI sequences were used: a Trace-DWI and a new sequence for diffusion kurtosis imaging (DKI).

Surprisingly, no difference in infarct volume was found between control and preconditioned brains for any of the three infarct estimation methods. However, strong correlations for the infarct volumes were found for both DWI ( $R^2=0.6316$ ; p-value=0.0001) and DKI ( $R^2=0.8950$ ; p-value<0.0001) when compared to histology.

The study indicates that infarct volume can be reliably estimated by MRI, even after fixation. Furthermore, the correlation for DKI was superior to DWI, suggesting that DKI provides a more accurate infarct volume estimate. Both MRI methods may provide alternatives for infarct volume estimation in preclinical studies.

P23.05 Niels Dalsgaard  
Nielsen IS LUMBOSACRAL PLEXUS BLOCK AN EFFECTIVE AND SAFE ALTERNATIVE AS SURGICAL ANESTHESIA FOR TOTAL HIP REPLACEMENT?

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Background: An increasing number of patients for total hip replacement presents with cardiovascular comorbidities that render them fragile to traditional methods of anesthesia. The aim of this intended study is to

compare lumbosacral plexus blockade with continuous spinal anesthesia for surgical anesthesia in total hip replacement. We hypothesize that lumbosacral plexus blockade induces less hemodynamic impact compared to continuous spinal anesthesia.

Methods: Thirty patients (ASA I-III, age  $\geq$  50 years) will be included for elective hip replacement after informed consent. Hemodynamics will be monitored using calibrated pulse contour analyses of the femoral artery pressure. All patients will receive a lumbar spinal catheter as well as lumbosacral plexus blockade. Group 1: Ropivacaine for the plexus blockade and placebo for the spinal catheter. Group 2: Bupivacaine for the spinal catheter and placebo for the plexus blockade. Patients, anesthesiologist and observer will be blinded for the intervention. Hemodynamic parameters will be recorded during a 1-hour-period following the interventions.

Results: The primary endpoint will be the change in cardiac output from baseline to 30 minutes after the interventions. Secondary endpoints will include change in systemic vascular resistance, mean arterial pressure, central venous pressure and central venous oxygen saturation.

Conclusions: We expect that our findings will support the hypothesis of a reduced hemodynamic impact from lumbosacral plexus blockade compared to continuous spinal anesthesia. This might favor the future use of lumbosacral plexus blockade for patients with severe cardiovascular comorbidities.

P23.06 Mie Mathiasen

ASSISTED REPRODUCTIVE TECHNIQUES (ART) AND THE POSSIBLE EFFECT IN THE PROGRESSION OF ENDOMETRIOSIS SYMPTOMS

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Objective: Investigation of the impact of controlled ovarian stimulation (COS) during ART on quality of life (QoL) and pain in endometriosis patients compared to patients without endometriosis.

Methods: A prospective cohort study based on questionnaires containing Endometriosis Health Profile (EHP-30) and pain evaluated on a numerical rating scale, which were administered before and after COS in one ART cycle. No fixed COS protocols were used as patients were treated according to principals of personalized medicine.

Patients aged < 40 years were recruited from two fertility clinics, and endometriosis diagnosis was confirmed by previous laparoscopy, transvaginal ultrasound or MRI. EHP-30 and NRS scores were analyzed

using paired and unpaired t-tests.

Results: Preliminary results of 19 patients with endometriosis and 34 in the reference group:

Baseline mean total EHP-30 score in the endometriosis group was 26.2 (95% CI: 15.1; 37.4) and 9.6 (95% CI: 5.4; 13.7) in the reference group. Total EHP-30 change from baseline to post aspiration was non-significant in the endometriosis group (-2.7 (95% CI: -10.6; 5.1)  $p=0.472$ ), but it was significant in the reference group (9.8 (95% CI: 3.9; 15.7)  $p=0.002$ ). Changes in the two groups were significantly different from each other (-12.5 (95% CI: -22.1; -2.9),  $p=0.012$ ).

None of the pain parameters worsened significantly in the endometriosis group.

Conclusion: As negative change in EHP-30 score indicates improvement in health status, ART does not seem to diminish QoL or increase pain symptoms in endometriosis patients compared to the reference group.

P23.07 Peter Sieljacks

LOW-LOAD BLOOD FLOW RESTRICTED EXERCISE AS A GENTLE TRAINING ALTERNATIVE TO HEAVY RESISTANCE TRAINING IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Introduction: Patients suffering from rheumatoid arthritis (RA) experience inflammation, joint stiffness and pain, leading to reduced physical activity and impaired physical performance due to loss of muscle strength and muscle endurance. Heavy resistance training (HRT) has been shown to effectively improve muscle strength, muscle size and physical performance. However, this is often not tolerated due to the associated joint pain. Low-load blood flow restricted exercise (BFRE) can induce muscular adaptations comparable to HRT using training loads corresponding to as low as 20% of maximal muscle strength. Because of the low loads used during BFRE, we hypothesize that it may provide a gentle and effective training alternative to HRT for RA patients who are unable to tolerate the high mechanical loading on the joints inherent of HRT.

Methods: In total, 24 RA patients will be allocated to either 4 weeks of BFRE or HRT. Measures of muscle function, muscle size, disease activity and physical performance will be conducted before, during and after the 4-week training period.

Pilot results and perspectives: Preliminary results show that low-load BFRE

potentially increases muscle size and strength in RA patients. Furthermore, mean joint pain score and time consumption during training appear to be lower for BFRE compared to HRT. Collectively, these results suggest that BFRE has potential to serve as an effective, gentle and time-efficient training strategy to improve muscle function in patients suffering from RA. In perspective, BFRE may be a promising training alternative to HRT for patients with RA or other conditions that affect their ability to tolerate the heavy loads inherent of HRT.

P23.08 Rasmus Hansen Olesen INSULIN RESISTANCE AND INFLAMMATION IN THE DORSOLATERAL PREFRONTAL CORTEX

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Since the 1980s, obesity has become an increasing global problem. At the same time, there has been a large increase in patients with type 2 diabetes. Excess body weight is often seen in diabetic patients. Obesity constitutes an increased risk factor for mortality and morbidity, but it also increases the risk of cardiovascular disease, cancer and diabetes. Moreover, obesity has been implicated in the development of dementia; the risk of developing Alzheimer's disease is 2-5 times higher if diabetes is also present. The link between these two diseases is currently unknown. However, chronic low-grade inflammation, altered insulin receptor signaling and glucose utilization are known to play a role in both diseases. This has led to Alzheimer's disease, which is also referred to as "Type 3 diabetes". We want to investigate how obesity and the related low-grade inflammation affect the brain in otherwise healthy subjects, and how it increases their risk of developing Alzheimer's disease. For the first step in this project, we use data from the dorsolateral prefrontal cortex obtained in the BrainSeq project at Lieber Institute for Brain Development. From their dataset, we selected RNA-Seq data from 169 human neurological and psychiatric healthy samples. We excluded samples with known diabetes and cases known to have used antidiabetic medicine. Likewise, we excluded subjects with a low BMI number, i.e. a BMI lower than 18.5. From this data, we want to investigate if there are alterations in the expression of key inflammatory markers and pathways involved in insulin resistance and glucose transportation. Preliminary results are expected to be presented at the PhD Day.

P23.09 Louise Nissen DAN-NICAD: DANISH STUDY OF NON-INVASIVE TESTING IN CORONARY ARTERY DISEASE: STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL

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Background: The primary objective of the Dan-NICAD study is to determine the diagnostic accuracy of cardiac magnetic resonance imaging (CMRI) and myocardial perfusion scintigraphy (MPS) as secondary tests after a primary coronary computed tomography angiography (CCTA), where coronary artery disease (CAD) could not be ruled out. Invasive coronary angiography (ICA) is used as gold standard. Secondary objectives include evaluation of an acoustic technology, which analyses the sound from coronary blood flow. It may potentially provide better stratification prior to CCTA than clinical risk stratification alone.

Methods and design: Dan-NICAD is a multi-centre, randomized and cross-sectional unit with 1676 enrolled patients without known CAD referred to CCTA due to a history of symptoms suggestive of CAD and a low-intermediate risk profile evaluated by a cardiologist. Patient interview, sound recordings and blood samples are obtained in connection with the CCTA. All patients with suspected obstructive CAD by CCTA are randomized to either stress CMRI or stress MPS followed by ICA with fractional flow reserve (FFR) measurements. Obstructive CAD is defined as FFR below 0.80 or as high-grade stenosis (>90% diameter stenosis) by visual assessment.

Diagnostic performance is evaluated as sensitivity, specificity, predictive values, likelihood ratios and C statistics. Enrolment commenced in September 2014 and completed in May 2016.

Discussion: Dan-NICAD is designed to assess whether a secondary perfusion examination after CCTA could safely reduce the number of ICAs, where revascularization is not required. The results are expected to add knowledge about the optimal algorithm for diagnosing CAD.

P23.10 Christian Philip Rønn FUNCTIONAL STUDY OF SELECTED ATP1A3 DISEASE-CAUSING MUTATIONS

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Recent studies have shown that mutations in the ATP1A3 gene, encoding the alpha subunit of the Na<sup>+</sup>/K<sup>+</sup>-ATPase, are associated with

the severe neurological diseases rapid-onset dystonia-parkinsonism (RDP), alternating hemiplegia of childhood (AHC) and cerebellar ataxia, areflexia, pes cavus, optic atrophy and sensorineural hearing loss (CAPOS) syndrome. The mutations are, with one exception, found to be disease-specific, even though some AHC and RDP mutations affect the very same residues. It has been speculated that, in fact, the diseases are not separate disorders but rather represent a phenotypic continuum of one underlying disease with RDP in the less severe end of the scale and AHC in the other.

Now, having identified the disease-causing mutations, the next step is to functionally characterize the mutations by functional assays.

We have introduced selected RDP, AHC, and CAPOS mutations into mammalian COS-1 cells in order to allow a functional characterization of the recombinantly expressed mutant enzyme. All of the mutants of our study were successfully expressed transiently in the plasma membrane. However, we find most of the mutants unable to sustain cell growth under ouabain selection pressure, thus indicating that the ion-transporting properties are severely disturbed.

P24.01 Tua Gyldenholm HISTONE-DNA COMPLEXES AND THROMBIN GENERATION AFTER INTRACRANIAL HAEMORRHAGE

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Intracranial haemorrhage (ICH) is a condition with high mortality. Animal studies suggest histone-DNA complexes (HDCs) as a contributing factor to the haemostatic disturbances seen in ICH.

The aim was to quantify levels of HDCs and thrombin generation with and without added anti-histone antibodies in blood samples from ICH patients. Samples were obtained at arrival to hospital, 6, and 24 hours after symptom onset. HDC levels were quantified with Cell Death Detection ELISA<sup>PLUS</sup>. Thrombin generation was quantified with Calibrated Automated Thrombogram<sup>®</sup>. Anti-histone antibodies were kindly donated by Dr. Charles T. Esmon, Oklahoma, USA. A commercially available control antibody was used.

We included 77 patients. HDC levels were significantly higher at arrival compared to 24 hours after symptom onset ( $p < 0.0001$ ). Thrombin generation decreased significantly between the arrival sample and the 24-hour sample, indicated by an increase in lagtime ( $p < 0.0001$ ) and time to peak thrombin ( $p = 0.003$ ), and a decrease in peak thrombin and the endogenous thrombin potential (both  $p = 0.0001$ ). Addition of anti-histone antibodies decreased thrombin generation, but the effect could

not be distinguished from the effect of adding the control antibody. The study demonstrated higher levels of HDCs and an increased thrombin generation in the acute phase after an intracranial haemorrhage, compared to 24 hours after symptom onset.

Addition of anti-histone antibodies as well as a control antibody decreased thrombin generation.

In conclusion, the interaction between HDCs and thrombin generation did not seem to be of significant importance after an ICH.

P24.02 Charlotte Ibsen DEVELOPMENT OF A PATIENT-REPORTED OUTCOME INSTRUMENT FOR PATIENTS WITH LUMBAR RADICULAR PAIN

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Background: Low back pain (LBP) is a complex biopsychosocial phenomenon, for which assessment needs to be comprehensive. Patient-reported outcome (PRO) instruments have been used to assess functioning, but lack of standardization makes comparison among studies difficult. The International Classification of Functioning, Disability and Health (ICF) is a globally agreed framework and classification to define functioning.

Purpose: To develop and evaluate a patient-reported outcome instrument based on the ICF in order to systematise and qualify the description of functioning among patients with lumbar radicular pain.

Methods: The PRO will be based on ICF Core Sets and existing items from The Patient-Reported Outcomes Measurement Information System (PROMIS<sup>®</sup>). The development process contains five steps:

1. Linking PROMIS items to ICF and identifying items that correspond to ICF categories in the Core Sets.
2. Developing new items corresponding to the ICF categories not covered by PROMIS items.
3. Engaging patients and clinicians; focus groups with patients (n=16) and a workshop with clinicians (n=8).

4. Alfa test among the participating patients and clinicians.
5. Beta test among patients in the target population (n=100).

The PRO is tested for face validity, construct validity and content validity.

Results: The linking results show that 89% of the PROMIS items were successfully linked to ICF. The PROMIS items cover 22% of the ICF Core Sets. To ensure full coverage of the ICF Core Sets, new items will be developed within the framework of the PROMIS methods and terminology.

Conclusion: The development process is in progress, and next step is to engage patients and clinicians.

P24.03 Peter Lund  
Ovesen

#### THE ROLE OF SORCS1 IN GABAERGIC SIGNALLING IN THE BRAIN

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The balance between excitatory and inhibitory activity in the brain is crucial for controlling and organising neuronal output. Issues within this system are core features of neurological diseases like autism and schizophrenia. The Vps10-p Domain receptor SorCS1 is highly expressed in the brain, dominating at embryonic and early postnatal stage of development within the hippocampus and neocortex (S. Oetjen et al., 2014; Allen Brain Institute). SorCS1 is shown to interact with and regulate axon-dendritic sorting of synaptic adhesion protein neurexin and affect the function of inhibitory synapses in single cortical neurons (N. Savas et al., 2015). Additionally, members of the neurexin family have been shown to interact with GABA<sub>A</sub> receptors and depress development of GABAergic signalling (Zhang C. et al., 2010).

We have investigated neuronal network inhibition in the hippocampus of mice absent of SorCS1 (SorCS1<sup>-/-</sup>) using field recording electrophysiology supplemented with expression analysis of several genes involved in GABAergic signalling. In SorCS1<sup>-/-</sup> mice, we found a pronounced reduction of paired-pulse inhibition (PPI) in the dentate gyrus; this indicates reduced general inhibition of the granule cells. Additionally, we observed a marked reduction of GABAergic induced network oscillations in the pyramidal cell layer of the hippocampus. Finally, expression analysis revealed a distinctive reduction of the GABA<sub>A</sub> receptor  $\alpha$ 2 subunit in the hippocampus.

Altogether, our data support a role of SorCS1 in regulating the inhibitory tone of the brain. Dysfunction of SorCS1 might, therefore, be involved in the pathology of GABAergic associated brain disorders.

P24.04 Charlotte Bodin INCIDENCE AND PREGNANCY OUTCOME OF PRENATALLY DIAGNOSED SPINA BIFIDA IN DENMARK

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Objectives: All Danish pregnant women are offered a prenatal ultrasound screening for fetal anomalies. The aim of this study was to estimate the incidence, the detection rate by fetal ultrasound and the outcome of spina bifida (SB) in Denmark.

Methods: Data was retrieved from the Danish Fetal Medicine Database, which includes data on > 90% of all pregnancies in Denmark, including ICD-10 codes for prenatally or postnatally diagnosed malformations and pregnancy outcome. Pregnant women with a screening scan and a due date between 1 January 2008 and 31 December 2015 were included. SB diagnosis was identified by ICD-10 codes. Cases with SB occulta, lipomyelomeningocele and isolated tethered cord without neurological deficits were excluded.

Results: A total of 231 fetuses were diagnosed with SB in the national cohort of 443,617 screened women in 2008-2015. The yearly incidence of SB was thus 5.2:10,000. The prenatal detection rate was 91.1% for those who attended screening < week 22 (205/225), with 15.7% diagnosed in first trimester and 84.3% diagnosed in second trimester. In total, 90.7% opted for termination (186/205). Of all cases (231), 36 were liveborn, 6 miscarried and 189 were terminated. 91.2% of all SB cases were isolated malformations, of these 57% were karyotyped with abnormal findings in 10.9% of these.

Conclusions: The incidence of SB in Denmark was 5.2/10,000 per year and thus in accordance with the data reported by the European Surveillance of Congenital Anomalies. The national prenatal detection rate of SB in Denmark is high, with only 36 cases not diagnosed before 22 weeks. The vast majority of SB cases were terminated and were isolated malformations and had a normal karyotype.

P24.05 Bente Kjær  
Lyngsøe MATERNAL DEPRESSION AND OFFSPRING ATTENDANCE IN ROUTINE HEALTH CARE

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## University

Background: Depression is one of the most common mental illnesses worldwide. Women have a risk twice as high as that of men. During pregnancy, birth and postpartum, this risk increases even further. Depression can be debilitating for both the affected person and his/her network. International research has shown ambiguous results regarding the association between maternal depression and utilization of health care.

Aim: To evaluate the association between maternal depression and offspring attendance to the Danish routine childhood care and vaccination program.

Materials: Our population is all live-born children from 1997 to 2013 and their mothers, approximately 1 million children and 600,000 mothers. Informations are obtained from the Danish Register of Medicinal Product Statistics, the Danish National Patient Register, the Danish National Health Insurance Service Register and the Danish Civil Registration Register.

Preliminary results: The results of our first population-based cohort study indicate that children of depressed mothers have a significantly lower attendance to the Danish routine childhood care and vaccination program compared to children of non-depressed mothers. Furthermore, it seems that having a depressed father also affects the attendance. We are in the process of investigating these associations further.

Perspectives: Our results will contribute with important knowledge in the process of improving the contact with vulnerable families in general practice.

P24.06 Simon Skov

### METAL WEAR AND CORROSION AFTER GROWTH ROD INSTRUMENTATION (GR) IN CHILDREN WITH SEVERE EARLY ONSET SCOLIOSIS

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Background: Wear in certain metal-on-metal hip implants has caused great concern. Evidence of wear in spinal implants, especially in children, is sparse.

Purpose: To determine metal ion levels in children with cobalt-chromium/titanium GR undergoing interval lengthening procedures.

Materials and methods: A cross-sectional study of 34 patients, including 8 children prior to surgery, median age 11.0 (3.3-15.8). Eligible patients were included during 1.7 years. Standardized venous blood samples were taken, median 2.9 years (0.5-10), after surgery. Contamination-free consensus guidelines were followed. Blinded analysis was performed for

serum chromium (Cr), cobalt (Co), molybdenum (Mo), titanium (Ti), aluminium (Al) and vanadium (V) using high-resolution mass spectrometry at a certified laboratory.

Results: Cr levels at index were median 1.9 ppb (0.5-10) vs. 1.1 ppb (0.5-80) during elongation,  $p=0.46$ . Cr levels exceeded the 7 ppb warning threshold given by MHRA ([www.gov.uk](http://www.gov.uk)) in 26% after GR. Cr levels after GR returned below threshold within the following year, despite presence of metal debris in most operated patients. Co levels increased from median 0.2 (0-0.4) ppb to 0.5 (0-2.6) ppb,  $p<0.0001$ . Ti levels at index were median  $<1$  ppb (max 3.4) vs. 10.6 ppb (1.1-48.4) during elongation,  $p<0.001$ . Al, Mo, V levels did not differ.

Conclusion: In total, 26% of patients had transient Cr levels above the warning threshold after GR, but the levels returned below threshold within the next year. The children with elevated ion levels did not differ clinically from the remaining group. Minimizing and monitoring iatrogenic metal ion exposure in these children is important due to the increased risk of genotoxicity and mutagenicity. This study did not confirm an increased risk.

P24.07 Andrey Chuhutin PRECISION AND ACCURACY OF DIFFUSION KURTOSIS ESTIMATION AND THE INFLUENCE OF B-VALUE SELECTION

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Diffusion Kurtosis Imaging (DKI) is an extension of Diffusion Tensor Imaging that accounts for leading non-Gaussian diffusion effects. In DKI studies, a wide range of different gradient strengths (b-values) is used, which is known to affect the estimated diffusivity and kurtosis parameters. Hence, there is a need to assess the accuracy and precision of the estimated parameters as a function of b-value. This work examines the error in the estimation of the mean of the kurtosis tensor (MKT) with respect to the ground truth, using a biophysical model for gray and biexponential model for white matter. The parameters of the models are derived from the human and ex vivo rat brain data. Additionally, the variability of MKT is studied using densely sampled ex vivo rat and in vivo human brains. Several prevalent fitting protocols are implemented and investigated. The results show strong dependence of net relative error and standard deviation of error on the maximum b-value for all of the fitting protocols. The minimum error and standard deviation of error for gray matter are achieved with much lower b-values than normally utilized by most DKI studies (less than  $1 \text{ ms}/\mu\text{m}^2$ ). Averaged over multiple voxels, a net average error of 15% for gray and white matter was observed for the optimal b-values choice. When the maximum b-value is increased above  $2 \text{ ms}/\mu\text{m}^2$ , a strong linear dependence between the evaluated MKT and biophysical parameter (neurite density) is observed

in the gray matter. These results suggest caution when using the DKI generated metrics for microstructural modeling and when comparing the studies that use different fitting techniques and gradient strengths.

P24.08 Mette Holm Hjorth METAL-ON-METAL HIP RESURFACING ARTHROPLASTY: ANTERO-LATERAL VERSUS POSTERIOR SURGICAL APPROACH: A 2-YEAR RANDOMIZED RADIOSTEREOMETRIC AND DUAL X-RAY ABSORPTIOMETRY STUDY OF 49 PATIENTS

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Background: Different surgical approaches can be used for metal-on-metal hip resurfacing arthroplasty (MoM HRA). The antero-lateral (AL) approach may spare the blood supply to the femoral head and potentially improve implant fixation, lessen bone mineral density (BMD) loss, and improve outcome scores.

Material and methods: A randomized clinical trial was carried out at Aarhus University Hospital between Nov 2008 and Jan 2012. A total of 49 patients (28 males) was allocated to MoM HRA by the AL (n=25) or the posterior (P) (n=24) surgical approach. Patients were followed with: radiostereometric analysis (RSA), measurements of periprosthetic BMD, outcome scores of Harris Hip Score (HHS) and Visual Analogue Scale (VAS), and levels of serum metal ions.

Results: At 3 months, the acetabular cups in the AL group had more pronounced total translations (TT) of mean  $1.00 \pm 0.70$  mm versus mean  $0.64 \pm 0.45$  mm in the P group ( $p=0.04$ ), and more pronounced total rotations (TR) of mean  $2.44 \pm 1.36^\circ$  versus mean  $1.39 \pm 1.17^\circ$  in the P group ( $p=0.002$ ). All migrations were similar at 1 year and 2 years ( $p>0.07$ ). Periprosthetic BMD since postoperative at the medial side of the stem was reduced in the AL group by mean 98.45 (8.57%) and increased in the P group by mean 105.57 (11.07%) at 1 year ( $p=0.02$ ), but measurements were comparable at 2 years ( $p=0.05$ ). Outcome scores of HHS, VAS and serum metal ions were similar ( $p>0.09$ ).

Conclusion: Cups in the AL group migrated more at 3 months and had lesser periprosthetic BMD at the medial side of the femoral stem at 1 year compared with the P group. However, the difference was small and not present at the 2-year follow-up. We will continue to follow these patients closely.

P24.09 Didde Haslund UNRAVELING THE MOLECULAR DISEASE MECHANISMS IN HEREDITARY ANGIOEDEMA BY ESTABLISHMENT OF A NEW CELLULAR SCREENING SYSTEM

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Hereditary angioedema (HAE), caused by C1 inhibitor (C1INH) protein deficiency, is a rare disease caused by mutations in the serping1 gene. Erroneous production of C1INH leads to unpredictable and life-threatening edema attacks in HAE patients. Heterozygous HAE patients maintain production of functional C1INH from a single normal serping1 allele. Yet, in Type I HAE patients, the C1INH plasma level is 20% of normal level. This is consistent with a disease pathology in which the mutated allele negatively affects proteins derived from the normal allele, which is referred to as 'trans-inhibition'. A detailed understanding of the cellular mechanisms leading to trans-inhibition in HAE is crucial for improved treatment of HAE and for development of genetic therapies.

Here, we describe a new cellular screening system by which it is possible to study the dominant negative effect of mutated serping1 genes on the normal serping1 gene encoding C1INH. By fluorescence tagging normal C1INH, we can study the effect of mutated serping1 gene variants on secretion and intracellular accumulation of normal C1INH by measuring fluorescence intensity in the medium and cells, respectively. Also, by wide field microscopy, we can determine the intracellular location of C1INH.

We demonstrate reduced secretion and increased intracellular accumulation of normal C1INH when HAE-causing serping1 genes are present. Furthermore, the presence of mutated serping1 gene variants leads to intracellular aggregation of normal C1INH, as determined by wide field microscopy. These results show that mutated serping1 genes inhibit the secretion of normal C1INH by inducing intracellular aggregation of normal C1INH.

P24.10 Ana Carlota Gonzalez-Ebsen ANALYSIS OF THE METABOLIC STATE IN CULTURED FIBROBLASTS FROM PATIENTS WITH MULTIPLE ACYL-COA DEHYDROGENATION DEFICIENCY (MADD), A MONOGENIC MITOCHONDRIAL DISORDER

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Multiple acyl-CoA dehydrogenation deficiency (MADD) is an inborn error of the mitochondrial metabolism. This genetic disorder is caused by mutations in either the electron transfer flavoprotein (ETF) or electron transfer flavoprotein ubiquinone oxidoreductase (ETF-QO), which links

mitochondrial fatty acid oxidation to energy/ATP production in the respiratory chain. Patients with this condition experience mitochondrial dysfunction with a specific decline in ATP production, and with increased production of cytotoxic reactive oxygen species (ROS). MADD can be categorized into S:MADD (S-severe), which corresponds to an early onset of the disease, where death is unavoidable, and RR:MADD (RR-riboflavin responsive), which corresponds to a later onset of the disease and response to riboflavin treatment. An important common hallmark of MADD and other conditions with mitochondrial dysfunction is a metabolic reprogramming towards enhanced aerobic glycolysis and low or impaired mitochondrial respiration, the so-called Warburg effect. In the present project, we want to investigate this metabolic reprogramming in the two patient groups, using skin fibroblasts. The SeaHorse XF96 extracellular flux analyzer allows us to measure cellular changes in mitochondrial respiration (oxygen consumption rate, OCR) and glycolytic lactate production (extra cellular acidification rate, ECAR) in order to determine the metabolic state of the cells.

P25.01 Mads Christian Larsen ONCE VERSUS TWICE DAILY ASPIRIN TREATMENT IN PATIENTS WITH ESSENTIAL THROMBOCYTOSIS

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Background: Insufficient platelet inhibition has been reported in up to 40% of aspirin-treated patients and is likely explained by several mechanisms, including accelerated platelet turnover. Patients with essential thrombocytosis (ET) serve as a biological model of increased platelet turnover.

In order to maintain sufficient platelet inhibition, a shorter dosing interval with aspirin has been suggested.

Aim: To investigate the antiplatelet effect of low-dose aspirin given twice-daily compared to standard once-daily dosing in patients with ET.

Methods: We included 22 patients with ET meeting at 4 visits: baseline (prior to intervention, after 14 days aspirin-washout), day 7 (after 7 days with aspirin 75 mg x 1), day 21 (after 14 days washout) and day 28 (after 7 days with aspirin 37.5 mg x 2). Blood samples were obtained 1h and 24h after last pill intake at each visit.

Laboratory analyses: Platelet aggregation was measured by Multiplate analyzer® using arachidonic acid (ASPItest 0.5 mM) as agonist. Thromboxane B<sub>2</sub> levels were determined using ELISA.

Preliminary results: The increase in platelet aggregation from 1h to 24h

was used to compare the two regimens. We demonstrated a lower increase in platelet aggregation in the twice-daily regimen compared to the once-daily: mean of difference = 227 AU\*min (95% CI: 92 to 363,  $p < 0.01$ ). Furthermore, a lower increase in serum thromboxane B<sub>2</sub> was demonstrated in the twice-daily regimen compared to once-daily: mean of difference = 10.3 ng/mL (95% CI: 6.3 to 14.3,  $p < 0.01$ ).

Conclusion: According to these preliminary results, twice-daily low-dose aspirin provides a more persistent platelet inhibition compared to standard once-daily dosing.

P25.02 Niels Sanderhoff CAN SORCS2 MODULATE BDNF SIGNALING AND DISEASE  
Degn PROGRESSION IN HUNTINGTONS DISEASE?

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Huntington's disease (HD) is an autosomal dominantly inherited neuro-degenerative disorder caused by a CAG repeat expansion in the huntingtin gene. HD is characterized by a hyperkinetic movement disorder, psychiatric symptoms and cognitive decline. Binding of Brain Derived Neurotrophic Factor (BDNF) to its receptor TrkB on medium spiny neurons in the striatum is required for maintaining neuronal integrity and for induction of long-term potentiation (LTP) in corticostriatal synapses. Disruption of BDNF signaling is a central aspect of impaired synaptic plasticity in cortico-striatal synapses and selective degeneration of medium spiny neurons in HD. This is accounted for by both reduced cortical expression of BDNF as well as reduced TrkB expression and impaired downstream signaling in the medium spiny neurons. Recently, we reported that SorCS2, a member of the Vps10p-domain receptor family, is indispensable for induction of BDNF-dependent LTP in the hippocampal CA3/CA1 synapse by activity dependent recruiting of TrkB into the postsynaptic density (Mol Psych, 2016). The current project aims to characterize the effect of SorCS2 on synaptic plasticity in the striatum and its effect on HD progression in R6/1HD mice. We find that SorCS2 is expressed in medium spiny neurons, and initial experiments suggest that late-phase LTP in dorsomedial striatum is impaired in SorCS2 knockout mice. To study motor dysfunction, we have, in a first paradigm, carried out a longitudinal testing for hindlimb clasping. Preliminary data indicate that SorCS2KO aggravates the clasping phenotype in R6/1HD mice. Our preliminary data suggest that SorCS2 is critical for the functionality of medium spiny neurons.

P25.03 Line Stjernholm  
Tipsmark ORGANISATIONAL DESIGN OF EMERGENCY CARE: POLICY EVALUATION

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Background: Organisation of emergency care holds a great impact on the health care system-level functioning. In recent years, the growing issue of patient crowding has increased the demand on ED staff and poses a threat to patient safety. To improve ED flow and quality of care in Denmark, emergency services are currently under reorganisation. This reorganisation is based on six strategies: centralisation, visitation, interdisciplinary teams, staff qualification upgrades, availability of specialised equipment, and senior physicians day and night. The reorganisation is intended to improve the quality of care, increase hospital sector effectiveness and optimise resource use, but this does not seem to be based on scientific evidence. The aim of this project is to assess the evidence behind the ongoing reorganisation of emergency care in Denmark and to investigate its effects on health outcome, patient-experienced quality of care, and costs.

Method: A first systematic literature review study aims at identifying the evidence base behind the six strategies of reorganisation. A second study is an online questionnaire-based survey aiming at assessing the status of reorganisation using closed-ended questions. A third registered-based longitudinal study, including acute patients treated from 2005 to 2016, aims at identifying the effect of the reorganisation on Triple Aim goal achievement. A comparative analysis of effects before and after the reorganisation will be made using a Difference-in-Difference approach. A fourth interview study aims at exploring how consultants and senior nurses can contribute to the overall understanding of the relation between effect and organisational design.

P25.04 Johan Fredrik  
Borg REGULATED EXPRESSION OF THE NA/K-ATPASE IN COLONIC EPITHELIUM BY BILE ACIDS

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Bile acid malabsorption (BAM) is a common cause of diarrhea in patients with Irritable Bowel Syndrome. The mechanism underlying the development of diarrhea during BAM is unclear. I aimed to determine if expression levels of mRNA and protein as well as localization of Na/K-ATPase are influenced by BA in colonic epithelial cells during BAM.

Rats were fed 1% Na-Cholate (NC) containing diet for three days. Colonic epithelium was isolated using  $\text{Ca}^{2+}$ -chelation and prepared for protein analysis and RT-qPCR. Colonic tissue was prepared for immune-

histochemistry (IHC).

The treated rats developed diarrhea with an increased feces water content compared to controls.

In a previous experiment with similar results, we used liquid chromatography tandem mass spectrophotometry (LC-MS/MS) on colonic epithelial tissue from the animal model of BAM to create a protein profile. We found that the Na/K-ATPase  $\beta_1$  subunit (NKA  $\beta_1$ ) was significantly down-regulated in the colon during BAM. In our BAM model, western blotting confirmed the down regulation of the NKA  $\beta_1$  in colon. Na/K ATPase  $\alpha_1$  subunit (NKA  $\alpha_1$ ) abundance was also decreased in proximal, but not distal colon. RT-qPCR analysis showed no regulation of ATP1B1 or ATP1A1 at the mRNA level. IHC showed no morphological differences in cross-sections from NC treated rats, nor any change in NKA  $\beta_1$  or  $\alpha_1$  localization.

In conclusion, we have found the NKA  $\beta_1$  to be down-regulated at the protein level in the colonic epithelium of rats after 3 days of NC treatment. Due to the central role of NKA in the absorption and secretion of water and electrolytes in the colon, this regulation could be central in the development of diarrhea during BAM.

P25.05 Linda Aagaard Rasmussen THE PATIENT PATHWAY FOR RECURRENT AND NEW PRIMARY CANCER: INVESTIGATING THE ROLE OF GENERAL PRACTICE

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Background: The number of cancer survivors in Denmark is increasing, and the Danish post-cancer follow-up programmes are currently under revision. The prognoses for cancer survivors depend on the ability of the health-care system to respond adequately to early signs of cancer recurrence. Knowledge about the complete pathway to cancer recurrence is sparse, and research enhancing effective follow-up programs and early detection of recurrence is warranted. However, as recurrence of cancer is not routinely registered in the Danish patient registries, we need to develop methods to identify these patients.

Objective: To develop and validate algorithms to identify patients with cancer recurrence in Danish national patient registries.

Methods: The study is an observational cohort study. The study population is incident cancer patients diagnosed during 2008-2014 according to the Danish Cancer Registry. Diagnostic and procedure codes in the Danish National Patient Registry and malignant pathology codes in the Danish National Pathology Registry will serve as indicators of cancer recurrence.

Validation of the algorithms are conducted by comparing the identified

cancer recurrence cases from the algorithms with a gold standard, being either data from national clinical cancer databases or relevant cohort studies or review of medical records.

Perspectives: This study will enable further research in cancer recurrence by generating valuable information that may improve targeted attention from general practitioners and other health-care professionals and promote more timely diagnosis of recurrent cancer.

P25.06 Karoline Knudsen GASTROINTESTINAL FUNCTION IN PARKINSON'S DISEASE

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Background: The majority of patients with Parkinson's disease (PD) experience gastrointestinal (GI) symptoms. Despite the high prevalence, data on objective GI tract testing is scarce, especially in the small intestine. Thus, we aimed to study GI symptoms and objective function in PD patients and healthy controls (HC).

Methods: Thirty-two PD patients and 26 HC were included. Colonic transit time (CTT) was evaluated with the radio opaque marker (ROM) technique, segmental colonic volume was estimated on a computed tomography scan (CT), and gastric emptying time (GET) was measured scintigraphically.

Transit time in the stomach, small intestine, and coecum-ascending colonic segment were assessed over a 24-hour period using the 3D-transit system, monitoring an ingested electromagnetic capsule. Subjective GI symptoms were evaluated by three different questionnaires.

Results: Seventy-nine percent of PD patients showed significantly prolonged CTT ( $p < 0.0001$ ), and 66% had significantly increased colonic volume ( $p = 0.0002$ ). There was no group difference in scintigraphy-based GET.

PD patients displayed significantly increased 3D small intestinal (STT) and coecum-ascending transit time (CATT) ( $p = 0.03$ ,  $p = 0.0063$ ). Again, no difference was seen in 3D-based GET ( $p = 0.91$ ). The prevalence of subjective constipation ranged from 3% to 38% depending on questionnaire type.

Conclusion: Significantly delayed CTT, increased volume, and prolonged 3D STT and CATT were seen in PD patients compared to HC. Objectively measured dysfunction was considerably more prevalent than subjective symptoms and could have potential as diagnostic tools in PD.

P25.07 Anne Højager  
Nielsen CONSOLATION OR CONFRONTATION WHEN CO-AUTHORING A DIARY  
IN THE ICU

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Background: A nursing intervention of introducing relatives to writing a diary for the critically ill patient can be a rewarding experience for the relative as it provides the relative with new insights and promotes wellbeing. Co-authoring of a diary has not been explored.

Aim: To explore relatives' experience of co-authoring a diary for the critically ill patient.

Method: Seven adult relatives, who had written a diary when their close relative was admitted to an ICU at a regional hospital in Denmark, were interviewed after the patient's discharge exploring their experience. Data were analysed using a phenomenological-hermeneutical approach drawing on the theory of interpretation by Ricoeur.

Results: Co-creation of a diary for the critically ill patient by fragile relatives increased their wellbeing by allowing them to share emotions. However, difficult relationships could keep relatives from sharing feelings and understandings and thus cause suffering among relatives and co-creation of the diary to fail. The relationship between relatives determined authorship, which could be both a powerful position to shape the story unfolding in the diary or a burdensome responsibility.

Conclusion: Administering a diary intervention among several relatives could increase wellbeing in critical situations, although precautions should be taken in families with troublesome relationships. Co-authoring the diary provided relatives with the power to influence the narrative in the diary and allowed the relatives to incorporate the illness experience into a personal narrative as well as a family narrative. The patients' perception of a diary written by relatives needs further exploration.

P25.08 Jonathan Yde AQUAPORIN WATER CHANNEL-EXPRESSION IS ALTERED IN RAT MODEL  
OF CHRONIC DIARRHOEA DUE TO BILE ACID MALABSORPTION

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Background: Bile acid malabsorption (BAM) is a condition where excess amounts of bile acids (BA) in the colon cause chronic watery diarrhea via unknown mechanisms. My aim is to determine if aquaporin water channels (AQPs) in the colonic epithelium are involved in the development of diarrhea during BAM.

Methods: Rats kept in metabolic cages were fed a diet containing 1% bile acids (BA) for 10 days as a model for BAM. Colonic epithelial cells were isolated by Ca<sup>2+</sup>-chelation. Cells were processed for RNA and protein analyses.

Results: BA rats had greater feces dry weight and feces water content compared to rats fed standard chow. In contrast to controls, BA rats did not gain weight over time. The difference in weight was significant at the end of the experiment. Semi-quantitative real-time PCR of epithelial cells showed that Ost- $\beta$  mRNA was increased in the BA-treated group, indicating activation of the nuclear bile acid receptor (FXR). Aqp3 mRNA was increased in the distal colon in the BA-treated group, while mRNA for Aqp8 was increased in both the proximal and the distal colon. mRNA for Aqp1, -4 and -7 was not different between groups. AQP3 was detected as a non-glycosylated and a glycosylated form by western blotting. The glycosylated form was significantly reduced in the BA rats compared to controls.

Conclusion: In a rat model of BAM, we find increased expression of Aqp3 and Aqp8 mRNA in the distal colon. This finding indicates a role for AQPs in the development of diarrhea during BAM.

P25.09 Lone Kirkeby

DO HIGH OCCUPATIONAL MECHANICAL EXPOSURES INFLUENCE THE RISK OF FAILURE OF TRAPEZIOMETACARPAL JOINT ARTHROPLASTY?

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Background: The influence of occupational mechanical exposures on the risk of implant failure and revision in trapeziometacarpal (TM) total joint arthroplasty (TJA) in younger and active patients remains unclear.

Aim: To determine the prognosis with respect to risk of revision after TM TJA, evaluating the hypothesis that occupational mechanical exposures are negative prognostic factors for implant survival.

Materials and methods: A register-based follow-up study of 133 patients aged 39-65 years (mean: 56) who in the period 2003-2013 had a total of 164 TM TJA operations. Prospectively collected clinical data concerning DASH, VAS, and grip strength before the operation and 3 and 12 months after the operation plus data concerning revision were combined with self-reported job title and information about labour market attachment from the Danish National Register on Public Transfer Payments. Job title was linked with a job exposure matrix to obtain estimates of occupational mechanical hand-arm exposures. Univariate

and multivariable Cox regression models were used.

Findings and results: A total of 45 of the 164 implants had been revised due to failure. Implant type with a cup with collar predicted a high DASH score after 12 months and implant revision during the observation period. Implant fixation (cementless/cemented) was not a predictor. Forceful work increased the risk of implant revision, however, not significantly ( $p=0.17$ ) in a multivariate analysis.

Conclusion: The prognosis for implant survival after TM TJA in younger and active patients is relatively poor and highly influenced by implant design. High occupational mechanical exposures may be important, and studies with larger number of patients are needed.

P25.10 Steffan Tábori  
Jensen FUNCTION, HEALTH STATUS AND SATISFACTION AFTER SURGERY WITH  
THA FOLLOWING FEMORAL NECK FRACTURE OR OSTEOARTHRITIS

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Background: Displaced femoral neck fracture (FNF) is a common injury. Treatment with total hip arthroplasty (THA) has low complication and revision rate, but less is known about the functional results after ended rehabilitation.

Purpose: To investigate function, health status and satisfaction in patients treated with primary THA after displaced FNF.

Material and method: From 2005 to 2011, a total of 414 consecutive FNF patients were operated with Saturne Dual mobility (DM) THA.

At min 1-year follow-up, 124 (95 women) responded to an invitation and were evaluated with Oxford Hip Score (OHS), a general health-related quality of life measure (EQ-5D) and two functional tests: Timed Up and Go (TUG) and Sit To Stand 10 times (STS). The FNF patients were matched 1:2 by age, sex and surgery date with patients receiving THA due to osteoarthritis (OA group) with 1-year OHS and EQ5D. EQ-5D for the FNF group was matched to the general population index.

Results: At mean follow-up of 2.8 (1.0 - 7.7) years, the mean EQ-5D score was 0.79 (sd 0.15) in the FNF group, which was similar to the index of the matched general population ( $p=0.4$ ), but lower ( $p=0.001$ ) when compared to the OA group. Mean OHS was 36.4 (sd 9.5) in the FNF group and 38.4 (sd 7.2) in the OA group ( $p=0.05$ ). Hip pain (Q1 from OHS) was similar between groups ( $p=0.10$ ). Mean TUG was 13.5 (sd 4.9) sec, and mean STS was 37.9 (sd 15.3) sec in the FNF group. Mean VAS at

rest was 1.0 (sd 1.7) and during activity 2.1 (sd 2.7); 89% were satisfied with the result of the operation.

Conclusion: Patients with DM THA following displaced FNF had a good functional and satisfactory result. EQ-5D was similar to the age- and gender-matched population index, but it was lower compared with OA THA patients.

P26.01 Kailash Rani  
Kumar

#### EVALUATION OF BLOOD FILTRATION MEMBRANES FOR MULTIPLEXED POINT-OF-CARE DIAGNOSTIC DEVICES

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Background and aim: Recently, a new method for measuring molecules in solution was developed (DETECT project)<sup>1</sup>. The method allows for fast measurement of biomarkers in the near patient setting, such as the ICU or prehospital. The aim of this study is to evaluate pre-analytical conditions for DETECT, including evaluation of methods for preparation of human blood samples by filtration instead of centrifugation. The pre-analytical methods will be evaluated for the measuring of various biomarkers and compared with standard reference methods (e.g. LCMS, UHPLC).

Methods: Experiments were carried out to evaluate four different types of whole blood plasma filter (GR, GX, S/G & NX) in relation to: 1) recovery, 2) practicability (time and volume), and 3) hemolysis. Blood samples were prepared by filtration and conventional centrifugation. More than 50 biomarkers (proteins, hormones, lipids, electrolytes, enzymes and drugs) were measured with reference methods.

Results and conclusions: Our results revealed that sufficient amounts of plasma (250µl/500 µl blood) can be obtained from full blood by all four filters within < 5 minutes. Plasma could be recovered without applying external force. Generally, recovery of most the biomarkers are near 100% when compared to traditionally centrifuged blood samples. The NX filter performed best, showing recovery of near to 100% for almost all biomarkers. The GR filter showed the lowest recovery (50 to 85%). Results on protein binding, hemolysis and recovery of the four types filter will be presented. In conclusion, passive filtration of whole blood is possible with acceptable recovery.

1) Zhang, Z. et al. J. Am. Chem. Soc. 2014, 136, 11115-11120.

P26.02 Zenthuja  
Sivalingam

THE PREDICTIVE ROLE OF NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (NGAL) IN PATIENTS WITH STABLE CORONARY ARTERY DISEASE

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**Aim:** We aimed to investigate the characteristics of neutrophil gelatinase-associated lipocalin (NGAL) as a risk marker for acute myocardial infarction (AMI), ischaemic stroke, and cardiovascular death in patients with stable coronary artery disease (CAD).

**Background:** NGAL is a protein of the lipocalin family. NGAL is highly expressed in atheromatous plaques and may contribute to the weakening of the cap causing rupture and thrombus formation. Recently, high NGAL levels were found to be associated with an increased risk of all-cause mortality and major adverse cardiovascular events (MACE) in healthy individuals and patients with ST-elevation myocardial infarction.

**Methods:** We included 900 patients with stable CAD. All patients had previous AMI or type 2 diabetes and/or reduced kidney function. Patients were followed for a median of 3.05 years (min 1.95; max 5.10). The primary endpoint was the composite of cardiovascular death, AMI and ischaemic stroke. Endpoint assessment was based on data from the Western Denmark Heart Registry, the Danish Stroke Registry and the Danish Register of Causes of Death. Citrate plasma concentrations of NGAL will be measured using the Cobas 6000® instrument from Roche Diagnostics.

**Results:** All patients have been included. However, NGAL analysis have just commenced, thus we have no results to present now.

**Expected outcomes and perspectives:** We hypothesize that patients included in the primary endpoint have elevated plasma NGAL levels. Elevated NGAL levels may indicate a poor prognosis in patients with stable CAD. The perspective is to utilize NGAL to identify stable CAD patients with a high risk of MACE.

P26.03 Anders Kristensen EFFECTS OF CALCIUM ON THE FORCE-VELOCITY RELATIONSHIP IN ISOLATED RAT SOLEUS MUSCLES

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**Aim:** In dynamically contracting muscles, increased curvature of the force-velocity (FV) curve contributes to the loss of power during fatigue. It has been proposed that this increased curvature is caused by fatigue-induced reduction in tetanic  $[Ca^{++}]_i$ . We hypothesized that a decreased tetanic  $[Ca^{++}]_i$  would increase the curvature in isolated skeletal muscle.

**Methods:** Freshly isolated rat soleus muscles were incubated in a standard Krebs-Ringer buffer at 30°C. Force and velocity were measured during electrical stimulation at a frequency of 60Hz (baseline) and subsequently during interventions that either lowered tetanic  $[Ca^{++}]_i$  (10  $\mu$ M dantrolene and submaximal stimulation at 30Hz) or increased tetanic  $[Ca^{++}]_i$  (2 mM caffeine). FV curves were obtained by fitting data on force and shortening velocity at different loads to the Hill equation. The curvature was measured as the ratio  $a/F$  based on the Hill equation parameters. Increased curvature was reflected in decreased  $a/F$ .

**Results:** Compared to baseline, lowering tetanic  $[Ca^{++}]_i$  with dantrolene and submaximal stimulation increased  $a/F$  by 12% and 13%, respectively. However, these interventions reduced maximal power by 51% and 41%, respectively, due to a decrease in maximal force and velocity. Increasing tetanic  $[Ca^{++}]_i$  with caffeine decreased  $a/F$  by 18%, but increased maximal power by 24% due to increases in maximal force and velocity.

**Conclusion:** Contrary to our hypothesis, interventions that reduced tetanic  $[Ca^{++}]_i$  caused a decrease in the curvature of the FV curves, while increasing tetanic  $[Ca^{++}]_i$  increased the curvature. These results reject a causal relation between  $[Ca^{++}]_i$  and an increased curvature during fatigue.

P26.04 Cecilie Siggaard TRANSANAL COLONIC IRRIGATION IS EFFECTIVE IN FUNCTIONAL FECAL INCONTINENCE

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**Objectives:** Functional fecal incontinence (FFI) is a chronic condition, which is often related to constipation. Transanal colonic irrigation is widely used in neurogenic fecal incontinence, but it is less studied in functional patients. The aim of the study was to evaluate the feasibility

and efficacy of transanal colonic irrigation in treatment of FFI.

Study design: A retrospective follow-up study was performed of children with treatment resistant FFI treated with irrigation. The initial regimen was to perform irrigation three times weekly and subsequently titrated according to response.

Results: Seventy-two children (mean age  $9.2 \pm 2.2$  years, 47 males) were identified. All children accepted treatment, and 35% ( $n = 25$ ) were titrated to daily sessions. Fifty children (69%) showed full response with complete remission of incontinence episodes, and 13 children (18%) showed partial response ( $\geq 50\%$  reduction). Sixty-three children (88%) fulfilled the ROME III criteria of constipation, whereas nine children met one criterion and were characterized as non-retentive. We found no significant difference in terms of reduction in incontinence episodes between the children with retentive (87%) and non-retentive (68%) fecal incontinence ( $p = 0.11$ ). However, more children characterized as retentive showed full or partial response (57 children (90%) vs. 6 children (67%),  $p < 0.05$ ).

Conclusion: Transanal colonic irrigation is an effective, well-tolerated and safe choice in children with retentive FFI. No clinical parameters seem to predict response to treatment. The number of children with non-retentive fecal incontinence was low, but the irrigation seems effective also in this group of children.

P26.05 Gunhild Mo  
Hansen

CONSTRAINT-INDUCED MOVEMENT THERAPY (CIMT) AND SHOULDER  
FUNCTION

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Background: Every year, 10,000-15,000 people in Denmark get a stroke. In total, 50% of the people surviving a stroke regain functional use of the upper extremity. CIMT, which is a highly recommended intensive approach for the rehabilitation of upper limb function following stroke, is recognized as being effective on the overall arm function. We know less about the proximal function and specific movement components; something that is sought after in newer studies. 3D kinematic movement analysis can contribute with specific objective details about the shoulder function in CIMT patients. The aim of this study is to evaluate longitudinal changes in the shoulder function before and after CIMT.

Method: A total of 40 persons will be included in the study, which is a prospective observational study with repetitive measurements before and three months after CIMT. Until now, 25 persons are included. Characteristics and further results will be presented.

Primary hypothesis: The shoulder function will improve from before to

after CIMT measured with 3D kinematic parameters in two functional tasks, and this improvement will persist after three months.

Secondary hypothesis: There is a correlation between outcome of 3D kinematic measurements of the shoulder, clinical tests and the patient's own experience of change in the shoulder function.

Perspective: The study can contribute with knowledge about changes in the shoulder function after CIMT and may thus contribute to development of CIMT as a treatment approach.

P26.06 Marie-Louise Ladegaard Baun ACCESS TO FAST TRANSVAGINAL ULTRASOUND THROUGH GENERAL PRACTICE FOR EARLIER DIAGNOSIS OF OVARIAN CANCER

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Background: Ovarian cancer (OC) is a disease with a poor prognosis due to diagnosis at late stage. Early-stage OC presents with non-specific and vague symptoms. Therefore, OC usually is not detected until an advanced stage. From 2008, Danish general practitioners (GPs) could urgently refer patients suspected of having OC to standardized cancer patient pathways (CPPs). The CPP is designed for women presenting specific signs and alarm symptoms and is intended to shorten the pathway from suspicion to treatment.

Direct access to fast transvaginal ultrasound (TVU) is only available through referral to the CPP. However, 60% of all OC patients do not present alarm symptoms, and the GP must refer to ordinary waiting list or use time as a diagnostic tool. This may cause diagnostic delays. Thus, there is a need for methods to facilitate earlier diagnosis of OC in general practice.

Aims: This PhD project has 3 overall aims.

1: To investigate the route to OC diagnosis.

2: To analyse the association between use of TVU and OC stage distribution.

3: To develop and evaluate training for GPs in OC diagnosis combined with direct access to fast TVU.

Methods: The first part of the study (aims 1 and 2) are observational studies, where the data are based on registry data. The second part is a clinical study, where all GPs from the Central Denmark Region are invited to participate.

Results: Data are not yet available.

Perspectives: This study may provide important new knowledge of how to improve the diagnostics of OC in the future, reduce the time to diagnosis and improve the survival.

P26.07 Sidsel Hastrup CENTRALIZATION AND SPECIALIZATION OF ACUTE STROKE TREATMENT

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Introduction: In 2012, a centralization and specialization of the acute stroke services was implemented in the Central Denmark Region (CDR) to save costs. It implied that only two designated hyper-acute units with re-vascularization therapy were to provide the care.

Objective: To investigate the impact on length of acute hospital stay (AHS), rate of thrombolysis (IV tPA), evidence-based clinical care and mortality.

Methods: Population-based before-and-after registry study. The study cohort included all stroke cases in Denmark, with patients outside the CDR being used as comparison to account for general changes in stroke care. The period before (May 2011 - April 2012) was compared to the period after (May 2013 - April 2014) using regression methods, including difference-in-differences (DID) analysis.

Results: Median length of AHS (days) in the CDR decreased from 5 (IQR 7) to 2 (3) vs. from 5.5 (9) to 5 (8.5) in the rest of Denmark. IV tPA rates increased from 15% to 19% of all acute ischemic strokes in CRD and from 9% to 14% in the rest of Denmark (DID RR 0.78 (0.66-0.92)). All-or-none rates of 11 process performance measures of in-hospital care increased from 51% to 63% in the CDR vs. 49% to 60% in the rest of Denmark (DID RR 0.99 (0.93-1.05)). Adjusted 30-day mortality rate decreased non-significantly and comparable to the rest of the country; OR 0.92 (0.67-1.18) vs. OR 0.91 (0.76-1.07) (DID OR 1.03 (0.74-1.42)).

Conclusions: Centralization of acute stroke care was associated with a significant reduction in AHS length. The use of IV tPA and the quality of acute stroke care also improved, but the trend was not different from the rest of Denmark. No changes in the adjusted 30-day mortality were observed.

P26.08 Gudrun Winther EFFECT OF PERINATAL OBESITY AND EXERCISE ON OFFSPRING METABOLISM AND MENTAL HEALTH

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Obesity during pregnancy can influence the long-term health in the offspring. Regular exercise might have an anti-inflammatory effect of an acute bout of exercise and might protect against chronic low-grade inflammation, but such a potential link between the acute effect of exercise and long-term benefits has not yet been proven. We wanted to investigate whether a nonpharmacological intervention, perinatal exercise, might improve offspring health.

Female rats were randomized into 4 groups (n = 8 in each group) with 2 subgroups per diet, exercise and sedentary: control diet group, high-fat diet group, control diet and exercise group and high-fat diet and exercise group. When receiving their corresponding diets for 6 weeks, rats were assigned randomly to be either in the runner or sedentary group by keeping them in standard cages individually equipped with either an unlocked or a locked wheel. Female rats were exposed to voluntary exercise wheels 5 weeks prior to mating.

Adult offspring exposed to perinatal high-fat diet and exercise were evaluated for anxiety- and depressive-like behavior using the elevated plus-maze (EPM), open field test (OFT) and forced swim test (FST). Hippocampal cytokines, neurotrophic factors and downstream signaling molecules were evaluated by RT-qPCR and Western Blot.

Here we suggest that exercise may be involved in mediating health-beneficial effects and may play an important role in the protection against diseases associated with obesity.

P26.09 Thomas Kristoffersen LEPTIN POTENTIATES THE PRO-INFLAMMATORY EFFECT OF PSORIASIS-RELATED CYTOKINES IN THE DERMAL FIBROBLAST POSSIBLY LINKING PSORIASIS TO OBESITY

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Psoriasis is often associated with obesity and cardiovascular diseases. Leptin, secreted mostly by the white adipose tissue, is an adipokine that regulates appetite and energy expenditure, thus playing a role in obesity. Leptin also participates in inflammatory responses. Increased serum levels of leptin are observed in obese individuals and psoriasis patients.

Moreover, leptin expression is increased in psoriatic skin.

Obesity predisposes to psoriasis and affects the efficacy of psoriasis treatment. Thus, understanding the association between obesity and psoriasis may enable us to improve psoriasis treatment. We, therefore, hypothesized that leptin could play a role in psoriasis. We have shown that, in the dermal fibroblast, leptin induced a pro-inflammatory response that was different for cells from psoriatic and from healthy skin. The purpose of this study was to investigate how leptin mediates its effects in psoriatic skin. In particular, we aimed to investigate whether the effect of leptin in the dermal fibroblast modulates other known psoriasis-related pro-inflammatory cytokines.

Dermal fibroblasts were isolated from psoriatic or from healthy skin, grown in vitro and assessed for a pro-inflammatory response after stimulation. Leptin stimulus was provided alone or in combination with IL-1 $\alpha$ , TNF- $\alpha$  or IL-17 for 24 hours. The cell culture medium was then analyzed by ELISA for the expression level of the inflammatory marker IL-6.

Our results suggest that leptin potentiates the effect of the selected psoriasis-related cytokines in human dermal fibroblasts. These data may explain the pro-inflammatory mechanism through which obesity exacerbates skin diseases such as psoriasis.

P26.10 Kaj Verner  
Døssing

#### THE ACCURACY OF ULTRASOUND AS A SCREENING MODALITY ON SUSPICION OF EXTREMITY FRACTURE IN ADULTS

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**Purpose:** The objective of this study was to investigate whether ultrasound can be used as a screening tool to exclude extremity fractures in adults.

**Materials and methods:** The study was a prospective comparative study involving 91 patients aged >18 years and referred to radiography by suspicion of an extremity fracture. The patients were referred by their general practitioner. Ultrasound examination was consistently performed prior to the radiography. No clinical examination was performed. Radiography was performed as the gold standard method. Inter-rater agreement between one of the investigators and a blinded radiologist was conducted by evaluating 42 randomly selected ultrasound images.

**Results:** The prevalence of fractures in the study population was 27%. McNemars test found an OR equal to 2 and showed no systematic difference between the results of ultrasound and radiography ( $p = 0.69$ ) when extremity fractures were suspected. The discriminative ability of ultrasound was described by a sensitivity of 92% and a specificity of 94%.

The positive predictive value was 85%, and the negative predictive value was 97%. There seemed to be no association between disagreement of the results and the patient's age or specific body parts. The inter-rater agreement was 100%, equal to a kappa value of 1.

Conclusions: This study indicates that ultrasound as a screening modality when an extremity fracture is suspected has high accuracy and reliability. No systematic differences were found between the results of the two modalities, and ultrasound showed a high sensitivity and specificity. The inter-tester agreement was 100%.

P27.01 Karen Rokkedal  
Lausch BEHIND CANDIDAEMIA: DESCRIBING A HIGH INCIDENCE NATIONWIDE SETTING

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Introduction: The incidence of candidaemia is remarkably high in Denmark compared to our neighbouring countries; the population-based incidence rate in Denmark being 9.4 in 2010-11 per 100,000 inhabitants compared to 2.6-5.7 in the other Scandinavian countries. Population-based incidence rates are sparse in other parts of the world and differ greatly. The high national incidence rate in Denmark calls for further investigation to elucidate the drivers behind and the associated outcome. We here characterize the clinical aspects of candidaemia in a nationwide perspective.

Methods: The National Surveillance of Fungaemia identified all candidaemia patients from 2010 to 2011. Clinical information was retrospectively collected from patient charts by a local microbiologist. The CPR number of cases was merged with the CPR register to ensure follow-up on mortality. The data collection was approved by the Danish health authorities.

Results: Clinical data was available for 909 cases, accounting for 93.7% of all identified cases. In total, 31 cases were pediatric. The overall annual national incidence rate of candidaemia was 0.34 cases per 1000 admissions and markedly higher for ICU admissions with 6.08 per 1000 admissions. Distribution on departments will be presented in Table 1, and the clinical characteristics will be shown in Table 2.

Conclusions: The first nationwide data with clinical characteristics of candidaemia will be described and will add to the knowledge about

and the characterization of candidaemia. This insight will contribute to the understanding of candidaemia in a broader perspective.

P27.02 Simon Skouboe MOTION INCLUDING REAL-TIME DOSE RECONSTRUCTION FOR CALYPSO PATIENTS IN RADIOTHERAPY

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Background: Dose reconstruction, i.e. calculation of the delivered tumor dose for a given cancer treatment, is needed to quantify and understand the detrimental effects of tumor motion in radiotherapy treatments.

Methods: During radiotherapy treatments, relevant machine parameters and the position of the tumor are streamed to our in-house developed software, which calculates the tumor dose based on this information. The dose is calculated in the same points as in the treatment planning system (TPS), with which the results are compared. The dose is reconstructed three times: 1) without motion (the plan), 2) with motion and gating (turning the beam off depending on motion), 3) with motion and without gating.

Dose volume histograms for the GTV and PTV are calculated for each of the three scenarios. The difference in dose received by e.g. 95% of the volume is found with and without motion and gating. The same procedure is carried out in the TPS, and the results are compared.

Status and results: The doses are successfully calculated in real-time. The online implementation of the analysis of the data has almost been completed. While some of the doses yield very good results, others are too far from the expected result. The reasons for this are believed to have been identified, but the corrections have not yet been completed.

Perspectives: Once the dose reconstruction system has been thoroughly tested for patient data offline, it can subsequently be used online, eventually leading to higher accuracy of the treatment, resulting in a higher cure rate of patients and fewer side effects.

P27.03 Hanne Mørkenborg Bove PROVIDING NURSING CARE TO PATIENTS SUFFERING FROM HARMFUL ALCOHOL CONSUMPTION OR ALCOHOL DEPENDENCY IN SOMATIC ACUTE ADMISSION UNITS: A PHENOMENOLOGICAL STUDY IN AN ACUTE ADMISSION UNIT AT AARHUS UNIVERSITY HOSPITAL

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Background: Alcohol overuse is health damaging, and it is estimated that 600,000 persons suffer from harmful alcohol consumption or alcohol dependency. This patient group is characterized by complex problems and health pictures spawned by chaotic lifestyles and likewise registered with increased use of health services. However, there is lack of documentation considering the experience of hospitalization from a patient perspective and the challenges in caring from a nursing perspective. This dissertation focuses on how patients suffering from harmful alcohol consumption experience hospitalization; essential care and treatment needs are identified and the nurses' perspectives on the challenges of caring for this patient group are explored. The overall purpose of the dissertation is to develop a nursing skills program based on a systematic identification of factors important for establishing a positive partnership between patient and caregiver.

Method: The dissertation is anchored in the phenomenological philosophy. The methodology applied is the descriptive phenomenological method as defined by Dahlberg (2008). The intention is to identify and understand the essences, patterns and structures of a lived experience. Data will be collected from in-depth interviews with 12-16 patients and a similar number of nurses. Data will be analysed according to the guidelines given by Dahlberg (2008).

Perspectives: This project will provide new knowledge about nursing care for hospitalized patients suffering from harmful alcohol consumption or alcohol dependency. Furthermore, the findings in this study will add a new dimension to the existing medical knowledge of the complexity in this group of patients.

P27.04 Lasse Reimer INTERFERON INDUCIBLE PKR KINASE PHOSPHORYLATE SERINE129 ON ALPHA-SYNUCLEIN CAUSES ALPHA-SYNUCLEIN AGGREGATION-DEPENDENT CELL DEATH IN AN OLIGODENDROGLIAL CELL MODEL OF MULTIPLE SYSTEM ATROPHY

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Multiple System Atrophy (MSA), Parkinson's disease (PD) and Dementia with Lewy Bodies (DLB) together comprise the subgroup of neurodegenerative diseases termed Synucleinopathies. They are characterized by the presence of inclusion bodies in degenerating brain cells, which contains aggregated  $\alpha$ -synuclein (AS) phosphorylated on Ser129.

The role of neuroinflammation in Synucleinopathies draws increasing attention. The interferon inducible serine-threonine kinase, PKR, plays a vital role in cellular protection against viral and bacterial infections. We demonstrate a pro-degenerative role of activated PKR in an AS aggregation dependent cell-model of MSA, where inhibition with small molecule inhibitor and mRNA silencing of PKR kinase decrease cellular degeneration. Further, in vitro phosphorylation studies demonstrate that PKR can directly phosphorylate AS on Ser129, while inhibition or knockdown of PKR reduces Ser129 phosphorylation in different models (differentiated human neuroblastoma cells (SH-SY5Y ASYN), rat oligodendroglia cells (OLN-AS7), primary mouse hippocampal neurons and in acute brain slices from WT mice or mice overexpressing human AS (ASO)). Interestingly, treatment with the known activators of PKR, Herpes simplex virus variant HSV-1- $\Delta$ ICP34.5 and LPS, as well as PKR inducer, interferon IFN- $\beta$ -1b, led to elevated levels of phosphorylated Ser129 AS in differentiated SH-SY5Y ASYN cells, OLN-AS7 cells and cortical neuronal cultures. Together, these results reveal a direct link between PKR and the phosphorylation and toxicity of AS and thereby support a role for neuroinflammatory processes in modulating the pathogenicity of  $\alpha$ -synuclein.

P27.05 Mette Winther Andersen

#### GASTROINTESTINAL MOTILITY IN DIABETES PATIENTS

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Gastrointestinal (GI) symptoms are common in patients with diabetes mellitus (DM), often with severe consequences for daily activities and quality of life. Despite of this fact, the pathophysiology of diabetes bowel dysfunction is only scantily described.

Contractions of the GI tract are primary stimulated by nerves using cholinergic nerve transmission. It is likely that cholinergic denervation is a major factor in development of GI dysfunction in DM.

Two highly advanced methods for description of GI innervation and motility are given below:

[<sup>11</sup>C]donepezil PET tracer to quantify the density of acetylcholine esterase in abdominal organs. First-ever validated scan-method for in vivo measuring cholinergic denervation of the GI tract. 3D-transit for minimal invasive and ambulant describing of regional transit times and contractions pattern of the bowel.

Through studies based on the two methods, we aim to test the following hypotheses:

Is the [<sup>11</sup>C]donepezil PET signal of the intestinal wall weaker than normal in patients with DM and GI symptoms? Is reduced [<sup>11</sup>C]donepezil PET signal associated with prolonged transit times through the GI tract in DM patients? Are prolonged transit times through the GI tract in DM patients reversible, and can they approach normal transit times during acetylcholine esterase inhibitor treatment? Can patients with DM and severe GI symptoms be grouped objectively into phenotypes based on their regional transit times through the stomach, the small intestine and the colorectum? Are regional transit times through the stomach and the small intestine changing after Malone (antegrade continence enema operation) in DM patients?

P27.06 Andreas Ernst

INTRAUTERINE EXPOSURE TO OVER-THE-COUNTER PAINKILLERS AND PUBERTAL DEVELOPMENT IN BOYS AND GIRLS: A NATIONWIDE COHORT STUDY

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Introduction: The underlying etiology of a continuing rapid decline in the timing of puberty remains largely unknown. Intrauterine exposure to over-the-counter painkillers may interfere with puberty timing and development through endocrine disruptive effects, as seen in several animal studies. Our study will be the first to examine these relationships in humans.

Materials and methods: We will use data from a large puberty cohort with 22,500 children born by women in the Danish National Birth Cohort. Data on over-the-counter painkillers was collected during pregnancy, and data on pubertal development are collected as the children go through puberty, which will continuously provide information on their current stage of puberty every six months until they reach full sexual maturation.

Results: Data currently undergo cleaning and analysis. Results will be presented.

Conclusion: Our study will shed novel light on the fetal endocrine programming effect of over-the-counter painkillers on puberty timing. Identifying preventable causes of early puberty is important, as early puberty is a predictor of a number of serious and widespread adult diseases.

P27.07 Morten Stokholm NEUROINFLAMMATION IN PREDIAGNOSTIC PARKINSON'S DISEASE: A MULTI-TRACER PET STUDY

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Objective: To investigate the in vivo occurrence of neuroinflammation in the brain of patients with idiopathic rapid-eye-movement sleep behaviour disorder (iRBD) and its relationship with striatal dopamine functioning using positron emission tomography (PET).

Background: Studies in patients with iRBD have shown that the majority eventually develop Parkinson's disease (PD) or dementia with Lewy bodies (DLB). The early pathological changes of these diseases could be detectable in iRBD prior to the full-blown clinical syndrome. Neuroinflammation in the form of microglial activation is present in PD and DLB and provides a possible therapeutic target to halt the progression of the underlying pathological process.

Methods: We recruited 15 iRBD patients and 19 matched controls. We used <sup>11</sup>C-PK11195 PET to detect levels of microglial activation and <sup>18</sup>F-DOPA PET to assess dopamine function in the nigrostriatal system.

Results: <sup>11</sup>C-PK11195 binding was increased in the substantia nigra of iRBD patients (left p=0.002; right p=0.032). Patients with highest nigral <sup>11</sup>C-PK11195 binding had raised <sup>11</sup>C-PK11195 binding in the ipsilateral putamen (r=0.61, p=0.0002). Putamen <sup>18</sup>F-DOPA uptake was reduced in iRBD (left p=0.0002; right p<0.0001). Patients with lowest putamen <sup>18</sup>F-DOPA uptake had highest putamen (r=-0.44, p=0.008) and nigral <sup>11</sup>C-PK11195 binding (r=-0.38, p=0.02).

Conclusion: In patients with iRBD, PET imaging detects increased microglial activation in the substantia nigra, and levels correlate with reduced putamen dopaminergic function. Immunotherapeutic strategies against microglia activation could be tested in iRBD patients to halt the ongoing neuropathological process towards PD or DLB.

P27.08 Marlene Beyer Eg CHILD ABUSE IN THE NORTHWESTERN PART OF DENMARK - A 12-YEAR RETROSPECTIVE STUDY

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Introduction: Recurrent childhood trauma, such as abuse, moulds and defines the personality (Herman, 1995). Early disclosure is crucial in order to hinder or diminish long-term consequences. Child abuse is associated with development of severe depression, anxiety, suicide attempts, alcohol and substance abuse, increased number of contacts to the health-care system due to physical health problems, as well as socioeconomic deviation (Fergusson, 2013).

Material and methods: This is a 12-year (2001-2013) retrospective register-based study, including every single child under the age of 15 years, on whom a police report on suspicion of child abuse has been filed with a subsequent clinical forensic examination.

Case material from the Department of Forensic Medicine, Aarhus University, and its four cooperating police districts, including judicial transcripts, has been made available to the project.

Additionally, for the cohort to be used in the first half of the project (2001-2007), a request for access to present data in public national databases has been made to supplement the existing data.

Results: A total of 765 cases meeting the inclusion criteria of the project have been identified. The forensic part of the data collection has been completed. So far, 28% (213/765) of the cases have been supplemented with data from police reports and judicial transcripts.

Discussion and conclusion: The project is expected to provide thorough knowledge on child abuse, including the approach demonstrated by the authorities and the possible long-term consequences in the child.

P27.09 Thomas Falstie-Jensen CAN LOW-GRADE INFECTIONS OF SHOULDER ARTROPLASTIES BE DIAGNOSED BEFORE REVISION?

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Introduction: Diagnosing infection of a shoulder arthroplasty is critical before planning revision surgery. However, low-grade infections are often diagnosed as unexpected positive cultures postoperatively.

Aim: To investigate if Dual Isotope In<sup>111</sup>Leucocyte/ Tc<sup>99</sup>Bone Marrow scintigraphy SPECT CT scan (L/BMS) can detect shoulder arthroplasty infection compared to tissue cultures obtained perioperatively.

Method: To diagnose infection as a possible cause of arthroplasty failure an L/BMS was planned for all referred patients with a painful shoulder arthroplasty during April 2014 to May 2015. If the arthroplasty later was revised, 5 tissue biopsies were obtained during surgery from an infection-suspicious site and cultured for 14 days to diagnose possible infection. Infection was defined as 3 of 5 biopsies with growth of the same bacteria.

Results: During the observation period, 72 patients were referred and 47 underwent an L/BMS scintigraphy. In 25 patients, both a scintigraphy result and a microbiological diagnose were available. One patient had a positive scintigraphy and positive cultures. Twenty-four patients had a negative scintigraphy, but positive cultures were found in 8 of these patients. Negative scintigraphy and negative cultures were found in 16 patients. L/BMS shows a sensitivity of 0.07 95% CI (0-0.19) and a specificity of 1.00 95% CI (1.00-1.00) in detecting an infected shoulder arthroplasty. The positive predictive value (PPV) is 1.00 95% CI (1.00-1.00) and the negative predictive value (NPV) 0.36 95% CI (0.16-0.56).

Conclusion: In<sup>111</sup>Leucocyte/ Tc<sup>99</sup>Bone Marrow dual isotope scintigraphy SPECT CT scan cannot be used as a screening method for infection of a failed shoulder arthroplasty.

P28.01 Dennis Graversen DEVELOPMENT OF A VALID AND RELIABLE QUALITY MEASUREMENT TOOL FOR GENERAL PRACTITIONER AND NURSE LED TELEPHONE TRIAGE IN OUT-OF-HOURS CARE

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Background and aim: Danish out-of-hours (OOH) healthcare services has in recent years changed. Hence, regional differences exist regarding the type of healthcare professional performing the telephone triage. Comparative studies on the quality of telephone triage performed by general practitioners (GP's) and nurses are sparse, and no measurement tool exists in Denmark to assess the quality. Thus, we aim to develop a valid and reliable quality measurement tool, which can be used for assessing quality of communication, safety and efficiency applicable in both GP- and nurse-led telephone triage in Danish OOH care.

Methods: The measurement tool was based on a validated Dutch tool, forward-backward translated into Danish, and input from a focus group meeting with patients. Face and content validity and applicability in Danish settings were secured through a semi-structured internet-based

two-round Delphi process with 26 relevant stakeholders. Reliability and clinimetric analysis will be tested in a pilot study in February 2017.

Results: In the 1<sup>st</sup> round of the Delphi process, experts were asked to rate readability, applicability and comment on 28 items and a scoring guide for each item. Response rates were 85% and 77%, respectively, in the two rounds. Comments were reviewed carefully, items were adjusted accordingly, and two items were excluded. In the 2<sup>nd</sup> round, >90% of experts found 25 out of 26 items to be applicable in its current form.

Conclusion: The measurement tool can be used in quality assurance and enhancement of telephone triage, and the tool will be used in a PhD study comparing the quality of GP-led and nurse-led telephone triage in real-life patient contacts in Danish acute care settings.

P28.02 Mathias Rædkjær COMORBIDITY AFFECTS DISEASE-SPECIFIC MORTALITY IN SARCOMA PATIENTS: A NATIONWIDE, POPULATION-BASED STUDY

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Objective: Comorbidity is an important prognostic factor for survival in cancers. The aims of this study were to examine the prevalence of comorbidity in sarcoma patients and estimate the prognostic impact of comorbidity on disease-specific mortality.

Methods: Through the validated national clinical database, Danish Sarcoma Registry (DSR), 2184 adult patients diagnosed with sarcoma in extremities and trunk between 1 January 2000 and 31 December 2013 were identified. We calculated a Charlson Comorbidity Index (CCI) score on the basis of the Danish National Patient Registry. We obtained all information on hospital contacts and diagnoses given 10 years prior to the date of the sarcoma diagnosis. Data on date and cause of death was obtained from the DSR, the Danish Civil Registration System and the Danish Register of Causes of Death.

Preliminary results: The overall prevalence of comorbidity was 20%. Patients with moderate/severe comorbidity had a significantly greater risk of dying from their sarcoma than patients without any comorbidity (HR: 1.61, 95% CI: 1.14-2.26, p=0.006). Patients with localized stage at diagnosis and moderate/severe comorbidity had a significantly greater

risk of dying from sarcoma than patients without any comorbidity (HR: 2.10, 95% CI: 1.37-3.22, p=0.001).

Conclusion: Patients with moderate/severe comorbidity and localized stage at diagnosis had significantly increased disease-specific mortality compared to patients without comorbidity, even when adjusting for important factors such as age. Improved knowledge and awareness of comorbid diseases is important to prevent complications and improve treatment.

P28.03 Sofie Eg  
Jørgensen

#### GENETIC DETERMINANTS UNDERLYING SEVERE INFLUENZA INFECTION

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Influenza infection usually causes self-limiting respiratory disease. However, a subgroup of influenza patients becomes so severely ill that hospitalization and ventilatory support is needed for survival. Recently, an increasing number of studies have shown that host genetics may play a major role in regard to disease susceptibility. In this study, we will investigate whether increased susceptibility to severe influenza infection is caused by primary immunodeficiencies.

We included 12 influenza patients, who had been hospitalized at the intensive care unit and received ventilatory support. We identified genetic variants in the immune system using whole exome sequencing (WES). Functional studies were performed using patient cells (PBMCs) and reporter cell assays, measuring how the genetic variants impacted on the innate immune response after influenza infection.

We identified genetic variants in several genes known to be important for host defence against influenza virus. One patient had two different variants in the cytosolic RNA sensor RIG-I. The RIG-I variants displayed much decreased activity compared to wild type RIG-I measured in the interferon (IFN) reporter assay. Ongoing studies will address the functional significance of the identified mutations in different cell types from the patient, including macrophages and fibroblasts.

Other mutations in two other patients include the transcription factor IRF7 and the IFN-induced antiviral gene RNASEL, respectively, and similar functional studies are carried out in cells from these patients.

P28.04 Randi Steensgaard

#### HOW DIRECT INVOLVEMENT OF NURSES IN RESEARCH CAN SUPPORT PATIENT PARTICIPATION IN REHABILITATION

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Background: Patient participation is essential in rehabilitation after spinal cord injury to achieve control and regain independence in life. However, patient participation is complex, and there is a lack of knowledge, clinical techniques and aids that take into account the patients' different needs and preferences. In a PhD study, we try to overcome the challenges of involving patient in their rehabilitation and to develop an approach and clinical aids to support the patient's path towards a meaningful life after a spinal cord injury.

Method: Knowledge is developed and practice changes as the iterative process of action research combines interaction, dialogue, action in practice and research. Together with seven nurses as co-researchers, data are generated, analyzed, discussed, and the result used as basis for new actions/tests. Changes will be implemented at the entire centre after thorough evaluations. The success rate for implementation and for improving patient participation will be studied 3 and 6 months after full implementation.

Results: A supporting management has enabled the co-researchers to participate actively throughout the entire study. The preliminary results show that the dynamic reflective process has increased the co-researchers attitudes, knowledge, competences and skills regarding patient participation. They have been empowered and are confident to work more actively with an open mind in patient participation. The co-researchers' professional awareness has been improved, and their dedication also affects their contribution to development and improvement of rehabilitation nursing in general at the centre.

P28.05 Julie Nelly Christensen

#### IDENTIFICATION OF MELANOMA-SPECIFIC REFERENCE GENES FOR QUANTITATIVE GENE EXPRESSION STUDIES

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Relative gene expression studies require validated reference genes for normalization of target gene expression. The RT-qPCR method of analyzing gene expression is a very powerful method. However, to control for technical variation, some general requirements to reference genes and the normalization process exist. This includes stable expression of reference genes throughout all samples under investigation. Additionally, normalization should be performed with at least two validated reference genes. Correct normalization procedures

will enable detection of small differences in gene expression and provide statistically more significant results. The stability of reference genes for relative gene expression studies is typically determined and validated in a preliminary study.

In melanoma, a systematic analysis of melanoma-specific reference genes has never been performed. Accordingly, stably expressed melanoma-specific reference genes have not yet been identified.

The present study aimed to identify the most robust melanoma-specific reference genes amongst 24 selected candidate genes evaluated across 13 metastatic melanoma cell lines. Commonly used reference genes, such as ACTB and GAPDH, were included in the selected panel, and we found that these genes varied considerably across the tested cell lines. Of the reference genes investigated in this study, CASC3 and RPS2 were the two most stably expressed. The two validated reference genes can thus be used for future melanoma cell-based experiments.

A similar approach to establish and validate candidate reference genes is currently being performed on primary melanoma tumor samples for future gene expression studies.

P28.06 Mette Saksø

#### DOSE-ESCALATED RADIOTHERAPY GUIDED BY FUNCTIONAL IMAGING FOR PATIENTS WITH HYPOXIC HEAD AND NECK SQUAMOUS CELL CARCINOMA

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Head and neck squamous cell carcinoma (HNSCC) is mostly treated with primary radiotherapy with curative intent in accordance to national guidelines. Overall, 80% of the patients are cured, but the prognosis varies significantly. A smaller group of patients are not being helped sufficiently with the current treatment strategy. The main purpose of this study is to introduce a dose-escalated treatment to patients with poor prognosis. First, the hypoxic PET tracer FAZA will be evaluated in order to select patients with poor prognosis. Next, a radiotherapy strategy will be introduced consisting of accelerated, hyperfractionated treatment with concomitant chemotherapy and a cell-sensitizer allowing for higher total dose to be delivered to the entire tumor. Dose-escalation will be assessed in terms of tumor control and cancer-free survival. Last, correlations of markers of radioresistance will be characterized in a prospective setting. This will aid in offering patients biologically adapted, individual therapy.

P28.07 Maj Ulrichsen SORTILINS AND NEUROTROPHIN SIGNALING IN SCHWANN CELLS

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Background: Schwann cells are the myelinating glial cells of the peripheral nervous system, and they play a crucial role in the regeneration of injured peripheral nerves. The family of sortilins is involved in neurotrophin signaling in Schwann cells of injured peripheral nerves, as two-chain SorCS2 induces apoptosis of injured Schwann cells. However, it is unknown if SorCS2 or Sortilin affects downstream neurotrophin signaling in Schwann cells.

Aim: To characterize the expression of the sortilins and neurotrophin receptors in cultured Schwann cells and to examine if SorCS2 or Sortilin affects expression of neurotrophin receptors and downstream signaling in cultured Schwann cells.

Methods: Schwann cells were cultured from neonatal wild type (wt), Sort1<sup>-/-</sup> or SorCS2<sup>-/-</sup> rat sciatic nerves and the expression of SorCS2, Sortilin, SorLA and the neurotrophin receptors, p75<sup>NTR</sup>, TrkA, TrkB and TrkC were examined by Western blotting of the culture lysates. Moreover, wt, Sort1<sup>-/-</sup> and SorCS2<sup>-/-</sup> Schwann cells were stimulated with neurotrophin-3 or BDNF and analyzed for downstream phosphorylation of MAPK by Western blotting to examine if Sortilin or SorCS2 mediates neurotrophin signaling in Schwann cells.

Results and conclusion: Cultured rat Schwann cells expressed SorCS2, Sortilin and SorLA and deficiency of SorCS2 or Sortilin did not affect the expression of Sortilin or SorCS2, respectively. Moreover, preliminary data indicated that lack of SorCS2 hampered downstream signaling of neurotrophin-3, while lack of Sortilin appeared to increase neurotrophin-3 mediated signaling. Furthermore, preliminary data indicated that cultured Schwann cells expressed TrkA and low levels of TrkC.

P28.08 Lisbet Grønbaek FAMILIAL ACCUMULATION OF AUTOIMMUNE HEPATITIS AND EXTRAHEPATIC AUTOIMMUNE DISEASES: A NATIONWIDE, REGISTRY-BASED COHORT STUDY

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Background and aims: Many patients with autoimmune hepatitis (AIH) have other autoimmune diseases, suggesting that they are genetically predisposed for autoimmunity. However, the scientific basis for this hypothesis is weak. We aimed to determine the prevalence of autoimmune diseases in a nationwide cohort of AIH patients and their relatives, and to compare this population with the background population.

Materials and methods: We collected data from Danish nationwide healthcare registries to identify and follow our study population from 1994 through 2015. The prevalence of selected extrahepatic autoimmune diseases was estimated and compared between AIH patients, their first and second-degree relatives and age- and gender-matched controls.

Results: We included 2,745 AIH patients (71% women), 17,812 relatives (49% women), and 27,450 controls (71% women). At all ages, the prevalence of autoimmune diseases was highest among AIH patients and lowest among controls. At age 70 years, the prevalence of autoimmune diseases among AIH patients was higher compared with controls (females: 42% vs. 17%, relative prevalence [RP] = 2.4, 95% CI 2.0-3.0; males: 25% vs. 13%, RP = 1.9, 95% CI 1.1-2.9). Also, the prevalence among AIH patients' relatives was higher compared with controls (females: 29% vs. 17%, RP=1.7 CI 1.4-2.1; males: 25% vs. 14%, RP 1.9 CI 1.4-2.5). Among all groups, autoimmune diseases of the gastrointestinal system were most prevalent until mid-life, whereas diseases of the endocrine system and connective tissue were most prevalent later in life.

Conclusion: AIH patients and their relatives have a higher risk of extrahepatic autoimmune diseases than the background population.

P29.01 Anne Bendix  
Andersen

THE INFLUENCE OF A POLICY DOCUMENT IN THE PRACTICE OF INTERSECTORIAL COLLABORATION IN DANISH HEALTHCARE: A CRITICAL DISCOURSE ANALYSIS

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Background: Policy documents are powerful actors in health care, and they play a significant role because they produce certain discursive and non-discursive conditions for intersectorial collaboration.

Central documents in Denmark are the Health Agreements. These policy documents set out the premises for collaboration between hospitals, municipalities, and general practitioners in the five regions. This area is traditionally contested, and the intention of the Health Agreements is to be a guideline for the allocation of tasks and responsibilities within the

collaboration.

Aims:

- To exemplify and discuss how linguistic features and wordings in the Health Agreement for the Central Denmark Region produce a certain understanding of intersectorial collaboration in the health care system.
- To show how a critical discourse analysis (CDA) can give health care providers and researchers a tool to critically assess a policy document.

Method: A CDA based on a three-dimensional model for discourse analysis.

Findings: Our analysis showed how wordings and grammatical features create and maintain certain perceptions or common-sense understandings of actors, responsibilities, and tasks in health care. The linguistic analysis of grammatical features present in the document enabled us to demonstrate how the authors of Health Agreements apply governing technologies to control the delivery of intersectorial health care in Denmark. Furthermore, the findings showed how this policy document, through its use of language, constructs the actors in intersectorial collaboration within the framework of a market-economy understanding, the goal being to increase productivity and efficiency in health care delivery.

P29.02 Vibe Bolvig  
Hyldegård

SOCIOECONOMIC INEQUALITY IN THE PROVISION OF BEST CLINICAL PRACTICE IN THE TREATMENT OF STROKE PATIENTS

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Introduction: In a setting where access to health-care services is allegedly free and equal, do we actually have equal treatment for equal needs? The aim of this study is to investigate horizontal inequality in the provision of stroke treatment in a publicly funded hospital setting in Denmark. Stroke patients represent an appropriate case for studying horizontal inequality because of their relatively uniform needs profile.

Methods: A cross-sectional study of 112,000 consecutive stroke patients discharged between 2004 and 2014. Data is drawn from national registries and a national quality-database regarding stroke care. Multilevel probit and logistic regression is used to estimate the opportunity-based, i.e. the proportion of available medically relevant treatment elements provided, and all-or-none treatment measures, respectively. The analyses are adjusted for stroke severity and prognostic factors to minimise potential confounding.

Scientific contribution: The study adds to previous research by utilizing a

large high-quality dataset of individual-level data from a validated database linked with personal socioeconomic registry data. The applied regression models are founded both on empirical evidence from the field and inspired by a theoretical framework drawing on John Roemer and Allan Williams' ideas. This allows for an investigation of a wider range of socioeconomic characteristics than in most previous studies. The study further provides an addition to the limited research focusing on the development of inequality in hospital treatment over time.

P29.03 Sarunas Dikinis SIMVASTATIN IMPACT ON LIVER REGENERATION IN HEALTHY RATS FOLLOWING LIVER RESECTION

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The approach to treatment of colorectal cancer (CRC) liver metastases has changed in the last two decades towards more extensive surgical procedures.

Normally, the turnover of liver cells is relatively slow. However, hepatocytes have an incredible regenerative capacity, and up to 90% of hepatocytes will start proliferation after a larger liver resection.

The regeneration ability of hepatocytes may be compromised by ischemic/reperfusion injury following the surgical procedure, ranging from mild enzymatic release to fulminant hepatic failure.

Recent animal studies in rat models have shown statins to have a protective effect on ischemic damage and may stimulate liver regeneration.

In order to test this hypothesis, we conducted an animal study to examine the liver regeneration after 70% liver resection in healthy rats treated preoperatively and postoperatively with different regimens of Simvastatin. The parameters tested were liver regeneration rate and treatment time, in particular preoperative, as this option is attractive in clinical practice.

Results: All surgical procedures are completed. Currently, Ki-67 index is tested together with different serological markers of liver regeneration.

The results of these will not be available until after deadline of this poster.

P29.04 Mats Bue BONE AND SUBCUTANEOUS TISSUE PHARMACOKINETICS OF VANCOMYCIN IN TOTAL KNEE REPLACEMENT PATIENTS

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Background: Adequate antimicrobial tissue penetration is essential for prevention of orthopaedic infections. Currently, studies investigating perioperative bone and soft tissue concentrations of antimicrobials are sparse and also challenged by a shortness of appropriate methods.

Purpose and aim: The objective of this study was to compare and describe plasma, subcutaneous tissue and bone pharmacokinetics of vancomycin in patients.

Materials and methods: One thousand mg of vancomycin was postoperatively administered as a single dose over 100 minutes to 10 male patients undergoing total knee replacement. Vancomycin concentrations in plasma, subcutaneous tissue, cortical and cancellous bone were measured over 8 hours. Microdialysis was applied for sampling in solid tissues.

Findings and results: For all extravascular tissues, an impaired penetration was demonstrated. Area under the concentration-time curve (AUC) and peak drug concentration ( $C_{max}$ ) were found lower for bone and subcutaneous tissue when compared to free plasma. For the same pharmacokinetic parameters, cortical bone differed from cancellous bone. Time to minimal inhibitory concentration (MIC) of 2 mg/L was attained after 110 min in bone. However, a MIC of 4 mg/L was not reachable in bone.

Conclusions: Bone and subcutaneous tissue penetration of vancomycin was found to be impaired and delayed. Particularly in cortical bone, adequate vancomycin concentrations may not be reached.

P29.05 Caroline Marie  
Andreasen RESPONSE TO PAMIDRONATE TREATMENT ASSESSED BY WHOLE BODY  
MAGNETIC RESONANCE IMAGING IN PAEDIATRIC CHRONIC NON-  
BACTERIAL OSTEOMYELITIS

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Background: Chronic non-bacterial osteomyelitis (CNO) causes pain due to multifocal sterile bone inflammation. Children are at risk of persistent pain, disability and vertebral fractures. Pamidronate (PAM) is a promising treatment. Our aim was to assess radiological and clinical disease activity in CNO after 1-year PAM treatment.

Methods: A retrospective study of CNO treated with i.v. PAM 1mg/kg on 3 consecutive days every 3 months for 1 year. At baseline and year 1, radiological disease activity was assessed by whole-body magnetic resonance imaging, and a paediatrician assessed clinical disease activity.

Results: We included 18 children, median age 10 years (range 5-13). At baseline, we identified 120 radiological active lesions (median 7, range 2-14). Most frequent locations were tibia (21%), femur (15%) and spine (12%). Radiological activity year 1: Total resolution was seen in 4 children. We identified 91 lesions (median 3, range 1-21). Compared to baseline, this reduction was significant (Wilcoxon rank test,  $p < 0.05$ ). We observed a total resolution of 63 lesions (median 4, range 0-8). We also identified 45 new lesions (median 2, range 1-12) and 46 stable or partially resolved lesions (median 1.5, range 0-11). The number of spinal lesions decreased from 15 to 3 lesions ( $p < 0.05$ ). Clinical disease activity after 1 year: Total resolution of pain ( $n=4$ ), partial resolution of pain ( $n=12$ ) and no resolution of pain ( $n=2$ ). Despite total radiological resolution, pain was still reported in 2 out of 4 children.

Conclusion: One-year PAM treatment is a potent treatment for CNO, particularly in spinal lesions. Persistent pain can exist despite radiological resolution.

P29.06 Rikke  
Smedegaard  
Rosbjerg

RETURN TO WORK SELF-EFFICACY (RTW-SE) AND ACTUAL RETURN TO WORK IN A DANISH POPULATION OF CANCER SURVIVORS

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Objectives: Cancer survivors have more sick days and increased risk of unemployment. Considering the implications for the quality of life of cancer survivors and their families as well as the economic costs associated with sickness absence for the individual and the society, improving the work ability and the process of return to work (RTW) for cancer survivors is of major importance.

Self-efficacy (SE) refers to the individual's belief in his or her own ability to handle specific future challenges. RTW-related self-efficacy (RTW-SE) has been shown to be a strong predictor of actual RTW in workers on sickness leave due to both psychological and physiological causes, but has not yet been investigated in employees on sickness leave due to cancer. The aim of the present study is to investigate the predictive value

of RTW-SE in cancer survivors on sickness leave when undergoing chemotherapy.

Methods: In a prospective study, cancer patients with various cancers (n = 400) from two Danish hospital wards will be included during a 12-month period. Inclusion criteria: age 18-62 years, employed but on sickness leave at baseline. At the time of chemotherapy initiation, the participants are asked to complete the 19-item RTW-SE questionnaire in addition to questions regarding demographic and illness-related factors. The main outcome measure is RTW at 3-, 6-, and 12-month follow-up.

Results: Inclusion of patients started in November 2016. Higher levels of RTW-SE at baseline are expected to be associated with shorter time to RTW.

Conclusion: To improve the work ability and the process of RTW for cancer patients, it is necessary to obtain a better understanding of the RTW process of cancer patients.

P29.07 Jakob Wetche

EFFECT OF ACUTE STRESS ON HPA AXIS ACTIVATION, GENE EXPRESSION AND BEHAVIOR IN A MOUSE MODEL POSSESSING AF GENETIC SUSCEPTIBILITY TO MENTAL ILLNESS

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Mental disorders are caused by intricate interactions between an abundant number of genetic risk variants and environmental risk factors (GxE). A connection between environmental risk factors and genetic liability has been reported. The majority of the biological basis for the complex GxE interaction in mental disorders has been suggested to origin in epigenetic regulation of expression of genes influencing brain development and function. The BRD1-gene has been implicated with susceptibility to mental disorders. BRD1 encodes a protein, which is responsible for histone H3K1-acetylation, and thereby regulates the transcription of numerous genes, among which schizophrenia genes are overrepresented.

This project builds on a newly developed mouse model (Brd1 +/- mice). These mice are heterozygous for a targeted deletion in the Brd1 gene and have approximately 50% less BRD1 mRNA and protein in their brains and display a spectrum of phenotypes related to mental illness. BRD1 is upregulated in the brains of rodents subjected to stress; this strongly suggests that BRD1 is involved in postnatal adaptation to stress. We, therefore, expect that Brd1 +/- mice show a different response to stress

compared to their wild-type littermates. This study investigates three different stress responses following exposure to an acute cold-swim-stress paradigm: extracellular, intracellular and transcriptional. The extracellular response includes activation of the HPA axis and the release of norepinephrine (NE). The intracellular response consists of signaling cascades inside the cell. The transcriptional response includes altered transcriptional activity of genes related to the general response to a stressor.

P29.08 Sara Buskbjerg  
Jager

#### THE FORGOTTEN CELL TYPE: SATELLITE GLIAL CELLS

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Neuropathic pain is a chronic pain condition seen in patients suffering a direct injury to the peripheral or central nervous system or an indirect injury due to, e.g., diabetes or multiple sclerosis. Neuropathic pain treatment falls short of preventing, or completely relieving, neuropathic pain.

For years, research has focused on understanding the role of neurons in neuropathic pain pathogenesis, while the role of supportive cells seems to have been overlooked in general and the supportive satellite glial cells in the dorsal root ganglion in particular. These cells not only support the neurons, they are also involved in controlling the electrical activity flowing through the neurons and in neuropathic pain pathogenesis.

The aim of this project is to understand the role of the satellite glial cells in neuropathic pain development and thereby aid in the identification of new drug targets for neuropathic pain treatment. We plan to investigate the mRNA expression profile in satellite glial cells from mice with or without peripheral nerve injury-induced neuropathic pain. Prior to the mRNA expression analysis, satellite glial cells will be isolated from freshly dissected dorsal root ganglions with FACS. The different methodical challenges of isolating satellite glial cells with FACS will be discussed.

The results from this project will elucidate the role of the satellite glial cells in neuropathic pain development and will hopefully pave the way for the discovery of new treatments for neuropathic pain.

P30.01 Mette Tranberg  
Nielsen

#### ACCURACY OF HRHPV TESTING IN SELF-COLLECTED CERVICOVAGINAL AND URINE SAMPLES

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**Purpose:** This study will compare the diagnostic accuracy of high risk human papillomavirus (hrHPV) analyses performed on home-based self-collected samples (cervicovaginal and urine samples) and conventional samples obtained by a general practitioner (GP). Further, the women's acceptability of the different procedures will be measured.

**Methods:** Three hundred consecutive women aged 30-59 years with abnormal GP-collected samples will obtain a self-collected cervicovaginal and urine sample at home and answer a questionnaire about the acceptability on the use of the self-sampling methods. All paired samples will be tested for hrHPV using the PCR-based Cobas 4800 and Clart assays. Thus, six hrHPV test results for every woman will be available. When two of the six yield positive results, the woman will be considered to be hrHPV infected. The hrHPV prevalence can thus be measured, and the sensitivity and specificity of hrHPV detection in each of the obtained samples, using each of the diagnostic assays, can be calculated. Finally, the acceptability among the participating women will be reported for each of the procedures.

**Conclusions:** For the first time in a Danish setting, this study will assess the diagnostic accuracy and acceptability of home-based, self-collected cervicovaginal and urine samples compared to GP-collected samples. This study can thus guide the future use of diagnostic assays in the laboratory. Depending on the results of the study, an additional perspective could be to use urinary hrHPV testing in subgroups of women who are reluctant to have a self-collected cervicovaginal sample or a GP-collected sample taken.

P30.02 Rikke Madsen EXPERIENCES OF PATIENTS AND SIGNIFICANT OTHERS CONCERNING TRANSITIONS DURING THE COURSE OF INCURABLE CANCER

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**Background:** Studies have reported that patients and significant others experience difficult transitions during the course of incurable cancer. However, more in-depth knowledge is needed to illuminate the life world experiences from a broad perspective of both patients and significant others.

**Aim:** To explore the lived experiences from everyday life, related to transitions during the course of incurable cancer, through the perspective of patients and bereaved spouses. In this study, transitions are

conceptualised as experiences concerning organisational, psychosocial and existential issues.

Method: Data will be collected through three sub-studies: a systematic literature review (2013-2017), interview of ten incurable cancer patients (2015), and interview of ten significant others (2015).

Results: The systematic literature review will provide an overview of findings from existing qualitative research. Data from interviews will be analysed using Ricoeur's phenomenological-hermeneutic theory of interpretation focusing on meaning units from the life world experiences of the participants. The interviews will generate in-depth knowledge from the life worlds of incurable cancer patients and significant others on a topic, which has not previously been explored.

P30.03 Morten  
Overgaard

### PSEUDO-OBSERVATIONS AND THE CHALLENGE OF VARIANCE ESTIMATION

*M. Overgaard*

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A jack-knife pseudo-observation is designed to say something about the influence of an observation on the size of a parameter estimate in a statistical model. Such pseudo-observations can hold valuable information about the association between covariates and a potentially unobserved outcome like 'surviving more than 5 years after treatment', which could be unknown if the person had dropped out of the study before 5 years. The pseudo-observations are, therefore, used in regression analyses to estimate parameters related to such an association.

When calculating pseudo-observations for the entire sample, the different calculations are very much based on the same information. Therefore, the pseudo-observations are likely going to depend on each other; in other words, they are correlated. This fact complicates matters in a regression analysis. It is now known that the variances of the parameter estimates look different from what they would have looked like had the pseudo-observations been independent. This means that the variance estimates provided by the typical statistical program packages are generally inappropriate in this case.

A new variance estimate, which is designed to be appropriate in large samples, has been suggested. The poster will explain how computer simulations are used to investigate how this new estimator performs in smaller samples and how it compares to the variance estimator from the typical statistical packages.

Based on lots of simulated data sets, the results illustrate that the new variance estimator is generally more appropriate, but that the difference between the two is often small.

P30.04 Peter Lykke  
Eriksen

## MAPPING OF METABOLIC LIVER FUNCTIONS IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Background: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in the western world. The incidence of NAFLD is increasing worldwide, and the complications related to the disease are now recognised as important causes of morbidity and mortality. It has been a ruling clinical and pathophysiological dogma that a fatty liver without established cirrhosis is a well functioning liver. Recent studies, though, report indications of reduced liver function. However, quantitative measurements of metabolic liver functions have never been systematically investigated in humans with NAFLD.

Objectives: To study and quantify specific metabolic liver functions in varying degrees of NAFLD.

Methods: In a human clinical study, metabolic liver functions are studied by a series of functional tests:

1) Galactose elimination capacity (GEC), to assess hepatocyte cytosol activity.

2) Aminopyrine breath test (ABT), to assess hepatocyte microsomal activity.

3) Functional hepatic nitrogen clearance (FHNC), to assess mitochondrial/cytosolic metabolic capacity.

4) Indocyanine green plasma disappearance rate (ICG-PDR), to assess hepatocyte excretory function.

Regional liver function quantified by positron emission tomography (PET) with the radioactive galactose analogue 2-[18F]fluoro-2-deoxy-D-galactose (FDGal) is compared to fat infiltration evaluated by magnetic resonance imaging (MRI) and histological disease severity.

Perspectives: We aim to challenge the dogma that hepatic metabolic function is not affected in NAFLD, and to improve the understanding of the relationship between disease severity, histology, metabolic functions, and imaging in NAFLD.

P30.05 Zhijia Wang

DEFINING ROLES OF BOTH CDK12/CYCK AND CDK13/CYCK TRANSCRIPTION ELONGATION KINASES IN THE CONTROL OF GENE EXPRESSION, PRE-MRNA PROCESSING AND CANCER

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Precise regulation of transcription and RNA processing in maintaining genome integrity is becoming increasingly vital across species. The Cdk12/CycK complex is a novel transcription-associated kinase that promotes expression of a subset of RNA polymerase II genes. Cells without Cdk12/CycK induce spontaneous DNA damage and are sensitive to a variety of DNA damage agents. Meanwhile, studies show that the polymerase associated factor (PAF1) complex is a critical regulator of paused Pol II release, and the subsequent recruitment of CDK12 is dependent on PAF1C. However, nothing is known about their cellular function in connection with the potential targets as well as how CDK12 mutations promote tumorigenesis. Here, in order to identify novel substrates, we collected nuclear and chromatin extracts of HEK293T cells expressing Cdk12 and CycK protein using the tandem affinity purification (TAP) method tethered to streptavidin and flag beads. After immunoprecipitation, Cdk12- or CycK-associated proteins were identified by mass spectrometry (MS). Meanwhile, in flavopiridol-treated cells which lack of CDK12 or CycK, the nascent mRNA transcripts for DDR genes were reduced to 15-35% of mock-treated controls, confirming a block in elongation (pause escape). Depleting CDK12 and CycK generate a mutation signature resembling SETD2 depletion at I-SceI-induced DNA double-strand break (DSB) sites, with significantly increased deletions arising through microhomology-mediated end-joining. We propose that CDK12 is a tumor suppressor of which loss-of-function mutations may elicit in multiple DNA repair pathway, leading to genomic instability underlying the genesis of the cancer.

P30.06 Berit Dalsgaard Nielsen

ATTENUATION OF FLUORINE-18-FLUORODEOXYGLUCOSE UPTAKE IN LARGE-VESEL GIANT CELL ARTERITIS AFTER SHORT-TERM, HIGH-DOSE STEROID TREATMENT: A DIAGNOSTIC WINDOW OF OPPORTUNITY

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Background: Untreated, giant cell arteritis (GCA) is associated with high morbidity. Fluorine-18-fluorodeoxyglucose (FDG) PET/CT is increasingly used to diagnose GCA. However, PET/CT is not always readily available, which may compel the clinician to either delay steroid treatment at the risk of GCA related complications, or to initiate treatment at the expense

of diagnostic PET/CT sensitivity. Evidence of a possible "FDG PET/CT diagnostic window" after initiation of treatment is needed.

Methods: Twenty treatment-naïve patients (14 women), mean age of 69 years (range: 56-83 years), with FDG PET/CT-proven GCA, repeated FDG PET/CT after either 3 (PET3, n=10) or 10 days (PET10, n=10) of oral prednisolone treatment 60 mg daily.

FDG uptake in vascular regions was reviewed and graded relative to liver uptake (grade 0-4). Vascular uptake > liver was considered consistent with vasculitis. Composite scores were calculated by summarizing grades for 3 thoracic aortic segments and 3 supraaortic branches.

Data was either continuous or binomial. Normality was checked using Q-Q plots. McNeemar's and Wilcoxon's signed-rank tests were used to test statistical significance.

Results: GCA was diagnosed in 10/10 patients after 3 days of treatment. By contrast, GCA could only be diagnosed in 5/10 patients after 10 days (PET0 vs. PET10, p=0.03). Composite scores in aorta did not decrease at PET3, whereas a significant decrease was observed in supra-aortic branches at PET3 (p<0.01) and both vascular domains at PET10 (p<0.01, both).

Conclusion: In large vessel-GCA, high-dose steroid treatment differentially attenuates FDG uptake, but diagnostic properties remain within the first three days.

P30.07 Anne-Birgitte Blavnsfeldt

LOW-DOSE PREDNISONE OR PREDNISOLONE DOES NOT AFFECT BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED, CONTROLLED STUDIES

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Background: Glucocorticoids (GCs) 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. Current meta-analyses of harms and benefits may be improved on a number of important parameters, including study selection, data extraction process and risk of bias assessment. 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 twice. 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 included 6 studies in the primary meta-analyses. Standard mean difference in change in BMD from 0 to 24 months was -0.04 [95% CI -0.18, 0.09] at the lumbar spine and -0.11 [95% CI -0.25, 0.02] at the hip. Studies were comparable regarding study population and intervention. Concomitant treatment of RA differed between studies, as did osteoporosis prophylaxis.

Conclusion: In these clinical studies, with a follow-up of two years, we found no difference in change in BMD between groups of RA patients who had either GCs or placebo treatment added to the anti-inflammatory therapy. This contradicts previous studies. Unbalanced distribution of bisphosphonates between groups may have influenced the results, and data incompleteness may have led to attrition bias.

P30.08 Rola Ismail

IMAGING BIOMARKERS IN SUBJECTS WITH ALZHEIMER'S DISEASE AND SUBJECTS AT RISK OF ALZHEIMER'S DISEASE:  
A STUDY OF THE TEMPORAL AND SPATIAL RELATIONSHIPS BETWEEN NEUROINFLAMMATION, BETA-AMYLOID AND TAU AGGREGATION IN SUBJECTS AT RISK OF ALZHEIMER'S DISEASE

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Introduction: Along with amyloid (A $\beta$ ) plaques and tau tangles, brain inflammation is a component of the neuropathology of Alzheimer's disease (AD). We are investigating their temporal and spatial inter-relationships in subjects with mild cognitive impairment (MCI) and AD in an in vivo longitudinal positron emission tomography (PET) study.

Methods: MCI and AD subjects are recruited via memory clinics and advertisements. <sup>11</sup>C-PiB, <sup>11</sup>C-PK111195 and <sup>18</sup>F-AV-1451 PET are used for measuring fibrillar beta-amyloid load, microglial activation (brain inflammation) and levels of tau aggregation, respectively, and compared with age-matched healthy controls (HC). All subjects have a T1 weighted MRI and standard neuropsychological testing.

Preliminary results: In total, 42 MCI subjects have had <sup>11</sup>C-PIB and <sup>11</sup>C-PK11195 PET. Twenty-nine MCI subjects also had <sup>18</sup>F-AV-1451 PET. Two AD subjects have been included. To date, 13 of 42 MCI have completed their 2-year follow-up. Two-thirds of our MCI cohort show cortical amyloid at baseline and two-thirds of these have evidence of neuro-inflammation. All MCI cases with cortical tau also have amyloid present. Interestingly, a PiB-and AV1451-positive MCI case at baseline shows decreased PK11195 binding at the 2-year follow-up.

Conclusion: Brain inflammation can be detected early in the neuro-pathology of AD but may decrease with time. Two-year follow-up will be completed in the first half of 2018.

CH.01 Willemijn Comuth STABILITY OF DABIGATRAN-SPIKED PLASMA AFTER STORAGE AT -80°C

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Background: Dabigatran etexilate is increasingly prescribed for the prevention of thrombo-embolic complications in patients with atrial fibrillation and in the prevention and treatment of venous thrombo-embolism. In some clinical situations, measurement of the anticoagulant effect of dabigatran is required. We expect that the calibrated automated thrombography (CAT) is a good method. To reduce analytical variation in studies, it is optimal to perform the CAT analyses batchwise at the end of the study, but this requires that the anticoagulant effect of dabigatran is stable during long-term storage at -80°C.

Aim: To evaluate the stability of dabigatran-spiked plasma at -80°C.

Methods: Pooled plasma from healthy volunteers was spiked with dabigatran (0-1000 ng/mL). Dabigatran concentrations were determined using liquid chromatography tandem mass spectrometry (LC-MS/MS) and the dabigatran anticoagulant effect using calibrated automated thrombography (CAT) at baseline and after 1, 3, and 6 months of storage at -80°C.

Results: Measurements were unaffected by 6 months of storage at -80°C. An unexpected decrease in endogenous thrombin potential (ETP) and an increase in lagtime after 1 month and 3 months can be explained by a reduction in activity of fluo-substrate over time. Results at 6 months, using a new vial of fluo-substrate, were similar to baseline results.

Conclusion: Dabigatran-spiked plasma is stable at -80°C for at least 6 months. This indicates that batch analysis of samples of patients treated with dabigatran etexilate is possible after storage at -80°C for up to 6 months at least.

CH.02 Kirstine Petrea IMPACT OF RECONSTRUCTION ALGORITHMS ON FUNCTIONAL 2-  
Bak-Fredslund [<sup>18</sup>F]FLUORO-2-DEOXY-D-GALACTOSE PET/CT OF HUMAN LIVER

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Introduction: It is known that, in small volumes of interest (VOIs), such as image-derived input functions from the aorta used in the current settings of 3D parametric imaging of the metabolic liver function by 2-[<sup>18</sup>F]fluoro-2-deoxy-D-galactose (<sup>18</sup>FDGal) PET/CT, resolution modelling can have substantial effects on the quantitative results obtained. We wanted to evaluate the effect of resolution modelling and the size of matrix on the estimates of the metabolic liver function by <sup>18</sup>FDGal PET/CT.

Methods: Teen subjects, i.e. six healthy subjects and four patients with cirrhosis, had two dynamic <sup>18</sup>F-FDGal PET/CT scans performed with an interval of median 15 days. The PET data were reconstructed with and without resolution modelling in both 168 and 336 matrix; in total, four reconstructions per scan. 3D parametric images of the hepatic metabolic function, expressed in terms of hepatic systemic clearance of <sup>18</sup>F-FDGal ( $K_{met}$ , mL blood/min/mL liver tissue), were generated using Gjedde-Patlak analysis. Regional liver VOIs were placed in the right lobe of the liver, and a whole-liver VOI encircling the liver was created semi-automatized.

Results: There was no significant day-to-day difference in  $K_{met}$  by either reconstruction methods or size of matrix. The absolute values were, however, overestimated systematically by reconstruction without resolution modelling in the 336 matrix as compared to the other three reconstructions.

Conclusion: Functional <sup>18</sup>FDGal PET/CT imaging is reproducible with low day-to-day variation. For reconstruction, we recommend no resolution modelling and 168 matrix.

CH.03 Helene Halkjær HOST CELL STRUCTURE, POLARITY AND PROTEIN ORGANIZATION  
Jensen DURING INFECTION WITH TWO PATHOGENIC ESCHERICHIA COLI STRAINS

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Escherichia coli (E. coli) are a commensal part of the microbiota. However, there are a number of E. coli strains which can infect epithelial tissues like the gastrointestinal (GI) tract and the kidney. Infection with

enteropathogenic *Escherichia coli* (EPEC) is a major cause of childhood death due to diarrhea in developing countries. In healthy adult women, 80% of all urinary tract infections are caused by uropathogenic *Escherichia coli* (UPEC).

We aim to understand EPEC and UPEC host cell: pathogen interactions in the GI tract and the kidney, respectively. Moreover, we aim to understand why patients with chronic kidney disease are more prone to acute pyelonephritis.

We use a wide range of techniques to model infections with EPEC and UPEC. Using cell culture, we can, in high detail, observe and measure the cellular changes that occur during infection. Live fluorescence microscopy allows us to follow individual proteins as well as the bacterial behavior when infecting. Also, we use animal models to study the protein expression profile in different models of renal disease to understand why they may be more susceptible to infection.

When infecting, EPEC attaches to the epithelial cell surface. We found that EPEC can manipulate local cell polarity by mediating translocation of basolateral proteins to the apical infection site to create a local basolateral domain. We also identified a potential host cell receptor for EPEC.

CH.04 Morten Høggild  
Pedersen

SUBSTRATE METABOLISM DURING FASTING IN OBESE HUMAN  
SUBJECTS: IMPACT OF GH BLOCKADE

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Introduction: Obesity is associated with insulin resistance and metabolic inflexibility. Prolonged fasting is a useful model to investigate the shift in metabolism from glucose to lipid oxidation and induction of insulin resistance. Since GH promotes lipolysis, we investigated the metabolic impact of GH blockade during fasting in obese subjects.

Methods: Nine obese males were studied on 3 occasions in a randomized, single-blinded cross-over trial: 1) After an overnight fast (Control), 2) After 72 hours of fasting saline administration (Fasting), and 3) After 72 hours of fasting and concomitant GH blockade by means of pegvisomant (GHA) injections (Fasting + GHA). Each study day consisted of a 4 h basal period followed by a 2 h hyperinsulinemic, euglycemic clamp (HEC).

Results: Fasting was associated with an increase in GH levels ( $P < 0.01$ ), and GHA enhanced the fasting-induced IGF-I reduction ( $P < 0.05$ ). Fasting alone induced a marked increase in FFA levels and lipid oxidation, which was not influenced by GHA, but GHA increased serum glycerol levels ( $P < 0.05$ ) without changing protein expression of glycerol transporters (AQP7) in adipose tissue. The Fasting-induced insulin

resistance ( $P < 0.01$ ) was abrogated by GHA primarily attributed to reduced hepatic glucose production ( $P = 0.03$ ) during the HEC, whereas glucose disposal only increased insignificantly in response to GHA ( $P = 0.18$ ).

Conclusions: 1) GHA-induced suppression of GH activity during fasting in obese subjects reverses hepatic insulin resistance, 2) and lowers hepatic IGF-I production, 3) GHA-induced elevated circulating glycerol levels in the presence of unaltered levels of glycerol transporters in adipose tissue.

CH.05    Henriette Holm  
            Stabel

RUPTURE OF A NON-TRAUMATIC ANTERIOR COMMUNICATING ARTERY ANEURYSM: DOES LOCATION OF ANEURYSM PREDICT FUNCTIONAL INDEPENDENCE AFTER NEUROREHABILITATION?

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Background: Several studies have reported that patients with rupture of a subarachnoid aneurysm (a-SAH) located at the anterior communicating artery (ACoA) often confabulate, show apathy and experience disabilities within executive functions. It is not known whether these disabilities affect their gain in functional outcome during post-acute neurorehabilitation.

Aim: To explore the predictive value of a-SAH located at the ACoA for functional independence measured by Functional Independence Measure (FIM) at discharge from post-acute neurorehabilitation. Age and FIM at admission were also explored.

Design: Historical cohort study.

Participants: 107 patients with first-time a-SAH.

Method: Multivariable logistic regression analysis was conducted to perform comparisons based on an aggregation of FIM.

Results: Patients with a rupture of an ACoA aneurysm gained the same level of functional independence at discharge from post-acute neurorehabilitation as patients with an aneurysm located elsewhere. Older age predicted statistical significant worse functional level in four of the 18 items of FIM; bowel OR 0.59 and bladder OR 0.54 management, comprehension OR 0.53 and memory OR 0.48. Overall, FIM at admission predicted level of functional independence significantly, with the exception of two items: stair walking OR 7.0 and bladder management OR 6.3.

Conclusion: Rupture of an ACoA aneurysm did not predict the level of functional outcome after post-acute neurorehabilitation. Older age predicted worse functional outcome in bowel and bladder functions and comprehension and memory. FIM at admission was the strongest

predictor for level of functional independence after neurorehabilitation.

CH.06 Mette Høj  
Lauridsen

2ND TRIMESTER HEAD SIZE IN FETUSES WITH CONGENITAL HEART DISEASE: A COHORT STUDY

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Background and aims: Congenital heart disease (CHD) is associated with neuro-developmental disorder. The influence of CHD on the brain begins during pregnancy. The aim of this study is to describe a 2-year cohort of fetuses with CHD and to investigate if and when during pregnancy cerebral growth is disrupted. We hypothesize that fetal cerebral growth is impaired as early as 2nd trimester.

Method: Pregnant women in Denmark (more than 95%) attend two publicly funded ultrasound scans. Fetal biometrics and abnormal ultrasound findings are registered. Fetuses in Western Denmark (2.9 mill inhabitants) screened between 1 January 2012 and 31 December 2013 and diagnosed with any structural, non-syndromic CHD during pregnancy or up to six months after birth were included in the study.

Results: Two hundred and ninety five fetuses with CHD were identified. One hundred and twenty (41%) were genetically screened. Data from 30 fetuses were excluded due to genetic syndromes. Data from 15 fetuses were excluded due to extra-cardiac malformations and from 26 due to multiple gestations. Data from 226 fetuses (77%) with presumed non-syndromic CHD were included, of which 89 had minor and 137 had major CHD. In week 12, bi-parietal diameter mean Z-score was 0.18 (95% CI -0.03; 0.4) (P= 0.1) in minor CHD and 0.11 (-0.07; 0.3) (P=0.2) in major CHD. Head circumference in week 19-20 in minor CHD was with a mean Z-score of 0.14 (95% CI -0.1; 0.4) (P=0.2) and in major CHD mean Z-score was -0.42 (95% CI -0.6; -0.2) (P<0.01).

Conclusions: Preliminary results suggest that fetal cerebral growth in children with CHD is normal in the 1st trimester, but may be disrupted as early as 2nd trimester in major CHD.

CH.07 Morten Lykke  
Olesen

PLATELET-RICH PLASMA LEADS TO NEW MATRIX FORMATION AROUND ARTICULAR CARTILAGE CHIPS EMBEDDED IN FIBRIN GLUE IN VITRO

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Purpose: Cellular outgrowth and formation of cartilaginous tissue around articular cartilage explants have been described in a number of recent experimental studies. We aimed to investigate the effect of platelet-rich plasma (PRP) on new tissue formation around articular cartilage chips in vitro.

Methods and materials: Cartilage biopsies were isolated from the femoral condyles of three skeletally mature Göttingen minipigs. The biopsies were prepared into 1mm<sup>3</sup> cartilage chips. Cartilage chips were embedded in fibrin glue and cultured in cell culture inserts up to 21 days in 1) control media (DMEM/F12, 10% PBS and 1% pen/strep), 2) control media with 10% autologous PRP or 3) 10% autologous platelet-poor plasma (PPP) supplementation. Toluidine blue pH 4, alcian blue pH 1 and H&E stainings were performed to characterize newly formed matrix.

Results: Cartilage chips were viable in all groups after 21 days of tissue culturing. There were no definite signs of chondrocyte outgrowth from the chips in any of the groups. Histologic evaluation revealed formation of negatively charged aggregates at the wound edges of the cartilage chips in the PRP group compared with the control and PPP groups. The majority of the cells found in these aggregates had a rounded shape. The highly acidic alcian blue stain of the extracellular matrix indicated the presence of glycosaminoglycans.

Conclusion: The addition of PRP to fibrin glue-embedded cartilage explants in vitro leads to formation of a glycosaminoclycan-rich and cell containing aggregate surrounding the cartilage surfaces. This suggests a potential role of PRP in new tissue formation when using cartilage explants embedded in fibrin glue.

CH.08 Martin Bøhme  
Rasmussen

ROUTINE USE OF POINT-OF-CARE TROPONIN T MEASUREMENT FOR PREHOSPITAL DIAGNOSIS AND RISK-STRATIFICATION IN PATIENTS SUSPECTED OF ACUTE MYOCARDIAL INFARCTION

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Background: Prehospital ECG acquisition and interpretation in patients with ST-elevation myocardial infarction (STEMI) is a prerequisite for field-triage directly to invasive centers, which is associated with earlier reperfusion and lower mortality. However, in patients suspected of acute myocardial infarction without classical ST elevations (NSTEMI) the diagnostic analysis in the prehospital setting can be difficult. Prehospital biomarker measurement may improve triage and preadmission assessment of these patients, but it has never been used routinely.

Purpose: We aim to determine the predictive value of prehospital point-

of-care troponin T (TnT) in NSTEMI patients and to compare the mortality among patients with elevated and normal prehospital TnT in a routine setting.

Design, materials and methods: We installed equipment (Cobas h232) for measurement of TnT in all prehospital vehicles in the Central Denmark Region. We aim to evaluate sensitivity, specificity and mortality by combining prehospital TnT results with data from national registries.

Results: We expect to identify ~2,300 patients with elevated prehospital TnT and expect a rate of AMI as final diagnosis in 15-20% of the patients suspected of AMI in the prehospital setting, resulting in a cohort of ~5,000 patients with AMI. We hypothesise that the sensitivity and specificity of prehospital TnT regarding AMI is above 50% and that patients with elevated prehospital TnT have a higher mortality.

Discussion: Patients with a suspected AMI and elevated values of prehospital TnT have a poor prognosis. This study will evaluate the predictive value of routine TnT measurement in the prehospital setting.

CH.09 Zongpei Zhao

#### INSIGHTS INTO THE STRUCTURAL BIOLOGY OF A NEURAL PROTEIN COMPLEX INVOLVED IN NEURODEGENERATION

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Neurodegenerative diseases are characterized by progressive dysfunction and death of neurons. A common cause of neuronal death is associated with multiple forms of cellular stress, such as absence of functionally important proteins, aggregation of misfolded proteins, and impairment of the protein degradation system. Neuronal macromolecular complexes are cellular machines that perform a wide array of vital tasks, such as regulation of a neuron-specific gene expression profile, vesicle formation, intracellular transport, and neurotransmission. Describing the protein structure of the involved proteins is crucial to understand the function of the proteins. In this project, we study a neuronal protein complex comprising the protein REST. In order to provide insights into the structural organization of the protein complex, we subcloned the involved genes in wild type and mutated form into suitable expression vectors. Specifically, we selected an insect cell expression system suitable for co-expression of human proteins. We successfully confirmed expression of the proteins by Western blotting, and we could also purify individual proteins and protein complexes by anti-FLAG affinity chromatography for biochemical, functional and structural analyses. Using our system, we could identify the inhibitory mechanism of two recently developed drugs. In particular, we demonstrated that the drugs inhibit the catalytic activity of the complex

rather than interfering with the assembly of the complex. Thus, our studies provide insights into the macromolecular assemblies involved in health and neurodegeneration.

CH.10    Andreas Fløe

## TUBERCULOSIS-SPECIFIC CD8 CELLS AND ACTIVE AND LATENT TUBERCULOSIS

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**Background:** Understanding the CD8+ response against Mycobacterium tuberculosis (MTB) may be a key to improved TB diagnostics and vaccine development.

**Aims and objectives:** To detect a CD8+ T-cell response against MTB in active tuberculosis (TB) and latent TB (LTBI) in HLA A\*02 positive patients.

**Methods:** We identified possible epitopes (antigen fragments) from 9 MTB antigens (Ag85B, ESAT-6, EsxH, Hsp65, EsxJ, rv1490, rv1614, rv2626c and 16 kDa antigen) by literature search, and by computer prediction of likely binding to MHC-1. We selected 24 epitope candidates, from which we constructed MHC multimers (Dextramers). Peripheral blood mononuclear cells (PBMC) from 7 TB patients, 16 LTBI patients and 8 MTB-exposed, IGRA-negative, healthy subjects (HE), all HLA A\*02 positive, were stained with the Dextramers and with anti-CD8 and anti-CD3, and analyzed on a flow cytometer. The epitopes were analyzed in 5 pools (3-7 epitopes each). Positive responses included >0.01 % of CD8+, CD3+ cells, supported by inspection of flow cytometry plots.

**Results:** MTB-specific CD8+ T-cells were detected more often in TB patients (57%) than in LTBI patients (41%) and in HE (25%), though differences were insignificant. CD8+ responses were seen against a broad spectrum of antigens, including not previously described Rv2626c epitopes. Reactivity against multiple antigens was observed in 3 of 7 LTBI patients and in 2 of 4 TB patients with detectable CD8+ responses.

**Conclusion:** Broad diversity in epitope-specificity was seen among MTB-specific CD8+ T-cells in HLA A\*02, which is consistent with previous reports. A trend of more common detection of MTB-specific CD8+ cells in TB than in LTBI and HE was found.

- CH.11 Rikke Hahn  
Kofoed A NEW POSSIBLE PATHWAY FOR TREATMENT OF PARKINSON'S DISEASE  
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Genetic studies of familial forms of Parkinson's disease (PD) imply that the level of the protein  $\alpha$ -synuclein (AS) is an important factor in the development of PD. It is, therefore, of great interest to find ways of decreasing the level of AS since this could lead to new targets for the treatment of PD; targets, which could treat the underlying pathology of the disease, not just the symptoms, in contrast to current treatments.

Such targets could be found in the investigation of polo-like kinase 2 (PLK-2) since this kinase has been shown to decrease AS levels upon overexpression. However, overexpression of a protein in human brains is not yet technically possible. The aim of this PhD project is, therefore, to unravel the underlying pathway and to search for targets, which upon inhibition could decrease AS levels.

The study has so far shown that PLK-2 regulates AS at a transcriptional level, which is in contrast to a previously published hypothesis suggesting that PLK-2 regulates AS degradation. Further studies will investigate which other proteins are involved in the pathway and if a specific part of the AS encoding sequence is involved.

- CH.12 Adrian Bauer ARE REDUCED HEPARIN LEVELS DURING MINIMAL INVASIVE EXTRACORPOREAL (MIECC) SAFE? SAFETY OF A NEW ANTI-COAGULATION STRATEGY  
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Introduction: The current standard approach for the use of extracorporeal circulation (ECC) aims at an anticoagulation strategy with a minimum activated clotting time (ACT) of 450 seconds or more. In contrast to conventional ECC, MiECC systems are predestined to reduce the level of heparin due to their closed design, the absence of areas of stagnating blood and the coated surfaces. This approach is not used at all MiECC centers. In a meta-analysis regarding MiECC, only fifty percent of 16 trials were using reduced heparin doses. Different authors found significantly reduced complement activation and less postoperative bleeding in patients with reduced heparin levels. On the other hand, reduction of systemic heparinization is associated with increased thrombin formation and could lead to hyperfibrinolysis or thromboembolic complications.

Aim: This safety trial investigates potential clinical benefits and risks during application of reduced heparin levels like induction of a consumptive coagulopathy.

Hypothesis: A level of 300 sec of ACT during MIECC is safe and sufficient to avoid thrombin formation assessed by thromboelastography and endogenous thrombin potential, and therefore has no negative influence on the activation of the coagulation system.

Materials and methods: To assess the potential activation of the coagulation system, the thromboelastograph (TEG® 5000, Haemonetics) was used. Furthermore, the ETP test with the ability to early detect thrombin-formation was chosen.

Results: In total, 70 patients have been investigated so far. Currently, the data are to be analysed.

CH.13 Rune Dall Jensen EXPLORING THE DEVELOPMENT OF TALENT IN SURGERY - A STUDY ACROSS THE PERFORMANCE DOMAINS OF SURGERY AND SPORTS

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Talent is highly regarded in high performance sports as a key feature for athletes to succeed. In surgery, talent is not a commonly held conversation, even though medical students are usually identified as high achieving, internally motivated individuals. We suggest that bringing talent into the conversation of health sciences education research will help us enrich how to design selection processes and pathways to excellence. Optimally, this may enhance health science students' transition to postgraduate professional domains. In order to bring talent into the conversation of medical education, we conducted a review.

This review aims to map existing literature about talent identification and talent development in the domains of surgery, sports and music. We conducted a five-step scoping study based on a literature search in six databases.

We included 243 studies from the performance domains of surgery (69 studies), sports (115 studies), music (34 studies) and cross-disciplinary studies (25 studies) published in the period of 1985-2014. Compared with the domains of sports and music, the domain of surgery was characterized by few studies focusing on 1) psychological and motivational factors or 2) environmental, demographic and structural factors influencing high performance.

Informed by the performance domains of sports and music, and their holistic, ecological approach to research, this study suggests that research in surgical education may benefit from broadening its view on talent by including psychosocial variables and environmental, demo-

graphic and structural influencers when considering how surgical talent may be identified and developed.

CH.14 Vibeke  
Lynggaard

PATIENT EDUCATION: LEARNING AND COPING STRATEGIES IMPROVE THE ADHERENCE IN CARDIAC REHABILITATION (LC-REHAB) – A RANDOMISED CONTROLLED TRIAL

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Background: Despite proven benefits of cardiac rehabilitation (CR), adherence to CR remains suboptimal. This trial aimed to assess the impact of the patient education 'learning and coping strategies' (LC) on patient adherence to an eight-week CR program.

Methods: In total, 825 patients with ischaemic heart disease or heart failure were randomised to either LC arm (LC plus CR) or control arm (CR alone) across three hospital units in Denmark. Patients in both arms received the same amount of training and education hours. LC consisted of individual clarifying interviews, participation of experienced patients as co-educators, situated and inductive teaching. Patients in the control arm received structured deductive teaching. The primary outcomes were patient adherence to at least 75% of the exercise training or education sessions. We tested for subgroup effects on the primary outcomes using interaction terms. The primary outcomes were compared across arms using logistic regression.

Results: More patients in the LC arm (80%) adhered to at least 75% of the exercise training sessions than controls (73%) (adjusted odds ratio (OR):1.48; 95% CI:1.07 to 2.05, P=0.018) and 75% of education sessions (79% versus 70%, adjusted OR:1.61, 1.17 to 2.22, P=0.003). Larger effects of LC were seen for patients with heart failure, low education and household income.

Conclusions: Addition of LC strategies improved the adherence in rehabilitation, both in terms of exercise training and education. Patients with heart failure, low levels of education and household income appear to benefit most from this adherence promoting intervention.

CH.15 Ardis Simonsen AUTOMATIC ACTION IMITATION IN SCHIZOPHRENIA

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**Introduction:** Imitation plays a key role in social learning and social interaction. It has been hypothesized that the social impairments seen in schizophrenia are in part due to deficits in imitation ability. However, most studies have assessed intentional imitation, which recruits several aspects of cognition not specific to imitation, e.g. attention, working memory, executive function. As these functions are known to be impaired in schizophrenia, this and not imitation may account for the deficits seen.

**Methods:** In order to overcome this issue, we used an automatic imitation paradigm with 33 patients with schizophrenia and 40 matched controls. Participants were required to lift either the index or middle finger according to the number shown on the screen, whilst observing a compatible or incompatible action (e.g. lifting middle finger while observing index finger lift). In order to control for attentional effects, we used a priming condition, where the fingers on the screen remained still, but a mask was added to either the compatible or incompatible finger.

**Results:** Although patients had longer reaction times in general, they showed an automatic imitation effect and priming effect similar to controls: reaction times on compatible trials were faster than on incompatible trials. In addition, the difference between the two conditions (imitation vs. priming) was larger in patients compared to controls. This effect was driven by a greater facilitation of finger movements during imitation trials compared to compatible priming trials in patients.

**Conclusion:** The results suggest that basic imitation ability is not impaired in schizophrenia.

CH.16 Michael Schriver UNDERSTANDING AND MEASURING THE QUALITY OF EXTERNAL SUPERVISION OF RWANDAN PRIMARY HEALTHCARE PROVIDERS

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This final-year PhD study explores the characteristics of external supervision of staff in Rwandan primary healthcare facilities, and how the quality of this supervision may be measured.

We developed a deeper understanding of external supervision with 2 qualitative studies focusing on: 1) the relationship between evaluative and formative functions of the supervision and 2) the relationship between primary healthcare providers and their external supervisors. Through focus group discussions with providers and supervisors, separated and mixed, their perceptions of supervision and the supervisory relationship were explored and compared.

Findings problematize the dominance of continuous performance pressures through regular performance evaluations and fault finding in a context of insufficient formative supervision content. Furthermore, they reveal a need for means to improve the supervisory relationship, including measuring of supervisor support.

Consequently, with the intention to measure the supportive qualities of external supervision, we developed the ExPRESS tool. This questionnaire was developed using qualitative data on supervision, a theoretical framework on supportive supervision and existing supervision questionnaires. An early version was field tested for explorative factor analysis and test-retest reliability. A subsequent version was relevance assessed by international experts as well as supervisors and providers in four African countries. A final version is in the process of field testing for confirmatory factor analysis and discriminative item functioning.

Results may be presented and discussed.

CH.17 Rasmus Aagaard ECHOCARDIOGRAPHY DURING RESUSCITATION: A PARADOX OF RIGHT VENTRICULAR DILATATION IN CARDIAC ARREST CAUSED BY HYPOVOLEMIA AND HYPERKALEMIA - A RANDOMIZED PORCINE STUDY

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Introduction: The interpretation of echocardiographic findings from patients with spontaneous circulation is often extrapolated to those in cardiac arrest. In patients with spontaneous circulation, severe hypovolemia causes a reduction in the right ventricular (RV) diameter, which may persist during cardiac arrest. In contrast, hyperkalemia may cause RV dilation by arresting the heart in diastole. Furthermore, animal studies have demonstrated RV dilation in ventricular fibrillation (VF).

Aim: To study the RV diameter during resuscitation from cardiac arrest caused by hypovolemia, hyperkalemia compared to VF as control.

Methods: Twenty-four pigs were randomized to 7 min of cardiac arrest induced by hypovolemia, hyperkalemia, or VF. Animals were then resuscitated in accordance with international guidelines.

Echocardiographic images were obtained before and during cardiac arrest. Primary endpoint: RV diameter at the third rhythm analysis.

Results: At the third rhythm analysis, the RV was dilated in all groups compared with baseline ( $P < 0.05$ ). In the hypovolemia group, RV diameter was 32 mm (95% CI: 29-35) and significantly larger than in the VF group at 25 mm (95% CI: 22-28) ( $P = 0.008$ ). In the hyperkalemia group, RV diameter was 29 mm (95% CI: 26-32), which was not different from hypovolemia and VF ( $P = \text{NS}$ ).

Conclusion: The right ventricle is dilated during resuscitation from cardiac arrest caused by hypovolemia, hyperkalemia, and ventricular fibrillation. The interpretation of echocardiographic findings in the patient with spontaneous circulation should not be extrapolated to those in cardiac arrest. Right ventricular dilation may be inherent to cardiac arrest, rather than specific to certain causes.

CH.18 Jakob Søgaard  
Juul

DIAGNOSTIC ACTIVITY IN GENERAL PRACTICE ONE YEAR PRECEDING INVITATION TO SCREENING FOR COLORECTAL CANCER

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Background: Lower gastrointestinal symptoms are prevalent in individuals with positive iFOBT in screening. An association between a positive iFOBT in screening and a high diagnostic activity in general practice preceding screening could indicate that iFOBT could be used in general practice.

Objectives: To investigate and compare the use of general practice for individuals who were invited to and participated in the screening programme for colorectal cancer (CRC) in the one year preceding the invitation to screening.

Method: Individuals invited to screening for CRC from 1 March to 31 December 2014 were eligible for inclusion in the study. Included individuals were divided into participants and non-participants, and participants were further divided into positive and negative iFOBT, and whether they were diagnosed with CRC. The groups were compared regarding daytime consultations and haemoglobin measurements in the one year preceding the invitation to screening.

Results: Participants had significantly higher consultation rates than non-participants throughout the study period (IRR = 1.16 (95% CI: 1.15-1.18)). For individuals with a positive iFOBT, the consultation rates were slightly higher compared to individuals with a negative iFOBT. However, it increased significantly in the last two months preceding the invitation to screening (IRR = 1.09 (95% CI: 1.06-1.13) and IRR=1.08 (95% CI: 1.05-1.12)). No significant difference in consultation rates were found between CRC cases and individuals without cancer.

Conclusion: Individuals with a positive iFOBT had an increase in consultation rates two months preceding the screening compared to individuals with negative iFOBT. This may indicate the usefulness of iFOBT in general practice.

CH.19 Carsten Behr-Rasmussen

#### MAGNETIC RESONANCE IMAGING OF THE INTRALUMINAL THROMBUS IN ABDOMINAL AORTIC ANEURYSMS - A QUANTITATIVE AND QUALITATIVE EVALUATION AND CORRELATION TO GROWTH RATE

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Introduction: The intraluminal thrombus (ILT) is still not fully understood regarding abdominal aortic aneurysm (AAA) growth. This study presents novel information on the presence and morphological traits of the ILT and growth rate of AAAs, evaluated with ultrasound (US) and magnetic resonance imaging (MRI).

Methods: In total, 46 patients from the VIVA study and 1 patient from the outpatient clinic were included. All underwent an MRI. Presence (yes/no) of an ILT was noted and, if present, divided into 5

morphological categories. Confounders were adjusted for in a multiple linear regression analysis.

Results: Mean age at the time of the MRI was 75.47 years  $\pm$  2.92 (SD). Mean growth rate was 1.96 mm/year  $\pm$  0.87 (SD). Observation time was 5.51 years  $\pm$  0.84 (SD). ILT was present in 20.00%, 88.89%, 81.25%, 100% and 100% in the AAA size groups measured by US 30-34.9 mm, 35-39.9 mm, 40-44.9 mm, 45-49.9 mm and 50-54.9 mm respectively.

Presence of any sort of ILT resulted in a significantly increased growth rate of 1.09 mm/year 95% CI [0.50:1.70] unadjusted and adjusted 1.28 mm/year 95% CI [0.69:1.88]. When we introduced thrombus categories based upon the visual morphology viewed on MRI, all types of thrombus were associated with increased growth rate compared to "no thrombus". The presence of a thin circumferential thrombus was associated with

most increased growth rate of 2.24 mm/year 95% CI [1.22:3.25].

Conclusion: In this small-scale study with long observation time, the presence of ILT is associated with increased growth rate of the AAAs. There is a tendency that certain types of thrombi are related to accelerated growth.

CH.20 Kathrine Bang Madsen DISCORDANCE BETWEEN PARENT-REPORTED BEHAVIOUR AND ADHD-DIAGNOSIS IN THEIR CHILDREN

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Background: Attention deficit hyperactivity disorder (ADHD) is a diagnosis linked to a substantial lifelong impact on social and academic performance as well as the health system in general. A scientific and public debate is ongoing regarding whether ADHD is systematically diagnosed according to the diagnostic criteria, and misdiagnosis has been reported.

Objective: We aimed to estimate the extent of discordance between the phenotypic parent-reported child behavior and ADHD diagnosis, and secondly to examine the characteristics of these children.

Methods: The present study was based on the Danish National Birth Cohort (DNBC). At 7-year-follow up, the parents of 57,282 children completed questionnaires including the Strength and Difficulties Questionnaire (SDQ). ADHD diagnosis was identified through Danish registers and phenotypical behaviour by the SDQ subscale.

Results: We identified children with ADHD behaviour, but no registered diagnosis (1.3 %), and children with normal behaviour, but a registered ADHD diagnosis (1.4%). Of the 692 children in the former group, 78.6% had other diagnoses than ADHD. The latter group represented more than half of the ADHD diagnosed children. When compared to the rest of the ADHD diagnosed children, these children were significantly more likely to have mothers with a high SOC status (OR<sub>adjusted</sub> low vs. high: 1.77; 95% CI: 1.22; 2.56) and were older at the time of diagnosis (OR<sub>adjusted</sub> ≤ 6 years vs. ≥ 11 years: 11.38; 95% CI: 7.28; 17.79). Conclusion: The results correspond with previous studies, which underline the need for more focus on the importance that the professionals who identify and diagnose children with ADHD follow the official diagnostic criteria.

CH.21 Søren Nielsen Skov NOVEL REMODELING MITRAL ANNULOPLASTY RING THAT PRESERVES AXIAL DYNAMICS OF THE NATIVE MITRAL ANNULUS

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**Introduction:** Despite acceptable results with mitral annuloplasty rings, there is still a need for innovations of annuloplasty devices that ensure a competent valve and maintain the natural out-of-annular-plane dynamics. In this study, we tested a prototype of a novel remodeling annuloplasty ring with built-in septal-lateral annular fixation and commissural axial flexibility. The aim was to evaluate the biomechanical performance of the new remodeling annuloplasty ring compared to two common commercially available remodeling annuloplasty rings.

**Methods:** The measurements were performed in-vivo in an 80 kg porcine model. In total, 28 animals were randomized evenly in four groups: no ring, novel remodeling ring, semi-rigid ring (CE Physio I Ring) and rigid ring (CE Classic Annuloplasty Ring). 3D dynamical geometry was measured with implanted sonomicrometry crystals.

**Results:** The novel remodeling, rigid and semi-rigid mitral annuloplasty rings equally restricted the annular geometry compared to the native valve. The mitral annular height of the semi-rigid and rigid rings was significantly lower in its maximum value and cyclic changes compared to the no ring group. There were no differences in annular height between the novel remodeling ring and the native valve, indicating that the intended function of the new device was obtained.

**Conclusion:** The annular systolic saddle shape is believed to protect the mitral valve function and decrease leaflet stress. This new concept for a remodeling annuloplasty ring with integrated septal-lateral annular fixation and apical flexibility is unique and could be an important step towards improved mitral valve reconstruction.

CH.22 Christina Friis  
Jensen

HYPOTHERMIA AND RESPIRATORY DISTRESS SYNDROME IN VERY PRETERM INFANTS

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**Background:** Hypothermia is thought to increase the risk of respiratory distress syndrome (RDS) and bronchopulmonary dysplasia (BPD) in very preterm born infants. However, the evidence of an association is sparse, and concerning RDS the possibility of reverse causality challenges the interpretation of a potential association.

**Objective:** We investigated the association between hypothermia and

RDS or death and the association with BPD or death in very preterm infants.

Methods: We studied a cohort of 676 inborn infants born before 32 weeks of gestation. Hypothermia was defined as a temperature  $< 36.5^{\circ}\text{C}$  upon admission. Primary outcome was severe RDS or death within the first 3 days of life. Secondary outcome was BPD or death before discharge. We performed multivariable logistic regression adjusted for early onset infection, gestational age, Apgar score, gender, treatment year and birth weight.

Results: We found a twofold increase in the odds for RDS or death if the infant had hypothermia upon admission. After adjustment, the estimate was smaller and not statistically significant (OR = 1.36; 95% CI 0.89; 2.08). Infants with hypothermia had an unadjusted twofold increase in the odds for BPD or death. After adjustment, no association was found between hypothermia and BPD or death (OR = 1.03; 95%CI 0.64 to 1.68).

Conclusion: Very preterm infants with hypothermia upon admission had increased odds for RDS or death. However, after adjustment, the results were not statistically significant. Admission temperature was not associated with the adjusted risk of BPD or death.

CH.23    Esben Søvsø    IMAGING PORCINE CARDIAC SUBSTRATE SELECTION MODULATIONS BY  
Szocska Hansen    GIK INTERVENTION: A HYPERPOLARIZED  
[1- $^{13}\text{C}$ ]PYRUVATE STUDY

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Cardiac metabolism has gained considerable attention, both in terms of diagnostic and prognostic purposes, as well as a novel target for treatment. As human trials involving hyperpolarized MR in the heart are imminent, we sought to evaluate the general feasibility of detecting an imposed shift in metabolic substrate utilization during metabolic modulation with glucose, insulin and potassium (GIK) infusion and thus the limitations associated with this strategy in a large animal model reassembling the human physiology. The study demonstrates that hyperpolarized [1- $^{13}\text{C}$ ]pyruvate, in a large animal, is a feasible method for cardiac studies with a generally high reproducibility in fasted animals. GIK infusion increases the metabolic conversion of pyruvate to its metabolic derivatives, lactate, alanine and bicarbonate, but with an increased variability.

CH.24 Pernille Falberg Rønn OBESITY-ASSOCIATED RISK OF CARDIOVASCULAR DISEASE AND THE INFLUENCE OF ETHNICITY: A COMPARATIVE STUDY IN INUIT AND EUROPEANS

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Background: Inuit populations have a lower prevalence of cardiovascular risk factors for the same obesity levels as Europeans. We, therefore, aimed to examine whether Inuit populations also have a different incidence of cardiovascular disease (CVD) in relation to obesity to test the predictability of different anthropometric measures for CVD.

Methods: We did a comparative cohort study based on data from three studies in Canada, Greenland and Denmark. Anthropometric measures collected at baseline included: BMI, waist circumference, waist-to-hip-ratio, waist-to-height-ratio and a body shape index. Participants were followed in national registers or medical files. CVD was defined as a fatal or non-fatal event from ischaemic heart disease, heart failure or stroke. Poisson regression analyses were used to calculate incidence rate ratios for CVD as an effect of obesity with adjustment for confounders. A total of 9759 participants without CVD diagnosis at baseline were followed for a median of 10.3 years.

Results: In total, 642 participants had a CVD event during follow-up, including 31 (4.3%) in Canadian Inuit, 117 (4.1%) in Greenlandic Inuit and 494 (8%) in Danes. After adjustment for confounders, all the anthropometric measures showed slightly positive but insignificant relations to CVD. Neither sex or study cohort modified the effect of obesity on CVD, but the Canadian Inuit had a higher absolute CVD incidence for a given anthropometric measure.

Conclusion: Inuit populations have a similar or higher CVD incidence for a given obesity level and measure compared to Europeans. None of the anthropometric measures were independent predictors for CVD, regardless of ethnicity.

CH.25 Anders Krogh Brøndberg NATIONWIDE EXPERIENCE OF CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA CAUSED BY RYR2 MUTATIONS

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**Objective:** To characterize disease penetrance, course of disease, prevalence and the use of implantable cardioverter defibrillator (ICD) therapy in a Danish nationwide cohort of patients with catecholaminergic polymorphic ventricular tachycardia (CPVT) due to mutations in the ryanodine receptor-2 gene (RYR2).

**Methods:** The study population was identified through the national hereditary heart disease database. The study population was divided into three groups: probands, symptomatic and asymptomatic relatives.

**Results:** We identified 23 symptomatic probands, 16 symptomatic and 12 asymptomatic relatives with a RYR2 mutation. We found a prevalence of one RYR2 mutation positive patient per 100,000 inhabitants. Twenty (87%) probands exhibited fatal or near-fatal events (Sudden cardiac death (SCD), aborted SCD (ASCD) or syncope) as first symptom.

As compared with symptomatic relatives, probands had lower age at onset of symptoms (16 years (IQR; 10-33) vs 43 years (IQR; 25-54),  $p < 0.0001$ ), and were more prone to fatal or near-fatal events (20 events vs 10 events,  $p < 0.0001$ ). Twenty-eight patients had an ICD implanted, and 8 experienced appropriate ICD therapy during follow-up (65 months (IQR; 43-175)). Electrical storm was seen in 2 of the 28 ICD treated patients (7%). No treated patients died during follow-up (57 months (IQR; 32-139)).

**Conclusions:** We found a prevalence of RYR2 mutation positive CPVT patients of 1:100,000 in Denmark. Fatal or near fatal events were presenting events in the majority of probands and were also seen in 36% of relatives identified through family screening. Probands were younger at disease onset and more prone to fatal or near-fatal events than relatives.

CH.26 Casper Larsen

## STRUCTURAL CHARACTERISATION OF COBALAMIN UPTAKE AND TRANSPORT: THE CUBILIN-AMNIONLESS INTERACTION

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Cobalamin (Cbl, also known as vitamin B<sub>12</sub>) plays a key role in the human metabolism, and deficiency can lead to anemia and neurological disorders. Humans must obtain the compound through dietary sources and have evolved a sophisticated absorption and transport pathway from the food to the cells in the body. Intestinal uptake is mediated by a protein complex named Cubam that recognizes and internalizes Cbl in complex with the carrier protein intrinsic factor (IF-Cbl). The Cubam complex is composed of the peripheral membrane protein Cubilin and the transmembrane Amnionless (AMN). Each protein has a distinct function during the endocytosis process; Cubilin is responsible for

binding of IF-Cbl, and AMN is responsible for membrane anchoring and internalization of the complex. Interaction between the two proteins is a prerequisite for proper processing of the receptor complex to the plasma membrane, as expression of Cubilin or AMN separately causes endoplasmic reticulum retention.

This project aims at providing a detailed three-dimensional crystal structure of the complex between Cubilin and AMN. Elucidating this structure will lead to a complete understanding of the Cubilin-AMN association and thereby give insight into how the interaction leads to proper processing and function of the receptor complex. Furthermore, the molecular basis for defects in the uptake of Cbl can be deduced, e.g. the autosomal recessive disorder termed the Imlerslund-Gräsbeck syndrome, which is caused by mutations in the encoding of genes, either Cubilin and/or AMN, and is manifested by intestinal Cbl-malabsorption and mild proteinuria.

CH.27 Sorosh  
Tabatabaeifar

#### MEDIAN NERVE AFFECTION DURING SEASONAL REPETITIVE WORK WITH MODERATE FORCE

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Little is known about the time course of changes in the median nerve function in relation to variations in occupational mechanical exposures to the wrist. We studied this relation using mink skinning as a natural experiment. Mink skinning is hand-intensive seasonal work.

We included 11 male workers without median nerve affection and performed dominant-sided nerve conduction studies (NCS) pre-, mid-, end-, and post-season. For a subset of the workers, we characterised the exposures by full shift technical measurements. Questionnaire information about symptoms and disabilities was obtained.

Mean age was 35.7 years (SD: 10.2) and mean number of seasons with skinning 8.9 (range: 2-26). The single-task job of skinning mink was characterised by a high median velocity of flexion/extension of the wrist (22°/s), 20% of the time in non-neutral wrist postures, and moderate forearm extensor force requirements. The season lasted 22 days with mink skinning on 20. From pre- to end-season, mean distal motor latency (DML) increased 0.41 ms (95% CI: 0.27-0.56,  $p < 0.001$ ), mean sensory nerve conduction velocity (SNCV) digits 2 and 3 decreased 6.3 m/s (2.5-10.2,  $p = 0.004$ ) and 6.2 m/s (1.9-10.6,  $p = 0.01$ ), respectively. DML and

SNCV were unchanged for the ulnar nerve across the wrist. Symptoms and disabilities increased significantly from pre- to end-season, where four workers had developed carpal tunnel syndrome according to symptoms and NCS. Three to six weeks post-season, the NCS parameters had reverted to normal as had symptoms and disabilities.

Reversible median nerve affection may result from 3 weeks of seasonal work with high repetitiveness and moderate force.

CH.28 Mia Bendix Rasch VITAMIN D TREATMENT INCREASES T CELLS PROGRAMMED DEATH RECEPTOR-1 EXPRESSION IN CROHN'S DISEASE

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Background: Vitamin D treatment may reduce the activity episodes in Crohn's disease (CD) by modulating immune cell functions. Programmed death 1 (PD-1) receptor is important for maintenance of immune tolerance. Vitamin D may modulate PD-1 mediated signalling in CD.

Aim: To investigate whether vitamin D treatment modulates the PD-1 mediated regulation of activated T cells from CD patients.

Methods: Plasma samples from forty CD patients were included; 20 treated with 1200 UI daily vitamin D in 26 weeks and 20 treated with placebo. Peripheral blood mononuclear cells (PBMCs) were isolated at baseline and at week 26 from 10 vitamin D and 10 placebo treated CD patients. Eight healthy controls were included. PBMCs were cultured with anti-CD3/CD28, and the expression of PD-1, PD-L1 and activation markers were analysed by flow cytometry. Soluble PD-1 plasma levels were measured by ELISA.

Results: Faecal calprotectin increased in placebo treated CD patients compared with the vitamin D treated group ( $p = 0.01$ ). Upon T cell receptor stimulation, vitamin D increased the PD-1 expression in CD4<sup>+</sup>CD25<sup>+</sup>T cells compared to placebo ( $p = 0.04$ ). This was not observed in CD4<sup>+</sup>CD25<sup>high</sup>T cells but in the remaining T cell population ( $p = 0.03$ ). Vitamin D treatment decreased the expression of the activation marker CD69 ( $p = 0.01$ ) compared to placebo ( $p = 0.26$ ). Soluble PD-1 plasma levels were not influenced by vitamin D.

Conclusion: Oral vitamin D treated CD patients increased the PD-1 expression in CD4<sup>+</sup>CD25<sup>+</sup>T cells combined with a decreased CD69 expression.

CH.29 Maria Wielsøe SERUM LEVELS OF ENVIRONMENTAL POLLUTANTS ARE ASSOCIATED WITH BREAST CANCER RISK

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Background: Environmental organic pollutants (POPs) have been hypothesized to influence the breast cancer risk by hormone disrupting effects, promoting disruption of epigenome mechanisms and development of obesity increasing the risk of breast cancer development.

Although the association between POPs and breast cancer has been widely studied, no clear conclusions on associations or mechanisms have been drawn. The present study examined the associations between serum levels of POPs and breast cancer with focus on the highly exposed Greenlandic Inuit population.

Method: The present study was designed as a case-control study, including Inuit women in two periods: 2000-2003 and 2011-2014. The serum level of 14 polychlorinated biphenyls (PCBs), 11 organo chlorine pesticides (OCPs) and 16 perfluoroalkyl acids (PFAAs) were determined.

Results: The study population included 77 breast cancer cases and 84 controls. We found that the level of POPs was significantly higher in cases than in controls for all tested compounds. The majority of the measured PCBs and OCPs and some of the amphiphilic PFAAs increased the breast cancer risk significantly. The associations were, however, weak with odds ratio estimates close to 1.00. Of the tested groups, the serum levels of PFSAs showed the strongest associations (OR: 1.01, 95% CI: 1.00; 1.02), whereas of the individual compounds perfluorohexane sulfonate (PFHxS) showed the strongest association (OR: 1.16, 95% CI: 1.02; 1.32).

Conclusion: Significant weak associations between breast cancer risk and POPs were observed. The weak associations indicate that exposure to POPs may be a factor increasing the risk of developing breast cancer.

CH.30 Vincent Kalumire UNDERSTANDING AND MEASURING PATIENT-PROVIDER  
Cubaka COMMUNICATION IN PRIMARY HEALTH CARE SETTINGS IN RWANDA

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Patient-provider communication (PPC) influences the quality of health care. This PhD work attempts to set baselines in the exploration of PPC in a sub-Saharan context using Rwanda as a case.

We conducted two qualitative explorations to deepen our understanding of PPC in primary health care (PHC) in Rwanda,

respectively from a patient and a provider perspective.

We are currently analysing data from in-depth interviews to deepen the insight into determinants of quality interaction between the patient and the provider in the PHC consultation room. Findings and lessons learned will be highlighted and discussed.

We additionally conducted a cultural adaptation from English to Kinyarwanda of the communication assessment tool (CAT). The CAT is a validated questionnaire that measures the provider's communication and interpersonal skills from a patient's perspective. The validation in the Rwandan context is still in progress.

This tool may be used for different purposes (direct feedback to providers, in teaching, in research, etc.) with the ultimate aim of improving the quality of the communication between the patient and the provider, and consequently improve health outcomes. We will describe and discuss the adaptation and validation process as well as the results of field-testing, including differential item functioning, test-retest reliability and factor analysis to explore dimensionality.

CH.31 Kasper Lisager  
Jønsson

IFI16 PLAYS A DUAL ROLE IN THE CGAS-STING PATHWAY BY PROMOTING BOTH PRODUCTION AND FUNCTION OF CGAMP

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Host innate sensing of microbial DNA is of major importance for several infectious diseases. However, dysregulation of the sensing machinery can lead to autoimmunity and inflammatory disorders. Sensing is mediated by cyclic GMP-AMP synthase (cGAS), which signals through stimulator of interferon genes (STING) via a second messenger molecule called cyclic GMP-AMP (GAMP), resulting in type I interferon (IFN) and cytokine induction. Interferon-gamma inducible factor 16 (IFI16) is another host factor shown to recognize foreign DNA and induce IFNs. However, the interrelation with the cGAS-STING pathway remains to be fully elucidated.

We show that IFI16 works on the cGAS-STING pathway at two distinct levels. Upon depletion of IFI16 in human macrophages, we see a strong impairment in cGAS activity upon DNA stimulation. Overexpression of IFI16, however, augments cGAS function. Additionally, IFI16 facilitates recruitment of TANK-binding-kinase 1 (TBK1) to STING resulting in IFN and cytokine induction upon cGAMP treatment. Our results prove that IFI16 is essential for effective innate sensing and signalling upon DNA stimulation to initiate IFN expression and induce an anti-viral state. Such insights into the regulation of innate sensing are critical for further understanding of how viruses, such as human immunodeficiency virus type 1 (HIV) or herpes, are detected. Furthermore, our study yields invaluable knowledge to the underlying pathologies associated with several autoimmune and inflammatory disorders, such as psoriasis, SAVI (STING-associated vasculopathy with onset in infancy) and Aicardi-Gourtières, which have been associated with activation of IFI16, cGAS and STING.

CH.32 Susan Larsen SHORT UNPLANNED ADMISSIONS IN HAEMATOLOGY

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Background: Unplanned admissions are known to impair treatment outcome for patients and to be indicators of the quality in patient care. Research also suggests that chemotherapy treated patients at home have unmet needs and unnecessary suffering, which may lead to unplanned admissions. Knowledge of the factors causing admissions is important to adjust care and support, and possibly prevent unplanned admission.

Aims: To describe the extent and causes of unplanned admissions (study 1), to explore and understand the impact of unplanned admissions on patients' lives (study 2). Resolve possible initiatives to prevent unplanned admissions.

The aims are achieved through a quantitative and qualitative approach. Results from study 1 will guide the selection of patients for study 2.

Preliminary results: A registration of all unplanned admissions during 6 months in the Department of Haematology shows that unplanned admissions have a duration of between 2 hours and 77 days. However, approx. 25% of the admissions have a duration of 24 hours or less.

On all admissions data concerning socio-demographics, sickness and treatment, patient condition, nursing problems, contact to primary care facility and time are collected. The problems or symptoms leading to these short admissions will be presented.

CH.33 Anders Laustsen VERSATILE PLATFORM FOR INVESTIGATING PLASMACYTOID DENDRITIC CELL DEVELOPMENT AND FUNCTION

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Plasmacytoid dendritic cells (pDC) are essential for immune competence. Consequently, they play an important role in the pathogenesis of several diseases, including viral infections, autoimmune diseases and cancer. However, due to their low frequencies within peripheral blood, progress in understanding their function has been limited. Thus, there is an urgent need for a flexible and reproducible pDC culture system, which facilitates the rapid elucidation of pDC developmental mechanisms, as well as recapitulation of pDC functions. Here we describe a novel method that allows for a high generation of pDCs.

Human umbilical cord blood derived hematopoietic stem cells (HSC) were cultured for 21 days with cytokines and growth factors, allowing the expansion and differentiation of pDCs. Starting from  $2 \times 10^5$  HSCs, we were able to generate on average  $15 \times 10^6$  pDCs, corresponding to what can be obtained from 10 litres of blood. Based on phenotypic and functional characteristics, cells were defined as precursors of canonical pDCs with low surface levels of CD123, CD303, CD304 and HLA-DR and low functional activity through TLR7/9. Finally, the versatility of this platform for gaining mechanistic insights into pDC development and function is illustrated by our discovery about pDC development; pDC precursors must experience interferon priming to become functional active. When primed, cells elicited a canonical pDC phenotype with high expression of CD123, CD303, CD304 and HLA-DR as well as functional TLR7/9-mediated responses. Collectively, we present a new model of pDCs, which is readily amenable to modifications that allow investigators to evaluate pDC development and function.

CH.34 Thomas Dahl  
Nielsen ULTRASOUND GUIDED OBTURATOR NERVE BLOCK - INVESTIGATING THE PROXIMAL SPREAD AND INVOLVEMENT OF THE HIP ARTICULAR BRANCHES

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Background: The femoral and obturator nerves are assumed to account for the primary nociceptive innervation of the hip joint capsule. The fascia iliaca compartment block and the so-called "3-in-1-block" have been employed in patients with hip fracture based on a presumption

that local anesthetic spreads to anesthetize both of these nerves. Evidence demonstrates that this presumption is unfounded, and knowledge about the analgesic effect of obturator nerve blockade in hip fracture patients pre-surgically is thus nonexistent.

**Objective:** The objective of this cadaveric study was to investigate the proximal spread of the injectate resulting from the administration of an ultrasound guided obturator nerve block, and to evaluate the spread around the obturator nerve branches to the hip joint capsule.

**Method:** 15 mL of methylene blue was injected into the interfascial plane between the pectineus and external obturator muscles in seven adult cadavers. The spread of the injectate into the obturator canal and around the obturator and accessory obturator nerve branches to the hip joint was evaluated by subsequent dissection.

**Results:** A preliminary estimation of the results suggest that the dye injected into the interfascial plane between the pectineus and the external obturator muscle effectively spread proximally to reach the obturator canal and colored all obturator branches to the hip joint capsule in all fourteen sides. Furthermore, the accessory obturator nerve was present in three of fourteen sides, and the nerve and its branches to the hip joint capsule were colored in all cases.

CH.35 Sara Bisgaard  
Jensen HUMAN ENDOGENOUS RETROVIRUSES (HERVS) IN MULTIPLE SCLEROSIS (MS)

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HERVs have been associated with MS through both genetic and biochemical approaches. We here propose experiments to investigate this association further; in vitro, ex vivo and in vivo.

**In vitro:** Microglia plays a role in all phases of MS pathogenesis. Depending on the stimuli, microglia polarized into one of two very different kinds of activated cells; the pro-inflammatory M1 or the anti-inflammatory M2. We have obtained a human microglia cell line (CHME3), which we will polarize into these two types and by means of qPCR and ELISA investigate for expression of HERVs. Later, we will overexpress HERVs in the cell line and investigate whether this promotes the polarization. This will clarify the causal relation between HERVs and MS.

**Ex vivo:** By ELISA, we will examine plasma in 65 MS patients and 65 healthy controls for presence of antibodies towards two peptides from HERV-K gag and pol, respectively. The level of antibodies towards these peptides has previously been shown to be increased in MS patients.

**In vivo:** The immunosuppressive domain of the HERV envelope could play a beneficial role in MS by repressing the immune response. Studies

in a murine model for rheumatoid arthritis (RA) show that HERV derived proteins ameliorate RA symptoms. We want to investigate the effect of these proteins in a mouse model for MS. The outcome will be analyzed by scoring of the animals, ELISA of plasma and immunohistochemistry.

All together, this will bring clarity to the causality between HERVs and MS, identify antibodies in MS patient plasma, and identify drug candidates for the treatment of MS.

CH.36    Rebeka Bodak    CAN LISTENING TO SOUNDS TRAIN MOTOR SKILLS?

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Brain imaging studies with highly skilled musicians show strong co-activation in the auditory and motor cortices during music performance. Interestingly, this co-activation has been shown while playing a familiar piece with no sound feedback, as well as during music listening in the absence of movement (Bangert et al., 2006; Lotze et al., 2003). After a short period of audio-motor training, this relationship between movement and sound production, known as audio-motor coupling, has also been observed in nonmusicians (Bangert & Altenmüller, 2003; Lahav et al., 2007).

Building on a recent behavioural study with nonmusicians by Stephan and colleagues (2014), this project will explore the impact of auditory exposure on the formation of new motor memories. Following an audiomotor mapping session, participants will be asked to listen to and memorise either Sequence A (Group A) or Sequence B (Group B). Using visuospatial stimuli to cue motor responses, all participants will be tested before the mapping session; half of each group immediately after exposure and the other half 6.5 hours later. It is predicted that Congruent Group A will perform faster than Incongruent Group B (between subjects), and that those tested 6.5 hours after exposure will perform faster than those tested immediately.

The findings of this study have the potential to be useful in motor rehabilitation settings, where the coupling of sound and movement patterns might help patients relearn motor tasks relevant to activities of daily living, particularly when regular physical practice is not possible.

CH.37 Troels Bille  
Folkmar

QUALITY OF LIFE IN PATIENTS WITH CHRONIC OSTEOMYELITIS OF THE MANDIBLE: A QUESTIONNAIRE SURVEY

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Objective: Chronic osteomyelitis of the mandible (COM) in adults is often accompanied by pain and swelling, leading to patient discomfort. Only few investigations report quality of life (QOL) in patients with chronic osteomyelitis and none for COM. The aim was to study the influence of COM on patient QOL.

Patients and methods: We recruited 23 patients from the outpatient clinic at the Department of Oral and Maxillofacial Surgery with pain for a median (range) of 4 years (23 years) at the time of inclusion. At the end of the survey, the final number was 16. The reasons for non-respondent dropout are unknown. At disease onset, the median (range) was 48 years of age (56 years). The diagnosis of COM was established from clinical and radiological examinations. Data on QOL were collected through a self-reported questionnaire survey based on the Health Survey Short Form scoring algorithms for 12-item physical and mental component summary measures (SF12v1) and pain on a visual analogue scale (VAS). The questionnaire was repeated three times during 10 months.

Results: QOL as measured with SF12 questionnaire did not show major changes over time, and those with only the mandible affected had a significantly better QOL than those with pain from more than the mandible. The SF12 questionnaire showed a tendency to a lower mental than physical score.

Conclusion: The findings of this study suggest that patients with COM have a reduced QOL that does not change much over time. This suggests that the previous treatment is inadequate. Therefore, more effective treatments must be established.

CH.38 Hanne Mari  
Jørgensen

BIOAVAILABLE TESTOSTERONE IS ASSOCIATED WITH BONE DENSITY IN MALE KIDNEY TRANSPLANT CANDIDATES

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Introduction: Hypogonadism is common in chronic kidney disease (CKD) and may contribute to bone fragility. We investigated associations between sex hormones and bone mineral density (BMD) in adult kidney transplant candidates.

Methods: Volumetric BMD of lumbar spine and femoral neck was measured by computed tomography. Intact parathyroid hormone (iPTH), testosterone (T), estradiol (E2) and sexual hormone binding protein (SHBG) were measured from fasting morning blood samples. Free and bioavailable (Bio) T and E2 were calculated based on constants for protein binding.

Results: In 102 male patients, hypogonadism was present in 15%. Z-scores were reduced in hypogonadal men, which were statistically significant in adjusted analyses. For example, femoral neck Z-score was -1.38 (1.10) vs. -0.89 (0.88),  $p=0.07$  with adjusted  $p=0.01$ . Bio T was positively correlated to both lumbar spine ( $r=0.24$ ,  $p=0.01$ ) and femoral neck vBMD ( $r=0.21$ ,  $p=0.03$ ), and Bio E was positively correlated to lumbar spine vBMD ( $r=0.23$ ,  $p=0.02$ ). In multiple linear regression analyses adjusting for age, body mass index, dialysis, diabetes and iPTH, Bio T and Bio E were confirmed as positive predictors of vBMD at lumbar spine: Bio T ( $\beta=6.12$ ,  $p<0.001$ ) and Bio E ( $\beta=0.26$ ,  $p=0.02$ ) and at femoral neck: Bio T ( $\beta=8.71$ ,  $p<0.001$ ) and Bio E ( $\beta=0.33$ ,  $p=0.03$ ). When including both Bio T and Bio E in the linear model, Bio T remained a significant positive predictor of vBMD at lumbar spine ( $\beta=4.16$ ,  $p=0.02$ ) and femoral neck ( $\beta=5.37$ ,  $p=0.04$ ), independently of Bio E.

Conclusions: Sex hormones may exert an important effect on bone health in male patients with advanced kidney failure.

CH.39 Charlotte Runge AN OBTURATOR NERVE BLOCK AND A FEMORAL TRIANGLE BLOCK COMBINED WITH SYSTEMIC DEXAMETHASONE IS AN EFFICIENT ANALGESIA AFTER TOTAL KNEE ARTHROPLASTY - A RANDOMIZED CONTROLLED STUDY

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Background and objectives: A multimodal strategy of systemic and regional analgesia is a mainstay in the pain management after total knee arthroplasty (TKA). Combined obturator nerve and femoral triangle blocks (OFB) reduce the opioid requirement after TKA more effectively than local infiltration analgesia (LIA) without impairing ambulation. High-dose systemic dexamethasone also has an analgesic effect on postoperative pain. The question is whether high-dose systemic dexamethasone equalises the analgesic effect of OFB compared to LIA.

Aim: To compare the analgesic effect of OFB vs. LIA after TKA, when

adding high-dose systemic dexamethasone to both techniques.

Methods: Eighty-two patients were randomly assigned either to OFB or LIA after primary unilateral TKA. Both groups were additionally given high-dose systemic dexamethasone. Primary outcome was morphine consumption after 20 postoperative hours. Secondary outcomes included nausea and dizziness.

Results: Seventy-four patients were included in the analysis. The total intravenous morphine consumption during the first 20 postoperative hours was 6 mg (IQR 2 - 18) in the OFB group and 20 mg (IQR 12 - 28) in the LIA group ( $P < 0.001$ ). The OFB group had less ondansetron consumption and dizziness than the LIA group.

Conclusion: A combined obturator nerve block and femoral triangle block reduces morphine consumption more than local infiltration analgesia after TKA, even after addition of high-dose systemic dexamethasone to both groups.

CH.40 Joan Fledelius

INTER-OBSERVER AGREEMENT IMPROVES WITH PERCIST 1.0 AS OPPOSED TO QUALITATIVE EVALUATION IN NON-SMALL CELL LUNG CANCER PATIENTS EVALUATED WITH F-18-FDG PET/CT EARLY IN THE COURSE OF CHEMO-RADIOTHERAPY

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Background: The purpose of this study is to determine whether a qualitative approach or a semi-quantitative approach provides the most robust method for early response evaluation with FDG PET/CT in non-small cell lung cancer (NSCLC).

Methods: Eight nuclear medicine consultants analyzed FDG PET/CT scans from 35 patients with locally advanced NSCLC. Scans were performed at baseline and after 2 cycles of chemotherapy. Each observer used two different methods for evaluation: 1) PET response criteria in solid tumors (PERCIST) 1.0 and 2) a qualitative approach. Both methods allocate patients into one of four response categories: CMR, PMR, SMD and PMD. The agreement was evaluated using Fleiss' Kappa, Cohen's Kappa and intraclass correlation coefficients (ICC).

Results: The agreement between observers determining percentage change in SUL peak was "almost perfect", with ICC=0.959. There was strong agreement amongst observers allocating patients to the different response categories with a Fleiss kappa of 0.76 (0.71-0.81). In 22 of the 35 patients, complete agreement was observed with PERCIST 1.0. The agreement was moderate when using the qualitative method (Fleiss

kappa of 0.60 (0.55-0.64)). Complete agreement was achieved in only 10 of the 35 patients. The difference between the two methods was statistically significant ( $p < 0.005$ ) (chi squared).

Conclusion: PERCIST 1.0 provides a higher overall agreement than qualitative evaluation. The inter-observer agreement is strong using PERCIST 1.0 even when the level of instruction is purposely kept to a minimum in order to mimic the everyday situation. The variability is largely owing to the subjective elements of the method.

CH.41 Jesper Weile

#### THE USE OF ULTRASOUND IN TRAUMA IN DENMARK

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Background: The Focused Assessment with Sonography in Trauma (FAST) protocol is considered beneficial in emergent evaluation of the trauma patients with blunt or penetrating injury and has become integrated in the Advanced Trauma Life Support (ATLS) protocol. No guidelines exist as to the use of ultrasound in trauma in Denmark. We aimed to investigate the usage of ultrasound during trauma in Denmark.

Methods: We conducted a two-phased cross-sectional investigation. The first phase was an Internet-based investigation of existing guidelines. The second phase was a series of structured interviews including on call trauma leaders, on call anesthesiologists and on call radiologists in all centers receiving traumatized patients in Denmark.

Results: Pending.

Conclusion: Ultrasound is used in a non-uniform fashion by multiple medical specialties in Danish trauma facilities. The training and certification of providers is non-uniform. National guidelines on training and usage of ultrasound in trauma are called for.

CH.42 Louise Møldrup  
Nielsen EFFECTIVENESS OF ASSESSMENT OF FUNCTIONAL ABILITY AND  
FOLLOW-UP AT HOME FOR ELDERLY MEDICAL PATIENTS

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Introduction: Elderly patients often experience limitations in their functional ability related to performance of daily activities. Limited functional ability in elderly is associated with increased risk of hospital readmission and may be a predictor of increased mortality

Objective: To examine the effectiveness of an intervention at an Emergency Department (ED) aimed at reducing elderly patients' risk of readmission.

Design: The study was conducted as a comparative intervention study (quasi-experimental design) with an intervention group and a usual care group.

Materials and method: The study population consists of 383 medical patients admitted to the ED, aged 65+ years. Patients were allocated by their personal identification number (CPR) to an intervention group (n=145) or a usual care group (n=238). The intervention was based on systematic assessment of functional ability, development of a rehabilitation plan and follow-up at home. At the home visit, an occupational therapist initiated training focused on increasing performance of daily activities. Outcomes at 4 and 26 weeks were readmission, mortality, contacts to general practitioner and emergency physician.

Results: Results are expected during the spring of 2017

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CH.43 Martin  
Christensen ABSTRACT TITLE

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Introduction: The association between preeclampsia and cardiovascular disease (CVD) is well established. In fact, the risk of cardiovascular disease (CVD) is more than doubled 10-15 years after preeclampsia. However, absolute risk is still very low, which reflects the need for stratification of post-preeclamptic cardiovascular risk. This study was undertaken to test if gestational age at diagnosis could help stratify CVD risk after preeclampsia.

Objective: To test the association between gestational age at diagnosis

and subclinical atherosclerosis 12 years after preeclampsia.

Methods: A follow-up study of preeclamptic women who gave birth in Randers from 1998 to 2008. Markers of subclinical atherosclerosis were carotid plaque presence and carotid intima-media thickness (cIMT).

Results: Forty-eight women were included. Data revealed a statistically significant association between gestational age at diagnosis and carotid plaque 12 years after preeclampsia. The odds ratio equalled 0.78 ( $P=0.03$ ). Hence, the higher the gestational age at diagnosis, the lower the odds of having carotid plaque 12 years after preeclampsia. The negative association was also shown for cIMT, but only the right cIMT estimate was statistically significant ( $P=0.02$ ).

Conclusion: Our results indicate an association between gestational age at diagnosis and subclinical atherosclerosis 12 years after preeclampsia. We found a statistically significant negative association between gestational age at diagnosis and carotid plaque presence as well as right cIMT 12 years after preeclampsia. Hence, gestational age at diagnosis might help stratify post-preeclamptic CVD risk, but large-scale data need to confirm our findings.

CH.44 Lena-Sophie  
Martis

CHRONIC MILD STRESS MODEL OF DEPRESSION SHOWS SIGNS OF  
IMPAIRED COGNITION IN TOUCHSCREEN TASK

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Major depressive disorder (MDD) is ranked worldwide as the leading cause of disability, affecting 350 million individuals and their social-economic environment. Cognitive impairments in attention, executive function and memory are often overshadowed by the more burdensome core symptoms of MDD; depressed mood, lack of energy and anhedonia. However, these cognitive symptoms can persist after remission of depressive symptoms and can negatively affect the patient's quality of life. Hence, a valid animal model of depression also displaying cognitive symptoms is vital to optimize pro-cognitive antidepressant treatment and enhance MDD patients' recovery.

We tested the cognitive performance of rats exposed to the chronic mild stress (CMS) paradigm, a valid rodent model of depression. We included rats that were susceptible to CMS and consequently exhibiting the core symptom anhedonia ( $N = 10$ ) and rats displaying resilience towards anhedonia ( $N = 9$ ). Employing the touchscreen operant platform, cognitive testing was conducted with the modified version of the human paired-associates learning task.

We observed a trend for mean number of trials to learn the task,  $F(2,26) = 3.30$ ,  $p = .053$ . Fisher's LSD post-hoc test revealed that non-stressed

controls (N = 10, M = 1307, SD = 556) required fewer trials to accomplish learning than anhedonic (M = 1824, SD = 460) but not resilient rats (M = 1428, SD = 342).

The results suggest impaired cognition in anhedonic rats. They needed more practice to learn the task. Hence, susceptible CMS-exposed rats, which are cognitively phenotyped with the touchscreen task, introduce a potential model for testing pro-cognitive antidepressant treatment.

CH.45 Kristian  
Wemmelund

#### FLUID THERAPY AND NOREPINEPHRINE ADMINISTRATION MASK THE DECREASE IN LEFT VENTRICULAR PRELOAD INDUCED BY PLEURAL EFFUSION - A PROSPECTIVE RANDOMIZED PORCINE STUDY

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Background: Pleural effusion (PLE) is frequent among critically ill patients and leads to circulatory instability and shock. This requires fluid and vasopressor resuscitation.

Objective: To disclose the impact of fluid therapy and norepinephrine on basic physiologic determinants obtained by ultrasonography during PLE.

Design: Prospective, randomised, laboratory study.

Subjects: Piglets (21.9±1.3 kg).

Intervention: PLE (75 mL/kg) and fluid therapy (n=12), norepinephrine infusion (n=12) or control (n=6).

Main outcome measures: Left ventricular preload, measured as left ventricular end-diastolic area (LVEDA). Indices of basic physiological determinants including inferior vena cava distensibility and invasive pressure-flow measurements. All measured at: baseline, PLE installation, each interventional step and PLE evacuation.

Results: PLE decreased LVEDA, mean arterial pressure and cardiac output (P<0.001), which were reversed by intervention subsequently (P<0.001). LVEDA reached baseline levels after 20 mL/kg fluid (P=0.369) and norepinephrine 0.05 ug/kg/min (P=0.061). Inferior vena cava distensibility remained stable (P≥0.085) besides after PLE evacuation in the control group, which was accompanied by a LVEDA increase (P≤0.006).

Conclusion: PLE reduced left ventricular preload. Both fluid therapy and low norepinephrine infusion rates reverted this preload decrease and normalised most other frequently measured haemodynamic parameters. Inferior vena cava distensibility was unreflective. The haemodynamic

significance of PLE may thus be underestimated and falsely attributed to hypovolaemia or vasodilatation that leads to unwarranted fluid or norepinephrine therapy and mask basic physiology.

CH.46 Kousik Sarathy  
Sridharan TREATMENT EFFECTS ON CONNECTIVITY BETWEEN MOTOR CORTEX  
AND FOREARM MUSCLE IN PARKINSON'S DISEASE PATIENTS

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Introduction: Parkinson's disease (PD) is a neurodegenerative disease, where patients are treated with dopaminergic medication, often at later stages with deep brain stimulation (DBS), to predominantly handle motor symptoms. Though PD patients respond well to both treatments, the effect-mechanisms of these treatments on motor cortex are still not well understood. We used corticomuscular coherence (CMC), a marker of cortico-peripheral functional connectivity, to assess the effects of treatment on cortical motor areas. CMC is variably affected by DBS, while medication has been shown to restore reduced CMC in the beta frequency range (12-30 Hz) in PD patients. We investigated two different tasks involving hand gripping (isotonic contractions) and flexing the wrist backwards (isometric contractions).

Methods: We recorded magnetoencephalography (MEG) and peripheral EMG from the extensor digitorum communis muscle in 5 PD patients while they performed isometric and isotonic contractions over both treatments. We calculated the CMC maxima in the beta range in the sensors over the motor cortex in both tasks.

Results: We observed similar trends in beta-CMC in both tasks with DBS ON, leading to diminished beta-CMC and dopaminergic medication leading to increased beta-CMC. The peak frequency of the beta-CMC seemed to shift to higher frequencies in the beta range (25-30 Hz) during the isotonic, more demanding, task (hand grips) compared to the isometric task (wrist flexed backwards, 18-23 Hz).

Discussion: These preliminary results seem to suggest that DBS and dopaminergic medication influence cortico-muscular connectivity differently, suggesting different effect mechanisms.

CH.47 Esben Næser  
PROBABABILITY OF CANCER FOR ROUTINE BLOOD TESTS AMONG  
PATIENTS REFERRED WITH NON-SPECIFIC, SERIOUS SYMPTOMS

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**Background:** An urgent referral pathway for patients with non-specific, serious symptoms was developed and implemented at Silkeborg Regional Hospital in 2009 and subsequently implemented throughout Denmark in 2011-2012. As part of the diagnostic workup, all referred patients are examined by a blood test panel. In this study, we analysed the post-test probability of the blood test panel in the diagnosis of cancer for patients referred by their general practitioner (GP) to the urgent referral pathway.

**Method:** We performed a cohort study including all patients aged 18 years or older who were referred by their GP to a panel of blood tests at Silkeborg Regional Hospital. All patients were followed for three months for a cancer diagnosis in the Danish Cancer Registry. The likelihood ratio and post-test probability of subsequent cancer were calculated in relation to abnormal blood test results.

**Results:** Among the 1499 patients included in the study, 12.2% were subsequently diagnosed with cancer. The probability of cancer increased with growing numbers of abnormal blood tests. Combinations of two abnormal blood tests had a 23%-62% probability of cancer. Only a few single abnormal blood tests had a high post-test probability of cancer, and most were unspecific to cancer.

**Conclusions:** A number of specific abnormal blood tests and combinations of abnormal blood tests increased the probability of cancer markedly. Still, abnormal blood test results should be interpreted with caution as most are non-specific to cancer. Thus, results from the blood test panel may strengthen the suspicion of cancer but cannot rule out cancer.

CH.48 Ellen Marie Høye CORRECTING FOR LINEAR ENERGY TRANSFER DEPENDENT QUENCHING IN RADIOCHROMIC THREE-DIMENSIONAL DOSIMETRY OF PROTON THERAPY

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Radiochromic 3D dosimetry has potential to become a useful tool for verification of proton therapy (PT). Linear energy transfer (LET)

dependent quenching of the signal in the Bragg peak (BP) results in an under-response of the dosimeter. In this study, we investigate whether the quenching can be corrected by adjusting the measured 3D optical density (OD) distribution using a calibration model generated from a Monte Carlo (MC) simulation and a calibration dosimeter.

A 3D dosimeter was irradiated with three spatially separated, unmodulated 60 MeV proton beams ( $\varnothing$  10 mm collimator), to plateau doses of 5, 10 and 20 Gy. The change in OD caused by the radiation was found by read-out in an optical CT scanner. MC simulation of  $10^8$  protons gave the dose and dose-averaged LET (dLET) distributions. A calibration model with respect to dose and dLET was generated from the 5 and 20 Gy BPs: Linear fits to OD as a function of dose was computed for all voxels within limited ranges in dLET. Voxels in the 10 Gy BP were calibrated using these variables and compared to the MC simulated dose.

Quenching results in a lower dose response in the BP of the proton beam ( $0.013 \text{ cm}^{-1}\text{Gy}^{-1}$ ) compared to the low-LET regions, such as the plateau ( $0.027 \text{ cm}^{-1}\text{Gy}^{-1}$ ). Good agreement between the calibrated signal and the MC simulated dose was found in the central part of the beam, but was less good towards the edges, where the MC beam model was suboptimal. Dose errors larger than 5% of maximum dose (2.7 Gy) was found in 3.5% of all calibrated voxels.

We present the first LET-corrected 3D dose measurements in a dosimeter for proton therapy, showing that verification for single fields has been made possible.

CH.49 Jenny Bertholet VALIDATION OF A FULLY AUTOMATIC REAL-TIME LIVER MOTION MONITORING METHOD ON A CONVENTIONAL LINAC

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Intrafraction motion is a challenge for accurate liver radiotherapy delivery. Real-time treatment adaptation may mitigate the detrimental effects of motion, but it requires reliable target motion monitoring. In this study, we develop and validate a framework for fully automatic monitoring of thoracic and abdominal tumors on a conventional linac by combining real-time marker segmentation in kV images with internal position estimation by an external correlation model (ECM). A pre-treatment CBCT is acquired with simultaneous recording of the motion of an external block on the abdomen. The 3D marker motion was estimated from the 2D projections and used to optimize an ECM of the internal marker motion  $\text{INT}(t)$  as a function of the external motion  $\text{EXT}(t)$ . During treatment,  $\text{INT}(t)$  is estimated from  $\text{EXT}(t)$ , while kV images are

acquired every 3s. The markers are segmented in real-time to update the ECM. The method was validated using internal and external motion recorded from 10 liver SBRT patients. The validation included both experiments with a programmable motion stage and simulations hereof for the first patient as well as simulations for the remaining patients. The real-time estimated 3D motion was compared to the known tumor motion. For comparison, the position estimation error was also calculated without ECM updates. The simulations agreed with the experimental root-mean-square error (rmse) within 0.4 mm. For all patients, the mean 3D rmse was 1.74 mm and 2.47 mm with and without ECM updates, respectively. The method is fully automatic and can be used for arbitrarily shaped fiducial markers in the thorax or abdomen on a conventional linac without additional time or hardware.

CH.50 Mathilde Borg  
Houlberg  
Thomsen

COMPREHENSIVE GENOMIC AND TRANSCRIPTOMIC  
CHARACTERIZATION OF HETEROGENEITY IN ADVANCED BLADDER  
CANCER BY MULTIREGIONAL ANALYSIS

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Background: Bladder cancer has the highest mutational load, only preceded by melanomas and lung cancer. Thus, it is speculated to be a highly heterogeneous disease, which may have huge implications on therapy response. Further, it is highly recurrent and often multifocal, which is proposed to be due to the presence of transformed fields in the urothelium.

Methods: Multiple tumors, lymph node metastasis, relapse biopsies and adjacent normal tissue from 4 patients with muscle invasive disease were analyzed. A targeted panel (illumina TruSeq Custom Amplicon v1.5) was designed from whole exome sequencing of bulk tumor DNA and germline DNA. Targeted sequencing was applied on 141 small cellular regions procured by laser-microdissection (LMD) from each tumor biopsy as well as adjacent normal biopsies generating a comprehensive genomic map of the bladder. Transcriptomic profiling (Fluidigm GE) was carried out using RNA from LMD procured regions matching the regions used for targeted sequencing.

Results: Preliminary results show varying degrees of intratumor heterogeneity at the genomic level in the four patients. Heterogeneity appears reflected at the transcriptomic level with evidence of different subclones. We identified 95, 380, 117 and 335 variants estimated to have a functional impact with 8, 14, 9, and 16 potential disease drivers in the 4 patients, respectively. Different disease drivers were clonal and

subclonal, and all tumors from individual patients were of monoclonal origin. The lymph node metastasis and local relapse samples showed gains of additional genomic variants. Ongoing mapping of the field disease indicates mutations in tumor suppressor genes.

CH.51 Jakob Toftegaard AN EXPERIMENTALLY VALIDATED COUCH AND MLC TRACKING SIMULATOR USED TO INVESTIGATE HYBRID COUCH-MLC TRACKING

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Purpose: Couch and MLC tracking are two novel techniques to mitigate intrafractional tumor motion on a conventional linear accelerator, but both techniques still have residual dosimetric errors. Here, we propose and experimentally validate a software tool to simulate couch and MLC tracking, and use the simulator to study hybrid couch-MLC tracking.

Materials and methods: The tracking simulator simulates the treatment plan delivery to a moving target. A series of couch and MLC tracking experiments were used to determine dynamic parameters for the simulator and to validate its tracking accuracy. All hybrid couch-MLC strategies divided the target motion into motion perpendicular and parallel to the MLC leaves. Couch tracking compensated for the following target motion: 1) all perpendicular motion, 2) residual perpendicular motion less than half a leaf width, and 3) persistent residual perpendicular motion. MLC tracking compensated for the remaining target motion. All strategies were tested for a combination of lung and prostate treatment plans and motion trajectories.

Results: The tracking simulator reproduces the experiments very well, both with regard to geometrical and dosimetric accuracy. All hybrid tracking strategies reduced the couch motion relative to pure couch tracking and improved the tracking accuracy compared with pure MLC tracking. For both lung and prostate motion, the tracking accuracy was best with hybrid tracking strategy 1).

Conclusion: A couch and MLC tracking simulator was developed and experimentally validated against a series of tracking experiments. All hybrid couch-MLC tracking strategies improved MLC tracking. Two strategies also improved couch tracking.

CH.52 Jacob Kinggaard RADIOSENSITIVITY IN OROPHARYNGEAL CANCER PATIENT-DERIVED Lilja-Fischer XENOGRAFTS

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Objective: Oropharyngeal squamous cell carcinoma (OPSCC) is now the most common type of head and neck cancer. The prognosis depends on tobacco smoking and HPV status.

Personalization of treatment is needed, which is the focus of ongoing clinical trials. However, adequate pre-clinical models are lacking.

The purpose of this study was 1) to create a number of patient-derived xenografts (PDX) reflecting the heterogeneity of OPSCC, 2) to compare the models with the corresponding original human tumors, and 3) to determine if radiosensitivity in the PDX model reflects the empirical findings.

Methods: PDX tumors were generated by implanting fresh tumor biopsies from patients with OPSCC into immunodeficient mice.

Xenograft tumors and human originals were compared using histology and immunohistochemistry. To characterize radiosensitivity, PDX tumors were subjected to low-dose irradiation in a growth delay assay (4-8 Gy, single fraction).

Results: Tumor biopsies from 26 OPSCC patients have been xenografted resulting in PDX growth in 15 cases (58%, 5 still awaiting evaluation). PDX models were established from OPSCC patients with HPV-positive and HIV-negative disease as well as a wide range of tobacco exposure. Most PDX tumors retained the histological appearance of squamous cell carcinoma and immunoprofile of the original tumor. Other tumors adopted a lymphoproliferative appearance. Low-dose irradiation of PDX tumors resulted in a reproducible growth delay.

Conclusion: It is possible to generate PDX models that represent the clinical heterogeneity of disease with a satisfactory success rate. Most PDX models retain the characteristics of the original tumor. The PDX model is suitable for radiotherapy research.

CH.53 Line M Hybel  
Schack

#### THE DANISH RADIOGENOMICS STUDY

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Purpose and objective: Radiotherapy (RT) provides an important means of anti-cancer treatment. It is estimated that half of all cancer patients in Europe can benefit from RT, either in a curative or a palliative setting. The curative potential of RT is highly dependent on the total dose delivered to the tumour. This total dose is limited by radiation-induced morbidity from the normal tissues surrounding the tumour. The extent of radiation-induced morbidity from the normal tissues varies with RT-related factors and with patient-related factors. A growing body of evidence points to normal variants in the genetic code as being one important patient-related factor. In this study, we aim to analyse normal genetic markers in patients with good scoring of radiation-induced morbidity following RT.

Material and methods: In two cohorts of 1221 head and neck cancer patients and 1208 breast cancer patients treated with RT with curative intent, we performed a genome-wide association analysis. Clinical endpoints on radiation-induced morbidity were provided by the Danish Head and Neck Cancer Group (DAHANCA) and the Danish Breast Cancer Cooperative Group (DBCG). DNA from buffycoats is genotyped on the Infinium OncoArray-500K BeadChip from Illumina. Imputation will be based on data from the 1000 Genomes Project, and data will be analysed using R Statistical Package and SNPTEST.

Results: Biological material is currently being genotyped. We expect preliminary results by mid-January 2017.

Perspectives: This study has the perspective to elucidate to what extent an unexplained variability in radiation-induced morbidity can be associated with normal genetic markers.

CH.54 Christian Andreas Hvid CONE BEAM CT-BASED APPROACH TO ADAPTIVE RADIOTHERAPY IN HEAD AND NECK CANCER

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Background: Radiation therapy (RT) is the most commonly used treatment for head and neck cancer (HNC). High local control rates are achieved at the cost of substantial side effects, including xerostomia and dysphagia. Advances in RT, including intensity modulated RT, have decreased morbidity, but these does not take into account the anatomical changes which can arise during the 5-6 weeks of treatment. These changes can cause increased dose to the parotid glands, which increases the risk of xerostomia. Currently, plan concordance with patient anatomy is checked once during treatment with a mid-course CT scan with plan adaptation in case of insufficient target coverage or overdose to critical normal tissue.

We propose a novel approach to adaptive RT, using cone beam CT monitoring instead of midcourse CT and including parotid glands when considering plan adaptation.

Materials and methods: In total, 50 consecutive patients entering curatively intended RT for NHC will be included. At RT plan approval, patients will be assigned a xerostomia risk level based on planned dose to the parotid glands. Patients for whom xerostomia is deemed unavoidable, or for whom the risk is very low, will have one midcourse cone beam check performed. Patients in intermediate/high risk of xerostomia will have weekly cone beam checks. In addition to target coverage and critical normal tissue overdose, a parotid gland dose increase of >2 Gy will prompt renewed CT scan and plan adaptation.

Results: Primary endpoint is spared parotid gland dose when comparing summed delivered dose with planned dose. Secondary endpoints are number of cancelled midcourse CT scans and time consumption of the new approach. Results are pending.

CH.55    Henriette Ejlsmark    DETERMINANTS OF BONE MICROARCHITECTURE IN THE GERIATRIC  
          Svensson                    POPULATION

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Introduction: Fragility fractures among elderly are a social and economic burden. The role of bone geometry and microarchitecture in the pathogenesis of fragility fractures has been recognised. Few studies have investigated determinants of bone microarchitecture in the geriatric population. To reduce the fracture rate, it is imperative to acknowledge determinants that are important for bone structure.

Aim: To assess determinants of bone microarchitecture in the geriatric population in aged-care facilities.

Design: A cross-sectional study including 87 participants (59% female) from 60 different aged-care facilities in Melbourne enrolled in the "Dairy and Fracture Trial".

Methods: Two days of dietary assessment with the nutritional method 'visual estimation of plate waste' was performed. Radius and tibia were scanned using high resolution peripheral quantitative computer tomography. A linear regression model was used to assess determinants for bone microarchitecture.

Results: For radius; significant determinants for trabecular separation were sex ( $p < 0.001$ ), BMI ( $p = 0.001$ ) and the use of thiazides ( $p = 0.034$ ), for trabecular thickness were BMI ( $p = 0.0026$ ) and the use of thiazides (0.015), for cortical porosity were sex ( $P < 0.001$ ) and vitamin-D suppl. ( $p = 0.011$ ). For tibia; significant determinants for trabecular separation,

trabecular number and trabecular bone volume were sex, BMI and dairy serves per day.

Conclusion: In the very old, bone geometry and structure is modified by the use of vitamin-D suppl., dairy intake, BMI, and the use of thiazides. Whether these indices also affect fracture risk needs to be further studied.

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