

PHD DAY

HEALTH

PROGRAMME & ABSTRACTS

26 JANUARY 2018



AARHUS
UNIVERSITY

PHD DAY 2018 PROGRAMME

LOCATION: THE LAKESIDE LECTURE THEATRES

26 JANUARY 2018

- 8.30 **Welcome by the Dean**
Lars Bo Nielsen, Dean, The Faculty of Health, Aarhus University
- 8.40 **Welcome and presentation of the programme by the chairman of the PHD Association**
Iben Bach Damgaard, PhD student, Chairman of the PhD Association, Health, AU
- 8.50 **“Believe in Science”, keynote lecture**
*Charles A. Dinarello, Professor of Medicine and Immunology at the University of Colorado School of Medicine, and Professor of Experimental Medicine at Radboud University in the Netherlands.
Introduced by Helene Nørrelund, Head of the Graduate School, Health, AU*
- 09.50 **Coffee/tea and fruit break**
- 10.15 **Poster presentations**
The Lakeside Lecture Theatres, the Bartholin Building (build. 1241) and Anatomy (build. 1230)
- 11.45 **Lunch /poster viewing**
The Lakeside Lecture Theatres, the Bartholin Building (build. 1241) and Anatomy (build. 1230)
- 12.30 **Oral presentations**
The Lakeside Lecture Theatres and the Bartholin Building (build. 1241)
- 14.00 **Break**
- 14.15 **“Believe in Science”, keynote lecture**
*Joseph Stephen Alpert, American cardiologist and professor of medicine at the University of Arizona Sarver Heart Center and editor-in-chief of the American Journal of Medicine.
Introduced by Helene Nørrelund, Head of the Graduate School, Health, AU*
- 15.15 **Coffee/tea and cake break**
- 15.40 **Fogh-Nielsen Competition**
Chaired by Professor Søren K. Moestrup, Chairman of the Fogh-Nielsen board and co-chairman Rasmus Pihl, PhD student, Health, AU
- 16.25 **Awards, Posters and oral presentations**
Professor, Bent Winding Deleuran and PhD student, Rasmus Pihl, Chair and Co-chair of the Organizing Committee, PhD Day 2018
- 16.35 **Closing remarks**
Helene Nørrelund, Head of the Graduate School, Health, AU
- 16.40 **The programme for the day ends**
-
- 18.30 **Dinner and awards ceremony for the JCD prize and the Fogh-Nielsen Competition**
Centralværkstedet; Aarhus C.
Festive speech
Pil Lindgreen, PhD student, Health, AU

Aarhus University
Graduate School of Health

PHD DAY
26 JANUARY 2018



Practical Information

- Posters should be hung up between 16:30 and 19:00 on 25 January or between 7:30 and 8:00 on 26 January. Posters may be removed from 12:30 on 26 January 2018. Posters that have not been removed at 15.15 will be placed near the reception desk in The Lakeside Lecture Theatres and can be collected after conclusion of the scientific programme of the PhD day
- Oral presenters for sessions O1-O5 must meet in the auditorium concerned between 7:30 and 8:00 on 26 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, (building: 1240-1241) Auditorium 2, 3, 4, Studyroom, Gardenroom, room 130 and halls

Poster session 23-29: Anatomy, (building 1230-1231): Hall and Colloquium room 1

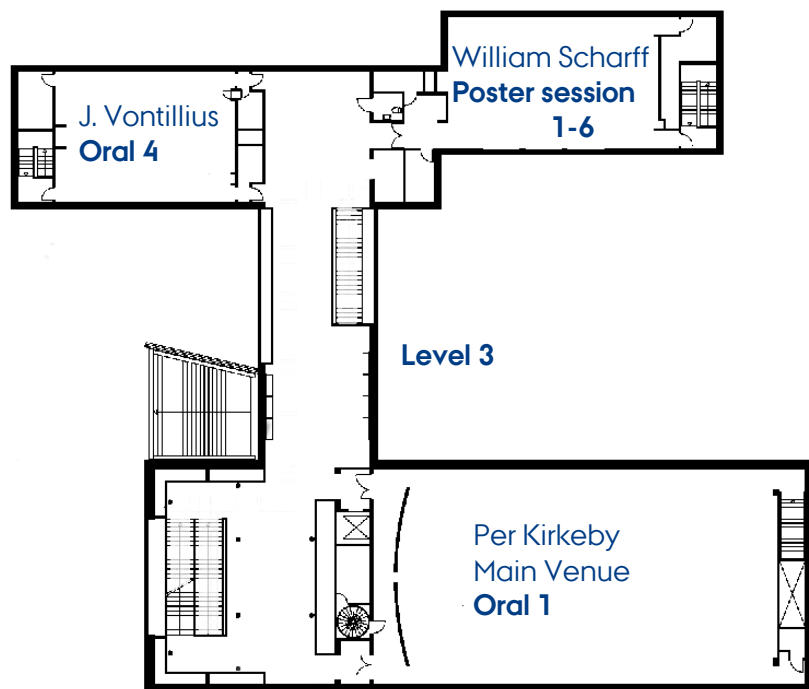
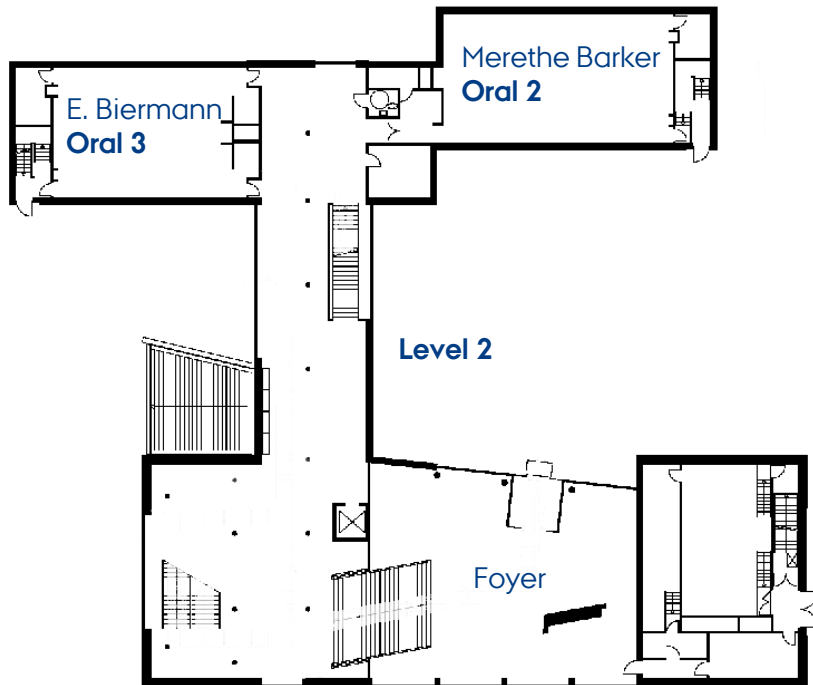
Organizing committee for PhD Day 2018:

- *Bent Deleuran, Professor, Department of Biomedicine, Chairman*
- *Rasmus Pihl, PhD student, Department of Biomedicine, Co-chairman*
- *Helle Møller, PhD Administration*
- *Johan Palmfeldt, Associate professor, Department of Clinical Medicine*
- *Khoa Manh Dinh, PhD student, Department of Clinical Medicine*
- *Louise Hauge Matzen, Associate professor, Department of Dentistry and Oral Health*
- *Martin Nors Skov, PhD student, Department of Clinical Medicine*
- *Pernille Thomasen, PhD student, Department of Biomedicine*
- *Rasmus Bysted Møller, Assistant professor, Department of Public Health - Sport Science*
- *Sashia Bak-Nielsen, PhD student, Department of Clinical Medicine*
- *Simin Berenji Ardestani, PhD student, Department of Clinical Medicine*
- *Stine Andersen, PhD student, Department of Clinical Medicine*
- *Terkel Rørkær Sigh, PhD Administration*
- *Trine Wigh Arildskov, PhD student, Department of Clinical Medicine*
- *Ulla Kampmann Opstrup, Postdoc, Department of Clinical Medicine*

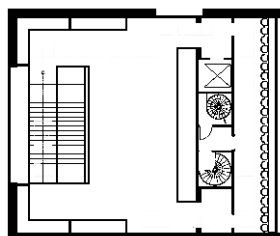
Social media:

- Facebook: PhD Association Health
- Instagram: #auhealthphdday

Lakeside Lecture Theatres



Level 4



Bartholin Building (building: 1240/1241)

- Oral 5
- Poster session 7-22

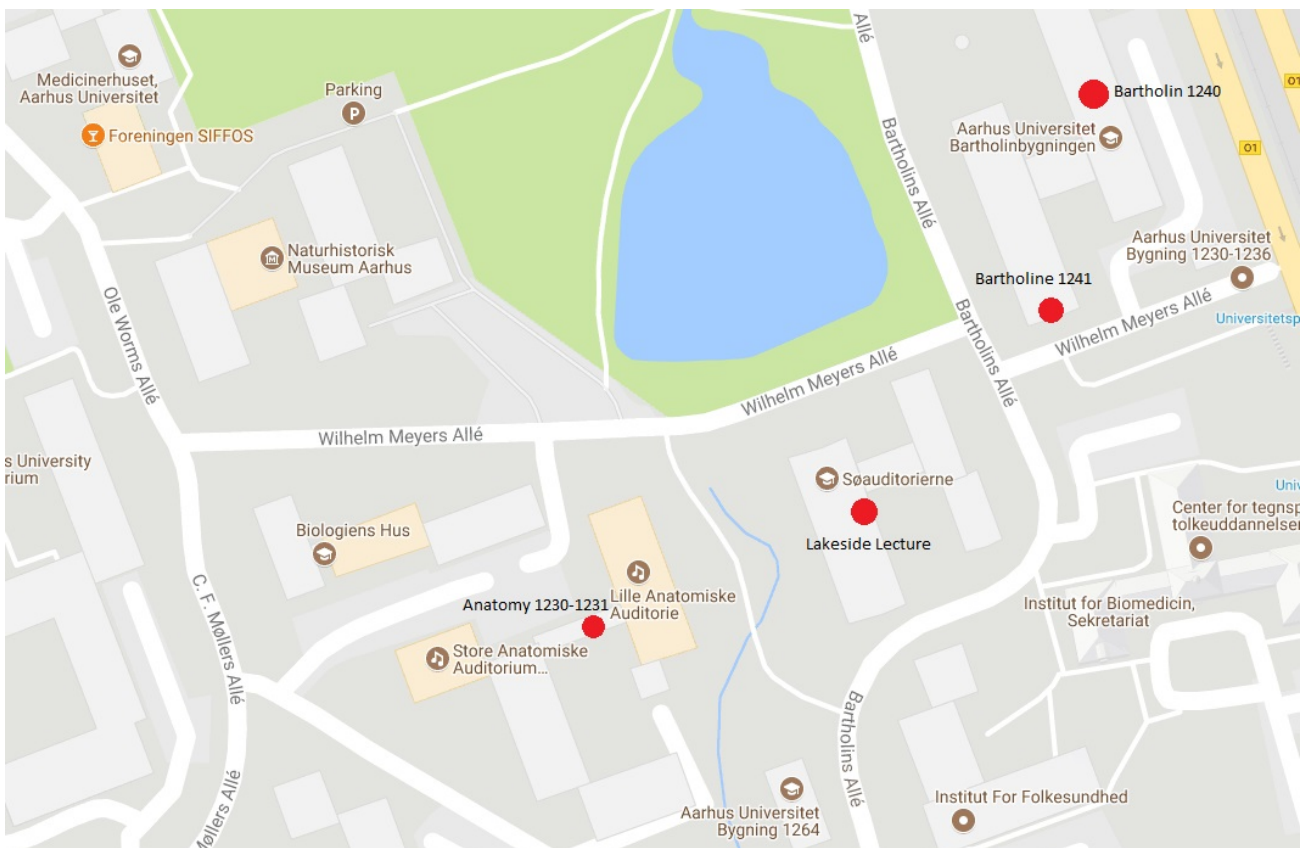
Anatomy (building 1230/1231)

- Poster session 23-29

Practical Information

Session overview:

- Oral session 1:** Lakeside Lecture Theatres, **Per Kirkeby Auditorium**
- Oral session 2:** Lakeside Lecture Theatres, **Merethe Barker Auditorium**
- Oral session 3:** Lakeside Lecture Theatres, **Eduard Biermann Auditorium**
- Oral session 4:** Lakeside Lecture Theatres, **Jeppe Vontilius Auditorium**
- Oral session 5:** Bartholin building (building: 1241/135), **Auditorium 1**
-
- Poster session 1-6:** Lakeside Lecture Theatres, **William Scharff Auditorium**
- Poster session 7-11:** Bartholin building, (building: 1241/211), **Studyroom**, (First floor)
- Poster session 12:** Bartholin building, (building: 1241/231), **Gardenroom**, (First floor)
- Poster session 13:** Bartholin building, (building: 1240-41), **Hall** (First floor)
- Poster session 14-15:** Bartholin building, (building: 1241/125+129), **Auditorium 2**
- Poster session 16-17:** Bartholin building, (building: 1241/119), **Auditorium 3**
- Poster session 18-19:** Bartholin building, (building: 1241/114), **Auditorium 4**
- Poster session 20-21:** Bartholin building, (building: 1240-41), **Hall** (Ground floor, at Aud.1)
- Poster session 22:** Bartholin building, (building: 1240-41), **Room 130** (Ground floor)
-
- Poster session 23-26:** Anatomy (building 1231/114), **Colloquium room 1**
- Poster session 27-29:** Anatomy (building 1230), **Hall**



Believe in Science

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 2018

You are invited to enjoy five oral and 29 poster sessions as well as the Fogh Nielsen Competition. This year's topic aims to inspire you to venture outside your comfort zone in pursuit of new insights within your research field. By balancing Methodological rigor with creative imagination, you are encouraged to make all of us *believe in science* by opening new pathways to better treatment.

This year we have two keynote speakers: Professor Charles A. Dinarello from University of Colorado, USA and Radboud University in the Netherlands and Professor Joseph S. Alpert from University of Arizona, USA.

Charles A. Dinarello will give you an outstanding perspective on how groundbreaking scientific discoveries can be put into valuable therapeutic use. He is considered one of the founding fathers of cytokines and has -received numerous awards and prizes for his contribution to the field of cytokines and medicine. He is regarded as one of the most influential biomedical researchers of our time and has been granted honorary degrees from various Universities around the world.

Joseph S. Alpert is a Danish-American cardiologist and editor-in-chief of the American Journal of Medicine. He is an honorary member of scientific societies in Denmark, Israel and Argentina and has received many awards for excellence in teaching. Prepare for a thrilling lecture on the importance of science in today's society.

By the end of the day we hope that our firm belief in science have been passionately revitalized by the new original ideas and perspectives presented.

Finally, a warm thank you to everybody who has participated and helped to make the PhD day 2018 a – hopefully – joyful and inspiring event.

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

Rasmus Pihl, PhD student
Co-Chairman of the Organizing Committee
Health, Aarhus University

Lars Bo Nielsen
Dean
Health, Aarhus University

Lise Wogensen Bach
Vice-dean
Health, Aarhus University

Helene Nørrelund
Head of Graduate School
Health, Aarhus University

The Keynote Lecture

Charles A. Dinarello, Professor of Medicine and Immunology



Charles A. Dinarello is Professor of Medicine and Immunology at the University of Colorado School of Medicine and Professor of Experimental Medicine at Radboud University in the Netherlands. He received his medical degree from Yale University, clinical training at the Massachusetts General Hospital and from 1971-77, he was at the National Institutes of Health in Bethesda. Dr. Dinarello is considered one of the founding fathers of cytokines. He was the first to purify interleukin-1 (IL-1) in 1977 and identified IL-1 in 1974. His group reported the first cDNA for IL-1 in 1984. He has published over 700 original research articles and 250 reviews and book

chapters on inflammatory cytokines, particularly on IL-1, the IL-1 family and related cytokines. He has trained over 50 investigators, many of whom are recognized experts in their fields. The Institute for Scientific Information listed Dinarello as the world's 4th most-cited scientist during the 20 years 1983-2002 and from 1996 to 2011, he was listed as one of 400 of the world's most influential biomedical researchers.

In 1998, Dinarello was elected to the United States National Academy of Sciences and in 2010, he was made a foreign member of the Royal Netherlands Academy of Sciences. He is a member of the Board of Governors of the Weizmann Institute (Israel) and Ben Gurion University (Israel). Dinarello has received honorary degrees from the University of Marseille (France), the Weizmann Institute (Israel), the University of Frankfurt (Germany) and Roosevelt University (USA), Albany Medical College (USA), Radboud University (Netherlands) and Trinity College (Ireland), University of Bonn (Germany) and Aarhus University (Denmark).

For his contributions to the field of cytokines and medicine, he received the Squibb Award (USA), Ernst Jung Prize in Medicine (Germany), Gold Medal of the Heilmeyer Society for Internal Medicine (Germany), Chirone Prize (Italian National Academy of Medicine), Carol Nachman Prize (Germany), Sheikh Hamdan bin Rashid al Maktoum Award (United Arab Emirates), Beering Prize (USA), Albany Prize in Medical Research (USA), Crafoord Prize of the Royal Swedish Academy of Sciences (Sweden), Paul Ehrlich Prize (Germany), Bonfils-Stanton Prize (USA), the Novartis Prize in Clinical Immunology (Switzerland), the Bonazinga Award (USA) and Drexel Prize in Immunology (USA). Dinarello received the Lifetime Achievement Award of the Eicosanoid Foundation for his pioneering studies on the role of lipids in cytokine-mediated inflammation. In 2017, Dinarello was awarded the Meinhard von Pflaundler Medal, Ludwig Maximilian University (Germany) and the Cerami Prize (USA). Dr. Dinarello donates the monies from his awards and prizes to The Interleukin Foundation, a charitable foundation he established in 2009, which supports research on cytokines, particularly to young investigators.

The Keynote Lecture

Dr. Joseph S. Alpert, Professor of Medicine



Dr. Alpert is Professor of Medicine in the Department of Medicine at the University of Arizona (UA).

Board-certified in internal medicine and cardiovascular disease, Dr. Alpert has received many awards for excellence in teaching from, among others, the Peter Bent Brigham Hospital, the United States Navy, the University of Massachusetts, and the University of Arizona. In 2004, he received the Gifted Teacher Award from the American College of Cardiology (ACC). Dr. Alpert is a past chairman of the Council on Clinical Cardiology of the American Heart Association from which he received the Distinguished Achievement Award in 2001.

He is a master of the American College of Physicians and a fellow of the Council on Clinical Cardiology of the American Heart Association, the American College of Cardiology (ACC), the American College of Chest Physicians, and the European Society of Cardiology.

He is an honorary member of the Danish Cardiovascular Society, the Israeli Heart Society, and the Argentina Cardiology Association. He has served on many national and international committees of professional organizations and is a former member of the Board of Trustees of the ACC and the Board of Directors of the American Board of Internal Medicine. He is a current member of the Board of Trustees of the Association of Professors of Medicine. His research interests are wide and varied and he has served as principal investigator, steering committee member, and data safety and monitoring committee member and chairman for many clinical trials.

Dr. Alpert is the former editor of the journals *Cardiology*, *Current Cardiology Reports*, and *Cardiology in Review*. He is the current editor-in-chief of *The American Journal of Medicine* ("the Green Journal"), a member of the editorial boards of 12 cardiovascular journals, and an editorial reviewer for 15 internal medicine and cardiovascular disease journals. He has authored or edited 50 books and monographs, and more than 700 publications including original articles, book chapters, reviews, and editorials, as well as many abstracts.

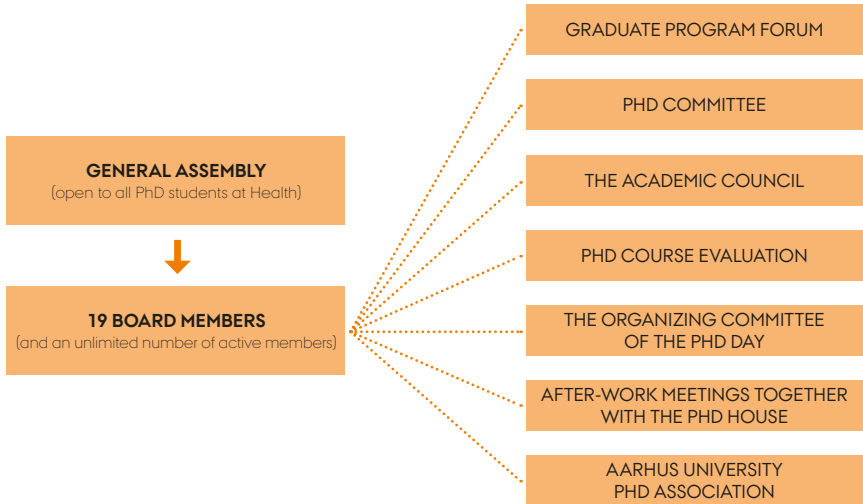


AARHUS UNIVERSITY

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

ALL PHD STUDENTS CAN JOIN!

**Working
hard
for you!**



NorDoc

is going to launch its

2nd Nordic Summit for Doctoral Students

at the

University of Helsinki, Finland, 23-24th August 2018

Find more information about the Summit **very soon** at the NorDoc website:

<https://www.nordochealth.net/>

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.

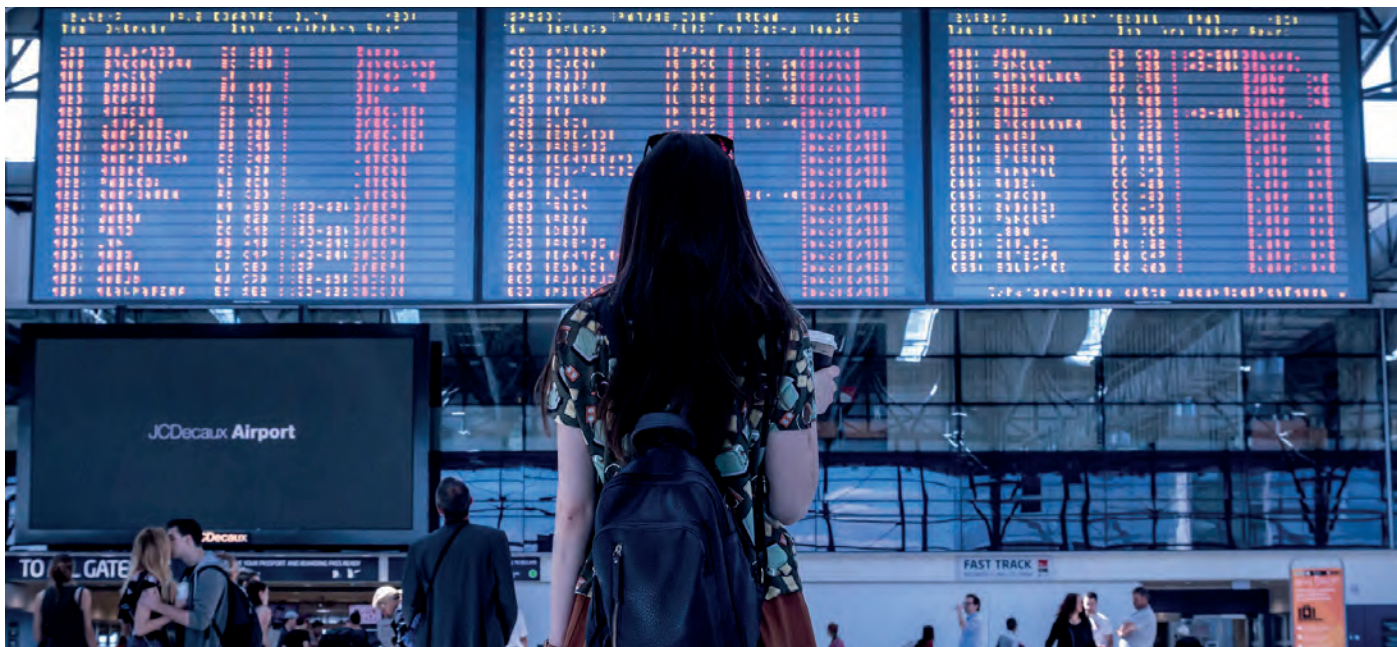
You are always welcome to contact the PhD student counsellor!

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



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OFFICE OF INTERNATIONAL RELATIONS

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

The core activities of the Office of International Relations include:

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

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

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

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



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Dean's Office

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Ph.D. Career Consultant
Phone: +45 2942 6029
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 talent.au.dk/career

Jane Midtgaard Madsen

Ph.D. Career Counsellor
Phone: +45 5122 6880
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 facebook.com/AUCareerPhDandJR

AU CAREER
PHD & JR

Graduate School of Health



To take place on

5th October 2018

at Aarhus University Hospital, Skejby

(an a preparatory event the day before)

Two tracks

A. Challenges

You solve a defined
challenge from a company

B. Innovative Ideas

You propose your idea to
investors

We offer you efforts and ideas and the opportunity to meet like-minded colleagues and start new collaborations.

Registration opens in spring 2018



DO YOU NEED FUNDING FOR YOUR RESEARCH?

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

www.au.dk/fse

Here you can:

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

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



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AU Health PhD Day
#auhealthphdday



Find Us On
Instagram

Dear PhD student

Do you know your PhD association?
And do you know why you need it?
In the PhD associations, we are ourselves PhD students. And we deal with the problems and questions that we meet ourselves - and the ones that you bring up.

For example, we:

- discuss rules and potential changes with the PhD school leaders
- try to create stronger PhD student networks at AU
- address issues such as stress, loneliness, and work/life balance
- are represented in boards that influence the PhD studies
- put awareness on specific topics like teaching duties, integration of international PhD students, finances, and courses

Check out your local association on Facebook:

ARTS:

 ARTS PhD Network

BSS:

 PHABUSS

HEALTH:

 PhD Association Health

ST:

 PHAUST

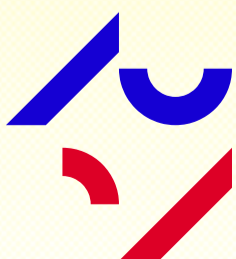
And visit us at:

 AUPA

or

www.phd.au.dk/aupa/

Love,
AUPA



AUPA
Aarhus University PhD Association

PhD Day 2018

Believe in Science

Do you dare to formulate bold research questions and hypotheses? Are you willing to challenge yourself and your research community in pursuit of new insights? Is the research community ready for you and your ideas?

These questions are in focus during the PhD Day 2018.

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 2018 is: *Believe in Science*.

The quest for excellence within the scientific community begins with a firm belief in your own research. This belief is displayed by methodology, as well as by creative imagination, and collectively by a supportive, yet critical dialog. It is also displayed by your passion for gaining novel knowledge within your research field, leading to new and better treatment options.

However, in a world of “alternative facts”, evidence alone no longer have the same weight and impact. It has therefore become increasingly important that we continue to *believe in science* as the road to human progress.

Within this framework, the PhD day offers lectures by international key note speakers and gives PhD and Research Year Students a great opportunity to present their research through oral or poster presentations, or to co-chair sessions.

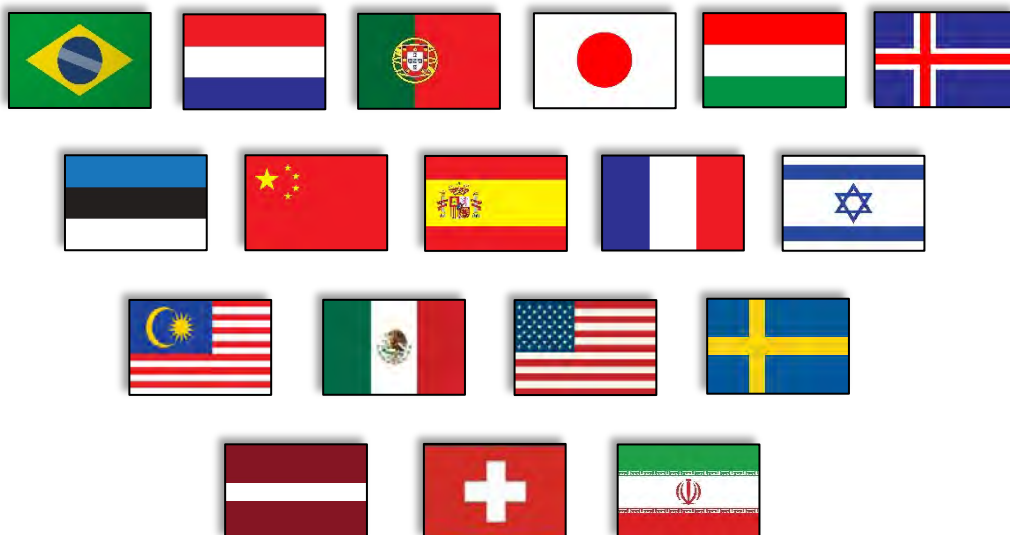
With the theme *believe in science*, the PhD Day 2018 will focus on the scientific achievements with special attention to the originality, perspectives involved, and on the challenge to make the community believe in our science.

Organizing Committee 2018
Health, Aarhus University

PhD Day
2018



We welcome
all our PhD students to the
PhD Day 2018



Session chairmen

Fogh-Nielsen Competition	Søren Kragh Moestrup & Rasmus Pihl (PhD student)
O1	Christian Holm, Hans Jürgen Hoffmann, Willemijn Comuth (PhD student) & Mikkel Carstensen Gjelstrup (PhD student)
O2	Therese Ovesen, Marina Romero-Ramos, Line Thorndal Moll (PhD student) & Velma Aho (PhD student)
O3	Michael R. Horsman, Jacob Giehm Mikkelsen & Steffen Nielsen (PhD student)
O4	Ebba Nexø, Vibeke Hjortdal & Farhad Waziri (PhD student)
O5	Cecilia Høst Ramlau-Hansen, Niels Uldbjerger, Ditte H. Jensen (PhD student) & Caroline Mejdahl (PhD student)
P1	Tue Wenzel Kragstrup, Sarah Fogh (PhD student) & Lise Sofie Bislev (PhD student)
P2	Tove Christensen, Allan Kjeldsen Hansen (PhD student) & Andrey Chuhutin (PhD student)
P3	Agnete Larsen, Ida Hovdenak Jakobsen (PhD student) & Iben Lyskjær (PhD student)
P4	Dorte Rytter, Daniel Ramskov Jørgensen (PhD student) & Martin Lund (PhD student)
P5	Henrik Kolstad, Nini Nørgaard (PhD student) & Niels Lyhne Christensen (PhD student)
P6	Peter Bross, Casper Sæbye (PhD student) & Mette Holm Hjorth (PhD student)
P7	Vladimir Matchkov & Niels Dalsgaard Nielsen (PhD student)
P8	Hatice Tankisi, Bente Skovsby Toft (PhD student) & Carsten Gleesborg (PhD student)
P9	Henrik Sørensen, Peter Lykke Eriksen (PhD student) & Ole Adrian Heggli (PhD student)
P10	Kristian Overgaard, Martin Langeskov Christensen (PhD student) & Kamilla Pedersen (PhD student)
P11	Mette Nørgaard, Karen Rokkedal Lausch (PhD student) & Louise Bang Grode (PhD student)
P12	Mette Spliid Ludvigsen, Cecilie Nørby Thisted (PhD student) & Anja Thiede (PhD student)
P13	Anna Starnawska, Karen Busk Nørøxe (PhD student) & Mette-Lise Simonsen (PhD student)

- P14 Vivi Schlünssen & Signe Voigt Lauridsen (PhD student)
- P15 Reimar W. Thomsen, Bawer Jalal Tofiq (PhD student) & Stine Thyssen (PhD student)
- P16 Arne Møller & Luise Aamann (PhD student)
- P17 Axel Forman, Pernille Gabel (PhD student) & Lise Roed Brogaard (PhD student)
- P18 Mette-Lise Simonsen, Anuj Pareek (PhD student) & Jesper Falkesgaard Højen (PhD student)
- P19 Natalya Fedosova, Mads Sørensen Larsen (PhD student) & Karoline Knudsen (PhD student)
- P20 Anders Børglum, Jesper Guldsmid Madsen (PhD student) & Morten Stokholm (PhD student)
- P21 Ulf Simonsen, Jacob Lynge Callesen (PhD student) & Cecilie Ejerskov (PhD student)
- P22 Thomas Reinert, Mats Bue (PhD student) & Kathrine Hald (PhD student)
- P23 Rikke Nørregaard, Marie Vad (PhD student) & Ina Qvist (PhD student)
- P24 Hanne Møller, Casper Kruse (PhD student) & Katrine Fuglsang (PhD student)
- P25 Anders Lade Nielsen, Dmitri Zintchouk (PhD student) & Bo Langhoff Hønge (PhD student)
- P26 Sebastian Frische, Daan Koppens (PhD student) & Jens Hartlev (PhD student)
- P27 Jens Leipziger, Laura Laine Herborg (PhD student) & Jesper Damsgaard (PhD student)
- P28 Robert Fenton, Birgit Rasmussen (PhD student) & Morten Overgaard (PhD student)
- P29 Christian Erikstrup, Steffan Tábori Jensen (PhD student) & Mia Glerup (PhD student)

Session overview

Fogh-Nielsen Competition

Chairmen: Søren Kragh Moestrup & Rasmus Pihl (PhD student)

Linn Håkonsen Arendt. EARLY LIFE EXPOSURES AND GENITAL ANOMALIES IN BOYS: NATIONWIDE COHORT STUDIES IN DENMARK AND SWEDEN

Nichlas Riise Jespersen. MITOCHONDRIAL MODULATION - A NEW CLINICAL TARGET FOR CARDIOPROTECTION?

Marie Maagaard Sørensen. ALTERED RIGHT VENTRICLE MORPHOLOGY AND CONTRACTILE FUNCTION IN SMALL, OPEN VENTRICULAR SEPTAL DEFECTS

Oral session 1

Chairmen: Christian Holm, Hans Jürgen Hoffmann, Willemijn Comuth (PhD student) & Mikkel Carstensen Gjelstrup (PhD student)

- O01.01 Sara Konstantin Nissen. WHOLE EXOME SEQUENCING OF HIV-1 LONG-TERM NON-PROGRESSORS IDENTIFIES RARE VARIANTS IN GENES ENCODING INNATE IMMUNE SENSORS AND SIGNALING MOLECULES
- O01.02 Juan Yuan. ANTI-TUMOR EFFECTS OF HDAC AND DNMT1 INHIBITORS ON MEDULLOBLASTOMA CELLS
- O01.03 Stefanie Luecke. THE INNATE IMMUNE SYSTEM IS ACTIVATED BY CYTOSOLIC DNA IN A LENGTH-DEPENDENT MANNER
- O01.04 Rasmus Pihl. ANALYSIS OF FACTOR D ISOFORMS IN MASP-3-DEFICIENT PATIENTS HIGHLIGHTS THE ROLE OF MASP-3 AS A MATURASE IN THE ALTERNATIVE PATHWAY OF COMPLEMENT
- O01.05 Christian Benner. FINEMAP: ULTRAFAST HIGH-RESOLUTION FINE-MAPPING USING SUMMARY DATA FROM GENOME-WIDE ASSOCIATION STUDIES
- O01.06 Jaakko Keinänen. LOW-GRADE INFLAMMATION IN FIRST-EPIISODE PSYCHOSIS IS DETERMINED BY WAIST CIRCUMFERENCE INCREASE

Oral session 2

Chairmen: Therese Ovesen, Marina Romero-Ramos, Line Thorndal Moll (PhD student) & Velma Aho (PhD student)

- O02.01 Janni Strøm Petersen. FACTORS ASSOCIATED WITH SYMPTOMS OF ANXIETY AND DEPRESSION IN ADULTS UNDERGOING SPINE SURGERY - A SYSTEMATIC INTEGRATIVE REVIEW
- O02.02 Kaj Verner Døssing. THE USE OF ULTRASOUND TO EXCLUDE EXTREMITY FRACTURES IN ADULTS
- O02.03 Kasper Faarkrog Høyer. SEVOFLURANE ANESTHESIA INDUCES HEPATIC AND SKELETAL MUSCLE INSULIN RESISTANCE AND REDUCES GLUCOSE UPTAKE IN THE BRAIN
- O02.04 Peter Lund Ovesen. THE SORTING PROTEIN SORCS1 REGULATES NEURONAL INHIBITION IN THE HIPPOCAMPUS

- O02.05 Gunhild Mo Hansen. SHOULDER FUNCTION AND CONSTRAINT-INDUCED MOVEMENT THERAPY (CIMT)
- O02.06 Sara Buskbjerg Jager. BELIEVE IN SATELLITE GLIAL CELLS' INVOLVEMENT IN NEUROPATHIC PAIN

Oral session 3

Chairmen: Michael R. Horsman, Jacob Giehm Mikkelsen & Steffen Nielsen (PhD student)

- O03.01 Rikke Kaae. E-LEARNING IMPROVES THEORETICAL KNOWLEDGE ON ULTRA-SONOGRAPHY-BASED ASSESSMENT OF UMBILICAL CATHETER PLACEMENT AMONG PEDIATRICIANS
- O03.02 Marie Bill. MAPPING THE CLEC12A EXPRESSION ON MYELOID PROGENITORS IN NORMAL BONE MARROW; IMPLICATIONS FOR UNDERSTANDING CLEC12A RELATED CANCER STEM CELL BIOLOGY
- O03.03 Marianne Bjerre. POTENTIAL NEW MINIMALLY INVASIVE DIAGNOSTIC BIOMARKERS FOR PROSTATE CANCER
- O03.04 Charlotte Madsen. UPFRONT RITUXIMAB MAINTENANCE AFTER INDUCTION THERAPY IMPROVES THE OUTCOME AND REDUCES THE RISK OF HISTOLOGICAL TRANSFORMATION IN PATIENTS WITH FOLLICULAR LYMPHOMA - A NATIONWIDE COHORT STUDY
- O03.05 Ying Liu. PWP1: A NOVEL NUTRITION-DEPENDENT GROWTH REGULATOR
- O03.06 Michael Roost Clausen. GRADE 3-4 NEUTROPENIA AFTER THE 1ST CYCLE OF CHEMOTHERAPY FOR DIFFUSE LARGE B-CELL LYMPHOMA IS ASSOCIATED WITH INFERIOR OUTCOME COMPARED TO GRADE 1-2 OR NO NEUTROPENIA - A DANISH COHORT STUDY

Oral session 4

Chairmen: Ebba Nexø, Vibeke Hjortdal & Farhad Waziri (PhD student)

- O04.01 Anders Valdemar Edhager. MAJOR METABOLIC PATHWAY ALTERATIONS IN THE MYOCARDIUM DURING DEVELOPMENT OF TYPE 2 DIABETES
- O04.02 Sheyanth Mohanakumar. THE REVEALING OF THE FORGOTTEN CIRCULATION
- O04.03 Kaare Terp Fjederholt. PERIOPERATIVE BLOOD TRANSFUSIONS INCREASES THE RISK OF ANASTOMOTIC LEAKAGE AFTER SURGERY FOR GEJ CANCER
- O04.04 Morten Fenger-Grøn. LEAN BODY MASS IS THE PREDOMINANT ANTHROPOMETRIC RISK FACTOR FOR ATRIAL FIBRILLATION
- O04.05 Stine Gunnarsen. CONDITIONAL DISRUPTION OF THE MYD88 GENE IN SMOOTH MUSCLE CELLS DOES NOT REDUCE THE DEVELOPMENT OF ATHEROSCLEROSIS IN MICE
- O04.06 Anne-Mette Oxvig. CONCOMITANT PROBE-BASED PROFILING OF METHYLGLYOXAL BLOOD METABOLISM AND POST-TRANSLATION MODIFICATION

Oral session 5

Chairmen: Cecilia Høst Ramlau-Hansen, Niels Ulbjerg, Ditte H. Jensen (PhD student) & Caroline Mejdahl (PhD student)

- O05.01 Brigitta Villumsen. EFFECT OF UNSUPERVISED HOME-BASED HEALTHY GAMING IN PROSTATE CANCER PATIENTS RECEIVING ANDROGEN DEPRIVATION THERAPY ON PHYSICAL FUNCTION, BODY COMPOSITION, QUALITY OF LIFE AND FATIGUE: A RANDOMIZED CONTROLLED TRIAL
- O05.02 Nasrin Tayyari Dehbaraz. WOMEN'S PREFERENCES FOR DELIVERY HOSPITAL: A DISCRETE CHOICE EXPERIMENT
- O05.03 Anne Højager Nielsen. THE CONTENT AND STRUCTURE OF ICU DIARIES WRITTEN BY RELATIVES - A NARRATIVE ANALYSIS
- O05.04 Anne Sofie Dam Laursen. AN EPIDEMIOLOGICAL INVESTIGATION OF DAIRY PRODUCT INTAKE AND SUBSEQUENT RISK OF STROKE
- O05.05 Lisbet Grønbæk. PREGNANCY AND BIRTH OUTCOMES IN A DANISH NATIONWIDE COHORT OF WOMEN WITH AUTOIMMUNE HEPATITIS AND MATCHED POPULATION CONTROLS
- O05.06 Mette Tranberg Nielsen. PREVENTING CERVICAL CANCER USING HPV SELF-SAMPLING: DIRECT MAILING OF TEST-KITS INCREASES SCREENING PARTICIPATION MORE THAN TIMELY OPT-IN PROCEDURES - A RANDOMIZED CONTROLLED TRIAL

Poster session 1

Chairmen: Tue Wenzel Kragstrup, Sarah Fogh (PhD student) & Lise Sofie Bislev (PhD student)

- P01.01 Morten Aagaard Nielsen. TOCILIZUMAB: THE DRUG OF CHOICE IN TREATING THE "FIBROBLAST PHENOTYPE" OF RHEUMATOID ARTHRITIS
- P01.02 Cecilie Blenstrup Patsche. TREATING TUBERCULOSIS WASTING WITH A PROTEIN-RICH SUPPLEMENT
- P01.03 Litten Sørensen Rossen. IDENTIFYING NOVEL SIGNAL TRANSDUCTION PATHWAYS OF CD46 ISOFORMS
- P01.04 Samuel Joseph Windross. MECHANISMS OF ACTIVATION OF STING SIGNALING AT THE ENDOPLASMIC RETICULUM
- P01.05 Georgios Katzilieris Petras. CHEMOATTRACTIVE SIGNALING IN THE RECRUITMENT OF MICROGLIA TO HSV-1 INFECTION FOCI IN THE BRAIN
- P01.06 Jesper Geert Pedersen. CCR5 EXPRESSION ON T CELLS DEPENDS ON THEIR ACTIVATION STATUS AND ENVIRONMENT
- P01.07 Kristian Juul-Madsen. BACTERIAL CELL WALL ULTRASTRUCTURE ANALYZED WITH NANOPARTICLE TRACKING ANALYSIS
- P01.08 Madalina Elena Carter-Timofte. MUTATIONS IN POLR3 GENES AND DEFECTIVE DNA SENSING IN PATIENTS WITH SEVERE VARICELLA ZOSTER VIRUS CENTRAL NERVOUS SYSTEM INFECTION
- P01.09 Alice Knudsen. MECHANISM OF ACTIVATION AND EFFECTS OF AN INNATE ANTIVIRAL PATHWAY AT MUCOSAL SURFACES

P01.10 Camilla Gunderstofte Nielsen. NRF2 INCREASES HSV INFECTION THROUGH IMPAIRED ANTIVIRAL INNATE IMMUNE RESPONSE

Poster session 2

Chairmen: Tove Christensen, Allan Kjeldsen Hansen (PhD student) & Andrey Chuhutin (PhD student)

- P02.01 Sidsel Andersen. MASTERS OF IMMUNE MANIPULATION
- P02.02 Katrine Schou Sandgaard. TCR REPERTOIRE AND THYMIC OUTPUT AFTER TREATMENT INTERRUPTION IN CHILDREN WITH HIV
- P02.03 Nina Breinholt Sørensen. A RANDOMISED CONTROLLED TRIAL OF A 12-DOSE RIFAPENTINE AND ISONIAZID REGIMEN USING DIRECT OBSERVED THERAPY VERSUS 6 MONTHS OF DAILY ISONIAZID FOR LATENT TUBERCULOSIS INFECTION IN SOCIALLY MARGINALISED PEOPLE
- P02.04 Cecilie Linneberg. CHARACTERISATION OF THE ZEBRAFISH ORTHOLOGUES OF HUMAN EXTRACELLULAR SUPEROXIDE DISMUTASE
- P02.05 Anna Halling Folkmar Andersen. DEVELOPMENT OF LONG-ACTING INJECTABLE HIV TREATMENT: ALBUMIN-BASED MACROMOLECULAR PRODRUGS MEDIATE ANTI-HIV EFFECTS WITH PROLONGED THERAPEUTIC INDEX TIME
- P02.06 Christina Lundgaard Ernstsén. ACUTE PYELONEPHRITIS: EFFECT OF UROPATHOGENIC E. COLI INFECTION ON RENAL EPITHELIAL CELLS
- P02.07 Anne Mette Fløe Hvass. HIGH COVERAGE OF THE POLIO IMMUNIZATION PROGRAM IN REFUGEES RESETTLING IN DENMARK
- P02.08 Maike Mose. A NEW MODEL OF ACUTE INFLAMMATORY DISEASE - COMBINING ENDOTOXEMIA, FAST AND BEDREST IN HEALTHY YOUNG MEN
- P02.09 Asta Linauskas. BODY FAT PERCENTAGE WAS ASSOCIATED WITH THE DEVELOPMENT OF RHEUMATOID ARTHRITIS - A DANISH FOLLOW-UP STUDY
- P02.10 Susan Mikkelsen. EXAMINATION OF ALLERGY AND ASTHMA RISK FACTORS IN THE DANISH BLOOD DONOR STUDY

Poster session 3

Chairmen: Agnete Larsen, Ida Hovdenak Jakobsen (PhD student) & Iben Lyskjær (PhD student)

- P03.01 Ann Taber. DEVELOPMENT OF PREDICTIVE BIOMARKER MODELS FOR STRATIFYING BLADDER CANCER PATIENTS TO OPTIMIZE THERAPY
- P03.02 Morten Herlin. MULTILEVEL ANALYSIS OF CHILDHOOD ACUTE MYELOID LEUKEMIA (AML)
- P03.03 Maibritt Nørgaard. PROSTATE CANCER TUMOR EVOLUTION AND IDENTIFICATION OF PROGNOSTIC AND PREDICTIVE BIOMARKERS
- P03.04 Pernille Christiansen Skovlund. FEEDBACK IN CANCER CONSULTATIONS - A DIALOGUE-BASED TOOL FOR THE SYSTEMATIC APPLICATION OF PATIENT REPORTED OUTCOME (PRO)
- P03.05 Maria Riedel. A NEW MOUSE MODEL FOR IDENTIFICATION OF KEY FACTORS DRIVING PROSTATE CANCER PROGRESSION AND METASTASIS

- P03.06 Sofia Spampinato. FUNCTIONAL SUB-STRUCTURES OF LOWER URINARY TRACT IN CERVIX CANCER: CONTOURING AND DOSE DISTRIBUTION
- P03.07 Michelle Simone Clement. MECHANISMS OF ACQUIRED RESISTANCE TO MET INHIBITION IN MET-AMPLIFIED RESISTANT NON-SMALL CELL LUNG CANCER
- P03.08 Karen Schow Jensen. FOLLOW-UP AFTER CESSATION OF TREATMENT FOR CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA - THE ABILITY TO DETECT RELAPSE AND THE NEEDS OF THE FAMILIES
- P03.09 Dianna Buus Hussmann. UNCOVERING THE CLINICAL POTENTIAL OF THE CLL METHYLOME
- P03.10 Laura Toussaint. DOSES TO BRAIN STRUCTURES ASSOCIATED WITH COGNITION IN PHOTON VS PROTON THERAPY OF CRANIOPHARYNGIOMA

Poster session 4

Chairmen: Dorte Rytter, Daniel Ramskov Jørgensen (PhD student) & Martin Lund (PhD student)

- P04.01 Frederik Frostholt Prip. COMPREHENSIVE CHARACTERIZATION OF MOLECULAR SUBGROUPS IN EARLY STAGE BLADDER CANCER
- P04.02 Astrid Lindman. RETURN TO EVERY DAY LIFE AFTER STEMCELL TRANSPLANT (MINI-HCT): EFFECT OF A MULTIMODAL INTERDISCIPLINARY REHABILITATION PROGRAMME
- P04.03 Jakob Haldrup Jensen. GENOME-WIDE CRISPR-CAS9 SCREENING IDENTIFIES GENETIC VULNERABILITIES AND POTENTIAL THERAPEUTIC TARGETS IN CASTRATION RESISTANT PROSTATE CANCER
- P04.04 Jesper Pedersen. THE VALIDITY OF PHOTON-BASED RECTUM NTCP MODELS TOGETHER WITH A CONSTANT RBE FOR PROTON THERAPY
- P04.05 Kia Busch. ON-LINE DOSE-GUIDED PROTON THERAPY TO ACCOUNT FOR INTER-FRACTIONAL MOTION: A PROOF OF CONCEPT
- P04.06 Maja Bendtsen Sharma. RADIATION THERAPY OF SINONASAL CANCER
- P04.07 Nadia Øgaard. ESTABLISHMENT OF A STANDARD OPERATING PROCEDURE FOR PRE-ANALYTIC PROCESSING OF CIRCULATING CELL-FREE DNA
- P04.08 Rikke Nørgaard Pedersen. LATE BREAST CANCER RECURRENCE: RISK AND PREVENTION
- P04.09 Margarita Sergeyevna Melnikova. HISTOLOGICAL PROFILING OF THE TUMOR MICROENVIRONMENT IN MOLECULAR SUBCLASSES OF COLORECTAL CANCER
- P04.10 Emil Aagaard Thomsen. IDENTIFICATION OF CANCER DRUG RESISTANCE MECHANISMS AND CELLULAR SIGNALING PATHWAYS BY GENOME-WIDE CRISPR/CAS9 SCREENS

Poster session 5

Chairmen: Henrik Kolstad, Nini Nørgaard (PhD student) & Niels Lyhne Christensen (PhD student)

- P05.01 Ann-Katrine Jakobsen. TARGETING REPAIR MECHANISMS IN CANCER TREATMENT
- P05.02 Anne Tranberg Madsen. IDENTIFICATION OF THE MECHANISM OF ACQUIRED RESISTANCE TO LORLATINIB IN AN ALK-REARRANGED NON-SMALL CELL LUNG CANCER CELL LINE
- P05.03 Anders Rosendal Korshøj. OPEN-LABEL PHASE 1 CLINICAL TRIAL TESTING PERSONALIZED AND TARGETED INTERVENTION WITH SKULL REMODELLING SURGERY TO MAXIMIZE LEVELS OF TT FIELD INTENSITY FOR HIGHER TREATMENT BENEFIT - THE OPTIMAL TTF STUDY
- P05.04 Trine Block Mattesen. DNA METHYLATION PROFILING OF COLORECTAL CANCER IDENTIFIES MOLECULAR SUBTYPES AND SUBTYPE-SPECIFIC BIOMARKERS FOR IMPROVED PREDICTION OF PATIENT PROGNOSIS AND TREATMENT RESPONSE
- P05.05 Anders Kindberg Boysen. THE PROGNOSTIC VALUE OF SIDEDNESS OF THE PRIMARY TUMOR AFTER LOCAL TREATMENT FOR METASTATIC COLORECTAL CANCER - A DANISH POPULATION-BASED STUDY
- P05.06 Sofie Gottschalk Højfeldt. GENETIC VARIANTS IN HLA GENES ARE ASSOCIATED WITH PEG-ASPARAGINASE ALLERGY - A GENOME-WIDE ASSOCIATION STUDY ON THE NOPHO ALL2008 PROTOCOL
- P05.07 Sarah Lindhøj Kvorning. CROSSTALK IN CANCER: SOLUBLE CD163 IN EXTRACELLULAR VESICLES IN PATIENTS WITH MULTIPLE MYELOMA
- P05.08 Johan Vad-Nielsen. EPIGENETIC REGULATION OF ALTERNATIVE SPLICING IN EPITHELIAL-MESENCHYMAL TRANSITION IN NSCLC
- P05.09 Mette Saksø. FAZA PET HYPOXIA AS A MARKER OF LOCO-REGIONAL RECURRENCE IN HEAD AND NECK CANCER?
- P05.10 Anita Tranberg Simonsen. CLONAL PROGRESSION DURING FIRST COURSE OF CHEMOTHERAPY IN ACUTE MYELOID LEUKEMIA SUBOPTIMAL RESPONDERS HERALDS REINDUCTION FAILURE AND EARLY DEATH

Poster session 6

Chairmen: Peter Bross, Casper Sæbye (PhD student) & Mette Holm Hjorth (PhD student)

- P06.01 Johanne Marie Holst. LYMPHOPROLIFERATIVE AND MYELOPROLIFERATIVE MALIGNANCIES OCCURRING IN THE SAME HOST: DESCRIPTION OF A NATIONWIDE DISCOVERY COHORT
- P06.02 Trine Vilsbøll Larsen. REGULATION OF PD-L1 IN NON-SMALL CELL LUNG CANCER
- P06.03 Julie Bondgaard Mortensen. ELEVATED PRE-THERAPEUTIC SERUM LEVELS OF SOLUBLE PROGRAMMED DEATH 1 PROTEIN (SPD-1) IDENTIFY DLBCL PATIENTS WITH ADVERSE PROGNOSTIC FEATURES
- P06.04 Julie Nelly Christensen. LOSS OF ENDOCYTIC RECEPTOR X (ERX) IN MELANOMA CELLS INDUCE EPITHELIAL-TO-MESENCHYMAL TRANSITION
- P06.05 Eva Boysen. CLINICAL CHARACTERISTICS AND SURVIVAL OF EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) MUTATED NON-SMALL CELL LUNG CANCER (NSCLC) (STAGE I-IV) IN A DANISH COHORT DIAGNOSED IN 2010-2017

- P06.06 Marianne Agerlund Petersen. EXAMINING THE LEUKEMIC STEM CELL COMPARTMENT IN CHILDHOOD AML
- P06.07 Pernille Byrialsen Elming. COMBINING HYPERTHERMIA AND CHECKPOINT INHIBITORS: A METHOD OF INCREASING TUMOUR IMMUNOGENICITY?
- P06.08 Lene Haldbø-Classen. COGNITIVE FUNCTION AFTER RADIATION THERAPY FOR BRAIN TUMOUR
- P06.09 Simon Skouboe. REAL-TIME DOSE RECONSTRUCTION FOR MOVING TUMOURS DURING LIVER RADIOTHERAPY
- P06.10 Sarah Østrup Jensen. CURING COLORECTAL CANCER WITH EARLY DETECTION: BLOOD-BASED BIOMARKERS FOR IMPROVED SCREENING

Poster session 7

Chairmen: Vladimir Matchkov & Niels Dalsgaard Nielsen (PhD student)

- P07.01 Julie Jacobsen. TENDON-RELATED ABNORMALITIES IDENTIFIED WITH ULTRASOUND ARE COMMON IN SYMPTOMATIC HIP DYSPLASIA
- P07.02 Eva Forsom. ANTIPSYCHOTIC MEDICATION AND THE DEVELOPMENT OF OSTEOPOROSIS IN PATIENTS WITH OR WITHOUT SCHIZOPHRENIA
- P07.03 Sebastian Mosegaard. IDENTIFICATION OF OUTCOME PREDICTORS FOR TREATMENT OF TRAPEZIOMETACARPAL OSTEOARTHRITIS WITH A TOTAL JOINT ARTHROPLASTY
- P07.04 Anders Kristensen. THE EFFECT OF AN INCREASED CURVATURE OF THE FORCE-VELOCITY RELATIONSHIP ON POWER IN ISOLATED RAT SOLEUS AND EDL MUSCLES
- P07.05 Ahmed Abdul-Hussein Abood. DEPOSITION OF ALLOGENIC AND AUTOLOGOUS CARTILAGE IN A PHYSEAL DEFECT SUGGESTS SIMILAR PHYSEAL ACTIVITY - AN EXPERIMENTAL PORCINE MODEL
- P07.06 Janni Kjærgaard Thillemann. BONE MODEL PRECISION IN DYNAMIC RSA ON THE ELBOW AND DISTAL FOREARM
- P07.07 Jakob Bie Granild-Jensen. ZOLEDRONATE AGAINST FRACTURES IN CHILDREN WITH CEREBRAL PALSY
- P07.08 Simon Skov. COMPARING 3D CORRECTION AND SPINAL GROWTH OF MAGNETICALLY CONTROLLED GROWTH-ENGINE (MCGR) DRIVEN DISTRACTION TO OPEN INTERVAL DISTRACTION OF TWO DOUBLE GROWING-ROD SYSTEMS WITH APICAL CONTROL IN EOS
- P07.09 Peter Sieljacks. COMPARATIVE EFFECTS OF LOW-LOAD BLOOD FLOW RESTRICTED EXERCISE AND HIGH-LOAD RESISTANCE EXERCISE ON MUSCLE ACCRETION AND MUSCLE STEM CELL ADAPTATIONS
- P07.10 Pelle Emil Hanberg. PHARMACOKINETICS OF SINGLE-DOSE CEFUROXIME IN PORCINE INTERVERTEBRAL DISC AND VERTEBRAL CANCELLOUS BONE DETERMINED BY MICRODIALYSIS

Poster session 8

Chairmen: Hatice Tankisi, Bente Skovsby Toft (PhD student) & Carsten Gleesborg (PhD student)

- P08.01 Ellen Kure Fischer. A MOLECULAR PATHWAY ANALYSIS STRESSES THE ROLE OF INFLAMMATION AND OXIDATIVE STRESS TOWARDS COGNITION IN SCHIZOPHRENIA
- P08.02 Karen Hansen Kallesøe. GROUP-BASED ACCEPTANCE AND COMMITMENT THERAPY (ACT) FOR SEVERE FUNCTIONAL SOMATIC SYNDROMES IN ADOLESCENTS - UNCONTROLLED PILOT STUDY
- P08.03 Malene Thygesen. EXPOSURE TO AIR POLLUTION IN EARLY CHILDHOOD AND THE ASSOCIATION WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER - A NATIONWIDE COHORT STUDY
- P08.04 Pil Lindgreen. THE SELF-MONITORING APP RECOVERY RECORD FOR EATING DISORDER TREATMENT: AN INTERPRETIVE DESCRIPTION OF THE INTERDISCIPLINARY CLINICAL PERSPECTIVE
- P08.05 Anita Tønder Nielsen. RISK OF DIABETIC COMPLICATIONS AND SUBSEQUENT MORTALITY IN INDIVIDUALS WITH SCHIZOPHRENIA AND DIABETES MELLITUS: A POPULATION-BASED REGISTER STUDY
- P08.06 Sanne Jensen. CHILDREN AND ADOLESCENTS WITH OBSESSIVE-COMPULSIVE DISORDER: PREDICTORS OF LONG-TERM TREATMENT OUTCOME
- P08.07 Janne Tidselbak Larsen. EARLY LIFE RISK FACTORS FOR EATING DISORDERS
- P08.08 Andreas Aalkjær Danielsen. PREDICTING MECHANICAL RESTRAINT BY APPLYING DATA MINING TECHNIQUES ON ELECTRONIC MEDICAL RECORDS
- P08.09 Pernille Kølbæk. CLINICAL VALIDATION OF PANSS-6 SCHIZOPHRENIA SEVERITY RATINGS OBTAINED USING THE SIMPLIFIED NEGATIVE AND POSITIVE SYMPTOMS INTERVIEW (SNAPSI)
- P08.10 Sara Højslev Avlund. AUTISM OVERLOOKED: CHARACTERISTICS OF CHILDREN WITH AN AUTISM SPECTRUM DISORDER DIAGNOSIS MISSED IN THE FIRST ASSESSMENT

Poster session 9

Chairmen: Henrik Sørensen, Peter Lykke Eriksen (PhD student) & Ole Adrian Heggli (PhD student)

- P09.01 Marie-Louise Ladegaard Baun. OVARIAN CANCER OUTCOME AND VARIATION IN REFERRAL RATES FOR TRANSVAGINAL ULTRASOUND EXAMINATION FROM GENERAL PRACTICE
- P09.02 Marzieh Katibeh. IMPROVING EYE HEALTH AT THE PRIMARY HEALTH CARE LEVEL THROUGH MHEALTH
- P09.03 Linda Aagaard Rasmussen. ACTIVITY IN GENERAL PRACTICE PRECEDING A DIAGNOSIS OF CANCER RECURRENCE
- P09.04 Tina Lützen. PSYCHIATRIC MORBIDITY AND GP ATTENDANCE PRIOR TO HPV VACCINATION AND RISK OF REFERRAL TO HPV CENTRE
- P09.05 Jose Omar Silverman Retana. TRAJECTORIES OF OBESITY BY SPOUSAL DIABETES STATUS IN THE ENGLISH LONGITUDINAL STUDY OF AGEING
- P09.06 Kathrine Pape Madsen. ACCURACY OF OFFSPRING-REPORTED PARENTAL SMOKING STATUS - THE RHINESSA GENERATION STUDY

- P09.07 Tine Vrist Dam. THE ANABOLIC EFFECT OF ENDOGENOUS AND EXOGENOUS ESTROGEN ON THE SKELETAL MUSCLES
- P09.08 Lea Lykke Lauridsen. PREECLAMPSIA AND TIMING OF PUBERTAL DEVELOPMENT IN DAUGHTERS AND SONS
- P09.09 Benedicte Marie Winther Johannsen. SELF-HARM IN WOMEN WITH SEVERE POSTPARTUM PSYCHIATRIC DISORDERS
- P09.10 Maria Keilow. SOCIAL GRADIENT PATTERNS IN MEDICAL ADHD TREATMENT

Poster session 10

Chairmen: Kristian Overgaard, Martin Langeskov Christensen (PhD student) & Kamilla Pedersen (PhD student)

- P10.01 Anne Ankerstjerne Rasmussen. PATIENT-REPORTED OUTCOMES IN PATIENTS SUFFERING FROM HEART FAILURE: ASSOCIATIONS BETWEEN PATIENT DEMOGRAPHICS AND PRO?
- P10.02 Diana Hedevang Christensen. THE ASSOCIATION OF METABOLIC RISK FACTORS WITH POLYNEUROPATHY IN RECENTLY DIAGNOSED TYPE 2 DIABETES PATIENTS
- P10.03 Martin Lund. THE DANISH COLORECTAL CANCER SCREENING PROGRAM AND THE DISTRIBUTION OF QUALITY INDICATORS PER COLONOSCOPIST IN THE CENTRAL DENMARK REGION
- P10.04 Signe Hjuler Boudigaard. RISK OF AUTOIMMUNE RHEUMATOLOGICAL DISEASES AFTER OCCUPATIONAL EXPOSURE TO RESPIRABLE QUARTZ: A COHORT STUDY OF THE DANISH WORKING POPULATION 1977-2015
- P10.05 Bishal Gyawali. PREVALENCE, ASSOCIATED FACTORS, AWARENESS, TREATMENT, AND CONTROL OF TYPE 2 DIABETES IN A SEMI-URBAN AREA OF NEPAL: A CROSS-SECTIONAL STUDY
- P10.06 Bente Kjær Lyngsøe. MATERNAL DEPRESSION AND OFFSPRING UTILIZATION OF PRIMARY HEALTH CARE: A POPULATION-BASED COHORT STUDY
- P10.07 Signe Timm. ASTHMA AND SELECTIVE MIGRATION AWAY FROM FARMING ENVIRONMENTS IN THE THREE-GENERATION COHORT STUDY RHINESSA
- P10.08 Jonas Boysen Fynboe Ebert. PAPER- OR WEB-BASED QUESTIONNAIRE INVITATIONS AS A METHOD FOR DATA COLLECTION? A CROSS-SECTIONAL COMPARATIVE STUDY OF DIFFERENCES IN RESPONSE RATE, COMPLETENESS OF DATA AND FINANCIAL COSTS
- P10.09 Mette Kielsholm Thomsen. SOCIOECONOMIC PREDICTORS OF INTERVAL CANCER AND ADHERENCE TO FOLLOW-UP COLONOSCOPY IN THE DANISH COLORECTAL CANCER SCREENING PROGRAM
- P10.10 Michael Bertelsen. A FRAMEWORK FOR THE ETIOLOGY OF RUNNING-RELATED INJURIES

Poster session 11

Chairmen: Mette Nørgaard, Karen Rokkedal Lausch (PhD student) & Louise Bang Grode (PhD student)

- P11.01 Marie Weinreich Petersen. PREVALENCE AND SOCIODEMOGRAPHIC CHARACTERISTICS OF FUNCTIONAL SOMATIC SYNDROMES IN THE GENERAL DANISH POPULATION
- P11.02 Liv Marit Valen Schougaard. PATIENT-REPORTED OUTCOME (PRO) MEASURE-BASED ALGORITHM FOR CLINICAL DECISION SUPPORT IN EPILEPSY OUTPATIENT FOLLOW-UP: A TEST-RETEST RELIABILITY STUDY
- P11.03 Anne Gedebjerg. PREVALENCE OF MICROVASCULAR AND MACROVASCULAR DIABETES COMPLICATIONS AT THE TIME OF TYPE 2 DIABETES DIAGNOSIS AND ASSOCIATED CLINICAL CHARACTERISTICS: A CROSS-SECTIONAL BASELINE STUDY OF 6958 PATIENTS IN THE DANISH DD2 COHORT
- P11.04 Inge Schjødt. LOW SOCIOECONOMIC STATUS IS ASSOCIATED WITH HIGHER RISK OF READMISSION AMONG PATIENTS WITH HEART FAILURE AND REDUCED EJECTION FRACTION: A POPULATION-BASED COHORT STUDY
- P11.05 Per Høgh Poulsen. THE EFFECT OF CHILDHOOD SOCIOECONOMIC POSITION ON MENTAL HEALTH IN ADOLESCENCE AND EARLY ADULTHOOD
- P11.06 Julie Jessen Hvidt. PUBERTAL DEVELOPMENT IN CHILDREN WITH FETAL GROWTH RESTRICTION
- P11.07 Helene Narvestad. MATERNAL SMOKING DURING PREGNANCY AND OFFSPRING UTILISATION OF HEALTHCARE SERVICES
- P11.08 Asser Hedegård Thomsen. KILL YOUR TEXT /// HOMICIDE IN DENMARK 1992-2016 - PRELIMINARY FINDINGS
- P11.09 Gitte Boier Tygesen. DEVELOPMENT OF A DANISH EMERGENCY DEPARTMENT PATIENT SAFETY MODEL USING A SYSTEMATIC SEARCH AND MODIFIED DELPHI PROCESS
- P11.10 Gitte Vrelits Sørensen. LONG-TERM RISK OF SOMATIC HOSPITALIZATION IN 5-YEAR SURVIVORS OF CHILDHOOD LEUKEMIA - A NORDIC POPULATION-BASED COHORT STUDY

Poster session 12

Chairmen: Mette Spliid Ludvigsen, Cecilie Nørby Thisted (PhD student) & Anja Thiede (PhD student)

- P12.01 Kathrine Håland Jeppesen. MANAGEMENT RELATED TO THE IMPLEMENTATION OF PATIENT INVOLVEMENT
- P12.02 Charlotte Dyrehave. "GOD CANNOT HELP ME IF I DON'T TAKE MY MEDICINE". BARRIERS TO RETENTION IN CARE AND HEALTH-RELATED QUALITY OF LIFE AMONG HIV-INFECTED AFRICAN MIGRANTS
- P12.03 Anne Mette Schmidt. JUSTIFICATION AND DESCRIPTION OF A NEW REHABILITATION PROGRAMME FOR PATIENTS WITH CHRONIC LOW BACK PAIN
- P12.04 Randi Steensgaard. A HIDDEN BARRIER TO IMPLEMENT A STRONGER FOCUS ON PATIENT PARTICIPATION IN REHABILITATION - HOW HEALTH PROFESSIONALS' POSITIONS URGE THEM TO RETAIN STATUS QUO

- P12.05 Anders Damgaard Møller. ACUTE EXACERBATION OF CHRONIC DISEASE: EVALUATION OF AN INTERSECTORAL INTERVENTION TO INTEGRATE AND OPTIMISE TREATMENT AND FOLLOW-UP
- P12.06 Charlotte Ibsen. "KEEP IT SIMPLE": INVOLVING PATIENTS WITH LUMBAR RADICULOPATHY IN DEVELOPING A PATIENT-REPORTED OUTCOME INSTRUMENT
- P12.07 Rikke Buus Bøje. NURSING PRACTICE AND EXPANSIVE LEARNING IN OLDER ADULTS' TRANSITION BETWEEN HOSPITAL AND PRIMARY CARE
- P12.08 Charlotte Arp Sørensen. SELF-ADMINISTRATION OF PATIENTS' OWN DRUGS DURING HOSPITAL STAY - A FEASIBILITY AND PILOT STUDY
- P12.09 Maria Pedersen. PROGNOSTIC ROLE OF NEUTROPHIL-LYMPHOCYTE RATIO IN LOCALIZED AND METASTATIC RENAL CELL CARCINOMA. A POPULATION-BASED COHORT STUDY
- P12.10 Lene Holst Pedersen. EARLY FOLLOW-UP AFTER DISCHARGE FOR GERIATRIC PATIENTS ADMITTED FROM THEIR OWN HOME

Poster session 13

Chairmen: Anna Starnawska, Karen Busk Nørøxe (PhD student) & Mette-Lise Simonsen (PhD student)

- P13.01 Cecilie Siggaard Jørgensen. TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION IN CHILDREN WITH MONOSYMPOMATIC NOCTURNAL ENURESIS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY
- P13.02 Stine Lohmann. DELAYED GRAFT FUNCTION IN A PORCINE AUTOTRANSPLANTATION MODEL
- P13.03 Stine Langaa. DETERMINATION OF RENAL BLOOD FLOW BASED ON PET/CT-RUBIDIUM-82 TECHNOLOGY
- P13.04 Jeanette Finderup. DEVELOPING AND PILOT TESTING A SHARED DECISION-MAKING INTERVENTION FOR DIALYSIS CHOICE
- P13.05 Yutao Lu. DIFFERENT DIURNAL VARIATION IN PATIENTS WITH CONGENITAL NEUROGENIC AND NON-NEUROGENIC LOWER URINARY TRACT DYSFUNCTION
- P13.06 Haiyun Qi. EFFECTS OF ANESTHESIA ON RENAL FUNCTION AND METABOLISM IN RATS
- P13.07 My Emma Sofie Malmberg. EFFECT OF TOLVAPTAN ON RBF AND GFR IN POLYCYSTIC KIDNEY DISEASE
- P13.08 Marie Houmaa Vrist. 18F-NAF PET/CT IN COMBINATION WITH BIOMARKERS FOR THE CLASSIFICATION OF RENAL OSTEODYSTROPHY IN HEMODIALYSIS PATIENTS
- P13.09 Malthe Pedersen. SLEEP AND NOCTURNAL ENURESIS
- P13.10 Christian Østergaard Mariager. HYPERPOLARIZED [¹³C,¹⁵N₂] UREA T₂ RELAXATION CHANGES IN ACUTE KIDNEY INJURY

Poster session 14

Chairmen: Vivi Schlünssen & Signe Voigt Lauridsen (PhD student)

- P14.01 Lene Andreasen. RATIONAL AND DESIGN OF THE RANDOMIZED EUROPEAN OPTICAL COHERENCE TOMOGRAPHY OPTIMIZED BIFURCATION EVENT REDUCTION (OCTOBER) TRIAL
- P14.02 Anders Sjørsløv Schmidt. THE CHESS TRIAL: COMPARISON OF HIGH VERSUS ESCALATING SHOCKS IN CARDIOVERTING ATRIAL FIBRILLATION: DESIGN AND RATIONALE FOR A RANDOMIZED CLINICAL TRIAL
- P14.03 Mathilde Stærk. AUTOMATED EXTERNAL DEFIBRILLATORS ARE WIDELY DISTRIBUTED IN DANISH HOSPITALS BUT INFREQUENTLY USED - A NATIONWIDE STUDY
- P14.04 Mads Dam Lyhne. PHARMACOLOGICAL SUPPORT OF THE FAILING RIGHT VENTRICLE IN ACUTE PULMONARY EMBOLISM
- P14.05 Asbjørn Petersen. CAN GENETIC DEFICIT OF KCA3.1 CHANNELS PREVENT THE DEVELOPMENT OF CIRCULATORY COLLAPSE AND LUNG OEDEMA IN ACID-INDUCED LUNG INJURY?
- P14.06 Kasper Krohn Korsholm. INTRACARDIAC ECHOCARDIOGRAPHY FROM THE LEFT ATRIUM FOR PROCEDURAL GUIDANCE OF TRANSCATHETER LEFT ATRIAL APPENDAGE OCCLUSION
- P14.07 Tine Billeskov. CENTRAL ROLE OF MUSCLE STEM CELLS IN REGENERATIVE FAILURE IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE
- P14.08 Laust Rasmussen. DANISH STUDY OF NON-INVASIVE DIAGNOSTIC TESTING IN CORONARY ARTERY DISEASE II (DAN-NICAD II) - AN INTERDISCIPLINARY MULTICENTRE STUDY IN THE CENTRAL DENMARK REGION
- P14.09 Estefano Pinilla. EFFECT OF TRANSGLUTAMINASE CONFORMATIONAL MODULATION ON VASCULAR TONE
- P14.10 Peter Carøe Lind. PROTECTIVE ROLE OF KCA3.1 ION CHANNEL BLOCKERS IN PULMONARY CIRCULATORY COLLAPSE AND OEDEMA

Poster session 15

Chairmen: Reimar W. Thomsen, Bawer Jalal Tofiq (PhD student) & Stine Thyssen (PhD student)

- P15.01 Anne Midtgaard-Thomsen. DIABETES INCREASES EARLY SIGNS OF ATHEROSCLEROTIC INFLAMMATION AND PLAQUE INSTABILITY IN LDLR^{-/-} MICE
- P15.02 Mine Onat. CONCOMITANT ABLATION FOR ATRIAL FIBRILLATION IN PATIENTS UNDERGOING CARDIAC SURGERY
- P15.03 Benjamin Kelly. NEAR INFRARED FLUORESCENCE IMAGING OF THE LYMPHATIC VASCULATURE IN THE HUMAN ARM - A VALIDATION STUDY
- P15.04 Tanja Charlotte Frederiksen. PROLONGATION OF THE QTC INTERVAL IN ANOREXIA NERVOSA
- P15.05 Simin Berenji Ardestani. ENDOTHELIAL FUNCTION AND CARDIOVASCULAR STRESS MARKERS AFTER A SINGLE DIVE IN AGING RATS (APOE KNOCKOUT RATS)

- P15.06 Anders Hostrup Larsen. LEFT VENTRICULAR MYOCARDIAL DEFORMATION CAPACITY DURING EXERCISE STRESS IN HEALTHY ADULTS. A TWO-DIMENSIONAL SPECKLE-TRACKING ECHOCARDIOGRAPHY STUDY
- P15.07 Marcell Juan Tjørnild. MITRAL LEAFLET AUGMENTATION AND RECONSTRUCTION USING PORCINE EXTRACELLULAR MATRIX: FUNCTIONAL AND BIOMECHANICAL ASPECTS
- P15.08 Gro Grunnet Pløen. RENIN AND ANGIOTENSINOGEN OVEREXPRESSING D374Y-PCSK9 MINIPIGS: A PIG MODEL PRONE TO DEVELOP HYPERTENSION AND ACCELERATED HUMAN-LIKE CORONARY ATHEROSCLEROSIS
- P15.09 Leila Louise Benhassen. CHARACTERIZATION OF TWO DIFFERENT SUBVALVULAR ANNULOPLASTIES FOR AORTIC ROOT REPAIR
- P15.10 Andreas Engel Krag. DOES REMOTE ISCHEMIC PRECONDITIONING INFLUENCE PLATELET AGGREGATION IN PATIENTS UNDERGOING HEAD AND NECK CANCER MICROSURGICAL RECONSTRUCTION? A RANDOMIZED CONTROLLED TRIAL

Poster session 16

Chairmen: Arne Møller & Luise Aamann (PhD student)

- P16.01 Johnni Rudbeck-Resdal. ETIOLOGIES OF ATRIOVENTRICULAR BLOCK IN YOUNGER PATIENTS - A NATIONWIDE DANISH STUDY
- P16.02 Kasper Glerup Lauridsen. MAJOR DIFFERENCES IN ADVANCED LIFE SUPPORT TRAINING STRATEGIES AMONG DANISH HOSPITALS - A NATIONWIDE STUDY
- P16.03 Camilla Mains Balle. PLATELET FUNCTION IN CRITICALLY ILL ADULTS TREATED WITH EXTRACORPOREAL MEMBRANE OXYGENATION
- P16.04 Sebastian Udholm. HEALTH PROFILE AND EXERCISE FUNCTION IN ADULTS WITH SMALL ATRIAL SEPTAL DEFECTS
- P16.05 Omeed Neghabat. UNCERTAIN DETECTION OF STENT FRACTURE BY THREE-DIMENSIONAL INTRAVASCULAR OPTICAL COHERENCE TOMOGRAPHY
- P16.06 Benjamin Asschenfeldt Arlander. IMPACT OF CONGENITAL HEART DISEASE ON BRAIN DEVELOPMENT
- P16.07 Julie Brogaard Larsen. A NEW CLOT FORMATION AND LYSIS ASSAY IN SEPSIS-RELATED DISSEMINATED INTRAVASCULAR COAGULATION
- P16.08 Jacob Gammelgaard Schultz. NO-SGC-CGMP PATHWAY STIMULATION LOWERS PULMONARY VASCULAR RESISTANCE IN A PORCINE MODEL OF ACUTE PULMONARY EMBOLISM
- P16.09 Mikkel Giehm-Reese. A RANDOMIZED STUDY OF CONTACT FORCE IN ATRIAL FLUTTER ABLATION
- P16.10 Stine Andersen. EFFECTS OF ENTRESTO IN PULMONARY HYPERTENSION AND RIGHT HEART FAILURE

Poster session 17

Chairmen: Axel Forman, Pernille Gabel (PhD student) & Lise Roed Brogaard (PhD student)

- P17.01 Eva Rydahl. WHY ALL THESE CESAREAN SECTIONS? CAN INCREASED MATERNAL AGE BE AN EXPLAINING FACTOR?
- P17.02 Trine Muhs Nielsen. EARLY TERM CAESAREAN SECTION AND COGNITIVE FUNCTION IN CHILDHOOD - A 7-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL
- P17.03 Christine Rohr Thomsen. NEW PRINCIPLES FOR QUANTITATIVE ELASTOGRAPHY OF THE HUMAN UTERINE CERVIX
- P17.04 Anne Raabjerg Kruse. CHALLENGES IN A CLINICAL TRIAL RANDOMIZING PATIENTS TO FAST-TRACK OR ROUTINE DISCHARGE AFTER ELECTIVE CESAREAN SECTION
- P17.05 Siri Nana Halling Steen. TZA QUANTIFICATION OF THE LATENT RESERVOIR IN HIV-1 PATIENTS: PREDICTING TIME TO VIRAL REBOUND DURING ART INTERRUPTION
- P17.06 Sara Larsen. ANGIOTENSIN RECEPTOR TYPE 1 AUTOANTIBODIES AND ENDOTHELIN RECEPTOR TYPE A AUTOANTIBODIES IN PREECLAMPTIC WOMEN: IS PREECLAMPSIA AN AUTOIMMUNE DISEASE?
- P17.07 Frederik Rothemejer Jacobsen. IMPACT OF A TLR9 AGONIST ON THE FUNCTIONAL CAPACITY OF NK CELL SUBSETS TO INHIBIT HIV-1 PROPAGATION EX VIVO
- P17.08 Julie Lyngsø. DOES COFFEE CONSUMPTION IMPACT ON FERTILITY TREATMENT?
- P17.09 Clara Faurby Maarup. THE POTENTIAL RISK OF ENDOMETRIAL CANCER IN WOMEN WITH ENDOMETRIAL HYPERPLASIA - A LONG-TERM FOLLOW-UP
- P17.10 Thomas Berger. IMPACT OF BOWEL GAS AND BODY OUTLINE VARIATIONS ON TOTAL ACCUMULATED DOSE WITH INTENSITY MODULATED PROTON THERAPY IN LOCALLY ADVANCED CERVICAL CANCER PATIENTS

Poster session 18

Chairmen: Mette-Lise Simonsen, Anuj Pareek (PhD student) & Jesper Falkesgaard Højen (PhD student)

- P18.01 Ole Nymark. MATERNOFETAL TISSUE DISTRIBUTION OF VITAMIN B12 INFLUENCED BY B12 STATUS AND FORM: AN EXPERIMENTAL STUDY IN PREGNANT RATS
- P18.02 Gitte Øskov Skajaa. PARITY INCREASES INSULIN REQUIREMENTS IN PREGNANT WOMEN WITH TYPE 1 DIABETES
- P18.03 Malou Eva Maria Pinto Barbosa. LONG-TERM OUTCOME AFTER LATE REPAIR OF THE ANAL SPHINCTER SECONDARY TO OBSTETRIC TRAUMA
- P18.04 Kristine Frederiksen. DOES REMOTE ISCHAEMIC PRECONDITIONING INFLUENCE THE COMPLEMENT SYSTEM IN PATIENTS UNDERGOING HEAD AND NECK CANCER SURGERY? A RANDOMIZED CONTROLLED TRIAL
- P18.05 Khoa Manh Dinh. LOW-GRADE INFLAMMATION AMONG HEALTHY PREMENOPAUSAL WOMEN TAKING COMBINED ORAL CONTRACEPTION DEPENDS ON DOSE AND TYPE OF PROGESTIN: RESULTS FROM THE DANISH BLOOD DONOR STUDY (DBDS)
- P18.06 Ida Charlotte Bay Lund. DETECTING CONFINED PLACENTAL AND FETAL MOSAICISM USING CELL-FREE DNA SEQUENCING ON MATERNAL PLASMA
- P18.07 Maria Birgitte Søndermølle. RISK FACTORS FOR NON-SUCCESSFUL TUBERCULOSIS TREATMENT

- P18.08 Simon Larsen. IDENTIFICATION OF NOVEL INNATE IMMUNODEFICIENCIES IN PATIENTS WITH PARALYTIC POLIOMYELITIS
- P18.09 Diana Skaaning. DOES PARENTAL SUPERVISION IN REGULAR ORAL STIMULATION PROLONG THE DURATION OF BREASTFEEDING AMONG PREMATURE INFANTS? A SINGLE-BLINDED RANDOMIZED CONTROLLED TRIAL
- P18.10 Line Kolding. DRUG SAFETY IN PREGNANCY - DRUG USE DURING PREGNANCY AND EFFECTS ON THE CARDIAC FUNCTION OF THE FETUS

Poster session 19

Chairmen: Natalya Fedosova, Mads Sørensen Larsen (PhD student) & Karoline Knudsen (PhD student)

- P19.01 Rasmus Fuglsang Nielsen. DIETARY FIBER AND WHEY PROTEIN: THE EFFECTS ON GLUCOSE METABOLISM IN SUBJECTS WITH ABDOMINAL OBESITY
- P19.02 Elin Rakvaag. EFFECTS OF WHEY PROTEIN AND DIETARY FIBER ON PLASMA TRIGLYCERIDES: A RANDOMIZED, CONTROLLED, DOUBLE-BLIND DIETARY INTERVENTION TRIAL IN ABDOMINALLY OBESE SUBJECTS
- P19.03 Elias Didrik Francis Zachariae. TWO STRUCTURES FROM A SINGLE GENE: INVESTIGATING THE DIFFERENTIAL FOLDING OF SOD3
- P19.04 Anne Sophie Koldkjær Sølling. TREATMENT WITH ZOLEDRONIC ACID SUBSEQUENT TO DENOSUMAB IN OSTEOPOROSIS
- P19.05 Katrine Meyer Lauritsen. THE EFFECT OF EMPAGLIFLOZIN ON CARDIAC AND KIDNEY METABOLISM IN PERSONS WITH TYPE 2 DIABETES
- P19.06 Karolina Snopek. SYMPTOMS OF DIABETIC POLYNEUROPATHY ARE RELATED TO FALLS IN PATIENTS WITH TYPE 2 DIABETES
- P19.07 Marlene Christina Nielsen. DEVELOPMENT AND VALIDATION OF AN ASSAY TO MEASURE CD163 BOUND TO EXTRACELLULAR VESICLES
- P19.08 Kristian Alsbjerg Skipper. INTERVENING GENETICALLY WITH TYPE II DIABETES
- P19.09 Mette Ji Riis-Vestergaard. β -ADRENERGIC REGULATION OF UNCOUPLING PROTEIN 1 IN A NEW HUMAN BROWN ADIPOCYTE CELL MODEL
- P19.10 Rasmus Kold-Christensen. MONITORING REACTIVE METABOLITES BY ELISA

Poster session 20

Chairmen: Anders Børghlum, Jesper Guldsmed Madsen (PhD student) & Morten Stokholm (PhD student)

- P20.01 Angela Pärn. THE ROLE OF PCSK9 IN BRAIN DEVELOPMENT AND BEHAVIOR
- P20.02 Sara Raquel Almeida Ferreira. INVOLVEMENT OF THE CD163 RECEPTOR IN THE ALPHA-SYNUCLEIN INDUCED NEURODEGENERATION IN PARKINSON'S DISEASE
- P20.03 Filomena Iannuzzi. FYN TYROSINE KINASE AS POTENTIAL TARGET FOR ALZHEIMER'S DISEASE TREATMENT
- P20.04 Sarah Christine Christensen. DRUG DELIVERY INTO THE BRAIN: BELIEVE IT TO BE THE RIGHT TARGET ON THE BLOOD-BRAIN BARRIER OR NOT
- P20.05 Camilla Højland Knudsen. HUMAN PLURIPOTENT STEM CELLS FOR SPINAL CORD REPAIR

- P20.06 Lasse Reimer. INFLAMMATION ASSOCIATED KINASE, PKR, BLOCKS ALPHA-SYNUCLEIN VESICLE-BINDING BY PHOSPHORYLATING NOVEL SERINE AND THREONINE SITES: A NEW MECHANISM IN NERVE TERMINALS?
- P20.07 Sérgio Eduardo Costa Almeida. LYSOSOMAL SORTING OF PROGRANULIN IN FRONTOTEMPORAL LOBAR DEGENERATION
- P20.08 Rikke Kristensen. TWO NOVEL ELECTROPHYSIOLOGICAL METHODS IN EVALUATION OF ALS PATIENTS - MSCAN MUNE AND MVRC
- P20.09 Giulia Monti. A NOVEL SORL1 VARIANT IS DOWNREGULATED IN ALZHEIMER'S DISEASE BRAIN

Poster session 21

Chairmen: Ulf Simonsen, Jacob Lynge Callesen (PhD student) & Cecilie Ejerskov (PhD student)

- P21.01 Majken Thomsen. SYNAPTIC DENSITY IMAGING IN RAT AND PIG BRAIN
- P21.02 Nick Larsen. CHARACTERIZATION OF MINICOLUMNS AND VOLUME TENSORS OF NEURONS IN BRODMANN AREA 46 IN NORMAL, SCHIZOPHRENIC AND DEPRESSIVE HUMAN AUTOPSY BRAINS
- P21.03 Simon Bang Kristensen. STATISTICAL METHODS FOR METACOGNITION
- P21.04 Rola Ismail. STUDY OF THE TEMPORAL AND SPATIAL RELATIONSHIPS BETWEEN NEUROINFLAMMATION, BETA-AMYLOID AND TAU AGGREGATION IN MILD COGNITIVE IMPAIRMENT AND ALZHEIMER'S DISEASE
- P21.05 Agnes Hauschultz Witt. MUSCLE VELOCITY RECOVERY CYCLES IN NEUROGENIC MUSCLES
- P21.06 Asbjørn Johan Krom-Thaysen. THE NUCLEAR ANATOMY AND FIBER CONNECTIONS OF THE GÖTTINGEN MINIPIG'S SEPTAL NUCLEI
- P21.07 Mette Habekost. DIRECT CONVERSION OF WILD-TYPE AND ALZHEIMER'S DISEASE PORCINE FIBROBLASTS TO NEURONS
- P21.08 Pernille Thomassen. SORCS2 IN MOTOR NEURON DEVELOPMENT AND INTEGRITY
- P21.09 Luca Bordoni. THE ROLE OF AQP4 AND CEREBRAL CAPILLARY BLOOD FLOW DYNAMICS IN DEVELOPMENT OF HYPONATREMIA INDUCED BRAIN EDEMA IN MICE
- P21.10 Annemarie Svane Aavild Poulsen. SORL1 IS A TARGET GENE OF NEUROD2

Poster session 22

Chairmen: Thomas Reinert, Mats Bue (PhD student) & Kathrine Hald (PhD student)

- P22.01 Leonardo Bonetti. RISK OF DEPRESSION ENHANCES THE DISCRIMINATION OF AUDITORY IRREGULARITIES: AN MEG STUDY
- P22.02 Ted Carl Andelius. CONSEQUENCE OF INSERTION TRAUMA - EFFECT ON EARLY MEASURES WHEN USING INTRACEREBRAL DEVICES
- P22.03 Anne Nielsen. ACUTE ISCHEMIC STROKE: ESTIMATING TREATMENT EFFECT USING A COMPUTER MODEL

- P22.04 Alexander Gramm Kristensen. DETECTION OF EARLY MOTOR INVOLVEMENT IN DIABETIC POLYNEUROPATHY USING A NOVEL MUNE METHOD: MSCANFIT MUNE
- P22.05 Denise Fabienne Happ. ESTABLISHING A RAT MODEL OF POST-STROKE EMOTIONAL DYSFUNCTION
- P22.06 Kathrine Stokholm. MILD MICROGLIAL ACTIVATION INDUCED BY ALPHA-SYNUCLEIN IN A RAT MODEL OF PARKINSON'S DISEASE
- P22.07 Suzi Ross. THE ROLE OF AUDITORY FEEDBACK IN MOTOR SEQUENCE LEARNING IN MUSICAL NOVICES
- P22.08 Daniel Gramm Kristensen. SIZE ILLUSIONS AND SURROUND MODULATION
- P22.09 Abdel-Rahman Al-Absi. BEHAVIORAL, STRUCTURAL AND MOLECULAR ALTERATIONS IN THE DF(H22Q11)/+ GENETIC MOUSE MODEL OF SCHIZOPHRENIA
- P22.10 Martin Nors Skov. NOVEL TELEMETRIC APPROACH TO ASSESS THE PROGRESSING IMPACT OF DIABETES ON THE PERIPHERAL NERVOUS SYSTEM

Poster session 23

Chairmen: Rikke Nørregaard, Marie Vad (PhD student) & Ina Qvist (PhD student)

- P23.01 Sophie-Charlott Seidenfaden. BIOMARKERS IN PREHOSPITAL MANAGEMENT OF TRAUMATIC BRAIN INJURY: THE PRETBI STUDY
- P23.02 Sandra Sif Gylfadottir. PAINFUL DIABETIC POLYNEUROPATHY DECREASES QUALITY OF LIFE IN DANISH TYPE 2 DIABETIC PATIENTS
- P23.03 Stine Derau Sørensen. INDIVIDUAL DIFFERENCES IN MUSIC REWARD EXPERIENCES IN DANISH ADOLESCENTS
- P23.04 Fernando Exposto. CHARACTERIZATION AND PREDICTIVE MECHANISMS OF EXPERIMENTALLY-INDUCED TENSION-TYPE HEADACHE
- P23.05 Saida Said. FUNCTIONAL STUDIES OF THE GABA TRANSPORTER BY SITE-SPECIFIC INCORPORATION OF A FLUORESCENT UNNATURAL AMINO ACID
- P23.06 Søren Bruno Elmgreen. THE LION PROCEDURE - DISRUPTING THE PARADIGM OF MOTOR REHABILITATION IN CHRONIC SPINAL CORD INJURY
- P23.07 Casper Schmidt. IMPULSIVITY AND COMPULSIVITY: THE ROLES OF DOPAMINE AND SEROTONIN IN REWARDS
- P23.08 David Ricardo Quiroga Martinez. A NEW MULTIFEATURE MISMATCH NEGATIVITY (MMN) PARADIGM FOR THE STUDY OF MUSIC PERCEPTION WITH MORE REAL-SOUNDING STIMULI
- P23.09 Klaus Ulrik Koch. INFLUENCE OF VASOPRESSORS AND INOTROPES ON BRAIN OXYGENATION AND CEREBRAL MICROCIRCULATION IN ANESTHETIZED PATIENTS WITH BRAIN TUMORS
- P23.10 Nina Stockfleth Buch. NEUROMAS AS THE CAUSE OF NEUROPATHIC PAIN IN AMPUTEES?

Poster session 24

Chairmen: Hanne Møller, Casper Kruse (PhD student) & Katrine Fuglsang (PhD student)

- P24.01 Anne Birkeholm Jensen. ANTIMICROBIAL SUSCEPTIBILITY TESTING OF AGGREGATIBACTER ACTINOMYCETEMCOMITANS COLLECTED GEOGRAPHICALLY WIDESPREAD SUPPORTS AMOXICILLIN AS A CONTINUED DRUG-OF-CHOICE IN PERIODONTAL TREATMENT
- P24.02 Trine Bertelsen. THE IL-17A/F HETERODIMER REGULATES PSORIASIS-ASSOCIATED GENES THROUGH $\text{I}\kappa\text{B}\zeta$
- P24.03 Maria Dietz Toppenberg. EVALUATION OF MOBILE X-RAY WITHIN THE TRIPLE AIM APPROACH
- P24.04 Susanna Botticelli. INFLUENCE OF CLEFT DIMENSIONS AT BIRTH ON DENTO-OCCLUSAL RELATIONS BEFORE ORTHODONTICS IN UNILATERAL CLEFT LIP AND PALATE PATIENTS: A SUBGROUP ANALYSIS WITHIN A RANDOMISED CLINICAL TRIAL
- P24.05 Arwa Gera. STABILITY AFTER ORTHODONTIC TREATMENT: HOW TO MAINTAIN TREATMENT RESULTS IN THE LONG TERM?
- P24.06 Dilde Haslund. DOMINANT-NEGATIVE EFFECTS IN HEREDITARY ANGIOEDEMA: INTRACELLULAR AGGREGATION AND RETENTION OF NORMAL C1 INHIBITOR INDUCED BY TRANS-INHIBITORY MUTANT C1 INHIBITOR
- P24.07 Anne Hald Rittig. THE ROLE OF STAPHYLOCOCCUS AUREUS IN CUTANEOUS T-CELL LYMPHOMA
- P24.08 Pankaj Taneja. SOMATOSENSORY INVESTIGATION OF OROFACIAL PAIN, UNPLEASANTNESS AND PLEASANTNESS
- P24.09 Yasser Haddadi. CLINICAL ACCURACY OF CROWNS BASED ON DIGITAL INTRAORAL SCANNING COMPARED TO CONVENTIONAL IMPRESSION METHOD: AN IN VIVO RANDOMISED SPLIT-MOUTH STUDY
- P24.10 Mads Hagen Pedersen. CORONECTOMY OF HIGH RISK MANDIBULAR THIRD MOLARS. LONG-TERM FOLLOW-UP OF TREATMENT OUTCOMES

Poster session 25

Chairmen: Anders Lade Nielsen, Dmitri Zintchouk (PhD student) & Bo Langhoff Hønge (PhD student)

- P25.01 Sidsel Rugberg Alsing. EXPERIMENTAL ANTI-ANGIOGENIC OCULAR GENE THERAPY
- P25.02 Wenqian Gu. THE DYNAMIC EFFECTS OF ISOSTEVIOL ON INSULIN SECRETION AND ITS ABILITY TO COUNTERACT THE IMPAIRED BETA-CELL FUNCTION DURING GLUCO-LIPO- AND AMINOACIDO-TOXICITY: STUDIES IN VITRO
- P25.03 Iben Bach Damgaard. BIOMECHANICAL STABILITY AFTER SMALL INCISION LENTICULE EXTRACTION (SMILE) FOR MYOPIA: AN EX-VIVO STUDY ON HUMANE DONOR CORNEAS
- P25.04 Anna Dons-Jensen. A_{2A} ADRENOCEPTOR STIMULATION REDUCES DILATATION OF RETINAL ARTERIOLES INDUCED BY FLICKERING LIGHT IN NORMAL PERSONS
- P25.05 Kristina Laugesen. CLINICAL INDICATORS OF ADRENAL INSUFFICIENCY FOLLOWING DISCONTINUATION OF ORAL GLUCOCORTICOID THERAPY: A DANISH NATIONWIDE SELF-CONTROLLED CASE SERIES ANALYSIS

- P25.06 Andreas Holmgaard. POSSIBLE DOMINANT-NEGATIVE EFFECTS IN MALATTIA LEVENTINESE/DOYNE HONEYCOMB RETINAL DYSTROPHY RESULTING IN ALTERED INTRACELLULAR FIBULIN-3 HANDLING
- P25.07 Kata Wolff Pedersen. ESTIMATING CYTOCHROME P450 EXPRESSION LEVELS IN POST-MORTEM HEPATIC TISSUE
- P25.08 Sashia Pernille Bak-Nielsen. KERATOCONUS OUTCOME RESEARCH QUESTIONNAIRE - A VALIDATION STUDY OF THE DANISH VERSION
- P25.09 Johanne Emy Sollid. PROTEIN INTERACTIONS OF THE AVP PROHORMONE AND THEIR ROLE IN FAMILIAL NEUROHYPOPHYSEAL DIABETES INSIPIDUS
- P25.10 Amanda Bæk. ADIPOSE TISSUE FIBROSIS IN PATIENTS WITH ACROMEGALY: BEFORE AND AFTER TREATMENT

Poster session 26

Chairmen: Sebastian Frische, Daan Koppens (PhD student) & Jens Hartlev (PhD student)

- P26.01 Tea Lund Laursen. SOLUBLE CD163 DECLINES DURING SUCCESSFUL DIRECT-ACTING ANTIVIRAL TREATMENT AND ASSOCIATES WITH INFLAMMATION AND FIBROSIS IN CHRONIC HEPATITIS C
- P26.02 Jakob Kirkegård. ACUTE PANCREATITIS AND PANCREATIC CANCER RISK: A NATIONWIDE MATCHED COHORT STUDY
- P26.03 Peter Andersen. OPEN VERSUS LAPAROSCOPIC RECTAL CANCER RESECTION AND RISK OF SURGERY FOR ADHESIVE SMALL BOWEL OBSTRUCTION: A NATIONWIDE POPULATION-BASED COHORT STUDY
- P26.04 Sissel Ravn. RISK FACTORS FOR METACHRONOUS PERITONEAL CARCINOMATOSIS: A NATIONWIDE POPULATION-BASED COHORT STUDY OF DANISH COLORECTAL CANCER PATIENTS
- P26.05 Anne Catrine Bjerre Mikkelsen. EFFECTS OF POTASSIUM DEFICIENCY ON LIVER PROTEIN AND UREA SYNTHESIS IN RATS
- P26.06 Nina Marie Videbech. RISK FACTORS OF RENAL FAILURE IN LONG-TERM CHILDHOOD CANCER SURVIVORS: AN ADULT LIFE AFTER CHILDHOOD CANCER IN SCANDINAVIA (ALICCS) STUDY
- P26.07 Frederik Rønne Pachler. FERTILITY IN PATIENTS WITH FAILURE OF RESTORATIVE PROCTOCOLECTOMY: A NATIONAL COHORT STUDY OF 1455 PATIENTS
- P26.08 Line Weisbjerg. DISTURBANCES IN THE RESPIRATORY CHAIN COMPLEXES AS A POSSIBLE CAUSE OF MITOCHONDRIAL DYSFUNCTION IN CHRONIC FATIGUE SYNDROME
- P26.09 Stine Karlsen. PATIENT SPECIFIC BIOMARKERS - A ROLE FOR CIRCULATING TUMOR DNA IN HEPATOCELLULAR CARCINOMA MANAGEMENT AND SURVEILLANCE?
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- P27.02 Louise Devantier. PET VISUALIZED STIMULATION OF THE VESTIBULAR ORGAN
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- P27.04 Hanne Nielsen. PROTON PUMP INHIBITOR PRESCRIPTIONS AND BREAST CANCER RECURRENCE: A DANISH NATIONWIDE PROSPECTIVE COHORT STUDY
- P27.05 Anne Sofie Borg Hammer. HYPODIPLOIDY IN CHILDHOOD ACUTE MYELOID LEUKEMIA: A RETROSPECTIVE COHORT STUDY BY THE INTERNATIONAL BERLIN-FRANKFURT-MÜNSTER STUDY GROUP, A MULTICENTER COLLABORATION
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- P27.08 Trine Line Hauge Okholm. CIRCULAR RNA EXPRESSION IS ABUNDANT AND CORRELATED TO AGGRESSIVENESS IN EARLY-STAGE BLADDER CANCER

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- P28.01 Mathias Kristensen. DOES ALDOSTERONE STIMULATE THE NA/CL COTRANSPORTER NCC INDEPENDENTLY OF HYPOKALEMIA?
- P28.02 Maria Linaa Markussen. STATINS AS A NEW TREATMENT DRUG FOR LITHIUM-INDUCED NDI
- P28.03 Julie Birkmose Axelsen. EFFECTS OF 6-MERCAPTOPYRIMIDINE IN PRESSURE OVERLOAD INDUCED RIGHT HEART FAILURE
- P28.04 Katrine Berg. SURVIVAL AND GRAFT FUNCTION IN HEART TRANSPLANT PATIENTS RECEIVING ADVERSE RISK PROFILE DONOR HEARTS
- P28.05 Lærke Dam Dengsøe Petersen. IMPLANTABLE CARDIOVERTER DEFIBRILLATOR THERAPY AND RELATED COMPLICATIONS IN YOUNG PATIENTS WITH INHERITED CARDIOMYOPATHY OR CHANNELOPATHY: A 17-YEAR COHORT STUDY
- P28.06 Anne Sif Lund Ovesen. NEUROHORMONAL AND INFLAMMATORY ACTIVITY IN ADULT PATIENTS WITH ATRIAL SEPTAL DEFECT
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- P28.08 Archana Kulasingam. NOVEL BIOMARKERS IN THE ACUTE PHASE OF ST-ELEVATION MYOCARDIAL INFARCTION

Poster session 29

Chairmen: Christian Erikstrup, Steffan Tábóri Jensen (PhD student) & Mia Glerup (PhD student)

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- P29.02 Anne Marie Hove. HUMAN PROSTATIC CELL RESPONSES TO INFECTION WITH PROPIONIBACTERIUM ACNES SUBSPECIES DEFENDENS
- P29.03 Stine Bruun. SELECTIVE SEROTONIN REUPTAKE INHIBITOR USE AND POSTOPERATIVE COMPLICATIONS, MORTALITY AND QUALITY OF CARE IN HIP FRACTURE PATIENTS
- P29.04 Charlotte Maria Jensen. APPROACHING PATIENT-CENTRED GOAL SETTING IN OUTPATIENT MULTIDISCIPLINARY REHABILITATION EXPERIENCES AND PERSPECTIVES OF PATIENTS AND HEALTH PROFESSIONALS
- P29.05 Camilla Darum Sørensen. MYELOID-DERIVED SUPPRESSOR CELLS AND MONOCYTES IN GRAFT-VERSUS-HOST DISEASE
- P29.06 Kaja Kristiane Eiksrud Kjørholt. NATIONWIDE TRENDS OF INFECTIONS AMONG HIP FRACTURE PATIENTS IN DENMARK, 2005-2016
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- P29.08 Mia Doherty. CLINICAL AND GENETIC EVALUATION OF DANISH PATIENTS WITH PYCNODYSTOSIS

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Abstracts

Fogh-
Nielsen

Linn Håkonsen EARLY LIFE EXPOSURES AND GENITAL ANOMALIES IN BOYS: NATIONWIDE
Arendt COHORT STUDIES IN DENMARK AND SWEDEN

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Background: Congenital abnormalities in the male reproductive tract are common, but the causes remain poorly understood.

Methods: In a nationwide register-based cohort study of all singleton boys born alive in Denmark (1978-2012), we studied the association between hypertensive disorders of pregnancy, including pre-gestational hypertension, gestational hypertension and preeclampsia, and the risk of the male genital anomalies cryptorchidism (undescended testes) and hypospadias (urethral meatus displacement).

Results: A total of 1,073,026 live-born singleton boys were included. Boys of mothers with pre-gestational hypertension had higher risk of cryptorchidism [adjusted hazard ratios (aHR): 1.31 (95% CI: 1.06; 1.62)] and hypospadias [aHR: 1.73 (95% CI: 1.28; 2.33)], whereas gestational hypertension was only slightly associated with cryptorchidism. For boys born of mothers with preeclampsia, the HRs increased with preeclampsia severity, for HELLP syndrome the highest risks were observed (cryptorchidism [aHR: 2.09 (95% CI: 1.37; 3.18)] and hypospadias [aHR: 3.91 (95% CI: 2.52; 6.08)]). The risks increased with lower gestational age at the time of the preeclampsia diagnosis. Boys of mothers with early-onset preeclampsia had the highest risks, whereas late-onset preeclampsia was only associated with a slightly increased risk.

Conclusions: We found an increased risk of genital anomalies among boys of mothers with hypertensive disorders of pregnancy. The highest HRs were observed for severe and early-onset preeclampsia. Future studies should seek to understand the potentially shared common aetiology of preeclampsia and genital anomalies.

Fogh-
Nielsen

Nichlas Riise
Jespersen

MITOCHONDRIAL MODULATION - A NEW CLINICAL TARGET FOR CARDIOPROTECTION?

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Background: Mitochondrial dysfunction plays a central role for ischemia
reperfusion injury. Pre-ischemic inhibition of the malate aspartate shuttle
(MAS) and succinate dehydrogenase (SDH) constitutes promising cardio-
protective interventions, but the underlying mechanisms remain unknown.

Method: Using a translational approach, we examined the mechanisms
behind MAS and SDH inhibition.

Study I: Cardioprotection by MAS inhibition was tested in isolated perfused
rat hearts. Mitochondrial respiration, changes in metabolites and infarct size
were examined to elucidate the mechanism.

Study II+III: Cardioprotection by SDH inhibition was tested in diabetic and
non-diabetic tissue from isolated perfused rat hearts and atrial strips from
patients undergoing by-pass surgery. Hemodynamic performance, infarct
size and mitochondrial function were examined to clarify the underlying
mechanisms.

Results:

Study I: MAS inhibition preserved post-ischemic mitochondrial respiration
and limited infarct size by attenuation of excessive ROS emission and
reduced oxidative damage in the intervention group.

Study II+III: Preliminary data show reduced hemodynamic performance,
increased infarct size and deteriorated mitochondrial respiration in rat and
human diabetic cardiac tissue. SDH inhibition did not reduce infarct size or
improve mitochondrial respiration in the animal trial, but showed improved
contractility and mitochondrial respiration in human tissue.

Conclusion: Although differences may be present between diabetic animal
models and diabetes in humans, MAS and SDH inhibition may provide
cardioprotection in non-diabetic as well as diabetic individuals and may
constitute new possible pharmacological targets.

Fogh-
Nielsen

Marie
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ALTERED RIGHT VENTRICLE MORPHOLOGY AND CONTRACTILE FUNCTION IN SMALL, OPEN VENTRICULAR SEPTAL DEFECTS

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Background: Patients with small, open ventricular septal defects (VSD) have traditionally been considered to have normal outcomes in adulthood. However, we have previously demonstrated a 20% lower functional capacity in these patients when compared with healthy peers. The mechanisms behind these findings remain unclear. Therefore, we performed magnetic resonance imaging (MRI) and transthoracic echocardiography (TTE) to evaluate biventricular morphology and function.

Methods: Adults with small, open VSDs and healthy controls underwent cine MRI for the evaluation of biventricular volumes and tissue Doppler TTE for the assessment of biventricular force-frequency relationship. MRI and TTE measurements were analysed post hoc in a blinded fashion by one main investigator.

Results: Thirty-two patients with open VSDs (26±6years) and 28 matched controls (27±5years) were included. Open VSDs were found to have larger right ventricular end-diastolic volume index (105±17ml/m²) compared with matched controls (88±13ml/m²), p<0.01. Left ventricular measurements displayed no differences. Additionally, the patients' right ventricles were visually characterized by abundant coarse trabeculations. TTE revealed lower isovolumetric accelerations at rest in patients compared with controls in right ventricle (111±48 vs. 149±43 cm/s², p<0.01), septum (100±44 vs. 154±77 cm/s², p<0.01), and left ventricle (93±46 vs. 166±72 cm/s², p<0.01).

Conclusions: An altered right ventricular morphology and contractile function was demonstrated at rest in adults with small, open VSDs. These findings may explain some of the mechanisms behind the exercise limitations that have previously been found in adulthood in these patients.

001.01 Sara Konstantin Nissen WHOLE EXOME SEQUENCING OF HIV-1 LONG-TERM NON-PROGRESSORS IDENTIFIES RARE VARIANTS IN GENES ENCODING INNATE IMMUNE SENSORS AND SIGNALING MOLECULES

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Among HIV-infected patients, <1% have no disease progression, but they can live for several years with viral control and unaltered CD4 T cell count without treatment. Factors associated with slow disease progression (CCR5 heterozygosity and protecting HLA alleles) can only explain 25% of the HIV long-term non-progressor (LTNP) phenotype. Hence, the cellular mechanisms underlying this immunological phenotype remain poorly understood.

Type I interferon (IFN) has been suggested to play a pathogenic role in driving chronic immune activation and CD4 T cell depletion during HIV infection. In the present study, we collected a cohort of HIV LTNPs based on data from the Danish HIV Cohort and performed whole exome sequencing together with functional immunological analyses. Through this approach, we identified several rare variants in genes involved in innate immune sensing, CD4 expression, HIV trafficking, and HIV transcription. Particularly, we identified two patients with homozygous variants in STING. STING is an adaptor molecule downstream DNA sensing leading to IFN production. We found decreased STING expression levels and decreased IFN responses to DNA challenge and HIV infection in patients with these variants compared to HIV-infected individuals with wild-type STING and normal disease progression.

In conclusion, our data suggest that homozygous variants in STING result in decreased innate DNA sensing and IFN production and, therefore, might contribute to reduced chronic inflammation and slow disease progression in HIV LTNPs. Furthermore, our data provide novel candidate genes for further studies on the basic biology, immunology, and potential therapeutic targets of HIV infection.

001.02 Juan Yuan ANTI-TUMOR EFFECTS OF HDAC AND DNMT1 INHIBITORS ON MEDULLOBLASTOMA CELLS

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Medulloblastomas are one of the most common aggressive brain malignancies in children. Considerable progress has been made in the treatment regimens. However, the patients are still at risk of developing neurologic and cognitive deficits. Most importantly, there are different subtypes of medulloblastoma, which need to be treated according to their clinical and molecular characteristics. Encouragingly, it has been reported that an epigenetic modification therapy based on histone deacetylase inhibitors (HDACi) alone or combined with DNA methyltransferase 1

(DNMT1) inhibitors has exhibited anti-cancer effects. Thus, epigenetic modifiers are promising drugs for personalized therapy of medulloblastoma. In our study, a panel of epigenetic drugs was tested for their effect on medulloblastoma cells under mild hypoxic conditions that reflect the physiological concentrations of oxygen in the brain. We selected a set of class I and II HDACi and a DNMT1 inhibitor, 5-aza-2'-deoxycytidine (5-aza-dC), to treat Daoy and D283 Med medulloblastoma cells. Cell viability, apoptosis and cancer sphere survival were assessed in both cell lines. We found that parthenolide was efficient in inducing cell death in both cell lines tested. Interestingly, when suberoylanilide hydroxamic acid (SAHA) and parthenolide were individually applied in combination with 5-aza-dC, a synergistic effect on cell survival was observed in both cell lines. Our current results suggest that the combination of HDACi with DNMT1 inhibitors may represent a promising treatment for medulloblastoma.

001.03 Stefanie Luecke

THE INNATE IMMUNE SYSTEM IS ACTIVATED BY CYTOSOLIC DNA IN A LENGTH-DEPENDENT MANNER

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The innate immune system is responsible for the first recognition of invading pathogens by using pattern recognition receptors (PRRs) to sense the presence of pathogen-associated molecular patterns (PAMPs). In the last decade, it has been discovered that cytosolic DNA acts as a potent PAMP, stimulating innate immune responses, including type I interferons (IFN) which have antiviral and immunomodulatory activities. Cyclic GMP-AMP synthase (cGAS) is one of the PRRs that recognize cytosolic DNA. It signals via the signaling adaptor STING to induce IFN production. Despite the importance of DNA in innate immunity, the nature of the DNA that stimulates IFN production is not well described.

Using low DNA concentrations, similar to those present during infections, we show that DNA induces IFN in a length-dependent manner in cell culture. This is observed over a wide length-span of DNA, ranging from the minimal stimulatory length to several kilobases, and is fully dependent on cGAS irrespective of DNA length. Importantly, in vitro studies reveal that long DNA activates recombinant human cGAS more efficiently than short DNA. This shows that length-dependent DNA recognition is an intrinsic property of cGAS independent of accessory proteins.

Collectively, this work identifies long DNA as the molecular entity stimulating the cGAS pathway upon cytosolic DNA challenge. This may allow cGAS to efficiently detect viral and bacterial genomes, which often consist of long DNA present at low concentrations, while avoiding autoimmunity due to the presence of shorter host-derived cytosolic DNA, such as the byproducts of DNA repair.

O01.04 Rasmus Pihl ANALYSIS OF FACTOR D ISOFORMS IN MASP-3-DEFICIENT PATIENTS HIGHLIGHTS THE ROLE OF MASP-3 AS A MATURASE IN THE ALTERNATIVE PATHWAY OF COMPLEMENT

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Background: Complement is part of our innate immune system and is a cascade of proteases that can be initiated by three routes. The alternative pathway (AP) is key to complement activity, as it greatly amplifies the response of the system. Factor D (FD) has been viewed as the first-acting protease of the AP and was believed to be synthesized as an activated protease. Recently, it was shown that Masp1^{-/-} mice, which lack the proteases MASP-1 and -3, have a defective AP due to the fact that FD circulates as a proenzyme (pro-FD).

Methods: We have developed a technique based on isoelectric focusing (IEF) that resolves FD variants in complex samples. The FD variant distribution was analyzed in serum and plasma samples from MASP-3-deficient patients and healthy donors. MASP-3 was injected intravenously into Masp1^{-/-} mice, and lysis of rabbit erythrocytes was used to follow the level of AP activity. Moreover, MASP-3 was immunoprecipitated from EDTA plasma, and its activation state was investigated by western blotting.

Results: Analysis of FD isoforms showed that samples from MASP-3-deficient patients predominantly contained pro-FD, whereas samples from healthy donors mainly contained FD. Noticeably, small amounts of FD were still detected in patient samples. Moreover, the importance of MASP-3 for the AP was highlighted by the fact that the AP in Masp1^{-/-} mice was rescued by injection of MASP-3. Lastly, we show that roughly half of the circulating MASP-3 is in an activated state, which explains why healthy donors mainly contain FD. Our results show that the AP, which is emerging as an attractive target for treating several autoimmune diseases, largely depends on MASP-3.

O01.05 Christian Benner FINEMAP: ULTRAFAST HIGH-RESOLUTION FINE-MAPPING USING SUMMARY DATA FROM GENOME-WIDE ASSOCIATION STUDIES

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Although Genome-Wide Association Studies (GWAS) have been successful in narrowing down the genome into regions underlying disease susceptibility, any one disease-associated region still harbours thousands of correlated genetic variants, which complicates biological follow-up. Fine-mapping aims to refine the large set of variants associated with the disease down to a much smaller set of variants with a direct effect on the disease.

This is, however, a hard combinatorial problem and requires advanced statistical methods to efficiently explore the high-dimensional model space. Recently, fine-mapping approaches have been extended to use GWAS

summary data, but they rely on computationally expensive exhaustive search, which limits their use to only a few hundred variants.

We introduce a software package, FINEMAP, which replaces the exhaustive search by an ultrafast stochastic search. We demonstrate that (1) FINEMAP opens up completely new opportunities by fine-mapping the HDL-C association of the LIPC locus with 20,000 variants in less than 90 seconds, while exhaustive search would require thousands of years. By jointly modeling the locus, (2) FINEMAP identifies a 3-SNP configuration with 190-fold higher likelihood than the top configuration from conditional analysis. We suggest that a missense variant and a promoter polymorphism are likely to be causal, whereas the lead variant in single-SNP testing has less evidence than a regulatory variant correlated with it. With extensive simulations, we further show that (3) FINEMAP is as accurate as exhaustive search when the latter can be completed and (4) achieves even higher accuracy when the latter must be restricted due to computational reasons.

O01.06 Jaakko
Keinänen LOW-GRADE INFLAMMATION IN FIRST-EPISODE PSYCHOSIS IS DETERMINED BY WAIST CIRCUMFERENCE INCREASE

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Psychosis is associated with low-grade inflammation as measured by high-sensitivity C-reactive protein (hs-CRP). We aimed to investigate the relationship between CRP and metabolic changes in people with first-episode psychosis (FEP) during the first treatment year. We recruited 95 FEP patients and 62 controls and measured the changes in hs-CRP, weight, waist circumference, insulin resistance and lipids. We used linear mixed models to analyze the relationship between CRP and metabolic changes.

At baseline, FEP patients (mean age: 26.1 years) had higher insulin resistance, total and LDL cholesterol, apolipoprotein B and triglyceride levels than controls. However, baseline weight and waist circumference, hs-CRP, fasting glucose and HDL cholesterol were similar between patients and controls. A robust change in anthropometric measures and inflammation was evident among patients by 12 months. Hs-CRP was significantly higher in patients at 12-month follow-up than at baseline (baseline hs-CRP 0.67 mg/l, IQR 0.33-2.54; 12-month 1.73 mg/l, IQR 0.49-4.21; Wilcoxon signed-rank $p=0.007$). Of patients, 59% were overweight or obese and 32% had abdominal obesity by 12 months. The median weight gain among patients was 9.6 kg (IQR 1.5-13.6 kg), and the waist circumference increase was 6.0 cm (IQR 2.0-13.0 cm). There was a strong positive relationship between waist circumference increase and hs-CRP.

In conclusion, patients with FEP are in a marked risk of developing abdominal obesity and subsequent low-grade inflammation. Prevention of the early metabolic changes in FEP is important, as abdominal obesity and inflammation are associated with increased risk of cardiovascular events and mortality.

O02.01 Janni Strøm Petersen FACTORS ASSOCIATED WITH SYMPTOMS OF ANXIETY AND DEPRESSION IN ADULTS UNDERGOING SPINE SURGERY - A SYSTEMATIC INTEGRATIVE REVIEW

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Background: Anxiety and depression are important outcome predictors of pain, physical impairments, and lower health-related quality of life among patients undergoing spine surgery. We aimed to identify factors associated with symptoms of anxiety and depression before and after spine surgery.

Method: A systematic literature search was conducted in PubMed, CINAHL, PsycINFO, Embase, Scopus, Cochrane, and Web of Science. A three-step selection and assessment process was conducted; titles and abstracts (N=1124) were skimmed for relevance, and the remaining articles (N=53) were read in full. Articles that did not meet the inclusion criteria (N=26) were excluded. Eligible articles (N=31) were critically appraised for methodological validity. The 14 remaining articles were synthesized and analysed using a convergent qualitative design to extract and synthesize findings from both qualitative and quantitative articles, thereby transforming results into qualitative findings.

Results: Fourteen studies were included and reported findings based on 4.833 participants: 3.017 males and 1.816 females (mean age: approximately 49 years). From 75 findings, five categories of factors associated with anxiety and depression both before and after undergoing spinal surgery were identified: pain, information, disability, employment and psychological disturbances.

Interpretation: Five categories of interacting factors both before and after surgery were identified: pain, lack of information, disability, return to work, and psychological disturbances. Furthermore, information appears to have a regulating effect on the other four factors that influence anxiety and depression.

O02.02 Kaj Verner Døssing THE USE OF ULTRASOUND TO EXCLUDE EXTREMITY FRACTURES IN ADULTS

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Background: The conventional diagnostic approach on suspicion of upper and lower extremity fracture consists of a clinical and a radiographic examination. Fifty per cent of the patients go through an X-ray examination although they have no fracture. Studies indicate that ultrasound (US) can effectively identify fractures in adults.

Aim of study: We aimed to determine the diagnostic accuracy of US screening to exclude extremity fractures in adults. Furthermore, we aimed to determine the inter-rater agreement of US images in this group of patients.

Materials and method: We consecutively enrolled 92 adults referred to X-ray at Viborg Regional Hospital on suspicion of extremity fracture. To ensure blinding, US was consistently performed prior to X-ray. Similarly, no clinical examination was performed. X-rays were reviewed for the presence of fracture and considered to be gold standard. Inter-rater agreement between one of the investigators and a blinded radiologist was conducted by evaluating 42 randomly selected US images.

Results: The prevalence of fractures was 27%. McNemars test found no systematic difference between the results of US and X-ray ($p=0.69$). The sensitivity of US in detecting fracture was 92% (95% CI: 74;1.0) and the specificity was 94% (95% CI: 85;1.0). The positive predictive value of US was 85% (95% CI: 66; 96) and the negative predictive value was 97% (95% CI: 0.89;1.0). The inter-rater agreement was 100%, equal to a kappa value of 1 (95% CI: 1;1).

Conclusion: US screening on suspicion of extremity fracture has a high accuracy and reliability. No systematic differences were found between the results of the two modalities.

O02.03 Kasper
Faarkrog
Høyer

SEVOFLURANE ANESTHESIA INDUCES HEPATIC AND SKELETAL MUSCLE INSULIN RESISTANCE AND REDUCES GLUCOSE UPTAKE IN THE BRAIN

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Background: The use of anesthetics severely influences insulin sensitivity and glucose metabolism. This poses challenges for patients in clinical settings and for the use of animals in diabetes research. However, little is known about the underlying mechanisms for the condition. The aim of the present study was to determine the tissue specificity of insulin resistance during sevoflurane anesthesia.

Methods: Fourteen mice were divided into two groups: conscious mice ($n=6$) and mice under sevoflurane anesthesia ($n=8$). All mice underwent a hyperinsulinemic clamp, where constant infusion of insulin and donor blood was administered during variable glucose infusion to maintain isoglycemia. 2-[1-¹⁴C]-deoxy-D-glucose was infused to determine tissue specific uptake of glucose in adipose tissue, heart, brain and skeletal muscle.

Results: Sevoflurane anesthesia severely impaired insulin stimulated glucose uptake, which was demonstrated by a 30% lower Glucose Infusion Rate (GIR). This was associated with a significantly decreased glucose uptake in brain, soleus, triceps and gastrocnemius muscles of sevoflurane-anesthetized mice compared to conscious mice. In addition, plasma FFA, a potent inducer of insulin resistance, increased by 42% in mice under sevoflurane anesthesia.

Conclusions: Sevoflurane inhalation anesthesia induce hepatic and skeletal muscle insulin resistance in mice, but anesthesia also involves reduced glucose uptake in less insulin-sensitive tissue as the brain. The underlying mechanisms may involve sevoflurane-induced mobilization of FFA.

O02.04 Peter Lund
Ovesen

THE SORTING PROTEIN SORCS1 REGULATES NEURONAL INHIBITION IN THE HIPPOCAMPUS

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Neuronal inhibition in the brain is crucial for controlling and organizing neuronal output. Issues within this system are core features of psychiatric disorders like autism and schizophrenia. The inhibitory system makes up 20% of the total neuronal population in the brain and consists of interneurons that use GABA as their transmitter molecule to control the activity and timing of excitatory neurons. They enable simultaneous activation of larger groups of excitatory neurons, resulting in rhythmic or repetitive neural activity measured as network oscillations. 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). SorCS1 interacts with and regulate axon-dendritic sorting of Neurexins (N. Savas et al., 2015), synaptic adhesion proteins with several functions within the synapse; one of them being binding and regulating postsynaptic GABA_A receptors (Zhang C. et al., 2010).

We have investigated neuronal network inhibition in the hippocampus of mice absent of SorCS1 (SorCS1^{-/-}). By electrophysiology, we found reduced general inhibition in the dentate gyrus along with impaired γ -oscillations. Protein expression analysis and immunohistochemistry of the dentate gyrus showed a reduction in the total number of inhibitory synapses and a strong reduction of one of the major GABA_A receptor subunits. Finally, working memory was impaired in SorCS1^{-/-} mice, which suggests a functional consequence of impaired γ -oscillations in the hippocampus.

Our results support a role of SorCS1 in regulating the inhibitory tone of the brain.

O02.05 Gunhild Mo
Hansen

SHOULDER FUNCTION AND CONSTRAINT-INDUCED MOVEMENT THERAPY (CIMT)

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Background: Reduced motor and functional performance in the upper extremity (UE) is a potential consequence after stroke. Shoulder function plays an important part in the UE function and is an essential prerequisite for many daily life activities. Improving shoulder function is, therefore, an important goal in rehabilitation. Constraint-induced movement therapy (CIMT) is an evidence-based intensive approach for patients with impaired UE motor function after stroke, but little is known about the specific changes in shoulder function following CIMT. The aim of this study was to identify

possible predictor variables for satisfactory shoulder function in patients with reduced shoulder function pre-CIMT.

Method: This retrospective cohort study is based on data of 229 patients who participated in CIMT-training at a neurorehabilitation hospital in Denmark from December 2008 until October 2015. Satisfactory function was defined as a sum score >16 of four items defining proximal function according to the Wolf Motor Function Test Functional Ability Scale (WMFT-FAS). Predictors of satisfactory shoulder function after CIMT were identified using multivariable logistic regression.

Results: Better distal UE function and good proximal shoulder function were strong predictors of satisfactory shoulder function, whereas age and time since stroke on admission to CIMT were not.

Conclusions: Intensive CIMT training comprising tasks that require both distal and proximal upper extremity function may increase the shoulder function in patients with a potential functional reserve.

O02.06 Sara Buskbjerg BELIEVE IN SATELLITE GLIAL CELLS' INVOLVEMENT IN NEUROPATHIC PAIN
Jager

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Neuropathic pain is a chronic condition seen in patients suffering a direct injury to the peripheral or central nervous system or an indirect injury due to, e.g., diabetes. Current treatment options fall short of preventing or completely relieving patients of their pain.

For years, research has focused on understanding the role of neurons in neuropathic pain pathogenesis while overlooking the role of supportive cells in general and satellite glial cells (SGCs) in the dorsal root ganglion in particular. These cells not only buffer the neuronal microenvironment; they are also believed to be 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 SGCs in neuropathic pain development and thereby aid the identification of new drug targets. The SGCs turned out to be difficult to study with traditional neuroscience methods, so we decided to develop a protocol for fluorescently activated cell sorting (FACS). This proved to be difficult, but we believed in our choice of method and finally succeeded in purifying SGCs from adult mice. We then ran RNA sequencing on SGCs after peripheral nerve injury to compare their transcriptome to that of uninjured cells at different time points. The results have confirmed that the SGCs react to peripheral nerve injury by regulating genes that are important for proliferation, cholesterol metabolism and immune system regulation.

Further research into the three SGC functions identified by our research is expected to enhance our understanding of how SGCs contribute to the development of neuropathic pain.

O03.01 Rikke Kaae E-LEARNING IMPROVES THEORETICAL KNOWLEDGE ON ULTRA-SONOGRAPHY-BASED ASSESSMENT OF UMBILICAL CATHETER PLACEMENT AMONG PEDIATRICIANS

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Background: The efficacy and potential limitations of e-learning for ultrasonography (US) are sparsely investigated.

Objective: To assess the improvement in theoretical knowledge after a 1.5 h e-learning program introducing US-based assessment of umbilical catheter placement.

Methods: The study is a comparative observational experiment. The e-learning program comprised video examples with voiceover. A 25-item multiple-choice questionnaire (MCQ) test of 'one best answer' type was developed and validated for this study. The MCQ was administered before and after e-learning. A total of 20 paediatricians, 12 fellows and 8 neonatologists with minimal or no experience in the use of US were included. The MCQ was scored as follows: 10 points for choosing the correct answer and 0 for an incorrect or blank answer. Maximum score was 250 points. The learning outcome was measured by the participants' change in the MCQ score.

Results: The participants' MCQ scores (mean±SD) before and after completing the e-learning were 161±30 and 234±14 points, respectively. Mean MCQ score difference was 73±30 points (P < 0,0001, two-tailed paired t-test). Participants with the lowest scores in the pre-MCQ test tended to have the largest improvement in score, resulting in a smaller post-test standard deviation of the mean.

Conclusion: E-learning homogenized and increased the pediatricians' theoretical knowledge in US-based assessment of umbilical catheter placement. The outcome related to practical skills and the need for additional hands-on training should be investigated before the e-learning program can be recommended as a part of paediatricians training.

O03.02 Marie Bill MAPPING THE CLEC12A EXPRESSION ON MYELOID PROGENITORS IN NORMAL BONE MARROW; IMPLICATIONS FOR UNDERSTANDING CLEC12A RELATED CANCER STEM CELL BIOLOGY

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The C-type lectin domain family 12, member A (CLEC12A) receptor has emerged as a leukemia associated and cancer stem cell marker in acute myeloid leukemia, and we have previously shown the relevance of this

marker in myelodysplastic syndrome. However, a detailed delineation of its expression in normal hematopoiesis is lacking.

Here, we have characterized the expression pattern of CLEC12A on the earliest stem and myeloid progenitor subsets by multicolor flowcytometry on bone marrow cells from 13 healthy individuals. In addition, sorted CLEC12A[±] myeloid progenitor cells from 6 donors were investigated in the colony forming cell (CFC) assay.

We demonstrate distinct CLEC12A expression in the classically defined myeloid progenitors, where on average 39.1% (95% CI [32.5;45.7]) of the common myeloid progenitors (CMPs) expressed CLEC12A, while for granulocyte-macrophage progenitors (GMPs) and megakaryocyte-erythroid progenitors (MEPs) the average percentages were 81.0% (95% CI [76.0;85.9]) and 11.9% (95% CI [9.3;14.6]), respectively. In line with the reduced CLEC12A expression on MEPs, functional assessment of purified CLEC12A[±] CMPs and MEPs in the CFC assay demonstrated CLEC12A⁺ subsets to favor non-erythroid colony growth.

In conclusion, we provide evidence that the earliest CLEC12A⁺ cell in the hematopoietic tree is the classically defined CMP, and we show that CLEC12A expressing CMPs and MEPs are functionally different than their CLEC12A negative counterparts. Importantly, these data can help determine which cells will be spared during CLEC12A-targeted therapy. Furthermore, we propose CLEC12A to be included in future detailed studies of myeloid cancer stem cell biology.

O03.03 Marianne
Bjerre
Cancellation

POTENTIAL NEW MINIMALLY INVASIVE DIAGNOSTIC BIOMARKERS FOR PROSTATE CANCER

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Overdiagnosis and overtreatment of prostate cancer (PC) is a major challenge, and use of the PSA test is not without issues. Consequently, there is an urgent need for novel diagnostic and prognostic molecular biomarkers for PC. Tumours shed genomic DNA into the blood, known as circulating tumour 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 tumour biopsy for PC and thus could be a source for discovery of new minimally invasive diagnostic biomarkers. We aimed to identify PC-specific hypermethylated CpG sites that are suitable for liquid biopsy testing in order to improve diagnostic accuracy.

We designed methylation specific PCR assays for the 11 top candidate markers, based on bioinformatically analysis of 5031 male tissue samples from Marmal-aid database. The sensitivity and specificity of these assays were tested on PC tissue (n=20) and BPH tissue (n=20) as well as leukocytes (n=40) before clinical validation on plasma (BPH, localized and metastatic PC).

We identified six novel epigenetic biomarker candidates with high specificity (84 - 100 %) and sensitivity (75-94 %) for prostate cancer in tissue-based analyses. Additionally, they displayed a promising potential for liquid tumour biopsy analyses, as none of the assays detected methylated DNA from leukocytes. We are currently investigating the diagnostic potential of our top candidate markers in plasma samples from a large patient cohort (n=150), including men with vs. without PC, recurrent vs. non-recurrent PC after radical prostatectomy, and localized vs. metastatic PC.

O03.04 Charlotte Madsen

UPFRONT RITUXIMAB MAINTENANCE AFTER INDUCTION THERAPY IMPROVES THE OUTCOME AND REDUCES THE RISK OF HISTOLOGICAL TRANSFORMATION IN PATIENTS WITH FOLLICULAR LYMPHOMA - A NATIONWIDE COHORT STUDY

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The introduction of the CD20 antibody rituximab in combination with chemotherapy (R-chemo) has improved the prognosis of patients with follicular lymphoma (FL). During the last decade, the addition of rituximab maintenance (MR) has been tested with the hopes of further improving the outcome of these patients. In the present study, we investigated the effect of upfront MR on time related endpoints as well as the rate of histological transformation (HT). Patients with FL or Diffuse Large B-cell Lymphoma (DLBCL) were identified through the Danish Pathology and Lymphoma Registries. HT was defined as biopsy-proven FL followed by a subsequent biopsy-verified FL grade 3B or DLBCL. Patients were included if they: (i) completed first-line induction treatment with R-chemo, (ii) were alive after induction treatment and eligible for MR, and (iii) had no evidence of HT at the same time point. Among 733 patients who completed their first R-chemo, 364 were consolidated with MR and 369 were not. Patients receiving MR had more often advanced clinical stage ($p<0.001$), high FLIPI score ($p<0.001$), and bone marrow infiltration ($p=0.016$). Despite of these adverse features, those consolidated with MR had an improved 5-year OS (89% vs. 81%; $p=0.001$) and PFS (72% vs. 60%; $p<0.001$) at both univariate and multivariate level. Interestingly, a trend towards a reduction of HT was also observed among MR treated patients (6% vs. 10%; $p=0.067$). When we compared induction treatments, the above mentioned advantages were more evident in patients receiving doxorubicin-containing regimens.

O03.05 Ying Liu

PWP1: A NOVEL NUTRITION-DEPENDENT GROWTH REGULATOR

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Tissue growth is closely regulated during animal development and displays a high degree of plasticity in response to environmental cues, such as nutrient availability. Studies in *Drosophila* and other genetic model systems have established the conserved role of insulin/mTOR signaling pathway in nutrient-dependent growth control. A key process controlled by insulin/mTOR signaling is ribosome biogenesis, which is a limiting process for growth through its impact on cellular protein biosynthetic capacity. However, how ribosome biogenesis is controlled by nutrients via mTOR signaling has remained insufficiently understood. Here, we demonstrate that a conserved chromatin-binding protein PWP1 is an essential regulator of ribosomal RNA expression and a key link between mTOR-mediated nutrient sensing and ribosome biogenesis-mediated growth control in vivo. Ribosome biogenesis is frequently deregulated in cancer, and our data shows that high expression of PWP1 in head and neck squamous cell carcinoma tumors strongly associates with poor patient prognosis. In conclusion, our study establishes PWP1 as a novel nutrient-responsive regulator of rRNA expression and tissue growth in vivo with a potential role in tumorigenesis in human.

O03.06 Michael Roost
Clausen GRADE 3-4 NEUTROPENIA AFTER THE 1ST CYCLE OF CHEMOTHERAPY FOR DIFFUSE LARGE B-CELL LYMPHOMA IS ASSOCIATED WITH INFERIOR OUTCOME COMPARED TO GRADE 1-2 OR NO NEUTROPENIA - A DANISH COHORT STUDY

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Hematologic toxicity of chemotherapy could be a biologic measure of treatment efficacy and has been correlated to positive outcome in other cancers. We investigated the prognostic implications of neutropenia, after the first cycle of chemotherapy for patients with diffuse large B-cell lymphoma (DLBCL).

Data from patients diagnosed with de novo DLBCL between 2000 and 2013 were retrieved from Danish registries and laboratories. Inclusion criteria were: treatment with combination chemotherapy containing doxorubicin and no primary CNS-lymphoma. We graded blood neutrophil values ($10^9/L$), measured 8 to 10 days after the first treatment cycle, as G3-4: <0.5 , G1-2: $0.5- <2$, and G0: ≥ 2.0 . The 5-year overall survival (OS) proportion was estimated with the Kaplan-Meier method. In a Cox regression model, we estimated the corresponding hazard rate ratios (HRs) using G3-4 as reference, both crude and adjusted for the NCCN International Prognostic Index (IPI) risk factors (age, tumor stage, LDH, performance and extra nodal disease).

Nadir values were available for 863 (24%) of 3531 patients. G3-4 neutropenia was present in 465 (54%) patients, and these patients had higher IPI than G1-2 and G0. In patients treated with rituximab-chemo, OS at five years was 53% (95%CI, 48-58) in G3-4, 72% (95% CI, 62-80) in G1-2, and

66% (95% CI, 0.60-0.72) in G0. After adjustment, this corresponded to a HR for death of 0.63 (95% CI, 0.43-0.93) in G1-2 neutropenia and 0.79 (95% CI, 0.60-1.04) in G0, when compared with G3-4.

In contrast to reports in other cancers, G3-4 neutropenia was associated with an inferior outcome in DLBCL compared to G1-2 or no neutropenia.

O04.01 Anders
Valdemar
Edhager

MAJOR METABOLIC PATHWAY ALTERATIONS IN THE MYOCARDIUM DURING DEVELOPMENT OF TYPE 2 DIABETES

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Congestive heart failure, cardiomyopathies, and myocardial infarction are all co-morbidities associated with the development of Type 2 diabetes (T2D), which could lead to pre-mature death. It is, therefore, of vital importance to investigate the effects of progressing T2D in the diabetic heart.

The aim of the study was to identify regulated proteins and intracellular metabolic pathways in the diabetic rat heart as T2D develops by mass spectrometry (MS) based proteomics.

Zucker Diabetic Fatty rats (ZDF^{fa/fa}) and their heterozygous lean controls (ZDF^{fa/+}) were euthanized at age 6 weeks (pre-diabetic state), 12 weeks (onset of T2DM), and 24 weeks (late T2D), and hearts were removed. Heart tissue was homogenized and trypsin digested, and resulting peptides were analyzed by MS. Proteins were quantified and sorted into functional pathways by KEGG and DAVID.

At an early stage (6 weeks, pre-diabetic state), only minor disturbances of the diabetic rat heart proteome were detected. At onset of T2D, proteins involved in major metabolic pathways (BCAA, glycolysis, TCA-cycle, fatty acid metabolism (FAM)) were upregulated, whereas OXPHOS proteins were mainly downregulated. Peroxisomes and insulin signaling were also perturbed. At late T2D, proteins of same metabolic pathways were downregulated, except FAM, which was upregulated. The most enriched pathways were the mitochondrion, glucose/ribitol dehydrogenase, and FAM.

We report here, for the first time, changes in the diabetic rat heart proteome as T2D develops. There is a shift in major metabolic pathways in the diabetic rat heart as the disease progresses from the pre-diabetic state to late T2D, which may have consequences for heart function.

O04.02 Sheyanth
Mohanakumar

THE REVEALING OF THE FORGOTTEN CIRCULATION

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Background: The lymphatic vasculature has been a neglected research area. The lack of human clinical research has predominantly been due to absence of in-vivo techniques to assess lymphatic morphology and function. Being one of few centres mastering NIRF imaging and MRI for assessing lymphatic function in humans, we significantly contribute to increasing the understanding of human lymphatics. Our ability to perform in-vitro and in-vivo tests of human lymphatic vasculature has generated the current translational PhD project.

Methods: In-vitro studies were conducted using human thoracic ducts (TDs). Vessels were mounted in a wire myograph for isometric force measurements to characterize the role of Cl⁻ for the human TD contractility. The in-vivo functional state of lymphatics is described using NIRF and MRI. Study subjects are patients with a Fontan circulation and post-menopausal women receiving CCB treatment.

Results: Spontaneous activity was fully stopped in Cl⁻-free conditions. The contractility achieved after a CCRC at 10 μ M NA under control conditions was 1.37 \pm 0.28N/m and reduced to 0.38 \pm 0.14N/m in the absence of Cl⁻ (p=0.0110). MRI shows that Fontan patients have a vast abnormal network of lymphatic and dilated thoracic ducts. Lymphatic function in the fontan group shows a contraction frequency: 0.8(0.1) min⁻¹, propulsion velocity: 2,1(0.2) cm/s and a significant lowering of the pumping pressure: 51(3) mmHg compared to the control group, p<0.05. CCB study results are still pending.

Conclusion: Our findings demonstrate that the human TD contractility is dependent on Cl⁻ and that lymphatics in Fontan patients are abnormal with respect to both morphology and function.

O04.03 Kaare Terp
Fjederholt

PERIOPERATIVE BLOOD TRANSFUSIONS INCREASES THE RISK OF ANASTOMOTIC LEAKAGE AFTER SURGERY FOR GEJ CANCER

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Aim: To investigate the effect of blood transfusions on the risk of anastomotic leakage in patients with gastro-esophageal-junction cancer.

Background: The incidence of gastro-esophageal-junction cancer is increasing in the western world. Surgery is the curative treatment of choice. Anastomotic leakage increases the mortality, morbidity and risk of cancer recurrence. In colorectal surgery, a relation between anastomotic leakage and blood transfusions have been demonstrated.

Method: The risk of anastomotic leakage in relation to blood transfusions was investigated in a cohort study. 253 consecutive patients undergoing surgery for gastro-esophageal-junction cancer were included. Data was based on a prospectively maintained database and analyzed using logistic regressions models adjusting for multiple confounders.

Results: We found an increased risk of anastomotic leakage when blood was transfused, OR: 3.47, (1.51; 7.99). This relation was consistent after adjustment for multiple confounders, OR: 4.60, (1.29; 16.4). Increasing number of blood units did not increase the risk of AL further.

Conclusion: We present data demonstrating a strong correlation between receiving blood transfusions and the risk of AL after surgery in gastro-esophageal-junction cancers patients.

004.04 Morten Fenger-Grøn LEAN BODY MASS IS THE PREDOMINANT ANTHROPOMETRIC RISK FACTOR FOR ATRIAL FIBRILLATION

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Background: Obesity is repeatedly emphasized as a risk factor for atrial fibrillation or flutter (AF). However, the underlying evidence may be questioned as the obvious correlations between various anthropometric measures hamper identification of the characteristics that are biologically driving AF risk.

Objectives: This study aimed to assess mutually adjusted associations among AF risk and height, weight, body mass index, hip and waist circumference, waist-to-hip ratio, fat mass, lean body mass, and fat percentage.

Methods: Anthropometric measures and self-reported life-style information were collected from 1993 to 1997 in a population-based cohort including 55,273 persons aged 50 to 64 years who were followed in Danish registers until June 2013.

Results: During a median of 17 years of follow-up, 3,868 persons developed AF. Adjusted hazard ratios (HRs) per population SD difference showed highly statistically significant positive associations for all 9 anthropometric measures (HRs ranging from 1.08 [95% confidence interval (CI): 1.05 to 1.12] for waist-to-hip ratio to 1.37 [95% CI: 1.33 to 1.42] for lean body mass). Pairwise mutual adjustment of the 9 measures left the association for lean body mass virtually unchanged (lowest HR: 1.33 [95% CI: 1.28 to 1.39] when adjusting for height), whereas no other association remained substantial when adjusted for lean body mass (highest HR: 1.05 [95% CI: 1.01 to 1.10] for height).

Conclusions: Lean body mass was the predominant anthropometric risk factor for AF, whereas no association was observed for either of the obesity-related anthropometric measures after adjustment for lean body mass.

004.05 Stine
Gunnensen CONDITIONAL DISRUPTION OF THE MYD88 GENE IN SMOOTH MUSCLE
CELLS DOES NOT REDUCE THE DEVELOPMENT OF ATHEROSCLEROSIS IN
MICE

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Background: Atherosclerosis is caused by lipoprotein-driven chronic inflammation in the arterial intima. In plaques, smooth muscle cells (SMCs) can modulate to an inflammatory phenotype, characterized by the secretion of pro-inflammatory cytokines. This modulation can be induced in SMCs in culture by signaling through the MyD88-dependent Toll-like receptors and the interleukin 1-receptor, but the role of this type of signaling for atherosclerosis development is unknown.

Methods: Cre recombinase activity was induced in male Myh11-CreERT2 x MyD88^{flx/flx} and Myh11-CreERT2 x MyD88^{wt/wt} mice at 6-8 weeks of age with daily injection of 1 mg tamoxifen i.p. for 10 days to remove loxP-spanned sequences, leading to onset of MyD88 knockout in the SMCs. Hypercholesterolemia was induced with a single injection of rAAV-D377Y-PCSK9 at 12 weeks of age and high-fat diet for 12 weeks. Lesion development was analyzed at 24 weeks age by en face quantification of Oil Red O-stained aortas and by cross-sections of the aortic root. Recombination efficiency was investigated by qPCR on DNA isolated from the arterial media.

Results: Recombination leading to a disrupted MyD88 gene was successfully induced by tamoxifen with an efficiency of 83.44±7.21%. Plasma cholesterol levels and body weight did not differ between genotypes. There was no significant difference in the amount of atherosclerosis in the aortic arch (7.2±4.9% vs 7.5±4.1%, p=0.83) or in the aortic root (0.097±0.06 mm² vs 0.107±0.06 mm², p=0.62) between Myh11-CreERT2 x MyD88^{flx/flx} and Myh11-CreERT2 x MyD88^{wt/wt} mice.

Conclusion: MyD88 deficiency in SMCs does not impair the development of atherosclerosis significantly.

004.06 Anne-Mette
Oxvig CONCOMITANT PROBE-BASED PROFILING OF METHYLGLYOXAL BLOOD
METABOLISM AND POST-TRANSLATION MODIFICATION

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Methylglyoxal is a metabolic byproduct formed spontaneously in the glycolysis. It is a highly reactive compound, which is known to react with amino acids, mainly arginines but also lysines and cysteines, causing post-translational modifications of proteins. These protein modifications are referred to as advanced glycation end-products (AGEs). As AGEs cause alterations of the native protein structure, these may disrupt the function of the protein, and methylglyoxal-derived protein modifications are generally accepted to be implicated in a range of age- and diabetes-related pathologies such as endothelial dysfunction. Commonly in biological research of endogenous compounds such as methylglyoxal, it is desirable to

follow the formation of protein modification along with the metabolism of the compound. However, for low abundant metabolites, this can be a painstaking process. With the use of small-molecule probes and click chemistry, we have developed a generic protocol to simultaneously study metabolism and post-translational modification in the same biological sample. Applying this new protocol with our methylglyoxal-analogue probe (AlkMG), we have detected enzymatic metabolism in blood and profiled modified proteins and the specific binding sites using in-gel fluorescence and tandem mass spectrometry.

O05.01 Brigitta
Villumsen

EFFECT OF UNSUPERVISED HOME-BASED HEALTHY GAMING IN PROSTATE CANCER PATIENTS RECEIVING ANDROGEN DEPRIVATION THERAPY ON PHYSICAL FUNCTION, BODY COMPOSITION, QUALITY OF LIFE AND FATIGUE: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Adverse effects, such as loss of muscle and bone mass, reduced physical function, decreased quality of life and increased fatigue, are commonly seen in prostate cancer patients treated with androgen deprivation therapy (ADT). Supervised exercise has shown positive results in reducing these adverse effects.

Objective: To investigate the effect of a 12-week unsupervised home-based exercise program using the interactive video gaming console Xbox 360 Kinect in prostate cancer patients receiving ADT.

Materials and methods: Randomized trial with two groups: a) intervention group (n=23) and b) control group (n=23).

Outcome measures: 6-minute walk test (6 MWT), leg extensor power, bioelectrical impedance analysis. Functional Assessment of Cancer Therapy-Prostate (FACT-P) and Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) questionnaires. The physical functioning and global health status was measured using the EORTC QLQ-C 30 questionnaire. Tests were done at baseline and 12 weeks.

Results: The adjusted analysis showed significant improvements in the intervention group compared to the control group in 6 MWT (p=0.002) and self-reported physical functioning (p=0.041) at 12 weeks. Neither skeletal nor cardiovascular events occurred during the study.

Discussion: To our knowledge, this is the first study to investigate the effect and safety of an unsupervised, off-the-shelf interactive videogame console and exercise games in prostate cancer patients undergoing ADT. This exercise intervention resulted in statistically significant improvements in the physical functioning and the self-reported physical functioning, and it also proved to be safe in patients with bone metastases.

O05.02 Nasrin Tayyari Dehbarez WOMEN'S PREFERENCES FOR DELIVERY HOSPITAL: A DISCRETE CHOICE EXPERIMENT

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Background: "Free choice of hospital" has been introduced in many health care systems to accommodate patients' preferences and incentivize hospitals to compete. Yet, little is known about what patients actually prefer. The aim of this study is to assess women's preferences with regard to delivery hospital by quantifying the utility and trade-offs of hospital attributes and investigate whether these differ across sub-groups of women.

Methods: We conducted a discrete choice experiment survey that presented women with 12 hypothetical choice scenarios in which they had to choose among three hospitals characterized by six attributes: continuity of midwifery care, availability of neonatal intensive care unit (NICU), specialization level to handle rare events under birth, hospital services offered and travel time. A random parameter logit model estimated utility and marginal willingness to travel for improvement in the other hospital attributes.

Results: 517 women completed the survey. Significant preferences were expressed for all of the attributes, with availability of NICU being the most important driver for the women's preferences; women were willing to travel 26 more minutes (95% CI: 24 to 29) to reach a hospital with a highly specialized NICU. Substantial heterogeneity was noted with respect to parity (women who have children: 19 minutes, others: 31 minutes).

Conclusion: Women appear to have strong preferences for minimizing catastrophic risk although they have no clinical reason. As this does further appear to be most influential for women without previous birth experience, information could play a pivotal role in affecting hospital choice.

O05.03 Anne Højager Nielsen THE CONTENT AND STRUCTURE OF ICU DIARIES WRITTEN BY RELATIVES - A NARRATIVE ANALYSIS

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Background: Undergoing critical care and ventilator treatment in the Intensive Care Unit (ICU) can be a traumatic experience for patients and relatives. A key to psychological recovery for patients and relatives can be diaries authored by relatives for the ICU patient, providing a narrative framework for understanding the ICU experience. However, there is little research on how patients and relatives use such diaries, and how it affects the patient in the aftermath of critical illness.

Aim: To explore the structure and content of diaries authored by relatives for critically ill patients in the ICU.

Methods: Qualitative narrative analysis of 12 diaries authored by 1 male and 11 female relatives of 12 ICU patients expecting to undergo ventilator treatment > 24 h and staying in the ICU > 48 hours; 11 patients survived their critical illness. Analysis and interpretation were based on Ricoeurs model of the text.

Findings: The structure of the diary consisted of 5 phases: Pre-ICU phase, Early ICU phase, Culmination, Rehabilitation phase and Post-ICU realization. Content of the diary were identified as: 1) Drawing on agreeing and conflicting sources of information when writing the diary, 2) Using the diary to continue the dialogue with the unconscious patient, 3) Using the diary to understand the patient's situation and reflect on their own feelings.

Conclusion: The diary had a clear narrative structure that potentially could promote understanding and reflection in relatives and patients. The diary allowed relatives to connect with the patient, and relatives expressed a full range of emotions. However, some might be unfit to share with the patient.

O05.04 Anne Sofie Dam Laursen AN EPIDEMIOLOGICAL INVESTIGATION OF DAIRY PRODUCT INTAKE AND SUBSEQUENT RISK OF STROKE

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A diet rich in low-fat dairy products and limited in high-fat dairy products is recommended for stroke prevention. However, the role of dairy products for stroke remains unclear. We investigated associations for substitutions between subgroups of dairy products and for dairy derived fatty acids in adipose tissue with incident stroke.

We used data from the Danish Diet, Cancer and Health (DCH) cohort and the Dutch arm of the European Investigation into Cancer and Nutrition (EPIC-NL), which included 57,053 adult men and 40,011 adult women. In both cohorts, information on dairy product intake was collected by validated food frequency questionnaires. In the DCH, the fatty acid composition of adipose tissue was determined by gas chromatography. Incident stroke cases were identified by linkage to national registers.

During follow-up, 1,897 ischemic and 396 hemorrhagic strokes were recorded in the DCH, and 503 ischemic and 244 hemorrhagic strokes in the EPIC-NL. In both cohorts, we observed that intake of whole-fat yoghurt in place of semi-skimmed yoghurt, cheese, buttermilk or milk regardless of fat content was associated with a lower rate of ischemic stroke, while no associations were observed for hemorrhagic stroke. In the DCH, a higher percentage of dairy derived fatty acids in adipose tissue was associated with a lower rate of ischemic stroke.

In conclusion, our results suggest that differences in intake of dairy products may be involved in the etiology of ischemic but not hemorrhagic stroke. Particularly, whole-fat yoghurt intake in place of other dairy products as well

as the presence of dairy fat in adipose tissue appear beneficial for ischemic stroke prevention.

O05.05 Lisbet
Grønbaek

PREGNANCY AND BIRTH OUTCOMES IN A DANISH NATIONWIDE COHORT OF WOMEN WITH AUTOIMMUNE HEPATITIS AND MATCHED POPULATION CONTROLS

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Background: Many patients with autoimmune hepatitis (AIH) are women of fertile age. Some major concerns for these patients are related to pregnancy. We conducted a nationwide study on risk of miscarriage, birth rate, and birth outcomes in women with AIH.

Methods: We collected data from Danish healthcare registries for 1994-2015. We included 1,947 women with AIH and 19,470 age- and gender-matched population controls. We calculated the risk of miscarriage and the birth rate in premenopausal women with AIH and controls. We used logistic regression to compare the odds of adverse birth outcomes (preterm birth, small for gestational age, congenital malformations, and stillbirth) between women with AIH and controls. We adjusted for mother's age and smoking habits, and we conducted separate analyses for AIH patients on vs. off immunosuppressive treatment and with vs. without cirrhosis.

Results: The risk of miscarriage was similar in women with AIH and controls: risk ratio 1.16 (95% confidence interval [CI] 0.80-1.69). The first-time birth rate per 1000 person-years in women with AIH was 37 (95% CI 29-46), in controls 32 (95% CI 30-35). In women with AIH, there were 176 births, 70 of which were first-time births: Women with AIH had an increased risk of preterm birth (adjusted odds ratio 3.29, 95% CI 1.62-6.67) and SGA (adjusted odds ratio 4.65, 95% CI 0.83- 26.04) but not of other adverse birth outcomes. Birth outcomes were similar in AIH patients on vs. off immunosuppression and with vs. without cirrhosis.

Conclusions: Fertility is unaffected in women with AIH. Women with AIH have an increased risk of preterm birth and SGA but not of other adverse birth outcomes.

O05.06 Mette
Tranberg
Nielsen

PREVENTING CERVICAL CANCER USING HPV SELF-SAMPLING: DIRECT MAILING OF TEST-KITS INCREASES SCREENING PARTICIPATION MORE THAN TIMELY OPT-IN PROCEDURES - A RANDOMIZED CONTROLLED TRIAL

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Background: Even in countries with organized screening programs, cervical cancer is a burden, especially in unscreened or underscreened women. This trial, the first of its kind, evaluates whether offering HPV self-sampling kits, either mailed directly to the women or using timely opt-in procedures for ordering the kit, increases screening participation when compared with a standard second reminder.

Methods: In this randomized controlled trial, 9,791 Danish women aged 30-64 who were due to receive the second reminder were randomized to either: 1) direct mailing of a second reminder and a self-sampling kit (directly mailed group); 2) mailing of a second reminder that offered a self-sampling kit to be ordered by e-mail, text message, phone, or website (opt-in group); or 3) mailing of a second reminder to attend regular cytology screening (control group). In an intention-to-treat analysis, we estimated the participation rate at 180 days post intervention by returning a self-sample or attending regular cytology screening. We calculated the proportion of HPV-positive self-samplers who attended follow-up testing within 90 days.

Results: Participation was significantly higher in the directly mailed group (38.0%) and in the opt-in group (30.9%) than in the control group (25.2%) (differences: 12.8%, 95% CI: 10.6-15.0% and 5.7, 95% CI: 3.5-7.9%, respectively). Within 90 days, 107 HPV positive self-samplers (90.7%, 95% CI: 83.9-95.3%) attended follow-up.

Conclusions: Offering HPV self-sampling as an alternative to regular cytology screening increased participation; direct mailing was the most effective invitation strategy. A high compliance with follow-up was seen.

P01.01 Morten
Aagaard
Nielsen

TOCILIZUMAB: THE DRUG OF CHOICE IN TREATING THE "FIBROBLAST PHENOTYPE" OF RHEUMATOID ARTHRITIS

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Introduction: There has been a remarkable progress in the treatment of patients (pt) with rheumatoid arthritis (RA), mainly due to the introduction of a still expanding palette of different biologic agents.

Rheumatoid arthritis is proposed to consist of three phenotypes: lymphocyte, macrophage, and fibroblast. This disease heterogeneity causes big challenges in choosing the right individual treatment.

Methods: Synovial fluid was obtained from patients with active rheumatoid arthritis (RA) or spondyloarthritis. Synovial fluid mononuclear cells (SFMCs) cultured for 48 hours were used to study the effect of different biological agents on secretion of Monocyte Chemoattractant Protein-1 (MCP-1) (n=14). Further, fibroblast-like synovial cells (FLSs) were co-cultured PBMCs and used to study the effects of the same biological agents (n=6). Finally, SFMCs cultured for 21 days were used to study the effects of the biological agents measured by Tartrate-resistant acid phosphatase (TRAP) (n=10).

Results: Tocilizumab decreased the production of MCP-1 by 50% in FLSs and PBMCs co-cultures. This effect was exclusively seen in the FLS co-cultures

and not in SFMC cultures. Tocilizumab had a very different response than Adalimumab and Etanercept. These two TNF α inhibitors had no significant reduction in the FLS co-cultures, but instead showed a significant decrease in both TRAP and MCP-1 levels from the SFMC cultures.

Conclusions: This study reveals a possible beneficial effect of anti-IL-6 (Tocilizumab) therapy to patients of the fibroblast RA phenotype where anti-TNF α has no effect. This study hereby points to a different treatment strategy for pts of the fibroblast RA phenotype.

P01.02 Cecilie
 Blenstrup
 Patsche

TREATING TUBERCULOSIS WASTING WITH A PROTEIN-RICH SUPPLEMENT

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Background: Undernutrition at the time of diagnosis of active tuberculosis (TB) is a risk factor for increased mortality, and lack of weight gain during TB treatment has been linked to an increased relapse risk. The World Health Organization has emphasized the need for studies examining the effect of protein-rich supplements during TB treatment. The main objective of this study is to test the effect of Lacprodan DI-8090 whey protein concentrate on anthropometric measures and treatment outcome on patients with TB with a body mass index (BMI) <20.

Methods: An open-labelled randomized, controlled, trial will be conducted in Guinea-Bissau from August 2017 until August 2020. Patients diagnosed with TB will be recruited from 4 trial sites in the health and demographic surveillance area in the capital Bissau. Inclusion criteria: i) age \geq 18 years, ii) BMI <20. Exclusion criteria: i) Pregnancy; ii) Mentally ill/disabled; iii) Creatinine levels outside national reference intervals; iv) Missing informed consent; and v) Commencement of treatment \geq 30 days prior to inclusion. The intervention arm will receive a daily dose of 62,5g Lacprodan DI-8090 whey protein concentrate for the duration of TB treatment (sponsored by Arla Foods Ingredients Group P/S). Patients will be followed bimonthly with clinical examinations, dietary intake evaluation, nutritional status assessment, and blood testing.

Results: Two-hundred and sixty patients will be included in the study. All results are pending.

Conclusions: Pending

P01.03 Litten
 Sørensen
 Rossen

IDENTIFYING NOVEL SIGNAL TRANSDUCTION PATHWAYS OF CD46 ISOFORMS

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Objective: The CD46 gene encodes multiple isoforms of a ubiquitously expressed membrane protein, CD46, which has important functions in the immune system. Co-stimulation of the receptors CD3 and CD46 on CD4⁺T

cells promotes T-cell activation and differentiation, resulting in increased production of the cytokines interferon-gamma (IFN- γ) and interleukin 10 (IL-10). CD46 is also used as an entry receptor by microorganisms, raising the question of the functional consequences of ligation of CD46 during infection. Further studies of CD46 and its signal transduction may provide important insight into the mechanisms used by pathogens to modulate the immune response.

Methods: Activated CD4⁺T cells purified from peripheral blood mononuclear cells were infected with human herpes virus 6A (HHV-6A), and IL-10 and IFN- γ secretion was measured using ELISA. The signaling pathways were studied by analysis of phosphorylated proteins extracted from antibody stimulated CD4⁺T cells using an LC-MS/MS proteomics approach. In addition, CD46 isoforms were cloned into a lentiviral vector for further studies of the individual function of each isoform.

Results: It was confirmed that CD4⁺T cells infected with HHV-6A secreted both IL-10 and IFN- γ . Stimulation of CD4⁺T cells with α CD3 vs. α CD3/ α CD46 antibodies led to identification of proteins by LC-MS/MS that were specifically regulated by CD46.

Conclusion: The data demonstrate that mass-spectrometry is a useful method for the identification of signaling pathways in primary T cells. Further investigation may map specific pathways of CD46 to provide novel insight into the adaptive immune response as well as immunomodulation induced by pathogens.

P01.04 Samuel Joseph Windross

MECHANISMS OF ACTIVATION OF STING SIGNALING AT THE ENDOPLASMIC RETICULUM

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The discovery of the cGAS-STING (STimulator of Interferon Genes) pathway and the important 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. How does STING form the dimeric form, which is essential for activation? How does DNA detection prime STING for activation at the ER? These two questions remain unanswered. In this PhD project, we will first focus on how STING becomes covalently dimerised at ER membranes. Previous work in the lab has shown that DNA stimulation induces a covalent STING dimer. To approach this, we will initially map the STING dimer using Mass Spectroscopy in order to determine the position of the disulphide bridge(s) mediating covalent dimerisation. After characterization, we will carry out additional experiments in order to investigate key proteins that are involved in mediating the STING monomer dimer transition. Initial experiments of STING dimer mutants in a HEK293T cell based reporter gene assay will then be used to show the effects of non-covalent dimer on innate immune responses. Secondly, we hope to investigate the role of ER stress on STING dimerisation and the potential role of innate immune responses during herpes virus infections. We hope to define how STING dimerisation is primed during the detection of viral nucleic acids through direct/indirect interaction with DNA sensors like cGAS, IFI16, and cyclic dinucleotides like cGAMP. This research aims to identify novel mechanisms in the early phases of the DNA-activated antiviral

pathway, which is essential for successful clearance of infection with DNA viruses.

P01.05 Georgios
Katzilieris
Petras

CHEMOATTRACTIVE SIGNALING IN THE RECRUITMENT OF MICROGLIA TO HSV-1 INFECTION FOCI IN THE BRAIN

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Herpes simplex virus 1 (HSV-1) is a DNA virus, which can cause a severe infection of the central nervous system (CNS), called herpes simplex encephalitis (HSE). The aim of this project is to identify the chemotactic signals that are released by infected brain cells in order to activate and recruit the resident immune cells of the brain, microglia, and infiltrating monocytes to the sites of infection. A mouse model of HSE was simulated by cornea scarification and infection with a neurotropic strain of HSV-1. Then, RNA extracted from brain stem, which is the major area of infection in the brain with potentially increased production of chemokines, was used to measure the expression levels of various chemokine genes. Ligands for chemokine receptors CCR2, CCR5 and CXCR3, but not for CXCR2, showed a cGAS- and STING-dependent induction of RNA levels in the infected brain stems 3 days post-infection (d.p.i.). However, after 4 days of infection, RNA induction of CCR2, CXCR3 ligands and CCL3 was observed in both wild-type and STING KO mice, whereas RNA levels of CXCR2 ligands, CCL4 and CCL5 displayed no significant upregulation. Ultimately, these data suggest that there is a cGAS- and STING-dependent induction of chemokine expression in the brain stem 3 d.p.i., while there is evidence of a STING-independent mechanism contributing to the production of chemokines after 4 days of infection. Therefore, it is essential to understand the role of these pathways in the recruitment of brain macrophages to the infected sites in the brain in order to gain a clearer understanding of the immune responses during the early stages of HSE.

P01.06 Jesper Geert
Pedersen

CCR5 EXPRESSION ON T CELLS DEPENDS ON THEIR ACTIVATION STATUS AND ENVIRONMENT

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The chemokine receptor CCR5 is well known for its crucial role during HIV infection, serving as a coreceptor for HIV entry. CCR5 is expressed on several cell types, including macrophages, dendritic, and T cells. CCR5 is expressed differentially among cell types, and there are indications that cytokines can increase CCR5 expression. However, it remains unknown as to which cells and cytokines control the CCR5 expression.

Here we examined the expression of CCR5 on primary CD4+ T cells. These T cells were either cultivated alone or in their complete PBMC culture. Cells were activated with either anti-CD3/CD28+IL-2 or PHA+IL-2 before analysis for CCR5 expression using FACS. Interestingly, we observed significantly more CCR5 positive cells within the PBMC-cultured T cells than in the T cells cultured alone. However, T cells activated and cultured alone showed higher CCR5 expression per cell (MFI values).

To investigate if cytokines produced by PBMCs increase CCR5 expression in T cells, we cultivated T cells using conditioned medium obtained from anti-CD3/CD28 + IL-2 activated PBMCs. We found that cultivation with conditioned medium increased the amount of CCR5 positive cells, indicating that PBMC secreted cytokines can increase CCR5 expression.

Finally, PBMC-cultured T cells showed increased susceptibility towards R5-HIV infection, but not towards X4-HIV.

In conclusion, activated CD4+ T cells cultured within PBMCs show increased CCR5 expression compared to CD4+ T cells cultured alone. Further, our data shows that PBMC secreted cytokines induce an increased amount of CCR5 positive. These results greatly influence how one should establish HIV studies in primary T cell cultures.

P01.07 Kristian Juul-Madsen BACTERIAL CELL WALL ULTRASTRUCTURE ANALYZED WITH NANOPARTICLE TRACKING ANALYSIS

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Introduction: Antimicrobial peptides (AMPs) act to destabilize the membrane of microorganisms through electrostatic interactions between the cationic AMPs and the anionic microbial membrane. The electrostatic interactions allow these peptides to permeabilize the membrane, leading to formation of membrane pores, cell depolarization, leakage of intracellular contents, and ultimately cell death.

Aims: To investigate the size of particles secreted from bacteria after AMP treatment by use of nanoparticle tracking analysis (NTA).

To determine the antimicrobial effect of LL-37 in perspective to their secretion of particles after treatment.

Methods: To investigate the effect of LL-37 as an AMP on different bacteria strains, three types of bacteria, Two Gram negative (Escherichia coli, E. coli and Pseudomonas aeruginosa, P. aeruginosa.) and a Gram positive (Staphylococcus aureus, S. aureus) have been investigated. NTA was used to assess the particles released from a solution containing bacteria and AMPs.

Results: Results obtained through NTA show that particles secreted from bacteria change with AMP treatment. This indicates that LL-37 disrupts the cell wall and reveals details about the ultrastructure of the cell wall. This could be due to a repeated structure with specific active sites for AMP's.

Conclusion: The ultra structure of bacteria could be a very promising target for new drugs against bacteria. AMPs are able to detect and insert into repeated structures in the cell wall causing the wall to disrupt and the cell to leak intracellular material leading to cell death.

- P01.08 Madalina Elena Carter-Timofte MUTATIONS IN POLR3 GENES AND DEFECTIVE DNA SENSING IN PATIENTS WITH SEVERE VARICELLA ZOSTER VIRUS CENTRAL NERVOUS SYSTEM INFECTION

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Chicken pox is caused by the Varicella Zoster Virus (VZV), which establishes life-long latency in the host following primary infection. During adult hood, the virus is able to re-activate causing herpes zoster, which is clinically distinct from the primary infection. Whilst most children and adults are able to clear the infection, in some, otherwise healthy individuals, the virus is able to spread to the central nervous system (CNS) and cause severe complications such as encephalitis. We predicted that the differential susceptibility to viral CNS infection can be explained by host genetics. Using whole exome sequencing (WES) of patients with severe VZV CNS infection, we identified various mutations in the cytosolic RNA polymerase III sensor, whose main function is to recognize foreign DNA virus infection. To functionally validate the mutants, we stimulated patient peripheral blood mononuclear cells (PBMCs) with viral mimics. We found that the patients with the identified mutations had a reduced anti-viral response and increased viral replication when compared to healthy controls. Our data identifies a novel association between mutations in the DNA sensor, RNA polymerase III, and the development of severe VZV CNS infections in both children and adults.

- P01.09 Alice Knudsen MECHANISM OF ACTIVATION AND EFFECTS OF AN INNATE ANTIVIRAL PATHWAY AT MUCOSAL SURFACES

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Early sensing of infection and immune defense activation is pivotal for fast clearance of pathogens and efficient disease prevention. Traditionally, the type I interferon (IFN)s have been characterized as the first line of defense against viral infections. A pathological role for IFNs has been observed later, however. Thus, research in early IFN-independent antiviral mechanisms is now emerging. The host laboratory has described the existence of an antiviral pathway that is initiated independent of IFNs at mucosal surfaces. Here, we will establish the molecular components involved in activation of this pathway as well as investigate the nature of its antiviral effects. HaCaT cells constitute our in vitro model system since they represent a type of epithelial cells, express a range of proteins involved in innate immune signalling and respond to relevant immunological stimuli. Using CRISPR/Cas9-mediated genome editing, we have produced HaCaT cells lacking specific immune signalling proteins. Our investigation of these cells shows that HSV-2 infection induces an IFNAR2-, IRF3-, p65- and STING-independent CXCL10 response. Furthermore, we have observed a virus-entry- and IFN-independent CXCL10 response to HSV-2 in HaCaT cells. We will finally clarify which proteins are involved in the virus-entry- and IFN-independent CXCL10 induction using a flow-based screen. Moreover, we will start characterising the effects of this response by RNA sequencing. We will confirm our findings in mouse models of viral infections at mucosal

surfaces. The project will provide novel, mechanistic knowledge on an innate antiviral pathway that acts before the IFNs.

P01.10 Camilla
Gunderstofte
Nielsen NRF2 INCREASES HSV INFECTION THROUGH IMPAIRED ANTIVIRAL INNATE IMMUNE RESPONSE

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Herpes simplex viruses (HSVs) are highly prevalent viruses that establish latency in neurons and the most frequent cause of viral meningo-encephalitis. Generation of reactive oxygen species (ROS) and the subsequent oxidative tissue damage is central to HSV-induced physiopathology. To reduce tissue damage caused by oxidative stress, cells possess antioxidant mechanisms that maintain redox homeostasis. Nuclear factor erythroid 2-related factor 2 (Nrf2) is a transcription factor involved in the activation of different antioxidant genes whose proteins products detoxicate and eliminate ROS and protect the cell. Yet, no studies have evaluated the importance of the Nrf2/Kelch-like ECH-associated protein 1 (Keap1) axis in the control of HSV-associated physiopathology. Comparison of antiviral gene expression profile by RNA-seq, analysis of wildtype (WT) and Nrf2 mutant macrophages showed an increase in the basal levels of the interferon-stimulated gene response in absence of functional Nrf2. The same basal increased antiviral profile was observed in the spleen of Nrf2 knockout (KO) mice. Interestingly, lack of Nrf2 increases the responsiveness to HSV-derived dsDNA. The in vivo vaginal herpes infection model showed that Nrf2 controlled early innate immune responses to HSV-2. Nrf2 KO mice exhibited reduced viral replication that were associated with higher level of type I interferons in vaginal washes. In addition, Nrf2 KO mice developed significantly reduced weight loss, lower disease scores and higher survival rates compared to WT animals. Collectively, these data identify Nrf2 as an upstream regulator of the antiviral response and a critical player in the course of HSV infection.

P02.01 Sidsel
Andersen MASTERS OF IMMUNE MANIPULATION

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Parasites have turned into true masters of host manipulation as they can dampen inflammation to optimize their own survival in tissues, but very little is known about the specific mechanisms by which they do so. Excretory-secretory antigens from parasites are important in this context, but a few recent studies have indicated that parasite EVs are crucial for host-parasite communication. Deciphering of this communication opens up for a new fundamental understanding of host-parasite interaction, which could thereby pave the way for novel drug targets and vaccines. This research project will provide fundamental and novel insight into how parasites manipulate an aggressive immune system and survive within their host. To do so, I am exploring the production of extracellular vesicles (EVs) among parasitic helminths such as *Ascaris suum*, also known as the giant roundworm. Adult *A. suum* have been collected from naturally infected pigs slaughtered at an abattoir and cultivated in the laboratory for 3 days. To

determine the presence of secreted EVs, we have used ultracentrifugation and/or size exclusion chromatography (qEV) to isolate the EVs and established their size profile using nanoparticle tracking analysis (NTA) by Nanosight. Furthermore, I have characterized the content of proteins in the secreted EVs by proteomic analysis (HPLC) and investigated the spectrum of molecular products released from this parasite. At the moment, we are looking at the function of EVs on host cells by adding helminth-secreted EVs to immune cells, where we try to identify the intracellular mechanisms affected by EV stimulation using bioassay, qPCR and ELISA.

P02.02 Katrine Schou Sandgaard TCR REPERTOIRE AND THYMIC OUTPUT AFTER TREATMENT INTERRUPTION IN CHILDREN WITH HIV

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The T cell receptor (TCR) repertoire is established in the thymus. As children become adults, thymic output declines, which results in a reduction of TCR diversity. In children with HIV, there is a loss of CD4⁺T cells that can be restored by antiretroviral therapy (ART), mainly as a result of the thymic output. However, the resultant clonal diversity is largely unknown and will be influenced by thymic output and peripheral cell division.

We have combined Flow Cytometry with high throughput sequencing of TCRs and the data analyzed using a novel bioinformatic platform. Thymic output and TCR diversity were measured in HIV-infected children following 48 weeks of ART interruption and HIV-infected children with continuous ART treatment.

IL-8, an important chemokine released from T cells and found to correlate with thymic output, was found to increase rapidly in naïve CD4⁺T cells when ART was stopped. This was associated with increased naïve CD4⁺T cell proliferation, as measured by Ki67. The combination of increased IL-8 and Ki67 following ART cessation is compatible with both increased thymic output and peripheral cell expansion. T cell IL-8 and Ki67 returned to pre-interruption levels when the children re-started ART, which indicates that it is a reversible response to the ART interruption. TCR repertoire diversity decreased when ART was stopped and increased to pre-interruption levels after ART re-introduction. Hence, the high levels of thymic output in children may be sufficient to reverse the impact of ART cessation. These important results indicate that periods of treatment interruption in children may not have a lasting detrimental impact on thymic output or TCR diversity.

P02.03 Nina Breinholt Sørensen A RANDOMISED CONTROLLED TRIAL OF A 12-DOSE RIFAPENTINE AND ISONIAZID REGIMEN USING DIRECT OBSERVED THERAPY VERSUS 6 MONTHS OF DAILY ISONIAZID FOR LATENT TUBERCULOSIS INFECTION IN SOCIALLY MARGINALISED PEOPLE

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Background: In low-incidence countries, most tuberculosis (TB) cases are found in high-risk groups, including immigrants from high-incidence countries, substance abusers, alcoholics and socially marginalised people (SMP). TB tracing and prevention in low-incidence settings should focus on these groups. Latent TB infection (LTBI) is a potential reservoir for future disease as 5-15% progress to active disease and preventive treatment of LTBI could potentially reduce the reservoir of disease, the number of active cases and thereby the number of secondary cases. Treatment of LTBI is often not offered to SMP due to expected low adherence. A study investigating the 12-dose weekly rifapentine and isoniazid (RPT+INH) regimen using direct observed therapy (DOT) showed promising results for adherence in the study population, but no studies have investigated the feasibility of treating SMP.

Objective: The primary objective of the study is to evaluate the feasibility of LTBI treatment with the 12-dose RPT+INH regimen compared with standard treatment in SMP. The secondary objective will be to obtain information on side effects and TB status at one-year follow-up.

Methods and materials: 150 socially marginalised persons with LTBI in Aarhus, Aalborg, Esbjerg and Copenhagen will be randomised to either weekly RPT+INH for 12 weeks or daily isoniazid for 6 months. The treatment will be administered at shelters or social institutions, where the patients already come. Blood samples will be collected at baseline and during treatment to control for side effects. Data will be collected on adherence to treatment, adverse events and one-year TB status after treatment completion.

P02.04 Cecilie Linneberg CHARACTERISATION OF THE ZEBRAFISH ORTHOLOGUES OF HUMAN EXTRACELLULAR SUPEROXIDE DISMUTASE

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Extracellular superoxide dismutase (EC-SOD) is a protein that converts extracellular superoxide (O_2^-) into hydrogen peroxide (H_2O_2). Superoxide and H_2O_2 are both reactive oxygen species (ROS), which in general are known to be harmful and associated with diseases like atherosclerosis, arthritis and neurodegeneration. However, research has established that ROS also are important secondary messengers in diverse biological processes, such as transcriptional regulation, cell-cell communication and inflammation. Especially H_2O_2 has evolved to be a key mediator of these processes, referred to as redox signalling. We hypothesize that EC-SOD provides spatiotemporal production of H_2O_2 to support redox signalling,

whereby the inflammatory response is modulated. To investigate this, we will use zebrafish, which is now an established model system. We aim to publish groundbreaking results that highlight the strong association between ROS and inflammation.

Data collected by RT-PCR, whole mount in situ staining, activity assays and size exclusion chromatography indicate that the structure and function of zebrafish EC-SOD orthologues are comparable to those of the human protein. Furthermore, in situ staining and RT-PCR suggest that EC-SOD is present throughout the embryonal development and is associated with the thymus and dopaminergic neurons.

These results represent the initial characterization of EC-SOD orthologues and will set the basis for studies using genetically manipulated zebrafish. Further studies will focus on regulation of extracellular redox signalling and its importance during the inflammatory response with a special focus on macrophage and neutrophil migration.

P02.05 Anna Halling
Folkmar
Andersen DEVELOPMENT OF LONG-ACTING INJECTABLE HIV TREATMENT: ALBUMIN-BASED MACROMOLECULAR PRODRUGS MEDIATE ANTI-HIV EFFECTS WITH PROLONGED THERAPEUTIC INDEX TIME

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One of the main obstacles to eradicating HIV is eliminating the latent reservoir. Histone deacetylase inhibitors (HDAC inhibitors), such as panobinostat (PANO), can contribute to exposing the latent HIV reservoir in patients. PANO has dose-limiting side-effects, which makes optimized delivery highly warranted. We use PANO as a proof-of concept drug to show that we can increase blood residence time with the consequence of lowering dose and avoidance of side-effects. One approach of improving circulation time is conjugation to albumin. Previously, conjugation to albumin has been limited to carrying only one molecule of drug without compromising albumin's natural functions. In contrast, synthetic polymers can carry multiple copies of drug. We combine for the two platforms, albumin and polymers. Polymers were synthesized by RAFT, which enabled us to design polymers with a defined molar mass and low dispersity, with control over the polymer terminal groups used for subsequent conjugation reactions. We used BALB/cJ mice and administered a fluorescently labelled prodrug either intravenously (IV) or subcutaneous (SC). Fluorescence intensity was measured by in vivo imaging system (IVIS). To determine the potency of the prodrugs, we used latently HIV infected lines and virus by p24 ELISA after stimulation with the prodrugs and with pristine drug. We show that our prodrug increases blood half-life by IV from 112 min. to 202 min. SC injection of the prodrug has increased the duration of maximum response, and thus the longitudinal therapeutic window from 2 to 9 hours. In vitro, we find that prodrug maintains the anti-latency activity of PANO when comparing to treatment with pristine PANO.

P02.06 Christina Lundgaard Ernstsén ACUTE PYELONEPHRITIS: EFFECT OF UROPATHOGENIC E. COLI INFECTION ON RENAL EPITHELIAL CELLS

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Urinary tract infections are one of the most common bacterial infectious diseases in humans and are, in at least 80% of the cases, caused by uropathogenic E. coli (UPEC). UPEC enters the urinary tract, migrates to the bladder and invades the bladder urothelium. UPEC can ascend from the bladder to the kidney and cause acute pyelonephritis (APN), which can result in permanent renal damage. This damage can lead to chronic kidney disease and potentially renal failure, requiring dialysis and transplantation.

Compared to bladder infections, the knowledge about UPEC infection mechanisms in the kidney is limited. We aim to understand the infection mechanisms and risk factors of UPEC infection in the kidney.

Several pathogens have been shown to disrupt intercellular junctions and to utilize compromised epithelial polarity during infection. It is not yet described if UPEC affects junctional proteins and polarity of renal epithelial cells. The influence of UPEC infection of intercellular junctions will be investigated by analyzing expression levels and subcellular localization of key junctional proteins. Time-lapse imaging of fluorescently tagged junctional proteins will show the effects during live infection of renal epithelial cells. Measuring the UPEC infection efficiency at different stages of renal epithelial polarity will show if there is an inverse relationship between epithelial polarity and UPEC infection efficiency.

Results from the first part of the PhD project will provide important information regarding the mechanisms of UPEC infection, which could contribute to minimizing the risk of infection, potentially prevention and treatment of renal damage following APN.

P02.07 Anne Mette Fløe Hvass HIGH COVERAGE OF THE POLIO IMMUNIZATION PROGRAM IN REFUGEES RESETTLING IN DENMARK

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Background: In Europe, vaccines have eliminated wild poliovirus (WPV) infection. Resettling refugees may lack immunity, and import of WPV through refugees remains a concern.

Methods: A cross-sectional survey was performed to determine the prevalence of poliovirus immunity in children and adult refugees resettling in Aarhus, Denmark. Immunity was evaluated by antibody response for serotypes 1, 2 and 3.

Results: This survey evaluated 475 children and adult refugees aged between 0,5 and 76 years. 59% were male. The survey was conducted

between February 2014 and May 2016. 65% of the refugees originated from Syria, 14% from Eritrea and the rest from Congo, Lebanon, Somalia, Afghanistan, Iran, Iraq, Ethiopia and Columbia. Of the 475 refugees, 27 were lacking antibodies against a least one serotype. 14 persons lacked antibodies against type 1, two against type 2, and 13 against type 3. (Two persons lacked antibodies against two serotypes). Of the 27 persons without sufficient antibody response, the majority came from Syria (48%) and Eritrea (33%). 29% had minor symptoms from the CNS, e.g. headache and visual impairment. None of the participants had paralysis or paresis.

Conclusion: This study demonstrated a complete WPV immunity in 448 of 475 (94%) recently resettled adult refugee population in Denmark. The study demonstrates a high coverage of the polio immunization program. Ensuring poliovirus immunity among refugees remains a priority until polio has been eradicated worldwide.

P02.08 Maike Mose

A NEW MODEL OF ACUTE INFLAMMATORY DISEASE - COMBINING ENDOTOXEMIA, FAST AND BEDREST IN HEALTHY YOUNG MEN

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Background: Inflammatory disease causes insulin resistance, increased lipolysis and loss of muscle mass. Great heterogeneity amongst patients complicates metabolic studies, which highlights the need for a Model of Inflammatory Disease. Endotoxin (LPS) can induce inflammation comparable with sepsis, and by combining this with fast and bedrest, we wanted to test whether the metabolic changes seen under real acute inflammatory disease can be imitated.

Aim: The aim of this study was to validate a new Model of Acute Inflammatory Disease.

Methods: In a randomized crossover design, 6 healthy young men (BMI 20-30) were subjected to the interventions "healthy" (overnight fast) or "Sick" (LPS 0.1 ng/kg + 36 hour fast and bedrest). Insulin resistance was quantified by clamp technique and protein-, glucose- and fat metabolism was investigated with tracer methodology using both whole-body and the forearm model. Overall energy consumption was estimated by indirect calorimetry, and intracellular signaling was investigated by western blotting in muscle and fat biopsies.

Results: The M-value, a measure of insulin sensitivity, was lower in "sick" 4.1 ± 0.23 mg/kg/min (MEAN \pm SEM) versus "healthy" 7.2 ± 0.95 mg/kg/min (paired t-test, $p < 0.05$), implying that our Model induces insulin resistance. Insulin stimulated glucose uptake in the forearm muscle was reduced by 80% in sick versus healthy (0.54 ± 0.24 μ mol/100 ml/min versus 2.73 ± 0.24 μ mol/100 ml/min, 2 way RM Anova, $p < 0.05$).

Conclusion: This Model mimics the glucose metabolic changes seen under real acute inflammatory disease. The Model is suited for future studies testing oral protein supplementation during acute inflammatory disease.

P02.09 Asta Linauskas BODY FAT PERCENTAGE WAS ASSOCIATED WITH THE DEVELOPMENT OF RHEUMATOID ARTHRITIS - A DANISH FOLLOW-UP STUDY

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammation of joints. The etiology of RA is basically unknown. Fat tissue contributes to the systemic inflammation. Therefore, several studies have investigated the association between overweight and the development of RA. Body Mass Index (BMI) has been the preferred measure in these studies. However, BMI correlates modestly with body fat volume.

Aim: To investigate the association between bio-impedance-derived body fat percentage and the development of RA.

Methods: We conducted a population-based cohort study among 54,284 persons enrolled in the Danish Diet, Cancer and Health cohort. Bio-impedance measurements and data on life style factors were collected at baseline. Persons who subsequently developed RA were identified by linkage with the Danish National Patient Registry. We assessed the associations between body fat percentage and incident RA using Cox proportional hazards regression models stratifying by gender and adjusting for known and potential confounders.

Results: During follow-up (median: 21 years), 283 women and 110 men developed RA. The risk of RA was higher in women with higher fat percentage (per 5% increment of body fat HR 1.16; 95% CI 1.06-1.28). There was no association between body fat percentage and the development of RA among men (HR 0.97; 95% CI 0.80-1.17).

Conclusions: Having higher fat percentage was associated with a higher RA risk in women.

P02.10 Susan Mikkelsen EXAMINATION OF ALLERGY AND ASTHMA RISK FACTORS IN THE DANISH BLOOD DONOR STUDY

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Background: The development of Allergic rhinitis and asthma depends on environmental factors, modified by the genetic background.

Aims: First, to explore whether the risk of allergy and asthma is associated with the degree of sensitization (elevated specific IgE to inhaled allergens) as well as exposure to airborne allergens. Second, to identify genetic variants associated with allergy, asthma and sensitization, in a genome-wide association study (GWA study).

Methods: DBDS is a prospective population-based cohort study and bio bank. Currently more than 40,000 blood donors have completed a questionnaire including questions about allergy, asthma and upbringing, based on the European Community Respiratory Health Survey questionnaire. GWA array analyses for all 40,000 participants will be completed in January 2018 (Global Infinium Array, Illumina). Cumulative exposure to air pollution will be modeled down to address level, and specific IgE (Phadiatop) will be completed in February 2018.

Results: In the cohort, 10.6% (10.1-11.1) have asthma and 21.2% (20.3-21.8) have allergic rhinitis. Our results support a protective effect of livestock farm upbringing compared to city upbringing for both allergic rhinitis and asthma (OR 0.65 (0.57-0.75) and 0.78 (0.65-0.92), respectively). Results on specific IgE and air pollution as well as data for the GWA study are not yet available.

Perspective: We believe that the large size and the widespread geographic distribution of our study population facilitate the ability to identify gene-environment interaction, by combining results from the GWA study with results on sensitization and environmental factors.

P03.01 Ann Taber

DEVELOPMENT OF PREDICTIVE BIOMARKER MODELS FOR STRATIFYING BLADDER CANCER PATIENTS TO OPTIMIZE THERAPY

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The progressive nature of bladder cancer (BC) and the heterogeneity in the response to chemotherapy raise some major concerns in the care of advanced BC. Previous research aiming at understanding cancer development and delineating biomarkers for treatment response have almost exclusively focused on the genomic alterations in the carcinoma cells. Consequently, contributions from other cell types in the tumor micro-environment (TME) and the patient's genetic basis (e.g. immune recognition) have not been taken into consideration.

The aim of this project is to develop a multi-omics prediction model for stratifying patients with advanced BC to the optimal treatment.

For model generation, we retrospectively identified 100 patients who received chemotherapy at the Department of Oncology, AUH. Whole exome sequencing of tumor and germ line DNA will be performed to determine mutational and neoantigen load, infer tumor heterogeneity and obtain data on MHC variants. Methylation analysis of tumor DNA will be carried out to identify patterns associated with e.g. immune cell composition and/or treatment response. Furthermore, we will perform total RNA-Seq analysis to characterize the composition of immune cell infiltrates and delineate gene expression signatures associated with treatment response.

Finally, we will identify the type and magnitude of immune cells present in the TME associated with response using a novel multiplex immunofluorescence method.

Successful implementation of prediction models will ultimately lead to a higher survival rate, reduce toxicity and decrease health care system expenses as ineffective treatments are avoided.

P03.02 Morten Herlin MULTILEVEL ANALYSIS OF CHILDHOOD ACUTE MYELOID LEUKEMIA (AML)

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Acute myeloid leukemia (AML) accounts for 15% of leukemias in children, with survival rates at 70%. The high risk of adverse effects hinders further intensification in the current treatment protocols. Genetic studies of leukemogenesis are pivotal in the search for new therapies in order to improve survival and lower toxicity. AML is currently classified according to WHO by recurrent genetic aberrations of prognostic relevance. However, as the WHO classification is largely based on adult studies, the applicability in childhood AML has been questioned. Moreover, the knowledge of molecular genetics in childhood AML still remains sparse.

This study aims to investigate the molecular biology of the large heterogeneous group of AML, not otherwise specified (NOS), which includes all patients with none of the recurrent genetic aberrations according to the WHO classification. We will use viable frozen bone marrow cells from about 25 pediatric patients with AML, NOS, taken at the time of diagnosis and stored in the Nordic AML biobank in Uppsala, Sweden. We will conduct a multi-level analysis including whole genome sequencing of paired leukemia-normal samples followed by studies of the methylome, transcriptome and proteome of the leukemia cells. Finally, we aim to study the clonality at the time of diagnosis using deep targeted sequencing.

We believe that the study will provide new insight into the role of molecular genetics in childhood AML development. Ultimately, the study may find new pathogenic genes that may serve as potential therapeutic targets.

P03.03 Maibritt Nørgaard PROSTATE CANCER TUMOR EVOLUTION AND IDENTIFICATION OF PROGNOSTIC AND PREDICTIVE BIOMARKERS

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Prostate cancer (PC) is the most common cancer among men in the western world and is associated with high mortality. Localized PC is curable by surgery or radiation therapy, but a significant fraction of the patients experience relapse and metastasis. At this stage, PC is treated with medical/surgical castration, but the cancer invariably develops resistance and becomes castration resistant (CRPC). The currently used prognostic and predictive tools are suboptimal, resulting in overtreatment of many indolent

PCs. Treatment of aggressive CRPC is also suboptimal, resulting in reduced quality of life and shortened lifespan.

In this project, we will investigate the evolution of aggressive PC from early carcinogenesis to death. From radical prostatectomy patients who have later progressed to CRPC, we will collect tissue from diagnostic biopsies, surgically removed prostates, and metastases. Moreover, we will collect blood (plasma) samples while the patients are in treatment to analyze circulating tumor DNA. With this patient material, we will use the newest genome sequencing methods (NGS) to investigate PC tumor evolution from the time of diagnosis, during treatment, and in metastases.

This project will generate novel knowledge about the tumor evolution in PC, which will facilitate identification of new and better prognostic and predictive biomarkers for PC and CRPC. Such markers could be used for clinically relevant patient stratification and thus pave the way for more personalized treatment of PC and CRPC.

P03.04 Pernille
Christiansen
Skovlund

FEEDBACK IN CANCER CONSULTATIONS - A DIALOGUE-BASED TOOL FOR THE SYSTEMATIC APPLICATION OF PATIENT REPORTED OUTCOME (PRO)

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Background: In recent years, treatment of metastatic melanoma has led to improved prognosis. However, because of new treatment regimens, concerns about health-related quality of life and coping with disease in everyday life have emerged. Systematic completion of PRO prior to a consultation enables the patient-physician dialogue to focus on what is most important for the patient to discuss and overcome. The aim of the study is to investigate the potentials using PRO as a dialogue-based tool.

Hypothesis: Using PRO as a dialogue-based tool will:

- Improve patients' self-efficacy for managing their own health
- Reduce perceived burden of physical symptoms and emotional dysfunction as reported by the patients
- Improve the quality of the patient-physician interaction

Methods: In this non-randomized controlled study, patients (N=282) will be assigned to either the intervention group (systematic completion of PRO-measures and feedback to physicians) or control group (treatment as usual).

Outcomes are measured at baseline, and after three, six and 12 months using the following questionnaires:

- Patient Activation Measure (PAM)
- Functional Assessment of Cancer Therapy - Melanoma (FACT-M)
- Cancer Behavior Inventory (CBI)
- Perceived Efficacy in Patient-Physician Interaction (PEPPI)

Perspectives: If results are positive, the intervention will be ready to apply in routine settings and, in a slightly adjusted form, to other patients in oncology practice.

- P03.05 Maria Riedel A NEW MOUSE MODEL FOR IDENTIFICATION OF KEY FACTORS DRIVING PROSTATE CANCER PROGRESSION AND METASTASIS
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- Prostate cancer is the second leading cause of cancer-related death in man worldwide. With increasing incidence, it is crucial to identify new key drivers involved in this heterogenic cancer and to establish a model for rapid validation of new candidate genes.
- Seeking to understand the function of the AP-1 transcription factor subunits JunB and c-Fos in prostate cancer initiation and progression to a metastatic state, we introduce a powerful new prostate cancer mouse model based on CRISPR/Cas9 technology.
- In this model, specific in vivo gene editing can be obtained in murine prostate epithelium cells that were infected with a self-engineered adeno-associated virus (AAV) in a mouse strain with Cre recombinase-dependent expression of the CRISPR associated protein 9 (cas9) endonuclease.
- In total, five genetically different viral constructs were designed expressing the Cre recombinase and different combinations of single guide RNAs (sgRNA) for Pten as main driver in prostate cancer and JunB, c-Fos, Trp53 and Smad4.
- Simultaneous gene knockouts (KO) reflect tumor heterogeneity. By only hitting few cells with the virus, the cell clones are able to clonally expand as seen in human scenario.
- The first results seen in histological sections of murine prostates three months post-injection confirm increased proliferation as well as increased AKT activation in cells that were infected with the AAV. Mice will be monitored for up to a year for tumor development and metastatic formation. Candidate gene function, alterations in downstream pathways and human relevance will, furthermore, be validated in vitro in JunB and c-Fos KO cell clones as well as in human biopsy samples.
- P03.06 Sofia Spampinato FUNCTIONAL SUB-STRUCTURES OF LOWER URINARY TRACT IN CERVIX CANCER: CONTOURING AND DOSE DISTRIBUTION
- S. Spampinato¹, L. Fokdal¹, E. Marinovski², S. Axelsen³, E.M. Pedersen⁵, R. Pötter⁴, J. Lindegaard¹, K. Tanderup¹*
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Purpose: Recent progress in Image Guided Adaptive Brachy Therapy (IGABT) has improved the understanding of dose effects for Locally Advanced Cervical Cancer (LACC). However, there is still poor understanding of the related late GenitoUrinary (GU) morbidity, a complex phenomenon consisting of various clinical endpoints (i.e. frequency, cystitis, incontinence, bleeding, fistula) that may be related to different anatomical bladder substructures. Currently, dose and correlation with morbidity is evaluated through contouring of the outer bladder wall. The aim of the study is to investigate contouring and dose evaluation in bladder substructures potentially responsible for GU morbidity in LACC treated with IGABT.

Material/Methods: 20 LACC patients treated with External Beam Radiation Therapy (EBRT) and IGABT were selected. Structures (outer bladder wall, trigone, bladder neck, urethra) were contoured, and dose parameters were extracted. Dose to Posterior-Inferior Border of Symphysis points (PIBS/PIBS+2cm) was also extracted as urethral sphincter surrogate. Finally, the vaginal reference length (VRL), defined as the distance from PIBS to vaginal radioactive sources, was measured.

Results: Bladder wall dose was systematically higher than trigone, and hotspots were often placed outside this area. Urethral sphincter dose correlated with PIBS dose. Hotspots in trigone and bladder neck correlated with VRL.

Conclusion: This study showed that parameters currently used for IGABT bladder dose reporting are not sufficient for describing dose distribution in the lower urinary tract. Further understanding of dose-effect relationships may be gained by systematic delineation of bladder substructures.

P03.07 Michelle
Simone
Clement

MECHANISMS OF ACQUIRED RESISTANCE TO MET INHIBITION IN MET-AMPLIFIED RESISTANT NON-SMALL CELL LUNG CANCER

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Background: Development of treatment resistance is a major issue in non-small cell lung cancer (NSCLC). Patients with mutations in the epidermal growth factor receptor (EGFR) are treated with EGFR tyrosine kinase inhibitors (TKIs), but inevitably resistance develops. One of the mechanisms causing this is amplification of MET, resulting in increased bypass signalling through the MET-receptor. Patients with MET amplification gain a good response from the MET TKIs crizotinib and capmatinib, but inevitably resistance also occurs to this treatment. The object of this study is to evaluate the potential mechanisms of this resistance.

Methods: HCC827-ER cells, a NSCLC cell line resistant to the EGFR TKI erlotinib, was treated with increasing doses of crizotinib (0.01-1 μ M) or capmatinib (0.5-12nM) in combination with erlotinib to develop resistant cell lines. The sensitivity of the resulting cell lines was investigated using MTS viability assays. To examine the mechanisms behind the resistance, the cells will be analysed by next generation sequencing (NGS) using the OncoPrint

Focus Panel (Thermo Fisher). This panel targets 52 genes with hotspot mutations, CNV gain and fusions.

Results: Resistance developed after four months of treatment confirmed by MTS analyses. At treatment with 1 μ M crizotinib or 12nM capmatinib, the resulting cell lines are highly resistant to MET-inhibition compared to the parental cells. Currently, we are performing NGS analyses of the cell lines.

Conclusion: Using a comprehensive NGS panel, we will be able to identify mechanisms causing resistance to MET targeted therapy, gain new knowledge about acquired resistance and ultimately improve the treatment strategy.

P03.08 Karen Schow Jensen FOLLOW-UP AFTER CESSATION OF TREATMENT FOR CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA - THE ABILITY TO DETECT RELAPSE AND THE NEEDS OF THE FAMILIES

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Background: Acute lymphoblastic leukaemia (ALL) is the most common cancer in children, accounting for about 200 new cases every year in the Nordic countries. Over the past decades, advances in treatment have led to an increasing number of children who survive cancer, and more than 85% of children with ALL have now become long-term survivors.

Objectives: 1: To evaluate the role of follow-up for the detection of relapses, and if the mode of detection (routine visit vs. symptoms) affects the outcome measured as survival. 2: To analyse quality of life, parental fear, expectations and need of reassurance after discontinuation of maintenance treatment for ALL. 3: To evaluate the long-term use of health care services in the population of long-term ALL survivors.

Method: 1: Retrospective study on ALL relapses after cessation of maintenance therapy in the Nordic countries. Patients are identified in the NOPHO register (Nordic Society of Paediatric Haematology and Oncology). From medical charts and results of blood tests, it will be decided if the relapse was diagnosed at a routine visit in an asymptomatic child or if the relapse was diagnosed because of symptoms. 2: A cross-sectional study of the Danish population of ALL survivors 0-5 years after end of treatment. Questionnaires are under development. 3: Register study where the Danish population of long-term ALL survivors are compared to a control group.

Perspective: Results of this population-based relapse study will provide an evidence-based background for planning optimal and relevant follow-up programs for children after therapy of ALL.

P03.09 Dianna Buus Hussmann UNCOVERING THE CLINICAL POTENTIAL OF THE CLL METHYLOME

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Patient stratification remains one of the major challenges in the clinical management of chronic lymphocytic leukemia (CLL), leaving an urgent need for improved markers to discriminate aggressive from indolent disease. This project aims to uncover the methylome of CLL patients to identify novel DNA methylation-based biomarkers for prognostication and gain insights into the underlying disease mechanism.

CLL is the most common hematological cancer amongst adults, displaying a remarkably heterogeneous disease course. Epigenetic alterations affect the gene expression and are often detectable early in cancer development as changes in the DNA methylation pattern. These measurable, disease-specific alterations show great promise to be highly advantageous in clinical molecular testing and in precision medicine.

Using genome-wide screening of >850K DNA methylation sites in a cohort of 137 CLL patients, I see that these patients separate into three clinically significant CLL sub-groups. By performing genomic, pathway and clinical correlation analyses, I will characterize the DNA methylation signatures of each CLL-subgroup, and validate a selected number marks for biomarker usage. I will further study how these methylation changes affect the cells by in vitro studies using CRISPR-Cas9 epigenome-editing.

With this project, I will thoroughly characterize the methylome of CLL-subgroups for promoting the clinical use of methylation-based biomarkers. I will identify potential drivers of disease in each subgroup, gaining insights into the molecular mechanisms of CLL. Ultimately, this will bring us closer to understanding CLL and improving treatment for CLL patients.

P03.10 Laura
Toussaint

DOSES TO BRAIN STRUCTURES ASSOCIATED WITH COGNITION IN PHOTON VS PROTON THERAPY OF CRANIOPHARYNGIOMA

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Purpose: Pediatric craniopharyngioma patients are at great risk of developing neurocognitive late effects after radiotherapy (RT). Craniopharyngioma are typically located in the suprasellar brain, in close proximity to several structures related to cognition (hereafter referred to as cognitive brain structures (CBSs)). The aim of this study was, therefore, to explore the pattern of doses delivered to CBSs for contemporary photon versus proton therapy techniques.

Material and methods: CT and MRI scans from ten pediatric craniopharyngioma patients were used to delineate conventional critical structures

(brainstem, optic nerves, chiasm) as well as CBSs (limbic system and Papez circuit, frontal and temporal lobes, anterior and posterior cerebellum, subventricular zones, corpus callosum and left frontal white matter). Photons volumetric modulated arc therapy (VMAT) and intensity modulated proton therapy (IMPT) plans were generated for a prescribed dose of 54Gy. For each CBS, we compared the fraction of volume receiving low (V10Gy), intermediate (V40Gy) and high (V50Gy) doses, as well as the mean doses (Dmean). Wilcoxon signed-rank tests were performed to compare the dose/volume parameters for VMAT vs. IMPT plans.

Results: In general, V10Gy were reduced with IMPT compared to VMAT. V40Gy and V50Gy were comparable. IMPT significantly reduced Dmean to twelve CBSs, while the choice of field incidence resulted in slightly higher Dmean compared to VMAT for some CBSs.

Conclusion: Dmean and V10Gy were reduced by the use of IMPT compared to VMAT, while V40Gy and V50Gy were comparable. The ability of IMPT to spare some of the CBSs was influenced by the choice of beam orientations.

P04.01 Frederik COMPREHENSIVE CHARACTERIZATION OF MOLECULAR SUBGROUPS IN
 Frostholtm Prip EARLY STAGE BLADDER CANCER

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Background: About 50%-70% of patients with non-muscle invasive bladder cancer (NMIBC) have disease recurrence and 10%-15% progresses to muscle invasive bladder cancer. To optimize treatment and follow-up regimens, it is essential to understand and to be able to predict disease aggressiveness. For that, several biomarkers of aggressiveness have been identified, and these biomarkers reflect distinct molecular subtypes in NMIBC.

Aim: To investigate the underlying biological mechanisms responsible for the molecular subclasses identified in NMIBC.

Method: This will primarily be accomplished by construction of a tissue microarray (TMA) containing tissue cores from approximately 200 cases previously analyzed by RNA-Seq. We will perform Immunohistochemistry (IHC) against well-known subtype markers (luminal-like, basal-like, EMT markers and stem cell markers), and results will be quantified using digital image analysis. We will compare the protein IHC data to genomic alterations (obtained from DNA-seq and RNA-seq data), methylation changes and gene expression changes. Finally, the multi-omics data will be correlated to clinical outcome by univariable and multivariable Cox regression analysis.

Expected impact: Understanding the molecular mechanisms behind the observed molecular subtypes in NMIBC can be the first step towards more efficient targeted therapy for this patient group. This will hopefully increase patient survival and prevent side-effects from unnecessary treatment.

P04.02 Astrid Lindman RETURN TO EVERY DAY LIFE AFTER STEMCELL TRANSPLANT (MINI-HCT): EFFECT OF A MULTIMODAL INTERDISCIPLINARY REHABILITATION PROGRAMME

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Non-myeloablative haematopoietic stem cell transplantation (MiniHCT) is associated with a high treatment-related mortality and innumerable complications and side-effects. Thus, it is a challenge for MiniHCT patients to maintain physical and psychosocial functioning, quality of life, and participation in society.

The aim of this project is to develop and evaluate the effect of a multimodal interdisciplinary rehabilitation programme targeted at patients undergoing MiniHCT.

In accordance with the framework of "Complex Interventions" three studies will be performed:

1) An interview study with focus groups of experienced MiniHCT patients. The object is to develop a MIR programme based on patient experiences and perspectives combined with existing evidence, and thereby involve patients in the research process.

2) A prospective feasibility study. The object is to investigate whether MIR developed in study I is feasible, safe and effective.

3) A clinical trial with matched controls. The object is to investigate the effects of the MIR programme compared to usual care.

The project will contribute with knowledge about the effects of a rehabilitation programme targeted at a vulnerable group of chronic cancer patients. If the intervention leads to an increased level of empowerment, functioning and fewer treatment-related symptoms, it will not only reduce the number of hospitalizations and healthcare services, but also imply that more patients will be able to maintain contact with the labour market and a meaningful life. Additionally, the study will document the impact of an interdisciplinary intervention anchored in the hospital setting but aimed at reaching patients at home.

P04.03 Jakob Haldrup Jensen GENOME-WIDE CRISPR-CAS9 SCREENING IDENTIFIES GENETIC VULNERABILITIES AND POTENTIAL THERAPEUTIC TARGETS IN CASTRATION RESISTANT PROSTATE CANCER

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Background: Treatment options for castration-resistant prostate cancer (CRPC) are limited, and only a few agents (e.g. enzalutamide, docetaxel) are routinely used in the clinic. However, CRPC tumors will invariably develop resistance to these agents, and only a subset of patients will respond. The duration of treatment response is highly individual, and there is

currently no accurate way to monitor for treatment failure and disease progression. Thus, novel predictive biomarkers are urgently needed to ensure that an expensive and potentially harmful agent is given only to patients who will benefit from it. Furthermore, to enable new treatment strategies, a better understanding of drug resistance mechanisms is required

Methods: To identify novel drug resistance genes and mechanisms of therapy resistance, we performed genome-wide CRISPR-Cas9 loss-of-function screens in the C4 CRPC cell line. Using 77,441 unique sgRNAs, 19,114 protein-coding genes were tested for their potential functional role in enzalutamide and docetaxel resistance. IC50 and IC90 values were used for selection, resulting in successful positive (gain of resistance) and dropout (loss of resistance) screens for both drugs.

Results: The screens identified genetic vulnerabilities and potential therapeutic targets in CRPC, as knockout of specific genes sensitized C4 cells to enzalutamide. In addition, our results suggest that disruption of specific transcription factors may modulate docetaxel resistance in C4 cells.

Conclusion: Drug resistance is a major clinical problem. Here, we identified genetic vulnerabilities that may be translated into predictive biomarkers and/or novel combination therapies for CRPC.

P04.04 Jesper
Pedersen

THE VALIDITY OF PHOTON-BASED RECTUM NTCP MODELS TOGETHER WITH
A CONSTANT RBE FOR PROTON THERAPY

P04.05 Kia Busch

ON-LINE DOSE-GUIDED PROTON THERAPY TO ACCOUNT FOR INTER-FRACTIONAL MOTION: A PROOF OF CONCEPT

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Purpose: Dose-guided proton therapy (DGPT) is when online dose re-calculations of possible isocenter shifts are performed to find the best re-positioning of a patient. The aim of this study was to investigate the potential of DGPT exemplified by inter-fractional pelvic motion.

Materials/methods: Five models were created from a locally advanced prostate cancer patient using a planning CT (pCT) and four repeat CTs (rCTs) with the Hounsfield Units overwritten to water, air and the average of bone. Intensity-modulated PT (IMPT) plans were created on the pCT (Eclipse, Varian Medical Systems) using two lateral opposed beams. To simulate inter-fractional motion, we moved the prostate and seminal vesicle planning target volumes 3-15 mm along the three axes in all CTs. Image-guided PT (IGPT) was investigated by moving the plan isocenter according to the simulated motion and re-calculating the plan. DGPT was explored by calculating multiple dose distributions with the isocenter shifted 1-15 mm from the field position used for the IGPT re-calculation. The targets were evaluated using V98%, and normal tissue (NT) was evaluated based on D1cc.

Results: DGPT improved the dose distribution in all targets and NT in half of the simulated scenarios compared to IGPT. The largest benefits of DGPT were seen for large anterior motion, and the best strategy was clearly to move the fields back towards their original position.

Conclusion: Using a simplified patient model, we showed that DGPT has the potential to improve dose coverage and spare NT compared to IGPT, with the greatest benefits for large organ motion.

P04.06 Maja Bendtsen RADIATION THERAPY OF SINONASAL CANCER
Sharma

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Background: Radiation therapy is a cornerstone in the treatment of sinonasal cancer. Radiation with X-rays, used today, presents a considerable challenge because of important structures in close proximity to the tumor, including the brain, the optic pathways and the pituitary gland. Damage to these may have large impact on the patient's quality of life. Proton therapy is a novel treatment for these tumors, available in Denmark in 2018. Protons have different depth-dose characteristics, which makes it possible to deliver a high radiation dose in a precise location, and hereby spare the normal

tissue and reduce side effects. Because of certain physical entities and the limited capacity, it is of great importance to form a model for patient selection as well as investigate physical insecurities in order to establish suitable treatment protocols.

Aim: The aim of the study is to form the basis for establishing a model for patient selection via investigation of outcome and toxicity as well as investigate the need for adaptive/robust dose planning in proton therapy of sinonasal cancer.

Methods: We have planned four studies. A retrospective database study will determine outcome, a clinical cross-sectional study will investigate late toxicity, a planning study will determine the need for adaptive radiotherapy, and finally a prospective study will evaluate patients receiving proton therapy in Denmark.

Perspectives: We may be able to offer patients a new treatment that is superior in both effect and toxicity. These studies provide the data necessary for both proper patient selection and treatment planning. Thus, it will be of benefit for all future patients with sinonasal cancer.

P04.07 Nadia Øgaard ESTABLISHMENT OF A STANDARD OPERATING PROCEDURE FOR PRE-ANALYTIC PROCESSING OF CIRCULATING CELL-FREE DNA

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Analyses of circulating cell-free DNA (cfDNA) have great potential for non-invasive diagnosis, prognosis, and treatment/recurrence monitoring in cancer patient management. However, absence of standardization of pre-analytical conditions hinders inter-study comparability.

This study describes the development of a standard operating procedure (SOP) for pre-analytic management of cfDNA in biomarker studies. Including the development of quality control assays for, assessing the cfDNA purification efficiency, leucocyte DNA contamination and for quantifying the cfDNA level in the purified sample and an approach for up-concentration of cfDNA.

cfDNA is quantified using digital PCR assays targeting genomic regions rarely affected by mutations in cancer. CfDNA extraction efficiency is assessed using a spike-in oligo and a digital PCR assay targeting the spike-in. Contamination with leucocyte DNA is estimated using an assay targeting the rearranged immunoglobulin locus found in B-cells.

Lysis of blood leucocytes potentially contaminates plasma samples with irrelevant cellular DNA. We present results showing how standard steps in plasma processing affects lysis. Our cfDNA quantification assay targets a cytosine free region of the genome, making it suited for DNA-methylation studies by enabling assessment of cfDNA recovery both before and after bisulfite conversion. We also present procedures for assessing bisulfite conversion efficiency.

To exploit the benefits of cfDNA applications in the clinic, reproducible results are essential. We present an easy-to-implement SOP with appropriate quality controls, which will facilitate the clinical translation of cfDNA studies.

P04.08 Rikke
Nørgaard
Pedersen

LATE BREAST CANCER RECURRENCE: RISK AND PREVENTION

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Background: There are over 60,000 female breast cancer survivors in Denmark. About 70% of women with breast cancer survive at least 10 years after primary diagnosis. The high survival of breast cancer calls for a need to identify women at risk of late breast cancer recurrence. Data on the risk and prevention of late recurrent breast cancer are sparse.

Methods: Using nationwide Danish registries, we will estimate the risk of late recurrence, identify factors that may increase the risk of late recurrence, as well as drugs that may help prevent late recurrence. We will define late recurrence as local, regional or distant recurrent breast cancer diagnosed ≥ 10 years after primary breast cancer diagnosis. Our algorithm includes codes to identify metastatic cancer in the DNRP; recurrent cancer in the Patobank and/or DNRP; and surgery for recurrent breast cancer in the DNRP. We will supplement the algorithm with information on cancer-directed treatment registered in the DNRP ≥ 10 years after the date of primary breast cancer diagnosis. The algorithm has a positive predictive value of 71% (95%CI = 54%, 85%), with sensitivity, specificity and negative predictive value $>90\%$.

Results and conclusion: Awaiting data. No results available yet.

Perspectives: We anticipate that this study will provide important information on clinicopathological and other predictors that will help identify patients with increased risk of late recurrence, who may benefit from extended therapies.

P04.09 Margarita
Sergeyevna
Melnikova

HISTOLOGICAL PROFILING OF THE TUMOR MICROENVIRONMENT IN MOLECULAR SUBCLASSES OF COLORECTAL CANCER

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Background: Colorectal cancer (CRC) is the third most common cancer globally. CRC treatment selection and prognostication are based on pathological classification, grading, and TNM (tumor/node/metastasis) staging. Current CRC classification has limited prognostic and predictive value, partly because of inter-tumor molecular diversity. Therefore, there is a need to complement pathological staging with molecular sub-classification of CRC to improve prognosis prediction and personalized cancer treatment.

Our group stratified CRC into five molecular subtypes based on gene expression profiling: goblet-like, stroma-like, sessile serrated carcinoma-like, depleted in AU-rich element and chromosomal instable. We found subtype-specific prognostic biomarkers at RNA level and emphasize that the tumor microenvironment is a novel determinant of CRC progression. These molecular subtypes cannot be applied in routine clinical settings due to high cost and technically demanding gene expression analysis.

Aim and hypothesis: The aim of my PhD study is to establish a novel framework for molecular subtyping of CRC based on conventional, low-cost technique (immunohistochemistry (IHC)). We hypothesize that IHC-based molecular classification can be used in CRC diagnostics and as a predictor of high relapse risk TNM stage II patients.

Planned studies:

- 1) Selection of IHC biomarkers for molecular subtypes
- 2) Evaluation of biomarkers in a discovery cohort
- 3) Validation of biomarkers in a large clinical cohort
- 4) Quantification of intra-tumor stroma within the primary tumor

P04.10 Emil Aagaard Thomsen IDENTIFICATION OF CANCER DRUG RESISTANCE MECHANISMS AND CELLULAR SIGNALING PATHWAYS BY GENOME-WIDE CRISPR/CAS9 SCREENS

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The capacity of malignant cells to develop resistance to immuno- and chemotherapies is a continuous challenge in cancer therapies. Treatment of Diffuse Large B-cell Lymphoma (DLBCL), an aggressive B-cell cancer form characterized by extensive clinical and biological heterogeneity, with the standard R-CHOP treatment is often affected by acquired or inherent drug tolerance. This project takes its origin in establishment of lentiviral CRISPR-based genetic screening. These approaches offer a new and unique approach to identifying the causative resistance genes relevant for patients suffering from DLBCL. By employing CRISPR screens, the high complexity in biological settings can be reduced and translated into clinically relevant discoveries. Using genome-wide lentivirus-based CRISPR/Cas9 libraries, I will identify genes affecting R-CHOP tolerance and analyze their functional relevance in cellular signaling and clinical datasets. The functional role of genes that I have already identified as modulators of the cell response to rituximab will be studied in detail. The project will provide new knowledge about drug tolerance, allowing the use of genetic variants as biomarkers and development of individualized cancer treatment.

- P05.01 Ann-Katrine Jakobsen TARGETING REPAIR MECHANISMS IN CANCER TREATMENT
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- Lack of response to chemotherapeutics occur in the treatment of some cancer patients. This problem also exists for the camptothecin (CPT) family of chemotherapeutic drugs including Irinotecan and Topotecan. CPT drugs trap the enzyme topoisomerase 1 (TOP1) on DNA, resulting in breakage of the DNA backbone and ultimately cell killing. However, the enzyme tyrosyl-DNA phosphodiesterase 1 (TDP1) has been shown to be a key enzyme in the repair of TOP1-mediated DNA damage and thereby counteracting the effect of CPT drugs. This suggests that the effect of cancer treatment with CPT drugs can be increased if combined with TDP1 inhibiting drugs.
- To establish if TDP1 is a relevant target in cancer treatment, TDP1 and TOP1 activities have been measured in paired non-tumor and tumor tissue from a cohort of 130 patients with non-small cell lung cancer.
- Both TDP1 and TOP1 activity were significantly upregulated from non-tumor to tumor tissue. The results indicate that TDP1 is relevant to inhibit when treating cancer patients with CPT drugs. Furthermore, some patients from the cohort had a lower TOP1 activity in the tumor tissue compared to the non-tumor tissue. This suggests that screening for TOP1 activity before treating with CPT drugs should be considered.
- Another part of the PhD study focuses on the development of small molecular compounds capable of inhibiting TDP1. The compounds are synthesized by chemists in Spain. In this PhD project, the compounds are tested for their ability to inhibit TDP1. Four compounds have so far showed promising results by reducing the survival of cancer cells in combination with CPT treatment when tested using established cancer cell cultures.
- P05.02 Anne Tranberg Madsen IDENTIFICATION OF THE MECHANISM OF ACQUIRED RESISTANCE TO LORLATINIB IN AN ALK-REARRANGED NON-SMALL CELL LUNG CANCER CELL LINE
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- A subset of non-small cell lung cancer (NSCLC) patients harbor oncogenic rearrangements of the receptor tyrosine kinase ALK and can be treated with the potent ALK inhibitor lorlatinib. Unfortunately, drug resistance inevitably emerges, and the mechanisms underlying lorlatinib resistance remain largely undescribed. In vitro models have proven to be valuable tools for understanding the molecular mechanisms of resistance to targeted therapies in NSCLC. Thus, we aimed to discover novel mechanisms of resistance to lorlatinib treatment by establishing a lorlatinib-resistant NSCLC cell line.
- Resistant H3122LR cells were generated by treating the cell line H3122 with gradually increasing doses of lorlatinib. Following 4 months of treatment, the

cells were insensitive to treatment with different ALK inhibitors. To examine the H3122LR cells, we employed targeted next generation sequencing of 52 relevant genes and found that H3122LR cells had not gained any mutations or copy number variations compared to H3122 cells. However, using RT-qPCR and immunofluorescence microscopy, we found that H3122LR cells presented with epithelial-to-mesenchymal transition (EMT) features resulting in a distinct phenotypic shift. This was evident from the upregulated mRNA and protein levels of the mesenchymal marker vimentin, as well as downregulation of the epithelial marker E-cadherin in H3122LR. Furthermore, mRNA levels of genes encoding the mesenchymal markers N-cadherin and snail were also upregulated.

EMT is a known mechanism of resistance to several other targeted therapies, and future studies will further investigate the role of EMT as a potential novel lorlatinib resistance mechanism.

P05.03 Anders Rosendal Korshøj

OPEN-LABEL PHASE 1 CLINICAL TRIAL TESTING PERSONALIZED AND TARGETED INTERVENTION WITH SKULL REMODELLING SURGERY TO MAXIMIZE LEVELS OF TT FIELD INTENSITY FOR HIGHER TREATMENT BENEFIT - THE OPTIMAL TTF STUDY

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We present a new and ongoing investigator initiated (Aarhus, DK) open label phase 1 clinical trial (NCT02893137) investigating safety and efficacy of a novel therapeutic concept for recurrent glioblastoma. The intervention combines best physician's choice chemotherapy with tumor treating fields (TTFs) and personalized skull remodeling surgery (SR-surgery), incl. minor craniectomy, burr hole formation and skull thinning. We performed finite element calculations, which indicate that SR-surgery provides a marked and focal enhancement (~100%) of TTFs without significantly compromising patient safety. Accrual began in Dec 2016 and will end at fifteen patients. Eligibility criteria include: Age > 18 years; first recurrence of focal glioblastoma (WHO, RANO) < 2 cm to cortical surface; Karnofsky performance score (KPS) > 60; lack of uncontrollable epilepsy and significant co-morbidity. Primary endpoint is severity/frequency of adverse events (AEs). Secondary endpoints include overall survival, progression free survival (PFS), PFS at six months, objective response rate (RANO), Quality of life (QoL) assessment, KPS and steroid dose. Follow-up is 18 months and includes regular toxicity assessment every 6 weeks, and QoL and response assessments (incl. MRI) every 3rd month. Patients are censored upon finished scheduled follow-up, occurrence of serious or unacceptable AEs, withdrawal of consent, or loss to follow-up.

The tested concept holds promising potential for a new and superior implementation of TTFs for intracranial tumors. The presented trial will hopefully lay the foundation for future efficacy investigation.

P05.04 Trine Block
Mattesen

DNA METHYLATION PROFILING OF COLORECTAL CANCER IDENTIFIES MOLECULAR SUBTYPES AND SUBTYPE-SPECIFIC BIOMARKERS FOR IMPROVED PREDICTION OF PATIENT PROGNOSIS AND TREATMENT RESPONSE

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By analysis of RNA profiles from >1000 fresh-frozen colorectal cancer (CRC) samples, we recently established that CRC is comprised of distinct molecular subtypes with different etiology, prognosis and treatment response. Furthermore, we found preliminary evidence in retrospective CRC cohorts that patients may benefit from being treated according to their molecular subtype rather than according to their tumor (TNM) stage. The clinical validation and utilization of this exiting knowledge is, however, complicated by the unavailability of high quality RNA from clinical collected formalin-fixed paraffin-embedded (FFPE) samples. Here we, therefore, establish a novel CRC subtyping approach "methCORR", which only requires DNA from FFPE tissue to stratify CRC into subtypes. The approach is based on DNA methylation profiles. Using methCORR, we are able to identify different epithelial CRC developmental pathways, which induce clearly distinct tumor microenvironments (TMEs). Very notably, we found that CRC aggressiveness was associated with specific and different immune cell type subsets within each TME subtype. To facilitate clinical translation of this knowledge, we developed simple PCR-based DNA methylation biomarkers, which simultaneously stratified patients into epithelial subtypes and quantified subtype-specific prognostic immune cells. Thereby, patients with poor and favorable prognosis could be identified. The results illustrate that our novel subtyping framework, combining DNA methylation-based subtyping and subtype-specific biomarkers, could contribute to improved patient prognostication and may form a strong basis for future studies.

* contributed equally to this work

P05.05 Anders
Kindberg
Boysen

THE PROGNOSTIC VALUE OF SIDEDNESS OF THE PRIMARY TUMOR AFTER LOCAL TREATMENT FOR METASTATIC COLORECTAL CANCER - A DANISH POPULATION-BASED STUDY

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Background: Local treatment of metastatic colorectal cancer (mCRC) includes resection, radiofrequency ablation (RFA) and stereotactic radiotherapy (SBRT) of liver and/or lung metastases. The aim of this study was to analyse the prognostic value of the primary tumors sidedness after local treatment of mCRC in a national population based study.

Methods: Data was retrieved from the Danish Cancer Registry and the Danish National Patient Registry (DNPR) for all patients who underwent surgery for CRC in 2000-2013. Additional data from the DNPR included liver and/or lung metastasectomy, RFA or SBRT. Survival was calculated from the date of last recorded local treatment until death from any cause or end of follow-up. A Cox proportional hazard model was used to compute hazard ratios (HRs) for mortality between groups adjusting for age, gender, co-morbidity, nodal stage and site of local treatment.

Results: A total of 38,131 patients had surgery for a primary CRC and 2,912 patients underwent a total of 3,602 metastasis directed procedures. The median age was 64.9 years (range 20-92 years), and 59% were male. Local treatment modalities comprised liver surgery (n=1,616), lung surgery (n=1,075), liver RFA (n=705), liver SBRT (n=124) and lung SBRT (n=82). For patients with a right and left sided tumor, the median survival reached 3.2 years (95% CI 2.7-3.5) and 4.0 years (95% CI 3.8-4.2), respectively. With left sided as the reference, the adjusted HR 1.20 (95% CI 1.07-1.38, p=0.003).

Conclusion: We report a longer median survival for CRC patients with a left sided primary as compared to right sided primary tumor after local treatment for liver and lung metastasis.

P05.06 Sofie
Gottschalk
Højfeldt

GENETIC VARIANTS IN HLA GENES ARE ASSOCIATED WITH PEG-
ASPARAGINASE ALLERGY - A GENOME-WIDE ASSOCIATION STUDY ON THE
NOPHO ALL2008 PROTOCOL

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Asparaginase is a cornerstone in treatment of childhood acute lymphoblastic leukemia (ALL). However, balancing positive anti-leukemic effect against toxicities has proven difficult. A frequent toxicity is allergy; 13% of children treated according to the Nordic NOPHO ALL2008 protocol develop an allergic reaction to pegylated asparaginase (PEG-asp.) and must truncate their treatment.

To investigate a genetic predisposition to PEG-asp. allergy, we performed a genome-wide association study (GWAS) on 1288 children treated according to the NOPHO ALL2008. Of these, 178 (13.8%) were registered with an allergic reaction to PEG-asp. Registration relied solely on the physician's ability to recognize symptoms of an allergic reaction, which can be difficult because of the diverse clinical manifestations. To define allergy and increase specificity, we used asparaginase enzyme measurements, only including children with available enzyme measurements; after quality control, 63 children with clinical allergy and without enzyme activity and 360 children with enzyme activity were included as cases and controls.

The variant rs3998159 on 6p21.32 showed the strongest association to PEG-asp. allergy ($P=1.23 \cdot 10^{-6}$; OR=3.7). This SNP is located 27kb upstream of the HLA-DQA2 gene. Our top 17 SNPs are all located in close proximity to the top SNP and are in high linkage disequilibrium ($R^2=1$).

This study associates variants in the HLA-region with PEG-asp. allergy, a region highly involved in the immune responses. These results fit into the

exiting literature in the field on allergic pathways and expand our knowledge about the genetic background for PEG-asp. allergy.

P05.07 Sarah Lindhøj Kvorning CROSSTALK IN CANCER: SOLUBLE CD163 IN EXTRACELLULAR VESICLES IN PATIENTS WITH MULTIPLE MYELOMA

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Background: Multiple myeloma (MM) is an incurable hematological cancer, where malignant plasma cells are localized in the bone marrow (BM). Tumor associated macrophages (TAMs) in the BM support cancer development, e.g. by stimulating neo-angiogenesis and by inducing resistance to chemotherapy. These functions may be executed via extracellular vesicles (EV) released from the TAMs. We have recently shown that some circulating EVs contain the macrophage specific protein CD163, which is highly expressed on TAMs. This EV-CD163 fraction of the total soluble CD163 in plasma may be a sensitive biomarker for monitoring treatment response and relapse identification.

Hypothesis: We hypothesize that the fraction of EV-CD163 is increased in peripheral blood in MM patients compared to reference persons, and that the fraction is increased during active disease episodes. We aim to measure EV-CD163 and relate the concentration to disease activity and other macrophage biomarkers.

Methods: We enroll MM patients with different disease activity at the Department of Haematology, Aarhus University Hospital. The reference group is blood donors from the Department of Clinical Immunology. From whole blood samples, we will detect and measure EV-CD163 and total sCD163 with ELISA. Furthermore, we will measure CD163 mRNA levels in blood monocytes and EV with qPCR and measure monocyte CD163-expression using Flowcytometry.

Perspectives: This research year study is the first to explore EV-CD163 in cancer, and it holds prospects for the identification of new biomarkers in MM and potential targets for therapeutic intervention.

P05.08 Johan Vad-Nielsen EPIGENETIC REGULATION OF ALTERNATIVE SPLICING IN EPITHELIAL-MESENCHYMAL TRANSITION IN NSCLC

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Lung cancer remains the leading cause of cancer-related deaths worldwide, with a disappointing 5-year survival rate of <10%. Approximately 80% of cases are non-small cell lung cancer (NSCLC). The prognosis is often poor, and therapeutic options are limited. A mechanism of acquired resistance to current therapies in NSCLC that has received increasing

attention is the process of Epithelial-Mesenchymal Transition (EMT). The EMT program involves the disruption of cell-cell adherence and loss of cell polarity of the epithelial cancer cell for the acquisition of a more mesenchymal-like phenotype. EMT occurs on the basis of major changes in gene expression and especially transcript isoform diversity produced by alternative splicing (AS). Evidence of epigenetic mechanisms in the regulation of AS is now emerging, wherein histone modifications and their interaction with non-histone proteins as well as DNA-methylation can modulate AS. However, despite substantial independent evidence for the interplay between epigenetics, AS and EMT, a direct link between epigenetic changes and AS in the context of EMT has yet to be demonstrated.

This project aims at providing an in-depth characterization of the functional relationship between alternative splicing, epigenetics, and EMT in NSCLC. This will include genome-wide characterization of alternative splicing and epigenetics during EMT as well as in vitro studies of functional cause-and-effect mechanisms.

These results will permit the prediction of not only gene expression but also transcript isoform diversity specific for EMT from the chromatin level. This may have applications in NSCLC diagnostics through circulating nucleosomes in "liquid biopsies".

P05.09 Mette Saksø FAZA PET HYPOXIA AS A MARKER OF LOCO-REGIONAL RECURRENCE IN HEAD AND NECK CANCER?

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Background and purpose: Hypoxia in head and neck squamous cell carcinoma (HNSCC) is an important risk factor when assessing clinical outcome after primary chemo-radiation (RCT). We hypothesized that the hypoxic sub-volumes are areas in the tumor with special radiation resistance. The volumes can be visualized using PET/CT and a hypoxia-specific tracer ¹⁸F-fluoroazomycin arabinoside (FAZA). The purpose of this study was to test the hypothesis of the hypoxic sub-volumes as seen on pretreatment FAZA PET/CT being the predominant sites of treatment failure.

Material and methods: In 2009-2011, 40 patients with HNSCC planned for primary RCT were included in the prospective phase II trial, DAHANCA 24. All were imaged with static 2h-post-injection FAZA PET/CT prior to treatment. Recurrence was verified by histology and MRI or PET/CT imaging. The attenuation CT of the FAZA scan was merged with recurrence imaging, and the spatial information was visually compared.

Results: Twenty-five of 40 patients had FAZA-avid, hypoxic tumors before treatment (63%). In total, 38 patients completed treatment as prescribed. With a median follow-up of 4.9 years, 9 loco-regional recurrences were observed, and 8 of these were identified in patients with initially hypoxic tumors (cum. incidence of 32% and 8%, respectively, p=0.04). Eight patients

had recurrence imaging sufficient for co-registration with the FAZA PET/CT. Seven of these had hypoxic primary tumors. In less than half of these patients, the recurrence was in or overlapping with the hypoxic sub-volumes.

Conclusion: The pattern of failure does not convincingly support the hypothesis of the hypoxic sub-volume being the major origin of recurrent disease.

P05.10 Anita Tranberg CLONAL PROGRESSION DURING FIRST COURSE OF CHEMOTHERAPY IN
Simonsen ACUTE MYELOID LEUKEMIA SUBOPTIMAL RESPONDERS HERALDS
REINDUCTION FAILURE AND EARLY DEATH

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We hypothesized that by studying clonal architecture changes during AML treatment another dimension could be added to the chemotherapy response assessment.

Patients included: Group 1: 7 AML CR_{MRD+} (patients achieved CR but with positive MRD levels between 0.02% and 1%) and Group 2: 18 AML pts. who did not achieve CR after the first course of chemotherapy. In Group 1; MRD cells from bone marrow samples taken after 1st treatment course were isolated using cell sorting. All samples from both groups were analyzed using a 26-gene panel.

In Group 1, clonal architecture in unsorted diagnosis samples were compared to clonal architecture in the sorted products. 3/7 cases were informative; 2/3 showed a persistence of a TET2 mutation. In the third patient, one of two clones containing IDH2 persisted.

In Group 2, 16/18 cases were informative regarding development of clonal architecture between diagnosis and regeneration after first course of chemotherapy. 9/16 cases were clonally stable. In 7/16 cases, clonal development was seen: In 4 cases, one or more subclones were selectively eradicated, leaving the more resistant clones. In 3/7 cases, subclones emerged during chemotherapy. The 2-year survival of patients was significantly different in the three groups (clonally stable (n=9): 0.58, AMLs with persisting subclones (n=4): 0.25, AMLs with emerging subclones (n=3): 0, P = 0.01).

Conclusion: subclonal architecture changes can happen even in patients with minute amounts of residual leukemia. We envisage that an approach like the one applied here can assist the decision of further treatment in patients experiencing suboptimal treatment response.

P06.01 Johanne Marie LYMPHOPROLIFERATIVE AND MYELOPROLIFERATIVE MALIGNANCIES
Holst OCCURRING IN THE SAME HOST: DESCRIPTION OF A NATIONWIDE
DISCOVERY COHORT

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Myeloid and lymphoid malignancies have been considered as diseases with distinct pathogenetic mechanisms. However, recent studies have reported an increased risk of lymphoid malignancies in patients with chronic myeloproliferative neoplasms (MPN). Genomic studies in patients with angioimmunoblastic T-cell lymphoma have revealed mutations in epigenetic modifier genes, which are usually not seen in lymphomas, while they are commonly found in patients with myeloid diseases. The objective is to identify and validate a nationwide cohort of patients, who were diagnosed with MPN and a lymphoid malignancy either simultaneously or sequentially.

Patients diagnosed with both MPN and a lymphoid malignancy within the period 1990-2015 were identified through the Danish Pathology Register. Formalin-fixed paraffin-embedded tissue specimens were collected and reviewed.

The cohort consists of ninety-seven patients, and 48.5% of the patients were females. The age at diagnosis ranged between 18.5 and 93.7 years, and the median age at MPN diagnosis was 70.8 years (interquartile range: 62.8-79.9 years). An excess of peripheral T-cell lymphomas was observed (17%) at a frequency almost double as high as the one expected in a Caucasian population-based non-Hodgkin lymphoma cohort (8-10%). Interestingly, most peripheral T-cell lymphomas diagnoses were of angioimmunoblastic T-cell lymphoma type.

The establishment of this unique series of tissue specimens from patients with co-existing myeloid and lymphoid malignancies creates a basis for genomic studies to search for shared pathogenetic steps explaining the development of both MPN and lymphoid malignancies in the same host.

P06.02 Trine Vilsbøll REGULATION OF PD-L1 IN NON-SMALL CELL LUNG CANCER
Larsen

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Immunotherapy targeting the PD-1/PD-L1 pathway (PD therapy) is a treatment option for some patients with non-small cell lung cancer (NSCLC). However, a positive response to PD therapy is seen in some patients who currently do not qualify for PD therapy, and not all patients who receive PD therapy respond. In order to improve and further develop this treatment, this project aims to understand how PD-L1 expression is regulated in NSCLC and how this regulation affects T-cell activity.

The project will investigate how site-specific DNA methylation in PD-L1 correlates with PD-L1 expression in NSCLC cell lines. To ascertain the regulatory function of DNA methylation levels on PD-L1 expression and thereby T-cell activity, co-cultures of T-cells and tumor cells with epigenome editing of PD-L1 will be carried out.

To further understand how PD-L1 is regulated, NSCLC cell lines will be examined to detect splice variants of PD-L1. The functional effect of the different splice variants on T-cell activity will be examined using co-cultures of T-cells and new NSCLC cell lines expressing only one type of splice variant. Splice switching oligonucleotides will be utilized to shift expression patterns of PD-L1 transcript variants to specifically encode PD-L1 isoforms without T-cell inhibitory activity.

In a last attempt to better understand the regulation of PD-L1, CRISPR library screening will be performed to identify novel genes involved in PD-L1 regulation, and the regulatory importance of the gene(s) on T-cell activity will be examined.

Finally, the project will examine if significant findings in the NSCLC cell lines apply in tumor tissue from NSCLC patients.

P06.03 Julie
Bondgaard
Mortensen

ELEVATED PRE-THERAPEUTIC SERUM LEVELS OF SOLUBLE PROGRAMMED DEATH 1 PROTEIN (SPD-1) IDENTIFY DLBCL PATIENTS WITH ADVERSE PROGNOSTIC FEATURES

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Background: Checkpoint proteins regulate the immune system, and their down-regulation of effector mechanisms is exploited by malignant cells to evade antitumor response. Membrane bound programmed death 1 protein (PD1) and its ligand 1 are checkpoint proteins reported as adverse prognostic factors in lymphoma, and suppressing these proteins with targeting antibodies can re-establish antitumor immunity. A soluble form of PD1 is detectable in blood, but its biological and clinical significance is yet to be clarified.

Aims: Measure pre-therapeutic soluble PD1 (sPD1) levels in lymphoma and investigate the potential correlation with the International Prognostic Index (IPI) including age, stage, performance status, LDH and extranodal sites.

Methods:

- sPD-1 measurement: Time Resolved Immunofluorometric Assay based on commercial antibodies, validated and optimized by the research group
- Study population: Pre-therapeutic serum samples from lymphoma patients(n=84) and serum from healthy controls(n=22)
- Statistics: Mann-Whitney, linear regression and Spearman's rank correlation

Results:

- Higher sPD1 in patients compared to controls (p=0.002). In a diagnostic subgroup analysis, patients with Diffuse large B-cell lymphoma (DLBCL) and

Chronic lymphocytic leukemia still had significantly higher sPD1 ($p=0.009$ & $p=0.002$) than controls

- Positive correlation between sPD1 and adverse prognostic factors (IPI-score)($p=0.007$) in DLBCL

Conclusion: Pre-therapeutic sPD1 are elevated in selected lymphomas and levels correlate with presence of clinical adverse prognostic factors in patients with DLBCL. Correlation analyses between sPD1 and clinico-pathological features, clinical behaviour and outcome are ongoing.

P06.04 Julie Nelly Christensen LOSS OF ENDOCYTIC RECEPTOR X (ERX) IN MELANOMA CELLS INDUCE EPITHELIAL-TO-MESENCHYMAL TRANSITION

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Melanoma is a very aggressive cancer with a poor prognosis if the disease is detected after spreading from the primary tumor has occurred. The molecular changes initiating the spread from the primary tumor remain poorly described, and currently no established biomarkers can predict melanoma metastasis at early stages of the disease and thus indicate the need for adjuvant treatment.

We have discovered the endocytic receptor protein x (ERX) to be highly expressed in cutaneous melanomas and metastases hereof. In addition, we have found ERX expression in cultured cell lines derived from metastatic melanomas.

We are currently investigating the relationship between ERX expression and the metastatic potential of melanoma cells in dual fashion in cell-based model systems, where 1) modulation of ERX is obtained using CRISPR/Cas9 technology and 2) epithelial-to-mesenchymal transition (EMT) is induced by TGF β .

We hypothesized that modulation of ERX expression in melanoma cells would alter their ability to metastasize, and we have found that decreased ERX expression induces EMT. Identification of a shift in expression patterns of established EMT markers was achieved by qPCR and western blotting. Furthermore, the induced change in expression of the EMT markers resulted in functional changes mimicking those normally described during EMT, e.g. decreased adhesion and increased migration. ERX and EMT marker expression was evaluated after induction of EMT by TGF β . TGF β stimulation resulted in down regulation of ERX, which occurred prior to the observed change in EMT markers.

We conclude that downregulation of ERX expression in melanoma cells induces EMT and promotes a metastatic phenotype.

P06.05 Eva Boysen CLINICAL CHARACTERISTICS AND SURVIVAL OF EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) MUTATED NON-SMALL CELL LUNG CANCER (NSCLC) (STAGE I-IV) IN A DANISH COHORT DIAGNOSED IN 2010-2017

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Background: In a Caucasian patient population, approximately 10% of patients with NSCLC will harbour an EGFR mutation. This patient group is of specific interest because presence of EGFR mutations enables targeted therapies that are more efficient and less toxic than traditional chemotherapy. In an Asian population, the frequency of EGFR mutations has been reported to be as high as 64%. Thus, most research on this patient group is conducted in Asia. The objective of this study was to describe characteristics, treatment and survival of this specific patient group in the Central Denmark Region.

Methods and materials: All patients (n=255) with EGFR mutated NSCLC diagnosed at the Department of Histopathology at Aarhus University Hospital from 1 January 2010 to 31 July 2017, regardless of disease stage, were identified. Pathology analysis of the Therascreen EGFR RGQ PCR v2 Assay, which detects 29 of the most commonly known EGFR mutations, was used. Clinical data was extracted from the Aarhus Lung Cancer Database. Data cutoff was set to 20 October 2017. Retrospective analyses for clinical characteristics, treatment response and survival will be performed.

Results: Frequency distribution of the different subtypes of EGFR mutations were roughly as expected with del19 and L858R as the 83% of the patients (exp. 80-90%). A surprisingly high number of patients (15%) harboured two mutations simultaneously.

Analyses and calculations on treatment and survival were not yet completed at the time of abstract deadline.

P06.06 Marianne Agerlund Petersen EXAMINING THE LEUKEMIC STEM CELL COMPARTMENT IN CHILDHOOD AML
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Acute myeloid leukemia (AML) is a rapidly developing and highly aggressive cancer. The majority of childhood AML patients achieve complete remission, but relapse is still seen in 1/3 of the patients. In these cases, the prognosis is poor. Conceptually, AML is propagated by leukemic stem cells (LSC) that share properties with normal hematopoietic stem cells, such as self-renewal and quiescence, the latter related to chemo resistance. Consequently, persistent LSC can induce relapse disease. In adults, LSC have been characterized and isolated using flow cytometry, and the proportion of LSC at diagnosis and after therapy is linked to inferior outcome. Data on this in childhood AML is sparse.

We will perform extensive immunophenotypic profiling and cell sorting on blood and bone marrow samples for in-depth analyses using cell culturing

for functional assays and examination of the genetic aberrations using molecular and cytogenetic analyses for profound investigation of the LSC subset in paediatric AML. When relevant, evaluation will be conducted on both diagnostic and relapse samples. Data will be correlated to clinical data. Translating detailed knowledge about the LSC compartment is essential in understanding AML biology, developing targeted therapies and hopefully obtaining improved prognosis of childhood AML

P06.07 Pernille
Byrialsen
Elming

COMBINING HYPERTHERMIA AND CHECKPOINT INHIBITORS: A METHOD OF INCREASING TUMOUR IMMUNOGENICITY?

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Purpose: Checkpoint inhibitors (CIs) affect a small percentage of patients. Methods to increase efficacy are needed. We are currently doing experiments with the combination of CIs and heat treatment. The CI of our interest is the anti-CTLA-4.

Methods: CDF1 male mice were inoculated on the right rear foot with a C3H mammary carcinoma. When tumour size was 200 mm³, treatments were performed. These included control mice, heat (42.5°C for 1 hour) on day 0, injection with anti-CTLA-4 (10 mg/kg i.p.) on day 1, days 1 and 3, or days 1-4, or the combination of heat with anti-CTLA-4. Tumour size was measured daily. Endpoint was the time to reach five times treatment volume (TGT5). Results are listed as Mean (\pm SE). One-way ANOVA comparison of group means was performed, and a $P < 0.05$ was considered significant.

Results: The TGT5 for the control group was 6.6 days (+ 0.2). For the groups treated with anti-CTLA-4 on day 1, days 1 and 3, or days 1-4, the TGT5 was 5.8 days (+ 0.4), 5.8 days (+ 0.4) and 6.8 days (+0.3), respectively. None of these were significantly different from controls. In the heat treated group, the TGT5 was significantly increased to 11.1 days (+ 0.9). When combined with the anti-CTLA-4, this value was increased to 11.6 days (+ 1.2) for treatment on day 1, 12.9 days (+ 2.7) for days 1 and 3, and 15.4 days (+ 0.8) for days 1-4. Thus, when heat and anti-CTLA-4 on days 1-4 were combined, we saw a significant increase in treatment days ($p=0.004$). One mouse even showed tumour control.

Conclusion: The C3H mammary carcinoma is a non-immunogenic tumour. However, when treated with heat, the tumour becomes CI sensitive to anti-CTLA-4 administered on days 1-4.

P06.08 Lene Haldbo-
Classen

COGNITIVE FUNCTION AFTER RADIATION THERAPY FOR BRAIN TUMOUR

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Aim: To assess the cognitive function in patients with a primary brain tumour treated with radiation therapy (RT) and generate radio-sensitivity and volume effect parameters for the development of cognitive dysfunction.

Background: RT to brain tumours causes cognitive dysfunction. The extent of RT induced changes in cognitive function and radio-sensitivity of the brain is unknown. RT with protons instead of photons spares the healthy brain tissue more and is believed to reduce the risk of cognitive dysfunction. There is modest knowledge on which parts of the brain we need to spare to prevent cognitive dysfunction.

Methods: The project contains two studies: Study A is a cross-sectional study assessing cognitive function in patients with brain tumours who have previously been treated with RT compared to a similar non-RT group. 104 patients with specified brain tumours treated at Aarhus University Hospital will be included. Study B is a longitudinal nationwide study including 60 brain tumour patients from the four neuro-oncology centres in Denmark. In both studies, the patients answer questionnaires and have their cognitive function tested. The correlation between cognitive scores and RT dose-volume parameters to specific areas in the brain will be tested.

Results: 94 patients have been tested in study A and 37 in study B. The analysis is ongoing.

Perspective: This study will elucidate the dose-response relationship in radiation-induced damage to substructures of the brain, such as hippocampus, thalamus, temporal and frontal lobes. This will allow the clinician to prioritize these structures in planning of proton radiotherapy.

P06.09 Simon Skouboe

REAL-TIME DOSE RECONSTRUCTION FOR MOVING TUMOURS DURING LIVER RADIOTHERAPY

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Background: Dose reconstruction, i.e. calculating the delivered dose of radiotherapy treatment for cancer, is important to understand the effects of tumor motion on the dose distribution.

Methods: Treatment delivery parameters and the tumor position are streamed to our in-house developed software, which calculates the dose in real-time. The treatments are simulated offline, and the doses calculated 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. This is also done in the clinical treatment planning system (TPS).

The motion-induced reduction (relative to the plan) in the dose to 95% of the tumor volume, ΔD_{95} , is found with and without gating. The same is done in

the TPS, and the results are compared. Our system does not yet use CT heterogeneities, so another set of calculations were made in the TPS assuming water density, matching our system's assumption.

Results: Over a total of 24 motion-including dose reconstructions, the dose is reconstructed in real-time with a root-mean-square error for $\Delta D95$ of 0.6%-points (water) and 1.2%-points (CT) when compared to the slow and cumbersome calculations performed in the TPS.

Perspectives: The developed software shows promising results, allowing immediate evaluation of radiotherapy treatment quality. It could be used to trigger more elaborate dose analysis and plan adaptation in case of large motion-induced dose degradation, with minimally added workload to the clinic. This may lead to a higher accuracy of the treatment, resulting in a higher cure rate of patients with fewer side effects.

P06.10 Sarah Østrup
Jensen CURING COLORECTAL CANCER WITH EARLY DETECTION: BLOOD-BASED BIOMARKERS FOR IMPROVED SCREENING

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Background: The survival of colorectal cancer (CRC) patients is much higher for patients diagnosed with early stage than late stage disease. Therefore, early detection is vital. CRC screening using a fecal occult blood test (FOBT) is currently implemented in Denmark and has proven efficient for early detection and for reducing CRC mortality. However, the patient compliance of the FOBT test is low, and the sensitivity is limited because many bowel tumors bleed only intermittently. Consequently, many cancers in the screening population go undetected.

Objective: To improve the performance of CRC screening, this study aims to develop and validate novel blood-based biomarker assays with high patient compliance, sensitivity and specificity.

Methods and materials: We apply a genome-wide biomarker discovery strategy to identify CRC-specific DNA methylation biomarkers and use digital droplet PCR for highly sensitive biomarker detection.

Results: We have identified candidate hypermethylation biomarkers discriminating CRCs from controls and verified these in tissue and blood. The biomarkers were evaluated in plasma samples from 114 CRC patients and 86 colonoscopy-confirmed healthy controls. Combined, three biomarkers resulted in a sensitivity of 89% and a specificity of 99%. We are currently performing prospective validation of those in a nested cohort of 1000 samples from the Danish CRC screening program, thereby mimicking real life clinical application.

Conclusion: Our systematic biomarker discovery and validation study resulted in a three-gene DNA methylation panel. In 200 clinical plasma samples, it showed superior performance compared to the currently used FOBT test.

P07.01 Julie Jacobsen TENDON-RELATED ABNORMALITIES IDENTIFIED WITH ULTRASOUND ARE COMMON IN SYMPTOMATIC HIP DYSPLASIA

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Introduction: The primary aim was to report the prevalence of tendon-related abnormalities identified by ultrasound in 100 patients with symptomatic hip dysplasia. The secondary aim was to investigate correlations between tendon-related abnormalities identified with ultrasound and muscle-tendon-related pain identified clinically.

Materials and methods: One hundred patients (17 men) with a mean age of 29 ±9 years were included. The prevalence of tendon-related abnormalities was identified with a standardized ultrasound examination. Correlations between tendon-related abnormalities identified with ultrasound and muscle-tendon-related pain identified clinically were tested with spearman's rank correlation coefficient.

Results: Iliopsoas-, adductor- and abductor-related abnormalities had the highest prevalence (iliopsoas: 50% (95% CI: 40; 60), adductor longus: 31% (95%: 22; 40) and gluteus medius/minimus: 27% (18; 36)). Significant correlations between ultrasound findings and muscle-tendon-related pain were found for the iliopsoas tendon (Rho=0.24 and p=0.02) and the gluteus medius/minimus tendons (Rho=0.35 and p=0.0004).

Conclusions: Tendon-related abnormalities in the hip and groin region are common in patients with symptomatic hip dysplasia, and the ultrasound findings of the iliopsoas-related and gluteus medius/minimus tendons are weakly to moderately correlated to muscle-tendon-related pain in these structures. Both the iliopsoas and the gluteus medius/minimus have a pronounced stabilizing role in the dysplastic hip joint, and the common tendon-related abnormalities found in these patients may be caused by overuse injury or degenerative changes in the tendon tissue.

P07.02 Eva Forsom ANTIPSYCHOTIC MEDICATION AND THE DEVELOPMENT OF OSTEOPOROSIS IN PATIENTS WITH OR WITHOUT SCHIZOPHRENIA

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Background: Patients with schizophrenia have a higher mortality and morbidity compared to the background population and have been shown to have a higher risk of osteoporosis. Some antipsychotics have been linked

to decreased bone mineral density (BMD) and an increased risk of developing osteoporosis.

Aim: This project aims to investigate the possible negative effect anti-psychotic treatment on bone density, structure, and remodelling parameters among patients with or without schizophrenia. Further, the relative usefulness of different types of bone health indicators will be investigated through an examination of the overall relationship between BMD, structural and remodeling parameters, and vertebral compression.

Methods: The material will consist of QCT scans, bone biopsies from L2 and crista iliaca, and venous blood from approximately 320 autopsied individuals diagnosed with schizophrenia and/or positive toxicological analysis for antipsychotic medication. The blood will be tested for prolactin. The biopsies will be embedded in methylmetacrylate before undergoing micro-CT-scanning and histomorphometric analysis. The QCT scans will be used to calculate BMD as well as vertebral compression. Age- and sex-matched controls will be used for BMD and vertebral compression.

Perspectives: A better understanding of the effect of antipsychotic medication on bone is important as it could enable future researchers to develop better medicine and/or the use of osteoporosis prophylaxis when starting antipsychotic treatment. The study will also contribute to the general knowledge of the mechanisms of osteoporosis and the relative usefulness of different bone health indicators.

P07.03 Sebastian Mosegaard

IDENTIFICATION OF OUTCOME PREDICTORS FOR TREATMENT OF TRAPEZIOMETACARPAL OSTEOARTHRITIS WITH A TOTAL JOINT ARTHROPLASTY

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Purpose: The purpose of this study was to identify outcome predictors of no clinically important improvement following treatment of trapeziometacarpal osteoarthritis with a total joint replacement.

Hypothesis: Minor preoperative disability (VAS, DASH, grip strength) results in small postoperative improvement.

Methods: We included 286 patients (224 women, 62 men) undergoing total joint replacement of the trapeziometacarpal joint with a mean age of 58.8 years (range: 41-80) in a prospective study. We collected data (DASH score, grip strength and VAS at activity and rest) preoperatively and 12 months postoperatively.

Results: We found a statistically significant improvement in pre- and post-operative measurements of DASH (26.11, $p < 0.001$), VAS at rest (2.89 cm, $p < 0.001$), VAS at activity (5.46 cm, $p < 0.001$) and grip strength (5.42 kg, $p < 0.001$). When using DASH as outcome, there was no predictive effect of preoperative VAS rest/activity, grip strength, age and gender. Using grip strength as outcome, there was no predictive effect of preoperative VAS at rest/activity and DASH. Using VAS at activity as outcome, there was no predictive effect of preoperative VAS at rest and age. Using VAS at rest as

outcome, there was no predictive effect of preoperative VAS at activity, DASH and grip.

Conclusion: Low preoperative disability increases the risk of low postoperative improvement. Increased risk of low postoperative improvement in VAS at rest/activity and grip strength was seen in female patients. Higher age increases the risk of low postoperative improvement in VAS at rest and grip strength. We were unable to identify one isolated predictor for all outcome measures.

P07.04 Anders
Kristensen

THE EFFECT OF AN INCREASED CURVATURE OF THE FORCE-VELOCITY RELATIONSHIP ON POWER IN ISOLATED RAT SOLEUS AND EDL MUSCLES

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Exercise performance is determined by the ability of the skeletal muscles to generate mechanical power. This ability is determined by the muscular force-velocity curve, which relies on three key parameters: 1) Maximal isometric force (F_{max}), 2) Maximum contraction velocity (V_{max}) and 3) Curvature of the force-velocity curve. During fatigue, F_{max} and V_{max} are depressed with a larger rate of fatigue in fast than in slow muscles. However, it has not been studied how curvature changes during fatigue in different muscle types. Therefore, we investigated the development of curvature during fatigue and determined the contribution of curvature change to the loss of power in fast and slow twitch muscles.

Isolated rat soleus (slow twitch) and EDL (fast twitch) muscles were incubated in Krebs-Ringer buffer and stimulated electrically at 60 Hz (soleus) and 150 Hz (EDL) with a series of dynamic contractions leading to fatigue. Force-velocity curves were obtained by fitting data on force and shortening velocity to the Hill equation. Curvature was determined as the ratio a/F (inversely related to curvature).

During fatigue, maximal power decreased by $58 \pm 5\%$ (soleus) and $69 \pm 4\%$ (EDL) compared to initial values in unfatigued muscles. The curvature increased in both muscle types as judged from the decrease in a/F by $81 \pm 20\%$ (soleus) and by $31 \pm 12\%$ (EDL). The increased curvature contributed significantly more to the loss of maximal power in soleus muscles compared to EDL ($53 \pm 13\%$ and $18 \pm 8\%$, respectively; $P = <0.001$).

In conclusion, increased curvature of the force-velocity relationship is a substantial contributor to loss of power during fatigue, particularly in slow twitch muscles.

P07.05 Ahmed Abdul- DEPOSITION OF ALLOGENIC AND AUTOLOGOUS CARTILAGE IN A PHYSEAL
Hussein Abood DEFECT SUGGESTS SIMILAR PHYSEAL ACTIVITY - AN EXPERIMENTAL
PORCINE MODEL

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Introduction: Bone bridges (BBs) can occur as a result of physal injury, which can lead to partial growth arrest and bone deformities. The current treatments have proven ineffective.

Methods: Eleven immature pigs were included into two groups: A (n=5) and B (n=6). Standardized cylindrical drilling defects were created in both hind legs of all animals mimicking a defect after resection of a physal BB.

In group A, each animal was randomized for treatment of the physal defect with autologous cartilage (AuC) chips and fibrin glue (FG) in one leg and FG alone in the contralateral leg. In group B, each animal was randomized for treatment with allogenic cartilage (AIC) chips in FG and platelet-rich-plasma (PRP) in one leg and FG with PRP in the contralateral leg.

The AuC was harvested perioperatively from a non-weight bearing area of the distal femoral joint cartilage in the same leg in which it was deposited. PRP was prepared using a blood sample and a commercial PRP kit (GPS®III, ZimmerBiomet). AIC was harvested prior to intervention.

All animals were housed for 14 weeks before undergoing MRI with water content (WC) assessment. A mean defect ratio (DR) was defined as the ratio between WC of defect and WC of the whole physis.

Results: No BBs were observed in defects treated with AIC or AuC. One BB occurred in both control groups. In group A, DR=1.50 was for the defects filled with AuC and DR=1.40 in the control defects. In Group B, DR=1.05 for the defects treated with AIC and DR=0.99 in the control group.

Conclusion: The addition of AuC or AIC may be used in preventing a BB from re-occurring after surgical resection. Water Content assessment indicates continuous physal activity.

P07.06 Janni
 Kjærsgaard
 Thillemann

BONE MODEL PRECISION IN DYNAMIC RSA ON THE ELBOW AND DISTAL FOREARM

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Background: Dynamic radiostereometric (dRSA) analysis can be used to quantitatively measure changes in the three-dimensional in-vivo movements of bones. However, analysis of the radius and ulna bones in both the elbow and forearm is challenging due to the long cylindrical shape. Using digitally reconstructed radiograph (DRR) based RSA, the position and orientation of the bones can be determined without markers.

Aim of Study: To validate the precision of DRR based RSA compared to marker-based analysis.

Materials and methods: Custom motorized fixtures to perform clinically relevant wrist (11 arms) and elbow (8 arms) motions were made. Subject specific bone models were created from CT, and tantalum markers were inserted. Model-based RSA (RSA core) was used to calibrate the first frame

and initialize the bones. The complete recording was subsequently automatically analyzed by custom developed AutoRSA software. Marker analysis was independently performed in 3 images per dynamic recording. Precision was evaluated as systematic bias (mean difference) and random error ($1.96 \times SD$) for translations and rotations.

Results: In the elbow, the mean systematic bias for translations (mm) was 0.21). No systematic bias was found for rotations. Precision was ≤ 0.55 mm and $\leq 1^\circ$. In the distal forearm, the mean systematic bias (mm/ $^\circ$) was 0.17) and 0.26). Precision was ≤ 0.18 mm and $\leq 1^\circ$.

Conclusions: DRR-based RSA analysis using bone models provides a good precision for investigation of kinematics in the elbow and forearm. The method can be used for automated analysis of markerless dRSA studies for both pre-operative diagnostics and to evaluate kinematics after ligament or implant surgery.

P07.07 Jakob Bie
Granild-
Jensen

ZOLEDRONATE AGAINST FRACTURES IN CHILDREN WITH CEREBRAL PALSY

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Introduction: Low bone mineral density is highly prevalent in non-ambulant cerebral palsy (CP) and is associated with a high risk of fractures. In most cases, these fractures occur with no or minimal trauma. We hypothesise that zoledronate treatment significantly increases bone mineral density after 1 year compared with placebo.

Method: We plan to include 80 children aged 5 to 17 years with non-ambulant CP. Each child is randomized to 2 double-blinded treatments of i.v. zoledronate or placebo at a 6-month interval. The primary endpoint is the change in bone mineral density after 12 months as measured by Dual-energy X-ray Absorptiometry (DXA).

Results: The first child was included in October 2017. Aalborg and Randers sites are recruiting. Kolding, Viborg, Herning and Aarhus plan to start recruiting. Inclusion will continue until 2019. Results are expected in 2020.

Conclusion: The results may change the fracture prevention strategy and improve the quality of life in children with non-ambulant CP. Further, health care spending on fracture management may be reduced.

P07.08 Simon Skov

COMPARING 3D CORRECTION AND SPINAL GROWTH OF MAGNETICALLY CONTROLLED GROWTH-ENGINE (MCGR) DRIVEN DISTRACTION TO OPEN INTERVAL DISTRACTION OF TWO DOUBLE GROWING-ROD SYSTEMS WITH APICAL CONTROL IN EOS

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Background: MCGR use in severe early-onset scoliosis (EOS) treatment has increased worldwide. Our aim was to compare non-surgical 3-month interval MCGR lengthening to 6-month interval intraoperative manual lengthening in EOS; focusing on spinal growth and 3D correction.

Methods: Two cohorts of each 18 children were analyzed. The MCGR hybrid cohort, median age 8.9 (6.4-15.8), received a new MCGR hybrid principle, using a single MCGR to drive concave distraction combined with an apical control passive sliding rod construct on the convexity, median follow-up 1.6 years (0.9-2.1). The second cohort, median age 10.5 (4.5-14.8), received the similar principle CB system with conventional surgical distractions, median follow-up 1.5 years (0.9-1.9).

Results: Frontal Cobb angle improved in both groups; from mean 64° to 31° after MCGR hybrid, ($p < 0.01$), and from mean 77° to 38° after conventional technique, ($p < 0.01$). This 51% initial correction after MCGR hybrid vs. 49% after conventional technique was maintained in both groups. The mean rotation of the apical vertebra improved significantly in both groups, but was partially lost. There was a significant decrease in thoracic kyphosis from 27° to 20° after MCGR hybrid and from 33° to 17° after conventional technique, and largely unchanged lordosis.

T1-S1 spine growth rate was 11 mm/year in the MCGR hybrid group vs. 7mm/year in the conventional group, ($p = n.s.$)

Conclusion: We found significant early 3D scoliosis correction by double-rod systems with apical control. Spinal growth seemed to be superior following short interval MCGR lengthening. This may underline the negative effect of posterior tethering following long interval distraction.

P07.09 Peter Sieljacks COMPARATIVE EFFECTS OF LOW-LOAD BLOOD FLOW RESTRICTED EXERCISE AND HIGH-LOAD RESISTANCE EXERCISE ON MUSCLE ACCRETION AND MUSCLE STEM CELL ADAPTATIONS

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Introduction: Low-load blood flow restricted resistance exercise (BFRRE) has been shown to stimulate muscle accretion and strength gains using training loads corresponding to as low as 20% of maximal strength. Intriguingly, previous results have indicated that muscle fiber hypertrophy and proliferation of muscle stem cells (MSC) is stimulated to a greater extent with BFRRE than usually observed with high-load resistance exercise (HLRE). Accordingly, BFRRE may provide a mechanically gentle, yet efficient, training alternative to HLRE for muscle rehabilitation in patients with various musculoskeletal diseases. However, no study has compared muscle cellular adaptations to BFRRE and HLRE. Thus, the primary aim of the present study was to conduct a comparative investigation on muscle fiber, muscle stem cell and muscle function responses to BFRRE vs. HLRE.

Methods: 34 healthy, sedentary males were randomized to 6 weeks of either BFRRE, HLRE or non-exercise control. Tests of muscle function and collection of muscle biopsies were performed pre- and post-training. D₂O (stable isotope) was orally administered throughout the study to assess long-term myofibrillar fractional protein synthesis rate.

Preliminary results and perspectives: Preliminary results suggest that both BFRRE and HLRE are able to increase muscle accretion to a similar extent compared to control. Furthermore, muscle strength gains seem to be more pronounced with HLRE (~12%) compared to BFRRE (~7%). Analysis of muscle fiber cross-sectional area and number of MSCs still awaits, but our results indicate that BFRRE may be an efficient and gentle training alternative to HLRE.

P07.10 Pelle Emil Hanberg

PHARMACOKINETICS OF SINGLE-DOSE CEFUROXIME IN PORCINE INTERVERTEBRAL DISC AND VERTEBRAL CANCELLOUS BONE DETERMINED BY MICRODIALYSIS

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Aim: Spondylodiscitis is associated with prolonged antimicrobial therapy and high relapse rates. Nevertheless, tissue pharmacokinetic studies of relevant antimicrobials in both prophylactic and therapeutic situations are still sparse. Previous approaches based on bone biopsy and discectomy exhibit important methodological limitations. The objective of this study was, therefore, to assess intervertebral disc (IVD), vertebral bone, subcutaneous tissue (SCT) and plasma pharmacokinetics of cefuroxime after single-dose administration by use of microdialysis (MD) in a porcine model.

Method: Ten pigs were assigned to receive 1.5 g of cefuroxime. Measurements of cefuroxime were obtained from plasma and the respective tissues for 8 hours thereafter. Cefuroxime concentration was determined using UHPLC.

Results: For both the IVD and the vertebral bone, the area under the concentration curve was significantly lower than that of plasma. Tissue penetration of cefuroxime was incomplete for the IVD, whereas for vertebral bone and SCT it was not. Furthermore, the penetration of cefuroxime from plasma to IVD was delayed. Additionally, a prolonged elimination rate of cefuroxime in the IVD was found. The maximal concentration and the elimination of cefuroxime were reduced in IVD compared to both SCT and vertebral bone. Regarding the time with concentrations above the minimal inhibitory concentration (T>MIC), this was significantly higher in IVD than in SCT, vertebral bone and plasma for MICs up to 6 µg/ml.

Conclusions: Penetration of cefuroxime from plasma to IVD was found to be incomplete and delayed. However, due to a prolonged elimination, the best results regarding T>MIC were found in IVD.

- P08.01 Ellen Kure Fischer A MOLECULAR PATHWAY ANALYSIS STRESSES THE ROLE OF INFLAMMATION AND OXIDATIVE STRESS TOWARDS COGNITION IN SCHIZOPHRENIA
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- Background: Cognitive processes have a genetic component and are impaired in Schizophrenia (SKZ). The exact nature of such impairment escapes definition. The aim of the present contribution was to identify molecular pathways enriched with mutations (SNPs) associated with cognitive performance during antipsychotic treatment.
- Method: 765 individuals from the CATIE study, males = 559, mean age 40.93 ± 11.03 were included. Working memory and the verbal memory were the evaluated outcomes. A mixed regression model for repeated measures served in R for clinical and molecular pathway analysis. The analysis of quality was conducted under the following criteria: minor allele frequency [0.01, genotype call rate [95%, missing data frequency \5%, Hardy-Weimberg equilibrium threshold [0.0001. The inflation factor was controlled by lambda values. Input for the pathway analysis was SNPs at a p level \0.05 of association genome-wide. Gender, age, education and the duration of the disease were the clinical and sociodemographic variables associated with the cognitive performance. 4,268,977 SNPs were available after imputation and quality analysis.
- Results: Pathways related to inflammation and oxidation were most strongly associated with verbal memory and working memory at a conservative adjusted p value \ 0.01. We report that inflammation, and in particular the pathway associated with arachidonic acid, was enriched in mutations associated with poorer performance at the verbal memory and working memory tasks in SKZ patients.
- P08.02 Karen Hansen Kallesøe GROUP-BASED ACCEPTANCE AND COMMITMENT THERAPY (ACT) FOR SEVERE FUNCTIONAL SOMATIC SYNDROMES IN ADOLESCENTS - UNCONTROLLED PILOT STUDY
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- Background: Approximately 5-10% of adolescents report recurrent functional somatic symptoms. Some experience persistent symptoms and may receive functional somatic syndromes (FSS) diagnoses, characterised by severe disability and reduced quality of life. Despite a high need for care, there is lack of empirically supported treatments for adolescents.
- Objectives: To examine the feasibility and change after treatment of group based ACT for adolescents with severe FSS.

Method: Twenty-one patients attended a manualized group-based ACT programme (30 hrs) specifically developed for adolescents (15-19 years) with severe FSS. Close relatives participated in a workshop to increase their support to the patient. Change in health status was evaluated by self-reported physical health (SF-36 aggregate score; primary outcome). Feasibility was assessed by questionnaires evaluating the patient's and the relatives' opinions of the treatment.

Results: Nineteen patients (90.5 %) completed the treatment. The patients' physical health improved considerably from group start to 3 months after treatment, with a mean difference of 5.5 points (95 % CI 2.8 - 8.2). All patients would recommend the treatment to a friend with similar problems. Close relatives rated it valuable to meet other relatives to adolescents with FSS.

Conclusion: The ACT-based treatment was associated with clinically relevant improvement in physical health. An ongoing RCT will evaluate treatment effects by self-reported outcome measures and objective markers for physiological stress and physical activity. If the treatment is effective, this may result in significant improvement in the well-being and overall quality of life of these young patients.

P08.03 Malene Thygesen

EXPOSURE TO AIR POLLUTION IN EARLY CHILDHOOD AND THE ASSOCIATION WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER - A NATIONWIDE COHORT STUDY

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Background: Exposure to air pollution in early life has been linked to cognitive deficits and adverse neurodevelopmental effects. However, studies examining associations between air pollution and attention-deficit hyperactivity disorder (ADHD) have had conflicting findings. Hence, further investigation of this association is needed.

Methods: All individuals born in Denmark in 1992-2007 (n= 809 654) were followed for the development of ADHD during 1997-2012. Data on cumulative exposure of NO₂ and PM_{2.5} within the first 5 years of life was linked to the residential address of each cohort member. We estimated incidence rate ratio (IRR) for ADHD, according to an increase in exposure, while adjusting for age, calendar year, sex, obstetric factors, parental education and income, and family history of psychiatric disorders.

Results: Exposure to air pollution within the first 5 years of life was associated with ADHD, with an IRR of 1.38 (95% CI: 1.35-1.42) for increases of 10 µg/m³ in NO₂ and an IRR of 1.51 (95% CI: 1.40-1.62) for increases of 5 µg/m³ in PM_{2.5}. Estimates were robust across all geographical regions. However, when adjusted mutually for the other air pollutant, the IRRs for ADHD were 1.35

(95% CI: 1.31-1.39) and 1.07 (95% CI: 0.98-1.16) for exposure to NO₂ and PM_{2.5}, respectively.

Conclusion: Exposure to NO₂ early in life was associated with a 35% higher risk of developing ADHD. This result supports the hypothesis that, although ADHD is a highly heritable disorder, the etiology of ADHD also includes environmental risk factors. Future studies should examine how interactions between genetic and environmental risk factors affect susceptibility.

P08.04 Pil Lindgreen THE SELF-MONITORING APP RECOVERY RECORD FOR EATING DISORDER TREATMENT: AN INTERPRETIVE DESCRIPTION OF THE INTERDISCIPLINARY CLINICAL PERSPECTIVE

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Introduction: The smartphone app Recovery Record is a self-monitoring tool for individuals recovering from eating disorders. As an alternative to traditional pen-and-paper meal diaries, the app allows for in-app patient-clinician linkage enabling clinicians to access patient app data anytime. The aim of our study was to explore the interdisciplinary clinical perspective on Recovery Record and its impact on eating disorder treatment.

Method: 23 clinicians from a Danish eating disorder treatment facility participated in interviews and an additional eight in field studies. Data were collected and analyzed concurrently by applying the inductive methodology of Interpretive Description.

Results: Results will be presented at the PhD Day.

Discussion: Recovery Record induced new and affected pre-existing treatment and work conditions for clinicians. They were preoccupied with challenges associated with the app, e.g. an added workload and potential harm to the patient-clinician collaboration. Thus, prior to adopting the app, we encourage clinicians and managements to discuss the objectives, advantages and disadvantages of adopting the app and outline specific guidelines for patient and clinician app usage.

P08.05 Anita Tønder Nielsen RISK OF DIABETIC COMPLICATIONS AND SUBSEQUENT MORTALITY IN INDIVIDUALS WITH SCHIZOPHRENIA AND DIABETES MELLITUS: A POPULATION-BASED REGISTER STUDY

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Background: Schizophrenia constitutes a high risk of morbidity and mortality from physical illness. Individuals with comorbid schizophrenia and diabetes mellitus have been found to have a three- to four-fold higher risk of death than the general population, which may be explained by a higher rate of diabetic complications. We aim to study incidence of diabetic complications and subsequent mortality in hospitalized individuals with schizophrenia compared to hospitalized individuals with diabetes mellitus only.

Methods: The entire Danish population will be followed in 1994-2016 using nationwide population-based registries. Incidence of diabetic complications and subsequent mortality will be compared in hospitalized individuals with and without schizophrenia. Cox regression will be used to estimate incidence rate ratios (IRR) and mortality rate ratios (MRR).

Perspectives: We expect our results to show that hospitalized individuals with comorbid schizophrenia and diabetes mellitus will have higher rates of diabetic complications and subsequent mortality compared to individuals with diabetes mellitus only. These results may indicate an increased need for improved somatic care of individuals with schizophrenia if the burden of diabetes mellitus morbidity and mortality should be reduced.

P08.06 Sanne Jensen CHILDREN AND ADOLESCENTS WITH OBSESSIVE-COMPULSIVE DISORDER: PREDICTORS OF LONG-TERM TREATMENT OUTCOME

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Background: Little is known about predictors of long-term treatment outcome in pediatric OCD. Several previous studies are limited by small and heterogeneous samples, non-systematic assessment strategies, and retrospective designs. However, several factors seem to indicate an increased persistence of OCD. These include: earlier age of OCD onset, longer duration of OCD, and in-patient status. Larger, prospective studies are needed to replicate these findings.

Objective: To identify long-term outcome predictors in pediatric OCD according to symptom severity and functional impairment up to three years after treatment.

Methods: 269 children and adolescents aged 7-17 with OCD from Denmark, Norway, and Sweden participated in the Nordic Long-term OCD Treatment Study (NordLOTS). Treatment was provided using a stepped-care design: Step 1 was an open, uncontrolled trial with all participants receiving cognitive-behavioral therapy (CBT). Non-respondents were randomized in Step 2 to receive either further CBT or Sertraline. Step 3 consisted of Aripiprazole augmentation to Sertraline. Thorough assessments were performed at baseline, during treatment, at the end of treatment, and 6, 12, 24, and 36 months after Step 1.

Results: Initial data are undergoing statistical analyses.

Perspectives: Predictors of long-term treatment outcome will aid the early detection of patients who are vulnerable to relapse, and this will highlight essential focus areas in the treatment.

P08.07 Janne
Tidsebak
Larsen

EARLY LIFE RISK FACTORS FOR EATING DISORDERS

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Background: Eating disorders are severe psychiatric illnesses associated with increased mortality and other adverse outcomes. It is crucial to identify those at high risk of developing an eating disorder in order to improve early detection and to identify possible differences between the different types of eating disorders.

Aim: To investigate possible early life risk factors for later onset of eating disorders.

Methods: Using nationwide registers, we performed cohort studies including all individuals born in Denmark in 1989 or later. We evaluated exposure to prenatal and perinatal complications and to early childhood adversities before the age of 6 years. All individuals diagnosed with anorexia nervosa, bulimia nervosa, or eating disorder not otherwise specified (EDNOS) in a hospital were identified. Using survival analysis and comparing exposed and unexposed individuals, we calculated relative risks for being diagnosed with an eating disorder later in life.

Results: Exposure to early childhood adversities was associated with increased risks of bulimia and EDNOS but decreased risk of anorexia. All three eating disorders were significantly associated with exposure to few prenatal and perinatal complications.

Perspectives: Identification of early risk factors contributes to the understanding of the etiology of eating disorders and improves the possibilities for early detection and better and more personalized treatment. Anorexia seems to stand out, both among eating disorders and psychiatric disorders in general, as possibly having alternate risk pathways. Ultimately, a deeper comprehension of the causes of these disorders can lead to improved quality of life and fewer adverse outcomes.

P08.08 Andreas
Aalkjær
Danielsen

PREDICTING MECHANICAL RESTRAINT BY APPLYING DATA MINING TECHNIQUES ON ELECTRONIC MEDICAL RECORDS

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Background: Mechanical restraint (MR) is often used to counter severe aggressive behavior in patients admitted to psychiatric hospitals and is associated with many adverse outcomes. Early identification of risk factors associated with MR may enable targeted interventions to reduce the use of this procedure.

Objective: The objective of this ongoing study is to identify risk factors assessed within one hour of admission to predict MR.

Materials & methods: This is a retrospective cohort study based on data from the electronic medical records (midtEPJ) from Aarhus University Hospital, Risskov, and the Danish population registers. Patients with visits at AUH unrecorded in midtEPJ are excluded. The cohort will be randomly divided into a training and test dataset and using the training dataset, machine-learning methods will be applied to build a prediction model on data available one hour after admission. Structured data is transformed to categorical features. Features from clinical notes in natural language is constructed using unsupervised topic modeling. For classification, supervised statistical learners are trained. Results for the best performing learner is validated using the test set.

Results: We have identified 5007 adult patients who have been hospitalized. Within this cohort, a total of 189 patients experienced MR.

Conclusion: Early identification of patients at risk of MR will enable more targeted and intensified treatment programs to be initiated early during admission. The feature space could later be expanded using medication data, lab results and genetics to create models with unprecedented accuracy and speed in risk assignments.

P08.09 Pernille
Kølbæk

CLINICAL VALIDATION OF PANSS-6 SCHIZOPHRENIA SEVERITY RATINGS OBTAINED USING THE SIMPLIFIED NEGATIVE AND POSITIVE SYMPTOMS INTERVIEW (SNAPSI)

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Background: Schizophrenia is a severe mental disorder requiring multimodal treatment. Monitoring the severity of schizophrenia during treatment is essential to a successful outcome. The most widely used schizophrenia rating scale is the 30-item Positive And Negative Syndrome Scale (PANSS-30), which takes approximately an hour to administer. This is too long for routine clinical use. Recently, our group has extracted a 6-item scale (PANSS-6), which has shown promising psychometric properties. Also, our group produced a brief semi-structured interview, the Simplified Negative and Positive Symptoms Interview (SNAPSI), which can be used to collect information for PANSS-6 rating.

Hypotheses: PANSS-6 ratings obtained using the SNAPSI are clinically and psychometrically valid measures for the severity of schizophrenia and tap

into the core construct of the full PANSS. The inter-rater reliability for PANSS-6 ratings obtained using the SNAPSI is high.

Method: A total of 75 patients with a diagnosis of schizophrenia who are currently undergoing inpatient treatment will be recruited. The SNAPSI and the structured clinical interview for PANSS (SCI-PANSS) will be conducted by independent interviewers followed by independent PANSS-6 and PANSS-30 ratings at two time points: as soon after admission as possible and as close to discharge as possible. Statistical analyses: The degree to which PANSS-6 (rated via the SNAPSI) corresponds to PANSS-6 extracted from PANSS-30 (rated via the SCI-PANSS) will be tested by Spearman correlation analysis and the scalability of PANSS-6 by Mokken analysis. The interrater reliability will be assessed by calculation of the intra-class coefficient.

P08.10 Sara Højslev
Avlund AUTISM OVERLOOKED: CHARACTERISTICS OF CHILDREN WITH AN AUTISM SPECTRUM DISORDER DIAGNOSIS MISSED IN THE FIRST ASSESSMENT

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Background: Autism spectrum disorders (ASD) are pervasive developmental disorders, where symptoms usually present early in life. Yet, around 40% are diagnosed after the age of 6. Co-existing disorders may obscure autism symptoms, but despite suspicion in early childhood, it remains unknown why some children go unrecognized before school age. Studies examining how time affects diagnosis, phenotype and comorbidity are needed since early diagnosis and intervention are found to be important for the course and quality of life.

Objective: To characterize children who fail to meet the diagnostic criteria for an ASD diagnosis at first assessment in preschool age (≤ 7 years), but who meet diagnostic criteria at a later age (> 7 years), compared to children diagnosed at first assessment or who never meet the diagnostic criteria.

Methods: A total of 900 preschoolers suspected of ASD are included. All children were assessed at the Centre for Child and Adolescent Psychiatry, Aarhus University Hospital, in the period of 2000-2010. Data will be collected from medical records and national registers. Variables include age at diagnosis, gender, type of diagnosis, IQ, socioeconomic status, predisposition in the family and birth data. Data are analysed using appropriate regression methods.

Results: Data collection is ongoing.

Perspectives: The project is expected to enlarge our knowledge on factors important for missed diagnoses of ASD. The possibility of early diagnosis and intervention will increase, thereby improving the quality of life in children and adolescents with ASD. The study is expected to produce knowledge that may inform the clinic and help affected families and society in general.

P09.01 Marie-Louise Ladegaard Baun OVARIAN CANCER OUTCOME AND VARIATION IN REFERRAL RATES FOR TRANSVAGINAL ULTRASOUND EXAMINATION FROM GENERAL PRACTICE

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Background & aim: Ovarian cancer (OC) is the seventh most common cancer in women worldwide. As the disease is often diagnosed at a late stage, OC has a poor prognosis. In Denmark, 74% are diagnosed in FIGO stages III and IV with a 5-year survival of 30% and 15%, respectively, compared to 83% in FIGO stage I.

Knowledge is sparse about the consequences of variation in referral rates to transvaginal ultrasound (TVU) examination through general practice. We aim to investigate the association between referral rates to TVU examination in general practice and OC-related outcomes in Denmark.

Method: We conducted a national register-based ecological cohort study based on data collected in 2004-2014 and included women who were cancer-free, living in Denmark and aged ≥ 40 years. The analyses consisted of two steps. First, we ranked the women's general practices into four groups based on their annual TVU referral rate. Second, these groups were used as exposure for both OC stage distribution and complete resectability in the following years, and results were compared in the four groups.

Results: We hypothesize that higher propensity to TVU referral through general practice will lead to a more favorable OC stage distribution and lower OC tumour burden in patients. We found an almost three-fold higher referral rate among the group that referred the most compared to the group who referred the least. The study is ongoing, and detailed results will be presented.

Conclusions: Variation in the referral to TVU from general practice may have consequences for the practice populations. This study will provide an evidence base for the benefits of open access to TVU through general practice.

P09.02 Marzieh Katibeh IMPROVING EYE HEALTH AT THE PRIMARY HEALTH CARE LEVEL THROUGH MHEALTH

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Blindness is a global health issue, and 80% of causes are avoidable in less advantaged areas. This PhD project aims to establish a screening program for improving eye health.

First, through a participatory qualitative study, we identified the content and target group for this program. Then we developed an mHealth tool with 2 main components: a mobile application and a web-based software. The mobile application consisted of digital survey forms, integrated software for obtaining visual acuity (VA) and for optimizing retinal imaging, as well as a

management system. The primary health care workers collected population-based data in the field. After access to the internet, information was transmitted to a secure server and the customized web-based software.

The web-based software was used for data storage and management. Participants who had VA \leq 20/40 in either eye were automatically referred to an eye doctor. In addition, it was used as an online reading centre by retina specialists who made referral plans based on fundus evaluation. All participants who fulfilled the screening program got their screening result using an automated SMS system.

The sampling frame was an area with 4 counties (Varamin, Qarchak, Pishva, Pakdasht) in Iran. 30 clusters were randomly selected from the list of all urban and rural residential areas and assigned randomly to one of 3 arms: mHealth intervention, conventional intervention (paper-based forms, Snellen chart and fundus photography equipment), and control arm without any intervention.

We will describe/compare study outcomes, including eye care utilization, the efficacy of the interventions, acceptability and validity of the screening tests.

P09.03 Linda Aagaard Rasmussen ACTIVITY IN GENERAL PRACTICE PRECEDING A DIAGNOSIS OF CANCER RECURRENCE

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Introduction: The prevalence of cancer survivors increases rapidly. The post cancer follow-up programmes are under revision, and general practice will play a key role in the future cancer follow-up in Denmark. A central focus is early detection of cancer recurrence. To work out qualified follow-up programmes in general practice, we need more knowledge about the patient pathway for cancer recurrence.

Objective: To describe the activity in general practice in the year preceding a diagnosis of bladder cancer (BC) recurrence.

Methods: The study population was curatively treated BC patients, diagnosed in 2008-2014. Patients diagnosed with BC recurrence by October 2016 were matched 1:5 with BC survivors without recurrence. Activity in general practice one year preceding the diagnosis of cancer recurrence was estimated as number of contacts per month and number of urine dip-sticks per month, and compared to the activity in the matched population by incidence rate ratios (IRR).

Results: By October 2016, 303 of 1427 patients developed BC recurrence. IRR (95% confidence interval) for number of contacts in general practice per month increased from 1.4 (1.2-1.6) seven months before recurrence to 2.0 (1.8-2.3) one month before recurrence. Correspondingly, IRR for number of urine dip-sticks per month increased from 1.8 (1.1-3.1) to 3.3 (2.1-5.1).

Conclusion: Patients cured for BC who experience a recurrence have an increased activity in general practice from seven months before the diagnosis of the recurrence. Thus, general practice may play an important role in detection of cancer recurrence.

- P09.04 Tina Lützen PSYCHIATRIC MORBIDITY AND GP ATTENDANCE PRIOR TO HPV VACCINATION AND RISK OF REFERRAL TO HPV CENTRE
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- Background: The study aims to examine the association between psychiatric morbidity and general practitioner attendance prior to HPV vaccination and the risk of referral to an HPV centre due to suspected adverse events.
- Materials and methods: Register-based, matched case-control study. Cases were defined as women referred to an HPV centre in 2015 (n=1,496). Each case was matched with 5 controls on age, region and time of first vaccine registration. The total study population consisted of 8,976 women.
- Results: Overall, referred women above 18 years were more likely to have used psychiatric medication or to have been hospitalized due to a psychiatric disorder within five years prior to the first vaccine registration. Specifically, referred women were more likely to have used antipsychotics, antidepressants, ADHD medication or anxiolytics, and to have been hospitalized for affective disorders or anxiety, but not to have been hospitalized for schizoid, ADHD or eating disorders. In addition, they were more likely to have had talk therapy or a psychometric test performed prior to vaccination. Referred women of all ages had higher use of GP before vaccination. Population attributable fraction analyses indicated that psychiatric medication, hospitalization due to a psychiatric disorder and use of talk therapy or psychometric test explained 13%, 10%, 11% and 12% of the referrals, respectively. Results did not change substantially when adjusted for potential confounders.
- Conclusion: Women referred to HPV centres due to suspected adverse events after vaccination more often had preexisting psychiatric conditions, psychological symptoms or frequent GP attendance prior to vaccination.
- P09.05 Jose Omar Silverman Retana TRAJECTORIES OF OBESITY BY SPOUSAL DIABETES STATUS IN THE ENGLISH LONGITUDINAL STUDY OF AGEING
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- Background and aims: The likelihood of becoming obese is increased in people with an obese spouse; most likely due to assortative mating and their shared home and social environment. We aimed to examine whether the development of obesity trajectories with age was different for individuals with and without a spouse with diabetes.

Methods: We analyzed the English Longitudinal Study of Ageing (n=7,187 individuals, 51.2% men), including four follow-up assessments, 1998-2012. Our main exposure was having a spouse with diabetes; outcomes of interest were body mass index (BMI) and waist circumference (WC). We fitted age-related trajectories using mixed effects models stratified by sex and adjusted for spousal diabetes status, education, smoking, quadratic age and interaction terms between age and spousal diabetes status.

Results: At age 50 years, BMI levels were not different between individuals with and without a spouse with diabetes; across all groups, BMI increased with age until 70 years and then showed a slight decline. Men with a wife with diabetes experienced a steeper increase in BMI than men with a wife without diabetes. Women with a husband with diabetes had a similar BMI trajectory to women with a husband without diabetes; WC trajectories showed a similar shape by spousal diabetes status for men and women. Individuals with a spouse with diabetes had higher levels of WC throughout follow-up.

Conclusions: Middle-age spouses of individuals with diabetes may benefit from obesity assessment. Widening the scope of obesity prevention interventions by targeting the family network as well as couples could make more effective public health strategies to tackle the obesity epidemic.

P09.06 Kathrine Pape ACCURACY OF OFFSPRING-REPORTED PARENTAL SMOKING STATUS - THE
Madsen RHINESSA GENERATION STUDY

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Background: With increasing interest in exposure effects across generations, it is crucial to assess the validity of information given on behalf of others.

Aims: To compare adult offspring's report of their parents' smoking status with the parents' own report and examine predictors for discrepant answers.

Methods: We studied 7185 offspring (18-51 yrs) and one of their parents, n=5307 (27-67 yrs) participating in the Respiratory Health in Northern Europe, Spain and Australia (RHINESSA) generation study. Information about the parent's smoking status during offspring's childhood was obtained by questionnaires from parents and their offspring. We calculated sensitivity, specificity and Cohens Kappa [κ] for agreement using the parent's own report as the gold standard. We performed logistic regression to examine if offspring's sex, age, educational level, asthma status, or own smoking status as well as the parent's sex and amount of smoking during childhood predicted disagreement.

Results: The sensitivity for offspring's correct report of parent's smoking status during childhood was 0.82 (95% CI 0.81-0.84), specificity was 0.95 (95% CI 0.95-0.96), and a good agreement was seen, $\kappa=0.79$ (95% CI 0.78-0.80). Multivariate logistic regression analysis showed that offspring's age, amount of parents tobacco consumption and sex of the parents were predictors for discrepant answers. Offspring's own sex, asthma status, educational level or smoking status was not related to discrepant answers.

Conclusions: Offspring quite correctly report their parents' smoking status during the offspring's childhood and during pregnancy. In the absence of the parents' direct report, offspring's reports could be valuable.

P09.07 Tine Vrist Dam THE ANABOLIC EFFECT OF ENDOGENOUS AND EXOGENOUS ESTROGEN ON THE SKELETAL MUSCLES

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

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

Design & methods: The trial is designed as a randomized, controlled double-blinded intervention study, where 30 healthy postmenopausal women perform 12 weeks of resistance exercise. Half of them are randomized to transdermal estrogen administration (17 beta estradiol, 100 mg pr. 24 hour) during the training period. The other half will wear placebo patches. Primary endpoint: muscle cross sectional area (CSA) of quadriceps femoris, measured by MRI.

Secondary endpoints: CSA of specific fiber types by histology. Protein synthesis and mRNA levels in muscle and fat biopsies are measured by western blotting, and qPCR.

Perspectives: The novel results from the present study will help to elucidate the influence of estrogen on the degenerative changes in skeletal muscle,

which take place when women enter menopause. The new knowledge may be helpful in optimization of rehabilitation programs for elderly women.

P09.08 Lea Lykke
 Lauridsen

PREECLAMPSIA AND TIMING OF PUBERTAL DEVELOPMENT IN DAUGHTERS AND SONS

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Background: Preeclampsia is a critical pregnancy condition that affects 3-8% of all obstetric patients worldwide. Severe preeclampsia has been associated with low birth weight, which has been linked to increased risk of rapid postnatal weight gain, insulin resistance and hyperandrogenism in childhood. Few studies have investigated the potential association between preeclampsia and pubertal development in daughters and in sons, and the results from these are inconclusive. The aim of this large cohort study is to investigate whether preeclampsia is associated with timing of pubertal development in daughters and sons.

Materials and methods: We will use the Danish National Birth Cohort (DNBC), including additional follow-up of 15,822 of their children in the Puberty Cohort. These cohorts hold information on pregnancy-related factors collected through interviews during and after pregnancy, including preeclampsia and covariates, as well as detailed information on pubertal development collected biannually from the age of 11 years and onwards - until the child was fully sexually matured or 18 years of age. Further information on preeclampsia will be obtained from the Danish National Patient Register to ensure highest possible sensitivity of the preeclampsia diagnosis. We will analyze the data using a regression model for normally distributed, interval-censored data and adjust for potential confounders.

Results: Preliminary results will be presented at the PhD Day.

Conclusions: This study will expand our knowledge on the possible association between preeclampsia and timing of pubertal development in daughters and sons.

P09.09 Benedicte
 Marie Winther
 Johannsen

SELF-HARM IN WOMEN WITH SEVERE POSTPARTUM PSYCHIATRIC DISORDERS

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Objective: The postpartum period carries the highest risk of first onset of psychiatric disorders in women. Receiving a psychiatric diagnosis in general is a well-established risk factor of self-harm. However, to our knowledge, no previous study has described the incidence of self-harm in women with severe postpartum psychiatric disorders.

Methods: We conducted a population-based cohort study based on national Danish registers. A total of 1,076,163 Danish women born January 1st 1963 or later were included, with a maximum follow-up of 34 years. Severe postpartum psychiatric disorders were defined as a first inpatient or outpatient

contact to a psychiatric facility within 90 days after giving birth to the first child. Survival analyses were conducted (Cox regression), and the outcome of interest was any first hospital record of self-harm.

Results: Preliminary results showed that among 1,278 cases of severe postpartum psychiatric disorders 55 women had at least one episode of self-harm, providing a hazard ratio of 6.5 (95% CI: 5.0-8.5) when compared to mothers from the healthy background population.

Among the 55 cases of self-harm, a total of 16 episodes occurred within the first year after diagnosis and 5 women later completed suicide.

Conclusions: Women with severe postpartum psychiatric disorders are at increased risk of self-harm, and 9.0% of the women recorded in our data later committed suicide. These results highlight the necessity for treatment and prevention strategies in this group of vulnerable women.

P09.10 Maria Keilow SOCIAL GRADIENT PATTERNS IN MEDICAL ADHD TREATMENT

M. Keilow

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Background: International studies show that the prevalence of ADHD varies across socioeconomic characteristics. In Denmark, healthcare is universal, and the diagnosis and treatment rates are low compared to international levels. Still, we see considerable geographic variation in the prevalence and significant interactions with community level SES. However, the associations between individual level socioeconomic characteristics and ADHD have not been explored systematically although the comprehensive Danish statistical registers provide a unique potential for such analyses.

Objective: The study will explore social gradient patterns in the initiation and timing of ADHD health care in Denmark.

Methods: We combine data from Danish medical and demographic registers to study the likelihood of entering medical ADHD healthcare across socioeconomic characteristics in a birth cohort including all children born in Denmark in 1990-2000. We investigate how family socioeconomic characteristics are associated with the likelihood and timing of entering ADHD healthcare. Estimates are adjusted for diagnostic time trends, geographic variation, gender, and birth characteristics.

Results: Preliminary results support a social gradient pattern in ADHD health care: Entering treatment is significantly associated with several indicators of socioeconomic disadvantage including parent income, educational attainment, labor market attachment, and lone parenthood.

Perspectives: The findings will form the basis of further studies of whether children diagnosed with ADHD in families with fewer socioeconomic resources suffer cumulative disadvantage effects in terms of own academic attainment.

- P10.01 Anne Ankerstjerne Rasmussen
- PATIENT-REPORTED OUTCOMES IN PATIENTS SUFFERING FROM HEART FAILURE: ASSOCIATIONS BETWEEN PATIENT DEMOGRAPHICS AND PRO?
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- Background: Heart failure (HF) is a serious condition with frequent contacts to the healthcare system and high mortality. The prevalence in Denmark is approximately 100,000 individuals. A range of clinical and socio-demographic prognostic factors are well-established while a substantial need remains for clarifying the prognostic significance of self-reported information. Patient-reported outcome (PRO) data reflects the patient's subjective assessment of health status and quantifies the patient's perspective on the disease, symptoms and impact on every day life. We propose a project that evaluates the prognostic value of PRO information obtained at hospital discharge.
- Objective: To examine the association between demographic patient characteristics and PRO in a Danish population of patients suffering from heart failure.
- Methods:
- Design: cross-sectional cohort study.
- Inclusion: 1,537 patients with a HF diagnosis who answered The DenHeart Questionnaire at discharge from one the five heart centres in Denmark in 2013-2104.
- PRO instruments include: SF-12, HeartQoL, Hospital Anxiety and Depression Scale, Edmonton Symptom Assessment Scale, EQ-5D, Brief Illness Perception Questionnaire and data on lifestyle. The questionnaire data is linked to the following data sources: Danish Civil Registration System, Register of Medicinal Product Statistics, National Patient Register, Cause of Death Register and medical records.
- Perspectives: PRO data may help identify vulnerable patients with HF who could benefit from a closer and more regular contact to the healthcare system. This could potentially reduce the risk of readmission and improve the quality of life.
- P10.02 Diana Hedevang Christensen
- THE ASSOCIATION OF METABOLIC RISK FACTORS WITH POLYNEUROPATHY IN RECENTLY DIAGNOSED TYPE 2 DIABETES PATIENTS
- D.H. Christensen^{1,5}, S.K. Nikolaisen¹, S.T. Knudsen², N.B. Finnerup^{3,5}, T.S. Jensen³, J.S. Nielsen⁴, H. Beck-Nielsen⁴, R.W. Thomsen¹*
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- Background: Diabetic polyneuropathy (DN) is a common diabetic complication. Strict glycemc control only modestly reduces DN risk in type 2

diabetes (T2D) clinical trials. In contrast, inflammation and elements of the metabolic syndrome may play a central role for DN risk, but data are scarce. Moreover, it is unknown why some patients develop pain while other patients do not. Understanding of risk factors for painful and non-painful DN is a prerequisite for future prevention of DN in T2D patients.

Aim: To investigate the association between specific metabolic risk factors and painful/non-painful DN among patients with T2D.

Method: We sent out a detailed questionnaire on presence of poly-neuropathy and pain to 6,726 T2D patients enrolled in the Danish Centre for Strategic Research in Type 2 Diabetes (DD2) Cohort and received a remarkable response rate of 85% (N=5,750). The DD2 Cohort holds information on metabolic variables around T2D debut in all subjects, including central obesity (waist-hip ratio), physical activity, C-reactive protein, fasting blood glucose and C-peptide (allowing calculation of HOMA insulin resistance). Linkage with data from the Danish Diabetes Database for Adults provides further data on blood pressure, lipids and glycemic control. By using Poisson regression analysis, we will calculate crude and adjusted prevalence ratios with 95% confidence intervals of presence of painful/non-painful DN associated with each metabolic risk factor.

Perspectives: The study will improve our understanding of risk factors for developing painful and non-painful DN in T2D patients and thus form the scientific basis for improved prevention of these conditions in the future.

P10.03 Martin Lund

THE DANISH COLORECTAL CANCER SCREENING PROGRAM AND THE DISTRIBUTION OF QUALITY INDICATORS PER COLONOSCOPIST IN THE CENTRAL DENMARK REGION

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Purpose: To validate the registrations made in the Central Denmark Region (CDR) in connection with the screening of colonoscopies, and to describe the distribution of quality indicators per colonoscopist along with the patient-experienced comfort, the use of sedation and the quality of the bowel preparation.

Methods: This register-based study has its starting point in 11,164 colorectal cancer screening colonoscopies performed in the CDR from the 1st of July 2015 until the 30th of June 2017, (men (n=6,425), women (n=4,739), mean age 64 years (range: 49-78)). The validation of the data was conducted as a check of a random sample of screening colonoscopies.

The distribution of quality indicators per colonoscopist was assessed by the finding of mean values and confidence intervals (CI). Only colonoscopists, who have performed >30 screening colonoscopies in the period have been considered in the calculations of the adenoma detection rate (ADR), the cecal intubation rate (CIR), the withdrawal time (WT) and the polyp recovery (PR).

Results and conclusion: The registrations have a high level of validity, which makes the data very useful for scientific work. The only colonoscopist-dependent quality indicator that meets the requirements is the ADR. The CIR, WT and PR are all too low. However, this is based on the mean values, which indicates that the focus should be on the part of colonoscopists who do not meet the requirements in terms of more supervision and training.

- P10.04 Signe Hjuler
Boudigaard RISK OF AUTOIMMUNE RHEUMATOLOGICAL DISEASES AFTER OCCUPATIONAL EXPOSURE TO RESPIRABLE QUARTZ: A COHORT STUDY OF THE DANISH WORKING POPULATION 1977-2015

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Epidemiological studies suggest exposure to respirable quartz as an aetiological factor of autoimmune rheumatological diseases like systemic sclerosis, rheumatoid arthritis, systemic lupus erythematosus, and small vessel vasculitis. However, there is limited information on the quantitative exposure response relation, and earlier study results may have been recall biased and included few patients due to disease rarity.

The aim of this study is to examine the association between exposure to respirable quartz dust and autoimmune rheumatological diseases, and to explore any dose-response relationship.

We will follow the entire working population of Denmark in 1977-2015 (n=6.5 million). We combine national hospital register information on autoimmune diseases since 1977 with employment history provided by several national databases of job, tax payment and pension since 1970. Based on an international job exposure matrix for airborne quartz and measurements of quartz exposure conducted in Denmark, each study member will be assigned an individual exposure level for each year of work based on their occupation (job) in that year. We will estimate rate ratios (RR) with 95% confidence interval in a discrete survival function with person year as the unity of analysis. Since women are at higher risk of these diseases, gender may modify the effect of quarts. Hence, we will stratify all analyses on gender. We will adjust analyses by calendar year, social status and estimates for smoking status.

This study provides the potential to manage earlier methodological problems, and thereby contribute to a healthy working environment and to the knowledge on possible causal mechanisms.

- P10.05 Bishal Gyawali PREVALENCE, ASSOCIATED FACTORS, AWARENESS, TREATMENT, AND CONTROL OF TYPE 2 DIABETES IN A SEMI-URBAN AREA OF NEPAL: A CROSS-SECTIONAL STUDY

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Background: Type 2 diabetes is an escalating problem in semi-urban Nepal. This study aims to assess the prevalence, associated factors, awareness,

treatment, and control of type 2 diabetes in a semi-urban area of Western Nepal.

Methods: A population-based cross-sectional survey was conducted on 2,310 adults aged 25-64 years from a semi-urban Pokhara-Lekhnath Metropolitan area during October 2016 to April 2017 using the World Health Organization-STEPS approach. Data on demographic, behavioral risk factors, blood pressure, anthropometric measurements (weight, height, waist and hip circumference), and fasting blood glucose were collected by face-to-face interviews during a door-to-door visit. Diabetes was defined as a fasting blood glucose ≥ 7 mmol/L, or previous diagnosis of diabetes by a physician or use of anti-diabetic medications. Awareness, treatment, and control of diabetes were defined as participants' self-reported previous diagnosis, the use of medication or counseling for diabetes, and fasting blood glucose < 7 mmol/L, respectively.

Results: The overall prevalence of type 2 diabetes was 11.7%. Factors associated with type 2 diabetes were older age, being a male, Janajati ethnicity, abdominal obesity, being overweight or obese, low physical activity, hypertension, and family history of diabetes. Among diabetic participants, 65% were aware of their condition, 94% were on treatment, and 21% of those on treatment had controlled fasting blood glucose status.

Conclusions: The prevalence of type 2 diabetes was high among our study participants. Population-based intervention programs and policies are urgently required for prevention and control of type 2 diabetes.

P10.06 Bente Kjær
Lyngsøe

MATERNAL DEPRESSION AND OFFSPRING UTILIZATION OF PRIMARY HEALTH CARE: A POPULATION-BASED COHORT STUDY

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Background: Depression is a common mental illness worldwide. The lifetime risk among women is twice that of men and the perinatal and postnatal period forms a particularly sensitive period, where this risk increases further. Extant research finds maternal depression associated with higher utilization of non-routine health care and lower attendance to routine childcare in the offspring.

Aim: To investigate how mother's mental health in the form of depression affects the utilization of primary health care in the offspring. To investigate if exposure to recent, previous or past depression may affect this differently.

Design: Population-based cohort study using Danish National registries.

Methods: Participants are all live born children in the period 1 January 2000 until 31 August 2013 (approximately 800,000 children). Primary outcome is contact to the general practitioner (GP) divided into daytime contacts and out-of-hours-contacts. Secondary outcome is specific services used by the GP (strepA test, CRP, Urinary stix, tympanometry) to assess infectious disease in the children. Exposure is maternal depression in three categories (recent, previous and past).

Results: Preliminary results suggest a higher use of health care services in all contact categories for all groups of exposure.

Conclusion: Maternal depression is associated with higher use of both day-contacts and out-of-hours contacts to primary care. These findings could suggest a higher sickness in the child or a different pattern of behaviour in these women. Interestingly, the association sustains through all exposure categories, which suggests that this pattern of behaviour is consistent, even years after remission.

P10.07 Signe Timm

ASTHMA AND SELECTIVE MIGRATION AWAY FROM FARMING ENVIRONMENTS IN THE THREE-GENERATION COHORT STUDY RHINESSA

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Background: Several studies suggest that being born and raised on a farm reduces the risk of asthma. However, findings have been inconsistent. One would question if the protective effect from farming is due to greater microbial stimulation (hygiene hypotheses) or due to asthmatic parents raising their children away from farms (selective migration).

Objective: The aim of this study was to investigate if parents with asthma are less likely to raise their children on a farm.

Methods: RHINESSA (Respiratory Health in Northern Europe, Spain and Australia) is a cohort study of 8,260 offspring (18-51 years), 6,045 unique parents (44-73 years) and 9,784 unique grandparents. The parents originate from ECRHS (European Community Respiratory Health Survey), including men and women from 10 centres recruited in 1990 and followed up by questionnaires in 2000 and 2010. The parents also gave information about their parents (denoted grandparents).

Data were analysed in logistic regression conducting two identical analyses to investigate the association between parental asthma and offspring place of upbringing among parents' offspring and grandparents' parents.

Results: Having at least one asthmatic parent was not related to the likelihood of offspring growing up in the city (RR 0.99, 95 % CI 0.98-1.01). The same was found among grandparents' parents (RR 1.01, 95 % CI 0.98-1.05).

Conclusion: This study suggests no selective migration away from farms among parents' offspring nor grandparents' parents, and our findings thereby support the role of environmental exposures in the origin of asthma.

- P10.08 Jonas Boysen Fynboe Ebert PAPER- OR WEB-BASED QUESTIONNAIRE INVITATIONS AS A METHOD FOR DATA COLLECTION? A CROSS-SECTIONAL COMPARATIVE STUDY OF DIFFERENCES IN RESPONSE RATE, COMPLETENESS OF DATA AND FINANCIAL COSTS

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Background: Paper questionnaires have traditionally been the first choice for data collection in research. However, declining response rates over the last decade have increased the risk of selection bias in cross-sectional studies. A secure, online digital mailbox (e-Boks) became mandatory for all Danish citizens in 2014. Around 89% of the Danish population have a digital mailbox.

Objective: We aimed to compare response rates, completeness of data and financial costs for different invitation methods: traditional surface mail and digital mail.

Methods: Cross-sectional comparative study. An invitation to participate in a survey on help-seeking behaviour in out-of-hours care was sent to two groups of randomly selected citizens from three different age groups using either traditional surface mail (paper group) or digital mail sent to a secure online mailbox (digital group).

Results: A total of 3,600 citizens were invited in each group; 36.3% responded to the digital invitation and 46.0% to the paper invitation. The costs were EUR 1.51 per respondent for the digital group and EUR 15.67 per respondent for the paper group. Paper questionnaires generally had more missing values.

Conclusions: The digital invitations showed lower response rates, but were more cost-effective (by a factor of 10) and had slightly fewer missing values than the paper invitations. Invitations to questionnaire studies via digital mail may be a good option for collecting research data in the future. This study might serve as the foundational pillars of digital data collection in healthcare research.

- P10.09 Mette Kielsholm Thomsen SOCIOECONOMIC PREDICTORS OF INTERVAL CANCER AND ADHERENCE TO FOLLOW-UP COLONOSCOPY IN THE DANISH COLORECTAL CANCER SCREENING PROGRAM

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Background: In 2014, a national colorectal cancer (CRC) screening program was initialized in Denmark. Social inequality has been found in both colorectal cancer incidence and mortality. If socioeconomic factors are also associated with being diagnosed in the CRC screening program, it has the potential to inadvertently increase inequality.

Aim: The overall aim is to examine the influence of socioeconomic factors on the performance of the Danish CRC screening program. Specifically, we aim to evaluate socioeconomic predictors of adherence to follow-up colonoscopy (study 1), to estimate the incidence of interval cancer and compare characteristics of interval cancers with screen detected cancers (study 2), and to evaluate socioeconomic predictors of interval cancer (study 3).

Materials: Registry-based data from the CRC Screening Database, the Integrated Database for Labor Market Research, the Danish Central Person Registry, the Danish National Patient Registry, the Danish Pathology Registry, the Danish Psychiatric Central Research Register and the Danish National Prescription Registry.

Methods: Study 1 will be cross sectional, and logistic regression will be performed to estimate odds ratios of the potential predictors. Study 2 and 3 will be longitudinal studies. In study 2, incidence of interval cancer will be evaluated firstly by the proportional incidences method and secondly compared to the total number of detected cancers. To identify predictors of interval cancer in study 3, Poisson/Cox regression will be used.

Perspectives: The results will provide information on the performance and social impact of the CRC screening program.

P10.10 Michael Bertelsen

A FRAMEWORK FOR THE ETIOLOGY OF RUNNING-RELATED INJURIES

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The etiology of running-related injury is important to consider as the effectiveness of a given running-related injury prevention intervention is dependent on whether etiologic factors are readily modifiable and consistent with a biologically plausible causal mechanism. Therefore, the purpose of the present article was to present an evidence-informed conceptual framework outlining the multifactorial nature of running-related injury etiology. In the framework, four mutually exclusive parts are presented: (a) structure-specific capacity when entering a running session; (b) structure-specific cumulative load per running session; (c) reduction in the structure-specific capacity during a running session; and (d) exceeding the structure-specific capacity. The framework can be used to inform the design of future running-related injury prevention studies, including the formation of research questions and hypotheses, as well as the monitoring of participation-related and non-participation-related exposures. In addition, future research applications should focus on addressing how changes in one or more

exposures influence the risk of running-related injury. This necessitates the investigation of how different factors affect the structure-specific load and/or the load capacity, and the dose-response relationship between running participation and injury risk. Ultimately, this direction allows researchers to move beyond traditional risk factor identification to produce research findings that are not only reliably reported in terms of the observed cause-effect association, but also translatable in practice.

P11.01 Marie
Weinreich
Petersen

PREVALENCE AND SOCIODEMOGRAPHIC CHARACTERISTICS OF FUNCTIONAL SOMATIC SYNDROMES IN THE GENERAL DANISH POPULATION

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Background: Functional somatic syndromes (FSS) are prevalent in the general population, but more precise knowledge about their epidemiology is severely lacking. Prevalence rates vary tremendously because of considerable heterogeneity in diagnostic criteria and delimitation of the various FSS. Bodily distress syndrome (BDS) has been suggested as a unifying way of classifying FSS.

Aim: To establish prevalence and sociodemographic characteristics of FSS and BDS in the general Danish population.

Method: This study is part of the first coordinated larger study to address FSS in the general Danish population, the DanFunD study. A total of 9656 women and men from the adult general population answered self-reported questionnaires about physical symptoms, life style, and wellbeing. Prevalence estimates of FSS and BDS were given. Age-adjusted gender odds ratios were calculated with logistic regression. Associations between FSS, BDS and sociodemographic characteristics were measured as relative risk.

Results: Prevalence of any FSS and of BDS was 15.7 % (95 % CI: 15.0-16.4 %) and 16.0 % (95 % CI: 15.3-16.7 %), respectively. Both were more prevalent in women than in men (OR: 0.4, 95 % CI: 0.4-0.5). The majority of cases only fulfilled criteria of one FSS (12.6 %, 95 % CI: 11.9-13.2) or single-organ BDS (15.1 %, 95 % CI: 14.4-15.8). Cases had a higher risk of poor general health (RR: 8.2 %, 95 % CI: 7.1-8.5) and limitations in daily activities (RR: 6.0, 95 % CI: 5.4-6.7) than non-cases. No significant association with cohabitation, occupation, or vocational training were found.

Perspectives: This study unravels the epidemiology of FSS and may contribute to better diagnosis and treatment of FSS.

- P11.02 Liv Marit Valen Schougaard PATIENT-REPORTED OUTCOME (PRO) MEASURE-BASED ALGORITHM FOR CLINICAL DECISION SUPPORT IN EPILEPSY OUTPATIENT FOLLOW-UP: A TEST-RETEST RELIABILITY STUDY

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Background: Patient-reported outcome (PRO) measures have been used in epilepsy outpatient clinics in Denmark since 2011. The patients' self-reported PRO data are used by clinicians as a decision aid to support whether a patient needs contact with the outpatient clinic or not, based on a PRO algorithm. The aim of this study was to evaluate the test-retest reliability of the PRO algorithm used in epilepsy outpatient clinics and to analyse whether the method of administration would influence the result.

Methods: Outpatients with epilepsy aged 15 years or more from three epilepsy outpatient clinics in the Central Denmark Region were included from August 2016 to April 2017. The participants completed questionnaires at two time points and were divided into four test-retest groups: web-web, paper-paper, web-paper, and paper-web. Reliability was assessed by kappa statistics and agreement by percentage.

Results: A total of 554 patients completed the questionnaire at two time points. Kappa with squared weight was 0.67 (95% CI 0.60; 0.74) for the pooled PRO algorithm, and perfect agreement was observed in 82% of the cases. In total, 166 patients completed web-web, 112 paper-paper, 239 web-paper, and 37 paper-web. There was a tendency towards higher test-retest reliability and agreement estimates within same method of administration (web-web or paper-paper) compared to a mixture of methods (web-paper and paper-web).

Conclusion: The PRO algorithm showed moderate to substantial test-retest reliability. Different methods of administration produced similar results, but an influence of change in administration method cannot be ruled out.

- P11.03 Anne Gedebjerg PREVALENCE OF MICROVASCULAR AND MACROVASCULAR DIABETES COMPLICATIONS AT THE TIME OF TYPE 2 DIABETES DIAGNOSIS AND ASSOCIATED CLINICAL CHARACTERISTICS: A CROSS-SECTIONAL BASELINE STUDY OF 6958 PATIENTS IN THE DANISH DD2 COHORT

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Some individuals with type 2 diabetes (T2D) remain undiagnosed until they develop complications. We conducted a cross-sectional baseline study

using health databases to examine the prevalence and associated characteristics of microvascular and macrovascular complications among newly diagnosed T2D patients enrolled in the Danish Center for Strategic Research in Type 2 Diabetes (DD2) cohort, 2010-2016. We calculated age- and gender-adjusted prevalence ratios (aPRs) of complications associated with clinical and lifestyle factors using log-binomial regression. Among 6958 T2D patients, 35% (n=2456) T2D patients had diabetic complications at diagnosis; 12% (n=828) had microvascular complications; 17% (n=1186) had macrovascular complications; and 6% (n=442) had both. HbA1c levels of $\geq 7\%$ were associated with microvascular (aPR: 1.35, 95% confidence interval (CI): 1.12-1.62) but not macrovascular complications. High C-peptide ≥ 800 pmol/L was associated with macrovascular (aPR 1.34, 95% CI: 1.00-1.80) but not microvascular complications. Macrovascular complications were associated with male sex, age >50 years, obesity, hypertriglyceridemia, low HDL cholesterol, smoking, elevated CRP levels, and anti-hypertensive therapy. Microvascular complications were associated with high blood pressure, hypertriglyceridemia, and absence of lipid-lowering therapy. One-third of patients with T2D in Denmark had diabetes complications at the time of diagnosis. Our findings of dysglycemia-related factors associated with microvascular complications, and metabolic syndrome-related factors associated with macrovascular complications corroborate hypotheses about different underlying pathophysiological mechanisms.

P11.04 Inge Schjødt LOW SOCIOECONOMIC STATUS IS ASSOCIATED WITH HIGHER RISK OF READMISSION AMONG PATIENTS WITH HEART FAILURE AND REDUCED EJECTION FRACTION: A POPULATION-BASED COHORT STUDY

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Introduction: Low socioeconomic status is associated with higher incidence of heart failure (HF) as well as higher mortality following a HF diagnosis. However, the role of low socioeconomic status on readmission risk remains unclear.

Objective: This study investigated the association between socioeconomic status and readmission following HF diagnosis.

Methods: This is a population-based cohort study based on data from nationwide public registries. We identified patients with incident HF with reduced left ventricular ejection fraction ($\leq 40\%$) in the Danish Heart Failure Registry between January 2008 and October 2015. Socioeconomic status consisted of cohabiting status, highest education attained, and mean family income. Outcomes included all-cause readmission, HF readmission and non-HF readmission within day 1-30, 31-90 and 91-365 after the HF diagnosis. We used Cox regression to estimate hazard ratios (HR) of readmission, controlling for potential confounders.

Results: We identified 17,214 patients with HF; 8,341 patients (48%) were readmitted at least once within the first year. Low socioeconomic status (living alone with a low education and a low income) was associated with higher risk of all-cause readmission (adjusted HR 1.42; 95% CI 1.14-1.78) and

non-HF readmission (adjusted HR 1.35; CI 95% 1.06-1.71) within day 31-90. Low income was associated with higher all-cause readmission risk (adjusted HR 1.20; CI 95% 1.04-1.38) and higher non-HF readmission risk (adjusted HR 1.31; CI 95% 1.12-1.52) within day 31-90.

Conclusion: Low socioeconomic status is associated with higher risk of all-cause readmission and non-HF readmission within day 31-90 following HF diagnosis.

P11.05 Per Høgh
Poulsen

THE EFFECT OF CHILDHOOD SOCIOECONOMIC POSITION ON MENTAL HEALTH IN ADOLESCENCE AND EARLY ADULTHOOD

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Introduction: According to the Danish National Health Profile 2013, 17.5% of young women and 8.2% of young men reported symptoms of poor mental health (MH). Low socioeconomic position (SEP) in childhood has previously been linked to increased risk of morbidity and mortality in adulthood. However, further research within exposure to early childhood SEP and health outcomes in adolescence are required due to limited evidence in this field. We aimed to examine the association between SEP in early and late childhood and poor MH in adolescence and early adulthood. In this study, the term poor MH covers symptoms of depression and not disease.

Methods/materials: Longitudinal study using data from Vestliv, an ongoing Danish survey following a complete cohort of young people born in 1989 and living in the former county of Ringkøbing in 2004 (N=3681). Questionnaires have been collected in 2004, 2007 and 2010.

Exposure: Yearly household income and parental highest education level (Statistics Denmark), parental labour market participation (LMP) (DREAM register) and family functioning (questionnaire 2004).

Outcome: MH was measured by the CES-DC at age 15, 18 and 21 years.

Statistical analysis: Logistic regression models, stratified by gender with mutual adjustments.

Results: Low income and poor family functioning increased the risk of poor MH 2-fold in girls at age 21, and 1.5-fold in boys at age 18. Father's low LMP increased the risk of poor MH 1.4-fold in boys at age 18.

Conclusion: Low income and poor family functioning in childhood increased the risk of poor MH at age 18 and 21 in both genders. Father's low LMP increased the risk of poor MH at age 15 and 18 in boys.

P11.06 Julie Jessen
Hvidt

PUBERTAL DEVELOPMENT IN CHILDREN WITH FETAL GROWTH RESTRICTION

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Background: Timing of puberty seems to have declined in the Western world during the last century. Different factors have been suggested to play a role, including fetal growth restriction. Most studies have investigated age at menarche as a marker of pubertal development in girls, and only few have used other markers of pubertal development like Tanner staging in both boys and girls. We aim to investigate how fetal growth restriction, in terms of small for gestational age and low birth weight, is associated with pubertal development in a large Danish cohort.

Methods: We will use data from a large puberty cohort, nested within the Danish National Birth Cohort. Approximately 22,500 children were invited to report current stage of pubertal development through web-based questionnaires every 6 month from the age of 11 years to 18 years or full maturity, whichever came first. Data on birth weight and gestational age were obtained from the Danish Medical Birth Registry.

Results: The analytic strategy is being planned, and we expect to present preliminary results at the PhD Day 2018.

Perspectives: This study will be the largest to assess the association between fetal growth restriction and pubertal development. Fetal growth restriction results from prenatal exposures and disease. If fetal growth restriction is related to timing of puberty, it may indicate that prenatal factors related to intrauterine growth restriction might be determinants for timing of puberty.

P11.07 Helene
Narvestad

MATERNAL SMOKING DURING PREGNANCY AND OFFSPRING UTILISATION OF HEALTHCARE SERVICES

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Objective: Maternal smoking during pregnancy has been associated with a wide range of adverse effects on the foetus. This study aims to investigate the long-term consequences of prenatal smoking exposure on offspring general health by examining contacts to the healthcare system in exposed compared to non-exposed offspring.

Design: Population-based cohort study.

Setting: Danish nationwide national registers.

Participants: Participants were all liveborn singletons born in Denmark 1996-2002 whose mothers participated in the Danish National Birth Cohort and completed two interviews during pregnancy and one 6 months after giving birth (n=63,868).

Methods: Information about maternal smoking was collected in three telephone interviews during and after pregnancy. Information about contacts to the healthcare system and use of redemption medicine was retrieved from nationwide registers. Negative binomial regression (attendance to general practitioner) and Cox regression (attendance to hospitals) were used to calculate incidence rate ratios and hazard ratios together with corresponding confidence intervals.

Main outcome measures: Number and type of contacts to general practitioner and hospital contacts for offspring of mothers who smoked during pregnancy compared to non-exposed offspring. A secondary

outcome measure was use of specific types of services provided by the general practitioner, and a third was reimbursement of prescribed medicine.

Results: Data are currently being cleaned and analysed. We expect to have results ready for presentation at PhD Day.

Conclusions: We expect to find an association between exposure to prenatal smoking and increased use of healthcare services.

P11.08 Asser
Hedegård
Thomsen

KILL YOUR TEXT /// HOMICIDE IN DENMARK 1992-2016 - PRELIMINARY FINDINGS

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Interpersonal violence has wide public attention and claims many lives, every year, all over the world. Is interpersonal violence a result of chaotic randomness, or can we study it systematically using scientific methods? If so, can we make this data accessible to the general public?

The project "Homicides in Denmark 1992-2016" includes ~1400 deaths by interpersonal violence. For each death, I quantify information about the victim and perpetrator, the circumstances of the homicide, the findings at autopsy and related information. The project is focused on estimating the severity of violence and how this varies over time and within subpopulations.

I will show how some of this information can be presented in a way that the general public and scholars alike will understand, explore and enjoy. Let's believe in the people's ability to understand and believe in science.

P11.09 Gitte Boier
Tygesen

DEVELOPMENT OF A DANISH EMERGENCY DEPARTMENT PATIENT SAFETY MODEL USING A SYSTEMATIC SEARCH AND MODIFIED DELPHI PROCESS

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Objective: To identify risk factors for a Danish Patient Safety Model aiming to support clinicians in early risk identification to prevent severe patient deterioration in the Emergency Department(ED).

Methods: Based on a systematic literature review, generic risk factors that can indicate change over time and be assessed bedside in the ED were extracted and included in a Delphi Process. A total of 68 experts recruited from three organizations representing emergency nurses and doctors and anesthesiologists participated in the Delphi Process. The Delphi Process was conducted electronically in two rounds: 1) Risk factors were ranked according to predefined criteria and new risk factors could be suggested, and 2) New risk factors suggested by at least two experts and risk factors not meeting consensus in the first round were presented with prior individual rank, the group's rank and comments. Finally, risk factors not meeting predefined consensus criteria were excluded by the research group and an independent ED doctor.

Results: 40 papers (of 4067) fulfilled the inclusion criteria. A total of 33 risk factors were extracted and presented to the expert panel. Six new factors were added and 26 eliminated, leaving 13 risk factors that reached consensus. These represented biochemistry (4), vital signs (6) and clinical assessments (3).

Conclusion: 13 risk factors for early identification of adult patients at risk of clinical deterioration in the ED were identified and deemed suitable for a new safety model. These risk factors should be tested to quantify their collective and individual performance in assisting clinicians in early detection of clinical deterioration in ED patients.

P11.10 Gitte Vrelits
 Sørensen

LONG-TERM RISK OF SOMATIC HOSPITALIZATION IN 5-YEAR SURVIVORS OF CHILDHOOD LEUKEMIA - A NORDIC POPULATION-BASED COHORT STUDY

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Background: Toxicities from childhood leukemia treatment may persist or progress years after the child is cured. We aim to give a comprehensive description of subsequent somatic hospitalization in five-year survivors of childhood acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML) and chronic myeloid leukemia (CML).

Methods: In the Adult Life after Childhood Cancer in Scandinavia (ALiCCS) study we identified 4,030 five-year survivors diagnosed with childhood leukemia from 1963-2008 in Denmark, Sweden, Iceland or Finland. Survivors were followed for first-time hospitalizations for 120 diseases in the national hospital registries. Hospitalization rates in survivors and in a large population comparison cohort 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 16 years from leukemia diagnosis, survivors of ALL (n=3,402), AML (n=385) and CML (n=94) had an increased overall hospitalization risk. The RR for any hospitalization was 2.0 (95% CI: 1.9, 2.1) for ALL, 3.1 (95% CI: 2.8, 3.4) for AML, and 4.3 (95% CI: 3.6, 5.3) for CML survivors. Corresponding AERs were 2.7 (95% CI: 2.5, 2.9), 5.8 (95% CI: 4.9, 6.7), and 10 (95% CI: 7.8, 13), respectively. Among survivors of ALL we found particularly high risk of secondary CNS tumors, epilepsy, and pituitary hypofunction. In survivors of AML, high risks were seen for heart failure, cataract, and epilepsy, while survivors of CML had a high risk of bone and joint diseases.

Conclusion: Five-year survivors of ALL, AML and CML had an increased risk of subsequent hospitalization for a broad range of somatic diseases.

- P12.01 Kathrine Håland Jeppesen MANAGEMENT RELATED TO THE IMPLEMENTATION OF PATIENT INVOLVEMENT
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- Background: The PhD study follows the systematic implementation of "The user-led Hospital" (Det Brugerinddragende Hospital) at Aarhus University Hospital. The purpose of "The user-led Hospital" is to implement two patient participation methods: Shared Decision Making and Patient Centered Care. Studies show that organizational changes in the health care system are necessary in order for the health care professionals to adopt their new roles to the demands of the patient-involving initiatives. These organizational changes make demands on the leaders on all levels. The PhD study explores the meaning of management during the implementation of "The user-led Hospital".
- Data are collected through three sub-studies. Sub-study one consisted of semistructured interviews with the top management related to the implementation project. The aim was to uncover assumptions on meaningful factors among key persons at top management level during the implementation process. These assumptions operate as the focus in the second and third sub-studies since the PhD study has an overall focus on how management initiatives spread, shape and form throughout the organization over time.
- Methods: The PhD study is designed as an explorative qualitative case study. The data collection consists of semistructured interviews and a few supplementary field observations. The department management team and the project team from three selected wards are included.
- P12.02 Charlotte Dyrehave "GOD CANNOT HELP ME IF I DON'T TAKE MY MEDICINE". BARRIERS TO RETENTION IN CARE AND HEALTH-RELATED QUALITY OF LIFE AMONG HIV-INFECTED AFRICAN MIGRANTS
- C. Dyrehave^{1, 2}, C. Wejse^{1, 2, 3}, H.T. Mainda^{β, 4}, L.Ø. Rodkjaer^{1, 2}*
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- Objectives: Studies find lower adherence and low retention to HIV care among migrant populations. Limited health literacy is a known barrier to adherence. It is important to identify subgroups at risk to non-adherence to tailor treatments for their specific needs. We did a pilot survey among 64 HIV-infected African migrants and found that 39% did not attend their appointments during a six-month period. The aim of this study was to gain insights into the reasons for missed appointments and non-adherence.
- Methods: Semi-structured interviews were carried out with 15 HIV-infected African migrants at the Department of Infectious Diseases at Aarhus University Hospital in 2016. Digital audio-recordings of the interviews were transcribed and analyzed using thematic analysis.

Results: The majority of the interviewed reported complex life-situations, facing several challenges and barriers for not attending their scheduled appointments and reasons to non-adherence.

Five thematic areas were identified to classify factors associated with adherence and retention to care: 1) Traumatic suffering, 2) Cultural/religious dilemmas, 3) HIV-related stigma, 4) Competing problems, 5) Loneliness/lack of family support. Lack of acceptance of HIV was consistent in all five themes. Religion was a mental support when facing problems

Conclusion: Our study demonstrated that African migrants have several challenges when living with HIV and revealed important barriers to adherence and attendance on both individual, social and system level. The cultural background and the specific life situation should be considered when targeted interventions are developed to increase attendance, adherence and health literacy.

P12.03 Anne Mette Schmidt

JUSTIFICATION AND DESCRIPTION OF A NEW REHABILITATION PROGRAMME FOR PATIENTS WITH CHRONIC LOW BACK PAIN

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Introduction: Rehabilitation programmes for patients with chronic low back pain are considered complex interventions and should, therefore, be described in detail in order to ease implementation and allow replication. However, descriptions of rehabilitation programmes are often either lacking or deficient.

Purpose: To justify and describe a new rehabilitation programme before its evaluation in a randomised controlled trial.

Methods: The new rehabilitation programme was justified based on a development and piloting stage following the Medical Research Council's guidance "Developing and evaluation complex interventions". The clinical activities comprising the new rehabilitation programme were described as part of the development stage following Template for Intervention Description and Replication (TIDieR) checklist.

Results: The development stage: 1. We found no studies of how to integrate learning into the patient's own environment. 2. The International Classification of Functioning, Disability and Health (ICF) was found to be an appropriate biopsychosocial framework. 3. Twenty-eight clinical activities were described and grouped into ten key components. The piloting stage: 1. Administrative procedures were fine-tuned. 2. Inclusion criteria were defined 3. A total sample size of 160 patients was estimated.

Conclusion: In this study, we justified and described a new rehabilitation programme for patients with chronic low back pain. The description is currently being used for successful structuring and standardisation of the new rehabilitation programme in a randomised controlled trial.

- P12.04 Randi Steensgaard A HIDDEN BARRIER TO IMPLEMENT A STRONGER FOCUS ON PATIENT PARTICIPATION IN REHABILITATION - HOW HEALTH PROFESSIONALS' POSITIONS URGE THEM TO RETAIN STATUS QUO
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- Introduction: In this action research study, co-researchers and nursing staff are involved in creating new processes and methods that can strengthen the patient's ability to reestablish and sustain a meaningful life after a spinal cord injury. However, this is challenged by the complexity of patient participation in rehabilitation and existing positions within the group of nurses and between nurses and other health professionals.
- Methods: The study has 5 cyclic stages: problem identification, planning, action, evaluation and dissertation. In the 5th phase, four new initiatives are disseminated and require change in tasks, attitude and time spent with the patient. Using theoretical concepts developed by P. Bourdieu, we analyzed findings regarding the dominating positions at the Centre and their effect on the ability to change the nursing care.
- Results:
- The position of the nurses:
- Before the dissemination: A subordinate part of the team, where the nurses' focus on patient participation is assigned to other health professionals' tasks.
- After the dissemination: The majority of the nurses recognize the need for allocated time with patients to plan and adjust care and support the patient's participation. However, it is still difficult to plan and find time with one patient only, without practical tasks involved. The interdisciplinary planning of the rehabilitation is unchanged just as the position appears to be.
- Conclusion: When the nurses' approach towards patient participation in rehabilitation changes, it challenges the positions both within the group and within the other health professionals. The effort to maintain the positions affects the ability to make sustainable changes.
- P12.05 Anders Damgaard Møller ACUTE EXACERBATION OF CHRONIC DISEASE: EVALUATION OF AN INTERSECTORAL INTERVENTION TO INTEGRATE AND OPTIMISE TREATMENT AND FOLLOW-UP
- A. Damgaard Møller¹, D.H. Christiansen², U. Fredberg¹, P. Vedsted^{1, 3}*
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The Diagnostic Centre at Silkeborg Regional Hospital has developed the 24-hour outpatient clinic, which allows outpatients to contact the hospital round the clock if the patient experiences an acute exacerbation.

The aim of the study is to investigate whether the flexible admission patient pathway reduces healthcare utilization and is cost-effective.

The intervention group consists of outpatients residing in the municipality of Silkeborg with at least one of the diagnoses: chronic obstructive pulmonary disease, inflammatory bowel disease, liver cirrhosis, cardiac fibrillation and congestive heart failure. A control group is established by 1:n propensity score matching in a Danish population.

The primary outcome measure is hospital total length of stay. Secondary outcomes are 30-day mortality after hospitalization, admissions, length of stay in intensive care units and general practice utilisation. The follow-up period is two years. Data is retrieved from Danish registers.

The effect is investigated by difference-in-difference (DID) analysis, which is robust against unobserved fixed differences between groups and time varying differences that equally affect both the intervention group and the control group. Mixed models regression analysis is used to accommodate the clustered structure of data. For the analysis of cost-effectiveness, a societal perspective is applied. The incremental cost effectiveness ratio per reduced bed-day is calculated by a two-part logistic and gamma regression model. 95 % confidence intervals are calculated by bootstrapping technique.

P12.06 Charlotte Ibsen

"KEEP IT SIMPLE": INVOLVING PATIENTS WITH LUMBAR RADICULOPATHY IN DEVELOPING A PATIENT-REPORTED OUTCOME INSTRUMENT

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Background: Patient-reported outcomes (PROs) can enhance patient-centered care. Patient involvement in developing PRO instruments gives instruments that are more meaningful for patients. Still, patients are rarely involved.

Aim: To involve patients with lumbar radiculopathy in developing a PRO instrument by exploring their perspectives on its ability to describe functioning and to inform clinical decision-making process.

Methods: First, we developed a draft PRO instrument based on the International Classification of Functioning, Disability and Health. Second, patients with lumbar radiculopathy completed the draft online. Third, two semi-structured focus group interviews were conducted.

Results: Seven patients participated in the two interviews. They found the items relevant and adequately describing how their symptoms affected their everyday lives. Three core themes were identified: simplicity, individuality and application. Simplicity signified that items should be kept at a minimum,

and overlapping items should be avoided. Individuality indicated the need for partly individualized answers describing the patient's specific functioning. Application related to the desire for providing useful information to be used in the clinical decision-making process.

Conclusions: This study yields important insight on how to involve patients in developing a PRO instrument. To obtain a patient-centered clinical consultation, the PRO instrument must be simple, allow for individuality and be applied actively in the clinical consultation. Simplicity, Application and Individuality are closely linked in a chain of important elements for the patients toward a patient-centered clinical consultation.

P12.07 Rikke Buus
Bøje

NURSING PRACTICE AND EXPANSIVE LEARNING IN OLDER ADULTS' TRANSITION BETWEEN HOSPITAL AND PRIMARY CARE

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Background: Transitions of older adults between healthcare sectors create challenges like inaccurate information, planning and coordination, leading to adverse outcomes. Older adults (65+) are particularly vulnerable to this due to comorbidity and polypharmacy. Despite targeted interventions to improve transitions, there is a lack of direction in how to educate healthcare staff in transition related tasks. The purpose of the project is to develop an educational intervention applicable to nursing practice in the transition of older adults between healthcare sectors.

Methods: The study design is based on the Change Laboratory Method drawing from cultural historical activity theory and consists of 3 parts:

- Investigating challenges in nurses' practice regarding the transition of older adults between healthcare sectors through a scoping review, participant observation, qualitative interviews of 2 leaders and 2 older patients and focus groups with 10 nurses.
- Developing solutions to identified challenges and investigating development of nurses' learning involving 10 nurses and 2 leaders through video-recorded change lab sessions.
- Investigating simulation as a method to transfer the results from part 2 to 15 other nurses using questionnaires and qualitative interviews.

Participants are recruited from Randers Regional Hospital and Favrskov Municipality.

Perspectives: The project will contribute with solutions to identified challenges in nursing in the transitions of older adults between sectors, knowledge of how learning can develop across healthcare sectors and enhance a common understanding of quality in transitions and an educational intervention applicable to practice.

P12.08 Charlotte Arp Sørensen SELF-ADMINISTRATION OF PATIENTS' OWN DRUGS DURING HOSPITAL STAY - A FEASIBILITY AND PILOT STUDY

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Background: When patients are hospitalized, the responsibility for their medication is taken over by the hospital staff. Medication errors can occur. Advantages of self-administration are e.g. improved adherence, independence and cooperation. However, the risk of medication errors is unknown.

Methods: A feasibility and pilot study was carried out to investigate uncertainties about the intervention and the study design. Eligible patients were able to self-administer drugs and usually did so at home. Numbers and reasons for exclusion were registered. The intervention (self-administration) was tested on 40 patients. The next 20 patients were randomized to either intervention group or control group (drug dispensing by a nurse). Dispensing errors were observed through direct observation, and secondary outcomes through questionnaires. Intervention costs were calculated.

Results: 512 patients were admitted (over 3 months); 60 patients were included (1 withdrawn) and 452 patients were excluded for various reasons. Many eligible patients did not bring their drugs. Dispensing errors were seen in both groups. Dispensing could not be observed in 11 patients as they were included in weekends/holidays. Not all procedures were possible in practice.

Conclusion: The intervention is complex, but feasible. Many patients are eligible, but do not bring their drugs. Dispensing errors can be detected by using the direct observational technique. The intervention and outcome methods must be adjusted before the randomized controlled trial.

P12.09 Maria Pedersen PROGNOSTIC ROLE OF NEUTROPHIL-LYMPHOCYTE RATIO IN LOCALIZED AND METASTATIC RENAL CELL CARCINOMA. A POPULATION-BASED COHORT STUDY

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Background: Inflammation is known to have an impact on several steps in tumor development, and an elevated neutrophil-lymphocyte ratio (NLR) has been associated with a poorer prognosis in several types of malignancies.

Objective: To examine the prognostic value of NLR in a large cohort of patients with localized or metastatic renal cell carcinoma (RCC) at the time of diagnosis and at RCC recurrence.

Design and methods: Using data from Danish medical registries, we identified all patients from the North Denmark Region and the Central Denmark Region with a diagnosis of RCC and an NLR measurement within 30 days prior to diagnosis in the period of 1995-2015. Patients were

categorized according to NLR levels (≤ 3.0 and >3.0) and were followed until death, immigration, or up to 5 years. We estimated survival probabilities using Kaplan-Meier curves and hazard ratios (HR) with 95% confidence intervals using Cox proportional hazards regression. Results were adjusted for age, sex and tumor stage.

Results: We included 979 patients. Among these, 416 had at the time of the initial diagnosis an NLR ≤ 3.0 and 563 had an NLR >3.0 . The 5 year-survival rate was 35.2% in RCC patients with elevated NLR (>3.0) compared with 69.4% in patients with NLR ≤ 3.0 . The unadjusted HR was 3.1 (95% CI, 2.5;3.9) and the adjusted HR was 2.5 (95% CI, 1.9;3.1). Of 151 patients with RCC recurrence, 122 had NLR measured at the time of RCC recurrence. Elevated NLR (>3.0) was associated with a poorer prognosis (adjusted HR =2.1 (95% CI, 1.2;3.6)).

Conclusion: An elevated NLR at the time of the initial diagnosis of RCC is associated with a poorer prognosis. At the time of RCC recurrence, an elevated NLR was similarly associated with an increased mortality.

P12.10 Lene Holst
Pedersen

EARLY FOLLOW-UP AFTER DISCHARGE FOR GERIATRIC PATIENTS
ADMITTED FROM THEIR OWN HOME

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Objective: To investigate the effect of an early multidisciplinary follow-up visit after discharge among geriatric patients admitted from their own home.

Outcomes: Readmission, length of hospital stay, and 90-day mortality.

Method: The study was a quasi-randomised controlled trial. The participants were 75 years or older and admitted to the emergency department with one of the following diagnoses: pneumonia, chronic obstructive pulmonary disease, dehydration, delirium, constipation, anaemia, heart failure, urinary tract infection or other infections. Nursing home residents were excluded.

The intervention consisted of a multidisciplinary geriatric follow-up visit carried out on the first weekday after discharge. This was compared to a control group receiving usual care.

Results: During the study period from June 2014 until December 2016, 1725 patients were consecutively included. Baseline characteristics showed no statistical significance differences between the intervention group and the control group. The intervention led to shorter length of hospital stay (3 vs. 5 median days). Readmission rate and time to first readmission were reduced in the intervention group compared to the control group (15% vs. 22%, $p < 0.001$) (adjusted hazard ratio (HR) = 0.65 (0.52-0.81)). Mortality 90 days after admission was less frequent in the intervention group compared to the control group (18% vs. 22%, $p = 0.05$) (adjusted HR = 0.80 (0.65-0.99)).

Conclusion: An early follow-up visit for patients admitted from their own home can lead to shorter length of hospital stay, fewer readmissions, and a lower 90-day mortality rate.

- P13.01 Cecilie Siggaard Jørgensen TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION IN CHILDREN WITH MONOSYMPTOMATIC NOCTURNAL ENURESIS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY
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- Introduction and objectives: Involuntary voiding during sleep, nocturnal enuresis (NE), affects 10-15% of all 7-year-olds and 0.5-2% of young adults. Approximately one-third of all children with NE are refractory to first line treatments. Transcutaneous Electric Nerve Stimulation (TENS) has been documented efficacious in children with daytime incontinence. The aim was to investigate the effect of TENS in children with monosymptomatic nocturnal enuresis (MNE) without nocturnal polyuria.
- Methods: We designed a randomized, double-blinded, placebo-controlled study. A total of 52 children with MNE were randomized to treatment with either active TENS or sham TENS for one hour twice daily for ten weeks with electrodes placed in the sacral region at the S2/S3 outflow.
- Results: Of the 52 children randomized, 47 completed treatment (mean age 9.5 ± 2.1 years, 38 males). No children experienced full response with complete remission of enuresis, whereas two children who received placebo treatment showed partial response ($\geq 50\%$ reduction). Treatment with TENS did not lead to significant changes in the number of wet nights, nocturnal urine production on wet or dry nights, maximum voided volumes or voiding frequency when comparing the parameters before and after treatment.
- Conclusion: The present study demonstrates no anti-enuretic effect of TENS in children with MNE without nocturnal polyuria. Nocturnal urine production and bladder capacity characteristics remained unchanged after treatment with TENS.
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- P13.02 Stine Lohmann DELAYED GRAFT FUNCTION IN A PORCINE AUTOTRANSPLANTATION MODEL
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- Objective: Delayed graft function (DGF) occurs in up to 80% of kidney transplantations when kidneys are from donation after circulatory death (DCD). The primary aim of this pilot study was to create a porcine one-kidney autotransplantation survival model of a DCD donor with primary DGF for future test of interventions to improve function. Secondary aims were to develop and test blood and urine sample measurements with minimal stress to the pig.
- Materials and methods: Kidneys from 7 female pigs (50 kg) underwent from 30 to 75 minutes of warm ischemia (WI), by clamping left renal artery and vein, followed by static cold storage until contralateral nephrectomy, transplantation and reperfusion. Observation period was 14 days. Blood

samples were drawn daily during the first week and every second day the following, using a semi-central venous catheter. An ostomy bag around genitals was used for urine collection. Glomerular filtration rate (GFR) was calculated by renal clearance of $^{51}\text{Cr-EDTA}$ on day 14.

Results: No animals died. Serum creatinine increased with prolonged WI. Pigs with WI of 75 minutes (n=2) had anuria on first day, peak P-creatinine of 1486 and 1317 $\mu\text{mol/L}$, respectively, reached on day 4. Highest levels of potassium were 5.6 and 6.8 mmol/L (upper limit 6.2) reached on day 2. P-creatinine fell to nearly normal values after eight days in all pigs, and GFR on postoperative day 14 decreased inversely proportional with duration of WI.

Conclusion: WI of 75 minutes caused DGF with highest peak P-creatinine and potassium without compromising animal welfare. Blood and urine were collected postoperatively without sedation or use of metabolic cage.

P13.03 Stine Langaa DETERMINATION OF RENAL BLOOD FLOW BASED ON PET/CT-RUBIDIUM-82 TECHNOLOGY

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Background: Changes in the renal blood flow (RBF) plays an important role in the widespread diseases hypertension and kidney disease. RBF-determination is difficult in humans. As the present methods are cumbersome and have multiple disadvantages, it is desirable to develop a new method. Myocardial blood flow is routinely assessed with PET/CT and the perfusion tracer rubidium-82 (Rb-82). Rb-82 has an ultra-short half-life and is accumulated in the kidney. A recent study demonstrated that renal PET-Rb-82 exhibits excellent image quality, with high image resolution and contrast, and suggests that renal PET-Rb-82 has great potential regarding determination of RBF.

Aim: The overall aim of the project is to develop a new reliable method to determinate RBF based on PET-Rb-82-technology using a 1-tissue compartment model. To minimize the radiation exposure related to renal PET-Rb-82, the input function in the compartment model and the kidneys has to be included in the same field of view. We, therefore, aim to determine the optimal use of the abdominal aorta as input function instead of the left ventricular blood pool, which is routinely used.

Methods: PET-scanner and the Rb-82-generator are used according to usual guidelines. The K1-parameter in the compartment model represents RBF.

Perspectives: A new reliable method to determine RBF will provide new knowledge regarding renal physiology and pathophysiology in humans. New knowledge of RBF and changes in RBF will form the basis of improved and more targeted diagnostic and therapeutic actions in diseases with changes in RBF.

P13.04 Jeanette Finderup

DEVELOPING AND PILOT TESTING A SHARED DECISION-MAKING INTERVENTION FOR DIALYSIS CHOICE

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Background: Evidence is inconclusive on how to guide the patient in decision-making concerning haemodialysis and peritoneal dialysis. International guidelines recommend involvement of the patient in the decision to choose the dialysis modality most suitable for the individual patient. Nevertheless, studies show a lack regarding involving the patient in decision-making.

Objectives: To develop and pilot test an intervention for shared decision-making targeting the choice of dialysis modality.

Methods: This study reflects the first two phases of a complex intervention design: Phase 1, the development process and Phase 2, feasibility and piloting. As decision aids were part of the intervention, the IPDAS guideline has been considered. The pilot test included both the intervention and the feasibility of the validated shared decision-making questionnaire (SDM Q9) and the Decision Quality Measure (DQM) applied to evaluate the intervention.

Results: A total of 137 patients tested the intervention. After the intervention, 80% of the patients chose dialysis at home. This reflects an increase by 23% in the group stating dialysis at home. The SDM Q9 showed that the majority of the patients experienced the intervention as shared decision-making. A small number of patients experienced to have made the decision concerning dialysis modality on their own.

Conclusion: An intervention based on shared decision-making and supported by decision aids seemed to increase the number of patients in home dialysis. The SDM Q9 and DQM were feasible evaluation tools. Further research is needed to gain insight into the patients' experiences of involvement and the implications for their choice of dialysis modality.

P13.05 Yutao Lu

DIFFERENT DIURNAL VARIATION IN PATIENTS WITH CONGENITAL NEUROGENIC AND NON-NEUROGENIC LOWER URINARY TRACT DYSFUNCTION

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Purpose: Urodynamics are used for evaluation of lower urinary, clinical assessment and treatment strategy. However, findings from conventional urodynamics are not always representative, which provides information leading to discrimination between neurogenic and non-neurogenic patients. We retrospectively reviewed ambulatory urodynamic traces to investigate possible differences between neurogenic and non-neurogenic patients.

Material and methods: Two groups of paediatric patients, with congenital neurogenic or non-neurogenic lower urinary tract dysfunction, were included with 10 in each group. Ambulatory urodynamics was performed overnight until the second day. Detrusor contraction (higher than 15 cm H₂O)

were detected, and area under the curve (AUC) was calculated by the Prism7 software. AUC were analysed in 4-hour sections (12 am-4pm, 4pm-8pm, 8pm-12pm, 12pm-4am, 4am- 8am, 8am-12am).

Results: There was no significant difference in total AUC of detrusor contraction between the neurogenic and non-neurogenic group, but the neurogenic patients had more contraction peaks. Concerning diurnal variations of AUC, the non-neurogenic patients had the bi-phasic peaks during the recording with the first peak in 4am-8am and the second in 4pm-8pm. The neurogenic patients had a plateau of high-grade contraction from 4am-8pm before a drop at 8pm-12pm. Both groups had a low AUC at 8pm-4am.

Conclusions: The preliminary results suggested that congenital neurogenic patients had different diurnal variance compared to non-neurogenic patients. Detrusor contraction may remain stable during the day in congenital neurogenic patients, but the variance in non-neurogenic patients was noteworthy.

P13.06 Haiyun Qi

EFFECTS OF ANESTHESIA ON RENAL FUNCTION AND METABOLISM IN RATS

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Performing MRI of animals typically requires anesthesia. However, anesthesia is known to modulate a wide variety of important metabolic and functional processes in the body, and as such represents potential limitations in the study design.

Here we investigated renal functional and metabolic consequences of three typical rodent anesthetics of sevoflurane, inactin and a mixture of fentanyl, fluanisone and midazolam (FFM), with hyperpolarized [$1\text{-}^{13}\text{C}$] pyruvate magnetic resonance imaging (MRI) and dynamic contrast enhancement (DCE) imaging. A similar body weight and kidney weight were observed between the three groups, whereas the rats receiving sevoflurane or FFM mixture had higher blood glucose level than rats receiving inactin. FFM increased renal lactate/pyruvate ratio and blood lactate concentration, as well as lowered arterial pH value. DCE functional MRI showed rats with FFM anesthesia had lower plasma flow in the renal cortex. Inactin and sevoflurane anesthesia had reasonable renal metabolism and function. This study demonstrates the influence of three different anesthetics on renal metabolic and function using hyperpolarized MRI and DCE imaging in rats. Inactin and sevoflurane were found to affect the renal function and metabolic status to a lesser degree than the FFM mixture, which indicates that inactin and sevoflurane are preferable when renal metabolism and function are the consideration of research. Sevoflurane anesthesia is particularly easy to induce and maintain during the whole anesthesia procedure in the MR applications, and as such represents a good alternative to inactin (endpoint only anesthetic), although sevoflurane alters the blood glucose level.

- P13.07 My Emma Sofie Malmberg EFFECT OF TOLVAPTAN ON RBF AND GFR IN POLYCYSTIC KIDNEY DISEASE
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Polycystic kidney disease (ADPKD) is a common genetic disorder, which is characterized by the formation of cyst in the kidneys, causing gradual renal failure. Previous studies have shown that reduced glomerular filtration rate (GFR) and renal plasma flow (RPF) play a role in the progression of renal disease in ADPKD. Tolvaptan is a vasopressin 2 antagonist, which seems to reduce the growth of total kidney volume and the decline in e-GFR in ADPKD. The mechanisms are not fully understood and could, at least partly, be due to changes in renal blood flow (RBF).

The purpose of this trial is to investigate if Tolvatan increase renal blood flow and subsequently glomerular filtration in 30 ADPKD subjects in a randomized, cross-over, double-blind, placebo-controlled study.

ADPKD patients (CKD 1-3) are investigated twice (min. 10 days apart) after acute treatment with either Tolvaptan 60 mg or placebo. Renal blood flow is estimated by ^{99m}Tc-DTPA renography after treatment.

Increased understanding of the mechanisms involved in the regulation of renal hemodynamics, as well as the water and salt balance in the kidneys in ADPKD patients, is expected to be of importance for future clinical practice in the treatment of ADPKD, consequently improving the prognosis in these patients.

- P13.08 Marie Houmaa Vrist 18F-NAF PET/CT IN COMBINATION WITH BIOMARKERS FOR THE CLASSIFICATION OF RENAL OSTEODYSTROPHY IN HEMODIALYSIS PATIENTS
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Background: Chronic Kidney Disease - Mineral and Bone Disorder (CKD-MBD) is a relatively new definition, which brings together the disturbances in vascular calcification, bone and mineral status in patients with Chronic Kidney Disease. Renal osteodystrophy (ROD) only refers to the bone disturbances in CKD-MBD. ROD is divided into subgroups depending on bone turnover, mineralization and volume. It is measured by tetracycline double-labelled transiliac bone biopsy and bone histomorphometric analysis. The method is the gold standard, but it has limitations: invasive, regional and requires expertise both in the performance, processing and interpretation. Bone biopsy is performed rarely. It will be of great value if it can be replaced by a simple and non-invasive method.

Purpose: We investigate whether 18F-NaF PET/CT in combination with biomarkers can classify ROD and furthermore give the profile of CKD-MBD.

Design: It is a pilot study with 20 hemodialysis patients. Bone status is investigated with static and dynamic ^{18}F -NaF PET/CT and at the following biomarkers: Bone Alkaline Phosphatase, Fibroblast growth factor 23, osteocalcin and Osteoprotegerin/Receptor activator of nuclear factor kappa-B ligand ratio. Subsequently, bone biopsy is made as control.

Perspective: ^{18}F -NaF PET/CT have shown promising potential in order to determine bone turnover and additionally give information of the cardiovascular profile; thereby it fits much better to the new definition CKD-MBD. The introduction of new and better biomarkers can be very useful in the clinic for ongoing control.

P13.09 Malthé
Pedersen

SLEEP AND NOCTURNAL ENURESIS

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Introduction and aims: Nocturnal enuresis (NE) is a common paediatric condition affecting 10-15% of all 7-year-old children. The spontaneous cure rate is 15% per year, but 0.5-1% of adults still suffer from NE. Three main factors participate in the pathophysiology of the condition: nocturnal polyuria, reduced bladder capacity and lack of awakening when needing to pass urine at night. Sleep has been investigated as one of the main factors in NE. The aim of our study was to investigate the sleep quality, architecture and the intra-individual variation from night to night in healthy children and children with NE using ambulatory polysomnography (PSG).

Methods: The study will recruit 30 healthy children and 30 children with mono-symptomatic NE (15 with polyuria and 15 with no polyuria). The children will be between 7 and 14 years of age. All the children will undergo ambulatory PSG performed at their homes. The healthy children will be subjected to two nights of PSG to be able to study night-to-night variability. Children with NE will only undergo one night with PSG. The primary measures to be evaluated are sleep quality, periodic limb movement, blood pressure (using peripheral arterial tone), respiration during sleep, nocturnal urine production and enuresis episodes.

Hypothesis:

- There is large intra-individual night-to-night variation in sleep quality and architecture.
- Children with NE have different sleep architecture than healthy children when looking at sleep quality and arousals.
- Periodic limb movements at sleep is more frequent in children with NE than in healthy children.

P13.10 Christian
Østergaard
Mariager

HYPERPOLARIZED [^{13}C , $^{15}\text{N}_2$] UREA T_2 RELAXATION CHANGES IN ACUTE KIDNEY INJURY

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Blood oxygenation level dependent (BOLD) T_2^* magnetic resonance imaging (MRI) is a surrogate marker of tissue pO_2 alterations associated with

renal disease, but is limited by perfusion. Hyperpolarized [^{13}C , $^{15}\text{N}_2$] urea is an alternative marker of renal function that correlates with normal renal oxygenation. We investigate the correlation between BOLD T_2^* and ^{13}C -urea T_2 relaxation rate in six male rats subjected to unilateral renal ischemia 24 hours before the MRI investigation.

Whole kidney ^{13}C -urea T_2 was significantly decreased in the the contralateral (CL) kidney compared to the post-ischemic (IR) kidney ($p=0.001$). A urea gradient was observed in the CL kidney ($p=0.008$), which was significantly different ($p=0.008$) compared IR kidney urea gradient ($p=0.0004$). Whole kidney T_2^* was similar ($p=0.14$), as was the T_2^* gradient ($p=0.26$). Oxygen availability dependency on ^{13}C -urea T_2 was investigated via the correlation with BOLD T_2^* ; a statistically significant difference ($p=0.03$) was found in the CL kidney ($p=0.0001$) but not in the IR kidney ($p=0.31$). Hypoperfusion in the IR kidney was investigated via arterial spin labelling (ASL), showing a decreased perfusion of 55% compared to the CL kidney ($p=0.08$). Additionally, an offset in the correlation between the perfusion and T_2 measurements indicates that ^{13}C -urea T_2 is modulated significantly by the blood volume in addition to oxygen availability. We conclude that hyperpolarized urea T_2 correlates with renal BOLD T_2^* in the CL, but not in the IR kidney, and that the whole kidney T_2 difference could originate from decreased perfusion or altered blood volume. ^{13}C -urea T_2 mapping, therefore, has potential to improve the BOLD estimation.

P14.01 Lene
Andreasen

RATIONAL AND DESIGN OF THE RANDOMIZED EUROPEAN OPTICAL COHERENCE TOMOGRAPHY OPTIMIZED BIFURCATION EVENT REDUCTION (OCTOBER) TRIAL

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Background: Stenosis in coronary bifurcations often requires treatment by complex stenting, with an elevated risk of suboptimal stent implantation result and poor clinical outcome. Intravascular optical coherence tomography (OCT) is an imaging modality, which can detect correctable factors that are not visible by standard angiography, improve procedural control and optimize stent implantation. No randomized OCT guiding trials have yet been adequately powered to clinical endpoints.

Aim: The aim of the OCTOBER study is to compare median two-year clinical outcome after OCT guided vs. standard angiografi guided revascularization of patients requiring complex bifurcation treatment.

Method: Investigator initiated, randomized, controlled, prospective, superiority trial with planned 1200 patients. Randomized 1:1 to either OCT guided or standard guided revascularization. Inclusion criteria are patients with stable or unstable angina pectoris, or clinically stable non-STEMI, and indication for revascularization of a coronary bifurcation lesion requiring complex treatment. The primary endpoint is a composite endpoint of major adverse cardiac events (MACE) after a median of two years.

Conclusion: The OCTOBER Trial is aimed to answer if routine use of stepwise OCT-guided treatment in complex bifurcation improves the clinical outcome. Patient inclusion started in September 2017 with an expected inclusion period of 2 years.

- P14.02 Anders Sjørøsløv THE CHESSTRIAL: COMPARISON OF HIGH VERSUS ESCALATING SHOCKS IN
Schmidt CARDIOVERTING ATRIAL FIBRILLATION: DESIGN AND RATIONALE FOR A
RANDOMIZED CLINICAL TRIAL

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Background: Atrial fibrillation is the most common heart rhythm disorder and carries a substantially increased risk of death from stroke and heart failure. Cardioversion is a pivotal treatment for reducing atrial fibrillation burden. However, the treatment is not always successful. The standard treatment uses low-energy escalating shocks, but it is unknown if using high-energy shocks improves the success without compromising safety.

Aim: To investigate the efficacy and safety of high energy shocks versus standard escalating shocks in cardioversion of atrial fibrillation.

Methods: Prospective, randomized clinical trial enrolling patients admitted for elective cardioversion of atrial fibrillation. Patients are randomized to either: 1) High energy shocks using 360-360-360 J or 2) Standard escalating shocks using 125-150-200 J. All cardioversion attempts will be performed with Lifepak 20, Physio-Control Inc., USA, through self-adhesive gel electrodes. The primary endpoint is cardioversion efficacy, i.e. the proportion of patients in sinus rhythm after one minute. Safety will be evaluated by electrocardiographic measurements, echocardiographic recordings, and measurement of changes in high-sensitive troponin I.

We estimate a sample size of 276 patients to be able to refuse the null-hypothesis of no or less than 10% difference between the treatments.

Perspectives: We hypothesize that high energy shocks are more efficient in cardioverting atrial fibrillation compared with standard escalating shocks, without compromising safety. An improved success following cardioversion will have profound implications for the atrial fibrillation patient.

- P14.03 Mathilde Stærk AUTOMATED EXTERNAL DEFIBRILLATORS ARE WIDELY DISTRIBUTED IN
DANISH HOSPITALS BUT INFREQUENTLY USED -
A NATIONWIDE STUDY

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Introduction: Use of automated external defibrillators (AEDs) increase survival after out-of-hospital cardiac arrest. In contrast, data on the effect of

in-hospital use of AEDs are conflicting, which may be due to suboptimal use and differences in distribution of AEDs.

Aim: To investigate and compare the distribution and use of AEDs and manual defibrillators in Danish hospitals.

Methods: All public somatic hospitals in Denmark with a cardiac arrest team were included. Hospitals treating outpatients only were excluded. A questionnaire was sent to the medico-technical hospital departments. Items focused on: 1) AED and manual defibrillator distribution, 2) usage of AEDs and manual defibrillators, and 3) model of AEDs and manual defibrillators.

Results: In total, 46 hospitals replied (response rate: 100%). All hospitals had either AEDs (93%) and/or manual defibrillators (93%). The median number of AEDs was 10 (Q1;Q3: 5;24), and for manual defibrillators 11 (7;20) ($p=0.74$). During the past year, AEDs were used less (median 2 times per hospital (0;10)) compared with manual defibrillators (median 15 times per hospital (2;50)) ($p=0.001$) equal to each AED has been used 0.7 times and each manual defibrillator 2.7 times. Only 33% of hospitals had compatible AEDs and manual defibrillators, i.e. AED electrodes could be directly connected to a manual defibrillator, and 55% of hospitals required an adaptor.

Conclusion: AEDs and manual defibrillators are widely distributed at Danish hospitals. AEDs are infrequently used compared with manual defibrillators. Only one third of hospitals have compatible AEDs and manual defibrillators regarding defibrillation electrodes.

P14.04 Mads Dam
Lyhne

PHARMACOLOGICAL SUPPORT OF THE FAILING RIGHT VENTRICLE IN ACUTE PULMONARY EMBOLISM

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Background: Pulmonary embolism (PE) is the third most common cause of cardiovascular death. Due to its uncharacteristic clinical presentation, the diagnosis is often missed or delayed. This is problematic since a majority of PE related deaths occur within the first 1-2 hours. Death occurs due to right ventricular (RV) failure.

Aim: The hypothesis is that right ventricular dysfunction in acute PE can be improved by inotropic and pulmonary vasodilatory support. It is additionally hypothesized that acute PE causes a shift towards anaerobic metabolism in the RV myocardium and that pharmacological inodilator support to the RV can influence pathophysiological changes in RV myocardial metabolism.

Methods: In a porcine model, we will induce high-risk PE. Three different inotropic agents (dobutamine vs. milrinone vs. levosimendan) and three different pulmonary vasodilators (sildenafil vs. bosentan vs. iloprost) will be compared head-to-head. Evaluation of the hemodynamic effects will be done by MRI, invasive pressure-volume measurements, echocardiography and blood samples. Western blotting, qPCR and the advanced technique of hyperpolarized MRI will evaluate the RV metabolism during acute PE and any changes due to the pharmacological support.

Perspectives: These studies will add to the sparse knowledge on optimal support to the failing RV in acute PE as well as to the basic understanding of acute right heart failure. Results from animal studies cannot be extrapolated directly to humans, but the porcine model of acute PE is very realistic. Data from this project will guide the design of future randomized clinical trials.

P14.05 Asbjørn Petersen CAN GENETIC DEFICIT OF KCA3.1 CHANNELS PREVENT THE DEVELOPMENT OF CIRCULATORY COLLAPSE AND LUNG OEDEMA IN ACID-INDUCED LUNG INJURY?

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Acute respiratory distress syndrome (ARDS) is an acute inflammatory lung injury, which is associated with increased vascular permeability, progressive lung oedema, and loss of aerated lung tissue. Studies have shown that endothelial ion channels (in particular TRPV4 and KCa3.1) plays a critical role in endothelial barrier integrity and circulatory homeostasis. Recently, we found that KCa3.1^{-/-} mice were protected against lung damage induced by pharmacological activation of the endothelial TRPV4 channel. So, to explore the possibility of using KCa3.1 blockers for treatment of pulmonary oedema and vascular collapse, a series of preclinical studies are needed. Acid exposure to the lung, e.g. by aspiration of gastrointestinal content, can lead to ARDS, and these experimental models have previously been used for induction of acute lung injury. In this experiment, wild type mice and mice deficient in KCa3.1 channels will be anaesthetized and instrumented for blood sampling and measure of arterial blood pressure. Both phenotypes will be exposed either to tracheal instillation of HCl or saline and treated in combination with a KCa3.1 blocker. At 5 h after instillation, the following measurements will be obtained for analysis: (1) airway resistance and other lung function parameters, (2) lung dry-to-wet weight to assess liquid accumulation, (3) injury scoring of sectioned lungs to measure histopathology, (4) and collection of bronchoalveolar lavage fluid to evaluate protein accumulation and activation of leukocytes. The perspective is that a successful development of new drug candidates for pulmonary collapse and oedema will reduce mortality and improve life quality for the surviving patients.

P14.06 Kasper Krohn Korsholm INTRACARDIAC ECHOCARDIOGRAPHY FROM THE LEFT ATRIUM FOR PROCEDURAL GUIDANCE OF TRANSCATHETER LEFT ATRIAL APPENDAGE OCCLUSION

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Aim: The aim was to compare the efficacy and the safety of intracardiac echocardiography (ICE) from the left atrium with transesophageal echocardiography (TEE) for procedural guidance of transcatheter left atrial appendage occlusion (LAAO).

Background: Currently, TEE with general anesthesia is the gold standard to guide LAAO. However, by using ICE from the left atrium, LAAO can be

performed in local anesthesia and may potentially have advantages over TEE.

Methods: A single-center cohort study of consecutive patients undergoing LAAO with the Amplatzer Cardiac Plug or Amulet (St. Jude Medical, USA). Procedures were guided by ICE from the left atrium with local anesthesia (n=109) or TEE using general anesthesia (n=107). All patients had pre-procedural cardiac computed tomography. Efficacy outcomes were technical success, procedural success, and peridevice leakage at TEE 8 weeks after LAAO. The safety outcome was a composite of periprocedural complications.

Results: Technical success was achieved in 99% of both the TEE and ICE group. Procedural success was similar between groups: 94.4% success rate for TEE-guided procedures and 94.5% for the ICE-guided. Major periprocedural complications occurred in 4.7% of the TEE group and 1.8% of the ICE group. Rate and degree of peridevice leak did not differ between groups at follow-up. Time in the catheter laboratory was significantly reduced with ICE.

Conclusion: ICE from the left atrium to guide LAAO as compared with TEE appears to be effective and safe, without increased procedure-related complications. The rate of peridevice leak is low and similar to TEE-guided procedures. Time spent in the catheterization room may decrease substantially.

P14.07 Tine Billeskov CENTRAL ROLE OF MUSCLE STEM CELLS IN REGENERATIVE FAILURE IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE

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Lower extremity peripheral artery disease (PAD) restricts blood flow in the dependent tissue due to stenosis and occlusion of the artery with a decrease in peripheral blood pressure. Therefore, the muscle becomes ischemic during exercise. PAD hypoxia is associated with reduced muscle fibre cross-sectional area (CSA), loss of type-II muscle fibres, clinical signs of myopathy and fatty degeneration. Clinical evidence suggests that the restoration of the circulation is not sufficient to restore regenerative function and muscle size as outcomes do not equate with return to pre-morbid state.

We hypothesize that peripheral arterial disease with critical limb ischemia leads to skeletal muscle satellite cell (MuSC) dysfunction due to chronic ischemia causing limited muscle regeneration. Consequently, the muscle fibre cross-sectional area is reduced compared to healthy people and unable to recover due to the maintained dysfunction of MuSCs and associated tissue fibrosis.

Muscle biopsies (MB) will be collected from PAD patients (n=24) admitted to revascularization surgery and age-matched controls (n=24) admitted to coronary artery bypass graft surgery. For the PAD patients, MB will also be collected at 3-month follow-up and 12-month follow-up. Immunohistochemistry is utilized for CSA, in vivo MuSC content/activity and fibrosis quantification. Fluorescence activated cell sorting (FACS) is utilized to quantify and isolate primary MuSCs. Cell culture experiments are utilized to

determine the proliferative and differentiation capacity of MuSC with/without patient serum added. These will also be utilized to evaluate the degree of MuSC senescence and mitochondrial content of the MuSCs.

P14.08 Laust Rasmussen DANISH STUDY OF NON-INVASIVE DIAGNOSTIC TESTING IN CORONARY ARTERY DISEASE II (DAN-NICAD II) - AN INTERDISCIPLINARY MULTICENTRE STUDY IN THE CENTRAL DENMARK REGION

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Background: Over the latest 10 years, cardiac computed tomographic angiography (CCTA) has become the preferred diagnostic modality for symptomatic patients with low to intermediate pre-test probability of coronary artery disease (CAD). CCTA has a well-known high negative predictive value of more than 95%. However, CCTA has consistently proven to have a low positive predictive value. Following CCTA, patients are hence unnecessarily invasively tested using gold standard coronary angiographies (ICA) with fractional flow reserve (FFR) estimation. These ICAs are frequently not followed by revascularization, but they still imply a small but not insignificant risk of complications as stroke and death. On this background, current guidelines recommend ischemic verification using secondary cardiac stress- and perfusion-based image modalities prior to ICA. However, the diagnostic accuracy of these examinations has not been investigated nor validated against the gold standard invasive FFR.

Methods: In three studies using invasive FFR as reference standard, we wish to investigate and compare the diagnostic precision of positron emission tomography (PET), cardiac magnetic resonance imaging (CMRI) and fractional flow reserve CT (FFR-CT) in symptomatic patients with low to intermediate pre-test probability of CAD, where CCTA does not exclude coronary stenosis.

Results: No results are yet available. Currently, patients are included.

Conclusion: Validating and clarifying the diagnostic precision of CMRI, PET and FFR-CT may reserve ICA examinations to patients with significant treatment requiring coronary stenosis and hence improve patient safety.

P14.09 Estefano Pinilla EFFECT OF TRANSGLUTAMINASE CONFORMATIONAL MODULATION ON VASCULAR TONE

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Background and hypothesis: Tissue transglutaminase (TG2) is a multi-functional and ubiquitously expressed member of the transglutaminase family of enzymes. In its open conformation, TG2 possesses transamidating activity, which has been associated with both arterial remodeling in hypertension and increment of vessel stiffness. On the other hand, its closed conformation presents GTP binding activity, which plays a role in trans-membrane signaling and opening of BK_{Ca} channels. Recently, we found that pharmacological inhibition of TG2 leads to vasodilation through opening of

voltage-gated potassium channels in the smooth muscle. Therefore, the hypothesis of the present work is that the promotion of the closed conformation of TG2 by pharmacological means will lower blood pressure (BP) in vivo by activation of potassium channels.

Methods: Male Wistar rats are used for: isometric myograph experiments to assess microvascular function, membrane resting potential measurements, patch-clamp studies in isolated smooth muscle cells, measurements of BP and heart function in vivo using solid-state catheterization and electrocardiogram.

Results: Intravenous infusion of TG2 specific inhibitor LDN-27219 induced a lowering of BP in vivo in anesthetized animals, without changing heart rhythm. Ex vivo, LDN-27219 induced endothelium-dependent vasodilatation sensitive to the inhibition of endothelial NO synthase (eNOS) and vascular smooth muscle hyperpolarization that was sensitive to the blockade of BK_{Ca} channels.

Conclusion: Pharmacological promotion of the closed conformation of TG2 leads to vasodilation by a mechanism dependent on the eNOS pathway and opening of BK_{Ca} channels.

P14.10 Peter Carøe
Lind

PROTECTIVE ROLE OF KCA3.1 ION CHANNEL BLOCKERS IN PULMONARY CIRCULATORY COLLAPSE AND OEDEMA

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Background: Acute respiratory distress syndrome (ARDS) is a severe condition characterized by acute inflammation, hypoxemia and an increased alveolar-capillary permeability, resulting in non-cardiogenic lung oedema. Currently, no pharmacological interventions exist that target directly the underlying pathophysiology of the disease, thus elucidating the need for novel pharmacological entities. Recent evidence suggests that a synergistic interplay between the cation-channel TRPV4 and the calcium-activated potassium-channel KCa3.1 plays a crucial role in the development of the disease. In this project, we wish to investigate the in vitro effect of KCa3.1 channel blockade in isolated murine intrapulmonary arteries.

Methods and results: Murine pulmonary arteries (300-500 µm) will be mounted in isometric wire myographs for tension recording. As in ARDS, pulmonary arterial relaxation will be induced by KCa3.1 channel activation, and a dose-response curve will be established for a series of KCa3.1 blockers (Senicapoc, TRAM-34, RA-2).

Perspectives: 10% of patients admitted to an intensive care unit have ARDS with a high mortality. Current treatment methods show no reduction in mortality and are thus unsatisfactory. This preclinical project will investigate novel drugs for pulmonary circulatory collapse and oedema, and the perspective is that a successful development of new drug candidates will reduce mortality and morbidity from the disease.

P15.01 Anne Midtgaard-Thomsen
DIABETES INCREASES EARLY SIGNS OF ATHEROSCLEROTIC INFLAMMATION AND PLAQUE INSTABILITY IN LDLR^{-/-} MICE
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Introduction: People with type 2 diabetes have 2-3 times increased risk of dying from cardiovascular events. Mice are the most frequently used preclinical species for atherosclerotic studies though the relevance of the mouse models for human atherosclerotic lesion is unclear. The aim of this study was to characterize the composition of atherosclerotic aortas in a diabetic mice model.

Methods: A 17-week study was performed on LDLR^{-/-} mice. Two groups were fed HFD (n= 23 and 23) to induce atherosclerosis, and one group was fed chow diet (n=23). Diabetes was induced in one HFD group by streptozotocin. Immune composition of murine aortas was analyzed by flow cytometry, and aortic cytokine production was determined by a protein array.

Result: This study showed that diabetes causes a significant increase in percentage of monocytes/neutrophils (VD⁻CD45⁺Cd11b⁺Ly6c⁺ as % of VD⁻CD45⁺CD11b⁺) in murine aortas even though atherosclerotic plaque size is the same. Additionally, diabetes causes a non-significant increase of MCP-1 and MMP-3 expression in the aortas. Furthermore, a tendency was observed of diabetes suppressing M2-like macrophage appearance (CD206 MFI on VD⁻CD45⁺Cd11b⁺).

Conclusion: An increased recruitment and infiltration of monocytes and increase in MMP-3 can cause more unstable plaque, which has been correlated to increased risk of cardiovascular events in humans. Translational biomarkers are potential targets or can be used for preclinical evaluation of treatment effects.

P15.02 Mine Onat
CONCOMITANT ABLATION FOR ATRIAL FIBRILLATION IN PATIENTS UNDERGOING CARDIAC SURGERY

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Background: Atrial fibrillation causes 25% of strokes, and concomitant surgical ablation to treat atrial fibrillation is indicated in patients who undergo open heart surgery, using a biatrial ablation (MAZE) procedure, or a less complex pulmonary vein ablation (PVI) procedure. The choice of choosing the MAZE or PVI procedure continues to be a subject of debate. Compared with PVI, the MAZE procedure is more effective in producing sinus rhythm, but it also causes more patients to need a permanent pacemaker. Therefore, patient and procedure specific predictors of postoperative rhythm and pacemaker status need to be developed.

Methods: A retrospective single center analysis will be performed, using the study population of 544 patients that underwent open cardiac surgery and concomitant surgical ablation for atrial fibrillation from 2004 to 2015. Multivariate logistic regression analysis will be used to determine predictors of sinus rhythm twelve months postoperatively. The parameters used for regression analysis will be CHA₂DS₂-VAsC score, CHADS₂ score, gender, age, left ventricle ejection fraction, type of AF (paroxysmal or non-paroxysmal), type of ablation (PVI or MAZE) and concomitant mitral valve surgery. The level of significance will be set to 5%.

Results: Results are pending.

Perspectives: This study aims to increase our knowledge about which patients should be treated with PVI and which patients should be treated with the MAZE procedure in order to achieve the highest possible rate of patients obtaining a sinus rhythm and reducing the risk of stroke, while also decreasing the number of patients in need of a permanent pacemaker.

P15.03 Benjamin Kelly NEAR INFRARED FLUORESCENCE IMAGING OF THE LYMPHATIC VASCULATURE IN THE HUMAN ARM - A VALIDATION STUDY

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Background: In health, the lymphatic circulation secures removal and transport of excess fluid, proteins and foreign materials from the interstitial space. Due to its various functions, disease of the lymphatic system can result in chronic edema, tissue fibrosis and susceptibility to infection. The current possibilities of treatment are limited, primarily due to a lack of research and knowledge on the area.

Aim: The aim of this study is to examine the basic function of the lymphatic circulation, the impact of different interventions and the viability of the near infrared fluorescence (NIRF) method when applied to the upper extremities.

Materials and methods: The study will examine the function of the lymphatic vasculature in 10 healthy male subjects aged between 20 and 30. Furthermore, the repeatability of the method and the different interventions will be elucidated by repeating the examination two weeks after first visit. The emerging technique NIRF imaging will be applied to visualize the lymphatic vessels. The technique represents a non-invasive way of visualizing the lymphatic vasculature in vivo, enabling detailed imaging and examination of frequency, velocity and general function of the vessels under normal circumstances and when exposed to various interventions.

Perspective: The NIRF technique provides multiple new possibilities in relation to research regarding the lymphatic circulation and diseases related to this.

P15.04 Tanja
Charlotte
Frederiksen

PROLONGATION OF THE QTc INTERVAL IN ANOREXIA NERVOSA

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Background: Patients with anorexia nervosa (AN) have a more than doubled risk of cardiovascular death compared with the background population, and prolongation of the corrected QT interval (QTc) on the electrocardiogram has been suggested as an explanation. However, the actual risk of QTc prolongation in AN is still highly controversial.

Methods: In this cross-sectional study, we included 430 female patients with AN and 123 healthy female controls. We aimed to estimate the difference in the QTc interval and the relative risk of QTc prolongation (QTc>440 ms). Furthermore, we investigated predictors of QTc prolongation in patients with AN.

Results: In an unadjusted regression analysis, the mean QTc was 6.6 ms longer in AN patients compared with controls (95% CI 1.7 ms to 11.5 ms, p=0.01). After adjusting for age, treatment with selective serotonin reuptake inhibitors and levels of potassium, sodium and magnesium, the association remained (mean difference 6.8 ms, 95% CI 1.6 ms to 12.0 ms, p=0.01). The relative risk (RR) of QTc prolongation was 3.72 in AN patients compared with controls (95% CI 1.37 to 10.08, p=0.01). The higher risk of QTc prolongation in AN patients did not change after multivariate adjustments (RR=3.74, 95% CI 1.36 to 10.27, p=0.01). In AN patients, purging was positively associated with the QTc interval, while potassium levels and body mass index (BMI) were negatively associated with the QTc interval.

Conclusions: Our results show that patients with AN have a longer QTc interval and a nearly fourfold risk of QTc prolongation and suggest that purging, low BMI, and low potassium may independently contribute to determine the severity of QTc prolongation.

P15.05 Simin Berenji
Ardestani

ENDOTHELIAL FUNCTION AND CARDIOVASCULAR STRESS MARKERS AFTER A SINGLE DIVE IN AGING RATS (APOE KNOCKOUT RATS)

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The compressed gas breath during diving augments the partial pressure of oxygen, which causes the oxygen concentration of the blood to increase above normal (hyperoxia). Hyperoxia in combination with gas bubbles that develop during the decompression (ascent) phase is likely to cause oxidative stress, including transient endothelial dysfunction in venous and arterial vessels. The number of aging divers is rising and aging itself is associated with a gradual impairment of the endothelial function. These alterations play a central role in the pathogenesis of atherosclerosis and coronary artery disease. While diving and aging are independent

modulators of cardiovascular function, little is known about their combined effect. The central question is: Does diving expose old divers to more oxidative stress or not?

Method: ApoE homozygous knockout rats with impaired cardiovascular function were used as a model for aging. 10 ApoE rats (male and female) exposed to 500 kPa heliox gas (80% helium/ 20% oxygen) for 1 hr in a pressure chamber to simulate diving. Endothelial function was examined in-vitro by myograph in pulmonary and mesenteric artery. The oxidative stress biomarkers were measured in the plasma (collected from heart) and lung tissue via TBARS assay. 10 ApoE rats served as a control group.

Results and conclusion: The results of this study demonstrated that a single dive causes endothelial dysfunction in pulmonary arteries of rats with aging cardiovascular system. This seems to be caused by a reduction in the relative contribution of all three major endothelium-dependent relaxing pathways (NO, COX product(s), and EDH). These responses were aggravated even more in male rats than females.

P15.06 Anders Hostrup Larsen LEFT VENTRICULAR MYOCARDIAL DEFORMATION CAPACITY DURING EXERCISE STRESS IN HEALTHY ADULTS. A TWO-DIMENSIONAL SPECKLE-TRACKING ECHOCARDIOGRAPHY STUDY

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Background: Myocardial strain analysis is a robust marker of systolic myocardial deformation. Exercise strain analysis may provide incremental value to resting strain evaluation by demasking compensated myocardial dysfunction. However, the left ventricular myocardial deformation capacity during exercise stress testing, and the influence of gender and age, has not been investigated.

Methods: In a cross-sectional design, 67 healthy adults were included (age range, 23-80 yrs.; 49% women). All subjects underwent comprehensive echocardiographic assessment at rest and during symptom-limited semi-supine exercise test. Global longitudinal strain (GLS) was determined by two-dimensional speckle-tracking echocardiography.

Results: Average absolute numeric increase in GLS was 5.3% (95% CI; 4.8 to 5.7%) equivalent to a 26.7% relative increase in GLS with no significant between-group differences observed ($p = 0.27$). GLS magnitude at peak exercise was without significant differences between age groups (group 1, -26.2%; group 2, -25.4%; group 3, -24.7%, $p = 0.07$). No difference was found in peak exercise GLS (women -25.5%; men -25.2%; $p = 0.48$). Linear regression analysis revealed a significant but weak correlation between peak GLS and age ($r = 0.30$, $p = 0.02$). We found no correlation between peak exercise GLS and maximal heart rate, between peak exercise GLS and mean arterial blood pressure, or between peak exercise GLS and body mass index.

Conclusion: In healthy adults, GLS increased significantly during exercise stress independently of gender and age. Peak exercise GLS was independent of maximum heart rate and mean arterial blood pressure.

P15.07 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 pericardial patches or extensive surgery on the leaflets. For new valve material, an improved generation of CorMatrix has been developed in order to adapt the high-pressure on the left side of the heart. CorMatrix will act as a scaffold that is recellularized with the patients own cells and, therefore, becomes the perfect material for reconstruction of the mitral valve. The aim of this study was to design and test a mitral valve posterior leaflet reconstruction.

Materials and methods: An open chest acute porcine model was used (n=6) together with a piece of 8x4 cm 2-ply CorMatrix that consisted of P1-P3 scallops with an arc cutout of 1x3 cm for P2. On cardiac bypass, through the left atrium, the native P1-P3 was excised. The new posterior leaflet was attached at two points on each papillary muscle and at the annulus with Prolene 4-0. Magic stitches were performed at the new commissures. An epicardial echocardiography was performed at baseline and after the reconstruction, together with pressure measurements.

Results: Annulus diameter closed: 23.2±4.0 mm VS. 18.7±1.6 mm*, Tenting area: 160±25 mm²VS. 90±7 mm²*, Tenting height: 9.5±0.8 mm VS. 7.2±1.4 mm*, Coaptation length: 7.8±1.3 mm VS. 10.1±1.2 mm*. *: Statistically different from baseline (p<0.05).

Conclusion: The reconstruction of the posterior leaflet showed to be fully functional and comparable to native valve with no gradient or regurgitation. The suture plasty downsized the annulus. Further investigation is needed to explore if a ring annuloplasty would be beneficial, and to evaluate the recellularization potential of the material.

P15.08 Gro Grunnet Pløen RENIN AND ANGIOTENSINOGEN OVEREXPRESSING D374Y-PCSK9 MINIPIGS: A PIG MODEL PRONE TO DEVELOP HYPERTENSION AND ACCELERATED HUMAN-LIKE CORONARY ATHEROSCLEROSIS

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Atherosclerosis is the leading cause of cardiovascular disease in the western world. It is a chronic inflammatory disease in the vascular wall, fueled by the retention and modification of LDL. Hypertension is a risk factor for atherosclerosis and the renin-angiotensin system plays a vital role in initiation and progression of the disease. Upon reduction in blood pressure, renin induces angiotensin II (ATII) activation. ATII induces smooth muscle cells (SMCs) of the blood vessels to contract and stimulates release of the hormone aldosterone, thereby raising the blood pressure. Similarities with humans with regard to lipoprotein metabolism and cardiovascular anatomy

make the pig an attractive disease model. Using genetic engineering and cloning by somatic cell nuclear transfer, we have previously created Yucatan minipigs overexpressing a mutated human gene, D374Y-PCSK9. The animals develop severe hypercholesterolemia and atherosclerotic lesions exhibiting several features of human atherosclerosis, though only to a lesser extent in the coronary arteries, which is the hallmark of human atherosclerosis. Coronary atherosclerosis can be accelerated several fold in these pigs by inducing hypertension through surgical banding of the suprarenal aorta (unpublished data). This procedure is cumbersome and impractical, and we envisage that genetically induced hypertension in our D374Y-PCSK9 pigs will accelerate the disease progression and pronounce the important coronary disease phenotype. The hypertensive minipig model created in this study may aid in developing novel therapeutic targets and validate imaging biomarkers for e.g. coronary atherosclerosis in humans.

P15.09 Leila Louise Benhassen CHARACTERIZATION OF TWO DIFFERENT SUBVALVULAR ANNULOPLASTIES FOR AORTIC ROOT REPAIR

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Background: 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 standardization or comparison have yet been made for the different types of annuloplasties.

Aim: The aim is to compare two different annuloplasties in a porcine experimental model after performing: a) Conventional Dacron-ring, b) Suture annuloplasty and c) Native control valve.

Material and methods: 21 pigs of 80 kg were enrolled. A force transducer was inserted in the aortic annulus to assess segmental stress distribution.

Results: Overall, we observed greater accumulated forces in the control group compared to the two interventions (native 4.4 N vs. Dacron 3.6 N vs. suture 3.6 N). For the native aortic valve, there was a significantly lower force at the non-left commissure compared to the left-right commissure. A similar pattern of force distribution was observed after the Dacron-ring. After the suture annuloplasty, another pattern of force distribution was observed, being significantly lower at the right-non commissure compared to the left-right commissure, shifting the maximal force distribution away from the right sinus to the left sinus.

Conclusion: As expected, the force measurements were smaller after both types of annuloplasties compared with the control group due to the support of the annuloplasties. The altered stress distribution after the suture

annuloplasty suggests a remodeling effect compared with the Dacron-ring. Our findings are clinically relevant for assessment of these procedures in vulnerable aneurysmatic tissue.

- P15.10 Andreas Engel DOES REMOTE ISCHEMIC PRECONDITIONING INFLUENCE PLATELET
Krag AGGREGATION IN PATIENTS UNDERGOING HEAD AND NECK CANCER
MICROSURGICAL RECONSTRUCTION? A RANDOMIZED CONTROLLED TRIAL

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Background: Cancer induces an increased risk of thromboembolism. Large head and neck tumors are primarily treated by surgical resection followed by reconstruction of the defect. An autologous free tissue flap is transferred to the defect, and the blood supply is reestablished by microvascular anastomoses to vessels on the neck. Thromboses in the microvascular anastomoses or the patient's systemic circulation is a major complication to head and neck cancer microsurgical reconstruction.

Aim: The aim of the trial is to investigate if remote ischemic preconditioning (RIPC) influences platelet aggregation in head and neck cancer patients undergoing microsurgical reconstruction.

Methods and materials: The effect of RIPC on primary hemostasis in head and neck cancer patients undergoing microsurgical reconstruction is investigated in an ongoing randomized controlled trial. Sixty patients will be randomized 1:1 to RIPC or sham. RIPC is carried out intraoperatively 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, intraoperative, and postoperative phase. Platelet aggregation, platelet count, von Willebrand factor, and P-selection will be analyzed.

Results: Fifty-six patients have been included in the trial. We expect to present data from sixty patients.

Conclusion: If RIPC attenuates platelet aggregation, the risk of perioperative thrombosis may be reduced. Hence, the chance of successful microsurgical reconstruction is increased, and patients can proceed to adjuvant oncologic therapy in a timely fashion.

- P16.01 Johnni ETIOLOGIES OF ATRIOVENTRICULAR BLOCK IN YOUNGER PATIENTS - A
Rudbeck- NATIONWIDE DANISH STUDY
Resdal

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Background: Atrioventricular block (AVB) is the most common indication for pacemaker implantation, and incidence increases with age. Idiopathic and age-related fibrosis of the cardiac conduction system is the most common cause of AVB. In younger patients, underlying diseases other than idiopathic fibrosis may cause AVB, but the knowledge about their prevalence is scarce.

Identifying an underlying disease may allow individualized device selection for these patients.

Purpose: To investigate the prevalence and etiologies of AVB in younger patients in Denmark.

Methods: Patients were identified from the Danish Pacemaker and ICD Register. We included all patients treated with a first pacemaker because of AVB during the period 1 January 1996 – 31 December 2015 who were younger than 50 years at implantation. Medical records were reviewed, and clinical information and test results were obtained to evaluate the etiology.

Results: We identified 1183 patients who met the inclusion criteria. In 142 patients, the medical record was missing. Underlying etiologies were as follows: structural heart disease 3.3%, ischemic heart disease 1.2%, congenital heart disease 40%, congenital AVB 93%, disease 0.2%, muscular dystrophy 1.4%, sarcoidosis 0.7%, Lyme disease 0.6%, genetic 0.4%, cardiac surgery complication 16.2%, radiofrequency ablation complication 3.7%, endocarditis 1.8%, other 7.9% and unknown 48.8%.

Conclusion: In a nationwide cohort, an underlying disease as cause of AVB is identified in half the patients referred for first pacemaker implantation at age <50 years. Whether more intensive and structured pre-implantation workout, including genetic testing, increases this proportion should be investigated.

P16.02 Kasper Glerup MAJOR DIFFERENCES IN ADVANCED LIFE SUPPORT TRAINING STRATEGIES
Lauridsen AMONG DANISH HOSPITALS - A NATIONWIDE STUDY

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Background: Advanced life support (ALS) training may increase survival from in-hospital cardiac arrest. Efficient ALS training includes practice of both technical and non-technical skills in a realistic setting with frequent retraining to avoid decay in ALS skills.

Aim: To investigate ALS training strategies in Danish hospitals.

Methods: We included all public, somatic hospitals in Denmark with a cardiac arrest team (n=46). Online questionnaires were distributed to resuscitation officers in each hospital.

Results: In total, 44 hospitals replied (response rate: 96%). ALS training was conducted in 43 hospitals (98%). Median (range) ALS course duration was 3.5 (1-8) hours. Retraining was conducted every year (28%), every second year (49%), less frequent (19%) and 4% retrained with different intervals depending on healthcare profession. E-learning was used as a part of ALS training by 21%. Overall, 28% conducted ALS training in a meeting room or auditorium, while 72% conducted ALS training in a simulation unit or clinical setting. Chest compressions were trained on a bed by 63%, on a stretcher or table by 27%, and no hospitals used a backboard for training. Median (range) time spent on team training was 2.0 (0.5-5) hours. Overall, 51% conducted ALS training for all cardiac arrest team members (i.e. nurses, physicians, and orderlies) and 18% performed in-situ simulated cardiac

arrests in addition to regular ALS training. Non-technical skills were evaluated during or after team training by 56%. Overall, 2% reported to practice specific team leadership skills.

Conclusion: There are major differences in duration, retraining interval, and methods for ALS training in Danish hospitals.

P16.03 Camilla Mains Balle PLATELET FUNCTION IN CRITICALLY ILL ADULTS TREATED WITH EXTRACORPOREAL MEMBRANE OXYGENATION

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Background: Extracorporeal membrane oxygenation (ECMO) is life-saving treatment by a heart-lung-machine that can support the functions of the heart and/or lungs in patients suffering from respiratory or cardiac failure. Introducing ECMO has greatly improved the treatment of these critically ill patients, but morbidity and mortality associated with ECMO remain high. This is predominantly due to a coagulopathy that occurs during ECMO treatment resulting in bleeding and/or thrombosis.

Aim: Our aim is to investigate platelet function in patients treated with ECMO. Secondly, we aim to investigate the association between platelet function and the incidence of bleeding and thrombosis during ECMO treatment.

Methods: We plan to include 25 patients undergoing ECMO treatment at Aarhus University Hospital. The first blood sample is collected on the first morning following ECMO initiation. Subsequently, blood samples are obtained every morning the next seven days and on the 14th and 21st day, if the patient is still receiving ECMO. Platelet function is estimated by impedance aggregometry (Multiplate®) and by flow cytometry. Furthermore, we measure standard coagulation parameters as well as immature platelet count and immature platelet fraction.

Results: The samples are currently being collected and analyzed. We expect the inclusion to be completed in March 2018.

Perspectives: We expect the present study to provide new knowledge regarding platelet function in patients treated with ECMO. By clarifying the underlying mechanisms of the coagulopathy occurring in these patients, we aim to improve their anticoagulant treatment and thereby reduce the incidence of bleeding and/or thrombosis.

P16.04 Sebastian Udholm HEALTH PROFILE AND EXERCISE FUNCTION IN ADULTS WITH SMALL ATRIAL SEPTAL DEFECTS

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Background: Our register-based analyses of all Danish patients with a small unrepaired atrial septal defect (ASD) showed higher mortality in ASD patients with no closure compared with both the general population and with patients with a closed ASD. Furthermore, the patients without closure had an increased risk of pneumonia, atrial fibrillation and stroke. We wish to characterize patients with small, unrepaired ASD and challenge the perception that these patients are as healthy as previously expected.

Methods: Nationwide descriptive study. The patient group consists of adult patients with small, unrepaired ASD. Exercise testing was performed using an ergometer cycle, and results were compared with healthy age-matched controls. Patients received questionnaires (National Health Profile), allowing us to compare patients with the general population.

Results: 111 patients were included (mean age: 31 yrs) and 238 excluded. The defect was still open in 22 patients (19.8%). Peak VO₂ was lower in patients when compared with the control group (29.4 vs. 42.3 mL/kg/min; p=0.001). One-third (32.1%) of ASD patients experienced higher levels of stress compared with the general population (22.5%; p=0.01). Most ASD patients (90%) self-assessed their health to be excellent or good, which is comparable to the general population (92.3%, p=0.66). A minority (19.5%) self-assessed their physical function to be excellent or good, which is fewer than in the general population (37.5%; p=0.001).

Conclusion: Most defects were spontaneously closed. Exercise impairment was present in the entire cohort. In addition, patients with small unrepaired ASD evaluate their physical function less well and experience higher levels of stress.

P16.05 Omeed
Neghabat

UNCERTAIN DETECTION OF STENT FRACTURE BY THREE-DIMENSIONAL INTRAVASCULAR OPTICAL COHERENCE TOMOGRAPHY

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Background: Three-dimensional (3D) intravascular optical coherence tomography (OCT) is available for online guiding during percutaneous coronary intervention and could be of particular value in detection of acute stent fracture. Cardiac motion during image acquisition can cause artifacts mimicking stent fracture, possibly leading to mistreatment. This limitation calls for physician awareness.

Methods: OCT scans from coronary arteries implanted with a fully bio-resorbable scaffold (Fantom, REVA Medical, San Diego, CA, USA) were analyzed for fractures using a dedicated 3D rendering software package (QAngio® OCT, Medis, Leiden, Netherlands). The Fantom scaffold is readily visualized in 3D OCT and allows for clear visualization of the struts. Identification of apparently discontinued struts led to careful evaluation of the scan for potential artifacts, including guide wire shadows, overlying tissue or thrombus, rotational artifacts, and other volume rendering errors.

Results: In 181 patients with fully analyzable 3D OCT images, we identified 9 (5%) cases with actual strut fractures and 92 (51%) cases with artifacts resembling strut fractures. Among artifacts, 26 (28%) were due to longitudinal compressed image distortion, 24 (26%) due to unflushed blood,

22 (24%) due to rotational artifact, 9 (10%) due to console error, 4 (4%) due to longitudinal elongated image distortion, 4 (4%) due to thrombus overlay, and 3 (3%) due to a wobbling wire artifact.

Conclusion: In-procedure detection of strut fracture by 3D OCT may emerge as gold standard in treatment with bioresorbable scaffolds. However, to avoid unnecessary intervention, physicians should be able to rule out artifacts mimicking fractures.

P16.06 Benjamin Asschenfeldt Arlander

IMPACT OF CONGENITAL HEART DISEASE ON BRAIN DEVELOPMENT

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Introduction: Survivors of congenital heart defect (CHD) surgery live with an involuntary cerebral burden. Magnetic resonance imaging of the brain has shown abnormalities in brain morphology and hence impaired neurodevelopment. The cerebral alterations are thought to be inflicted in utero and caused by the circulatory pathophysiology. As brain development and maintenance occur throughout adulthood, a main concern emerges whether CHD patients are affected into adulthood. The present study investigates the long-term neurodevelopmental outcome in adults who were diagnosed in childhood with a simple congenital heart defect to clarify late-life cerebral comorbidities.

Methods: A prospective long-term follow-up study on simple CHD patients treated at Aarhus University Hospital between 1975 and 1995. The study population will consist of 30 surgically closed ventricular septal defect patients, 30 unclosed atrial septal defect patients and 30 matched controls. All participants will have an MRI scan of the brain and a standard neuropsychological test, both completed on the same day. These data allow an examination of brain macrostructural and microstructural morphology and assessment of cognitive domains and abilities.

Results: Results are pending.

Perspectives: The present study will demonstrate how simple congenital heart defect affects the brain sequentially across the age continuum and into adulthood. Furthermore, it will contribute to uncover possible cerebral comorbidities and further clarify the necessity for late life follow-up on simple CHD patients.

P16.07 Julie Brogaard Larsen

A NEW CLOT FORMATION AND LYSIS ASSAY IN SEPSIS-RELATED DISSEMINATED INTRAVASCULAR COAGULATION

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Background: Changes in fibrinolysis may contribute to disseminated intra-vascular coagulation (DIC) and mortality in sepsis. We aimed to investigate associations between fibrinolysis and morbidity in septic shock patients using a new dynamic clot-lysis assay.

Materials and methods: Blood samples were obtained in 14 patients with septic shock within 24 hours after admission at an intensive care unit. We registered Sequential Organ Failure Assessment (SOFA) score, DIC score and 30-day mortality and analysed clot-lysis assay (in-house clot formation and lysis assay, activated with tissue factor and tissue-plasminogen activator (tPA)), plasma-tPA and -plasminogen activator inhibitor-1 and standard coagulation tests. Fibrin concentration (absorbance) was registered continuously for 2h, and 50% lysis time and total fibrin formation was registered.

Results: We observed three distinct clot-lysis patterns: a group with flat curves (no/little net fibrin formation) (n=4), a group with normal fibrin formation curves (n=6), and a group with normal fibrin formation but no lysis (lysis resistance) (n=4). Patients with flat curves and patients with lysis resistance had higher morbidity expressed with DIC and SOFA scores and also had more abnormal standard coagulation tests than the normal group, most pronounced for the flat curve group.

Perspectives: Due to the low number of patients, our preliminary results must be interpreted with care and should be validated in a larger cohort. However, an abnormal clot lysis seems to be associated with higher morbidity and more pronounced coagulation disturbances in septic shock and thus may have a place in future diagnosis and prognosis.

P16.08 Jacob Gammelgaard Schultz NO-SGC-CGMP PATHWAY STIMULATION LOWERS PULMONARY VASCULAR RESISTANCE IN A PORCINE MODEL OF ACUTE PULMONARY EMBOLISM

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Background: Pulmonary vasodilators as add-on to current treatment strategies in acute pulmonary embolism (PE) may improve right ventricular (RV) unloading and hence improve outcome in patients with acute PE.

Purpose: To investigate if stimulation of the nitric oxide (NO)-soluble guanylate cyclase(sGC)-cyclic guanosine monophosphate (cGMP) pathway by inhaled NO, intravenous riociguat or intravenous sildenafil causes pulmonary vasodilation and improves RV function in a porcine model of acute PE.

Methods: Two large autologous PEs (20cm x 1cm) were administered to Danish Landrace pigs (60 kg). Animals were randomized to four increasing clinical equivalent concentrations of either vehicle (n=6), NO (n=6), riociguat (n=6) or sildenafil (n=6). Sham animals (n=4) underwent instrumentation but received no PE or treatment. The hemodynamic and biochemical response was evaluated at baseline, after PE and after each concentration by biventricular catheterisation, invasive pressure measurements, respiratory

parameters and blood analysis. Data were analysed by two-way ANOVA with multiple comparisons and are presented as mean \pm SEM.

Results: Administration of the PEs caused a 3-fold increase in pulmonary vascular resistance (PVR) compared to sham (PE, vehicle: 352 ± 28 vs. sham: 118 ± 8 , $p < 0.0001$) All treatment strategies lowered PVR compared to Vehicle (Dose 4, vehicle: 313 ± 41 vs. NO: 157 ± 12 , riociguat: 155 ± 23 , sildenafil: 89 ± 6 , $p < 0.0001$). Systemic blood pressure was unaltered.

Conclusion: Stimulation of the NO-SGC-cGMP pathway by inhaled NO, riociguat, and sildenafil reduces pulmonary vascular resistance in a porcine model of acute PE without lowering of systemic blood pressure.

P16.09 Mikkel Giehm-Reese A RANDOMIZED STUDY OF CONTACT FORCE IN ATRIAL FLUTTER ABLATION

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Introduction: Atrial flutter (AFL) is a macro-reentry tachycardia in the right atrium. Cavotricuspid isthmus ablation (CTIA) using radiofrequency (RF) energy is a well-established first line therapy of typical AFL. When performing catheter ablation, contact force (CF) applied during radiofrequency energy delivery is a powerful predictor of creating transmural lesions. However, prospective data documenting the superiority of ablation guided by the real time CF monitoring over the standard procedure are missing. The Lesion Size Index (LSI) estimates the size of the lesion created by ablation. It takes account for the nonlinear relationship between the size of the lesion and its three main determinants (CF, power and duration) and may, therefore, be an effective means to precisely dose the amount of the delivered RF energy. This may prevent both insufficient lesion creation and complications due to excessive energy delivery.

Aim: The aim of the present study is to evaluate if CF-guided ablation targeting a specific value of LSI is superior to standard radiofrequency catheter ablation (RFCA).

Methods: 150 patients undergoing first time CTIA for typical AFL will be included in the study and randomized in a 1:1 manor into two groups. First group: RFCA will be guided by real-time CF monitoring and LSI, targeting a LSI of 7.0 with a minimum of 6.8 and CF 10-30 g. Second group: The operator will be blinded to real time CF and LSI. The primary endpoint will be reconnection measured at an invasive electrofysiological procedure 3 months after the primary RFCA. The two groups will be compared by intention-to-treat analysis.

P16.10 Stine Andersen EFFECTS OF ENTRESTO IN PULMONARY HYPERTENSION AND RIGHT HEART FAILURE

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Background: Right heart failure is the predominant cause of death in patients with pulmonary arterial hypertension. Entresto is a combined angiotensin II receptor blocker and neprilysin inhibitor used in the treatment of left heart failure. We aimed to evaluate if treatment with entresto could prevent the progression of right ventricular (RV) hypertrophy and failure in rats with pulmonary hypertension and right heart failure.

Methods and results: Pulmonary hypertension was induced in rats by combined exposure to the vascular endothelial growth factor-receptor antagonist SU5416 and hypoxia (SuHx). To separate pulmonary from cardiac effects, isolated right heart failure was induced by pulmonary trunk banding (PTB) in another set of rats. In both models, treatment with entresto (60 mg/kg/day) was initiated after establishment of RV dysfunction. In the SuHx rats, treatment with entresto reduced RV pressure (mean difference: -12 ± 4 mmHg, $p=0.004$) and RV hypertrophy (RV weight corrected for tibia length) (mean difference: -2.3 ± 0.7 mg/mm, $p=0.003$) compared to vehicle. In the PTB model, entresto had no effects on RV pressure or RV hypertrophy. Compared to vehicle, treatment with entresto reduced systemic mean arterial blood pressure in both the SuHx rats (mean difference: -12 ± 5 mmHg, $p=0.02$) and the PTB rats (mean difference: -20 ± 7 mmHg, $p=0.02$).

Conclusion: Treatment with entresto reduces RV pressure and hypertrophy in the SuHx model of pulmonary hypertension. This may be attributed to pulmonary effects, as similar results were not seen in the PTB rats. Further analyses are needed in order to assess effects on the pulmonary vasculature, RV contractility and RV remodeling.

P17.01 Eva Rydahl

WHY ALL THESE CESAREAN SECTIONS? CAN INCREASED MATERNAL AGE BE AN EXPLAINING FACTOR?

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Background: The cesarean section rate in Denmark has increased by 30% over the last decades. Cesareans are associated with adverse events and long-term health consequences for both mother and child. The increased cesarean rate may be due to advanced maternal age. Women with advanced maternal age (>35 years) have doubled over the last decades and have now exceeded 22%. Maternal age > 35 years correlates with complicated pregnancy outcomes and may influence the cesarean rate.

Methods: A retrospective cohort study on all Danish births 1998-2014 ($n=1,100,000$). Maternal age of less than 30 years serves as reference compared to the following age groups: 30-34; 35-39 and 40+. Primary outcome measure is cesarean section. Multivariate regression models with adjustment for demographic, health, pregnancy, fetal and obstetric characteristics were performed and further stratified by parity.

Results: A positive association between cesarean section and increased maternal age was found after adjusting for confounders. In comparison with

the reference group (women age <30), nulliparous women age 40+ experienced an OR 3.45, 95% CI [3.23-3.67] for cesarean section and multiparous women age 40+ experienced an OR 1.90, 95% CI [1.80-1.99], respectively.

Conclusions: This study finds a positive association between advanced maternal age and increased rate of cesarean sections. The association persists even after adjustment for several confounders. Management culture and care provider factors may also contribute to the increased cesarean rate.

P17.02 Trine Muhs
Nielsen

EARLY TERM CAESAREAN SECTION AND COGNITIVE FUNCTION IN CHILDHOOD - A 7-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL

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Background: Evidence suggests that children born early term (gestational week 37 and 38) experience more developmental problems than children born full term (gestational week 39 and 40). However, this evidence is from observational studies only. We previously conducted a randomized trial of elective caesarean section at 38 versus 39 weeks of gestation. The children who participated in this trial are now 6-8 years old, making it possible to obtain a valid assessment of their long-term development.

Materials and methods: Seven-year follow up of newborns from a randomized trial. All the mothers who participated in the trial (early term n=636, full term n=638) are invited to rate their children using the Strengths and Difficulties Questionnaire (SDQ). In a subset of 47 children in each group (the eldest children born in Aarhus), we will perform an intelligence test using the Wechsler Intelligence Scale for Children (WISC). Results will be analysed according to the intention-to-treat principle.

Results: Based on our power calculation, we will be able to detect a statistically significant mean difference of 10 points or more (significance level at 0.05) in the WISC with a power of 90%. No power calculation has been done for the SDQ, as all mothers are invited to participate. The background characteristics and methods will be presented in more detail. Data and results are pending.

Conclusion: This study aims to evaluate whether early term birth is associated with long-term developmental problems as indicated by several observational studies. The randomized design enables us to reduce the risk of confounding by underlying pathologies associated with or leading to early term birth.

P17.03 Christine Rohr Thomsen NEW PRINCIPLES FOR QUANTITATIVE ELASTOGRAPHY OF THE HUMAN UTERINE CERVIX

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Aim: The aim of this project is to develop a new principle for identification of pregnant women at risk of preterm birth. The principle is based on the ultrasound technique termed elastography combined with either 1) reference caps developed at Aarhus University, interposed between the ultrasound transducer and the cervix, or 2) a force measurement device, developed in collaboration with Massachusetts Institute of Technology, USA.

Background: Preterm birth is a leading cause of neonatal morbidity as well as mortality. Very often softening of the uterine cervix precedes preterm birth. Today, the methods for evaluating the biomechanical properties of the human uterine cervix are inconsistent. In a recently finished PhD project, we have shown that vaginal ultrasound scanning combined with elastography software constitutes a promising tool for evaluation of the cervix. In collaboration with engineers at Aarhus University and MIT, we have developed promising improvements of the technique.

Material and method: We will refine the two methods at both phantoms and pregnant women concerning the optimal force, analysis of the recording, evaluation of the heterogeneity of the cervix, intra- and inter-observer variability, physiological changes during pregnancy, association between our biomechanical assessment and the cause of labor induction.

Perspective: The perspective is better identification and treatment of pregnant women at risk of preterm delivery. In addition, the methods could be used to plan induction of labor for post-term pregnancy.

P17.04 Anne Raabjerg Kruse CHALLENGES IN A CLINICAL TRIAL RANDOMIZING PATIENTS TO FAST-TRACK OR ROUTINE DISCHARGE AFTER ELECTIVE CESAREAN SECTION

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Background: Cesarean section (CS) is a procedure with prolonged hospital stay compared to vaginal delivery in multiparous women. The hypothesis of this study is that reduced length of hospital stay can be performed without compromising quality. Different aspects must be evaluated before this approach can be implemented in clinical routine. The main purpose of this study is to examine fast-track discharge from the patient's perspective.

Methods: The study is a randomized controlled trial with 142 multiparous women allocated to either fast-track (<28 hours) or routine discharge (>48 hours) after elective CS. The participants answer questionnaires about their sense of security, pain, the use of analgesia, mobilisation measured by an activity monitor, breastfeeding and the use of the healthcare system.

Results: The study started recruitment in October 2016. Until November 2017, 118 patients were assessed for eligibility. Nineteen patients did not meet the

inclusion criteria. Seventy-eight patients accepted receiving written and oral information about the project, of which 47 patients accepted participation. Of the 31 patients who declined to participate, the main reasons were to avoid hospital stay for more than 48 hours (N=12) or to avoid fast-track discharge (N=11).

Discussion: The rate of participation is less than expected. To be able to finish the project within a specific deadline, we adjusted the procedure of recruitment in order to increase the rate of participation. Furthermore, a new site has been added to increase the amount of eligible patients.

P17.05 Siri Nana
Halling Steen TZA QUANTIFICATION OF THE LATENT RESERVOIR IN HIV-1 PATIENTS:
PREDICTING TIME TO VIRAL REBOUND DURING ART INTERRUPTION

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Background: Current HIV cure research aims to reduce the latent reservoir, leading to either total eradication of infected cells or a prolonged time of viral remission in HIV patients off antiretroviral therapy (ART). However, current assays cannot provide a precise estimate of the reservoir size and measures do not correlate with virological control off ART. Collectively, this challenges the clinical evaluation of cure strategies. The novel TZM-bl assay (TZA) has shown promising results in quantifying the reservoir. In this study, we aim to evaluate whether reservoir size as measured by TZA predicts the time to viral rebound during analytical interruption of ART.

Materials and methods: The TZA utilizes TZM-bl cells to quantify replication-competent HIV-1. CD4+ T-cells from HIV-1-positive patients are isolated and reactivated through anti-CD3/CD28 mAb-coated microbeads. Afterwards, they are cultured in a 96-well plate seeded with TZM-bl cells. This cell line carries an integrated copy of β -galactosidase (B-gal) under the control of HIV-1 LTR promoter. HIV-1 will infect the TZM-bl cells and chemiluminescence can be measured and determine the number of HIV-1-positive wells.

Results: No results from this study have been obtained yet.

Conclusion: The size of the latent HIV-1 reservoir is a potential predictor of the time to viral rebound in patients off ART, but no current assays provide an accurate measurement of the reservoir. If the TZA provides a more accurate estimate of the reservoir than existing assays, it will be able to guide future studies aimed at a cure for HIV or achieving ART-free remission.

Keywords: TZA; HIV-1 reservoir; Time to viral rebound

P17.06 Sara Larsen ANGIOTENSIN RECEPTOR TYPE 1 AUTOANTIBODIES AND ENDOTHELIN RECEPTOR TYPE A AUTOANTIBODIES IN PREECLAMPTIC WOMEN: IS PREECLAMPSIA AN AUTOIMMUNE DISEASE?

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Aim: To investigate Angiotensin Receptor Type 1 autoantibodies (AT1-AABs) and Endothelin-Receptor Type A autoantibodies (ETA-AABs) in pre-eclamptic women and in healthy pregnant women.

Background: Preeclampsia (PE) is a hypertensive disorder affecting 2-8% of all pregnant women. Autoimmune diseases are associated with increased risk of developing PE. Our hypothesis is that autoantibodies against the Angiotensin Receptor Type 1 and Endothelin Receptor Type A play a role in the development of PE.

Materials: Serum samples from patients with Gestational Hypertension (GH), Preeclampsia (moderate + severe/HELLP) and from healthy pregnant women, collected at Aarhus University Hospital.

Methods: Autoantibodies are detected using a bioassay consisting of spontaneously beating cardiomyocytes. Immunoglobulins from serum are prepared using ammonium sulfate precipitation and added to the cell culture. The specificity of the autoantibodies is identified using receptor specific antagonists.

Preliminary results: 42 serum samples from patients with GH or PE were analyzed. All serum samples were positive for AT1-AABs. Furthermore, 12 of these samples were also positive for ETA-AABs. Three serum samples from healthy, pregnant controls were also analyzed and were all negative for both AT1-AABs and ETA-AABs.

P17.07 Frederik Rothemejer Jacobsen IMPACT OF A TLR9 AGONIST ON THE FUNCTIONAL CAPACITY OF NK CELL SUBSETS TO INHIBIT HIV-1 PROPAGATION EX VIVO.

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Antiretroviral therapy effectively suppresses HIV replication to undetectable in blood, but does not cure HIV infection because of viral persistence. Recent clinical trials have induced transcription of persistent HIV using latency reversal agents but have not led to profound reductions in the size of the viral reservoir, thus indicating that the "killing" aspect of such "shock-and-kill" strategies must be improved. Therefore, enhancing the killing capacity of immune effector cells is a promising strategy for eliminating infected cells following HIV latency reversal. Now we are using Toll-like receptor 9 (TLR9) stimulation to enhance NK cell-mediated killing of HIV-transcribing cells in clinical studies. My research year project goal is to identify the most efficacious NK cell subset(s) for inhibiting HIV spreading in autologous CD4+ T cell cultures. To do this, we will stimulate peripheral blood mononuclear cells ex vivo with a TLR9 agonist followed by isolation of distinct NK cell subsets. We will then assess the capacity of these NK cell subsets to impact

longitudinal virus production by autologous CD4+ T cells. Furthermore, we will define the role of monocytes in the activation of these NK cell subset(s). The characterization of these effector NK cells will provide an accessible efficacy biomarker whose activation status can be followed longitudinally to predict endpoint outcomes (e.g. reductions in the HIV reservoir size) and as a therapeutic target in our clinical trials evaluating TLR9 agonist therapies.

P17.08 Julie Lyngsø DOES COFFEE CONSUMPTION IMPACT ON FERTILITY TREATMENT?

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Background: Infertility is a major public health concern. Yet, even though a great impact is expected, we still do not know the exact implications of modifiable lifestyle factors, such as coffee consumption, in relation to a successful fertility treatment.

Objective: To investigate whether daily coffee consumption is associated with the clinical pregnancy rate and live birth rate among Danish women in a Medically Assisted Reproduction (MAR) cohort.

Method: A cohort study with prospectively collected exposure data, including approximately 1,700 Danish women and their partners enrolled for start of treatment at the Fertility Clinic, Aarhus University Hospital, 2010-2015. Information about exposure to daily coffee consumption was obtained from self-administered questionnaires before start of treatment. Based on data from the questionnaires and treatment charts, the "Aarhus MAR cohort" was generated. Information on the outcome variables, clinical pregnancy rate and live birth rate, was obtained by linkage of data from Danish nationwide registries. The association between daily coffee consumption and a successful fertility treatment will be analysed using logistic regression. The main analysis will be restricted to the first treatment cycle and stratified according to type of treatment. A secondary analysis using cycle specific exposure data will be performed for all consecutive treatment cycles. Missing information will be handled using multiple imputation techniques.

Perspectives: Study results will be used in the counselling of women and couples seeking fertility treatment.

P17.09 Clara Faurby Maarup THE POTENTIAL RISK OF ENDOMETRIAL CANCER IN WOMEN WITH ENDOMETRIAL HYPERPLASIA - A LONG-TERM FOLLOW-UP

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Background: Endometrial hyperplasia (EH) is a precancerous lesion characterized by excessive proliferation of the endometrium and is strongly related to the development of endometrial cancer. The existing guidelines for clinical follow-up of women diagnosed with EH are sparse, and there are no studies including long-time follow-up in Danish women initially diagnosed with EH investigating the risk of recurrence of EH or endometrial

cancer. The aim of this study is to investigate the long-term prevalence of recurrence of EH or endometrial cancer in Danish women initially diagnosed with EH.

Methods: All women diagnosed with EH at Randers Regional Hospital between 2000 and 2015 are included. The women who did not receive a hysterectomy as initial treatment for EH are invited to gynaecological examination with ultrasound and endometrial biopsies taken using mini-hysteroscopy. Patient interviews, questionnaires and medical records are used to collect further data.

Results: Data will be collected from winter 2017 to summer 2018. The outcome measures are the prevalence of recurrence and endometrial cancer after initial diagnosis with EH along with the correlation between treatment method and recurrence and endometrium cancer.

Conclusion: The study can contribute to the goal of being able to identify women with EH who has a high risk of progression to cancer. Furthermore, data can be used to evaluate the need for long-term follow-up after the initial diagnosis of EH and help revise the existing guidelines on clinical follow-up of these women.

P17.10 Thomas Berger

IMPACT OF BOWEL GAS AND BODY OUTLINE VARIATIONS ON TOTAL ACCUMULATED DOSE WITH INTENSITY MODULATED PROTON THERAPY IN LOCALLY ADVANCED CERVICAL CANCER PATIENTS

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Background: Standard treatment in Locally Advanced Cervical Cancer (LACC) is a combination of: image guided adaptive brachytherapy, concomitant chemotherapy and External Beam Radio Therapy (EBRT) commonly delivered using X-Rays. Using protons for the EBRT phase could improve the sparing of the Organs at Risk (OARs), but proton dose deposition is sensitive to density changes.

Purpose: To quantify the dosimetric impact on targets and OARs of: 1) bowel gas cavities and 2) body outline variations occurring during a complete course of RT in LACC patients with Intensity modulated proton therapy (IMPT).

Material and methods: IMPT dose plans were generated targeting the internal target volume with 45Gy in 25 fractions and pathologic lymph nodes with 55-57.5Gy. In total, seven LACC patients were analyzed through 475 modified CTs that were generated to evaluate the effect of: 1) gas cavities, 2) outline variations and 3) the two combined. The anatomy of each fraction was simulated by propagating gas cavities contours and body outlines from each daily Cone Beam Computed Tomography to the planning CT. Hounsfield units corresponding to gas and fat were assigned to the propagated contours. D98 and D99.9 for targets and V43Gy for OARs were recalculated on each modified CT. Total dose was evaluated through dose volume histogram addition across all fractions.

Results and conclusion: Body outline variations had larger dosimetric impact than gas cavities. We found limited dosimetric impact of variations in bowel gas cavities and patient outline on the accumulated dose to target and

OARs during 25-fraction EBRT course using 4-field IMPT. (Valid for patients with no drastic weight loss.)

- P18.01 Ole Nymark MATERNOFETAL TISSUE DISTRIBUTION OF VITAMIN B12 INFLUENCED BY B12 STATUS AND FORM: AN EXPERIMENTAL STUDY IN PREGNANT RATS
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- Purpose: Vitamin B12 (B12) is mandatory for a normal fetal development. Here we question the influence of maternal B12 status on fetal transfer of cyano-B12 (CN-B12), the form present in vitamin pills, and hydroxy-B12 (HO-B12), the form present in food items.
- Method: Female Wistar rats were impregnated while on a B12-rich (n=12) or a B12-deficient diet (n=12) starting 4 weeks prior to pregnancy and continuing throughout pregnancy. Labeled CN-B12 (n = 6) or HO-B12 (n = 6) were administered orally 24 h prior to sacrifice, two days before term. Liver, kidney, and fetal compartment (uterus, placenta, and fetuses) were measured for labeled B12.
- Results: Mean (range) fetus weight was higher (2.8 (1.9-3.4) g) in the B12-replete than the B12-deplete group (1.4 (1.2-2.1) g) (p<0.0001), while the total number of fetuses were the same. Approximately 30% of the administered B12 was recovered in the examined tissue, independently of maternal B12 status or B12 form administered. In accord with previous studies, more HO-B12 than CN-B12 went to the maternal liver (p=0.031). More than 15% of administered dose homed for the fetal compartment with a significantly higher tissue accumulation of CN-B12 than HO-B12 in B12-deplete fetuses (p<0.0001), but not in B12-replete fetuses.
- Conclusions: Maternal B12 status influence fetal size and distribution of different forms of B12. It remains to be clarified whether the accumulated B12 is converted to active vitamin in the fetuses.
- P18.02 Gitte Øskov Skajaa PARITY INCREASES INSULIN REQUIREMENTS IN PREGNANT WOMEN WITH TYPE 1 DIABETES
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- Objective: The aim of the current study was to evaluate the insulin requirements in women with type 1 diabetes during pregnancy and to test whether parity affects insulin requirements.
- Research design and methods: We conducted an observational cohort study consisting of women with type 1 diabetes who gave birth at Aarhus University Hospital in 2004-2014. Daily insulin requirements and HbA1c were collected from every visit during pregnancy.

Results: 380 women with a total of 536 pregnancies were included in the study. The mean age was 31.1 yrs and pre-pregnancy HbA1c 6.7% (59.7 mmol/mol). Parity was: P0=43%, P1=40%, P2=14% and P3+4=3%. Insulin requirements from week 11-16 decreased statistically significantly 4% and rose significantly from week 19 to delivery with a peak of 70% at week 33-36. Overall, insulin requirements increased significantly with parity. The unadjusted differences between P0 and P1, P2 and P3+4 were 9, 12 and 23%, respectively. After adjusting for BMI, age, pre-pregnancy HbA1c and duration of diabetes, differences were 13, 20 and 36%. We also observed an adjusted difference between P1 and P3+4 at 20%.

Conclusions: Our data show that parity per se increases insulin requirements during pregnancy between 9% and 36% in type 1 diabetes and confirm that insulin dosages exhibit a characteristic pattern with a modest early decrease and a pronounced late increase during pregnancy. This provides valuable information to achieve tight glycemic control throughout pregnancy. Being the first report to show this, our findings may have direct clinical implications for pregnant type 1 diabetes patients.

P18.03 Malou Eva
Maria Pinto
Barbosa

LONG-TERM OUTCOME AFTER LATE REPAIR OF THE ANAL SPHINCTER SECONDARY TO OBSTETRIC TRAUMA

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Background: Vaginal delivery and obstetric anal sphincter injuries (OASIS) is the most common cause of fecal incontinence (FI) in women. Anal sphincter repair (sphincteroplasty) is the standard management of FI when a structural defect in the anal sphincter is recognized.

Objective: The aim of this study was to assess the long-term functional results following late anal sphincter repair secondary to obstetric trauma.

Methods and materials: 407 women operated with a late anal sphincter repair within a 15-year period in Denmark (1 January 1990 to 31 December 2005) were included. Functional outcome and symptom specific quality of life score were assessed by self-reported, validated questionnaires.

Results: Mean follow-up time was 11.0 years. At the time of follow-up, mean Wexner incontinence score was 8.1 (95% CI 7.7 - 8.6) and mean St. Mark's score was 10.7 (95% CI 10.2 - 11.2). 58% were fully continent for solid stools and 33% for liquid stools. Only 6% were completely continent for flatus. Long lasting incontinence symptoms (≥ 11 years) were significantly associated with a higher incontinence score (9.2 vs. 6.7, $p < 0,05$)

Conclusion: Later sphincter repair has acceptable long-term functional outcome. However, accurate patient selection is essential when choosing patient suitable for anal sphincter repair. Furthermore, realistic explanation of the likely outcome is necessary. Nonetheless, the operation is well tolerated and has a low morbidity.

- P18.04 Kristine Frederiksen DOES REMOTE ISCHAEMIC PRECONDITIONING INFLUENCE THE COMPLEMENT SYSTEM IN PATIENTS UNDERGOING HEAD AND NECK CANCER SURGERY? A RANDOMIZED CONTROLLED TRIAL
- K. Frederiksen^{1,3}, A.E. Krag^{1,2,3}, J.B. Larsen^{1,3}, B.J. Kii^{2,3}, S. Thiel⁴, A.M. Hvas^{1,3}*
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- Background: Surgical resection of large head and neck tumours often involves reconstruction of the defect with transfer of the patient's own tissue. This is a major surgical intervention with risk of ischaemia-reperfusion injury in the transferred tissue. Furthermore, surgical site infection is a frequent complication after head and neck cancer surgery. The lectin pathway of the complement system has been identified as a contributing factor in ischaemia-reperfusion injury and may be involved in postoperative infections defence. Remote ischaemic preconditioning (RIPC) is an innovative treatment against ischaemia-reperfusion injury.
- Aims: To investigate 1) if RIPC influences lectin pathway protein levels in head and neck cancer patients undergoing reconstructive surgery and 2) the association between lectin pathway protein levels and the risk of surgical site infections.
- Methods: Sixty patients undergoing head and neck cancer surgery are randomized 1:1 to RIPC or sham. RIPC is carried out intraoperatively by four 5-minute periods of upper extremity ischemia induced with an inflatable tourniquet. Each ischemia period is separated by five minutes of reperfusion. Blood samples are collected at baseline, 6 hours postoperatively, and on the 1st postoperative day. Lectin pathway protein levels are measured with time-resolved immunofluorometric assay.
- Results: Patient inclusion will be completed in December 2017. Samples will be analysed during the spring of 2018.
- Perspectives: If RIPC reduces ischaemia-reperfusion injury and surgical site infections, more patients can proceed to adjuvant radiotherapy in a timely fashion, thus improving treatment efficacy and survival.
- P18.05 Khoa Manh Dinh LOW-GRADE INFLAMMATION AMONG HEALTHY PREMENOPAUSAL WOMEN TAKING COMBINED ORAL CONTRACEPTION DEPENDS ON DOSE AND TYPE OF PROGESTIN: RESULTS FROM THE DANISH BLOOD DONOR STUDY (DBDS)
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- Background: CRP is a well-established marker of inflammation, and several lifestyle factors affect the CRP level. A slightly elevated CRP level, known as low-grade inflammation (LGI), is associated with increased risk of several diseases, e.g. cardiovascular disease. Combined oral contraception (OC) is

a strong predictor of LGI among premenopausal women, but the mechanism behind this effect is unknown. This study raises the question whether the increased risk of LGI associated with the use of OC differs between the types of progestin.

Methods: Plasma CRP levels in 6,989 women from the Danish Blood Donor Study were measured. All participants completed a standard questionnaire on lifestyle factors. Type of OC was identified by ATC codes in the Danish National Prescription Register. Association between LGI (CRP level >3 mg/L and ≤10 mg/L) and OC groups (2nd, 3rd and 4th generation) was explored by multivariable logistic regression analysis. Adjustment for BMI, age, smoking, and leisure physical activity was performed. Results are presented as OR with 95%CI.

Results: LGI was found more frequent among 2nd generation (35%) than 3rd generation (31%) and 4th generation (24%) OC users. 4th generation OC use predicted a lower risk of LGI than 2nd generation use (OR=0.68, CI: 0.46;0.98).

Conclusion: 4th generation OC users had a significantly lower risk of LGI than 2nd generation OC users. Our finding indicates that the CRP increase found in OC users depends on type and content of progestin. Interestingly, this demonstrates an inverse correlation between the increased risk of venous thromboembolism associated with 4th generation OCs and the risk of LGI. This issue must be further investigated.

P18.06 Ida Charlotte Bay Lund DETECTING CONFINED PLACENTAL AND FETAL MOSAICISM USING CELL-FREE DNA SEQUENCING ON MATERNAL PLASMA

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Introduction: Mosaicism is characterized by a normal and an abnormal cell-line. Test results on cell-free DNA (cfDNA) in maternal plasma can be compromised as the fraction of abnormal cells may be too low for detection. We wanted to explore the detection rate of confined placental and fetal mosaicism using cfDNA sequencing on maternal plasma.

Methods: We retrieved data on chorionic villus samplings (CVS) and amniocenteses (AC) from mosaic pregnancies obtained from January 2014 to July 2017. On maternal plasma, we retrospectively performed cfDNA testing by genome-wide massive parallel sequencing.

Results: CfDNA detected placental mosaicism in 64% (16/25): trisomy 21 (n=3), trisomy 13 (n=1), autosomal chromosomes trisomy 2,7,8,11,12,16,22 (n=7), sex (n=4) and a copy number variation (CNV) of 60 Mb (n=1). The nine false negative cases of placental mosaicism using cfDNA testing were: trisomy 21 (n=2), trisomy 13 (n=1), autosomal chromosomes trisomy 9, 12 (n=2), sex (n=3) and a CNV of 50 Mb (n=1). The mean level of mosaicism in the CVS was 62.0% (CI, 47.1-76.9) in the detected cases and 38.4% (CI, 17.9-59.0) in the false negative cases (p=0.0501). Fetal mosaicism, confirmed by AC, was detected by cfDNA sequencing in 80% (four out of five cases). A

mosaic trisomy 21 case, which was confirmed by CVS (84% trisomy 21 cells) and AC, was missed by cfDNA.

Conclusion: It seems that the level of mosaicism in the invasive samples predicts whether or not cfDNA testing is able to detect the abnormal cell-line. However, a high-level mosaicism of trisomy 21 was missed. More studies are needed to explore how mosaicism is distributed in the placenta.

P18.07 Maria Birgitte Søndermølle RISK FACTORS FOR NON-SUCCESSFUL TUBERCULOSIS TREATMENT

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Background: To end the global Tuberculosis (TB) epidemic, the World Health Organisation (WHO) requires an 85% treatment success. Despite well-developed healthcare systems, low-incidence countries still fail to reach this goal.

Aim: To develop a prognostic model including clinical risk factors to identify patients needing special attention to complete treatment.

Methods: A retrospective cohort study on TB-treated patients at Aarhus University Hospital, Denmark, from 2001 to 2007. Bootstrap-validated multivariate logistic regression on WHO-defined treatment outcome with construction of a nomogram to provide easy calculation of probability of non-successful outcome.

Results: The study included 381 cases. During TB treatment, 3.4% of cases died, while 5.5% were lost to follow-up (LTFU). Overall treatment success was 82.9%. Disseminated TB, Greenlandic origin and C-reactive protein >50 mg/L were the strongest predictors of non-success, while age 40-65 years predicted success. Sub-group analysis demonstrated that death was associated with bilateral infiltrates, haemoglobin, sedimentation rate and C-reactive protein, and LTFU was associated with Greenlandic origin and alcohol abuse.

Conclusion: This prognostic model allows valid prediction of non-successful TB treatment and informs treatment selection based on risk factors identifiable at time of diagnosis. Greenlandic origin needs special attention to complete treatment. Severe disease (assessed by X-ray and blood samples) and disseminated disease indicate early death, underlining the importance of earlier diagnosis of active TB.

P18.08 Simon Larsen IDENTIFICATION OF NOVEL INNATE IMMUNODEFICIENCIES IN PATIENTS WITH PARALYTIC POLIOMYELITIS

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Introduction and background: Polio virus (PV) is highly infectious and spreads by the fecal-oral route, with the majority of those infected developing

symptoms resembling a common cold or flu. Only in a small fraction (0.1-0.5%), the infection progresses to paralytic poliomyelitis involving the motor neurons of the spinal cord with severe outcomes ranging from neurological deficits to death. But why is this minority so severely affected? Much is yet to be discovered with regard to the mechanisms by which PV spreads to the CNS causing neuron destruction.

Hypothesis: We hypothesize that differential susceptibility to CNS infection may be caused by rare mutations in genes encoding parts of the innate immune system.

Methods: We have recruited a cohort of 18 Danish patients with paralytic poliomyelitis. Genomic DNA has been isolated and subjected to Whole Exome Sequencing and peripheral blood mononuclear cells (PBMCs) have been isolated and cryo preserved for functional studies with live attenuated PV or relevant ligands.

Results: In the bioinformatic analyses, we identified a number of rare genetic variants in genes encoding proteins involved in interferon induction, pro-inflammatory response and autophagy.

Further studies: We are currently doing functional studies with PBMCs stimulated with PV or relevant ligands. We will measure mRNA expression of various pro-inflammatory and antiviral cytokines as well as protein expression of components of autophagy to see if there is a link between the phenotype and the genetic variants identified.

P18.09 Diana Skaaning

DOES PARENTAL SUPERVISION IN REGULAR ORAL STIMULATION PROLONG THE DURATION OF BREASTFEEDING AMONG PREMATURE INFANTS? A SINGLE-BLINDED RANDOMIZED CONTROLLED TRIAL

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Breastmilk is the healthiest nutrition for all newborn infants. The Danish Board of Health recommends that premature infants are exclusively breastfed for 6 months (1). Today nearly all premature are exclusively breastfed at discharge, but this rate is rapidly decreasing to 30% before six months after birth (2).

Premature infants have low muscle tone and thereby lower capability to establish a sufficient intra-oral vacuum. Studies have demonstrated that intervention with oral stimulation may shorten the transition period from gavage to oral feeding (3). We hypothesized that professional oral stimulation prolongs the duration of breastfeeding in premature infants.

The trial includes 200 premature infants who are randomized to oral stimulation or control. Families in the intervention group are guided by occupational therapists providing a specific program of oral stimulation twice a day. The effect of oral stimulation will be evaluated by 1) duration of exclusively breastfeeding and 2) the level of intra-oral vacuum.

The study is ongoing and 158 infants have been included.

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- P18.10 Line Kolding DRUG SAFETY IN PREGNANCY - DRUG USE DURING PREGNANCY AND EFFECTS ON THE CARDIAC FUNCTION OF THE FETUS
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- Objectives: To investigate a potential effect of drugs on the fetal cardiac function by use of conventional, 3D, and 4D ultrasound assessments, by comparing exposed and unexposed pregnancies.
- Methods: We have constructed a normal reference group of 15 pregnant women in pregnancy week 26 without drug exposure during pregnancy. The following was recorded and measured: The ventricular shortening fraction by fetal tricuspid and mitral annular plane systolic excursion (f-TAPSE/f-MAPSE) by conventional and electronic Spatio Temporal Image Correlation (eSTIC). The atrial function by E/A index and the global cardiac function by modified Myocardial Performance Index (Mod-MPI). The heart size, valve function, flows, and an estimated weight were obtained for all of the fetuses. In the first study, we will compare the measurements from the normal reference group with pregnancies exposed to the antidepressant sertraline.
- Preliminary results: In the reference group, the mean gestational week was 26+2. The mean f-TAPSE and f-MAPSE by conventional M-mode was 5.81 mm (sd 0.71) and 4.02 mm (sd 0.75), respectively. The mean f-TAPSE and f-MAPSE by eSTIC M-mode was 5.28 mm (sd 0.56) and 3.69 mm (sd 0.77), respectively. The mean E/A ratio on the left and the right side was 0.68 (sd 0.04) and 0.74 (sd 0.05), and the mean mod-MPI on the left side was 0.47 (sd 0.06).
- Conclusion: We have constructed a reference group for future studies with medication exposure during pregnancy.
- P19.01 Rasmus Fuglsang Nielsen DIETARY FIBER AND WHEY PROTEIN: THE EFFECTS ON GLUCOSE METABOLISM IN SUBJECTS WITH ABDOMINAL OBESITY
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- Background: The Metabolic Syndrome (MeS) is associated with an increased risk of developing diabetes and cardiovascular disease. MeS is defined by central obesity in combination with glucose intolerance, hypertension and dyslipaemia (high triglycerides or low HDL cholesterol).
- These risk factors of MeS can be modified by diet. Research indicates that dietary fibers and whey protein have beneficial effects on the glucose metabolism. Long-term study results are, however, inconsistent.

Objective: The purpose of this trial was to examine the individual and combined effect of whey protein and dietary fibers from wheat in a 12-week dietary intervention. Outcomes were insulin resistance estimated by an oral glucose tolerance test (OGTT), fasting glucose, glucagon and insulin levels and incremental area under the curve following a 3-hour meal test.

Methods: 73 abdominally obese subjects were included in a randomized, double-blinded intervention study. Subjects were randomized to one of four intervention groups of either low/high protein and low/high fiber: LP/LF, LP/HF, HP/LF, HP/HF.

Bread and cereals based on wheat bran with either high or low fiber content were incorporated into the regular diet. Whey protein or Maltodextrin was consumed twice daily. OGTT and a meal test were performed at baseline and at the end of the intervention.

Results: We found no effect on the glucose and insulin parameters. We await the analyses of glucagon and incretin hormones GIP and GLP-1.

Conclusion: Whey protein or dietary fiber per se, and in combination, does not significantly affect glucose metabolism and insulin sensitivity in this 12-week study in subjects with MeS.

P19.02 Elin Rakvaag EFFECTS OF WHEY PROTEIN AND DIETARY FIBER ON PLASMA TRIGLYCERIDES: A RANDOMIZED, CONTROLLED, DOUBLE-BLIND DIETARY INTERVENTION TRIAL IN ABDOMINALLY OBESE SUBJECTS

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Background: The triglyceride (TG) response following a meal (postprandial) is a predictor of future cardiovascular events, and acute studies have indicated that both whey protein (WP) and dietary fiber may separately reduce postprandial TG. It is not known whether combining these two dietary factors provide synergistic benefits on the TG response.

Aim: We investigated the separate and combined effects of WP and dietary fiber on fasting and postprandial TG in a longer-term study.

Methods: We conducted a 12-wk intervention with 2x2 factorial design. 65 adults with abdominal obesity were randomized to 1 of 4 groups: WP-LoFi (60 g/d WP + 10 g/d fiber), WP-HiFi (60 g/d WP + 30 g/d fiber), MD-HiFi (60 g/d maltodextrin (MD) + 30 g/d fiber), MD-LoFi (60 g/d MD + 10 g/d fiber). Before and after the intervention, we conducted a standardized meal test; subjects consumed a fat-rich meal, and blood samples were collected fasting and for 6 h after the meal. Incremental areas under the curve (iAUC) for plasma TG responses were calculated.

Results: Postprandial TG was reduced in WP-LoFi compared with MD-LoFi (Δ iAUC: -110.7 mmol/L x 6h, 95% CI: $-220.0, -1.4$; $p = 0.046$). In addition, fasting TG was reduced in WP-LoFi compared with MD-LoFi (median ratio: 0.58, 95% CI: 0.44, 0.77, $p < 0.001$). No effects were observed for WP-HiFi (Δ iAUC: -82.2 mmol/L x 6h, 95% CI: $-188.2, 23.7$; $p = 0.18$. Fasting TG: median ratio 0.80, 95% CI: 0.61, 1.05; $p = 0.15$).

Conclusion: Compared with MD, 12 weeks of WP consumption reduced both fasting and postprandial TG, but only in the group receiving low fiber

products. The combination of WP and high fiber does not seem to provide additional benefits on postprandial TG.

P19.03 Elias Didrik
Francis
Zachariae

TWO STRUCTURES FROM A SINGLE GENE: INVESTIGATING THE DIFFERENTIAL FOLDING OF SOD3

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Extracellular Superoxide dismutase (SOD3) is a zinc and copper-containing enzyme that is responsible for the dismutation of the reactive oxygen species superoxide. SOD3 has previously been shown to exist in two distinct folding variants. These variants are characterized by the connectivity of their disulphide bridges and by their enzymatic activity. One folding variant presents enzymatic activity (α SOD3), while the other, iSOD3, is enzymatically inactive. It has previously been established that the folding of these variants is an intercellular process and not a result of extracellular regulation. Until now, SOD3 is the only protein identified in which the expression of a single gene leads to two distinct protein structures. However, the mechanisms involved in the folding and maturation processes are yet to be described.

In the present PhD project, we aim to elucidate the process by which this differential folding is achieved. With a set of SOD3 mutants, lacking key metal-coordinating amino acid residues, we investigated the importance of copper and zinc in the folding of SOD3. We show that substitution of amino acid residues involved in the coordination of zinc, copper or both copper and zinc leads to differences in the quantities of SOD3 that are expressed. Importantly, we observe that enzymatic activity is absent in all mutants. Furthermore, we have indications that the ratio between iSOD3 and α SOD3 expressed is affected by the loss of metal binding, suggesting that these cofactors are actively involved in the folding process.

This study could provide insight into the mechanisms that allow one gene to display two structures.

P19.04 Anne Sophie
Koldkjær
Sølling

TREATMENT WITH ZOLEDRONIC ACID SUBSEQUENT TO DENOSUMAB IN OSTEOPOROSIS

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Background: Denosumab (Dmab) is an antibody against receptor-activator of nuclear factor kappa-B ligand that prevents recruitment and differentiation of osteoclasts. Treatment with Dmab decreases bone resorption and fracture risk. After discontinuation, however, bone resorption increases and bone mass is lost. At present, treatment with Dmab is considered to be life-long. The purpose of the study is to investigate if infusion of zoledronic acid (ZOL) can prevent the increase in bone turnover and bone loss seen in patients stopping treatment with Dmab.

Methods: The study is a randomized, open label, interventional study in 60 patients with osteoporosis. Treatment with ZOL will be administered 6 months or 9 months after the last injection of Dmab or when bone turnover is increased (s-carboxy-terminal collagen crosslinks $> 1.26\mu\text{g/l}$ or BMD loss $>$

5% at any site). If s-CTX increases above 1.26 ug/l during the second year, another infusion of ZOL will be administered. Baseline characteristics will be presented using ANOVA. Changes in BMD 1 year after the ZOL infusion will be investigated using paired t-tests, and the proportion of patients who fails to maintain BMD will be compared between groups using chi-sq test. Multiple regression analyses will aim to identify factors affecting change in BMD.

Results: 42 patients have been included in the study, and the remaining participants are booked for baseline visit.

Perspectives: If bone loss can be prevented by ZOL expenses on otherwise life-long Dmab, treatment can be saved and potential long-term side effects of Dmab (atypical femur fractures and osteonecrosis of the jaw) can be prevented.

P19.05 Katrine Meyer Lauritsen THE EFFECT OF EMPAGLIFLOZIN ON CARDIAC AND KIDNEY METABOLISM IN PERSONS WITH TYPE 2 DIABETES

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Sodium-glucose cotransporter 2 (SGLT-2) inhibitors increase urine glucose excretion and are a novel treatment for type 2 diabetes. SGLT-2 inhibitor treatment has shown remarkable effects with a reduction in cardiovascular mortality by 38% and slower progression of diabetic kidney disease. It has been hypothesized that the observed increase in circulating ketone bodies during SGLT-2 inhibitor treatment may mediate these beneficial effects. Ketone bodies are an energy-efficient super fuel for the heart and kidney due to a lower oxygen consumption compared to glucose and fatty acid oxidation.

We aim to test this hypothesis in a randomized, placebo-controlled crossover study of the cardiac and renal effects of SGLT-2 inhibitor treatment in type 2 diabetes. 12 subjects will complete two four-week interventions of 25 mg once-daily Empagliflozin/placebo in random order with a one-week washout period in-between. We hypothesize that a modest but constant increase in circulating ketone bodies will reduce cardiac oxygen consumption and improve cardiac efficiency by increasing ketone body oxidation at the expense of free fatty acids and glucose oxidation. Cardiac oxygen consumption, energy efficiency, free fatty acid oxidation and glucose oxidation will be measured by PET tracer techniques. In addition, we will perform an oral glucose tolerance test, indirect calorimetry, muscle biopsy and fat biopsy to determine whole-body and tissue-specific effects of SGLT-2 inhibitor treatment.

P19.06 Karolina Snopek SYMPTOMS OF DIABETIC POLYNEUROPATHY ARE RELATED TO FALLS IN PATIENTS WITH TYPE 2 DIABETES

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Objective: Distal sensorimotor polyneuropathy may cause impaired balance and unstable gait, which combined with decreased joint mobility and incoordination leads to an increased risk of falls. Falls may have serious consequences, including decreased mobility, physical inactivity and higher morbidity and mortality.

Materials and methods: We performed a cross-sectional analysis of survey data on patients with type 2 diabetes included in the cohort established by the Danish Center for Strategic Research in Type 2 Diabetes (DD2) in 2011. Questionnaires were sent to 7,011 patients with type 2 diabetes, and 77% of patients returned the questionnaire with complete data on falls and neuropathic symptoms.

Results: We analyzed data from 5,315 patients with type 2 diabetes who had answered questions concerning MNSI and fall frequency (median age of 62 years, 40% females, and median diabetes duration of 6.4 years \pm 2.3).

Falls were reported in 17% (896) of patients during the past year, and 9% (505) had experienced two or more falls.

Conclusion: Cross-sectional data from this large national database show that patients with type 2 diabetes with 4 or more neuropathic symptoms have a 3-4 fold higher risk of falls unrelated to alcohol consumption, smoking, physical activity, BMI, gender and age.

P19.07 Marlene Christina Nielsen DEVELOPMENT AND VALIDATION OF AN ASSAY TO MEASURE CD163 BOUND TO EXTRACELLULAR VESICLES

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The receptor CD163 is expressed by human monocytes and macrophages, and a soluble form of the receptor (sCD163) is present in blood. sCD163 is a biomarker in a number of diseases, including acute and chronic liver inflammation. However, sCD163 is unable to distinguish between the two. Soluble CD163 can be subdivided into two fractions: a true soluble form related to ectodomain cleavage induced by acute inflammation (ecto-CD163) and an extracellular vesicle associated form (EV-CD163), which may be associated with chronic inflammation. Our hypothesis is that the amount of EV-CD163 is higher in chronic liver inflammation compared to acute.

Different methods for EV-isolation exist, and defining the optimal method is a subject of great debate. Therefore, the aim of this study was to compare

different isolation methods for EV-CD163 in respect to practicability, efficiency, and reproducibility.

EDTA plasma and serum from healthy donors were used, and EVs were isolated using two different isolation methods, ExoQuick and TX-114. After isolation, total sCD163, ecto-CD163, and EV-CD163 were measured using ELISA.

We found that 17% of sCD163 was EV-bound when isolating EVs from plasma using ExoQuick, whereas 36% of sCD163 was EV-bound in serum. Furthermore, when isolating EVs using TX-114, we found that 6% of sCD163 was EV-bound in plasma, compared to 8% in serum.

Our results indicate that the concentration of EV-CD163 in healthy donors greatly depended on the material used (plasma or serum) along with the isolation method chosen. These results highlight the importance of methods chosen for EV-isolation, which may heavily impact results from studies with EV-isolation and analysis.

P19.08 Kristian
Alsbjerg
Skipper

INTERVENING GENETICALLY WITH TYPE II DIABETES

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Clinical gene therapy treatments are currently showing great promise worldwide. Effective therapies of a wide range of severely disabling genetic conditions have raised hope for the development of genetic treatments of many other diseases.

Type II diabetes (T2D) is a worldwide epidemic disease with more than 250,000 diagnosed in Denmark alone. It is estimated that 800,000 Danes are at high risk of developing T2D. The disease is associated with increased mortality and morbidity and represents a major health problem. A recently identified transmembrane protein of the Vps10p-domain receptor family, SorCS1, has been shown to increase insulin sensitivity by modulating the activities of the insulin receptor. Furthermore, SorCS1-deficient mice develop pre-diabetes in adulthood and T2D at high age. Together, these unprecedented observations document increased IR expression and signaling upon delivery of SorCS1, and this calls for methods of establishing persistent production of SorCS1 in diseased animals. In the PhD project, presented here, the aim is to elucidate SorCS1 function in type II diabetes and to evaluate genetic modulation of SorCS1 activity as a potential new treatment for type II diabetes.

P19.09 Mette Ji Riis-
Vestergaard

β-ADRENERGIC REGULATION OF UNCOUPLING PROTEIN 1 IN A NEW HUMAN BROWN ADIPOCYTE CELL MODEL

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Aim: Brown adipose tissue (BAT) can increase energy expenditure via uncoupling protein 1 (UCP1), which makes BAT an attractive therapeutic target in the treatment of obesity and type 2 diabetes. However, little is known about the molecular and biochemical properties of human brown adipocytes due to lack of adequate cell models. Non-shivering thermogenesis in human BAT is primarily controlled by β -adrenergic innervation but the primary receptor involved remains unclear. We have developed an immortalized polyclonal human brown adipocyte cell line (hBA) from adipocytes obtained from neck surgery. The aim of the study was to evaluate the expression of β -adrenergic receptors and the effect of β -agonists on the thermogenic marker UCP1 in this cell model compared to an immortalized white adipocyte cell line (hWA) originated from the same donor.

Method: The two cell models (hBA and hWA) were cultured to maturity and evaluated for expression of adrenergic receptors using qPCR. Moreover, the effects of selective β -adrenergic agonists were estimated based on UCP1 expression.

Results: The β_1 receptor was the predominant adrenergic receptor expressed in mature hBA, whereas the β_2 - and β_3 receptors were equally expressed at a very low level in both cell types. However, the UCP1-response to the selective β_3 agonist CL316.243 (1 μ M) was greater in hBA compared to hWA, and no difference in response to the selective β_1 agonist denopamin (10 μ M) or β_2 agonist procaterol (0.1 mM) was observed in the two cell types.

Conclusion: This new human BAT cell model displays responsiveness, especially to β_3 agonists, and may represent a useful tool in the understanding of human brown adipocyte function.

P19.10 Rasmus Kold-Christensen MONITORING REACTIVE METABOLITES BY ELISA

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Rapid and high-throughput quantification of unstable metabolites in biological samples is difficult using conventional methods. To solve this problem, we have recently developed a novel type of enzyme-linked immunosorbent assay (ELISA), which utilizes a chemical probe that is able to react chemoselective with the metabolite of interest, thereby stabilizing it and allowing ELISA detection, a method we have termed ReactELISA.

A ReactELISA for the disease causing metabolite methylglyoxal is under development and is being optimized for quantification of methylglyoxal in blood plasma from diabetic patients. Another ReactELISA for the metabolite acetoacetate, a product from lipid metabolism, has been made and is being used to screen for small molecules that can perturb lipid metabolism.

P20.01 Angela Pärn THE ROLE OF PCSK9 IN BRAIN DEVELOPMENT AND BEHAVIOR

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Proprotein convertase subtilisin kexin 9 (PCSK9) induces lysosomal degradation of lipoprotein receptors and is recognized for its role in regulation of cholesterol metabolism. The main target of PCSK9 is hepatic LDL receptor, but it also targets related lipoprotein receptors VLDLR and ApoER2. In adults, PCSK9 is mainly produced by the liver, while it is highly and transiently expressed in the embryonic telencephalon; the structure that develops into cerebrum in the mature brain. In addition, PCSK9 is expressed at high levels in cerebellum. The function of PCSK9 in the brain is not known, however, the PCSK9 expression pattern has a significant overlap with VLDLR and ApoER2. During development, these receptors function in regulation of neuronal migration and neurite outgrowth as signaling receptors in the Reelin pathway. Impaired Reelin signalling results in a characteristic phenotype, where neurons fail to organize themselves into distinct layers of the cortical plate. Our preliminary results show that PCSK9 overexpression in the embryonic brain arrests neuronal migration, and we hypothesize that PCSK9 regulates migration by controlling the levels of VLDLR and ApoER2. To further investigate this, we will study the effect of PCSK9 on migration of neural progenitors in vivo by in utero electroporation. In addition, we will assess the levels of ApoER2 and VLDLR in tissue overexpressing PCSK9 by Western blotting. Finally, we will evaluate cortical and cerebellar function of a PCSK9 deficient mouse model by rotarod performance test, Barnes maze, and sociability three-chamber task. Results obtained from this research will greatly help to understand the role of PCSK9s in the brain.

P20.02 Sara Raquel Almeida Ferreira INVOLVEMENT OF THE CD163 RECEPTOR IN THE ALPHA-SYNUCLEIN INDUCED NEURODEGENERATION IN PARKINSON'S DISEASE

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The occurrence of inflammatory changes in the brain and periphery in Parkinson's Disease (PD) patients has been documented in recent years. However, the proteins involved in such process are yet to be defined. How the brain and the peripheral immune system interact, and how this interaction plays a role in the induced neuro-inflammatory processes taking place during PD, is still undetermined. Our fundamental hypothesis is that the immune system is actively involved in the neurodegenerative process in PD and, therefore, its modulation may have therapeutic potential. CD163 is a scavenger receptor expressed in macrophages but not in microglia in the brain. The CD163 receptor can be shed from the membrane and produce a soluble protein that can be measured in fluids. Our lab has observed infiltration of CD163+ cells into the area of neurodegeneration in a PD toxic rat model. In addition, we have data showing changes of CD163 (at cellular and soluble level) in PD patients. Altogether, our data strongly suggests a biological role for the CD163 macrophages in the disease, and we believe it may be a key population involved in the crosstalk between the periphery and brain. Therefore, we aim to determine whether the receptor CD163 is directly involved in the immune cascade occurring in PD and how it might relate to alpha-synuclein, a protein with a key role in the neurodegenerative

process occurring in the disease. We will analyse alpha-synuclein neurotoxicity in CD163 knock-out animals. In addition, we will perform experiments to evaluate the influence of alpha-synuclein in the CD163 population and shedding, as well as the interaction between alpha-synuclein and the CD163 receptor.

P20.03 Filomena Iannuzzi FYN TYROSINE KINASE AS POTENTIAL TARGET FOR ALZHEIMER'S DISEASE TREATMENT

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Alzheimer's disease (AD) is a severe neurodegenerative condition characterized by extracellular Amyloid- β -plaques and intracellular neurofibrillary tangles. A β plaques are the result of the amyloidogenic cleavage of the amyloid precursor protein (APP) due to defects in APP trafficking and processing in neurons. It has been previously reported that Tyr682 phosphorylation on the C-terminal domain of APP influences APP sorting and trafficking in neurons. Tyr682 phosphorylation is increased in AD neurons, and it is responsible for A β production in affected neurons. The goal of my PhD project is to investigate whether APP Tyr682 phosphorylation can be targeted to design new diagnostic strategies for AD patients. We analysed neurons from 10 patients and 6 healthy controls, and we found an increased APP Tyr682 phosphorylation in 7 out of the 10 AD neurons. We then questioned which Tyr kinase might be responsible for such increased Tyr682 phosphorylation. We found that Fyn Tyr kinase binds APP only when Tyr682 is phosphorylated, and this binding is increased in AD patients. Consistently, Tyr kinase inhibitors prevent APP Tyr682 phosphorylation and reduce Fyn binding to APP. WB analysis showed an increase in APP Tyr682 phosphorylation and in the APP cleavage to generate APP intracellular peptides when Fyn is overexpressed. Such increased Fyn-mediated APP cleavage results in an extensive neuronal toxicity. We plan to further investigate APP/Fyn interaction in neurons using a new procedure called Biomolecular fluorescence complementation (BiFC), in which APP and Fyn are fused to unfolded complementary fragments of a fluorescent reporter protein and then directly transfected in neurons.

P20.04 Sarah Christine Christensen DRUG DELIVERY INTO THE BRAIN: BELIEVE IT TO BE THE RIGHT TARGET ON THE BLOOD-BRAIN BARRIER OR NOT

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Delivery of antibody-based drugs into the brain is hindered by the blood-brain barrier. Consequently, only 0.1-0.2% of the systemically injected antibody will enter the brain under normal physiological conditions. In order to overcome this challenge, a promising strategy is to take advantage of the endogenous transport system present in brain endothelial cells. By targeting central transporter proteins, the approach aims to enhance the brain uptake and thereby substantially increase the probability of success for the immunotherapy.

In line with this strategy, we will investigate expression levels of Basigin, CD320, CD98hc, and Glut1, and their ability to transcytose across the brain endothelial cells. These transmembrane proteins have been shown to have high transcript levels in mouse brain endothelial cells 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 by a high-content imaging system.

Our investigation of the trafficking routes in brain endothelial cells may reveal new target candidates for improved antibody delivery across the blood-brain barrier.

P20.05 Camilla
Højland
Knudsen

HUMAN PLURIPOTENT STEM CELLS FOR SPINAL CORD REPAIR

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To date, spinal cord repair remains one of the most challenging problems in regenerative medicine, and there is currently no effective cure for spinal cord injury (SCI). Olfactory ensheathing cells (OECs) have shown great promise in promoting axon regeneration in the CNS after nerve damage. However, the availability and immune-compatibility of readily obtainable cells pose major limitations in the advancement of this exciting field of research. Producing OECs from human pluripotent stem cells (hPSCs) would allow for unlimited expansion of cells and at the same time permit the creation of cell lines that are immune-compatible to patients. In this manner, generating differentiation protocols that allow the production of OECs from hPSCs will enable us to further investigate the therapeutical use of OECs in spinal cord repair.

This project, therefore, aims to investigate the signaling pathways required for the differentiation of hPSCs into OECs. We will use next generation sequencing to analyse the transcriptome of primary rodent OECs to characterise transcription factors important for OEC specification. We will test the OECs by characterisational and functional in vitro studies and, finally, the reparative potential of the hPSC derived OECs in in vivo transplantation studies in rat SCI models.

P20.06 Lasse Reimer

INFLAMMATION ASSOCIATED KINASE, PKR, BLOCKS ALPHA-SYNUCLEIN VESICLE-BINDING BY PHOSPHORYLATING NOVEL SERINE AND THREONINE SITES: A NEW MECHANISM IN NERVE TERMINALS?

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Synucleinopathies are a group of neurodegenerative diseases, including Parkinson's disease, multiple system atrophy and dementia with Lewy bodies, with the common characteristics of accumulation of intracellular inclusions in the central nervous system containing β -sheet rich aggregated and Ser129 phosphorylated α -synuclein (α -syn). α -syn is characterized by its

N-terminal amphipathic lysine-rich region consisting of seven 11 residue imperfect repeats, which allows α -syn to interact with lipid membranes. Recently, multiple reports have suggested α -syns membrane-, vesicle- and exosome-binding to play a role in the malicious process of α -syn oligomerization and aggregation. Through ^{32}P -labeling and mass spectrometry, we have shown that the interferon inducible serine-threonine kinase PKR, besides Ser129 and Ser87, phosphorylate 11 novel α -syn sites, all of which lie within the amphipathic region. Further, α -syn in vitro phosphorylated by PKR and α -syn substituted on all novel α -syn Ser/Thr sites into phosphomimetic aspartic acid exhibits completely abrogated liposomes-binding capabilities. A kinase screen also revealed the ability of mitogen-activated protein kinase kinase 4 (MKK4) to phosphorylate novel sites within α -syn, although without affecting α -syn interaction with lipids. Label-free quantification revealed that PKR phosphorylated Thr59, Thr64 and Thr72 to a higher extent than MKK-4, suggesting a specific role of these 3 sites in enabling α -syn liposome binding. Together, our results suggest a novel mechanism where activation of specific kinases can alter α -syns interaction with lipid membranes and possibly play a role in its aggregation.

P20.07 Sérgio Eduardo Costa Almeida

LYSOSOMAL SORTING OF PROGRANULIN IN FRONTOTEMPORAL LOBAR DEGENERATION

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Frontotemporal lobar degeneration (FTLD) is the most common neurodegenerative disorder in individuals under the age of 65, characterized by selective atrophy of the frontal and temporal lobes of the brain. The major cause of familial FTLD is heterozygous loss-of-function mutation in the GRN gene. GRN encodes a secreted glycoprotein, known as progranulin (PGRN), which up until now has had an undefined biological function. Recently, it was discovered that homozygous loss-of-function mutations in GRN cause a lysosomal storage disorder called neuronal ceroid lipofuscinosis (NCL), implicating PGRN in a lysosomal function. Although the exact role of PGRN in lysosomes and its connection with FTLD and NCL is presently unknown, it is clear that sustaining or elevating PGRN levels is an appealing strategy for treating FTLD and NCL. The present project is based on our discovery of a novel progranulin sorting receptor, and we aim to determine its role in regulating progranulin levels and lysosomal function in primary neurons and patient-derived cells as well as in vivo using transcriptomics and behavioral studies of transgenic mice.

P20.08 Rikke Kristensen

TWO NOVEL ELECTROPHYSIOLOGICAL METHODS IN EVALUATION OF ALS PATIENTS - MSCAN MUNE AND MVRC

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Objective: To examine the clinical utility of MScan MUNE and MVRC in ALS patients, which also contributes to a better understanding of disease pathophysiology.

Background: Electromyography (EMG) is the most important standard examination in the diagnosis of ALS, but this method does not quantify the denervation process. Since ALS is characterized by progressive loss of motor units, a diagnostic use of Motor Unit Estimation Methods (MUNE), like MScan MUNE, seems of potentially great value. The Muscle Velocity Recovery Cycle (MVRC) is another method that can provide information about muscle membrane properties and may enlighten the effect of the denervation process on the muscle fibers.

Methods: At present, 21 ALS patients and 21 age-matched healthy controls have been included. All participants were evaluated electrophysiologically by a standard EMG and by the two novel methods: MScan MUNE and MVRC, all in m. tibialis anterior (TA). MScan MUNE values and MVRC parameters were compared between ALS patients and healthy controls using a parametric unpaired t-test.

Results: Preliminary results show that the MUNE value for ALS patients (62 (95% CI: 46-77)) was significantly lower than for the healthy controls (96 (95% CI: 82-109)) (p=0.0027). No MVRC parameters are significantly different between ALS patients and control subjects.

Discussion: The novel MScan MUNE method is sensitive in detecting loss of motor units in ALS patients in TA. The finding of no difference in MVRC for ALS patients compared to healthy controls indicate that the muscle fibers are not prominently affected by the denervation process, and this may support a more proximal pathology in ALS.

P20.09 Giulia Monti A NOVEL SORL1 VARIANT IS DOWNREGULATED IN ALZHEIMER'S DISEASE BRAIN

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SORL1 is a recently discovered risk gene for development of Alzheimer's disease (AD) that encodes the neuronal sortilin related receptor SORLA. Expression profiling studies reported reduced SORLA levels in AD brain, and genetic analyses validated the casual role for SORLA in AD, as several SORL1 coding variants and single nucleotide polymorphisms were identified in individuals affected by early-onset AD and late-onset AD (LOAD), respectively. All these data indicate SORL1 as a major contributor of genetic AD, with the result that it now could be even proposed as the fourth dominant AD gene alongside APP, PSEN1/2, and APOE.

By in silico analysis of the 3'end of the human gene, we have here identified a SORL1 variant containing a novel exon located between exon 38 and exon 39, that we named exon 38B, and encoding a truncated receptor that lacks four FnIII, transmembrane and cytoplasmic domains. Interestingly, this exon maps closely to a region in SORL1 known to be significantly associated with LOAD. By RT-PCR, this novel SORL1 variant was identified in various

human tissues. In the brain, we found that it was most strongly expressed in the cerebellum, known to express high SORLA levels. Next, we performed immunostaining of cells stably expressing either SORLA-wt or -38B, showing a surprisingly strong cellular retention for the novel variant lacking a transmembrane segment, but confirming the production of a stable translation product from SORL1-38B. Finally, by qPCR, we found that SORL1-38B level is significantly decreased in AD brain compared to controls, which strongly suggests that this transcript plays an important role in the development of the pathology.

P21.01 Majken Thomsen

SYNAPTIC DENSITY IMAGING IN RAT AND PIG BRAIN

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Background: The number of functionally active synapses can be used as a measure of neurological activity. Reduced synaptic function is observed in diseases such as Parkinson's and Alzheimer's disease and interictally in focal epilepsy. [¹¹C]UCB-J is a novel positron emission tomography (PET) tracer that binds to the synaptic vesicle 2A (SV2A) transporter, a transmembrane protein located in secretory vesicles in all areas of the brain.

Aim: Here we assess the potential of [¹¹C]UCB-J as a biomarker of regional cerebral synaptic function in the living rat and pig brain, as a prelude to future studies in animal models of disease.

Method: We performed [¹¹C]UCB-J PET on anesthetised rats and pigs with [¹¹C]UCB-J while sampling their arterial blood to measure tracer levels and the presence of its metabolites. We are currently comparing different kinetic models for describing tracer brain uptake kinetics and to determine its regional distribution. Furthermore, we have performed blocking experiments in rat with levetiracetam, an antiepileptic SV2A ligand, administered iv prior to the [¹¹C]UCB-J PET scan.

Results: The brain showed high and fast [¹¹C]UCB-J uptake in both species. The blocking experiments in the rat showed reduced uptake after levetiracetam compatible with specific binding being present.

Conclusion: These preliminary data indicate that [¹¹C]UCB-J PET is a good potential in vivo marker of synaptic function in the rat and pig brain. This opens the possibility to non-invasively investigate in vivo synaptic function longitudinally and in response to therapy in both small and large animal models of neurodegenerative diseases.

P21.02 Nick Larsen

CHARACTERIZATION OF MINICOLUMNS AND VOLUME TENSORS OF NEURONS IN BRODMANN AREA 46 IN NORMAL, SCHIZOPHRENIC AND DEPRESSIVE HUMAN AUTOPSY BRAINS

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Schizophrenia and depression are neuropsychiatric diseases that affect a person's feelings and behaviour. Both mental disorders are influenced by environmental and genetic factors, which lead to social problems for the individual patient, family and friends as well as economic costs for the society. fMRI studies and PET scans have shown abnormal activation in the dorsolateral prefrontal cortex (DLPFC), which is involved in the development of schizophrenia and depression. DLPFC is an area that handles attention, cognitive flexibility, abstract reasoning and emotional judgment. Schizophrenia and depression may be caused by impairment in DLPFC due to an altered 3-dimensional size, orientation and shape of the neurons in Brodmann Area 46 (BA46).

Using autopsy human brains from 11 control subjects, 10 subjects with schizophrenia, 11 suicidal patients with a history of depression, and 8 subjects with major depression without committing suicide, advanced methods from stochastic geometry and 3-dimensional reconstruction will be implemented for the characterization of minicolumns and volume tensors of neurons in BA46. BA46 will be identified from thick and thin histological sections, and the sampling of cells will be carried out by various forms of optical microscopy and serial sectioning bright field microscopy.

Assuming a difference in number, organisation or orientation of neurons in BA46 of normal subjects and patients with schizophrenia or depression, it will be a very significant step in a better understanding of the pathophysiology behind schizophrenia and depression.

P21.03 Simon Bang
Kristensen STATISTICAL METHODS FOR METACOGNITION
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In psychology, metacognition refers to the process through which a subject discerns the correctness of a decision or assertion. Metacognition is a congruent trait in many psychological fields of study, and metacognitive disability is characteristic of clinical diagnoses such as schizophrenia, Alzheimer's and certain brain injuries (David & al. 2012). Experiments to investigate consciousness are usually fairly complexly designed with many repeated observations at varying experimental settings to tease apart the underlying processes. Specifically, one would usually try to separate task performance from performance insight, the latter being the metacognitive abstraction, but at the same time the relationship between performance and insight is crucial due to their interaction.

A variety of statistical methods are applied in the analyses of consciousness experiments, each method having its advantages and disadvantages. We study more dedicated methods to model the bivariate processes (performance and insight) over time in a regression framework to account for different experimental factors. Such techniques for multivariate and longitudinal binomial and ordinal data are relevant in other clinical experiments as well as in epidemiology.

We also study how to couple these models to large, highly structured data usually in the form of diffusion weighted MR brain scans. Such approaches will aid our empirical understanding of brain functions in cognition, but they may also have direct relevance to prediction of health-related outcomes such as recovery from anoxic brain damage following stroke.

P21.04 Rola Ismail

STUDY OF THE TEMPORAL AND SPATIAL RELATIONSHIPS BETWEEN NEUROINFLAMMATION, BETA-AMYLOID AND TAU AGGREGATION IN MILD COGNITIVE IMPAIRMENT AND ALZHEIMER'S DISEASE

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Introduction: The neuropathological hallmarks of Alzheimer's disease (AD) of amyloid- β plaques (A β) and tau tangle along with brain inflammation. We are investigating the temporal and spatial inter-relationships of these pathologies in subjects with mild cognitive impairment (MCI) or established AD in a longitudinal study using positron emission tomography (PET).

Methods: MCI and AD subjects were recruited via memory clinics and advertisements. ^{11}C -PiB, ^{11}C -PK11195 and ^{18}F -AV-1451 PET were used for measuring A β plaque load, microglial activation (brain inflammation) and levels of tau aggregation, respectively. A group of age-matched healthy controls (HC) were included for comparison. All subjects also had a T1 weighted MRI scan and standard neuropsychological assessment.

Results (preliminary): Forty-four MCI subjects have completed their baseline ^{11}C -PiB and ^{11}C -PK11195 PET. Thirty-two MCI subjects also had ^{18}F -AV-1451 PET. Four AD subjects have also been scanned. To date, 22 of 44 MCI have completed a 2-year follow-up. Those MCI cases with raised A β , representing prodromal AD, showed stable cortical amyloid levels at 2-year follow-up. However, one quarter of our MCI cases showed a decline in their levels of inflammation (PK11195 binding) compared to baseline. Their mean MMSE score had declined from 27 at baseline to 25 at follow-up.

Conclusion: Brain inflammation is present in prodromal AD, but it can decrease with time. This suggests that it may play a protective role that fails. Collection of 2-year follow-up data will be completed in 2018.

P21.05 Agnes
Hauschultz
Witt
Canceled

MUSCLE VELOCITY RECOVERY CYCLES IN NEUROGENIC MUSCLES

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Objective: Muscle Velocity Recovery Cycles (MVRC) enable assessment of muscle membrane properties. MVRC has been studied in some myopathies, but the method has never been tested in neurogenic muscles. In this study, we aimed to examine whether MVRC differ in neurogenic and normal muscles and how MVRC variables correlate to the incidence of spontaneous activity in electromyography (EMG).

Methods: Thirty-two patients with confirmed peroneal neuropathy (twenty-seven) or L5 root lesion (five) were prospectively included. In addition to

EMG, MVRC was recorded in the anterior tibial muscle using Qtrac-software. Nine MVRC parameters comprised muscle relative refractory period and early, late and residual supernormality after 1, 2 or 5 conditioning stimuli. Results were compared to twenty age- and sex-matched healthy subjects (HS).

Results: There was significant difference in six MVRC parameters (muscle relative refractive period, early supernormality after 1 and 5 conditioning stimuli and late supernormality after 1, 2 and 5 conditioning stimuli) between patients and HS (t-test, $p < 0.05$). Linear regression analyses showed significant correlation between the same MVRC parameters and incidence of spontaneous activity ($p < 0.05$).

Discussion: Significantly prolonged MRRP and pronounced slowing in propagation velocity in early supernormal period suggest lower depolarization threshold in the denervated fibers.

Conclusions: MVRC may be a potential diagnostic tool of neuromuscular disorders and may provide information in understanding muscle pathophysiology.

Significance: Future studies are required with larger patient groups, including comparison of different nerve and muscle disorders.

P21.06 Asbjørn Johan Krom-Thaysen THE NUCLEAR ANATOMY AND FIBER CONNECTIONS OF THE GÖTTINGEN MINIPIG'S SEPTAL NUCLEI

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Background: Degeneration of the cholinergic neurons in the forebrain's septal nuclei (SeN) is well known in Alzheimer's disease (AD). Cholinesterase antagonists targeting the cholinergic system is at the forefront of medical practice for AD. Thus, more knowledge of the animal brain cholinergic system, such as SeN, is needed in the effort to find new AD treatments and interventions. Large animal models can validate such treatments prior to human trials.

Aim: The aim of this project is to make a detailed description of the septal anatomy and connectivity of the Göttingen minipig (GM).

Method: Firstly, 4-6 GM brains will be coronally, horizontally and sagittally embedded, sectioned, sliced, stained with ChAT ab, Nissl, Luxol fast blue, followed by microscopic analysis to elucidate the finer septal anatomy. Secondly, 6 GMs will be sedated, intubated, anaesthetized, and MRI scanned. Using MRI scan coordinates, neuronal tracers will be injected in specific locations of the histologically identified SeN. Three GMs will be injected with the anterograde BDA tracer, and three other animals will be injected with retrograde FluoroGold. After 4-6 weeks, the euthanized GMs will be perfused with paraformaldehyde. The brains will be removed, and the anatomical distribution of the traced connections will be described. Lastly, the tracing study will be compared with the projections calculated using DWI tractography.

Future significance: Based on animal studies, it has been hypothesized that septum might be a target for Deep Brain Stimulation (DBS) to treat drug

resistant temporal epilepsy. The SeN is also considered as a DBS target, which could enhance memory e.g. in AD.

P21.07 Mette
Habekost

DIRECT CONVERSION OF WILD-TYPE AND ALZHEIMER'S DISEASE PORCINE FIBROBLASTS TO NEURONS

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Alzheimer's Disease (AD) is characterized by progressive neurodegeneration, and the APP intracellular domain (AICD) has been implicated in the pathogenesis by acting as a transcriptional regulator of disease-relevant genes. With the purpose of studying the role of AICD, we aim to generate a relevant in vitro model of AD by directly converting aged wild-type and APPsw/PS1 double-transgenic porcine fibroblasts into neurons.

Direct conversion of human and mouse fibroblasts is most commonly achieved by ectopic expression of defined neuronal-lineage-specific transcription factors and small molecule approaches. Based on recent human and mouse studies, we used NGN2 and ASCL1-induced re-programming to directly convert adult dermal porcine fibroblasts into neuronal cells that expressed neuron-specific proteins, but the yield was insufficient for further downstream applications. This was consistent with previous studies, which reported that reprogramming efficiency is largely influenced by species, age of donors and passage number. As an alternative, we collected fetal fibroblasts from 35 days old porcine embryos, which we will reprogram in parallel to adult fibroblasts using improved conversion protocols. The neuronal identity will be compared to neurons differentiated from primary porcine neurospheres.

We believe that the fibroblast-derived neurons provide a valuable tool for modeling AD and analyzing the transcriptional role played by AICD, which may open new perspectives in understanding the molecular mechanisms leading to AD.

P21.08 Pernille
Thomassen

SORCS2 IN MOTOR NEURON DEVELOPMENT AND INTEGRITY

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Motor neuron development is dependent on several mechanisms, including axon guidance, growth cone collapse and synapse formation. Although highly studied, not all the proteins and pathways involved in this process and their interplay are yet fully described. Accumulating evidence implicates axon guidance proteins in neurological diseases, such as amyotrophic lateral sclerosis (ALS) and spinal muscular atrophy, demonstrating that improper wiring during development may lead to disease later in life. Axon guidance proteins are not only important during development, but they may also play a role in regeneration of nerves after injury. Further studies of axon

guidance proteins and their function may clarify how dysregulation cause disease and could help develop new therapeutic strategies.

In my PhD project, the function of the sorting receptor SorCS2 in motor neuron development is being studied through in vitro and in vivo studies in zebrafish and mice.

We have found that SorCS2 is expressed in motor neurons in both zebrafish and mice. To study the role of SorCS2 in motor axon guidance, we have knocked down expression of SorCS2 in zebrafish embryos by morpholino injections. We find that knockdown of SorCS2 results in abnormal length and aberrant branching in the primary motor neurons. Using the technique facial nerve crush injury, we similarly find that nerve outgrowth of SorCS2 in knockout mice is significantly slower than in wildtype mice. Together, the data suggests that SorCS2 plays an important role for motor neuron development and integrity, and ongoing studies aim at elucidating the molecular mechanisms underlying these phenotypes.

P21.09 Luca Bordoni THE ROLE OF AQP4 AND CEREBRAL CAPILLARY BLOOD FLOW DYNAMICS IN DEVELOPMENT OF HYPONATREMIA INDUCED BRAIN EDEMA IN MICE

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Introduction: Brain edema (BE) is part of the pathology of common conditions, such as traumatic brain injury (TBI) and hemorrhagic stroke. BE also contributes to chronic brain injury and potential death by intracranial pressure (ICP) elevation. Current treatment options are all relatively unspecific. Aquaporin 4 (AQP4) is a water and gas permeable membrane protein localized in astrocyte endfeet. AQP4 mediates the swelling of endfeet during the development of BE, and AQP4-KO mice show improved survival of BE. Recent studies (Østergaard, 2014) have emphasized the role of regulation of cerebral capillary flow heterogeneity in health and disease state. In BE, the mechanisms regulating capillary blood flow patterns are prone to disturbances by, for example the swelling of astrocyte endfeet.

Hypotheses: Capillary dysregulation plays a role in BE early etiology. AQP4, due to its localization at blood brain barrier, may have a role in regulation of capillary blood flow heterogeneity. Altering AQP4 functionality will show less disturbed capillary flow patterns during the development of BE.

Aim of the study: To determine the effect of brain capillaries heterogeneity in the development of BE. We also aim to test specific treatment strategies, AQP4-inhibition and H₂-exposure, which could be clinically relevant.

Methodologies: BE will be induced by Water intoxication (WI). B6 mice will be anesthetized with isoflurane to monitor changes in arterial pressure, ICP and blood gases during BE (with or without treatment). Other mice (B6, α -synaptrophin-KO) will receive WI awake and freely running during head fixation. Two Photon Microscopy (TPM) will be used for brain-imaging studies.

- P21.10 Annemarie Svane Aavild Poulsen SORL1 IS A TARGET GENE OF NEUROD2
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- The sortilin-related receptor (SorLA) is present in the brain and is associated to Alzheimers disease (AD). SorLA levels are decreased in some late onset AD patients, suggesting SorLA to be important for development of AD. The mechanisms behind SorLA regulation, encoded by the SORL1 gene are still poorly understood.
- To study SORL1 regulation, we investigated the SORL1 promoter and the NeuroD family of basic-loop-helix transcription factors (ND-bHLH-TFs). By 5' RACE, we identified transcriptional start site for SORL1 in human brain. In silico studies helped identify the SORL1 promoter. Using deletion experiments, we found a minimal SORL1 promoter sufficient for luciferase activity (LA) in ARPE-19 cells. The promoter region (P3) contained two enhancer motifs (E-boxes).
- The influence of ND-bHLH-TFs on P3 promoter activity was examined, showing NeuroD2 (ND2) to increase LA. This was validated by performing mutations/deletions of a canonical E-box. CHIP was performed on mouse chromatin to study genome wide interaction between ND2 and SORL1. A sequence for the promoter region P3 was confirmed together with two sequences for enhancer regions, which are to be investigated in future studies. For the visualization of promoter inducing effects, we cloned the P3 into a GFP-reporter. This plasmid was used to produce a transgenic mouse model that can help us investigate SORL1 regulation in vivo in future studies.
- In conclusion, we identified ND2 as an activator of SORL1 expression. ND2 is known to induce neuronal differentiation and promote neuronal survival, thereby favoring a possible important interaction with SORL1, which may promote proper brain development and function.
- P22.01 Leonardo Bonetti RISK OF DEPRESSION ENHANCES THE DISCRIMINATION OF AUDITORY IRREGULARITIES: AN MEG STUDY
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- Depression is a disorder characterized by a general aversion to activity and low mood that modulates behavior, thoughts, feelings and sense of well-being. According to the trait congruency hypothesis, individuals affected by depression tend to respond more to auditory and visual unpleasant stimuli. Furthermore, the individual depression risk is associated with altered auditory cortex activation and appraisal of the affective content of sounds.
- Mismatch negativity (MMN) responses to acoustic feature changes (pitch, timbre, location, intensity, slide and rhythm) inserted in a tonal sequence played in major or minor musical mode were recorded using magnetoencephalography (MEG) in 98 subclinical participants with risk of

depression, assessed through the Montgomery-Åsberg Depression Rating Scale (MADRS).

We revealed correlations between the MMN amplitudes to slide and pitch deviants and the depression level reported by participants, indicating that higher MMN amplitudes for these feature changes corresponded to higher level of depression. Furthermore, we reported significantly higher MMN amplitudes to mistuned pitches within a major context compared to MMNs to pitch changes in a minor context.

This study shows a link between depression trait and the central auditory discrimination of pitch-related sound features, suggesting possible implications for prevention and screening of individuals with depression risk.

P22.02 Ted Carl
Andelius

CONSEQUENCE OF INSERTION TRAUMA - EFFECT ON EARLY MEASURES WHEN USING INTRACEREBRAL DEVICES

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Introduction: A variety of intracerebral devices is used to quantify biological processes in cerebral tissue. Installing such a device causes an insertion trauma, which may affect early measures. Current literature proposes minimum one hour of observation before acquiring first measures by microdialysis. It is unknown whether this applies to other intracerebral devices. We, therefore, aimed to investigate time to reach steady state when using microdialysis and two intracerebral probes in a piglet model.

Material and methods: 10 piglets < 24 h of age were anaesthetized. Two probes (Codman® and Oxford Optronics®) and a microdialysis catheter (CMA Microdialysis®) were installed 10 mm into the left hemisphere. Probes measured intracranial pressure, blood flow through laser Doppler, and oxygen tension. Microdialysis measured lactate, glucose, glycerol, and pyruvate. After insertion, measures were acquired hourly for 20 hours. Steady state was assessed through eyeballing of data plots.

Results: Glucose and pyruvate reached steady state 2 hours after insertion, while lactate and glycerol required 6 hours. Blood flow reached steady state after 2 hours, intracranial pressure after 5 hours, and oxygen tension after 15 hours. Inter-individual variability decreased for the majority of measurements until 6-7 hours.

Conclusion: Steady state occurred later than expected in all measures. Microdialysis and the two probes required at least 2 hours, although numerous hours were needed for some measures. Inter-individual variability also decreased over time. Consequently, sufficient observation time is crucial to obtain correct baseline values and valid comparisons between individuals.

P22.03 Anne Nielsen ACUTE ISCHEMIC STROKE: ESTIMATING TREATMENT EFFECT USING A COMPUTER MODEL

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Background: Every year, 13 million people suffer acute ischemic stroke. Reperfusion treatment with e.g. intravenous recombinant tissue plasminogen activator (iv-rtPA) is crucial but might have serious side effects. We wish to develop a model capable of automatically predicting the final lesion volume given treatment.

Methods: Using acute magnetic resonance imaging, we implemented a convolutional neural network (CNN) to predict final imaging outcome. A total of 222 patients were included, of which 187 were treated with iv-rtPA. To assess whether the CNN is capable of estimating treatment effect of iv-rtPA, patients not receiving iv-rtPA were also included. The model performance was assessed using visual inspection and the size of the final infarct (mean [min, max]).

Results: The visual inspection showed patients with different diffusion and perfusion weighted imaging lesions to have a substantial treatment effect, whereas patients with similar lesions showed almost no treatment effect. This is consistent with the well-esteemed penumbra model. The mean volume of the infarcted areas was lower (16.44 ml [0,121.21]) for +iv-rtPA compared to -iv-rtPA (29.40 ml [0,108.17]) with a slightly significant difference (p=0.048).

Conclusions: The treatment effect was significant, with -iv-rtPA yielding a higher volume of final infarct. The new model paradigm has shown treatment effect estimation and thereby a potential for use in automated decision support systems providing recommendations for personalized treatment and thereby hopefully better outcome for the individual patient.

P22.04 Alexander Gramm
Kristensen DETECTION OF EARLY MOTOR INVOLVEMENT IN DIABETIC POLY-NEUROPATHY USING A NOVEL MUNE METHOD: MSCANFIT MUNE

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Aim: To examine whether a novel Motor Unit Number Estimation (MUNE) method, the so-called MScanFit MUNE (MScan), can detect motor involvement in diabetic polyneuropathy (DPN) earlier than nerve conduction studies (NCS), which are delayed by collateral sprouting.

Methods: We prospectively included 45 patients with diabetes mellitus type II and 15 healthy subjects (HS). NCS of three motor (median, peroneal, tibial) and three sensory (bilateral sural and median) nerves and MScan in median nerve by recording from abductor pollicis brevis (APB) muscle were done in

all participants. NCS results were compared to laboratory controls. All participants with carpal tunnel syndrome were excluded.

Results: DPN diagnosis was given using Dyck's criteria requiring NCS abnormality in at least two nerves. Twelve patients (26.6%) had DPN (DPN+), and 33 patients had normal NCS (DPN-). Median nerve motor action potential amplitude from NCS was normal in all DPN+ patients, whereas MScan showed a significantly lower number of motor units (78.58 ± 8.01) in DPN+ patients compared to both HS (106.1 ± 7.0) ($p=0.015$) and DPN- patients (113.4 ± 6.4) ($p=0.005$). There was no difference in number of motor units between HS and DPN- patients ($p=0.509$). Motor unit size was significantly larger in DPN+ patients (6.6 [$5.4-8.0$]) compared to DPN- patients (3.8 [$3.3-5.2$]) but not compared to HS (DPN+ vs controls, $p=0.169$; DPN- vs controls, $p=0.321$).

Discussion: MScan abnormality while median motor amplitude is normal suggests that MScan may be a sensitive measure of early motor involvement in DPN. Further studies with larger patient groups and application of MScan in lower extremity muscles are needed.

P22.05 Denise
Fabienne
Happ

ESTABLISHING A RAT MODEL OF POST-STROKE EMOTIONAL DYSFUNCTION

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Stroke survivors commonly experience depression and anxiety. This is linked to poorer functional and cognitive recovery, poorer quality of life, and higher mortality rates. Unfortunately, post-stroke depression (PSD) and anxiety (PSA) are usually undertreated, and many cases may remain undiagnosed. Animal models can be used to study the underlying pathophysiology, to develop diagnostic tools, and to identify new treatment strategies. However, current models of PSD and PSA, using middle cerebral artery occlusion, may be confounded by motor deficits that can affect tests of depression and anxiety. Additionally, most research focuses mainly on PSD.

Since lesions in prefrontal-subcortical circuits are commonly associated with PSD and PSA, a unilateral ischemic lesion in the medial prefrontal cortex (mPFC) was induced in male Sprague-Dawley rats ($n=8$) using micro-injections of the vasoconstrictor endothelin-1. Sham-operated animals ($n=8$) were injected with vehicle. Animal behavior was evaluated after 2 and 6 weeks using Open Field, Horizontal Ladder, Elevated Plus Maze, and Forced Swim Test.

We found increased anxiety-like behavior in the Elevated Plus Maze in stroke animals compared to sham-operated animals at 2 weeks, but no differences in locomotor activity (Open Field), sensorimotor function (Horizontal Ladder), and depression-like behavior (Forced Swim). At 6 weeks, we found no effect of endothelin-1 injections on any of the behavioral tests.

Our results suggest that damage to a secondary area may be necessary to induce depressive-like behavior. However, this model may be useful for investigating pathophysiology and treatments for post-stroke anxiety.

P22.06 Kathrine
Stokholm

MILD MICROGLIAL ACTIVATION INDUCED BY ALPHA-SYNUCLEIN IN A RAT
MODEL OF PARKINSON'S DISEASE

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Background: Parkinson's disease (PD) is associated with microglial activation, a sign of neuroinflammation, which may contribute to the neurodegeneration characteristic of PD. The PK11195 ligand binds to the translocator protein expressed on activated microglia. Positron Emission Tomography (PET) studies using PK11195 show increased microglial activation in human PD brains. We recently developed an early model of PD in which changes in the dopamine system were found in the absence of cell death.

Objective: Here we investigated potential microglial activation in the α -synuclein (ASYN) overexpression rat model of early PD using the PK11195 ligand.

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 substantia nigra. Twelve weeks after the injections, rats were either PET imaged with ¹¹C-PK11195 or decapitated for autoradiography with ³H-PK11195.

Results: PET imaging revealed a significant increase in ¹¹C-PK11195 binding in the whole brain in the ASYN vs GFP group. Significant increases of 5% in the striatum and 8% in the midbrain were observed in the ASYN vs GFP group. Autoradiography data showed significant increases of 10-11% in the ipsilateral side of the substantia nigra and the striatum compared to the contralateral side and the GFP group.

Conclusion: Our results show that ASYN overexpression leads to mild, but significant, microglial activation, suggesting that the immune system responds early in the disease and supporting anti-inflammatory agents as potential treatment for PD.

P22.07 Suzi Ross

THE ROLE OF AUDITORY FEEDBACK IN MOTOR SEQUENCE LEARNING IN
MUSICAL NOVICES

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Is learning to play a musical instrument a purely motoric process, or does the auditory feedback contribute to learning and memory of motor sequences in music learning? Prior research shows that auditory feedback facilitates learning of novel piano sequences in highly-trained pianists (Finney & Palmer, 2003). However, this result cannot be generalised to the role of auditory feedback in non-experts. We, therefore, investigated the effect of auditory feedback on motor sequence learning in novices. Forty-eight participants with little-to-no previous musical training learned to play a novel musical sequence on the piano. Half of the participants heard the sound

(auditory feedback) from the piano during learning, while the other half did not hear any sound. We tested memory for the sequence immediately after practice and following a 24-hour retention interval. Performance at both the immediate test and 24-hour test were better in the group who learned without sound, with this group performing significantly fewer errors than the group who learned with sound. This contrasts the result that has previously been found in expert musicians and suggests that auditory feedback interferes with motor sequence learning processes in novices. I will present data from the study described above as well as an ongoing replication in a new group of participants.

Finney, S. A., & Palmer, C. (2003). Auditory feedback and memory for music performance: sound evidence for an encoding effect. *Memory & Cognition*, 31(1), 51-64.

P22.08 Daniel Gramm SIZE ILLUSIONS AND SURROUND MODULATION
Kristensen

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Perceptual illusions are a central part of basic cognitive neuroscience as they allow us to identify brain activity related to conscious experiences of object features that are not physically present, and they allow us to investigate the very basic principles of neural systems processing. Here, we examine the Ebbinghaus illusion, a classic illusion of size. We argue that the effects seen in the Ebbinghaus illusion are the same effects (or a subtype of the effects) as seen in Surround Modulation, and we test this through a series of behavioural experiments. Next, we expand upon the already known mechanisms of surround modulation by building a computational model that incorporates ideas from information theory and natural image statistics. This gives rise to hypotheses about the fundamental functional properties of Surround Modulation. The model predictions are then tested on behavioural and fMRI data from healthy human subjects. Finally, given the early stages of this research, there are many caveats to consider, and we attempt to outline the most prominent. If our hypothesis of the origin of the Ebbinghaus illusion is true, we will have provided a much more basic and principled explanation of the Ebbinghaus illusion, and we will have provided an advanced computational model of Surround Modulation with testable predictions, some of which are novel ways of creating visual illusions of size.

P22.09 Abdel- BEHAVIORAL, STRUCTURAL AND MOLECULAR ALTERATIONS IN THE
Rahman Al- DF(H22Q11)/+ GENETIC MOUSE MODEL OF SCHIZOPHRENIA
Absi

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Schizophrenia is a highly heritable neuropsychiatric disorder that disturbs the patient's thoughts, feelings and behavior, resulting in a 2-3 fold increase in

their mortality rate. Although the etiology is poorly understood, emerging candidate risk genes for schizophrenia, along with clinical findings, implicate various aspects of GABAergic neurotransmission with the cognitive symptoms of schizophrenia.

Through behavioral, molecular, biochemical, and brain morphometric characterization of a new genetic mouse model of schizophrenia (Df(h22q11)/+), which mimics the 22q11.2 human microdeletion syndrome, we investigate dysfunctions in the cortical GABAergic system with potential translational relevance to schizophrenia.

Df(h22q11)/+ displays behavioral changes which are related to deficits in both visuospatial memory and sensory motor functioning. Furthermore, pyramidal neurons from the prefrontal cortex of Df(h22q11)/+ mice show structural changes at the level of spines and dendrites.

Our findings from the behavioral tests are similar to observations from the 22q11.2 human carriers, who experience multiple intellectual disabilities during their early adulthood. However, results from the morphological study still needs to be confirmed in the corresponding human 22q11.2 carriers.

P22.10 Martin Nors Skov

NOVEL TELEMETRIC APPROACH TO ASSESS THE PROGRESSING IMPACT OF DIABETES ON THE PERIPHERAL NERVOUS SYSTEM

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In my PhD study, I will investigate the early development of autonomic and sensory diabetic neuropathy (DN) using longitudinal electrophysiological measurements of both the sensory and sympathetic nerves, and relate findings with changes in mean arterial blood pressure (MAP), intrinsic diffusive properties of axons and nerve loss. This PhD Study will address the challenges associated with continuous measurements of the autonomous (renal) and sciatic nerve function using novel telemetric devices. The PhD study will be performed in three consecutive projects: 1) Implementation and benchmarking of a telemetric device for the stimulation and registration of peripheral nerve activity. 2) Longitudinal progression of DN in the renal autonomic nerve. 3) Longitudinal progression of DN in the sciatic nerve.

Telemetric recordings of nerve activity in animals have recently been shown, but there is today no established protocol for longitudinal studies of DN. The purpose of study 1 is to implement a telemetric device for activity recording in the renal nerve, and to elucidate its biocompatibility. The proposed implant should not affect the tissue in any critical way, and at the same time, it should send quality recordings. In study 2, the purpose is to investigate the progressing denervation of the autonomic nerve in diabetic rat. Diabetes will be induced by a selective destruction of the insulin-producing β -cells of the pancreas with a single i.v. injection of streptozotocin (STZ). The purpose of study 3 is to investigate the longitudinal denervation of the sciatic nerve in the progressing of diabetes in STZ diabetic induced rat.

- P23.01 Sophie-Charlott Seidenfaden BIOMARKERS IN PREHOSPITAL MANAGEMENT OF TRAUMATIC BRAIN INJURY: THE PRETBI STUDY
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- Background: Traumatic brain injury (TBI) is the leading cause of death and disability among young adults worldwide. Difficulties in clinical assessment and triage of TBI patients in the prehospital phase results 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 clinical-decision-making.
- Aim: To investigate the potential of early biomarker measurements in prehospital management of TBI patients
- Methods: 3 prospective, observational studies were designed to investigate ROC characteristics of S100B, GFAP and NSE in relation to clinically relevant endpoints. 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 Neurosurgical 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 neuro-trauma. Ultimately to elucidate the need for development of a point-of-care analysis.
- P23.02 Sandra Sif Gylfadottir PAINFUL DIABETIC POLYNEUROPATHY DECREASES QUALITY OF LIFE IN DANISH TYPE 2 DIABETIC PATIENTS
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- Background and aims: Painful diabetic polyneuropathy (DPN) is a disabling complication of diabetes. This study aims to determine its prevalence and relationship with Quality of Life (QoL) in a nationwide prospective cohort of incident recently diagnosed Danish type 2 diabetic patients.
- Methods: We sent a detailed questionnaire on neuropathy, pain and QoL to 6,726 patients prospectively enrolled from general practitioners and hospital

specialist outpatient clinics into the Danish Centre for Strategic Research in Type 2 Diabetes (DD2) cohort. Patients who reported pain in both feet and a score ≥ 3 on the Douleur Neuropathique (DN4) questionnaire were considered to have possible painful DPN. QoL and pain intensity were measured on a numeric rating scale (NRS, 0-10). The Michigan Neuropathy Screening Instrument (MNSI) was used to assess neuropathy.

Results: A total of 5372 (80.0 %) returned a complete questionnaire. Of the 837 patients with pain in both feet who completed the DN4 questionnaire, 536 (64.0%) had a DN4 score ≥ 3 , corresponding to a prevalence in the total population of possible Painful DPN of 10%. Mean pain intensity was 5.2 (SD 2.1). Patients with possible DPN had a substantially lower QoL score than those without PPN (median QoL score 6 versus 8 ($p < 0.001$)), also when correcting for MNSI score.

Conclusion: Ten percent of newly diagnosed type 2 diabetic patients in Denmark had possible painful DPN. Patients with possible painful DPN had lower QoL than patients without.

P23.03 Stine Derau Sørensen INDIVIDUAL DIFFERENCES IN MUSIC REWARD EXPERIENCES IN DANISH ADOLESCENTS

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The ability to convey emotions and induce pleasure is one of the most important aspects of the way that music becomes meaningful to humans (Vuust & Kringelbach, 2013). Affective responses to music are specific to both cultural and personal preferences (Mas-Herrero, Marco-Pallarés, Lorenzo-Seva, Zatorre, & Rodríguez-Fornells, 2013), but little is known about the source of this individual variability. The Barcelona Music Reward Questionnaire (BMRQ) is a new psychometric measure that identifies five distinct factors associated with musical pleasure: musical seeking, emotion evocation, mood regulation, social reward, and sensory-motor (Mas-Herrero et al., 2013). With this study, we first wish to explore the individual differences in music reward experiences in Danish adolescents. Secondly, we will correlate the results of sensitivity to these different factors with a measure of musical discrimination ability. The study is part of a larger study involving children and adolescents from 330 schools across Denmark. Participants from 7th grade and up (N = 4837, 51.6 % girls, age range = 12-20 years old) took part in this additional study. We administered a Danish version of the BMRQ online and a test of melodic and rhythmic discrimination abilities. We will do exploratory analyses of the individual differences and investigate the extent to which they can be explained by demographic factors, including age and musical training, and discrimination abilities.

P23.04 Fernando Exposto CHARACTERIZATION AND PREDICTIVE MECHANISMS OF EXPERIMENTALLY-INDUCED TENSION-TYPE HEADACHE

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Background: Experimental tooth clenching has previously induced headache in healthy individuals. Despite this, the headache that may develop after clenching has not been assessed and could possibly be classified as tension-type headache, myalgia or headache attributed to temporomandibular disorders (TMD). Importantly, in this model, only around 20% of healthy participants develop headache, and the reason for this is unknown.

Objectives: To use a clenching task to trigger headache in healthy volunteers and assess if parameters assessed before the clenching task can predict who develops headache and who does not. Furthermore, to assess what kind of headache develops.

Methods: Healthy individuals participate in 2 sessions separated by 2 hours. In the 1st session, the participants are assessed according to the DC/TMD and the ICHD-3. After this, participants have their pericranial tenderness assessed by total tenderness score (TTS), their pain modulation profile assessed through a conditioned pain modulation (CPM) task and temporal summation (TS) over the temple and thenar region. Finally, pressure pain thresholds (PPT) are assessed over the temple and the thenar. After these assessments, a clenching task is performed. Two hours after the clenching task, the participants return to the laboratory and are assessed for TMD, headache, TTS and PPT. After leaving the laboratory, the participants are asked to rate, every 2 hours, any experienced head and facial pain in a diary up to 24 hours after the clenching task.

Results: Up to now, we have included 12 of the 60 participants, and results will follow shortly.

P23.05 Saida Said FUNCTIONAL STUDIES OF THE GABA TRANSPORTER BY SITE-SPECIFIC INCORPORATION OF A FLUORESCENT UNNATURAL AMINO ACID

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The γ -aminobutyric acid (GABA) is the major inhibitory neurotransmitter in the brain, and GABA transporter 1 (GAT-1) belongs to the solute carrier 6 (SLC6) gene family together with the other neurotransmitter transporters, such as the serotonin, dopamine, norepinephrine and glycine transporters. The neurotransmitter transporters from this family are located in the plasma membrane of neurons and glia cells. The specialized members of this family transport different neurotransmitters across the cell membrane, thereby regulating signaling between neurons. Most of these transporters are

important drug targets in treating affective disorders, such as depression and epilepsy.

The role of the GABAergic system in mental disorders in general and in depression in particular is gaining momentum, thus studies of GAT-1 at the molecular level is highly attractive for understanding how it fulfills its biological role, how it could possibly be targeted better pharmacologically, and how disease-related mutations may manifest themselves in both epilepsy and depression.

Despite structural elucidation of related transporters, little is still known about the transport mechanism and conformational changes of GAT-1. A fundamental understanding of the pharmacological, functional, conformational and structural aspects of GAT-1 by combining electrophysiological, fluorescence-based methods and unnatural amino acid mutagenesis will provide detailed knowledge of how ligand and ion binding control conformational change, and thus can provide the basis for developing drugs that target it.

P23.06 Søren Bruno
Elmgreen

THE LION PROCEDURE - DISRUPTING THE PARADIGM OF MOTOR
REHABILITATION IN CHRONIC SPINAL CORD INJURY

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In Denmark, around 6,000 individuals live with the consequence of a spinal cord injury (SCI). While there are no reliable estimates of worldwide prevalence, the WHO estimates there are up to 500,000 new cases every year of which 80-90% are traumatic.

Recovery after inpatient rehabilitation is at best modest, and the conversion rate of the American Spinal Injury Association Impairment Scale (AIS) grade remains poor for grades A and B. Likewise, the rate of motor improvement stagnates over time; 9-12 months after their injury, patients have essentially exhausted the possibility of further restorative treatments.

In 2014, Possover made the observation that four patients with chronic traumatic SCI regained significant motor and sensory function following laparoscopic implantation of neuroprosthesis (LION) for bladder and bowel dysfunction.

As the only centre outside Zürich, the SCI Centre of Western Denmark has first-hand experience with the LION procedure; alongside three other subjects, a 26-year-old woman SM underwent the LION procedure in April 2017. SM was rendered paraplegic with an AIS A and a neurological level of T4 by a motor vehicle accident December 2015.

After three months of neurostimulation, we have found increased amplitude of the compound muscle action potential and reduced threshold for activation of the right anterior tibial muscle. Also, SF has established voluntary contraction of the right rectus femoris muscle.

Restoring motor function in chronic SCI by the LION procedure may significantly disrupt current paradigms in SCI rehabilitation. We are currently conducting a randomized controlled trial of the LION procedure and hope to share our results in 2018-2019.

P23.07 Casper Schmidt

IMPULSIVITY AND COMPULSIVITY: THE ROLES OF DOPAMINE AND SEROTONIN IN REWARDS

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Within the neuroscience of addiction, there is lack of evidence both in terms of assessing its mechanisms and treating its different forms. This Cambridge-Aarhus PhD project currently seeks to delineate the relationship between the roles of dopamine and serotonin in rewards, and their roles in the neuropsychological measurements of impulsivity and compulsivity. Although a lot is known about these separate roles, no research has been devoted to the basics of these neurochemical mechanisms when exposed to humans in combination.

The experiments were carried out during 2017 in a between-subjects double-blinded design and contained testing of 127 subjects, including four different arms of approx. 25 healthy volunteers (HV) and a fifth arm of 25 subjects with pathological gambling disorder (PG), a psychiatric patient group with profound deficits in impulsivity and compulsivity. This was done in order to isolate the neural and behavioural correlates of both increasing dopamine and depleting serotonin to investigate:

1) how this affected the neural activity in a task-based fMRI experiment on different forms of rewards

2) cognitive components of impulsivity and compulsivity through behavioural testing

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

4) a connectome-based DTI sequence assessing structural neural networks across HV and PG groups.

In conclusion, this project, which is currently underway and finished in its initial stages, holds great promise to infer mechanistically about the neural and behavioural processes associated with dopamine and serotonin, thus providing a novel foundation for future treatment options within the neuroscience of addiction.

P23.08 David Ricardo Quiroga Martinez

A NEW MULTIFEATURE MISMATCH NEGATIVITY (MMN) PARADIGM FOR THE STUDY OF MUSIC PERCEPTION WITH MORE REAL-SOUNDING STIMULI

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The MMN is a brain response elicited by deviants in a series of repetitive sounds that has been valuable for the study of music perception. However, most MMN experimental designs use simple tone patterns as stimuli, failing to represent the complexity of everyday music. Our goal was to develop a new paradigm using more real-sounding stimuli. Concretely, we wanted to assess the perception of non-repetitive melodies when presented alone and when embedded in two-part music. An Alberti bass used previously served both as a comparison and as the second voice in the two-part stimuli. We used MEG to record nonmusicians' responses to four deviants (mistuning, intensity, timbre and slide), while they watched a silent movie and listened to music in four conditions: bass only ("bass"), melody only ("melody"), bass in a high pitch range ("bass high"), and bass and melody together ("together"). We found MMNs for all deviants in the "melody" condition. However, mistunings and slide MMNs were reduced compared to the "bass high" condition, probably due to the higher pitch complexity of the melodies. Moreover, we found reduced MMNs in the two-part excerpts, likely due to competition for neural resources. Interestingly, this reduction did not hold for mistunings and slide in the melody, probably due to interval mistuning and the high voice superiority effect. Our results indicate that it is possible to use the MMN for the study of more real-sounding music and that stimulus complexity plays a crucial role in auditory discrimination as reflected in the MMN.

P23.09 Klaus Ulrik Koch

INFLUENCE OF VASOPRESSORS AND INOTROPES ON BRAIN OXYGENATION AND CEREBRAL MICROCIRCULATION IN ANESTHETIZED PATIENTS WITH BRAIN TUMORS

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Background: During anesthesia for brain tumor surgery, adequate cerebral perfusion pressure (CPP) is required to maintain adequate cerebral oxygenation. Frequently, we use vasopressors (phenylephrine or ephedrine) to maintain adequate blood pressure and CPP. Studies of the commonly used vasopressors show that brain oxygen saturation is reduced after phenylephrine administration, but unaltered by ephedrine. This difference may be caused by different influences of the vasopressor drugs on brain microcirculation as measured with capillary transit time heterogeneity (CTH).

Aim and hypotheses: Do vasopressors effect brain microcirculation and oxygenation differently? We hypothesize that phenylephrine is associated with a local increase in CBF and CTH compared with ephedrine, and that

phenylephrine is associated with reduction in OEF and CMRO₂ compared with ephedrine.

Methods: 24 patients with brain tumors were randomized to infusion of either phenylephrine or ephedrine during anesthesia until a mean arterial blood pressure (MABP) above 60 mmHg or an increase of 20% from baseline was reached. Near-infrared spectroscopy (NIRS) and MRI-parameters were measured before and during infusion. With MRI cerebral blood flow (CBF), cerebral blood volume (CBV), cerebral metabolism rate of oxygen (CMRO₂), oxygen extraction fraction (OEF) and CTH were measured.

Conclusion: NIRS measurements were significantly lower with infusion of phenylephrine compared to ephedrine. Δ CTH, Δ CBV, Δ CBF, Δ CMRO₂ and Δ OEF were not different between the two groups, significant differences on CBV and CBF were found within the ephedrine group. This study cannot recommend one vasopressor over the other for brain tumor surgery.

P23.10 Nina Stockfleth NEUROMAS AS THE CAUSE OF NEUROPATHIC PAIN IN AMPUTEES?
Buch

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Background and aims: Post-amputation pain is highly prevalent, but it remains a challenging condition to treat. Peripheral nerve injury caused by amputation may lead to the formation of neuromas, which can be painful. However, the association between neuromas and neuropathic pain in amputees is not fully understood. This ongoing study examines whether neuromas are more frequent in patients experiencing pain after amputation than in patients without pain.

Methods: In this observational cohort study, 80 patients with amputation will be recruited. Patients will undergo an interview, answer pain questionnaires and go through a clinical examination. This examination includes testing of sensory abnormalities, including allodynia and hyperalgesia. Neuromas are identified using high resolution (6-18MHz) ultrasound by an investigator blinded to the patient's history of pain.

Results: Patient inclusion is ongoing. At present, 45 amputees have participated: 29 males and 16 females, aged 25-84 years. 73% of all patients included had at least one neuroma. 21 patients suffered from either persistent phantom pain or attacks of phantom pain. 16 patients suffered from stump pain. 11 patients were pain-free. There was no significant difference in the prevalence of stump pain, intermittent phantom pain, and persistent phantom pain when comparing patients with and without ultrasound-verified neuromas.

Conclusions: Preliminary data show no association between the occurrence and severity of either stump or phantom pain and the presence of neuromas at the amputation site. Sensory abnormalities are common findings at the site of the stump, regardless of the occurrence of neuromas.

P24.01 Anne Birkeholm Jensen ANTIMICROBIAL SUSCEPTIBILITY TESTING OF AGGREGATIBACTER ACTINOMYCETEMCOMITANS COLLECTED GEOGRAPHICALLY WIDESPREAD SUPPORTS AMOXICILLIN AS A CONTINUED DRUG-OF-CHOICE IN PERIODONTAL TREATMENT

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Aim: The combination of amoxicillin and metronidazol is recommended in the treatment of *Aggregatibacter actinomycetemcomitans* (Aa)-associated periodontitis when indicated. Resistance to amoxicillin is reported for Aa. The present study aims to clarify this important issue by investigating a large collection of strains cultured from patients of different age groups and from 22 countries on five continents.

Methods: Two hundred and fifty-nine Aa strains were serotyped using a multiplex PCR, and minimal inhibitory concentration (MIC) values of amoxicillin were determined using the agar dilution method (range 0.25 to 8.0 mg/L). The plates were spot-wise inoculated with approximately 10⁴ colony-forming units, incubated in 5 % CO₂ at 37 °C, and visually inspected after 24 and 48 hours. A MIC ≤ 2.00 mg/L was categorised as susceptible using EUCAST interpretative criteria for *Haemophilus* species.

Results: Amoxicillin MIC-values varied from 0.25 mg/L to 2.00 mg/L, and all tested strains, including isolates previously reported as resistant, were susceptible to amoxicillin. Minor differences in MIC were observed between various serotypes of Aa.

Conclusion: Meticulous testing could not support reports of emerging resistance to amoxicillin among clinical strains of Aa. A continuation of the use of amoxicillin as an integrated part of the periodontal therapy in certain patients with aggressive periodontitis can still be recommended.

P24.02 Trine Bertelsen THE IL-17A/F HETERODIMER REGULATES PSORIASIS-ASSOCIATED GENES THROUGH IκBζ

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Antagonists of IL-17 have proven to be highly effective in the treatment of psoriasis. However, the underlying molecular mechanisms involved in the pathogenesis of psoriasis are not fully understood. Recently, we presented evidence that IκBζ (encoded by the NFKBIZ gene) is a key regulator in the development of psoriasis through its role in mediating IL-17A- and IL-17F-driven effects. IL-17A and IL-17F are both increased in the skin of psoriatic patients and can exist as homodimers or heterodimers. Like IL-17A/A and IL-17F/F, the IL-17A/F heterodimer is produced by a variety of immune cells and signals through the same receptors.

The aim of this study was to characterize the role of the IL-17A/F heterodimer in the regulation of NFKBIZ expression and in the regulation of psoriasis-associated genes through I κ B ζ .

We demonstrated that stimulation with the IL-17A/F heterodimer significantly induced NFKBIZ expression. We found that the IL-17A/F-mediated induction of NFKBIZ mRNA expression reached its highest level after 1.5 hour of stimulation, and that IL-17A/F combined with TNF α increased the induction of NFKBIZ additionally. Moreover, silencing I κ B ζ by siRNA revealed that I κ B ζ is a key regulator of IL-17A/F heterodimer-inducible psoriasis-associated genes, including DEFB4, S100A7, CCL20, IL-8 and CHI3L1.

In conclusion, we present I κ B ζ as a novel key regulator of the IL-17A/F heterodimer-driven effects in psoriasis. Thus, antagonists of I κ B ζ could potentially provide a more targeted approach for treating psoriasis as well as for treating other inflammatory and immune-mediated diseases for which IL-17-targeting drugs have proven to be highly effective.

P24.03 Maria Dietz
Toppenberg

EVALUATION OF MOBILE X-RAY WITHIN THE TRIPLE AIM APPROACH

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Background: In other countries, mobile X-ray is used when transfer of patients to the radiology department at the hospital may be an obstacle. When using mobile X-ray, the X-ray examination is performed in the patient's home (nursing home, rehabilitating centre or psychiatric ward) with transportable equipment.

Aim: The overall aim is to evaluate the project 'mobile X-ray' and conclude if mobile X-ray improves the health care for fragile patients.

Method: The overall method used is the Triple Aim Approach that seeks to optimize health care performance for a specific population and contributes to the improvement of the effect of an intervention. The Triple Aim Approach has three dimensions: 1) Improving the health of the defined population, 2) Assessing the experience of care and 3) Reducing, or at least controlling, the per capita cost of care. They will each represent a sub-study in the PhD study using both qualitative and quantitative methods, such as quasi-randomized controlled study, observation study, interviews and questionnaires. Image quality will be determined by two radiologists, who will analyse all picture data sets in an anonymized way using a five-point scale. The economic impact of mobile X-ray will be evaluated by a cost consequence analysis.

Results and conclusion: Results are not presently available.

Perspectives: The ambition is to contribute to a study of mobile X-ray. Does it improve health care, and is it a way to get more value from the resources invested in the health care at Aarhus University Hospital when the focus is on X-ray examinations of fragile patients? The project will also create new knowledge about which practice that gives the best patient care with the available resources.

- P24.04 Susanna Botticelli INFLUENCE OF CLEFT DIMENSIONS AT BIRTH ON DENTO-OCCLUSAL RELATIONS BEFORE ORTHODONTICS IN UNILATERAL CLEFT LIP AND PALATE PATIENTS: A SUBGROUP ANALYSIS WITHIN A RANDOMISED CLINICAL TRIAL
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- Section of Orthodontics, Department of Dentistry and Oral Health, Aarhus University
- Aim: To explore the association between cleft dimensions at birth and occlusal outcome in unilateral cleft lip and palate (UCLP) patients.
- Design: Subgroup analysis within an ongoing multicentre RCT of primary surgery.
- Methods: A total of 122 UCLP infants received primary cheilo-rhinoplasty and soft palate closure at age 4 months and were randomised for hard palate closure at age 12 or 36 months in one surgical centre. A novel 3D analysis of cleft size and morphology was performed on digitised pre-surgical models. Occlusion was scored on 8-year models using the MHB Index and the Goslon Yardstick.
- Results: The crude analysis showed no difference between the two surgical groups ($P=0.17$). Adjustment for cleft size by multiple linear and logistic regression showed that the delayed hard palate closure group scored better when the cleft was posteriorly large ($P<0.001$).
- Conclusions: From an occlusal perspective, the timing of hard palate closure should be planned in relation to the posterior cleft size if the soft palate is closed first.
- P24.05 Arwa Gera STABILITY AFTER ORTHODONTIC TREATMENT: HOW TO MAINTAIN TREATMENT RESULTS IN THE LONG TERM?
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- Introduction: Lingual fixed retainers are crucial for maintaining stability in the mandibular anterior region after orthodontic treatment. So far, long-term orthodontic stability has been unpredictable, and the best method for preventing tooth relapse has not been resolved. Posttreatment results should be stable, and retention strategy should be with limited side effects.
- Aim: To improve orthodontic posttreatment stability and investigate posttreatment dental changes in the long term.
- Methods: Enroll 550 consecutive patients, 400 from the postgraduate orthodontic clinic, and 150 from the undergraduate orthodontic clinic at Aarhus University. This project consists of 3 studies:
- First study: RCT. Compare CAD/CAM retainer to traditional fixed retainers.
Aim: To assess and compare survival rate, long term stability and side effects of both retainers 1 to 24 months after placement.
- Second study: Retrospective. Recall patients who finished orthodontic treatment 5 to 10 years ago. Aim: To assess long-term post-treatment

stability, and to relate it to initial malocclusion, orthodontic treatment and retention protocol.

Third study: Population study. Calculate the prevalence of malocclusion, previous orthodontic treatment and retreatment upon dental students. Aim: To assess prevalence of orthodontically treated students and their occlusion several years after treatment.

Perspectives: We aim to provide new knowledge in the field of orthodontic posttreatment stability. Furthermore, the study will evaluate stability with a new type of digital retainer compared to conventional retainer. This technology might offer better stability due to increased accuracy, and consequently fewer posttreatment complications.

P24.06 Didde Haslund DOMINANT-NEGATIVE EFFECTS IN HEREDITARY ANGIOEDEMA: INTRACELLULAR AGGREGATION AND RETENTION OF NORMAL C1 INHIBITOR INDUCED BY TRANS-INHIBITORY MUTANT C1 INHIBITOR

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Hereditary angioedema (HAE) is an autosomal dominant disease characterized by recurrent edema attacks associated with significant morbidity and occasional mortality. HAE results from mutations in the SERPING1 gene, which encodes C1 inhibitor (C1INH), a serine protease inhibitor. Reduced plasma levels of functional C1INH lead to enhanced activation of the contact system, triggering high levels of bradykinin and increased vascular permeability. Until now, the cellular mechanisms leading to reduced plasma levels of C1INH in heterozygous HAE type I patients (20-30% of normal) remain obscure.

Here, we show that mutated C1INH encoded by HAE-causing SERPING1 alleles affect C1INH protein derived from the normal SERPING1 allele in a dominant negative fashion by triggering formation of intracellular C1INH aggregates trapped in ER and, thus, reducing secretion of functional C1INH. This cellular phenotype is prominent for a subset of HAE-causing SERPING1 gene variants and evident primarily in cells co-expressing normal and mutated C1INH. Importantly, intracellular aggregation, C1INH retention, and abnormal ER structures are observed in HAE type I patient-derived fibroblasts carrying a severe dominant negative SERPING1 gene variant. Notably, we demonstrate that this condition is effectively treated by viral delivery of the normal SERPING1 gene, leading to markedly increased C1INH secretion, which suggests that the dominant negative disease

mechanisms are not likely to obstruct the development of future gene therapies for HAE.

Collectively, our data link abnormal C1INH accumulation with dominant negative disease mechanisms as the prime drivers of reduced C1INH plasma levels in HAE type I patients.

P24.07 Anne Hald Rittig THE ROLE OF STAPHYLOCOCCUS AUREUS IN CUTANEOUS T-CELL LYMPHOMA

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The pathogenesis of Cutaneous T-Cell Lymphoma (CTCL) is elusive. For decades, microbes have been suspected to play a key role in CTCL; both as an etiologic agent and as drivers of severe co-morbidity. *Staphylococcus aureus* (SA) is often responsible for increased morbidity in CTCL. Most studies estimate that infection rates are generally high, varying from 44% to 76%. Originally, it was suspected that SA directly triggered proliferation of malignant T cells through the release of staphylococcal enterotoxins (SE), but this hypothesis never gained convincing experimental support. Instead, we have now discovered that SE stimulate malignant T cells through an indirect mode of action involving non-malignant T cells as providers of growth factors for malignant T cells.

The purpose of this study is to investigate whether aggressive antibiotic treatment can halt or reverse progression in CTCL.

Fifteen patients with advanced CTCL will be admitted at the Department of Dermatology for anti-bacterial treatment. Anti-bacterial therapy consist of ten days of daily infusion of cefuroxime 1500 mg x 3 and metronidazole 500 mg x 3 followed by 2 weeks of oral treatment with amoxicillin and clavulanic acid 500 + 125 mg x 3 daily. The observation period will be 8 months. During this period, punch biopsies (from lesional and non-lesional skin), skin swaps, serum, peripheral blood mononuclear cells and a panel of blood samples will be obtained at baseline and at six follow-up visits after initiation of treatment. Responsiveness will be measured by decline in skin involvement, degree of inflammation and subjective symptoms. Moreover, photographs of the skin lesions will be obtained at each visit.

P24.08 Pankaj Taneja SOMATOSENSORY INVESTIGATION OF OROFACIAL PAIN, UNPLEASANTNESS AND PLEASANTNESS

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Introduction: In the pain field, the scientific focus has been primarily on the sensation of pain and unpleasantness or problems with lack of normal

sensations like touch and temperature in the mouth and face, e.g. as a sequela of nerve damage. However, lack of sensation of stimuli normally considered as pleasant is rarely taken into account.

Aim: To apply established psychophysical tests of tactile and pain sensitivity as well as standardised pleasant stimuli, and to evaluate their potential capacity for evocation of perceived painful, pleasant and unpleasant sensations in the orofacial region.

Method: 20 healthy adult female participants underwent standardised quantitative sensory testing (QST) and dynamic tactile stimulation on the right infraorbital region. The QST included thermal and mechanical stimuli. For each stimulus modality, the level of evoked pleasantness, unpleasantness and pain was assessed. Psychological questionnaires used: Positive And Negative Affect Scale, Pain Catastrophising Scale and Social Touch Questionnaire.

Results: Brush stimuli was significantly more pleasant compared to other stimuli ($p < 0.05$). Unpleasantness and pain scores were positively correlated with each other ($P < 0.05$) at pin prick forces of 64 mN, 128 mN, 256 mN and 512 mN when compared to 8 mN. Significant positive correlations were seen between Negative Affect Score and pain for pinprick stimuli of 8, 16 and 128 mN ($p < 0.05$).

Conclusion: Brush stimulation is the most pleasant. The level of Negative Affect is associated with pain intensities of pin pricks at 8, 16 and 128 mN. The results from this study will contribute to a larger study in the multisensory integration of facial pain.

P24.09 Yasser
Haddadi

CLINICAL ACCURACY OF CROWNS BASED ON DIGITAL INTRAORAL SCANNING COMPARED TO CONVENTIONAL IMPRESSION METHOD: AN IN VIVO RANDOMISED SPLIT-MOUTH STUDY

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Objectives: The aim of this prospective in vivo study was to compare the accuracy of the marginal and internal fit of crowns based on conventional impression (CI) or intra oral scan (IOS) in a randomised, split-mouth set-up.

Materials and methods: 19 patients needing full coverage crowns, fitting a split-mouth design were provided with two lithium disilicate crowns; one based on a CI and one based on an IOS. The marginal and internal accuracy of the crowns was assessed with the replica technique and clinically using California Dental Association (CDA) quality evaluation form.

Results: At the preparation margin, the median gap was 60 μm (IQR = 55.75 μm) for IOS and 78 μm (IQR = 51.75) for CI. For the other points, the median gap ranged from 91 to 156 μm for IOS and from 109 to 181 μm for CI. The accuracy of the IOS was statistically significantly better at all points, except at the cusp tip. All crowns were rated R or S at both 6 and 12 months follow-up appointment. The results for the clinical evaluation with CDA for marginal integrity showed no statistically significant difference between the two impression methods for either evaluator at both 6 and 12 months of evaluation.

Conclusions: Crowns based on IOS show statistically significantly better marginal and internal adaptation before cementation compared to conventional impression. However, the clinical evaluation showed similar marginal adaptation.

Clinical relevance: Crowns based on a fully digital workflow can provide clinically acceptable marginal adaptation comparable to crowns based on CI.

P24.10 Mads Hagen Pedersen CORONECTOMY OF HIGH RISK MANDIBULAR THIRD MOLARS. LONG-TERM FOLLOW-UP OF TREATMENT OUTCOMES

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Aim: The aim of the study was to evaluate the long-term outcomes of coronectomy of mandibular third molars with close relationship to the inferior alveolar nerve (IAN) with sensory disturbances of the IAN and root migration as the primary outcome variables.

Material and methods: In the period 2005-2016, a total of 231 coronectomies of the mandibular third molar were performed. The indication for a coronectomy in favour of complete removal of the third molar was based on a CBCT scan, which had indicated lack of bone between the root and the IAN. After surgery, the patients were followed for a median of 5.8 years (range: 1-12 years). Clinical variables were subjective and objective measures of sensory disturbances of the IAN, pathological findings, and any postoperative infections or removal of the root complex. Radiological variables were root migration, bone formation, any pathological changes, and healing in cases of root complex removal.

Results: A temporary sensory disturbance of IAN was reported after 3 coronectomies (1.3 %). In two cases (0.9%), a mild sensory impairment persisted. 27 patients were treated with antibiotic therapy due to a postoperative infection (11.7%), and in 7 cases the root was removed (3%). One patient sustained a mandibular fracture following a coronectomy; this was treated by osteosynthesis and healed uneventfully. A common radiological finding within the first year was a coronal root migration.

Conclusion: The early results of this prospective follow-study demonstrated a low incidence of permanent IAN impairment following coronectomy. Postoperative infection (11.3%) and need for removal of the root (3%) were the most common complications.

P25.01 Sidsel Rugberg Alsing EXPERIMENTAL ANTI-ANGIOGENIC OCULAR GENE THERAPY

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Age-related macular degeneration (AMD) is the leading cause of blindness in the elderly in the western world. Current treatments target vascular endothelial growth factor (VEGF), which has been found to be

overexpressed exudative AMD (eAMD). While effective, these treatments demand repeated administrations for sustained effect and thus burden both patients and healthcare systems. In contrast, development of safe and efficient ocular gene therapy offers the possibility of achieving lifelong effects with only a single treatment.

The aim of this project is to bring ocular gene therapy for eAMD closer to a clinical setting by making advances terms of safety, efficacy, specificity, and translatability. The project comprises four subprojects.

Subproject one regards the delivery of anti-VEGF miRNAs and an anti-angiogenic protein using adeno associated viral (AAV) vectors. Subproject two concerns the use of Dicer independent short hairpin RNAs (DIshRNAs), which may prove superior to conventional shRNAs or miRNAs in terms of specificity as they produce no passenger strand. In subproject three, the possibility of establishing a porcine model for evaluation of anti-angiogenic therapies is investigated as well as the possibility of performing subretinal injections in pigs. Subproject four concerns the in vivo investigation of viral delivery of the Cas9 protein from the CRISPR-Cas9 system in order to avoid long-term expression of the Cas9 protein.

Collectively, these four subprojects have the potential to bring ocular gene therapy closer to a clinical setting.

P25.02 Wenqian Gu THE DYNAMIC EFFECTS OF ISOSTEVIOL ON INSULIN SECRETION AND ITS ABILITY TO COUNTERACT THE IMPAIRED BETA-CELL FUNCTION DURING GLUCO- LIPO- AND AMINOACIDO-TOXICITY: STUDIES IN VITRO

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Background: Isosteviol (ISV), a diterpene molecule, is an isomer of the backbone structure of a group of substances with proven antidiabetic capabilities. The aim of this study was to investigate if ISV elicits dynamic insulin release from pancreatic islets and if it is able to counteract gluco-, lipo- and aminoacido-toxicity in a clonal beta cell line (INS-1E) in relation to cell viability and insulin secretion.

Materials and methods: Isolated mice islets were placed into the perfusion chambers and perfused with 3.3mM and 16.7mM glucose with/without 10^{-7} M ISV. INS-1E cells were incubated for 72 h with 30mM Glucose or 1mM Palmitate or 10mM Leucine with or without 10^{-7} M ISV. We measured cell viability with Cytotoxic Fluoro-test, and insulin secretion was measured in KRB at 3.3mM and 16.7mM glucose.

Results: In the presence of 3.3mM glucose, 10^{-7} M ISV did not change basal insulin secretion from perfused islets. However, at high glucose level of 16.7mM, 10^{-7} M ISV elicited a 3-fold increase. After 72h gluco-, lipo- or aminoacido-toxicity in INS-1E cells, ISV was not able to change cell viability (glucotoxicity, \pm ISV: $19.23 \pm 0.83\%$, \pm ISV: $18.41 \pm 0.90\%$; Lipotoxicity, \pm ISV: $60.14 \pm 2.28\%$, \pm ISV: $59.72 \pm 2.72\%$; aminoacidotoxicity: \pm ISV: $8.12 \pm 0.63\%$; \pm ISV: $7.75 \pm 0.38\%$, all NS.) ISV showed no counteractive effect regarding insulin secretion (data will be shown in poster).

Conclusion: ISV acutely stimulates insulin secretion at high but not at low glucose. However, ISV could not counteract cell viability or cell dysfunction after exposure to gluco-, lipo- and aminoacido-toxicity in INS-1E cells.

P25.03 Iben Bach
Damgaard

BIOMECHANICAL STABILITY AFTER SMALL INCISION LENTICULE EXTRACTION (SMILE) FOR MYOPIA: AN EX-VIVO STUDY ON HUMANE DONOR CORNEAS

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Background: Small Incision Lenticule Extraction (SMILE) is a surgical technique for correction of myopia. To flatten the cornea, an intrastromal lenticule is cut with laser and removed through a small incision. The lenticule is normally removed from the anterior and strongest part of the cornea (110µm depth). However, the biomechanical stability may be better preserved by removing the lenticule in the deeper corneal layer (160µm depth).

Aim: To examine the biomechanical stability after SMILE performed in 110 and 160µm depth.

Methods: A total of 32 humane donor corneas were allocated to four groups, by the combination of two depths (110 and 160µm) and two corrections (-4 and -8D). Each cornea was mounted on an artificial chamber. The radius (r) of the anterior and posterior corneal curvature was registered before and after SMILE at a chamber pressure of 15 and 40 mmHg. The average changes after surgery ($\Delta r: r_{\text{post}} - r_{\text{pre}}$) and with increased chamber pressure ($\delta r: r_{40\text{mmHg}} - r_{15\text{mmHg}}$) were compared using mixed ANOVA.

Results: SMILE in 110µm depth caused more anterior flattening (Δr_{15} : 0.74 ± 0.22 vs. 0.43 ± 0.27 mm) and less posterior steepening (Δr_{15} : -0.19 ± 0.12 vs. -0.46 ± 0.19 mm) than SMILE in 160µm depth for the -8D groups ($p < .002$), but not for the -4D groups ($p > .059$). After SMILE, increased chamber pressure caused an anterior steepening in all four groups ($p < .014$) that was similar for SMILE in 110 and 160µm depth ($\delta r_{\text{post}, -4D}$: -0.13 ± 0.14 vs. -0.09 ± 0.05 mm, $p = .171$).

Conclusion: SMILE in 160µm depth caused less anterior curvature flattening than in 110µm depth, and consequently less myopic correction. However, the corneal compliance was comparable after SMILE in 110 and 160µm depth.

P25.04 Anna Dons-
Jensen

A_{2A} ADRENOCEPTOR STIMULATION REDUCES DILATATION OF RETINAL ARTERIOLES INDUCED BY FLICKERING LIGHT IN NORMAL PERSONS

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Background: Disturbances in the retinal blood flow are involved in the pathophysiology of the most common vision threatening diseases, but the mechanisms underlying these disturbances are unknown. Previous in vitro studies have shown that A_{2A}adrenoceptor agonists induce retinal vasodilatation, but it is unknown whether these results are reproducible in vivo,

and whether A_{2A} is involved in vasodilatation during changes in retinal metabolism.

Methods: 20 normal persons aged 22-31 were studied in an open controlled interventional study. A dynamic vessel analyzer was used to study the diameter of retinal vessels during rest and during stimulation with flickering light before and after administration of the A_{2A} adrenoceptor agonist regadenoson (A_{2A}). The examinations were repeated on a second day during hypoxia induced by inhalation of a gas mixture of 12.5% oxygen/87.5% nitrogen.

Results: Hypoxia induced dilatation of retinal arterioles at baseline ($p=0.0008$), which persisted during simultaneous A_{2A} administration ($p=0.03$), but was absent during A_{2A} administration alone ($p=0.17$). The flicker-induced dilatation of retinal arterioles was significantly reduced after A_{2A} administration, both alone ($p=0.02$) and simultaneously with hypoxia ($p<0.0001$) as well as during hypoxia alone ($p=0.0009$).

Conclusion: A_{2A} adrenoceptor stimulation and hypoxia both reduce flicker-induced dilatation of retinal arterioles. Further investigations should elucidate whether these effects are mediated by the same pathway.

P25.05 Kristina Laugesen

CLINICAL INDICATORS OF ADRENAL INSUFFICIENCY FOLLOWING DISCONTINUATION OF ORAL GLUCOCORTICOID THERAPY: A DANISH NATIONWIDE SELF-CONTROLLED CASE SERIES ANALYSIS

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Background and aim: Adrenal insufficiency (AI) caused by glucocorticoid withdrawal is a potential severe adverse effect of glucocorticoid therapy. The risk of biochemically verified AI is approximately 50% in oral glucocorticoid users. However, knowledge on the clinical consequences is lacking. We aimed to investigate the clinical indicators of AI during and following oral glucocorticoid withdrawal.

Methods: We conducted a population-based study utilizing data from national registries. We specified clinical indicators of AI (hypotension, syncope, cardiovascular collapse, hyponatremia, gastrointestinal symptoms and CNS deprivation). We defined four risk periods of 2 months each: risk period 1 or withdrawal period (1 month before cessation to 1 month after), risk period 2 (month 2-3 after cessation), risk period 3 (month 4-5 after cessation) and risk period 4 (month 6-7 after cessation). Finally, a reference period was defined as month 3 and 2 before glucocorticoid initiation. We conducted a self-controlled case series analysis. Each individual serves as his or her own control, and adverse event rates in the predefined risk periods can be compared to a reference period.

Results: N=2,853 cases of clinical indicators were identified. The incidence rate ratio (IRR) comparing risk period 1 with the reference period was 2.7 (95% CI: 1.4-5.3) for hypotension, 1.7 (95% CI: 1.5-1.8) for gastrointestinal symptoms, and 1.4 (0.9-2.0) for hyponatremia. The risk of hypotension and gastrointestinal symptoms remained elevated during risk period 2-4.

Conclusion: Our findings suggest that AI caused by glucocorticoid withdrawal has clinical consequences and thus should receive more attention.

P25.06 Andreas Holmgaard

POSSIBLE DOMINANT-NEGATIVE EFFECTS IN MALATTIA LEVENTINESE/DOYNE HONEYCOMB RETINAL DYSTROPHY RESULTING IN ALTERED INTRACELLULAR FIBULIN-3 HANDLING

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Malattia Leventinese/Doyne Honeycomb Retinal Dystrophy (ML/DHRD) is a rare inherited autosomal dominant disorder characterized by drusen formation and subsequent geographic atrophy of the photoreceptor cells at the macular region. A p.Arg345Trp missense mutation of the Efemp1 gene causes (ML/DHRD). Following transfections of N2A and RPE-J cells, we found that compared to wild-type fibulin-3, less of the p.Arg345Trp variant protein was secreted. As well, co-transfections with increasing amounts of plasmid encoding p.Arg345Trp variant protein and stable amount of wild-type Efemp1 plasmid resulted in intracellular retention of wild-type fibulin-3. Concomitantly, preliminary experiments indicate a corresponding decrease in secretion of wild-type fibulin-3.

While the pathogenesis of ML/DHRD is not fully elucidated, we here demonstrate altered intracellular handling of fibulin-3 wild-type caused by p.Arg345Trp Efemp1 variant protein, which might result in induction of ER stress and altered RPE cell function.

As our experiments suggest that the p.Arg345Trp Efemp1 variant protein causes a dominant disease phenotype on the cellular level, we have performed initial experiments toward developing allele-specific targeting of this allele by CRISPR/Cas9. The involved missense mutation creates a PAM sequence for the SaCas9 to specifically cut the p.Arg345Trp Efemp1 allele. Thereby, we would like to further demonstrate the potential of the CRISPR/Cas system for retinal targets and autosomal dominant disorders.

P25.07 Kata Wolff Pedersen

ESTIMATING CYTOCHROME P450 EXPRESSION LEVELS IN POST-MORTEM HEPATIC TISSUE

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The activity of cytochrome P450 (CYP) enzymes in the liver is central for the elimination of a large number of drugs. There is a great inter-individual variability in the CYP enzyme activity due to both genetic polymorphisms and differences in the expression levels of the CYP enzymes. Genetic polymorphic can be determined by genotyping and may result in enzymes with altered activities. However, large variations in enzyme activity are observed within genotypes, thus genetic analysis cannot stand alone as a precise estimate of CYP enzyme activity. Inter-individual differences in CYP protein expression levels have been observed due to both environmental and genetic factors.

Knowledge about the CYP activity of an individual is relevant in forensic cases involving intoxication to determine cause of death. Post-mortem hepatic CYP enzymes quickly lose their activity, which makes it impossible to

estimate the ante-mortem hepatic CYP activity by standard methods. Therefore, there is currently no method to estimate ante-mortem enzyme activity in a deceased individual.

The aim of this study is to develop a mass spectrometry based method to quantify the expression levels of selected CYP enzymes relevant for drug metabolism in post-mortem liver tissue. In combination with genotyping, the CYP expression levels can be used to estimate ante-mortem CYP activity in deceased individuals.

P25.08 Sashia Pernille KERATOCONUS OUTCOME RESEARCH QUESTIONNAIRE - A VALIDATION
Bak-Nielsen STUDY OF THE DANISH VERSION

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Background: Keratoconus (KC) is a bilateral corneal disease with typical onset of reduced visual acuity in adolescence. Reduced quality of life (QoL) has been reported among KC patients. However, the validity of the patient reported outcome (PRO) instruments have been questioned, as they are neither disease-specific nor satisfy modern scale validation. The Keratoconus Outcome Research Questionnaire (KORQ) is the first instrument developed specifically to measure two domains of QoL in KC patients.

Purpose: To translate the KORQ into Danish and validate it in a population of Danish KC patients.

Method: The KORQ was translated using standardised translation techniques. 191 responses were included from KC patients at the Department of Ophthalmology, Aarhus University Hospital. Data will be analysed using a polytomous Rasch model.

Preliminary results: Participants characteristics: Mean age: 34.5 (\pm 12.1) years. 75.4 % male. KC severity distribution grade 1-4: KC 1: 7.1 % KC 2: 35.5 % KC 3: 52.5 % KC 4: 4.9%. Correlation showed the majority of items to be nicely correlated in both the activity limitation and symptoms scale, except for two items in the symptoms scale that were poorly correlated. The poster will include further elements of the Rasch analysis.

Perspectives: PROs are becoming increasingly important tools in the treatment of the patient as a whole person and not just an individual with a specific disease. However, the validity of the instruments is of critical importance for their usability.

P25.09 Johanne Emy Sollid PROTEIN INTERACTIONS OF THE AVP PROHORMONE AND THEIR ROLE IN FAMILIAL NEUROHYPOPHYSEAL DIABETES INSIPIDUS

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Familial neurohypophyseal diabetes insipidus (FNDI) is an autosomal dominant disorder, where patients develop excessive thirst and polyuria in early childhood. Many (>70) mutations in the AVP gene that cause a clinically invariable phenotype of FNDI exist. The clinical homogeneity of the disease is thought to relate to a uniform mechanism of protein misfolding and ER retention, followed by neuronal cell death.

We aim to determine the factors involved in cellular processing of AVP prohormone. We will do this by characterizing the protein interactions of the WT and mutant AVP prohormone in neuronal cells upon varying levels of AVP prohormone expression. We hypothesize that the factors involved in cellular processing of AVP prohormone can also be involved in AVP misfolding.

To optimally imitate AVP producing neurons, we will by transfection express variable levels of WT or mutant AVP cDNA (Ser18del, Ala19Thr) in a neuronal cell line (SH-SY5Y). We will measure the AVP secretion capacity of the cell by radioimmunoassay. We will use immunocytochemistry and confocal laser scanning microscopy to determine how different levels of AVP affects the intracellular handling of AVP. By protein cross-linking, co-immunoprecipitation followed by mass spectrometry, protein interactions of the AVP prohormone will be evaluated. Additionally, we will investigate what domains of the AVP prohormone bind to other proteins.

We expect that our studies will give new insight into the cellular handling of the AVP prohormone. In the long term, this could potentially lead to new therapeutic interventions directed to modulate cell stress response.

P25.10 Amanda Bæk ADIPOSE TISSUE FIBROSIS IN PATIENTS WITH ACROMEGALY: BEFORE AND AFTER TREATMENT

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Background: Acromegaly is caused by chronic overproduction of growth hormone (GH), which has substantial effects on adipose tissue (AT), such as excess lipolysis causing a lean body composition. Fibrosis in the AT causes a pathological tissue state that has been linked to obesity-associated diseases, seemingly irrespective of fat mass. GH has been shown to induce fibrosis in various tissues, and acromegalic patients might thus exhibit an unhealthy leanness, but the connection between GH and fibrosis in human AT lacks exploration.

Aim: To study AT biology with specific emphasis on AT fibrosis in patients with acromegaly before and after treatment.

Patients and methods: We examined adipocyte size, extracellular matrix (ECM) content and mRNA expression of fibrosis-associated genes in subcutaneous AT biopsies obtained before and after treatment from 17 patients newly diagnosed with acromegaly.

Results: A significant decrease in lean body mass and an increase in fat mass were recorded after treatment, with a median increase in absolute fat mass of 19.5 % (P < 0.05). Surprisingly, no changes in adipocyte size were observed. Collagen gene expression and ECM content were significantly decreased after treatment by a median of 53.4 % (P < 0.05) and 53.5 % (P < 0.05), respectively.

Conclusion: Our results show that GH is negatively associated with fat mass and positively associated with gene expression and accumulation of ECM proteins in the AT, but without affecting adipocyte size. It remains to be studied if the lipolytic and fibrotic effects are causally linked, and to which extent they interact with substrate metabolism and insulin sensitivity.

P26.01 Tea Lund
Laursen

SOLUBLE CD163 DECLINES DURING SUCCESSFUL DIRECT-ACTING ANTIVIRAL TREATMENT AND ASSOCIATES WITH INFLAMMATION AND FIBROSIS IN CHRONIC HEPATITIS C

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Background: Soluble (s)CD163 is released from activated liver macrophages in chronic viral hepatitis C (HCV) and serum levels reflect liver disease severity. The impact of direct-acting anti-viral (DAA) treatment on sCD163-levels and the ability of sCD163 to predict the presence of liver fibrosis remain unclear. Thus, we aimed to investigate changes in sCD163 with DAA-treatment to investigate associations between sCD163 and histological activity and fibrosis, and to validate the sCD163-based fibrosis score in HCV patients.

Methods: We examined 3 groups of patients: an Australian group (n=28) treated with pegylated-interferon and a first-generation DAA, a Danish group (n=38) treated with sofosbuvir-based DAA-regimens, and a Japanese group (n=562) assessed for activity and fibrosis (Metavir) in liver biopsies. Serum sCD163-levels were quantified by ELISA.

Results: Thirteen (46%) of the Australian patients achieved sustained virological response (SVR), and only these patients had significant decreases in sCD163-levels (p=0.008). In the Danish group, 37 (97%) patients achieved SVR at 12-weeks of post-treatment with 32% reduction in sCD163-levels (p<0.001). The decline was rapid and persisted 12 months after treatment

cessation ($p < 0.007$). sCD163 levels increased in parallel with inflammatory activity and fibrosis ($p < 0.001$). The sCD163-based fibrosis score outperformed established fibrosis scores for significant fibrosis ($p < 0.001$).

Conclusion: sCD163 levels decline rapidly with successful DAA treatment and are associated with histological activity and fibrosis. This confirms a key role for macrophages in HCV inflammation and fibrosis and supports sCD163 as a biomarker of treatment response.

P26.02 Jakob Kirkegård

ACUTE PANCREATITIS AND PANCREATIC CANCER RISK: A NATIONWIDE MATCHED COHORT STUDY

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Background: Acute pancreatitis may be a risk factor for pancreatic cancer, although previous studies have yielded inconsistent results. We examined the association between acute pancreatitis and pancreatic cancer.

Methods: We conducted a nationwide, population-based, matched cohort study of all patients admitted to a Danish hospital with a diagnosis of acute pancreatitis from 1 January 1980 to 31 October 2012. We constructed a comparison cohort by matching each patient on age and sex with five subjects from the general population. Using the Cox model, we computed hazard ratios (HRs) and 95% confidence intervals (CIs) of pancreatic cancer, adjusting for age, sex, year of pancreatitis, alcohol- and smoking-related conditions, and Charlson Comorbidity Index score.

Results: We included 41,669 patients diagnosed with incident acute pancreatitis and 208,340 comparison individuals. Median age was 55.8 years and 54.7% were men. In total, 1,175 pancreatic cancers were diagnosed within a total of 2,758,907 years of follow-up. Patients with acute pancreatitis had a higher burden of comorbidity including alcohol- and smoking-related conditions. Throughout the follow-up period, acute pancreatitis patients had an increased risk of pancreatic cancer compared with the comparison subjects. The risk attenuated over time but remained elevated after more than five years of follow-up (adjusted HR: 2.02; 95% CI: 1.57-2.61).

Conclusions: Acute pancreatitis patients have an increased risk of pancreatic cancer compared with age- and sex-matched comparison subjects from the general population. Our findings suggest that acute pancreatitis should be considered as a risk factor for pancreatic cancer.

P26.03 Peter Andersen OPEN VERSUS LAPAROSCOPIC RECTAL CANCER RESECTION AND RISK OF SURGERY FOR ADHESIVE SMALL BOWEL OBSTRUCTION: A NATIONWIDE POPULATION-BASED COHORT STUDY

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Background: Laparoscopic surgery has been reported to reduce formation of adhesions following colorectal surgery. The aim of this nationwide cohort-study was to investigate the risk of surgery for adhesive small bowel obstruction (ASBO) following open and laparoscopic rectal cancer resection.

Method: Patients undergoing rectal cancer resection between 2005 and 2013 were identified in the database of the Danish Colorectal Cancer Group. The primary outcome of surgery for ASBO was identified in the Danish National Patient Register. The risk of ASBO surgery was estimated as cumulative incidence proportions, treating death as a competing risk. We used cox proportional-hazard regression analysis with multivariable adjustment to compute hazard ratios (HR). The secondary outcome was 30-day mortality following surgery for ASBO.

Result: Among 7 657 patients, 340 (4.4 per cent) underwent surgery for ASBO. The 5-year risk of surgery for ASBO was 4.5 per cent among patients undergoing open resection (n = 4 472) and 3.0 per cent among those undergoing laparoscopic resection (n = 3 185). Laparoscopic rectal resection was associated with lower risk of subsequent surgery for ASBO (adjusted hazard ratio (aHR) = 0.65, 95 per cent c.i. 0.50 to 0.86; P = 0.002)). The aHR of mortality after ASBO was 0.84 (95 per cent c.i. 0.37-1.91; P = 0.671) when comparing patients with previous laparoscopic and open resection.

Conclusion: Laparoscopic rectal cancer resection was associated with a decreased risk of surgery for ASBO. No substantial difference in the 30-day mortality after surgery for ASBO according to surgical approach at rectal resection was observed.

P26.04 Sissel Ravn RISK FACTORS FOR METACHRONOUS PERITONEAL CARCINOMATOSIS: A NATIONWIDE POPULATION-BASED COHORT STUDY OF DANISH COLORECTAL CANCER PATIENTS

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Aim: To identify risk factors for metachronous peritoneal carcinomatosis (M-PC) after curative colorectal cancer (CRC) surgery.

Method: The study was a nationwide register-based study of all Danish CRC patients in 2006-2015. Patients were identified using the Danish Colorectal Cancer Group, the Danish Pathology Register and the Danish National Patient Register. Patients were excluded if another cancer appeared within

5 years prior to CRC diagnosis and if following occurred within 180 days after CRC diagnosis: death, another cancer, synchronous peritoneal carcinomatosis or non-curative resections. Potential predictors of M-PC were estimated by multivariable absolute risk regression, treating death and other cancer as competing risks. One- and 3-year risk differences (RD) are presented as the absolute difference between groups.

Results: In total, 22,587 patients met the criteria for inclusion. The following variables were associated with a higher risk of M-PC: right-sided colonic cancer (1-year: right colon vs. rectum, 0.60% (0.22, 0.98) and 3-year: 0.93% (0.34, 1.51)), advanced tumour stage (T4- vs. T1-category 1-year: 2.97% (2.19; 3.75) and 3-year: 6.12% (4.98; 7.25)) and lymph node metastasis (N2 vs. N0 1-year: 2.58% (1.87; 3.27) and 3-year: 4.32% (3.29; 5.34)).

A subanalysis revealed that the radicality of surgery was associated with an increased risk of M-PC (1-year: R1 vs. R0: 4.16% (1.77, 6.54) and 3-year: 6.18% (2.81, 9.55)).

Conclusion: T-category and lymph node metastasis is associated with increased risk of M-PC, with a significant increase in the risk from 1 year until 3 years after surgery. Right-sided colonic cancers are associated with an increased risk of M-PC.

- P26.05 Anne Catrine Bjerre Mikkelsen **Cancellation** EFFECTS OF POTASSIUM DEFICIENCY ON LIVER PROTEIN AND UREA SYNTHESIS IN RATS
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- Purpose: We aim to investigate the effect of hypokalemia on liver protein and urea synthesis in a hypokalemia rat model.
- Background: Potassium depletion reduces gene expression, protein synthesis, and growth in plants, bacteria, rodents and humans. Potassium seems intimately related to peptide bond formation, yet surprisingly the mechanism is still obscure. The effect of hypokalemia on liver protein synthesis is scarcely described. However, in a pilot study, we found reduced protein synthesis leading to diminished urea synthesis with increased ammonia levels. This may be important as hypokalemia and hyperammonemia is frequent in chronic liver disease complicated with hepatic encephalopathy.
- Material and methods: The animal study consists of 105 female Wistar rats allocated into three groups: controls, pair-fed controls and potassium depleted in order to compare hypokalemic rats to normokalemic rats. Hypokalemia is induced by potassium-free diet and distilled water. Blood, liver, muscle and kidneys are collected, and various elements, such as production of hormones, plasma proteins, mRNA levels of liver proteins and enzymes, will be analyzed. Furthermore, the capacity of urea synthesis in vivo will be estimated.
- Results: For the present time, the animal study is running. Data and results are pending.
- Conclusion: In a hypokalemia rat model, we aim to investigate the effect of hypokalemia on circulating levels of ammonia and liver protein and urea

synthesis. If our hypotheses can be confirmed, it will have major impact on the understanding of the role of potassium in liver functioning.

- P26.06 Nina Marie Videbech RISK FACTORS OF RENAL FAILURE IN LONG-TERM CHILDHOOD CANCER SURVIVORS: AN ADULT LIFE AFTER CHILDHOOD CANCER IN SCANDINAVIA (ALICCS) STUDY

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Background: As a result of continuous advances in childhood cancer treatment, the survival rates have improved remarkably in the past half century. Today, 80% of affected children can be expected to be long-term survivors, which has led to a growing population of survivors and an increased knowledge of long-term effects of childhood cancer treatment. Childhood cancer treatment has been associated with long-term risk of renal failure, but risk factors remain to be comprehensively investigated.

Methods and materials: We identified a study cohort of 21,258 five-year survivors of childhood cancer diagnosed before the age of 20 years in the period of 1970-2008 in the five Nordic countries. We randomly selected 600 survivors from the study cohort. This sub-cohort represents the entire survivor cohort with respect to level and type of antineoplastic treatment, cancer diagnosis and demographics. Furthermore, 168 survivors with renal failure were identified from the study cohort as our cases. Detailed information on treatment from the individual medical records was collected for both groups. The group of cases will be compared to the sub-cohort to fully assess the risk factors of the serious late effect - renal failure.

Results and conclusion: No results or conclusion is yet available. The data is currently in the process of getting prepared for analyses.

Acknowledgements: Aarhus University

Keywords: Childhood cancer, late effects, renal failure

- P26.07 Frederik Rønne Pachler FERTILITY IN PATIENTS WITH FAILURE OF RESTORATIVE PROCTO-COLECTOMY: A NATIONAL COHORT STUDY OF 1455 PATIENTS

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Background: Birth rates are decreased in females after restorative proctocolectomy, while it is increased in males. Birth rates after failure of restorative proctocolectomy have not been studied.

Method: All patients with ulcerative colitis in 1980-2010 were identified. Records for parenting a child, surgery and failure were cross-linked, and birth rates were calculated.

Results: We included 28,834 patients with ulcerative colitis, 13,549 males. 1,455 had restorative proctocolectomy, 737 males and 199 had failure, 83 males.

Females with failure have lower birth rate at 15.9 children/1000 years, compared with females with no failure at 30.4 children/1000 years and females with ulcerative colitis at 46.2 children/1000 years, $p < 0.05$. Males with failure have a birth rate at 39.3 children/1000 years, similar to patients with ulcerative colitis at 40.8 children/1000 years, $p = 0.8$. Males with no failure have a higher birth rate at 49.0 children/1000 years compared with males with ulcerative colitis, $p < 0.05$.

Conclusion: Failure of restorative proctocolectomy adds a further negative impact on birth rates in females, while it diminishes the positive impact of restorative proctocolectomy seen in males.

P26.08 Line Weisbjerg DISTURBANCES IN THE RESPIRATORY CHAIN COMPLEXES AS A POSSIBLE CAUSE OF MITOCHONDRIAL DYSFUNCTION IN CHRONIC FATIGUE SYNDROME

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Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a debilitating illness with yet unknown etiology, making diagnosis and treatment challenging. Research in ME/CFS is hampered by heterogeneity in the clinical expression and the diagnostic criteria. Recent research has shown mitochondrial dysfunction with mitochondrial energy deficiency and oxidative stress in ME/CFS patients. We hypothesize that this mitochondrial dysfunction is caused by a vicious cycle of overproduction of reactive oxygen species (ROS), lipid peroxidation of the inner mitochondrial membranes, and damage to the respiratory chain complexes. From six unrelated patients diagnosed with ME/CFS, we have collected peripheral blood mononuclear cells (PBMCs) for in vivo studies and skin fibroblasts to establish an ex vivo model and study stress induced cellular changes. Mitochondrial function will be assessed using an extracellular flux analyzer that enables real-time measurement of glycolysis and oxidative phosphorylation. Preliminary results on PBMCs from the six patients showed an increased mitochondrial proton leak together with a decreased ability to couple maximum oxygen consumption to ATP production. Additionally, ROS production will be quantified with image cytometry using the MitoSOX™ Red probe and fluorescence upon reaction with superoxide, the main ROS. Initial results show signs of increased ROS in cultured fibroblasts from the ME/CFS patients when exposed to metabolic stressed. Results from both tissues support each other and indicate oxidatively damaged mitochondrial membranes that affect mitochondrial respiration efficiency, which supports our hypothesis of mitochondrial dysfunction in ME/CFS.

P26.09 Stine Karlsen PATIENT SPECIFIC BIOMARKERS - A ROLE FOR CIRCULATING TUMOR DNA IN HEPATOCELLULAR CARCINOMA MANAGEMENT AND SURVEILLANCE?

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Background: Cancer treatment and surveillance is associated with significant costs, both financial and personal costs. It is, therefore, crucial to be able to evaluate the clinical response to treatment efficiently. We have yet to identify a biomarker able to detect progression, relapse or stable disease in hepatocellular carcinoma (HCC). Mutations in the promotor region of TERT are frequent in HCC and may influence the prognosis. CTNNB1, a gene in the β -catenin pathway, often harbors mutations in HCC. It is known that the mutational landscape of HCC is dependent of the etiology of disease. Previous studies arise from areas of with a high prevalence of chronic viral hepatitis. In Denmark, the etiology of liver cirrhosis and HCC is primarily alcohol consumption (ALC) and non-alcoholic fatty liver disease (NAFLD).

Aim: To investigate whether CTNNB1 and TERT mutations can be detected in cell free plasma DNA derived from patients with HCC of different etiologies. To investigate, in individual patients, changes in the amount of mutated DNA fragments after treatment and over time. To investigate if detection of circulating tumor DNA can be used to detect relapse after curative treatments or progression after palliative treatments.

Methods: Inclusion commenced in November 2016. Blood samples are obtained before starting a new treatment, 1 month after treatment and every 6 months hereafter. The digital droplet PCR technique is used for detection of mutated DNA fragments, presence and frequency. Material for next generation sequencing is obtained for future analysis.

Results: 65 patients have been included. TERT and CTNNB1 assays have been tested. Patient samples are run within the coming weeks.

P26.10 Helene Mathilde Larsen THE PATHOGENESIS OF CHRONIC WATERY AND LOOSE STOOL AFTER RIGHT-SIDED HEMICOLECTOMY FOR CANCER

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Background: Colon cancer patients treated with right-sided hemicolectomy (RHC) are shown to have long-term bowel dysfunction, such as watery and loose stool, which affects their quality of life. However, the pathophysiology of the chronic loose stool is unknown. Therefore, the aim of this study is to investigate the aetiology of the chronic watery and loose stool among RHC patients curatively operated for cancer in cecum and the ascending colon.

Method: Fifty cases with chronic watery and loose stool after RHC will be compared to a control group of 20 RHC patients without loose stool. The patients will be recruited based on a questionnaire survey from 2016 regarding bowel function after treatment for colon cancer. All participants will undergo selenium-75 homocholeic acid taurine (SeHCAT) scan and glucose breath test, which will determine whether the patients have bile acid malabsorption and/or small intestinal bacterial overgrowth, respectively. The gastrointestinal transit time (GITT) will be determined by the Gothenburg method. In addition, cases and controls will be asked to complete a questionnaire regarding bowel function and quality of life.

Perspectives: We expect that the findings of our study will provide new knowledge of the mechanisms of chronic watery and loose stool after RHC. We assume that the cases will have a higher frequency of bile acid malabsorption and bacterial overgrowth compared to the control group. Furthermore, we assume the GITT to be shorter among the patients with chronic loose stool. These findings will allow sufficient treatment, which may improve the quality of life in long-term colon cancer survivors.

P26.11 Anne
Kraushaar
Martensen

ESTABLISHING AN EXPERIMENTAL ANIMAL MODEL OF POSTOPERATIVE ILEUS

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Introduction: Paralytic postoperative ileus (POI) is a significant problem after especially abdominal surgery. The condition increases both morbidity and mortality as well as represents a significant cost on hospital budgets. Options for treatment of POI are sparse and not very efficient.

Aim: The aim of this study was to establish an experimental animal model of POI for further research in treatment options of POI.

Method: The study material comprises 8 Danish Landrace pigs weighing 60 kg each. In a pilot series, the operative technique was established: A midline laparotomy was performed, followed by peritonectomy and cholecystectomy. The content from the gallbladder was distributed intraperitoneally. In addition, the adherence of the colon was dissected and the spiral colon mobilized. Finally, the gastrointestinal tract was manipulated for two hours using cotton gloves. A SmartPill (Giving Imaging) was inserted in the stomach, enabling us to analyze the intestinal motility wirelessly. The pigs were observed at the animal housing facility for up until ten days.

Results: Of the eight pigs, six had POI, defined as no stools for 3 days or more. One pig died of asphyxia, and one pig died of colon necrosis. Data from the SmartPill are pending.

Discussion: This study established an animal model of POI, which is essential for further research in potential treatments. These animal experiments are a prerequisite before any clinical studies of new treatments can be initiated. POI increases morbidity as well as mortality, and a potential treatment will thus have great socio-economic impact as patients will have a faster hospital discharge and recovery with less complications.

P27.01 Thomas Skovhus Prior TRANSLATION AND INITIAL VALIDATION OF THE SAINT GEORGE'S RESPIRATORY QUESTIONNAIRE, IPF-SPECIFIC VERSION

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Introduction: The Saint George's Respiratory Questionnaire, idiopathic pulmonary fibrosis (IPF)-specific version (SGRQ-I) is a validated, disease-specific health-related quality-of-life questionnaire. The study aimed to translate SGRQ-I from English into Danish and conduct the initial validation.

Methods: The questionnaire was translated into Danish following acknowledged guidelines. Initially, the questionnaire was translated following a forward-backward procedure. Consensus was reached in the presence of differences between the translations, and the translation was reviewed by the original author. The questionnaire was then completed by a group of patients with IPF. Patient interviews were performed to determine face validity, content validity, relevance and comprehensiveness. Adjustments to the questionnaire were sent to the original author for review and final approval.

Results: After completing the SGRQ-I, 5 patients with IPF were interviewed; 3 men, 2 women, mean age 67 (range 53-72), mean FVC% predicted 82 (range 65-97), mean DLCO% predicted 55 (range 42-61). Only minor alterations were made to the translation after the original author's review of the back translation and after patient interviews. The questionnaire had a high face and content validity according to the patients and expert clinicians.

Conclusions: The translated version of SGRQ-I was easily completed and demonstrated high face and content validity. It is a relevant and comprehensive measure of health-related quality of life in patients with IPF. A nationwide study investigating the internal consistency, concurrent validity, test-retest reliability and responsiveness of the questionnaire is ongoing.

P27.02 Louise Devantier PET VISUALIZED STIMULATION OF THE VESTIBULAR ORGAN

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Background and objective: Our knowledge of the vestibular cortical network in humans is variegated. With the exception of the vestibular system, all sensory systems have been localized to specific cortical areas of the human brain. A well-defined and unique vestibular cortex is still to be found. The current knowledge of vestibular cortical processing in humans is mostly based on studies where PET or fMRI were performed during a non-physiological stimulation either with caloric testing, galvanic stimulation, or

vestibular evoked myogenic potentials (VEMP). However, the use of non-physiological stimulation to localize a vestibular cortex is questionable. For instance, a caloric test not only stimulates the vestibular organ but also the vagal, thermal, nociceptive and tactile sensory receptors leading to a complex and potential misleading cortical activation. The specific objective of this study is to visualize the cortical and subcortical activity owing to a physiologic stimulation of the human vestibular organ.

Method: 12 healthy right-handed trial participants underwent three FDG-PET scans, one baseline scan and two scans after physiologic stimulation of the vestibular organ. Whilst sitting in our specially designed self-propelled chair, the trial participant was injected with an FDG-tracer. Right after the injection, the chair was set in motion for 35 minutes. Subsequently a brain PET-scan was obtained. The chair was not set in motion prior to the baseline scan; the participant simply remained seated for 35 minutes.

Results: Data from all 12 healthy participants will be presented and discussed.

P27.03 Michael Brun
Andersen CT TEXTURE ANALYSIS OF PULMONARY LESIONS IN PATIENTS SUSPECTED OF LUNG CANCER

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Objective: In this report, we evaluate the impact of CT texture analysis (CTTA) of pulmonary lesions when compared to final tumor stage in patients with suspected lung cancer on contrast enhanced CT.

Methods: Using texture analysis, we analysed 104 lesions in 104 patients suspected for lung cancer with a positive CT correlate. The analysis was performed using TexRAD (developed by TexRAD Ltd. UK). Histology was our reference standard. Malignancy was present in 92 lesions. CTTA comprised a filtration-histogram technique, where filtration extracted and enhanced features of different sizes (fine, medium, coarse - scales) followed by histogram analysis using Mean (M), Entropy (E), Uniformity (U), Total no. of voxels and Kurtosis (K) within the entire volume of the suspected lesion. The operator performing the CTTA was blinded to the histological results.

Results: In 58 malignant lesions with histologically verified TNM tumour stage, a Spearman's rank correlation found significant positive correlations between Kurtosis and tumour stage at coarse filter scales. ($\rho(58)=0.476$, $p<0.0005$). We also found a significant positive correlation between Total no. of voxels and tumour stage on unfiltered data ($\rho(58)=0.387$, $p=0.003$).

Conclusion: A significant correlation between texture figures and final tumor stage was found in patients with lung lesions suspected of lung cancer. Texture analysis may add complementary information to CE-CT.

P27.04 Hanne Nielsen PROTON PUMP INHIBITOR PRESCRIPTIONS AND BREAST CANCER RECURRENCE: A DANISH NATIONWIDE PROSPECTIVE COHORT STUDY

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Background: Proton Pump Inhibitors (PPI) and H₂-antagonists (H₂A) are indicated for gastrointestinal reflux disease and peptic ulcers. Research in breast cancer cell lines suggests that PPIs inhibit tumorigenesis, induce apoptosis, and disrupt the tumor microenvironment acidity, potentially enhancing the effectiveness of cancer-directed treatment. We, therefore, investigated the association of PPIs and H₂As (as an active comparator exposure) with breast cancer recurrence.

Methods: Our cohort included all Danish women diagnosed with non-metastatic breast cancer registered in the Danish Breast Cancer Group (DBCG) between 1996 and 2008. We ascertained information on PPIs, H₂As, and potentially confounding drugs from the National Prescription Register. Follow-up began on the date of diagnosis and continued until the first of breast cancer recurrence, death or immigration, ten years, or 30 June 2016. We used Cox regression models to calculate crude and adjusted hazard ratios (HRs) and associated 95% confidence interval (95% CI) of recurrence. PPIs, H₂As and potentially confounding drugs were modelled as time-varying exposures lagged by 1 year. Other variables were modelled as baseline variables.

Results: We identified 33,841 patients with 210,512 person-years of follow up. 6,146 patients developed recurrent disease. Neither PPI use nor H₂A use were associated with recurrence (HR_{adjusted}=0.99, 95% CI =0.66;1.48, and 1.13, 95 % CI= 0.66;1.96, respectively). Additional analyses (cumulative exposure, stratified analyses and sensitivity analyses) are ongoing.

Conclusion: Our analyses to date do not suggest an association of PPIs with risk of breast cancer recurrence.

P27.05 Anne Sofie Borg Hammer HYPODIPLOIDY IN CHILDHOOD ACUTE MYELOID LEUKEMIA: A RETROSPECTIVE COHORT STUDY BY THE INTERNATIONAL BERLIN-FRANKFURT-MÜNSTER STUDY GROUP, A MULTICENTER COLLABORATION

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Background: Survival in childhood acute myeloid leukemia (AML) reaches 70%, but relapse remains a frequent event. Cytogenetic abnormalities have prognostic impact and are used in risk stratification of patients. Hypodiploidy defined as a modal number of less than 46 chromosomes is associated with a poor outcome in pediatric acute lymphoblastic leukemia. In childhood,

AML loss of chromosome 7 has an adverse prognosis, but the survival and the clinical characteristics of other monosomies have only received scant attention.

Material and methods: This study is a descriptive, retrospective cohort study including patients diagnosed with de novo AML between January 2000 and December 2015. All study groups affiliated with the international Berlin-Frankfurt-Münster AML study group (I-BFM-AML) have been invited to participate. Patients below 18 years of age with a hypodiploid karyotype detected by G-banding were included. Cases with constitutional hypodiploidy are excluded, as are cases with composite karyotype, monosomy 7 and t(8;21) with sex chromosome loss.

Results: Data have been collected since December 2015 and will be completed by January 2018. Sixteen affiliated study groups worldwide have provided data on a total of 108 eligible cases. So far, cytogenetic review has been performed on 80 patients. 17 have been excluded; hence, 63 patients are included by October 2017. Cytogenetic review will finish by November 2017. The frequency of hypodiploidy is yet to be evaluated. Data are currently prepared for analyses, and preliminary results will be presented at the PHD day.

Acknowledgements: This study is supported by the Danish Cancer Society

Keywords: childhood cancer, cytogenetics, leukemia

P27.06 Anne-Sofie Skou SENSITIVE METHODS FOR MONITORING RESIDUAL DISEASE IN CHILDHOOD ACUTE MYELOID LEUKEMIA

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Background and aim: Detection and interpretation of minimal residual disease (MRD) in childhood acute myeloid leukemia (AML) is complex, and the best method remains debatable. Flow Cytometry (FC), Real-Time quantitative PCR (qPCR), Droplet digital PCR (ddPCR) and Next-generation sequencing (NGS) are all techniques of MRD detection and differ in sensitivity and applicability, but no useful monitoring regimen exist. We aim to elucidate molecular genetics of relapsed childhood AML and identify new putative MRD markers by collecting peripheral blood (PB) samples at monthly intervals during first complete remission (CR) in a large cohort of patients.

Methods: Since 2014, monthly PB samples from patients in CR at the end of chemotherapy or hematopoietic stem cell transplantation (HSCT) treated on the NOPHO-DBH-AML 2012 protocol in the Nordic countries and the Netherlands have been biobanked. In patients suffering hematological relapse, NGS will be applied to identify a diagnostic mutational signature. Subsequent ddPCR quantification of applicable targets and the longitudinal expression profile of six leukemia-associated genes (qPCR of CCL23, PRAME, ST18, SPAG6, MSLN and GAGED2) in PB during follow-up will be performed and compared between patients suffering hematological relapse and patients in long-term CR. Furthermore, a leukemic stem cell

related antigen flow cytometric assay will be employed in the follow-up samples.

Perspectives: We hope that our study will demonstrate that longitudinal MRD quantification in PB during follow-up based on a patient-specific molecular profile may be applicable in most childhood AML patients and serve to predict imminent hematologic relapse.

P27.07 Nanna Holt
Jessen

THE DEVELOPMENT OF A COMPREHENSIVE ABDOMINAL 'YES-NO' PATHWAY FOR PRIMARY CARE PATIENTS WITH VAGUE NON-SPECIFIC ABDOMINAL SYMPTOMS

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Background: To optimise cancer diagnosis in Denmark, a 3-legged strategy has been proposed with urgent referral for alarm symptoms, referral to diagnostic centres for patients with serious non-specific symptoms and lastly a 'yes-no' pathway for patients with vague non-specific symptoms.

Aim: The overall aim of this project is to explore the epidemiological and clinical need for an abdominal 'yes-no' pathway, which general practitioners (GPs) can use for diagnostic work in patients with vague non-specific abdominal symptoms and to develop such a pathway.

Methods: Study 1 is a national cohort study exploring the number of abdominal cancer patient pathways (CPPs) and investigations undertaken in the year prior to a diagnosis of an abdominal cancer.

Study 2 consist of: a) a literature review regarding abdominal symptoms and diagnostic pathways in general practice, and b) focus group interviews with participants with expertise regarding patients with abdominal symptoms and abdominal cancers and other abdominal diseases. We will develop a rapid, stepped abdominal 'yes-no' pathway. In study 3, we set-up the clinical abdominal 'yes-no' pathway and combine it with evidence-based clinical training for GPs, and assess the feasibility of the abdominal 'yes-no' pathway.

Results: Data are not yet available.

Perspective: In patients with vague non-specific abdominal symptoms, who do not fulfil the access criteria for the CPPs, but in whom the diagnosis of an abdominal cancer should not be missed, this study may provide important knowledge on how to reduce the time to diagnosis and improve the diagnostic pathway of abdominal cancers or other serious abdominal disease in the future.

P27.08 Trine Line
Hauge
Okholm

CIRCULAR RNA EXPRESSION IS ABUNDANT AND CORRELATED TO AGGRESSIVENESS IN EARLY-STAGE BLADDER CANCER

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The functions and biomarker potential of circular RNAs (circRNAs) in various cancer types are a rising field of study, as emerging evidence relates circRNAs to tumorigenesis. Here, we profiled the expression of circRNAs in 457 tumors from patients with non-muscle-invasive bladder cancer (NMIBC). We show that a set of highly expressed circRNAs have conserved core splice sites, are associated with Alu repeats, and enriched with Synonymous Constraint Elements as well as microRNA target sites. We identified 113 abundant circRNAs that are differentially expressed between high- and low-risk tumor subtypes. Analysis of progression-free survival revealed 13 circRNAs, among them circHIPK3 and circCDYL, where expression correlated with progression independently of the linear transcript and the host gene. In summary, our results demonstrate that abundant circRNAs possess multiple biological features, distinguishing them from low-expressed circRNAs and non-circularized exons, and suggest that circRNAs might serve as a new class of prognostic biomarkers in NMIBC.

P28.01 Mathias
Kristensen

DOES ALDOSTERONE STIMULATE THE NA⁺CL⁻ COTRANSPORTER NCC INDEPENDENTLY OF HYPOKALEMIA?

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The hormone aldosterone stimulates Na⁺reabsorption and K⁺excretion by the kidney. Aldosterone increases activity of the epithelial Na⁺channel (ENaC) and potentially the abundance of the Na⁺-Cl⁻-cotransporter (NCC) in the distal convoluted tubule (DCT). Whether the effects of aldosterone on NCC are direct, or only due to the ENaC mediated accompanying hypokalemia that in itself increases NCC abundance, are unclear. The present study aims to investigate the direct effect of aldosterone on DCT cells and NCC abundance by increasing plasma aldosterone levels while maintaining normal plasma K⁺level. An initial in vivo study aims to maintain a normal plasma K⁺level by administering the ENaC inhibitor, amiloride, in addition to aldosterone. Mice will be followed for 6 days using the following protocols: 1) standard diet + vehicle, 2) standard diet + aldosterone, 3) standard diet + aldosterone and amiloride and 4) low K⁺diet + vehicle. After 6 days, plasma K⁺level and kidney NCC and ENaC abundances will be determined using western blotting (WB). Immunohistochemistry (IHC) will be performed to compare NCC abundance in DCT1 and DCT2 - as only DCT2 is regarded as aldosterone-sensitive. Two ex vivo studies will be performed on: 1) isolated kidney tubules and 2) kidney slices. The tissue will be kept in

cell media with various concentrations of aldosterone and K⁺ for 24 hours. Levels of NCC and ENaC will subsequently be determined using WB and IHC.

- P28.02 Maria Linaa Markussen STATINS AS A NEW TREATMENT DRUG FOR LITHIUM-INDUCED NDI
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- Background: Lithium (Li) is used to treat bipolar disorders. Li also affects the kidneys' ability to concentrate urine, and patients may develop nephrogenic diabetes insipidus (NDI). Li-NDI is associated with severe polyuria and downregulation of AQP2. Statins are cholesterol-lowering drugs, which increase AQP2 translocation to the membrane and improve urine concentration in Brattleboro rats. Statins also appear to have protective effects in Li-NDI patients. This project will investigate if statins are able to prevent the Li-induced changes in the kidney.
- Methods: Male C57BL/6 mice (n=6 in 3 groups) were given: control; Li; Li/atorvastatin (Ator) food for 21 days. Urine output and osmolality were measured in metabolic cages for the last 5 days. At day 21, kidneys were taken out for western blot (WB) and immunohistochemistry. A collecting duct cell line (n=3 per group) was treated with: control; Li; Li/Ator; Ator. AQP2 protein levels were analyzed by WB.
- Results: Li increased urine output (0.46 ± 0.04 vs 0.07 ± 0.01 ml/BW, $p=0.002$) and decreased urine osmolality (425 ± 38 vs 1855 ± 232 mOsm/kg, $p<0.001$) compared to controls, but there were no differences between Li and Li/Ator in urine output (0.46 ± 0.04 vs 0.59 ± 0.1 ml/BW, $p=0.39$) and osmolality (425 ± 38 vs 423 ± 52 mOsm/kg, $p=0.9999$). Li reduced AQP2 compared to controls (0.48 ± 0.05 vs. 1.0 ± 0.10 , $p=0.043$), but there were no differences between Li and Li/Ator (0.48 ± 0.05 vs. 0.57 ± 0.22 , $p=0.877$). In the cell exp., both Li (0.67 ± 0.03 vs. 1.0 ± 0.10 , $p=0.013$) and Li/Ator (0.52 ± 0.03 vs. 1 ± 0.10 , $p=0.001$) reduced AQP2 compared to controls.
- Conclusion: Atorvastatin appear not to have a positive effect on Li-induced NDI.
- P28.03 Julie Birkmose Axelsen EFFECTS OF 6-MERCAPTOPYRINE IN PRESSURE OVERLOAD INDUCED RIGHT HEART FAILURE
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- Background: Pulmonary arterial hypertension (PAH) causes right ventricular (RV) failure, which is the predominant cause of death in PAH patients. The chemotherapeutic agent 6-mercaptopurine (6-MP) reduces pulmonary vascular remodeling and improves RV function in a rat model of PAH. In this

study, we investigate the direct cardiac effects of 6-MP in a rat model of isolated right heart failure caused by pulmonary trunk banding (PTB).

Methods: Male Wistar rat weanlings (112 g ± 12 g) were randomized to sham operation (sham, n=10) or PTB. The PTB animals were randomized to placebo treatment (PTB-control, n=9) or 6-MP treatment (7.5 mg/kg/day) with treatment start before the PTB procedure (PTB-prevention, n=10) or two weeks after (PTB-reversal, n=9). Effects were evaluated by echocardiography, MRI scans, and invasive pressure-volume measurements before the rats were euthanized and the RV stored for histology and molecular analyses.

Results: PTB increased RV afterload and caused RV hypertrophy and failure, which was evident by decreased cardiac output and RV dilatation in all PTB rats compared to sham. In the PTB rats, treatment with 6-MP did not improve RV function nor reduce RV hypertrophy in any of the treatment groups compared to PTB control. The end body weight and white blood cell count were reduced in the PTB-reversal group compared to PTB-control.

Conclusion: The PTB caused RV failure in all rats subjected to the procedure. Treatment with 6-MP did not improve RV function nor reduce RV hypertrophy. Further analyses are needed to clarify potential molecular effects of 6-MP in right heart failure.

P28.04 Katrine Berg SURVIVAL AND GRAFT FUNCTION IN HEART TRANSPLANT PATIENTS RECEIVING ADVERSE RISK PROFILE DONOR HEARTS

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Aim: To investigate if use of adverse cardiovascular risk profile (ACRP) grafts is associated with impaired graft function and adverse long-term outcome in heart transplant patients.

Methods: Survival status was obtained from Scandia transplant and a local prospective database. ACRP donors had at least one of the following characteristics: donor age ≥ 55 years, known diabetes mellitus, history of arterial hypertension, death caused by hypoxemia, impaired LVEF < 60%. Normal risk profile (NRP) donors met none of these criteria. Graft function was evaluated by echocardiography in patients alive up to 3 months before censoring on 11 September 2019. Cardiac allograft vasculopathy status (CAV) was obtained in all patients by coronary angiography.

Results: From 31 December 1992 to 11 August 2016, 302 heart transplantations were performed in 296 patients. Median survival was 16.5 years (95% CI, 14.3 - 22.9). We found no difference in survival between ACRP and NRP recipients (HR 0.63 (95% CI, 0.33 - 1.19), p=0.15). Survival rates remained comparable after adjustment for transplantation period (HR 0.62 (95% CI, 0.33 - 1.18), p=0.15). Median donor age increased significantly over time with median survival of 13.3 years (10.1-) when donor age >55 years and 18.4 years (14.9-) when donor age <55. LV systolic function was better in ACRP compared with NRP group in terms of higher LVEF (p<0.05) and ventricular GLS (p<0.05). Relation between donor age and cumulative incidence of CAV will be analysed.

Conclusion: Graft function and survival were excellent in ACRP recipients. The strategy to expand donor availability using marginal donors performed in our center seems safe and feasible.

- P28.05 Lærke Dam
Dengsøe
Petersen IMPLANTABLE CARDIOVERTER DEFIBRILLATOR THERAPY AND RELATED COMPLICATIONS IN YOUNG PATIENTS WITH INHERITED CARDIOMYOPATHY OR CHANNELOPATHY: A 17-YEAR COHORT STUDY

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Aim: To quantify appropriate and inappropriate therapy and complications related to treatment with Implantable Cardioverter Defibrillator (ICD) in young Danish patients who have received an ICD for a hereditary cardiomyopathy or channelopathy.

Methods and results: This was a retrospective study including 117 patients who had an ICD implanted at Aarhus University Hospital, Denmark, from 1999 to 2015. Patients were followed from the date of ICD implantation until the event of interest, migration, death, heart transplantation or end of follow-up on 1 February 2017. The events of interest were appropriate ICD therapy, inappropriate ICD therapy and complications related to the ICD. Mean age at implantation was 30.5 ± 12.8 years, and the patients were followed for a mean period of 7.2 ± 4.3 years. The cumulative incidence at 1, 5 and 10 years was 16.2%, 28.2% and 43.4% for appropriate therapy, 6.0%, 12.2% and 18.5% for inappropriate therapy, and 6.8%, 17.4% and 30.4% for implant-related complications, respectively.

Conclusion: We demonstrated a high risk of appropriate ICD therapy in patients implanted with an ICD because of a hereditary cardiomyopathy or channelopathy. Nevertheless, the risk of inappropriate therapy and complications are not neglectable and should be balanced against the possible benefits.

- P28.06 Anne Sif Lund
Ovesen NEUROHORMONAL AND INFLAMMATORY ACTIVITY IN ADULT PATIENTS WITH ATRIAL SEPTAL DEFECT

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Background: Atrial septal defect (ASD) is either treated conservatively or by surgical/transcatheter closure. Conservative treatment is chosen for patients with hemodynamically insignificant defects or with severe comorbidity. Our previous studies showed a higher prevalence of atrial fibrillation and pneumonia in adult patients with an unrepaired ASD compared to both the general population and to patients with a closed ASD. Both atrial fibrillation and pneumonia are associated with increased levels of inflammatory and neurohormonal biomarkers. The aim of this present study is to evaluate

biomarkers in adult patients with unrepaired ASD and compare them to patients with closed ASD and a healthy control group.

Material and methods: We are including patients with unrepaired ASD aged 18-65 years. The patients are divided into open ASD and spontaneously closed ASD. Furthermore, patients with a closed ASD as well as healthy, age- and gender-matched controls subjects are included as reference groups. Plasma concentration of inflammatory and neurohormonal biomarkers are assessed, including interleukin (IL)-6, pro-atrial natriuretic peptide and pro-brain natriuretic peptide.

Results: At present, 127 patients with unrepaired ASD have participated, as well as 22 patients with closed ASD and 22 healthy controls. Blood samples are currently being analysed.

Discussion/perspectives: Results will improve the understanding of the pathological mechanisms of the complications related to ASD. A complete understanding of the physiological and hormonal changes in these patients will facilitate follow-up and might change indications for closure of atrial septal defects.

P28.07 Josephine
Johnsen

RAPID CYCLE DELIBERATE PRACTICE VERSUS LEARNING CONVERSATION IN TEACHING LAYPERSONS BASIC LIFE SUPPORT - A RANDOMIZED CONTROLLED TRIAL

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Background: Feedback is a cornerstone in skill acquisition at basic life support and automated external defibrillation (BLS/AED) courses. The learning conversation (LC) is the standard European Resuscitation Council (ERC) feedback method, where the learner receives feedback after skill training. Contrary, using the novel teaching approach rapid cycle deliberate practice (RCDP), feedback is provided throughout skill training. Errors are corrected immediately as they occur, and the learner is exposed to repetitive practice of skills to ensure muscle memory. We aim to investigate the effect of using RCDP compared with LC at BLS/AED courses for laypersons. We hypothesize that RCDP is superior to LC when comparing learning outcome.

Methods: The study is a randomized controlled superiority trial. Laypersons will be randomized 1:1 to BLS/AED training using either RCDP or LC. They will be instructed in single-rescuer adult BLS/AED according to ERC Guidelines 2015. All participants will be tested immediately after the course and after three months to assess skill acquisition. Both training and tests will be audio- and video-recorded for later quality assessment. Questionnaires

on self-confidence, self-evaluated BLS/AED skills and participants' perception of teaching methods will be distributed.

Perspectives: If RCDP is superior to LC, it will provide evidence that may change the current teaching practice in BLS/AED courses worldwide. RCDP is a simple method that may improve learners' learning outcome and skill acquisition from BLS/AED courses. If so, implementation of RCDP can potentially improve the quality of BLS/AED delivery and thereby ultimately increase the survival from cardiac arrest.

P28.08 Archana
Kulasingam NOVEL BIOMARKERS IN THE ACUTE PHASE OF ST-ELEVATION MYOCARDIAL INFARCTION

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Background: ST-elevation myocardial infarction (STEMI) is caused by thrombus formation as a result of plaque rupture. Major players in STEMI are activation of inflammation, platelets, coagulation and fibrinolysis. Myocardial ischaemia may lead to necrosis and, in consequence, a poor prognosis with possible fatal result. Recently, new proximity extension assays, including a panel of biomarkers for atherosclerosis, have been developed. It is now possible to analyze many cardiovascular related biomarkers simultaneously by using proximity extension assay.

Aim: To investigate the expression of a wide range of cardiovascular protein biomarkers in the acute phase of STEMI compared with the expression in the stable phase 3 months after STEMI.

Methods: The study is a prospective observational study, including 48 STEMI patients treated with primary percutaneous coronary intervention (PPCI). Blood samples have already been collected and were obtained immediately prior to PPCI, 4 and 12 hours after PPCI and again 3 months later. Levels of 92 biomarkers evaluating inflammation, platelets, coagulation or fibrinolysis are assessed by a proximity extension assay based technique Olink CARDIOVASCULAR III®.

Results: The data collection has been completed, and data are currently being prepared for analysis. Preliminary results will be presented.

Perspectives: Novel biomarkers in the acute phase of STEMI will improve our knowledge about the pathophysiology of STEMI and may facilitate the development of improved diagnostics and treatment options for STEMI patients.

P29.01 Henrik Thyge Corfitsen INSIGHT GAINED FROM GENOME-WIDE INTERACTION AND ENRICHMENT ANALYSIS ON WEIGHT GAIN DURING CITALOPRAM TREATMENT

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Background: Weight gain is a possible side effect of the pharmacological antidepressant treatments. Defining antidepressant prescriptions based on personal genetic makeups would decrease the risk of weight gain.

Methods: Clinical and genetic data from the STAR*D study were accessed through the NIMH. 643 individuals (63.45% females) were included. All patients received citalopram (40 mg/day). Weight gain was measured as "Weight (Increase) Within the Last Two Weeks" and ranges from 0 ("no weight change") to 3 ("has gained 5 pounds or more"). SNPs were excluded for allele frequency <0.01 and low genotype call rate. Deviations from the Hardy-Weinberg equilibrium were accepted under a P-threshold of 0.0001. Enrichment analysis SNPs associated with the investigated phenotype were ranked according to the p-value of association. The first 1000 SNPs showing a stronger association with the phenotype were selected. The genes that harbored such variations were investigated for enrichment.

Results: The axon guidance (p.adjust = 0.005) and the developmental biology pathway (p.adjust = 0.01) were enriched in variations associated with weight gain. A number of variations were harbored by genes whose products are involved in the synthesis of collagen (COL4A3, COL5A1 and ITGA1), activity of the thyroid-hormones (NCOR1 and NCOR2), energy metabolism (ADIPOQ, PPARGC1A) and myogenic differentiation (CDON).

Conclusion: A molecular pathway analysis conducted in a sample of depressed patients identified new candidate genes. Future investigation of these genes may provide insights into the molecular events that drive weight gain during antidepressant treatment.

P29.02 Anne Marie Hove HUMAN PROSTATIC CELL RESPONSES TO INFECTION WITH PROPIONIBACTERIUM ACNES SUBSPECIES DEFENDENS

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Worldwide, more than 670,000 men are diagnosed with prostate cancer (PCa) each year, making it the most common non-cutaneous malignancy in men of western countries. The exact causes of PCa are unknown; many studies have presented evidence that inflammation of the prostate is an important contributing factor. Infecting microbes are culprits of the formation of an inflammatory environment in the prostate, directly or indirectly initiating or supporting a cancer-promoting microenvironment.

The Gram-positive anaerobic bacterium *Propionibacterium acnes* has frequently been isolated from cancerous prostates. It is debated if the bacterium is part of the natural microbiota of the prostate or represents an infectious agent. A recent large cohort study revealed that most PCa-associated isolates belong to a specific subspecies (subsp.) of *P. acnes*, subsp. *defendens*, which is distinct from the main type found on human skin.

This project investigates the response of prostatic cells to infection with different subsp. of *P. acnes*. First, we will analyze the inflammation signature of human prostate cells exposed to *P. acnes* by determining innate immunity markers. Second, we will investigate subsp.-specific infection consequences for the host cell fate regarding cellular proliferation and transformation. Third, bacterial host-interacting factors, such as tad pili, will be evaluated for their role in tissue adhesion and biofilm formation.

The identification of an inflammatory signature specifically induced by *P. acnes* subsp. *defendens* would fortify a causal link between *P. acnes* and PCa development. Results of this project could thus have profound consequences for PCa prevention and treatment.

P29.03 Stine Bruun

SELECTIVE SEROTONIN REUPTAKE INHIBITOR USE AND POSTOPERATIVE COMPLICATIONS, MORTALITY AND QUALITY OF CARE IN HIP FRACTURE PATIENTS

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Background: Prescription medication use is common in elderly hip fracture patients. It is unknown whether selective serotonin reuptake inhibitor (SSRI) use is associated with adverse outcomes after hip fracture surgery.

Objective: To examine the association between SSRI use and postoperative complications, mortality and quality of care in hip fracture patients.

Methods: We conducted a cohort study using Danish medical databases to identify hip fracture patients aged 65 years or older during 2006-2016. Using Cox and Poisson regression, we estimated crude and adjusted hazard ratios (HR) for postoperative complications and mortality and relative risks (RR) for fulfilment of care indicators with 95% confidence intervals (CI) comparing current and former SSRI users with non-users.

Results: Among 68,487 patients, 20% redeemed at least two prescriptions for SSRIs within 200 days prior to surgery. Current SSRI users had a 16% higher risk of dying within 30 days compared to non-users. Comparing current SSRI users with non-users, there was no increased risk of venous thromboembolism (HR 0.85; CI 0.66-1.10), myocardial infarction (HR 0.97; CI 0.78-1.22), stroke (HR 0.86; CI 0.73-1.02), or bleeding (HR 1.07; CI 0.88-1.29). The results regarding the association between SSRI use and quality of care will be presented at the meeting.

Conclusions: SSRI use is associated with a 16% increase in 30-day mortality among hip fracture patients. However, there is no effect on the risk of postoperative complications. Our data stress the importance of continued clinical awareness of fragility in hip fracture patients and potentially monitoring any evidence of adverse drug effects of SSRI treatment.

- P29.04 Charlotte Maria Jensen **Cancellation** APPROACHING PATIENT-CENTRED GOAL SETTING IN OUTPATIENT MULTIDISCIPLINARY REHABILITATION EXPERIENCES AND PERSPECTIVES OF PATIENTS AND HEALTH PROFESSIONALS

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Objective: The aim of the PhD project is to explore the patient's and the health professional's experiences and perspectives on patient-centred goal setting and its application in outpatient multidisciplinary rehabilitation.

Background: Patient-centred goal setting, while central to contemporary rehabilitation, has been associated with growing uncertainty regarding its application in clinical practice. There is a lack of studies exploring applied practice regarding patient-centred goal setting in rehabilitation that provide insight into the complexity of this process.

Method: A qualitative research design will be applied to this project using Interpretive Description as the methodology to answer the research questions, along with the theoretical framework Symbolic Interaction. Data will be generated through five months of ethnographic fieldwork using multiple sources (individual and focus group interviews, participant observation and clinical documentation), including patients and health professionals. Data transcripts will be analysed inductively using an interpretive description approach. The study will be conducted at the Specialised Hospital for Polio and Accident Victims, Rødovre and Aarhus.

Perspectives: The PhD project will contribute with knowledge to support that the rehabilitation programme is organised on the basis of research-based knowledge by optimising patient-centred goal setting in outpatient multidisciplinary rehabilitation in order to enhance patient rehabilitation outcomes.

- P29.05 Camilla Darum Sørensen MYELOID-DERIVED SUPPRESSOR CELLS AND MONOCYTES IN GRAFT-VERSUS-HOST DISEASE

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Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potentially curative treatment of hematological malignancies. The efficacy of allo-HSCT is largely caused by the "graft versus leukemia" (GVL) effect, an immunological response mediated by mature T cells present in the donor graft. T cells also contribute to the induction of acute graft versus host disease (aGVHD), a major clinical complication of transplantation. It is observed in 40-60% of cases and is one of the major causes of non-relapse mortality after allo-HSCT.

Inflammatory signals induced during allo-HSCT might favor accumulation of immuno-modulatory cells. One such cell type, the myeloid-derived suppressor cells (MDSC), have recently emerged as a highly heterogenic

immuno-regulatory population that can expand in response to inflammatory signals and repress allogeneic T cell responses.

The overall aim of this study is to investigate the role of myeloid cell subsets in aGVHD: to identify key myeloid cell subsets in patients undergoing allo-HSCT and to characterize these cells based on phenotype and immuno-regulatory potential.

Peripheral blood (PB) from 15 patients subjected to allo-HSCT has been collected before transplantation and at five time-points post-transplantation and analyzed by flow cytometry for the presence of distinct myeloid cell subsets. In vitro studies, including sorting and co-culturing with T cells, will reveal the immuno-regulatory potential of the myeloid cells.

P29.06 Kaja Kristiane Eriksrud Kjørholt NATIONWIDE TRENDS OF INFECTIONS AMONG HIP FRACTURE PATIENTS IN DENMARK, 2005-2016

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Background: Infections is a major cause of hospitalization and mortality among elderly, and a leading cause of death among hip fracture patients. The aim of this project is to examine the temporal trends of hospital-treated infections among hip fracture patients, using a Danish nationwide cohort from 2005-2016.

Methods: This prospective, population-based cohort study collected data by linking the Danish Multidisciplinary Hip Fracture Register, the Danish National Patient Register, the Danish National Health Service Prescription Database and the Danish Civil Registration System. We included a total of 74,791 patients aged > 65 years, who underwent hip fracture surgery in 2005-2016 in Denmark. To evaluate the risk of infections, we identified any first-time hospital admission or outpatient clinic visit with a bacterial infection at a private or a public hospital after the surgery (index) date.

Results: Results will be presented at the PhD Day. The results will include the standardized incidence rate of infections per 1000 person-years and cumulative incidence of infections, treating death as competing risk, per calendar year. Based on Cox proportional-hazards regression, 30-day (short-term) and 31-365-day (long-term) adjusted incidence rate ratio (IRR) will be calculated and included.

Conclusions: Conclusions will be presented at the PhD Day.

P29.07 Ingrid
Villadsen
Kristensen

EXPERIENCES OF LIVING WITH END-STAGE RENAL DISEASE:
A QUALITATIVE METASYNTHESIS

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Background: Treatment of end-stage renal disease is complex and involves fluid and dietary restrictions, prescribed medications, and dialysis or kidney transplantation. Increasing qualitative research is an important attempt to understand the experiences of living with end stage renal disease.

Aim: To explore the experiences of individuals with end-stage renal disease by examining the qualitative research focused on individuals' experiences of end-stage renal disease.

Method: This qualitative metasynthesis follows parts of the method of Sandelowski & Barroso in order to increase the usefulness of qualitative studies in practice by gathering and synthesizing knowledge from existing research. Sandelowski & Barroso describe a systematic method of searching for and retrieving qualitative research rapports, appraisal, classifying the findings in qualitative research rapports, and synthesizing and integration of qualitative research findings within a specific topic. The qualitative metasynthesis is derived through a constant comparative analysis.

Preliminary findings: The preliminary findings of the synthesis show that patients with end-stage renal disease experience existential contradictions: Perception of body - being between connection and separation, Maintaining life - being between freedom and captivity, Uncertainty - being between hope and despair, Enduring technology - being between object and subject.

P29.08 Mia Doherty

CLINICAL AND GENETIC EVALUATION OF DANISH PATIENTS WITH
PYCNODYSTOSIS

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Background: Pycnodysostosis is a rare autosomal recessive osteosclerotic skeletal dysplasia. The clinical features include short stature, bone fragility and acro-osteolysis of the distal phalanges. Patients suffer from complicated bone fractures. Various mutations in the Cathepsin K gene are responsible for the disease. The present study originates from earlier research from Herning Regional Hospital. The aim of our study is to describe the Danish population of patients with pycnodysostosis and report their genotype, phenotype and the prevalence of complications.

Methods: The study is a cross-sectional descriptive study comprising one meeting with the patients. Our study includes 10 patients with a median age of 32 years. The meeting involves history taking, clinical examination, blood and urine sample and a DXA and HRpQCT scan. Information about complications to the disease, bone mineral density and bone markers in blood and urine are collected and compared with previous findings.

Results: The study is still ongoing, and results will be presented at the PhD Day 2018. The preliminary data shows major variation in the type and severity of complications. Furthermore, all the patients have high bone mineral density compared to normal values.

Perspectives: Our study will be the first to investigate possible phenotype-genotype correlations and will provide an increased molecular genetic and pathophysiological knowledge of a yet incurable disease. The results will contribute to improve individual diagnosis and treatment outcomes for the patients. Pycnodysotosis research may contribute to the future of osteoporosis treatment as the gene mutation might increase bone density.

CH.01 Mikkel Carstensen Gjelstrup PRO-INFLAMMATORY MONOCYTE SUBSETS ARE AUGMENTED IN INCIPIENT AND PROGRESSED MULTIPLE SCLEROSIS

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Background: Peripheral blood mononuclear cells hold the potential to unveil new aspects of multifactorial diseases such as multiple sclerosis (MS). The monocyte subsets are particularly important due to their central roles in inflammatory diseases. An in-depth characterisation of the differentiation of monocyte subsets during MS by analysis of surface protein expression, combined with analyses of genetic and epigenetic regulation, will contribute novel insights in MS pathogenesis and diagnostics. This is particularly relevant considering the recent therapeutic strategies for MS, involving depletion of specific cell populations.

Methods: Flow cytometry is used for analysis of monocyte differentiation (CD14, CD16, CD40, CD163, and CD192) as well as expression of Human Endogenous RetroVirus (HERV) -H/F and -W Env epitopes. This will be combined with analysis of genetic and epigenetic regulation patterns using Precision Nuclear Run-On (PRO-seq) and Chromatin Immunoprecipitations (ChIP).

Results: Initial results from flow cytometric analyses of samples from patients with MS and controls indicate that several pro-inflammatory markers of monocyte differentiation (CD40, CD163, and CD192) are significantly modulated ($P < 0.004$), particularly on the non-classically activated monocyte subset, as is the expression of HERV-H/F and HERV-W Env epitopes ($P < 0.0005$), indicating a common regulatory mechanism.

Perspectives: Flow cytometric analyses hold the potential to aid or even replace some of the elaborate diagnostic work-up necessary for the MS diagnosis and may, together with the other proposed analyses, contribute to a better understanding of the disease.

CH.02 Willemijn Comuth COMPREHENSIVE CHARACTERISTICS OF THE ANTICOAGULANT ACTIVITY IN RELATION TO THE PLASMA CONCENTRATION OF DABIGATRAN

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Background: Dabigatran can be detected by various coagulation assays. Important problems include: 1) Do the assays reflect the dabigatran plasma concentration? 2) Spiked plasma samples may not mirror the in vivo effect in

treated patients, and 3) The long-term stability of dabigatran after storage at -80°C is unknown.

Aim: The aim of this study is to evaluate the correlation between the plasma concentration (liquid chromatography-tandem mass spectrometry (LC-MS/MS)) and the anticoagulant effect of dabigatran. The difference between plasma samples spiked with dabigatran and ex vivo samples obtained from patients treated with dabigatran etexilate. Stability of these samples was seen after long-term storage at -80°C.

Methods: ROTEM®, ecarin chromogenic assay (ECA), a laboratory-developed diluted thrombin time (LD-dTT), and LC-MS/MS were used to measure anticoagulant activity and plasma dabigatran concentrations in blood/plasma spiked with dabigatran (0-1000 ng/mL) from donors and in ex vivo samples from dabigatran-treated patients. Samples were frozen, stored at -80°C, and then thawed 1, 3, 6 and 12 months later and analysed.

Results: EXTEM and FIBTEM clotting time (CT), ECA and LD-dTT have good correlation with dabigatran plasma concentrations. With the exception of few ROTEM® parameters, there were no differences between spiked and patient samples. Samples were stable for at least 12 months at -80°C.

Conclusions: EXTEM and FIBTEM CT, ECA and LD-dTT are suitable for measuring the effect of dabigatran in treated patients. In general, results from spiked samples are similar to those of patient samples. Storage of dabigatran plasma samples for up to 12 months does not influence measured levels.

CH.03 Line Thorndal MRI OF THE CERVICAL SPINE: AN INTRA- AND INTER-RATER RELIABILITY
Moll STUDY OF ASSESSMENTS OF DEGENERATIVE CHANGES COMPARING THREE
DIFFERENT HEALTH CARE PROFESSIONALS

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Background: The use of magnetic resonance imaging (MRI) in the assessment of neck pain has increased over the past five years in Denmark. Although subject to concern among some researchers and clinicians, patients are more content when MRI is performed; they believe MRI to reveal the truth about their pain. Knowledge about the reliability of the most commonly reported pathologies is a prerequisite for precise and consistent communication about MRI findings. However, no comprehensive reliability studies on MRI of the cervical spine have compared several different health care professionals while addressing common clinical conditions by using MRI scans from different hospitals.

Objective: To assess the inter- and intra-rater reliability of assessments of degenerative findings on MRI of the cervical spine.

Methods: A radiologist, a chiropractor and a second year resident of rheumatology evaluated 50 MRI scans of the cervical spine from a subset of patients with neck pain. The evaluation comprised cervical alignment, disc height, disc contour, vertebral endplate signal changes, spinal canal stenosis, foraminal stenosis and osteoarthritis in the uncovertebral and

zygapophyseal joints for the disc levels C2-Th1. A codebook with definitions, scoring systems and illustrative examples was distributed to the readers. Prior to the full study, the first 10 MRI scans were evaluated twice followed by consensus meetings, where relevant adjustments in both the codebook and the habits of the readers were agreed upon. Reliability measures were calculated by means of quadratic weighted kappa statistics.

Results: Will be presented at the PhD day.

Discussion: Will be presented at the PhD day.

CH.04 Velma Aho PARKINSON'S DISEASE AND THE HUMAN MICROBIOME

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The causes of Parkinson's disease and the factors affecting its progression are not yet well understood. Based on early non-motor symptoms, epidemiological evidence and animal experiments, it has been suggested that a microbial agent might be involved. Instead of a single organism, many medical conditions have recently been associated with a general shift in the microbial communities residing in the body. To look for such changes in relation to Parkinson's disease, we used 16S rRNA gene amplicon sequencing to explore the microbiota of three body locations which are important contact surfaces with the environment and the sites of some of the earliest changes seen in the disease: the gut, the mouth and the nose. We compared the bacterial abundance data from nasal and oral swab and stool samples from 76 Parkinson's patients and 88 age- and sex-matched control subjects. There were notable differences in the gut and oral, but not the nasal bacterial communities when looking at either the overall community composition or the abundances of specific bacteria. This warrants further research into whether microbes might be involved in the disease process.

CH.05 Steffen Nielsen BIOLOGICAL DIFFERENCES IN FIBROBLASTS IRRADIATED WITH PROTON AND PHOTON BEAMS

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Background: Radiotherapy is an essential cancer treatment method. Photon beams have been used conventionally, but proton beams are emerging as a treatment option. Proton beams deliver a more conformal dose distribution than the best photon modality, thereby diminishing dose to the normal tissues. The inflammatory response to photon radiation initiates the development of normal tissue complications. These effects are well established for photons, but they are largely unexplored for protons.

The study aim was to identify signal transduction pathways regulated differently by proton and photon radiation.

Methods: Mono-layered primary fibroblasts were irradiated at positions in the entrance and distal edge of the proton beam profile. Photon irradiation was used as reference. RNA sequencing was performed to map coding transcriptomes using Illumina NextSeq 500 with high-output kit. The Tuxedo suite protocol was employed for data analysis. Real-time qPCR will be performed to validate RNA sequencing.

Results: Cytokines involved in the modulation of the JAK-STAT pathway appears to be more heavily upregulated in fibroblasts irradiated with photons than in proton irradiated fibroblasts. The profibrogenic genes COL3A1 and COL3A3 coding collagen type III are more upregulated by proton irradiation at the distal edge position compared with photon irradiation at the entrance region position.

Conclusion: Signal transduction pathways involved in normal tissue damage development may be regulated differently depending on the radiation type. An improved understanding of the transcriptomic changes in normal tissues will undoubtedly be helpful in optimizing proton therapy in the future.

CH.06 Farhad Waziri PULMONARY PRESSURE IMPROVES BUT REMAINS PATHOLOGICALLY ELEVATED DURING EXERCISE AFTER PULMONARY ENDARTERECTOMY

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Background: Pulmonary endarterectomy (PEA) is a potentially curative treatment of chronic thromboembolic pulmonary hypertension (CTEPH), resulting in improved functional status, hemodynamics and overall survival. However, the effect of PEA on invasive exercise hemodynamics is not well examined.

Hypothesis: We describe the effect of PEA on exercise capacity and invasive hemodynamics.

Methods: Twenty consecutive CTEPH patients were examined before PEA and three months after. Invasive hemodynamic parameters were measured at rest and during exercise test using a Swan-Ganz catheter.

Results: The average age was 61 ± 14 years. Significant improvement was noticed in NYHA-classification (2.9 ± 0.4 vs. 1.5 ± 0.7 , $p < 0.001$) before and 3 months after PEA. Maximal exercise load was increased (38 ± 16 vs. 65 ± 33 W, $p < 0.005$) and the same applied for oxygen uptake VO_2 -max (936 ± 229 vs. 1223 ± 358 ml/min, $p < 0.005$). Cardiac output increased after PEA, both at rest (4.3 ± 1.1 vs. 5.0 ± 1.1 L/min/m², $p < 0.05$) and after exercise (6.8 ± 2.6 vs. 10.7 ± 3.9 L/min/m² ($p < 0.0003$)). Pulmonary vascular resistance at rest decreased (802 ± 358 vs. 319 ± 172 dyne \cdot sec/cm⁵, $p < 0.0001$). mPAP dropped at rest (51 ± 12 vs. 29 ± 8 mmHg, $p < 0.0001$) and at maximal work load (75 ± 15 vs. 50 ± 12 mmHg, $p < 0.0001$). The mPAP-CO slope decreased significantly from 7.5 ± 4.2 to 3.3 ± 2.9 mmHg \cdot L⁻¹ \cdot min⁻¹, $p < 0.001$.

Conclusion: Significant improvements in both resting and exercise cardio-pulmonary function were seen after pulmonary endarterectomy. However, exercise hemodynamic parameters revealed that 45% of the patients had an abnormal increase in mPAP in response to CO (mPAP-CO slope > 3) 3 months after PEA.

- CH.07 Ditte H. Jensen **Canceled** PATIENT SELF-REFERRAL AND INTERNET-DELIVERED PSYCHOLOGICAL TREATMENT FOR PATIENTS SUFFERING FROM SEVERE HEALTH ANXIETY: A RANDOMISED CONTROLLED TRIAL

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Background: Severe health anxiety (HA), or hypochondriasis, is a prevalent, costly and disabling disorder. It is characterised by preoccupation with fear of having a serious illness. Currently, few treatment options exist. Furthermore, accessibility is limited due to health care administered referral. Therefore, easily accessible, specialised treatment is needed for this debilitating illness.

Objectives: To test the feasibility of a new procedure for patient self-referral and to evaluate the effectiveness of an internet-delivered Acceptance and Commitment Therapy (iACT) programme for HA, respectively.

Methods: Patients with HA were recruited through online self-referral and were diagnostically assessed using a video-based interview. Patients fulfilling study criteria were randomised to 12 weeks of either iACT (containing psychoeducation, exercises and therapist support) or an online discussion forum. Self-report questionnaires were obtained at baseline, at post-treatment and at 6-month follow-up. The primary outcome was level of HA symptoms assessed by Whiteley-7 (range: 0-100).

Results: In total, 151 patients were assessed after self-referral. Of these, 101 patients (65% females) were randomised. The mean age was 39.6 years (SD=9.9), illness duration was 15.9 years (range: 0.5-46 years), and the mean level of HA symptoms at baseline was M=73.9 (SD=16.0). Further, results based on between-group analysis will be presented. However, results are pending due to follow-up.

Conclusion: Patient self-referral is feasible. If iACT shows to be effective, this new treatment approach may broaden the availability and accessibility of specialised treatment for HA.

- CH.08 Caroline Mejdahl WHAT HAPPENS WHEN WE ASK THE PATIENTS? AN INTERPRETIVE DESCRIPTION OF THE PATIENT PERSPECTIVE ON PRO-BASED FOLLOW-UP IN EPILEPSY

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Background: PRO-based follow-up (PBFU) is implemented at three neurological departments in the Central Denmark Region. In PBFU, patients with epilepsy receive a questionnaire instead of routine visits in the outpatient clinic. The questionnaire encompasses self-assessments of HRQoL, symptoms and wellbeing. Potentially, this system can result in patients becoming more involved in their follow-up by which their self-management may improve.

Aim: In our study, we aim at describing patients' experiences with the system in order to explore mechanisms of action related to self-management.

Methods: We chose Interpretive Description as the methodology for this interview study and let Critical Realism constitute a research paradigm. Through in-depth interviews with 29 patients with epilepsy, we explored patients' experiences with PBFU.

Findings: Using a constant comparing analysis, we identified two thematic patterns illuminating possibilities and barriers for PBFU as a means of self-management support. Possibilities included awareness on psychosocial problems, improved communications, increased understanding of symptoms, changes in health behaviour and strengthened autonomy. Barriers included feeling rejected and disconnected, incomprehension of PROs, lack of confidence in own ability to assess health status and PROs being painful reminders.

Conclusion: PRO-based follow-up may support patients' self-management. Yet, applying PBFU into clinical practice does not automatically involve the patients and support their self-management. There seems to be both structural and individual barriers. We suggest supplementary clinical initiatives to strengthen the patient-involving benefits.

CH.09 Sarah Fogh

BI-ALLELIC NULL-MUTATIONS IN THE SHORT CHAIN ACYL-COA DEHYDROGENASE GENE RESULTS IN TOXIC LEVELS OF BUTYRIC ACIDS

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Hypothesis: Short Chain Acyl-CoA dehydrogenase (SCAD) deficiency is a toxicity disease, where its substrate butyrate accumulates. So bi-allelic null-mutations are rare, compared to null-mutations in the homolog protein MCAD.

Objective: Compare the genotype frequency of bi-allelic null-mutations and monoallelic null-mutation in combination with a missense variation in SCAD and MCAD deficient patients. The variant data has been collected over the last 20+ years at the Research Unit for Molecular Medicine, Aarhus University Hospital.

The variant spectrum of SCAD is dominated by two common variants, c.511C>T and c.625G>A. They are present in 69% of the SCADD patients, but surprisingly also in 29% of the healthy population.

The symptoms observed in SCAD deficiency differ from other acyl-CoA dehydrogenase deficiencies. We speculate that this might be a result of the toxicity of butyrate. Butyric acid is also known to be a Histone Deacetylase

(HDAC) inhibitor, known to maintain acetylation of histones, and thereby modify gene expression.

Results: No bi-allelic null-mutations were detected in ACADS, and only three patients had a monoallelic null-mutation, with the common variant c.625G>A on the other allele. In comparison, six MCAD deficiency patients had bi-allelic null-mutations and 31 monoallelic null-mutations.

Conclusion: The high frequency of null-mutations in MCADD patients compared to SCADD patients supports our hypothesis that bi-allelic null-mutations of ACADS, and the resulting accumulation of butyric acid, are toxic and thereby promote apoptosis.

CH.10 Lise Sofie
Bislev

THE EFFECT OF VITAMIN D TREATMENT ON CARDIOVASCULAR SURROGATES IN VITAMIN D INSUFFICIENT WOMEN - A RANDOMIZED CONTROLLED TRIAL

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Introduction: Vitamin D3 supplementation seems causally related to reduced all-cause mortality. One theory is that vitamin D may lower blood pressure and reduce plasma concentrations of angiotensin 2 and aldosterone. A positive association between PTH and aldosterone has been reported. However, recent studies fail to show a beneficial effect of Vitamin D on cardiovascular endpoints, possibly because most studies investigated subjects with normal vitamin D levels.

Methods: In a double-blind placebo-controlled clinical trial, 81 healthy postmenopausal women with secondary hyperparathyroidism (PTH>6.9 pmol/L) and vitamin D deficiency (25OHD) were included. Participants were randomized to 12 weeks of daily placebo or 70 microgram D3. For the first two weeks, the participants were co-randomized to daily placebo or 80 mg Valsartan.

Results: Vitamin D levels increased steadily during 12 weeks of vitamin D supplementation. Vitamin D3 only reduced PTH after the two first weeks. Valsartan reduced blood pressure, increased renin and caused a non-significant reduction in aldosterone levels. Valsartan did not reduce PTH, and vitamin D did not reduce the concentration of angiotensin 2 or aldosterone; these findings reject both of our two co-primary hypotheses. Vitamin D therapy did not affect ambulatory or 24 h measurements of blood pressure or vascular stiffness.

Conclusion: In healthy vitamin D insufficient women, improvement of vitamin D status does not seem to have a protective effect on indices of cardiovascular health.

CH.11 Andrey
Chuhutin

DEVELOPING NEW BIOMARKERS FOR MULTIPLE SCLEROSIS

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Multiple sclerosis is a demyelinating, inflammatory, neurodegenerative disease of the central neural system, affecting millions of people. For therapies to be successful in slowing disease progression or improving relapse frequency, early intervention is crucial. The development of new biomarkers can play an essential role by enabling earlier diagnosis and providing additional information about neural tissue microstructure. Diffusion weighted MRI is an imaging modality that produces not only biomarkers, but can also reveal the relationship between the biomarkers and the tissue microstructure when combined with biophysical modeling. In this work, the biomarkers provided by an extension of diffusion weighted MRI analysis (diffusion kurtosis imaging, DKI) were scrutinized.

Firstly, MRI biomarkers were analysed with the aim to establish the connection to tissue microstructure. The choice of gradient strength for optimal estimation of mean kurtosis tensor was found to depend on the target tissue. In particular, higher b-values (~2.5 ms/μm²) were found to be more suited for the examination of white matter while yielding low accuracy and precision when used in grey matter. Secondly, we studied the effects of using different pulse sequences on the estimation of kurtosis tensor parameters.

The final study is based on the imaging setup and fitting protocol suggested by the first two projects. Consequently, the experimental protocol that yields the kurtosis tensor metrics most closely related to the neural microstructure was chosen to test the biomarkers on a rodent model of multiple sclerosis (experimental autoimmune encephalomyelitis [EAE]).

CH.12 Allan Kjeldsen
Hansen

TAU PATHOLOGY IN PARKINSON'S DISEASE DESCRIBED WITH FLORTAUCIPIR PET

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Background: Cortical tau pathology in the shape of neurofibrillary tangles is a mandatory finding for a neuropathological diagnosis of Alzheimer's disease, along with beta-amyloid plaques. Recently, it has become possible to describe the presence of neurofibrillary tangles *in vivo*, using positron emission tomography (PET) with the radiotracer [¹⁸F]-flortaucipir, even in preclinical Alzheimer's disease. Neurofibrillary tangles also occur as co-pathology in up to 50% of patients with Parkinson's disease at post mortem, and these patients have generally had faster progression to dementia, which is common in Parkinson's disease, affecting around 75% of patients 10

years after initial diagnosis of Parkinson's disease. We attempted to use flortaucipir PET to detect neurofibrillary tangles in pre-dementia Parkinson's disease.

Methods: Twenty-six Parkinson's disease patients and 23 healthy controls had flortaucipir PET. Further, we performed a neuropsychological evaluation to detect mild cognitive impairment and describe performance in five cognitive domains.

Results: We found no significant differences between healthy controls and Parkinson's disease with (N=9) or without (N=17) cognitive impairment using both a regional and voxel-wise analysis of flortaucipir PET. No correlation was found with cognitive domain z-scores. One patient with mild cognitive impairment showed slightly increased PET signal, but not to the extent seen in Alzheimer's disease.

Conclusion: Neurofibrillary tangles as described by flortaucipir PET do not seem to commonly occur in pre-dementia Parkinson's disease, despite being common at post-mortem and in pre-clinical Alzheimer's disease.

CH.13 Ida Hovdenak Jakobsen GUIDELINES SYNTHESIS: FOLLOW-UP OF PATIENTS AFTER CURATIVE INTENT TREATMENT FOR COLORECTAL CANCER

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Aim: It is common clinical practice to follow patients for a certain period after curative intent treatment for colorectal cancer, but follow-up strategies vary widely. The aim of this study was to provide an overview of recommendations and evidence for follow-up after primary colorectal cancer treatment with curative intent, as stated in national and European guidelines.

Method: Five medical databases were systematically searched for guidelines and consensus papers for follow-up after colorectal cancer. Only guidelines used in European countries were included. Main topics were identified and divided into subtopics. For each subtopic, a conclusion was made followed by the degree of consensus and the highest level of evidence. The AGREE-II tool was used for the quality assessment.

Results: Twenty-one guidelines were included; the majority recommended that structured follow-up should only be offered to patients who are able to receive further treatment if recurrence is detected. It is generally agreed that medical history, physical examination, CEA measurement, chest, liver and pelvic imaging and endoscopy should be part of follow-up, but consensus regarding timing and modality was regularly lacking. A sufficient level of evidence was only found for the intensity of follow-up and the role of CEA measurement and liver imaging.

Conclusion: In the currently available guidelines, consensus and sufficient evidence on the follow-up after curative intent treatment of colorectal

cancer are lacking. Ongoing and future clinical trials comparing different follow-up regimens are required in order to determine the right follow-up strategy.

CH.14 Iben Lyskjær PREDICTION OF IRINOTECAN EFFICACY IN METASTATIC COLORECTAL CANCER USING CIRCULATING TUMOR DNA

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Development of biomarkers determining chemotherapy efficacy is vital to ensure optimal treatment of metastatic colorectal cancer (mCRC).

In this phase II study of 1st line Irinotecan-treated mCRC patients, the primary aim was to assess whether alterations in plasma cell free (cfDNA) and circulating tumor DNA (ctDNA) could be used as a marker of therapeutic effectiveness.

mCRC patients diagnosed with metastatic disease and with indication for first-line Irinotecan-based combination chemotherapy were prospectively enrolled. Blood samples were drawn prior to the first chemotherapy cycle, at day one and seven during the first and second cycle, and hereafter every third week and during treatment breaks until progression. The levels of cfDNA and ctDNA were determined using sensitive digital droplet PCR assays. ctDNA assays were designed either to mutations identified by targeted sequencing or on the basis of known tumor mutations detected in primary or metastatic lesions using a panel of hyper-sensitive and specific qPCR based assays (KRAS, NRAS, BRAF).

Twenty-four mCRC patients with a median of thirteen (range: 3-25) plasma samples collected were enrolled. Twelve patients had a known KRAS, NRAS or BRAF mutation that were used as a patient-specific ctDNA marker. ctDNA markers for the remaining patients were identified either by targeted sequencing of their tumor or matched germline samples (n=12). Changes in ctDNA levels were correlated with the clinical outcome parameters: time to progression (TTP), progression free survival (PFS) and overall survival (OS).

CH.15 Martin Lund ACTIVATION OF PROTECTIVE SYSTEMS IN FATTY ACID OXIDATION DISORDERS CAN LEAD TO DELETERIOUS OUTCOMES

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The peroxisome proliferator-activated receptors (PPARs) agonist bezafibrate has been proposed as a potential therapy for mitochondrial long-chain fatty acid oxidation (FAO) disorders. In vitro studies have shown promising results, but two small clinical trials less so.

The cellular consequences of pharmacologically activating the PPAR system are well studied. Effects could include potentially deleterious aspects, such as activating mitogenesis of inherently dysfunctional mitochondria. Conversely, PPAR activation also initiates protective systems.

We set out to investigate cellular protection against oxidative stress and survival under external heat stress after bezafibrate treatment. We found that, during heat stress, mitochondrial superoxide levels increase in very long-chain acyl-CoA dehydrogenase deficient patient fibroblasts treated with bezafibrate, compared to similarly treated controls. Superoxide levels were also greater in bezafibrate treated patient fibroblasts undergoing heat stress than in patient fibroblasts undergoing heat stress without prior bezafibrate treatment. Likewise, the capacity of bezafibrate-treated patient fibroblasts to maintain peptide antioxidant (glutathione) levels during decreased, which leads to faster cell death during heat stress. The increased predisposal to stress-induced cellular damage may counteract the beneficial aspects of the ability of bezafibrates to increase the baseline FAO capacity. This underscores the importance of supportive adjuvant therapy, especially during the periods of additional stress, such as fever, associated with disease manifestation in the milder phenotypes.

CH.16 Daniel
Ramskov
Jørgensen

RUN CLEVER – MORE RECREATIONAL RUNNERS ARE NOT INJURED BY PROGRESSION IN RUNNING INTENSITY. A RANDOMISED TRIAL

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Introduction: The Run Clever trial investigated if there was a difference in injury occurrence across two running schedules, focusing on progression in running intensity or in running volume. It was hypothesised that 15% more runners with a focus on progression in volume of running intensity would sustain an injury compared with runners with a focus on progression in total running volume.

Methods: Healthy recreational runners were included and randomly allocated to Sch-I or Sch-V. In the first 8 weeks of the 24-week follow-up, all participants (n=839) followed the same running schedule. Participants (n = 447) not censored during the first 8 weeks, entered the 16-week specific focus-training period with a focus on either progression in intensity (Sch-I) or volume (Sch-V). A Global positioning system collected all data on running. During running, all participants received real-time, individualised feedback on running intensity and running volume. The primary outcome was running-related injury.

Results: A total of 80 runners sustained a running-related injury. The cumulative incidence proportion (CIP) in Sch-V (reference group) after preconditioning were: CIP_{2-weeks} 4.6%; CIP_{4-weeks} 8.2%; CIP_{8-weeks} 13.2%; CIP_{16-weeks} 28.0%. The risk differences (RD) and 95% CI between the two schedules were: RD_{2-weeks}=2.9%[-5.7%;11.6%]; RD_{4-weeks}=1.8%[-9.1%;12.8%]; RD_{8-weeks}=-4.7%[-17.5%;8.1%]; RD_{16-weeks}=-14.0%[-36.9%;8.9%].

Conclusion: More recreational runners following a running schedule focused on progression in volume of running intensity did not sustain an RRI compared with recreational runners following a running schedule focused on progression in total running volume.

CH.17 Nini Nørgaard METHOTREXATE INTOLERANCE IN DANISH CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS OR ACUTE LYMPHOBLASTIC LEUKAEMIA TREATED WITH LOW-DOSE METHOTREXATE

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Low-dose methotrexate (LD-MTX) plays a key role in the treatment of juvenile idiopathic arthritis (JIA) and in the maintenance treatment of acute lymphoblastic leukaemia (ALL). MTX intolerance is defined as gastro-intestinal adverse effects associated to LD-MTX, including anticipatory, associative and behavioural symptoms, and may be semi-quantitatively measured using the methotrexate intolerance severity score (MISS). Our aim is to compare the level of MTX intolerance in Danish JIA- and ALL-patients. We enrolled patients followed at our outpatient clinics, diagnosed with either JIA or ALL, treated with LD-MTX and aged 9 years or above. Patients were excluded if cognitively impaired or not fluent in Danish. Enrolment period was December 2013 - August 2017. For every patient, the MISS and a physician's global assessment of the patient's level of MTX intolerance (PGA) were completed. 120 JIA patients and 23 ALL patients were enrolled and had the MISS and PGA completed. The mean LD-MTX dose was 4.65mg/m² (95% CI: 1.95; 7.34) higher in the ALL group than in the JIA group. The median duration of LD-MTX treatment was longer for the JIA group than for the ALL group (p-value =0.0006). The median MISS score was higher in the JIA group than in the ALL group (p-value <0.0001), and there were more MTX intolerant children (defined by the MISS) in the JIA group than in the ALL group (p-value <0.001). There was no statistically significant difference between the two groups' median PGA (p-value = 0.078). In conclusion, despite receiving a lower LD-MTX dose, the level of MTX intolerance is higher in the JIA group than in the ALL group when assessed by parents, but not physicians.

CH.18 Niels Lyhne Christensen LUNG CANCER GUIDELINES IN SWEDEN, DENMARK, NORWAY AND FINLAND: A COMPARISON

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Introduction: The Nordic countries are similar in terms of demographics and health care. Moreover, lung cancer remains the primary cause of cancer-related death in all four countries, yet the mortality rate is highest in Denmark. All countries have national guidelines for lung cancer care. We aimed to investigate differences and similarities in both the actual clinical care recommendations and also the methodology by which the guidelines are developed.

Methods: We evaluated the available clinical care guidelines from the four countries with emphasis on the specific clinical care recommendations regarding non-small cell lung cancer (NSCLC) and key methodological attributes. Finally, we compared the integrated cancer pathways in the countries that have implemented such pathways.

Results: The Norwegian guidelines are developed with methodological rigor and stand out as the most comprehensive and so far the most often updated set of guidelines. In general, the guidelines are in accordance. However, based on our findings, lung cancer care differs in the four countries in several areas, including cerebral imaging for identification of brain metastases, algorithms for follow-up, whether smoking cessation algorithms are included, Bevacizumab therapy, and dosing regimens for radiotherapy.

Conclusion: Based on the included guidelines, non-small cell lung cancer patients in Sweden, Denmark, Norway and Finland are treated differently in key areas of clinical care. This could partly explain the differences in outcome seen between the countries. Areas with discordance in the recommendations should be subjected to further research in order to obtain consensus on optimal clinical care.

CH.19 Mette Holm
Hjorth

HIGHER PREVALENCE OF MIXED OR SOLID PSEUDOTUMORS IN METAL-ON-POLYETHYLENE TOTAL HIP ARTHROPLASTY COMPARED TO METAL-ON-METAL TOTAL HIP ARTHROPLASTY AND RESURFACING HIP ARTHROPLASTY

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Background: Pseudotumors are common in metal-on-metal (MoM) total hip arthroplasty (THA) and resurfacing hip arthroplasty (RHA). However, information on pseudotumors in (metal-on-polyethylene) MoP THA is limited. We compared the pseudotumor prevalence, level of metal ions, and clinical scores between the 3 bearing types.

Methods: 111 patients with 148 hip articulations (30 MoM THA, 47 MoM RHA and 71 MoP THA) participated in a cross-sectional case-control study at Aarhus University Hospital. Patients were evaluated with metal artefact reducing sequence (MARS) magnetic resonance imaging (MRI), measurements of metal ions, and clinical scores of Harris Hip Score (HHS), Oxford Hip Score (OHS), and the Copenhagen Hip and Groin Outcome Score (HAGOS).

Results: Pseudotumors were present in 13 of 30 (43%) MoM THA, 13 of 47 (28%) MoM RHA, and 29 of 71 (41%) MoP THA, which was a similar prevalence ($p=0.10$). The prevalence of mixed or solid pseudotumors was higher in patients with MoP THA ($n=10$) compared to MoM THA ($n=3$) and MoM THA ($n=0$), ($p=0.01$). Hips with a mixed or solid pseudotumor had significantly poorer clinical scores of HHS ($p=0.01$) and OHS ($p<0.01$) and higher serum metal-ion levels of cobalt ($p<0.01$) compared to hips without a pseudotumor or with a cystic pseudotumor.

Conclusion: Pseudotumors have mostly been associated with MoM hip articulations, but we found a similar prevalence in MoP THA, which is the most common THA bearing worldwide. Mixed or solid pseudotumors were more often seen in patients with MoP THA compared to MoM hip articulations, and these patients had poorer clinical scores and higher metal-ion levels than patients without a pseudotumor or with a cystic pseudotumor.

CH.20 Casper Sæbye STRENGTH IN SOFT TISSUE SARCOMA PATIENTS AFTER LIMB-SPARING SURGERY IN THE EXTREMITIES

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Background: Only few studies have investigated the strength in soft tissue sarcoma patients by using objective measurements. This study intends to determine the effects of limb-sparing surgery on the functional outcome measured by strength at the first 3 months in soft tissue sarcoma patients.

Methods: Patients who underwent surgery for a soft tissue sarcoma in the extremities at Aarhus University Hospital were included. Patients completed a dynamometric muscle test with the Biodex System 3 dynamometer before surgery, 1 month and 3 months after surgery on both the disease-affected and the healthy side. The results were compared to normative data. A percentage between the obtained value compared to the expected value was calculated.

Results: This study included 26 patients who completed pre-operative measurement, while 14 and 17 patients completed 1 month and 3 months after surgery measurement, respectively. There was no significant difference found between healthy and disease-affected side pre-operatively ($p=0.51$). However, 1 month and 3 months after surgery, the healthy side was significantly stronger ($p<0.01$ and $p=0.02$, respectively). Before surgery, patients had an overall mean strength of 78.93% of the expected (95% CI: 72.37-85.50). One month after surgery, they had a mean strength of 76.56% of the expected (95% CI: 67.43-85.70). Three months after surgery, patients had a mean strength of 78.83% of the expected (95% CI: 69.47-88.20).

Conclusion: We found a significant difference in the strength between the disease-affected side and the healthy side after 3 months. Furthermore, soft-tissue sarcoma patients have significantly reduced strength when compared to healthy people.

CH.21 Niels
Dalsgaard
Nielsen

SPREAD OF ULTRASOUND GUIDED INJECTATE BETWEEN THE ILIOPSOAS MUSCLE AND THE ILIOFEMORAL LIGAMENT - A CADAVER STUDY

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Background: A femoral nerve block reduces postoperative pain after total hip replacement, but it is contra-indicated as it increases the risk of falling. We propose to selectively block the sensory articular branches from the femoral nerve to the hip joint by injections, in the plane between the

iliopsoas muscle and the iliofemoral ligament, into the iliopsoas plane. This novel nerve block has the potential to provide analgesia of the hip joint without motor blockade. We aimed to verify the block in a cadaveric study.

Methods: Fifteen cadaver sides were injected with 5 mL of dye in the iliopsoas plane under ultrasound guidance. Dissection was subsequently performed to visualize the spread of dye to the femoral nerve and its branches.

Results: In 10 dissections (67%), the dye was contained in the iliopsoas plane staining all branches from the femoral nerve to the hip joint. In 4 dissections (27%), the dye was found to have been unintentionally injected into the iliopectineal bursa, leading to an unpredictable spread of dye. In 1 dissection (7%), adhesions in the iliopsoas plane partially prohibited the spread of dye.

Conclusions: We demonstrate that an injection of 5 mL of dye in the iliopsoas plane can spread to all sensory branches from the femoral nerve to the hip joint. If these findings in cadavers translate to living humans, injection of local anesthetics into the iliopsoas plane will result in a sensory nerve block of the articular branches but not in the motor branches from the femoral nerve. The clinical implication would be a nerve block that provides analgesia after total hip replacement without motor blockade.

CH.22 Bente Skovsby TOFT BEING A LARGE BODY IN ACTIVITY: EXPERIENCES OF SUFFERING AND WELL-BEING

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Background: Health interventions towards people living with severe obesity are often directed towards weight loss, though it may be more relevant to address physical activity (PA) and the challenges it may entail. Facilitators and barriers to physical activity are related to the sense of self. However, in-depth knowledge of their experiences over time is lacking.

Aim: To explore and describe severely obese adults' experiences of being physically active.

Design and methods: Repeated individual interviews (n=36) were conducted in combination with repeated gender-specific focus group interviews (n=4). 8 male and 8 female patients admitted to lifestyle intervention were included according to the criteria: age ≥ 18 y and BMI ≥ 40 kg/m². A phenomenological-hermeneutic approach was performed using the domains of existential philosophy and sensitised by a theoretical framework of suffering and well-being.

Results: Preliminary findings point at failure and the feeling of being unable to affect the sense of self negatively, causing suffering. Focusing on small progress in well-being may increase the feeling of "homecoming" in activity. Further results will be presented orally.

Conclusion: The existential perspective on PA in the health care setting may help the patients in finding settlement in their sense of self and enable an authentic mode of living. Understanding and addressing the experiences of suffering and emotional well-being may be instrumental in inducing

permanent changes in everyday life through lifestyle interventions targeting severely obese patients aiming to make PA possible and pleasant.

CH.23 Carsten
Gleesborg

OLFACTORY NETWORK IMBALANCE IN A TREATMENT-NAÏVE DEPRESSED POPULATION

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Introduction: Depression is the leading cause of disability worldwide and is projected to become the primary contributor to the global burden of disease by 2030. As we still do not fully understand the mechanisms of this disease, we set out using computational whole-brain modelling to look at differences between the structural networks in the brains of healthy controls and depressed individuals.

Methods: 28 first-episode treatment-naïve patients with Major Depressive Disorder (MDD) and 30 healthy controls underwent DTI scanning. Using a whole-brain parcellation approach combined with probabilistic tractography, we acquired structural connectivity matrices that were further analysed by employing graph-theoretical measures.

Results: We found an overall loss of structural connectivity in the left hemisphere in the patient group, with a possible compensation through strengthening of the connections between caudate and putamen, as well as hippocampus and amygdala. Particularly the olfactory network seems highly affected. Modularity analysis shows highly increased segregation and loss of olfactory cortex as an information-integrating region for the patient population.

Discussion: Our results support the evolving literature on transient hyposmia throughout episodes of depression. The increased link between amygdala and hippocampus suits the trait anxiety often found as comorbidity in depression.

CH.24 Ole Adrian
Heggli

THE EFFECT OF RHYTHMIC CONTEXT ON INTERPERSONAL COORDINATION

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Humans are highly adept at coordination movements with another, an imperative ability for performing music. For a successful musical interaction to take place, we must mutually predict and adapt to the other's action on a

millisecond timescale. This requires a shared model of the fundamental aspects of the task at hand, which in music often is meter and rhythmic subdivisions. We designed an experiment wherein two musicians performing joint finger tapping were subject to either a consistent or a conflicting rhythmic context. This allowed us to measure the effect of a shared model on interpersonal coordination. Our results indicate an effect of rhythmic context on synchronization, and that the conflicting rhythmic context perturbed mainly the start of the interaction. Furthermore, the musicians trend towards mutual adaptation in all condition. This supports the hypothesis that mutual adaptation requires a fusion of predictive models to take place.

CH.25 Peter Lykke
Eriksen IN VIVO QUANTITATIVE 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 NAFLD 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 clinical study, metabolic liver functions are studied in 25 patients with NAFLD and 10 healthy volunteers 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.

Results: All subjects have completed the study, and preliminary results may be available at the PhD Day.

Perspectives: To challenge the dogma that hepatic metabolic function is not affected in NAFLD and improve our understanding of the relationship between disease severity, histology, and metabolic liver functions in NAFLD.

CH.26 Kamilla
Pedersen

THE IMPACT OF PREPARATORY TEACHING FORMATS ON MEDICAL STUDENTS' ATTITUDES AND PATIENT-CENTEREDNESS IN PSYCHIATRY CLERKSHIP

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Introduction: Addressing attitudes and patient-centered interviewing skills are recommended as learning targets in introduction to clinical psychiatry. Little is known about the influence of various teaching formats on patient-centeredness and attitudes. The study objective was to compare the effect of two different teaching formats on patient-centeredness and attitudes towards psychiatry in medical students in psychiatry clerkship.

Method: Context was the preparatory lecture in the diagnostic interview in the four-week psychiatry clerkship for 204 medical students at Aarhus University, Denmark. Students were allocated to two groups (intervention and control). The teaching formats were an interactive video portraying a simulated psychiatrist and patient designed for the purpose (intervention) compared to the conventional lecture using text-based material (control). We assessed students' attitudes and confidence in exhibiting patient-centered behaviors using the Attitudes Towards Psychiatry (ATP 30) and the Self-efficacy in Patient-centeredness (SEPCQ-27) questionnaire in a pre-post design.

Results: We found significantly higher scores ($p=0,02$) in SEPCQ-27 in the intervention group. We found a significant change in the negative direction in the control group on items related to attitudes towards psychiatrists and interest in the diagnostic process.

Conclusion: Video-based patient-cases improved the medical students' self-efficacy in communicating with psychiatric patients in psychiatry clerkship better than using conventional text-based teaching material.

CH.27 Martin
Langeskov
Christensen

EFFECTS OF AEROBIC EXERCISE ON BRAIN HEALTH IN PEOPLE WITH MULTIPLE SCLEROSIS - PHD STUDY PROTOCOL

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Multiple Sclerosis (MS) is a physically and cognitively disabling chronic autoimmune disease of unknown etiology. The disease causes damage of white and grey matter in the central nervous system, leading to brain atrophy. The accumulation of lesions and the accelerated whole-brain atrophy correlate with the progressing disabilities that clinically characterize MS patients (MSP). Aerobic exercise represents a promising approach towards preservation or even expansion of hippocampal volume and cognitive functioning in MS.

The purpose of the project is to investigate how aerobic exercise affects total brain volume, specific brain regions, neurotrophins and cognition in MSP.

It is hypothesized that aerobic exercise can slow down brain atrophy, increase the size of hippocampus, upregulate the secretion of neurotrophins and improve cognitive performance in MSP.

This ongoing study is a 6-month randomized (stratified for gender) controlled trial with a cross-over design. A total of 86 MSP have been enrolled. Participants have been randomized into two groups; aerobic training or control (continuation of habitual lifestyle). The exercise intervention consists of 6 months of supervised aerobic training (bicycling, rowing, crosstrainer) performed two times a week at moderate to high intensity (progressively increasing from 30-60 min. at 70-95% of heart rate max).

The primary outcomes of the study will be MRI-obtained structural measurements of the brain associated with disease progression at week 0, 24 and 48 (i.e. rate of global/regional atrophy).

In case of positive findings, this would provide the first convincing human evidence of a disease-modifying effect of exercise in MS.

CH.28 Karen
Rokkedal
Lausch

TREATMENT OF CANDIDAEMIA IN A NATIONWIDE SETTING: ADHERENCE TO GUIDELINES AND EFFECT

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Objective: Primary antifungal treatment (AFT) of candidaemia with echinocandins has been the national recommendation in Denmark since 2009 in accordance with international guidelines. We describe management of candidaemia in a national cohort, including impact of prophylactic AFT on species distribution, adherence to national recommendations for AFT and effect on patient outcome.

Methods: Incident candidaemia cases from 2010 to 2011 were included. Information on AFT was collected from patient charts. Mortality information was obtained from the Danish Civil Registration System. Hazard ratios (HR) for mortality were reported with 95% confidence intervals (CI).

Results: 841 patients were identified. One fifth of patients (19.3% (162/841)) received antifungals prior to candidaemia, with non-albicans species more

frequent among these cases (59.3% vs. 45.5% among non-treated). Echinocandins as primary AFT was given in 44.2% (302/683) of patients. Echinocandins resulted in a higher proportion of patients adequately treated (97.7% vs 72.1%) and was associated with lower 0-14-day mortality (adj.HR 0.76, 95%CI 0.55; 1.06) compared to azole treatment. The lower mortality was significant for *C. glabrata* and *C. krusei* cases (adj.HR 0.50 95%CI 0.28; 0.89), whereas choice of AFT had no effect on mortality in patients with *C. albicans* or *C. tropicalis*.

Conclusion: Compliance with national recommendations was low, although similar to previously reported international rates. Primary treatment with echinocandins was associated with higher proportion of adequately treated patients and better survival. This real-life setting supports guideline recommendations and warrant for further focus on compliance.

CH.29 Louise Bang
Grode

REPRODUCTIVE LIFE IN WOMEN WITH CELIAC DISEASE: A NATIONWIDE, POPULATION-BASED STUDY OF DANISH CELIAC WOMEN

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Background: Celiac disease (CD) is an immune-mediated disease induced by ingestion of gluten and induces inflammation of the small bowel. CD is often diagnosed in childhood or in the childbearing years and has been associated with infertility and adverse pregnancy outcomes.

Aim: To investigate whether CD may influence the reproductive life of women.

Methods: A nationwide cohort of women with CD was established using the Danish National Patient Register (DNPR). Women with a diagnosis code of CD during the period of 1977-2016, were identified. Data on reproductive outcomes was obtained from the DNPR, the Medical Birth Register and the Danish In Vitro Fertilization Register. The celiac cohort was compared to an age-matched control cohort of women with no diagnosis of CD. Outcomes were number of fertility treatments, live and stillbirths, molar and ectopic pregnancies, spontaneous and induced abortions. We estimated rate ratios of reproductive outcomes before the diagnosis of CD (latent disease) and HRs for risk of reproductive events after date of diagnosis.

Results: In total, the cohort consisted of 69,969 women, of whom 6363 were exposed to CD and 63,606 were non-exposed. When we compared the reproductive outcomes in the period before the diagnosis (exposed to latent CD), the exposed women had slightly higher rates of still birth (RR 1.51 95% CI 1.03-2.18), ectopic pregnancy (RR 1.27 95% CI 1.06-1.52), spontaneous abortion (RR 1.12 95% CI 1.04-1.21) and lower rates of induced abortion (RR 0.91 95% CI 0.85-0.96) and IVF treatment (RR 0.81 95% CI 0.66-0.98) than the unexposed women. Results on reproductive outcomes in the period after the CD diagnosis are pending and will be presented at the PhD day.

CH.30 Cecilie Nørby MANAGING DEPRESSION IN EMPLOYEES FROM THE PERSPECTIVES OF
 Thisted EMPLOYEES, CO-WORKERS AND EMPLOYERS: AN INTEGRATIVE REVIEW

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Purpose: To synthesize evidence on factors promoting or hindering work participation of employees with depression from the employees', co-workers' and employers' perspectives, alongside an additional focus on the influence of the employee's occupation.

Methods: An integrative review was conducted. Pre-defined eligibility criteria guided study selection. Papers were critically appraised using the Mixed Methods Appraisal Tool and tools developed by Joanna Briggs. Qualitative inductive content analysis was used to analyse and synthesise findings.

Results: Seventeen studies were included: 12 quantitative studies, three qualitative studies and two mixed methods studies. From these, 144 findings were extracted and combined into six categories from which two syntheses were developed. One synthesis demonstrates that employees, co-workers and employers hold different perspectives on rehabilitation stakeholders' responsibilities hindering work participation. The other synthesis reveals that work participation is influenced by interactions between individual and occupational factors.

Conclusions: Employees, co-workers and employers agree that sufficient treatment from health professionals promotes work participation. Employees' fear of stigmatization hinders work participation. Co-workers and employers find that utilizing open communication is important. However, employers are concerned about entering employees' private sphere. Managing employees' depression, employers often intervene on the individual level. There is a need for structural interventions to promote work participation among employees with depression.

CH.31 Anja Thiede ATYPICAL SPEECH SOUND PROCESSING IN NEWBORNS WITH FAMILIAL
 RISK OF DYSLEXIA

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Developmental dyslexia is a heritable learning disorder that compromises neural processing of linguistic auditory information. An identification of individuals at highest risk would enable interventions already during infancy, compared to current interventions at school age. During the period of high neural plasticity in infancy, it could be particularly effective to alleviate later deficits associated with the learning disorder. However, the neural basis of speech sound processing in predisposed infants as early as at birth has been examined only scarcely.

In this first part of a longitudinal study on dyslexia, we determined whether a familial risk for dyslexia influences the processing of speech sounds in healthy sleeping Finnish newborns. Mismatch negativity (MMN) responses to speech sound changes, reflecting neural change detection, were recorded with electroencephalography (EEG) from both infants with a high familial risk for dyslexia and a control group without diagnosed language deficits among their close relatives. During the experiment, the Finnish pseudoword /tata/ and its deviations in frequency, duration and vowel identity were presented to the infants in an MMN paradigm.

The results demonstrate abnormal neural detection of all variants in speech sounds in infants at high risk of dyslexia, as reflected by diminished or absent MMRs compared to healthy control infants. Further, speech sound processing was found to be left-lateralized in high-risk newborns, but right-lateralized in controls. Taken together, these findings on speech processing in infants at risk of dyslexia suggest that deficient low-level auditory processing is evident and detectable already at birth.

CH.32 Mette-Lise
Simonsen

PATIENTS WITH ACUTE DRUG POISONING

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Most patients with drug poisoning are currently treated on presumption. Urine screenings as a "rapid test" are not accurate enough. With blood screenings, it can take up to 48 hours before a result is available. A new analysis method available at Department of Forensic Medicine, Aarhus University, makes it possible to perform a blood screening for several hundred drugs in three hours. We want to evaluate if this blood screening for drugs can improve the treatment of patients with altered mental status and drug poisoning, so that observation level and treatment match the patient's needs. Thereby undertreatment and overtreatment of these patients may be avoided, and this may ultimately help utilize the hospital resources in the best possible way.

In a four-year period (2008-2011), 805 deaths due to poisoning were registered in Denmark among persons above age 18 years. Current knowledge of patients with poisoning in Denmark is limited. Another part of the study is, therefore, to use several Danish registers to describe risk factors and prognosis in this population. We want to determine what happens with the patients admitted for poisoning: in-hospital mortality and mortality after discharge. Along with this, we want to determine the risk of a new poisoning, the risk of a subsequent psychiatric diagnosis or another somatic diagnosis, and the risk of suicide after index poisoning. This new knowledge may help identify patients at risk of a new poisoning and death.

CH.33 Karen Busk
Nørøxe GENERAL PRACTITIONER BURNOUT IN RELATION TO SELF-ASSESSED
WORKABILITY AND PATIENTS' CHANGE OF PRACTICE

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Introduction: Mental distress such as perceived stress and burnout is common among general practitioners (GPs). GP burnout may impair the quality of patient care and patient satisfaction.

Aims: To examine GP burnout in relation to self-assessed workability and patients' change of practice (used as a proxy for dissatisfaction with care).

Methods: Information on burnout and self-assessed workability was obtained from a questionnaire survey (N=1.678). Burnout was measured by the Maslach Burnout Inventory and was categorized as moderate or severe. Workability was measured by a single item from the Workability Index Scale; assessment of current workability compared with lifetime best on a scale from 0 ('completely unable to work') to 10 ('workability at its best'). Impaired workability was defined as a score < 7. Information on patients' change of practice is obtained from Danish national registers. Associations are assessed by regression analyses and adjusted for GP age, gender, practice organization, and case-mix in practice populations.

Results: GPs with burnout were more likely to report impaired workability than GPs without burnout (moderate burnout; OR = 5.9 (95% CI: 4.4-8.0), severe burnout; OR = 19.9 (95% CI: 13.5-29.1). Among GPs without burnout, 8% reported impaired workability, whereas this was the case for 34% of GPs with moderate burnout and 63% of GPs with severe burnout. The work regarding patients' practice change is in progress.

Conclusion: Burnout was strongly associated with GPs reporting impaired workability. If burnout is also found to associate with patients' change of practice, this will accentuate the importance of physician mental health in relation to quality of patient care.

CH.34 Signe Voigt
Lauridsen HAEMOSTATIC FUNCTION AFTER SPONTANEOUS SUBARACHNOID
HAEMORRHAGE

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Background: Changes in the haemostatic function after spontaneous subarachnoid haemorrhage (SAH) are well-known, however only sparsely investigated with global coagulation assays. The aim was to describe SAH patients' haemostatic function in the acute phase at admission and compare this to healthy individuals.

Methods: This study included 46 patients with SAH admitted to the Department of Neurosurgery, Aarhus University Hospital, Denmark, from 2014 to 2016. Blood samples were collected on admission, 2-3 hours after

admission and 24 hours after symptom onset. Dynamic whole blood coagulation was performed by thromboelastometry (ROTEM®). Thrombin generation was quantified by Calibrated Automated Thrombogram®.

Results: Compared with healthy individuals, SAH patients had a significantly increased maximum clot firmness (MCF) on admission (EXTEM $p < 0.0001$; INTEM $p = 0.001$; FIBTEM $p < 0.0001$). Endogenous thrombin potential (ETP) did not differ significantly compared to healthy individuals at admission.

Conclusion: Non-anticoagulated SAH patients have a preserved haemostasis in the acute phase at admission. Except for significantly elevated ROTEM®MCF, SAH patients have a haemostatic function similar to healthy individuals according to ROTEM®, thrombin generation and conventional coagulation tests.

CH.35 Bawer Jalal
Tofig

RECURRENCE AFTER PULMONARY VEIN ISOLATION IS ASSOCIATED WITH LOW CONTACT FORCE

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Objectives: Recurrent arrhythmia after pulmonary vein isolation (PVI) by radiofrequency (RF) ablation in patients with atrial fibrillation (AFIB) remains a significant challenge. Using contact force (CF) sensing ablation catheters, we aimed to identify procedure-related parameters associated with recurrence after de-novo PVI in patients with AFIB.

Methods: Consecutive patients undergoing a de-novo PVI procedure ($n = 120$, 63% paroxysmal and 37% persistent AFIB) employing a force-sensing ablation catheter were included. A clinical control, including electrocardiogram and 120 hour of Holter-recording at 12-months, was performed in all patients. Recurrence was defined as any documented AFIB or atrial flutter of more than 30 seconds on Holter-recording after an initial blanking period of three months.

Results: Recurrence occurred in 44 patients (37%). Mean CF was lower in patients with recurrent arrhythmia (22.2 ± 9.5 vs. 28.8 ± 9.3 g, $p < 0.001$). In multi-variable analyses, lower mean CF (OR 0.9 (95% CI 0.8-1.0), $p = 0.03$) and higher percentage of ablation time with a CF < 10 grams (OR 1.1 (95% CI 1.0-1.1), $p = 0.004$) were both associated with recurrence in two distinct models. Dragging during ablation compared with point-by-point ablation technique was associated with recurrence in both models (OR 19.2 (95 % CI 2.9-130.0), $p = 0.002$, and OR 21.7 (95 % CI 2.7-176.2), $p = 0.004$).

Conclusions: Low CF and dragging during ablation as compared with point-by-point ablation technique were associated with recurrent arrhythmia in patients with AFIB undergoing de-novo PVI by RF ablation.

CH.36 Stine Thyssen CALORIC RESTRICTION IS AFFECTING THE WAY WE AGE

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Ketone bodies are a major energy supply during caloric restriction. Acetoacetate (AcAcO) is one of the key ketone bodies. Despite being important for energy supply, AcAcO has shown beneficial properties in various diseases, including cancer, cardiovascular diseases, and diabetes. The reason for these beneficial effects is still not completely understood. However, a common denominator of these diseases is an imbalance in the cellular redox state due to an overall increase in reactive oxygen species (ROS). ROS can oxidize proteins, giving rise to cysteine sulfenic acid formation. Considering the C-nucleophilic properties of AcAcO, we propose that AcAcO can react with the electrophilic sulfenic acid residue, resulting in a novel protein modification. As caloric restriction is known to have a beneficial effect on aging and age-related diseases, we therefore hypothesize that some of these effects may be associated with protein modification by AcAcO.

To investigate this novel modification, we synthesized an AcAcO analog containing an alkyne group suitable for click chemistry. In a click reaction, we were able to attach a fluorophore for visualization of modified proteins. Additionally, a biotin can also be attached in order to identify the modified proteins. Using this analog, we confirmed that AcAcO can modify proteins and that the modification occurs on sulfenylated cysteine residues. Furthermore, we demonstrated that several proteins were modified by AcAcO in a cell lysate. These findings may contribute to the overall understanding of the connection between caloric restriction and age-related diseases.

CH.37 Luise Aamann RESISTANCE TRAINING IMPROVES PHYSICAL PERFORMANCE, QUALITY OF LIFE AND NUTRITIONAL STATUS IN PATIENTS WITH LIVER CIRRHOSIS

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Background: Malnutrition is a severe complication in liver cirrhosis, affecting physical performance, muscle mass, quality of life and mortality. Resistance training reverses the loss of functional ability and muscle mass in frail elderly. Adequate nutritional supplements limit malnutrition and loss of muscle in cirrhotic patients. The effect of combining resistance training and adequate dietary protein intake on nutritional status, quality of life and performance status in cirrhotic patients was examined.

Methods: 39 patients with cirrhosis Child Pugh A/B were randomly allocated to resistance training in groups of five exercising 3x60 min/week for 12 weeks or a control group, where the level of activity was recorded. Everyone received a controlled diet of 1.2-1.5 g of protein/kg/day. Anthropometric measurements, the Short-Form Health Survey (SF-36) testing quality of life, and 6-minute walk test (6MWT) were assessed by the same blinded dietician before and after the intervention.

Results: The exercise group improved the 6MWT by 32.4m (± 42.4 SD, $p=0.005$), calf circumference increased by 0.56cm (± 0.65 SD, $p=0.002$) and the mental component score (SF-36) by 4.1 points (± 6.2 SD, $p=0.01$) within the group. The control group improved non-significantly affecting between group analyses.

Conclusion: Resistance exercise as an "add-on" to protein supplements improves physical performance, quality of life and increases calf circumference in patients with cirrhosis.

CH.38 Pernille Gabel COMMUNICATING DETAILED INFORMATION ABOUT COLORECTAL CANCER SCREENING TO CITIZENS WITH LOWER EDUCATIONAL ATTAINMENT USING AN ELECTRONIC DECISION AID: A QUALITATIVE STUDY

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Background: Compared to average educational attainment citizens, citizens with lower educational attainment (LEA) less frequently take up colorectal cancer (CRC) screening and more seldom read and understand conventional screening information. The information needs in LEA citizens range from a clear recommendation to elaborating information. Some decision aids (DAs) are designed to support informed decision-making about CRC screening participation, but none embrace the diversion in information needs. The aim of this study was to develop such a DA tailored to LEA citizens.

Methods: A prototype of the DA was developed based on the IPDAS guidelines along with LEA citizens' information needs. The online DA presented information in steps. Value clarification questions were included and answers were summarized in a choice-barometer on the last page. Statistics were presented in both relative and absolute numbers. User testing, peer review and field testing were conducted using focus group and telephone interviews and email correspondences with LEA citizens and healthcare professionals. Data was analyzed using thematic analysis.

Results: The citizens found the DA easy to understand and the text of suitable length. They easily and intuitively navigated around the DA and stated that they felt encouraged to think about benefits and harms of CRC screening without being overloaded with information.

Conclusions: This DA represents a new way of communicating detailed information about CRC screening to LEA citizens. Further, this work might serve as an inspiration when developing information material in other screening programs.

CH.39 Lise Roed Brogaard IS NON-TECHNICAL PERFORMANCE THE KEY TO HIGH CLINICAL PERFORMANCE IN OBSTETRIC TEAMS?

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Background: The risk of maternal death by postpartum haemorrhage can be reduced if the obstetric team performs well (1,2). However, the literature does not describe which behaviours characterise a high performing obstetric team (3).

Aim: To describe the relationship between non-technical skills and clinical performance in obstetric teams managing real-life major postpartum haemorrhage.

Methods: The inter-rater agreement between raters assessing clinical and non-technical performance was described by Intra Class Correlation (ICC) and Bland-Altman analysis. The relationship between clinical and non-technical performance was described by a simple linear regression.

Results: A total of 99 video recordings was included in the study. Inter-rater agreement was high for non-technical performance ICC 0.97 (95% CI; 0.96-0.98) as well as for clinical performance ICC 0.84 (95% CI; 0.76-0.89). The relationship between non-technical skills and clinical performance during real-life major postpartum haemorrhage can be described as a simple linear regression. The regression line had a coefficient of 0.40 (95% CI 0.23-0.57). The non-technical skill "Situation awareness" was the category of most impact in relation to clinical performance.

Discussion and conclusion: Our results show that better non-technical performance is related to higher clinical performance during real-life major postpartum haemorrhage. Our study found that "situation awareness" was a key behaviour for the obstetric team's management of postpartum haemorrhage.

CH.40 Anuj Pareek DIAGNOSTIC ACCURACY OF LUNG ULTRASOUND IN THE NEONATAL INTENSIVE CARE UNIT

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Background: Approximately 30% of premature neonates present with respiratory distress at birth. These neonates typically require multiple chest radiographs in order to uncover their medical condition. Several scientific articles emphasize that these radiological examinations account for a significant radiation exposure, which may be harmful and lead to development of cancer later in life. There is a clear consensus amongst medical doctors regarding the need for a safer imaging modality, which is both efficient and feasible in the neonatal intensive care unit (NICU) setting. Lung ultrasonography is a safe and relatively new diagnostic tool in the clinical setting. Although several studies have documented the efficacy of lung ultrasound in adults, there is currently a lack of data regarding neonatal patients.

Aim: To estimate the diagnostic accuracy of lung ultrasound for chest diseases in the NICU, using chest radiographs and clinical diagnosis as two separate reference standards.

Methods: All neonates admitted to the NICU at Aarhus University Hospital are considered for inclusion. Neonates who are subjected to a chest radiograph are included when the primary investigator can perform the lung ultrasonography within 30 minutes of the chest radiograph. Both chest radiographs and lung sonograms are evaluated by certified radiologists, who are blinded to clinical data. Diagnostic accuracy of lung ultrasound is reported as sensitivity, specificity, positive and negative predictive values.

Results and perspectives: 59 neonatal patients with respiratory distress are currently included in the research project. Ultrasound may be useful as a bedside diagnostic instrument in the NICU.

CH.41 Jesper
Falkesgaard
Højen

TREATMENT OF HIV-INFECTED INDIVIDUALS WITH THE HISTONE DEACETYLASE INHIBITOR PANOBINOSTAT RESULTS IN INCREASED NUMBERS OF REGULATORY T CELLS AND LIMITS EX-VIVO LPS-INDUCED INFLAMMATORY RESPONSES

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Histone deacetylase inhibitors (HDACi) modulate the transcriptional activity of all cells, including innate and adaptive immune cells. Therefore, we aimed to evaluate immunological effects of treatment with the HDACi panobinostat in HIV-infected patients during a clinical phase IIa latency reversal trial.

We investigated changes in T cell activation (CD69, CD38, HLA-DR) and the expression of CD39 and CTLA4 on regulatory T cells (Treg). Whole-blood stimulations were performed and cytokine responses measured using Luminex. Gene expression in purified PBMCs was evaluated using an Affymetrix HTA 2.0 gene chip.

We found that proportions of CD4+ and CD8+ T cells expressing CD69 increased 24hrs after initial panobinostat administration ($p < 0.01$), followed by an increase in CD38+HLA-DR+ co-expressing CD4+ T cells on day 4 ($p = 0.02$). Concurrently, proportions of Treg increased by 40% ($p = 0.003$). Treg CTLA4 median fluorescent intensity (MFI) increased by 25% ($p = 0.007$) and CD39 MFI on CD39+ Treg increased by 12% ($p = 0.02$). LPS-induced inflammatory responses (IL-1b, IL-6, IL-12p40 and TNF- α) in whole blood were significantly down-regulated four days after initial dosing. Lastly, panobinostat induced significant changes in the overall gene expression pattern (fold-change > 1.5 , FDR-corrected $p < 0.05$). Importantly, measures of immune function returned to baseline levels after panobinostat treatment and follow-up revealed no sustained effect on overall gene expression.

Collectively, these results suggest that panobinostat has transient opposing effects on immune responses, but does not cause persistent epigenetic influenced transcriptional or immunomodulatory changes in HIV individuals.

CH.42 Mads
Sørensen
Larsen

PROTEIN INGESTION TO REDUCE MUSCLE WASTING DURING WEIGHT LOSS: A RANDOMIZED CONTROLLED STUDY

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The percentage of overweight Danish women has reached 44%. This development is largely driven by middle-aged and elderly women, the majority of whom wish to lose weight. While traditional hypocaloric diets (HCDs) are effective in reducing fat mass, this approach is a controversial one as up to 40% of a HCD induced weight-loss can be attributed to undesired loss of lean body mass. This may accelerate the age-related loss of muscle mass (sarcopenia), exacerbate fragility and ultimately reduce the ability to perform activities of daily living. To accommodate women wishing to lose weight, it is important to develop strategies to reduce the loss of muscle mass during weight-loss. The aim of the study is to determine the optimal protein-dose (high quality milk protein) per meal necessary to enhance muscle protein synthesis and thereby counteract muscle loss during weight-loss. We hypothesize that the muscle-protein synthetic response in women on a HCD is blunted compared to women eating an energy sufficient diet, and that the dose maximizing muscle-protein synthesis in women consuming a HCD is higher than the dose previously determined in weight-stable elderly men.

Methods: Forty women (~ 50 years) will be randomized to ingest 15g (n=10), 35g (n=20) or 60g (n=10) following a five-day HCD (total n=30) or an energy balanced diet (n=10). Muscle protein synthesis will be determined using stable isotope tracers at rest in the post-absorptive state as well as following ingestion of the different protein doses.

CH.43 Karoline
Knudsen

PANCREATIC POLYPEPTIDE PLASMA LEVELS IN PARKINSON'S DISEASE - A POTENTIAL MARKER OF PARASYMPATHETIC DENERVATION

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Background: Most patients with Parkinson's disease (PD) experience signs of decreased parasympathetic function. Lewy pathology is present in the vagus nerve and dorsal motor nucleus of the vagus early in the disease course. The pancreas is densely innervated by the vagus nerve, and the early peak (5-20 min) of the hormone Pancreatic Polypeptide (PP) after food intake or sham-feeding has been validated as a marker of vagal integrity. Thus, we aimed to study plasma PP concentration during sham feeding (chew-and-spit) in PD patients and healthy controls (HC).

Methods: Twenty-five early-to-moderate PD patients (H&Y 2 (1-3); 7 female) and 17 HC (5 female) were included. Blood sampling for PP, glucose, and insulin analysis were performed before, during, and 20 minutes after a 5-

minute sham feeding session with white bread and chocolate spread. Faeces samples from all participants were analysed for pancreatic elastase enzyme levels as a marker of exocrine pancreatic function.

Results: The PD group displayed significantly decreased plasma PP concentrations during the early phase after sham feeding compared to HC ($p=0.012$). No changes in glucose and insulin levels were seen in the groups as an indicator of pure sham feeding without food ingestion. No significant group difference was seen in pancreatic elastase levels ($p=0.69$).

Conclusion: Early-to-moderate stage PD patients showed significantly decreased PP plasma concentrations after sham feeding - an indication of decreased vagal function. Exocrine pancreatic function was not significantly different between groups. Glucose and insulin concentrations did not change in either group throughout the test, verifying pure sham feeding.

CH.44 Jesper
Guldsmed
Madsen

HBO TREATMENT FOR DIABETIC NEUROPATHY AND RETINOPATHY IN STZ-INDUCED DIABETES IN WISTAR RATS

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The neurodegenerative complications of type II diabetes, such as diabetic neuropathy and retinopathy, can have devastating consequences for the quality of life for the afflicted, ranging from limb amputation to blindness. Recent research has suggested that reduced oxygen delivery to tissues is a major contributing factor to nerve degeneration. In this study, we aim to test this hypothesis and test whether a massive and sustained increase in blood oxygen levels can have alleviating effects upon the disease. Wistar rats with STZ-induced diabetes were subjected to High Barometric Oxygen (HBO) treatment for two weeks, after which retina responsiveness and peripheral nerve conduction speed were measured and compared with non-HBO diabetic control animals to determine the effect of treatment. Along with electrophysiological data, nerve tissue and blood samples were also collected in order to visualize potential damage with histology and imaging and to determine the extent of possible oxidative damage caused by the treatment.

CH.45 Morten
Stokholm

EXTRASTRIATAL MONOAMINERGIC FUNCTION IN PRODROMAL PARKINSON'S DISEASE: A PET STUDY IN IRBD PATIENTS

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Idiopathic REM sleep behaviour (iRBD) patients have a very high risk of progressing to Parkinson's disease (PD) or dementia with Lewy bodies (DLB) over time. At this prodromal stage, iRBD patients have an increased

frequency of non-motor symptoms similar to manifest PD patients; these symptoms might be linked to alterations in the neurotransmitter systems localised to extrastriatal structures. We investigated whether monoaminergic extrastriatal changes are present in iRBD patients and if this is associated with an altered microglial response using in vivo PET imaging

Twenty-one iRBD patients were studied with ^{18}F -DOPA and ^{11}C -PK11195 PET to assess the monoaminergic system and levels of microglial activation, and comparisons were made to 29 healthy controls. Regions of interest were identified, and voxel-based Statistical Parametric Mapping (SPM) analysis was performed for both tracers.

iRBD patients showed a 15% mean reduction in ^{18}F -DOPA Ki-values in the thalamus compared to controls ($p=0.03$); no other regions of interest assessed showed significant changes with either ^{18}F -DOPA or ^{11}C -PK11195 PET. The voxel-based analysis identified significant clusters with increased ^{11}C -PK11195 binding in the occipital lobe bilaterally of iRBD patients.

Reduced thalamic ^{18}F -DOPA Ki-values in iRBD patients might reflect alterations in the monoaminergic structures projecting to the thalamus. Increased occipital binding of ^{11}C -PK11195 in iRBD patients might reflect possible future progression towards DLB or PD prone to visuospatial impairments and hallucinations. Future longitudinal follow-up studies of these patients will elucidate the clinical importance of these changes.

CH.46 Cecilie
 Ejerskov
 Canceled

A STUDY ON NEUROFIBROMATOSIS TYPE 1 EXPLORING CORRELATION BETWEEN PHENOTYPE, GENOTYPE AND GASTROINTESTINAL SYMPTOMS

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Background: Neurofibromatosis type 1 (NF1) is a complex genetic disease caused by a mutation in, or a deletion of, the neurofibromin gene NF1 and is inherited in an autosomal dominant mode. With a prevalence of 1:3,000, NF1 is one of the more common rare diseases. The characteristic of NF1 is café-au-lait spots on the skin and cutaneous neurofibromas. The prevalence of gastrointestinal involvement in the NF1 population has been estimated at 11%-25% and is mostly based on case reports studies. Study I and II of the current PhD project have showed that both children, adolescents and adults with NF1 have a higher likelihood of gastrointestinal symptoms, most often corresponding to constipation. The current study III explores potential correlation between NF1 phenotype, genotype and the gastrointestinal symptoms.

Method: Of 277 patients with NF1, 49 patients were found to have chronic constipation. Of 191 index patients, 124 had a mutational NF1 analysis performed during the course of the study, whereas 67 previously had a mutational NF1 analysis performed. The mutational spectrum of NF1 will be correlated to the presence of constipation and NF1 phenotype. Information on NF1 current severity, visibility grade, and self-perceived conception of NF1 symptoms, visibility and illness burden was collected, and regression analyses with constipation as dependent variable are pending.

Results: At the time of abstract submission, the results of the study are pending. Serious intestinal symptoms are often underreported in the clinic and considered stigmatizing for the individual. The results will possibly

improve future investigation, control, and treatment of NF1 and gastrointestinal disorders.

CH.47 Jacob Lynge Callesen TEST-RETEST AGREEMENT AND RELIABILITY OF THE SIX SPOT STEP TEST IN PERSONS WITH MULTIPLE SCLEROSIS

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Background: Valid and reliable gait outcomes provide valuable information on disease impact and progression in persons with multiple sclerosis (PwMS). The Six Spot Step Test (SSST) extend traditional walking outcomes by further challenging components of coordination and balance. Nonetheless, the agreement of the SSST has not been investigated.

Objective: To determine the within-day, day-to-day and interrater agreement of the SSST in PwMS. A secondary aim was to investigate the validity of handheld timing.

Methods: 38 PwMS with an Expanded Disability Status Scale (EDSS) <6.5 completed two SSSTs with a five-minute break in-between. Two days later, this procedure was repeated. Bland-Altman analysis was performed to determine the 95% Limit of Agreement (LOA), and the Interclass correlation coefficient (ICC) was calculated. In a subgroup of 18 PwMS, the SSSTs were video-recorded and timed by a second investigator.

Results: The relative LOA within and between days were $\pm 15\%$ and $\pm 19\%$, respectively, while the ICC was 0.987 and 0.983, respectively. A decrease in mean time of 6% was found over four tests. A timing error of ± 0.5 sec was observed when applying handheld timing as compared to video-based timing.

Conclusion: The SSST has an acceptable agreement and reliability. For interventional purposes, a change of >19% can be regarded as a real change. Valid timing can be performed by a handheld stopwatch.

CH.48 Mats Bue SINGLE-DOSE BONE PHARMACOKINETICS OF VANCOMYCIN IN A PORCINE IMPLANT-ASSOCIATED OSTEOMYELITIS MODEL

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The increasing incidence of orthopaedic methicillin-resistant *Staphylococcus aureus* (MRSA) infections represents a significant therapeutic challenge. Being effective against MRSA, the role of vancomycin may become more important in the orthopaedic setting in the years to come. Nonetheless, vancomycin bone and soft tissue penetration during infection remains unclear.

In 8 pigs, implant-associated osteomyelitis was induced on day 0, using a *Staphylococcus aureus* strain. Following administration of 1,000 mg of

vancomycin on day 5, vancomycin concentrations were obtained with microdialysis for 8 hours in the implant bone cavity, in cancellous bone adjacent to the implant cavity, in subcutaneous tissue (SCT) adjacent to the implant cavity, and in healthy cancellous bone and healthy SCT in the contralateral leg. Venous blood samples were also obtained. The extent of infection and inflammation was evaluated by post-mortem CT-scans, C-reactive protein levels and cultures of blood and swabs.

In relation to all the implant cavities, bone destruction was found. Ranging from 0.20 to 0.74, tissue penetration, expressed as the ratio of the area under the concentration-time curve from 0 to the last measured value, was incomplete for all compartments except for healthy SCT. The lowest penetration was found in the implant cavity.

In conclusion, *Staphylococcus aureus* implant-associated osteomyelitis was found to reduce vancomycin bone penetration, especially in the implant cavity. These findings suggest that it may be unsafe to rely solely on vancomycin therapy when treating acute osteomyelitis. Particularly when metaphyseal cavities are present, surgical debridement seems necessary.

CH.49 Kathrine Hald EXPANDED CARDIAC REHABILITATION IN SOCIALLY VULNERABLE PATIENTS WITH MYOCARDIAL INFARCTION: A 10-YEAR FOLLOW-UP STUDY FOCUSING ON MORTALITY AND NON-FATAL EVENTS

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Purpose: The purpose of the present study was to perform a long-term follow-up on a socially differentiated cardiac rehabilitation intervention and examine the impact of the intervention on mortality and non-fatal recurrent events 10 years after.

Methods: The study was conducted as a prospective register-based cohort study. The study population consisted of 208 socially vulnerable patients aged < 70 years admitted to Aarhus University Hospital, Denmark, with first episode myocardial infarction in 2000-2004 and participating in a socially differentiated cardiac rehabilitation intervention.

Results: There was no significant difference in mortality or non-fatal recurrent events (all P-values > 0.05) measured at 10-year follow-up when comparing the expanded cardiac rehabilitation intervention to standard cardiac rehabilitation.

Conclusions: At 10-year follow-up, the study found no significant differences between socially vulnerable patients receiving expanded cardiac rehabilitation and socially vulnerable patients receiving standard cardiac rehabilitation regarding mortality and non-fatal recurrent events.

CH.50 Marie Vad CHRONIC POSTOPERATIVE PAIN AFTER INGUINAL HERNIA REPAIR IN RELATION TO OCCUPATIONAL MECHANICAL EXPOSURES - A PROSPECTIVE COHORT STUDY IN THE DANISH HERNIA DATABASE

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Objectives: To evaluate the exposure-response relationship between specific occupational mechanical exposures and the risk of persistent postoperative pain after first-time inguinal hernia repair.

Methods: We conducted a prospective cohort study using the Danish Hernia Database, the Danish Civil Registration System and the Danish National Register on Public Transfer Payments. All men aged ≥ 18 -65 years, living in Denmark within the study period (1 October 2014-1 March 2017), with a first-time inguinal hernia repair according to the Danish Hernia Database, and active at the labour market according to the Danish National Register on Public Transfer Payments received a questionnaire by mail. A Job Exposure Matrix was used to assess occupational mechanical exposures based on job titles. Each exposure variable was categorised into 3 levels: number of hours/days spent standing/walking (<4 hours, 4-6 hours, >6 hours), total load lifted per day (0 kg, >0-1000 kg, >1000-4900 kg), daily frequency of lifting loads weighing ≥ 20 kg (<2 times/day, 2-10 times/day, >10 times/day). Outcome was a Numeric Rating Scale (NRS) of pain ≥ 2 . Poisson regression was used to estimate prevalence ratios.

Results: We found a significantly increased risk of postoperative among respondents with a high intensity occupational mechanical workload. The adjusted prevalence ratio of NRS ≥ 2 at 6 months postoperative was 1.38 (95% CI 1.12-1.71) in the group lifting 1000>-4900 kilos per day compared with the minimal exposed group.

Conclusion: In this nationwide prospective questionnaire study cohort, we found an increased risk of pain among participants with the highest occupational mechanical exposures.

CH.51 Ina Qvist CHARACTERISTICS ASSOCIATED WITH ADHERENCE TO PRESCRIBED DRUGS AMONG 65-74 YEAR-OLD MEN DIAGNOSED WITH ABDOMINAL AORTIC ANEURYSM OR PERIPHERAL ARTERIAL DISEASE IN VIVA: A CARDIOVASCULAR SCREENING TRIAL

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Purpose: We aimed to investigate the extent of adherence to antiplatelet and statin therapy for participants in a vascular screening trial diagnosed with AAA or PAD and to identify characteristics predicting adherence.

Methods: Data from the VIVA screening cohort for vascular disease were combined with register data from Danish registers from 2007 to 2016. For all participants, persistence was measured by time to the first breaks of > 100 days during 5 years of follow-up. Proportion of days covered \geq 80% and was used as categorical cut-off for adherence. For non-users at baseline, adherence to statin and antiplatelet treatment was measured as initiation within 90 days. Predictors of initiation and adherence were identified in multivariable logistic regression models and persistence in Cox proportional hazards regression models.

Result: Among 18,748 screened participants, we identified 618 with AAA and 2,051 with PAD. A total of 94 % and 91% initiated antiplatelet and statin treatment, respectively. 61% and 56% were persistent and 67% and 61% were adherent. Predictors of adherence were current user status at baseline of antiplatelet and statin, hypertension, and history of myocardial infarction. Among non-users at baseline, only 64% and 61% initiated antiplatelet and statin within 90 days, respectively. 43% and 38% were adherent during 5 years of follow-up.

Conclusion: The 5-year adherence to antiplatelet and statin treatment was suboptimal for participants in a screening trial for vascular disease. For non-users in screening, the adherence was low. Research initiatives are required to increase the adherence among non-users in screening to increase the screening efficacy in future trials.

CH.52 Casper Kruse IMPACT OF CONE BEAM COMPUTED TOMOGRAPHY ON PERIAPICAL ASSESSMENT AND TREATMENT PLAN AT FIVE TO ELEVEN YEARS AFTER ENDODONTIC SURGERY

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Introduction: Traditionally, healing after endodontic surgery (ES) in a tooth with apical periodontitis is assessed on 2D periapical radiographs (PR). Recently, the use of 3D Cone Beam CT (CBCT) has increased in dentistry. In general, CBCT detects more periapical lesions than PR.

Aim: To evaluate the impact of additional information from CBCT on periapical assessment and treatment planning in long-term follow-up of ES cases.

Methodology: ES patients treated in 2004-2010 were re-invited for clinical follow-up examination, PR, and CBCT. Of 108 reinvited patients (119 teeth), 74 patients (83 teeth) participated. Three observers initially assessed PR using the scoring criteria by Rud & Molven (4-grade scale, increasing severity); "Periapical Assessment A". By including clinical information, "Treatment Plan A" was made: 1) no treatment, 2) new ES, or 3) extraction. The CBCT volume was then assessed, and the combined information was used for "Periapical Assessment B" and "Treatment Plan B". Agreement between assessments and between treatment plans was described statistically by test for marginal homogeneity (Stuart-Maxwell).

Results: Nine teeth had been extracted. Thus, the final analysis included 74 teeth in 66 patients. The periapical assessment changed in 38 cases (51.4%), of which 35 (47.3%) received a higher score, $p < 0.001$. Treatment plans changed in 18 cases (24.3%), and in 14 cases (18.9%) from no treatment necessary to recommendation of invasive treatment (new ES or extraction), $p = 0.005$.

Conclusion: CBCT used for long-term follow-up after ES may lead to more cases diagnosed with persisting apical periodontitis. This may lead to a recommendation towards a more invasive treatment modality.

CH.53 Katrine
 Fuglsang

HUMAN PAPILOMA VIRUS GENOTYPING AND POSTSURGICAL MANAGEMENT IN CERVICAL CANCER

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Objectives: Human Papilloma Virus (HPV) is obligate for the development of cervical cancer. HPV has previously been detected in tissue from cervical tumors, lymph nodes and recurrent disease. The aim of this study was to evaluate the value of HPV genotyping in postsurgical management.

Methods: We conducted a hospital-based case-control study. All patients had previously undergone surgery for early-stage cervical cancer during 2003 to 2014 at the Department of Obstetrics and Gynaecology, Aarhus University Hospital, Denmark. Formalin-fixed, paraffin-embedded tissue from the primary tumor, pelvic lymph node stations, and recurrent disease were genotyped using INNO-LIPA HPV Genotyping Extra (Fujirebio, Europe, Ghent, Belgium).

Results: Eighteen recurrent and 15 non-recurrent patients with an HPV positive cervical tumor were included. Not surprisingly, women diagnosed with lymph node metastases were more likely to be diagnosed with recurrence than women without metastases (86% vs. 46%, $p = 0.10$). Metastatic lymph nodes were more likely HPV positive than non-metastatic lymph nodes (71% vs. 27%, $p > 0.05$). Women with HPV positive lymph nodes, with and without metastases, were more likely to be diagnosed with recurrence than women with HPV negative lymph nodes (83% vs. 38%, $p < 0.05$). From ten women with recurrence, tissue biopsies were available and sufficient for HPV genotyping; HPV was detected in eight (80%). For all women, the HPV genotype in the three tissues was consistent.

Conclusions (preliminary): The presence of HPV in the lymph nodes seems to be associated with an increased risk of recurrence, and HPV genotyping may very likely be valuable in postsurgical management.

CH.54 Dmitri Zintchouk COMPREHENSIVE GERIATRIC CARE IN A COMMUNITY REHABILITATION UNIT - A RANDOMIZED CONTROLLED TRIAL

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Objectives: To investigate the effect of geriatrician-performed Comprehensive Geriatric Care (CGC) in older adults referred to a community rehabilitation unit.

Design: Randomized controlled trial.

Setting: Two Danish community rehabilitation units.

Participants: Persons aged 65 years or older admitted from home or hospital.

Intervention: Medical history, physical examination, blood tests, medication adjustment, and related treatments performed by a geriatrician.

Measurements: Primary outcome was number of hospital admissions and emergency department (ED) visits. Secondary outcomes were ambulatory contacts, general practitioner (GP) contacts, activities of daily living (ADL) and Overall Quality of Life (OQoL). Outcomes were measured within 90 days of admission to the rehabilitation units.

Results: 368 persons were randomized; 185 to the intervention group (IG) vs 183 to the control group (CG). Baseline characteristics and length of stay at the rehabilitation units were not different between the groups. The number of hospital admissions and ED visits, ambulatory contacts and out- of-hours GP visits or phone calls did not differ between the groups. The number of daytime GP consultations and visits, phone and email consultations, or other GP services were lower in the IG ($P < .001$). There were no differences in the mean between the groups for ADL and OQoL measures, but more participants in the IG improved their OQoL (OR 1.63, 95% CI: 1.07 - 2.48, $P = .023$).

Conclusion: Geriatrician-performed CGC in older adults in a community rehabilitation unit had no effect on the secondary healthcare utilization, but may reduce primary healthcare utilization and improve OQoL during 90 days of follow-up.

CH.55 Bo Langhoff Hønge OPTIMIZING RECOVERY OF FROZEN HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS FOR FLOW CYTOMETRY

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Introduction: Live peripheral blood mononuclear cells (PBMCs) can be frozen and thawed for later analyses by adding and removing a cryoprotectant, such as dimethyl sulfoxide (DMSO). Laboratories across the world use various procedures, but published evidence of optimal thawing procedures is scarce.

Materials and methods: PBMCs were separated from blood collected from healthy Danish blood donors and stored at -80°C after adding of DMSO. The essential steps in the thawing procedure were modified, and performance was evaluated by flow cytometry with respect to the percentage and total yield of viable PMBCs.

Results: The best-performing washing medium was Roswell Park Memorial Institute (RPMI) 1640 at 37°C with 20% fetal bovine serum. When using 10 mL washing medium in a 15-mL Falcon tube, samples should be centrifuged for at least 10 minutes at 500 g. We failed to detect any differences between the tested methods of mixing PBMCs with washing medium. Likewise, neither the thawing duration nor the centrifugation temperature (20°C and 37 °C) had any effect. PBMCs could be incubated (rested) for up to eight hours in a 37°C 5% CO₂ incubator without affecting cell counts, but incubating PBMCs for 16 hours significantly decreased viability and recovery. In general, high viability was not necessarily associated with high recovery.

Conclusion: Changing the thawing procedure significantly impacted PBMC viability and live cell recovery. Evaluating both viability and live PBMC recovery is necessary to assess method performance. Investigation of differential loss of PBMC subtypes and phenotypic changes during thawing and incubation requires further evaluation.

CH.56 Daan Koppens EQUAL FIXATION OF FIXED-BEARING VERSUS MOBILE-BEARING CEMENTED PARTIAL KNEE REPLACEMENT. A RANDOMISED CONTROLLED RSA STUDY WITH 2-YEAR FOLLOW-UP

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Background: Medial unicompartmental knee arthroplasty (UKA) makes up 10-20% of all knee arthroplasties and gives good clinical outcomes. However, the revision rate is higher compared to total knee arthroplasty (TKA). Early implant migration is a predictor of implant loosening/ revision and can be measured with radiostereometric analysis (RSA). The mobile-bearing Oxford UKA has been on the market for 40 years and has a 7-year revision rate of 11.1% in national registries. The fixed-bearing Sigma UKA has been on the market since 2010 and presents a 7-year revision rate of 5.5% in national registries. Longtime follow-up for the Sigma UKA is yet unknown. This study aims to evaluate migration of the Sigma and Oxford UKA using RSA.

Materials and methods: A patient-blinded, randomised controlled RSA study with 24 months of follow-up was performed. Between January 2014 and October 2015, 62 patients were randomised to receive either a Sigma UKA (N=31) or Oxford UKA (N=31). Stereoradiographs were obtained postoperatively at 4.12, and 24 months. Mixed model analysis was used for statistical data evaluation. Currently, follow-up has been completed for 52 patients.

Results: No differences in translations or rotations were found between the Sigma UKA and the Oxford UKA. The size of measured translations and

rotations was comparable with reportings in the literature. For maximal total point motion (MTPM) of the tibial component, no difference was shown between groups.

Conclusion: Our study shows no difference in migration between the Sigma UKA and the Oxford UKA. This supports the low revision rates of the Sigma UKA in the national registries. Migration stabilises after 12 months.

CH.57 Jens Hartlev VOLUMETRIC CHANGES OF THE GRAFT AFTER LATERAL BONE AUGMENTATION

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Background: Lateral alveolar ridge augmentation by an autogenous bone block harvested from an intraoral donor site is associated with some graft resorption during the healing period.

Aim: The purpose of this study is to evaluate volumetric changes after lateral alveolar ridge augmentation by using an autogenous bone graft covered by 1) a PRF membrane (test group) or 2) an anorganic bovine bone substitute and a resorbable collagen barrier membrane (control group).

Material and methods: Twenty-seven partially edentulous patients (test group n=14, control group n=13) treated with bone augmentation were included in this analysis. To evaluate the alveolar ridge volume, the patients received cone beam computed tomography (CBCT) examinations prior to surgery and 14 days and 6 months after bone grafting. Differences in alveolar ridge area among the various observation times were evaluated by planimetric measurements on two-dimensional CBCT images of the grafted regions.

Results: A significant increase in the alveolar ridge dimensions, allowing implant placement, was obtained with both types of grafting procedure. The mean bone resorption was 15% SD ± 9% in the test group and 18% SD ± 13% in the control group. There was no significant difference between the two groups (3%; CI 95%: -6; 12%).

Conclusion: At 6-month follow-up, it was possible to place implants in all the operated sites. There was no difference in the bone resorption between the control and test group. However, there was significantly more bone resorption if the augmented site was anterior than posterior in the jaw.

CH.58 Jesper Damsgaard COMBINING LATENCY REVERSING THERAPY AND BROADLY NEUTRALIZING ANTIBODIES TO LIMIT THE ESTABLISHMENT OF THE HIV-1 RESERVOIR DURING ANTIRETROVIRAL TREATMENT INITIATION - A RANDOMIZED CONTROLLED TRIAL (ECLEAR)

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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 attacks the HIV-1 reservoir, which involves three steps: 1. Shutting down the virus spread and thus preventing de novo infection (by ART), 2. (Re)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/production. 3BNC117, one of the most potent broadly neutralizing antibodies (bNAbs) cloned to date, accelerates clearance of cell-free virus, induces antibody dependent cytotoxicity to kill infected cells, and produces 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 conducted among ART naïve HIV-infected patients randomized 1:1:1:1 to either:

1. ART (*INSTI-based regimens)
2. ART* + romidepsin
3. ART* + 3BNC117
4. ART* + romidepsin + 3BNC117

Results and conclusion: The trial started in early 2017, and the final results are expected at the end of 2019.

CH.59 Laura Laine
Herborg

THE FLOW CYTOMETRIC CORRELATE TO FLT3 AND NPM1 MUTATIONS IN ACUTE MYELOID LEUKEMIA: HIGH EXPRESSION OF CLEC12A AND CD123

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Introduction: Two robust markers associated with acute myeloid leukemia (AML) are the C-type lectin domain family 12, member A (CLEC12A) and the IL-3 receptor α -chain (CD123). At diagnosis, most AML patients are CLEC12A+, but, remarkably, the amount of CLEC12A+ blasts ranges from very few to almost 100%. Likewise, CD123 is widely expressed in AML. We hypothesized that the heterogeneous CLEC12A and CD123 expression observed in AML could be associated with the important prognostic molecular aberrations of FMS-like tyrosine kinase 3 (FLT3) and nucleophosmin (NPM1).

Methods: 140 consecutive cases of AML diagnosed in 2009-2013 were retrospectively identified from the records of the Hemodiagnostic Laboratory, AUH. Routine multiparametric flow cytometry was performed at diagnosis using the following antibodies: anti-CD34, anti-CD123, anti-CD45, anti-CD117, anti-CD14, and anti-CLEC12A. Capillary fragment analysis identified FLT3 and NPM1 mutations. Marker expression was defined as

percentage of live cells and analyzed using binary regression. Risk ratios (RR) are reported.

Results: Of the 140 AML patients, 17 were FLT3+, 23 were NPM1+, and 14 were FLT3+NPM1+. Next, we investigated the expression of single markers on blasts and found that the medians of both CD123 and CLEC12A were significantly higher for FLT3+ patients compared to wild type patients (RR 2.48, $P < 0.001$ (*), and RR 2.19*, respectively). Also, the median CLEC12A expression was increased in NPM1+ and FLT3+NPM1+ (RR 2.00*, and RR 1.55*, respectively).

Conclusion: Our results indicate that the heterogeneous level of CLEC12A and CD123 expression in AML may in part be explained by molecular aberrations in FLT3 and NPM1.

CH.60 Birgit Rasmussen

OLDER PEOPLE'S LIVED EXPERIENCES OF FACILITATORS AND BARRIERS FOR BEING ACTIVE AFTER HIP FRACTURE: A PHENOMENOLOGICAL HERMENEUTIC STUDY

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Background: Being physically active is vital in old age. However, after hip fracture (HF), older people seem to live a sedentary life. Pain, limited mobility and fear of falling being prevalent after HF are found to be barriers to activity; while the expectation of a well-being experience during activity can be motivating. Older people's own perspectives on being active after HF are not well understood. In this study, a framework of well-being is used to clarify older people's experiences at an existential level.

Aim: To explore facilitators and barriers for being active after HF.

Method: Semi-structured, individual interviews are conducted at 2 weeks and 6 months after discharge after HF. A hermeneutical interpretation of moving between the parts and the wholes of the transcribed interviews, while considering own pre-understandings and using a five-step procedure focusing on meaning is applied.

Findings: Data are still being interpreted. Three themes seem to be emerging, describing experiences of being challenged and supported in activities that are meaningful. "Inner dialogue" describes inner driving forces, inner limitations, and rhythms & routines. "Struggling and striving" describes the activity when being with others and handling complications. "Surroundings" describes aspects of the health care system, assistive devices and spatial components.

Conclusion: The findings underline that having a feeling of meaningfulness in activity is fundamental when striving to be active after HF. For interventions to be supportive of older people's possibilities for being active in the first six months after a HF, their struggles and well-being experiences should be taken into consideration.

- CH.61 Morten Overgaard THE PSEUDO-OBSERVATION METHOD BASED ON INVERSE PROBABILITY WEIGHTING
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The pseudo-observation method allows for regression analysis of a survival outcome that is not always observed due to censoring from, for instance, study dropouts. However, in its standard form, the method is known to rely on a strict assumption on the censoring mechanism, and it is known that violation of that assumption may lead to bias. We study how the pseudo-observation method based on more intricate inverse probability weighting estimators avoids bias under a milder assumption on the censoring mechanism.
- CH.62 Steffan Tábori Jensen LOW DISLOCATION RATE OF SATURNE® DUAL-MOBILITY THA AFTER MEDIAL FEMORAL NECK FRACTURE. A RETROSPECTIVE STUDY OF 966 HIPS WITH A MINIMUM 1.6-YEAR FOLLOW-UP
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Background: Displaced medial femoral neck fracture (FNF) may be treated with primary arthroplasty. However, dislocation is a serious complication. Large head-size dual-mobility (DM) total hip systems may increase range of motion to impingement and may thereby improve stability compared with conventional hip implants.
Purpose: To investigate the dislocation and revision rate of primary DM cups in patients with acute FNF.
Materials and methods: Since 2005 we used DM articulations as standard treatment for displaced medial FNF. 966 consecutive patients (676 women) at a mean age of 80.5 years (range: 42-104) were operated by residents and consultants by use of the posterior-lateral approach (PLA). We evaluated all patient files and X-ray archive for dislocations and revisions until death of the patient or August 2017. The Danish National Patient Register was checked for additional complications. Educational level of the surgeon was noted and cup position was measured.
Results: At a minimum of 1.6 year follow-up, 48 (5%) experienced dislocation and 8 (0.8%) cup revisions. The 30-day mortality was 9.2%, and 533 patients (55.2%) had died at the time of follow-up. The mean duration until first dislocation was 21 days (range: 1-63), and the number was between 1 and 4. Educational level of the surgeon was unrelated to the dislocation risk (p=0.52) and the revision risk (p=0.71). 225 stems (23%) and 551 cups (57%) were fixed with cementless technique. Cementless stem fixation was associated with higher dislocation risk (p=0.04) and higher rate of stem complications (p=0.002).
Conclusion: DM hip system inserted via a PLA results in a low dislocation and revision rate, regardless of the surgeon's educational level.

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Introduction: Juvenile Idiopathic Arthritis (JIA) is a hyperonym of childhood arthritis with onset before the age of 16 years that persists for more than 6 weeks and with unknown origin. For the physician and the patients, it is crucial to know the individual prognosis of the disease, preferably as early as possible to prevent a poor outcome. The question remains how well these children perform during long-term follow-up.

Objective: The primary aim of this study was to evaluate if remission is sustainable from 8 to 15 years after disease onset. Secondary aims included the clinical and disease activity features 15 years after JIA onset.

Methods: 509 consecutive cases of JIA with disease onset in 1997 to 2000 from defined geographical areas in Denmark, Norway, Sweden and Finland were prospectively included in a population-based 15-year follow-up study.

Results: Among 423 participants included, 28% still had an active disease 17.46 years \pm 4.4 after onset, 9% were in remission on medication and 44% were in remission off medication. This is consistent with the 8-year follow-up data. 9% was treated with DMARDs, 20% with biologics and 10% with a combination of DMARDs and biologics at last follow-up. VASpain was reported to be low with a median of 1 (iqr 0-4), and the disease activity score Jadas71 was 1 (iqr 0-4.5) 15 years after disease onset.

Conclusion: A significant proportion of the current JIA patients do still not reach remission even though treated in the biologic era. The data are consistent with the 8-year follow-up of the same cohort, which indicates that JIA is a chronic disease even 15 years after onset.

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