

Annual Report 2018

Academic Activities

Division of Surgery Akershus University Hospital

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ANNUAL REPORT ON ACADEMIC ACTIVITIES IN 2018

Division of Surgery, Akershus University Hospital

This is the eight annual report on research activities in the Surgical Division (SD).

We got a new leader for SD in May, Anne Karin Lindahl. She is personally active in research and established a new research group, Research group for quality and patient safety. She has also attended the committee meetings and signaled the importance of research in a university hospital.

One of our problems has been the lack of space for research in the main building at Ahus. Our new division leader made it possible to get a section from Dr. Kobro's road to use for researchers in SD. During the last part of 2018 the section was renovated and in 2019 we have available 12 desks to our researchers and in addition a nice meeting room.

The research outpatient unit has been under development during 2018 and I was a member in a committee that delivered a statement to the leader board in August. It is important to get this resource in Ahus. We are the only university hospital without this kind of service.

Ahus also got a new research leader, Helge Røsjø, in 2018. Helge says that our success is his success and that there are three main issues to gain good research: good ideas, good teams and good infrastructure/resources for research. SD definitively has the two first and some problems with the last. Our problem is external financing. SD has not had great success in external funding and that is why external funding and better applications has been the theme of the year for the SD research groups. Helge Røsjø has launched grants@ahus.no, a support to funding applications that SD researchers have started to use actively. We also organized an application seminar in November to improve the quality of our applications. Now it will be exciting to see the results.

We had a good year in terms of publication based funding. Our 71 publications in 2017 resulted in 597.742 kr to fund our research in 2018. A lot of this success was due to successful research activity in the Gastrointestinal surgery research group. This funding has been an important support for our start

phase projects. This is a very good achievement compared with the number of academic posts and amount external funding in SD. We are very efficient with the resources we have available and it means that our researchers have done a lot of good work.

We had 58 publications in 2018 that generated publication based funding for 2019. This is substantially less than in 2016 and 2017. The reason is partly normal annual variation in publications, but this is also an alert to be taken into consideration and look for possible problems in research activity.

We had three academic dissertations in 2018, and this is a reason to celebrate. This activity illustrates the high number of publications in 2016 and 2017. We had two dissertations in the Gastrointenstinal surgery research group, Marie Louise Sunde and Johannes Schultz, and one in the ENT research group, Peder Aabel. Congratulations to candidates, supervisors and research groups.

We launched our first PhD seminar in January 2018. It was a one and a half day event, and was a success. We had Editor-in-Chief Arne Anderson from Uppsala Medical Journal as a guest speaker. He was available for the whole seminar with valuable remarks to our researchers. All PhD candidates got their project presented with good discussion. As a result, we decided to have a PhD seminar annually.

We had a seminar to improve the quality for our funding approvals in November. This was also the kick off for using the invaluable grants@ahus.no. We evaluated two of our applications that did not have success and got a lot of valuable information and instructions. A very clear conclusion from the seminar was that applying for external funding requires professionalism, and hard work. It has to be done with long-perspective planning and it cannot be done half-hearted during evenings and weekends some weeks before deadlines. It is also teamwork, where we can, and should, help each other. We will never win without enough resources to produce really good applications.

In house PhD projects is the most important source that brings resources and visibility to Ahus research. An important resource needed to start and bring to completion a PhD project is the supervisor; our senior consultants. This can be taken for granted and left without focus. I think we should aim attention at involving new supervisors with enough time and resources. Actually, everyone in the postdoc phase

should have the possibility to supervise new projects. We need more supervisors and more PhD projects.

Again, I thank all our researchers for your successful and hard work in 2018. Good luck in 2019.



On behalf of the research committee and myself,

Juha Silvola, Associate professorDepartment of ENT, Akershus University Hospital Institute of Clinical Medicine, University of Oslo

Research Committee 2018

Head

Surgical Division
Dept of Anaesthesiology
Dept of Breast and Endocrine Surgery
Dept of ENT
Dept of GI Surgery
The Operating Department
Dept of Urology
Dept of Vascular and Thoracic Surgery
Palliative Medicine
Head of Division of Surgery-Campus Ahus
Research coordinators

Juha Silvola

Anne Karin Lindahl Vegard Dahl, Signe Søvik

Magnus von Unge Ola Røkke, Tom Øresland, Dejan Ignjatovic Lise Smith Jacobsen Stig Müller Jarlis Wesche Olav Magnus Fredheim Asbjørn Årøen Inger Helene Nådland and Merete Helgeland



From left: Jarlis Wesche, Merete Helgeland, Vegard Dahl, Juha Silvola, Asbjørn Årøen, Stig Müller, Tom Øresland, Olav Magnus Fredheim, Ola Røkke, Lise Smith Jacobsen.

Members are elected for a three-year period. The committee's tasks are to:

- keep track of research within the Division of Surgery
- follow-up and support research projects
- facilitate practicalities related to research
- provide support in grant applications
- keep track on university activities
- promote interdisciplinary research
- initiate common research meetings within the Division of Surgery

Overview of researchers at the University of Oslo/Campus Ahus

Department	University positions	Ph.D. Research fellows
Anaesthesiology	3	1
Breast and Endocrine Surgery	0	2
ENT	4	2
GI Surgery	4	6
Urology	1	0
Vascular and Thoracic Surgery	1	2
Total	13	13

Summary of Research Activity

Publications (peer reviewed) and dissertations in the Division of Surgery

Year	Publications	Dissertations
2014	24	1
2015	31	0
2016	62	1
2017	71	1
2018	58	3



ENT Research Group

Head: Professor Magnus von Unge

University employees:	Research fellows:
Professor II Magnus von Unge	Peder Aabel
Associate Professor Gregor Bachmann-Harildstad	Kjell-Arild Danielsen
Associate Professor Juha Silvola	Øystein Eskeland
Senior lecturer Erik S Lie	Thorarinn Olafsson
Senior lecturer Harald Hrubos-Strøm	Post Doc Harald Hrubos-Strøm
	Post Doc Ingebjørg Skrindo
	Post Doc Andreas Steinsvik
	Post Doc Marit Austeng

The ENT Department has three major research foci: the diagnostics and treatment of otitis media and obstructive sleep apnoea, and the diagnostics of rhinological diseases.

Treatments for otitis media have not seen major changes since the 1950s. In chronic otitis media, structural defects - particularly perforations of the tympanic membrane - cause hearing impairment and chronic infections and are still treated with surgery. Our research aims to engineer new autologous tissue, either in vitro for subsequent implantation or directly in vivo. We have identified regenerative centers in the human tympanic membrane and are currently optimizing cultivation methods and assays to assess the properties of cultivated cells, as well as trying to develop in vitro-based activation of these centers. Tympanic stem cells investigations are partly done in close collaboration with the Ear Science Institute Australia.

Since 2004, the ENT Department on Sleep (ENT Sleep) has performed >25,000 clinical sleep studies, most of which have been performed with a sound-based polygraphic device (ApneaGraph AG 200) validated only by a limited clinical sample against the gold standard, polysomnography. Akershus

University Hospital and the manufacturer of ApneaGraph AG 200 have received funding to validate a new version of the device. As a result, the Akershus Sleep Apnoea Diagnostics and Treatment Evaluation (ASADaTE) was designed. The project consists of 276 patients referred to ENT Sleep with suspected sleep apnea.

Follow-up registrations in the treatment evaluation part of the ASADaTE begins in 2019. The study population is one of two populations forming the Akershus Sleep Apnea Personalized medicine (ASAP) cohorts. Baseline examinations in the other, population based cohort were conducted between 2006 to 2008 in collaboration with the University of Oslo and Division of Medicine. The ASAP cohorts are the main, Norwegian contribution to the Nordic project "Nord Sleep" that is funded through Nordforsk (www.nordforsk.no). Overall aims of the project is to evaluate novel sensors, to optimize risk estimates associated with sleep apnea and to develop personalized risk communication models.

Finally, ENT Sleep has included participants in the regional quality register for sleep disorders since October 2017. The register is coordinated by Professor Bjørn Bjorvatn at Haukeland University Hospital.

In rhinology, the main focus is on endotype and phenotype of chronic rhinosinusitis. Recent literature has indicated that biofilm plays a crucial role in the treatment of chronic rhinosinusitis. We therefore aim to describe correlations between chronic rhinosinusitis and biofilm, anatomical patterns and to investigate for correlations between the presence of biofilm and PROM's clinical outcomes and the correlation with lower airway symptoms at 6 months postoperatively.

The second focus will be on the validation of a quality of life instrument SNOT-22. A quality control database on the quality of life and on the outcome of nasal function after nasal septal surgery was established.

The third project is on the evaluation of objective assessments of the nasal airway. The aim is to calculate possible correlations between objective and subjective parameters for nasal obstruction. Peak nasal inspiratory flow as objective parameter and nasal obstruction visual analogue scale as well as SNOT-22 will be performed in a large cohort both pre- and post-surgery. A third focus is planned on a study for the emergency treatment of complicated nose bleeds.

Dissertation



Peder AabelExploring the Molecular Phenotype and Specificity of Cultured Human Tympanic Membrane Keratinocytes

Main supervisor: Magnus von Unge Dissertation: November 16, 2018

As many as 200 million people worldwide suffer from defects in the tympanic membrane that causes draining, infections and hearing loss. A more thorough understanding of the specificity of the epidermal keratinocytes of the tympanic membrane is necessary for targeting future research on finding new and more effective treatment modalities for perforations.

The aim of the thesis is to describe the isolation of cells from the tympanic membrane and create a molecular profile or fingerprint of the tympanic membrane skin cells. Also, the authors investigated aspects of storing cultured skin cells for the purpose of transplantation.

In microarrays of cultured cells several highly expressed genes involved in migration were identified in the tympanic membrane cells. An assay measuring the migration of the cells showed that there are functional differences between tympanic membrane and ordinary skin cells.

Further investigations of microRNA arrays and proteomics analyses showed a similar preponderance of molecules involved in migration and actomyosin structure organisation.

The loss of site specific stem cells in the tympanic membrane is a plausible explanation to surgery resistant perforations. This provides a rationale for cell treatment. When cells are cultured for transplantation storage upon delivery to the patient is very important. In a study of skin cells stored at a span of storage temperatures between 4°C and 37°C, cells showed the best viability at 24°C. Cells stored at 12°C to 16°C showed the best preserved morphology. Storage at 12°C to 24°C was far superior to 4°C that has traditionally been chosen for storage to ensure low cellular metabolism. Low metabolism had the cost of great loss of viable cells.

Cultured tympanic membrane keratinocytes can provide a new treatment option and make a useful in vitro model for studying the molecular aspects of normal homeostasis and treatment of perforations and other pathologies.

Publications (peer reviewed)

Berling Holm K, Bornefalk-Hermansson A, Knutsson J, **von Unge M**. Surgery for Chronic Otitis Media Causes Greater Taste Disturbance Than Surgery for Otosclerosis. Otol Neurotol. 2019 Jan;40(1):e32-e39.

Bousquet J et al. MASK study group (including **Skrindo I**). MASK 2017: ARIA digitally-enabled, integrated, person-centered care for rhinitis and asthma multimorbidity using real-world-evidence. Clin Transl Allergy. 2018 Oct 25;8:45.

Bousquet J et al. Mobile Airways Sentinel Network (MASK) Study Group (including **Skrindo I**). Allergic Rhinitis and its Impact on Asthma (ARIA) Phase 4 (2018): Change management in allergic rhinitis and asthma multimorbidity using mobile technology. J Allergy Clin Immunol. 2018 Sep 29. Epub ahead of print.

Caspersen NF, Røsjø H, Flyvbjerg A, Bjerre M, Randby A, **Hrubos-Strøm H**, Omland T, Einvik G. The association between circulating adiponectin levels, lung function and adiposity in subjects from the general population; data from the Akershus Sleep Apnea Project. BMC Pulm Med. 2018 Apr 2;18(1):54.

Falkenberg-Jensen B, Hopp E, Jablonski GE, Pripp AH, **Silvola JT**. The cartilaginous Eustachian tube: Reliable CT measurement and impact of the length. Am J Otolaryngol. 2018 Jul - Aug;39(4):436-440.

Hessen-Söderman I, Knutsson J, Priwin C, **von Unge M**. Vilken typ av ventilationsrör ska man välja? Svensk ÖNH-tidskrift 2018;2(2). Svensk ÖNH-tidskrift. 26(2):16.

Knutsson J, Priwin C, Hessén-Söderman AC, Rosenblad A, **von Unge M**. A randomized study of four different types of tympanostomy ventilation tubes - Full-term follow-up. Int J Pediatr Otorhinolaryngol. 2018 Apr;107:140-144.

Liew LJ, Chen LQ, Wang AY, **von Unge M**, Atlas MD, Dilley RJ. Tympanic Membrane Derived Stem Cell-Like Cultures for Tissue Regeneration. Stem Cells Dev. 2018 May 15;27(10):649-657.

Luukkainen V, Kivekäs I, **Silvola J**, Jero J, Sinkkonen ST. Balloon Eustachian Tuboplasty: Systematic Review of Long-term Outcomes and Proposed Indications. J Int Adv Otol. 2018 Apr;14(1):112-126.

Lødrup Carlsen et al. (including **Skrindo I** in study group). Preventing Atopic Dermatitis and ALLergies in Children-the PreventADALL study. Allergy. 2018 Oct;73(10):2063-2070.

Menditto E et al. MASK group (including **Skrindo I**). Adherence to treatment in allergic rhinitis using mobile technology. The mask study. Clin Exp Allergy. 2018 Dec 31. Epub ahead of print.

Niklasson A, Gladiné K, Rönnblom A, **von Unge M**, Dirckx J, Tano K. An Optimal Partial Ossicular Prosthesis Should Connect Both to the Tympanic Membrane and Malleus: A Temporal Bone Study Using Laser Doppler Vibrometry. Otol Neurotol. 2018 Mar;39(3):333-339.

Sepehri E, **von Unge M**. Congenital Mastoidal Cholesteatoma in an 87-Year-Old Woman Treated by Watchful Waiting. OTO Open. 2018 Apr 2;2(2):2473974X18765700.

Vogt K, **Bachmann-Harildstad G**, Lintermann A, Nechyporenko A, Peters F, Wernecke KD. The new agreement of the international RIGA consensus conference on nasal airway function tests. Rhinology. 2018 Jun 1;56(2):133-143.

Värendh M, Andersson M, Björnsdóttir E, Arnardóttir ES, Gislason T, Pack AI, **Hrubos-Strøm H**, Johannisson A, Juliusson S. PAP treatment in patients with OSA does not induce long-term nasal obstruction. J Sleep Res. 2018 Sep 28:e12768. Epub ahead of print.

Aabel P, Utheim TP, Olstad OK, Rask-Andersen H, Dilley RJ, **von Unge M**. Transcription and microRNA profiling of cultured human tympanic membrane epidermal keratinocytes. J Assoc Res Otolaryngol. 2018 Jun;19(3):243-260.

Abstracts and posters

Olafsson TA, Bachmann-Harildstad G. The pneumatized nasal septum – reviewing a century's worth of sporadic reporting. 27th Congress of the European Rhinologic Society, London, April 22-26.

Gerl JMA, Bachmann-Harildstad G, Lie ES. A retrospecitive study of infections and perforations after nasal septoplasty. 27th Congress of the European Rhinologic Society, London, April 22-26.

Swift A, **Bachmann-Harildstad G**, Schlosser R, Battaglia P, Soyka M. CSF-leaks, roundtable. 27th Congress of the European Rhinologic Society, London, April 22-26.

Niklasson A, Rönnblom, A, Tano K, Gladiné K, Dirckx J, **von Unge M**. An Optimal Partial Ossicular Prosthesis Should Connect Both to the Tympanic Membrane and Malleus. A Temporal Bone Study Using Laser Doppler Vibrometry. 8th International Symposium on Middle Ear Mechanics in Research and Otosurgery, Shanghai, China, July 5-7.

von Unge M, Wales J, Gladiné K, Van de Heyning P, Topsakal V, **Silvola J**, Dirckx J. Minimally Invasive Intra-operative Laser Vibrometry (MIVIB) with a Floating Mass Transducer - A New Method for Objective Evaluation of the Middle Ear Function. 8th International Symposium on Middle Ear Mechanics in Research and Otosurgery, Shanghai, China, July 5-7.

Gladiné K, Wales J, Van de Heyning P, Topsakal V, **von Unge M**, Dirckx J. Minimally Invasive Laser Vibrometry (MIVIB) Using a Floating Mass Transducer: Technical Aspects. 8th International Symposium on Middle Ear Mechanics in Research and Otosurgery, Shanghai, China, July 5-7.

von Unge M. Komplikasjoner til ventilasjonsrör: skillnad mellan olika typer. The Norwegian Society of Otorhinolaryngology, Head & Neck Surgery, Annual meeting, Oslo, October 25-27.

Moene CA, Hauge MB, Bachmann-Harildstad G. Kan nesekateter med varmt vann brukes for behandling av epistaxis? The Norwegian Society of Otorhinolaryngology, Head & Neck Surgery, Annual meeting, Oslo, October 25-27.

Steinsvik EAS, Damhaug CA, Lie ES, Hellings W, Seys SF. MySinusitisCoach: behandlingsstøtte til pasienter med kronisk rhinosinusitt ved hjelp av mobilteknologi. The Norwegian Society of Otorhinolaryngology, Head & Neck Surgery, Annual meeting, Oslo, October 25-27.

Gupta Jacobsen G. Kasuistikk – Pasient med dårlig lukt fra nesen, septumperforasjon og manglende luktesans. The Norwegian Society of Otorhinolaryngology, Head & Neck Surgery, Annual meeting, Oslo, October 25-27.

Hrubos-Strøm H, Einvik G, Mitic S, Fiske E, **Olafsson T**, Bjorvatn B. Apné Hypopné index og selvrapportert søvnighet hos henviste pasienter før og etter ny førerkortforskrift. The Norwegian Society of Otorhinolaryngology, Head & Neck Surgery, Annual meeting, Oslo, October 25-27.

Butt J, Mitic S, Skrindo I. Kasuistikkserie – «Gutta fra Kløfta». The Norwegian Society of Otorhinolaryngology, Head & Neck Surgery, Annual meeting, Oslo, October 25-27.

Academic assignments

Opponent/member of adjudication committee

Opponent on the thesis: Functional-structural reorganization of the neuronal network for auditory perception in subjects with unilateral hearing loss. Peder O. Laugen Heggdal, University of Bergen, August 27. **Silvola J**.

Opponent on the thesis: Hearing in musicians. Carl Christian Lein Störmer, University of Tromsø, December 14. **Silvola J**.

Opponent on the thesis: Mechanics of a single ossicular ear: optical measurements and finite elementmodeling of the avian middle ear. Pieter Muyshond, University of Antwerp, Belgium, April 18. **von Unge M**.

Opponent on the thesis: Middle ear pressure regulation. Simona Paraduro, Aalborg University, Denmark, September 7. **von Unge M**.

Opponent at mid-term evaluation

Johan Steineger, mid-term evaluation, Oslo University Hospital, Rikshospitalet, Oslo, August 30. **Bachmann-Harildstad G**.

Jakob Skalleberg, mid-term evaluation, Oslo University Hospital, Rikshospitalet, Oslo, February 6. **von Unge M**.

Arranged meetings

XVI Skandinavisk Ørekirurgisk Møte. Geilo, March 8-10. Silvola J.

Other academic activities

Main supervisor for Torstein Grønseth, University of Oslo. Silvola J.

Main supervisor for Arne Rødvik, University of Oslo. Silvola J.

Main supervisor for Peder Aabel in his thesis «Exploring the Molecular Phenotype and Specificity of Cultured Human Tympanic Membrane Keratinocytes», University of Oslo, November 16. **von Unge M**.

Main supervisor for Andreas Forsmark, University of Oslo. von Unge M.

Supervisor for Kjell Arild Danielsen, University of Oslo. Bachmann-Harildstad G.

Supervisor for Øystein Eskeland, University of Oslo. **Bachmann-Harildstad G**.

Supervisors for Thorarinn Olafsson, University of Oslo. Hrubos-Strøm H, Bachmann-Harildstad G,

Steinsvik A.

Supervisor for Maria Värendh in her thesis «Nasal patency and sleep –Prevalence of obstruction, sleep disturbances, quality of life, and treatment», University of Lund, May 18. **Hrubos-Strøm H**.

Supervisor for Benedikte Falkenberg-Jensen, University of Oslo. Silvola J.

Supervisor for Lena Pöyhönen, University of Tampere, Finland. **Silvola J**.

Supervisor for Torstein Grønseth, University of Oslo. von Unge M.

Supervisor for Anders Niklasson, Umeå University, Sweden. von Unge M.

Reviewer for The International Journal of Pediatric Otorhinolaryngology. von Unge M.

Reviewer for Acta Otolaryngol, PlosOne, Scientific Reports/Nature, J Int Advances Otology,

Tissue Engineering. von Unge M.

Conference session Moderator. The session «Middle ear Pathology and Diagnostics»,

8th International Symposium on Middle Ear Mechanics in Research and Otosurgery, Shanghai, China, July 5-7. **von Unge M**.

Memberships

Editorial board member for Rhinology. Bachmann-Harildstad G.

Member of International Rhinologic Society Standardization Committee on Objective Assessment of the Nasal Airway – ISCOANA. European Rhinologic Society, London, April 22-26. **Bachmann-Harildstad G**.

Member of Deutsche Ärztegesellschaft für Akupunktur. Bachmann-Harildstad G.

Assigned member of the board and treasurer of the Norwegian Society for Sleep Research and Sleep Medicine. **Hrubos-Strøm H**.

Member of European Sleep Research Association. Hrubos-Strøm H.

Wice chairman NFAI (Norsk forening for allergologi og immunpatologi). Skrindo I.

Member of EAACI (Europen Academy of Allergology and Clinical Immunology). Skrindo I.

Editorial board member for The Journal of International Advanced Otology. von Unge M.

Member of the Acta Otolaryngology Society. von Unge M.

Member of the Advisory Board for Journal of International Advanced Otology. von Unge M.

Ongoing research projects

The cultivation on of epidermal keratinocytes for improved treatment of tympanic membrane perforations

Peder Aabel M.D., Tor Paaske Utheim M.D. Ph.D. (Oslo University Hospital), Torstein Lyberg M.D. Ph.D. (Oslo University Hospital), Jon Roger Eidet M.D. Ph.D., Helge Rask-Anderssen Professor M.D. Ph.D. (University of Uppsala), Magnus von Unge Professor M.D. Ph.D.

Background: Permanent tympanic membrane perforations cause ear draining and hearing impairment. Though the treatment modalities have not evolved in nearly a century, tissue engineering has recently become possible and may become a better modality with cell-based therapy in certain patient groups. However, a more thorough understanding of the normal regeneration of the eardrum is necessary. **Aim:** To study cultivated stem cells from human tympanic membranes and assess their phenotype, genetic, proteomics and functional characteristics.

Methods: Cells from the skin and eardrum are grown in cell cultures in optimized growth conditions. The cultured tissue is examined for morphology, phenotypes, viability, and a variety of gene, protein and enzyme expression.

Status: Data on optimal temperature intervals for keratinocyte cultivation were published. A manuscript on RNA characterization data highlighting the genes coding for migration is accepted for publication in JARO. Data on the down stream proteomics with association to migration, as well as corresponding functional assessment (scratch test) are being analyzed, in manuscript.

The Constitutive Migration of the Tympanic Keratinocytes

Andreas Hassel Forsmark, M.D., Juha Silvola Associate Professor M.D. Ph.D., Hilde Nilsen Professor (EpiGen), Magnus von Unge Professor M.D. Ph.D., Peder Aabel M.D.

Background: Permanent tympanic membrane perforations cause ear draining and hearing impairment. The TM keratinocytes migration is critical in reparation of the perforations. By studying the migrational properties on a macroscopic and molecular level we hope to obtain a better understanding of their function and subsequently help develop a less invasive treatment.

Aim: Characterize the tympanic membrane (TM) keratinocyte's migration in terms of speed, linearity and collective migration behavior. Demonstrate the effectors and upstream regulatory molecular mechanisms responsible for the constitutive migration of the TM keratinocytes. Explore how growth substrate and bioactive supplements influence the migration of cells TM keratinocytes.

Methods: Tympanic membrane cells and control cells from skin will be cultured in vitro, and migration will be assessed using live imaging facilities at EpiGen at Campus Ahus. By knocking in/out suspected genes and using different substrates their effect on migration will be evaluated.

Status: The project has obtained approval from the Regional Ethics Committee. The Ph.D.-student, Andreas Forsmark, has set up the live imaging equipment and started training in the cell lab. He has also enrolled in the Ph.D.-program at the University of Oslo and started on courses.

Assessment of the epithelial regeneration centers in the human tympanic membrane in normal and activated conditions

Elnaz Sepehri M.D. (Karolinska Institute and University of Oslo), Peder Aabel M.D., P.O. Eriksson M.D. Ph.D. (University of Uppsala), Magnus von Unge Professor M.D. Ph.D.

Background: This is a structural and functional study of the regeneration centers in the epithelium of the human tympanic membrane. Please see the background in the study description above.

Aim: To create a basis of knowledge for tissue engineering.

Methods: Fresh human material and immunohistochemical and ultra structural methods are used to identify regeneration centers and assess their activation patterns in response to experimental trauma. **Status:** Manuscript showing early cellular signs of activation in the tympanic membrane epithelium is published. The project is transferred to EpiGen, Akershus University Hospital.

Laser-Doppler vibrometry: Intra-operative measurement of hearing bone mobility, development of a minimally invasive intraoperative vibrometry method (MIVIB)

Jeremy Wales, M.D. Ph.D. (Karolinska University Hospital), Juha Silvola Associate Professor M.D. Ph.D., Joris Dirckx Professor Ph.D. (University of Antwerp), Magnus von Unge Professor M.D. Ph.D.

Background: Intra-operative assessment of hearing ossicle mobility in a partial fixation situation may help to direct the surgeon in choosing the most favourable technical solution in regards to the hearing outcome of the surgery.

Aim: To develop an intra-operative device to measure hearing bone mobility.

Methods: A laser-Doppler vibrometry method was evaluated in animal skulls and human temporal bones. An electromagnetic system was developed and software adjusted to simulate the outermost hearing bone (i.e., the hammer) with calibrated signals. The vibration velocity was measured at various points on the chain of hearing bones. Eventually was a floating mass transducer introduced into the model to replace the electromagnetic stimulation system.

Status: Final adjustments of the hardware and software are ongoing in the in vitro situation performed on fresh human temporal bones. A methods development has been successful in the design of a clinically practical vibrometry method. Recently published in Hearing Research. Results have been presented at several international conferences and in articles.

Fractures of the ossicular bones – an experimental study on the healing processes

Anders Niklasson M.D., Ph.D.-student, Krister Tano M.D. Ph.D., Magnus von Unge Professor M.D. Ph.D.

Background: Fractures on the handle of malleus are rare and therefore sometimes misjudged in the clinic. They cause hearing impairment. In experimental temporal bone studies different surgical repair methods were performed and the optimal surgical methods identified. Ossicular bone differs in some respects from common cortical bone and their repair processes are not clarified.

Aim: The healing process of experimental fractures on ossicles an an animal model will be assessed and compared with common type of bone.

Methods: Experimental fractures were made in sheep middle ear ossicles and on nasal and mandibular bone at the Veterinarian faculty of the University of Western Australia in Perth. The animals withstood the surgery well. After an observation time of 4 weeks biopsies were harvested from fracture sites. Assessment with micro-CT scan, optical coherence tomography and histology is ongoing. Then specific markers for repair processes in bone are studied in the specimen.

Status: Results under analysis. Dissertation scheduled for March 2019 at Umeå University, Sweden.

Staphylococcus biofilm in otitis media chronica

Torstein Grønseth M.D., Ph.D.-student, Magnus von Unge Professor M.D. Ph.D., Juha Silvola Associate Professor M.D. Ph.D.

Background: Biofilms can be the main source of recidivism for infections in otitis media chronica and cholesteatoma. These are often difficult to treat with systemic or even with local antimicrobial agents. This can lead to development of multiresistent bacterial strains. The two main bacteria are Staphylococcus aureus and Pseudomonas aeruginosa. The main research objective is St.aureus and three articles which will lead to academic dissertation.

Aim: To investigate different treatment methods against biofilm in otitis media chronica.

Methods: Growth of biofilm from otitis media chronica and to test other methods than antibiotics to eradicate biofilm.

Status: The first article is published, the second is submitted and the third will be completed in 2019.

Nonsense words as a hearing test for cochlear implanted adults and children

Arne Rødvik CI, Ph.D.-student, Ona Bøe Wie Professor (Institute for Special pedagogic, University of Oslo), Janne von Koss Torkildsen Associate Professor (Institute for Special pedagogic, University of Oslo), Juha Silvola Associate Professor M.D. Ph.D.

Background: Nonsense words are little used but very effective way to investigate hearing on the phoneme level.

Aim: The aim is to investigate how nonsense words can be used as a hearing measurement tool for pediatric and adult cochlear implanted patients. The goal is three articles that make the PhD thesis.

Methods: First article is a review and meta-analyze on nonsense words. The goal for the second article is to test nonsense words as a hearing test for adults. The goal for the third article is to test nonsense words as a hearing test for children.

Status: Review and meta-analyze article is published, adult article is submitted, and pediatric article is in the last phase of manuscript.

The distribution and prevalence of biofilm in chronic rhinosinusitis with or without polyposis nasi Kjell-Arild Danielsen M.D., Øystein Eskeland M.D., Katrin Fridrich M.D. Ph.D., Vivian Orszagh M.D., Gregor Bachmann-Harildstad M.D. Ph.D., Espen Burum-Auensen M.D. Ph.D.

Background: Since biofilm presents a relatively new explanatory model for chronic infectious diseases, its role in chronic rhinosinusitis is still unresolved.

Aim: To assess the correlation between the presence of biofilm in different types of chronic rhinosinusitis and signs of chronic inflammation in the nasal sinuses.

Methods: Biopsies were harvested and stored, thereafter studied with confocal microscopy. The findings were correlated with clinical symptom scores, follow-up data at 6 months, and histologic parameters for inflammation.

Status: The committee did not approve the written thesis. The candidate has a second chance to send in a revised thesis. A third paper has been published in the meantime.

Akershus Sleep Apnea Diagnostic and Treatment Evaluation (ASADaTE), diagnostic part

Thorarinn Olafsson M.D., Eivind Andreas S. Steinsvik M.D. Ph.D., Svetislav Mitic M.D., Gregor Bachmann-Harildstad Associated Professor M.D. Ph.D., Harald Hrubos-Strøm Associated Professor M.D. Ph.D.

Background: Diagnostic properties of the ApneaGraph Spiro have not been validated.

Aims: To compare diagnostic properties of «Apneagraph Spiro» with automatically and manually scored polysomnography. To explore differences in objective sleep registrations between patients with and without chronic rhinosinusitis.

Methods: Consecutive patients referred because of suspected OSA (male or female, aged 18–80 yrs) were eligible for inclusion. Eighty three patients have been examined by double sleep registration with polysomnography and Apneagraph Spiro. Polysomnography data have been scored by a rater blinded for patient characteristics. Chronic rhinosinusitis was assessed by the Sino Nasal Outcome Test (SNOT) 22 and clinical evaluation.

Status: Data acquisition completed for the diagnostic study, manuscripts are in progress.

Nord Sleep Akershus Sleep Apnea Personalized medicine (ASAP) cohorts

Svetislav Mitic M.D., Gunnar Einvik M.D. Ph.D., Anna Randby M.D. Ph.D., Pål Gulbrandsen Professor M.D. Ph.D., Toril Dammen Professor M.D. Ph.D., Harald Hrubos-Strøm Associated Professor M.D. Ph.D.

Background: There is a need for novel treatment methods for sleep onset insomnia, a disorder often co-morbid with sleep apnea. There is a potential value of sleep registrations in predicting continuous positive airway pressure (CPAP) adherence, cardiovascular events and sleepiness related traffic incidents. Shared decision making between doctors and patients with sleep apnea may increase treatment adherence with CPAP.

Aims: To conduct a feasibility study of a novel treatment method for sleep onset insomnia. To explore baseline sleep characteristics associated with cardiovascular events and traffic accidents. To assess the relation between shared decision making and CPAP adherence and to develop a personalized risk communication tool.

Methods: Participants with sleep onset insomnia will be invited to try a novel treatment device based on electroencephalographic neurofeedback. The materials consists of 535 persons included in the Akershus Sleep Apnea Project between 2006-2008 and a sample of 276 persons included in the Akershus Sleep Apnea Diagnostic and Treatment Evaluation between 2015-2016. A sub sample of the 100 first, consecutive persons with BMI >30 and AHI \geq 5 included in the latter were video filmed during the discharge consultation. Outcomes will be assessed after approximately 12-13 months and 4 years respectively. Independent variables will be explored with artificial intelligence.

Status: A PhD student and a research nurse will be employed. Data collection is coordinated in collaboration with the Division of medicine.

Thermal balloon treatment for epistaxis. A prospective, randomized interventional study in emergency hospital care

Lise Carine Moene Johansen M.D., Mats Hauge M.D., Juha Silvola Associated Professor M.D. Ph.D., Gregor Bachmann-Harildstad Associated Professor M.D. Ph.D.

Background: About 24.6 % of all emergency hospital admissions at an Ear-nose and throat (ENT) unit are related to acute epistaxis. The incidence has risen over the last 15 years.

Aim: To determine the lengths of hospital stay, the rate of invasive surgical interventions, the rate of RBC transfusions and the rate of re-admissions with hot water vs cold water nasal balloon as emergency treatment for posterior epistaxis.

Method: This prospective and controlled study will include adult patients admitted to hospital care because of posterior epistaxis. As randomized intervention hot water vs standard temperature nasal balloon emergency treatment is given.

Status: The regional ethical committee did not approve the study, further risk factors needs to be clarified.

PreventADALL: Is asthma or rhinitis in young children reduced in children subjected to primary prevention of atopic dermatitis and/or food allergy?

Anine Lie M.D. (Oslo University Hospital), Ingebjørg Skrindo M.D. Ph.D, Karin Lødrup Carlsen Professor M.D. Ph.D (Oslo University Hospital), Håvard O. Skjerven M.D. Ph.D. (Oslo University Hospital).

Background: The atopic march suggests that atopic dermatitis and/or sensitization to food allergens may lead to development of other allergic diseases in childhood.

Aim: To determine if asthma and rhinitis in pre-school children is reduced in children subjected to primary intervention of the two commonly earlies manifestations of allergic diseases; namely atopic dermatitis (AD) and food allergy.

Method: Data from the first three years of the children in the PreventADALL study will provide the basis for analyses.

Status: 36-months examinations ongoing.

Granted Funding

Project	Source	Amount
The Constitutive Migration of the Tympanic Membrane Keratinocytes	Akershus University Hospital Strategic Research grants	150,000 NOK
Magnus von Unge, Andreas Forsmark		
Total		150,000 NOK



Gastrointestinal Surgery Research Group

Head: Professor Ola Røkke

Department of GI surgery

University employees:	Research fellows:
Professor I Tom Øresland	Johannes Kurt Schultz
Professor II Ola Røkke	Marie Louise Sunde (resigned 2018)
Professor II Dejan Ignjatovic	Yngve Thorsen
Professor emeritus Arne Olav Bakka	Robin Gaupset
Lecturer Javier Luzon	Gurpreet Singh Banipal
	Yasir Malik

At the department of digestive surgery there are 45 doctors, fourteen have doctorial thesis at the end of 2018: Tom Øresland, Arne Bakka, Ola Røkke, Dejan Ignjatovic, Rolf Aamodt, Arne Færden, Nazir Naimy, Geir Arne Larsen, Marianne Merok, Lars Eftang, Odd Langbach, Lara Pasovic, Johannes Schultz, Marie Sunde.

We consider research as an important part of our clinical practice. Science should be a conscious part of the clinical work for all employees at our department. Doctors not directly involved in research programs should be aware of the importance of ongo-

ing project and contribute when possible. The plans for 2019 will be to continue to promote scientific work through regular discussions in clinical practice, regular meetings, attendance on scientific meetings and seminars, increase the efforts to obtain external financial resources, and initiation of PhD-projects, with a special focus on three subjects:

- 1) Cancer: colorectal, gastric, small bowel
- 2) Development of surgical techniques and virtual anatomic equipment
- 3) Pancreatic diseases, especially acute pancreatitis

Dissertation



Photo by Kristoffer Myhre

Marie Louise Sunde Studies on the ileal pouch-anal anastomosis Main supervisor: Arne E. Færden Dissertation: February 23, 2018

Ileal pouch-anal anastomosis (IPAA) is the treatment of choice for patients with ulcerative colitis in need of surgery. After having removed the colon and rectum, a pouch is constructed of the distal part of the small intestine and attached to the anal canal. The procedure is done to improve the patient's quality of life by maintaining an anal route of defecation. It is a technically demanding procedure, with a great variability in functional outcome. The reason for this variability is to a large extent unexplained.

The aim of the thesis was to investigate surgical, functional and sexual outcome after surgery, and to investigate the correlation between functional outcome and life quality, and functional outcome and sexual function. In addition, we wished to further examine well and poorly functioning patients to determine factors contributing to functional outcome.

All patients operated on between 2000-2013 (N=103) were interviewed regarding quality of life, sexual function and pouch function. The best and

worst functioning patients were further invited to undergo manovolumetric testing, pouch endoscopy and a pelvic MRI.

There were few complications and no pouch failures. The patients had similar quality of life and sexual function as the normal Norwegian population. We found poor pouch function to impair quality of life in all patients, and to impair sexual function in women. Well functioning pouches had a larger volume and shorter rectal cuff. Poor functioning patients had a higher incidence of histological inflammation, pouchitis and hand sewn anastomosis. There were no differences in MRI findings between the groups.

The thesis concludes that small improvements in function have an impact on the patient's quality of life, and that pouch function has a stronger correlation with sexual function in women compared to men. In this study volume is the most prominent predictor of functional outcome. The reason for variability in pouch volumes remains unexplained.

Dissertation



Johannes Kurt SchultzSurgical aspects of diverticular disease of the colon – a randomized controlled trial and a cohort study challenging traditional treatment

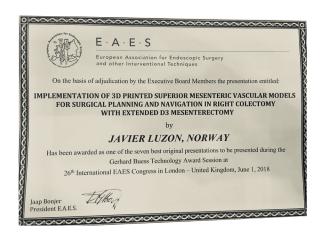
Main supervisor: Tom Øresland Dissertation: March 22, 2018

Diverticular disease of the colon is a common reason for hospitalization. At the beginning of the 19th century this condition was not yet described in surgical textbooks, nevertheless the British surgeon WHM Telling in 1917 found only one word to describe the treatment: surgery. Ever since, there has been a vivid debate among surgeons about how to prevent complications of diverticular disease and when and how to operate.

This thesis is based on two studies challenging mainstay treatments for diverticulitis. The randomized SCANDIV trial compared mini-invasive laparoscopic peritoneal lavage with conventional resection surgery of the diseased colon in perforated diverticulitis and purulent peritonitis. The 90-day results (Paper I) showed a higher reoperation rate for patients treated with laparoscopic lavage. At one-year follow-up (Paper II) the proportion of patients with a stoma was higher after resection. In conclusion laparoscopic lavage is an option for selected patients. The second study (Paper III) confirmed that antibiotic-free management is safe in uncomplicated diverticulitis. Complications are rare, and in contrast to previous beliefs, antibiotics do not prevent them.

Awards

Javier Luzon: Awarded as one of the seven best original oral presentation during the Gerhard Buess Technology award session during the 26th International congress of the EAES in London, May 30th - June 1st 2018.





Javier Luzon and Dejan Ignjatovic.

Javier Luzon: Awarded participation at the School of health innovation and entrepreneurship 2018 organized by the University of Oslo.

Javier Luzon: Was awarded entrance to the Business engineering surgical technologies (BEST) innovation course at the Institute of image-guided surgery in Strasbourg, France, August 2018.

Publications (peer reviewed)

Augestad KM, Keller DS, Bakaki PM, Rose J, Koroukian SM, **Øresland T**, Delaney CP. The impact of rectal cancer tumor height on recurrence rates and metastatic location: A competing risk analysis of a national database. Cancer Epidemiol. 2018 Apr;53:56-64.

Bemelman WA; S-ECCO collaborators (including **Øresland T**). Evolving Role of IBD Surgery. J Crohns Colitis. 2018 Jul 30;12(8):1005-1007.

Elfeki H, Thyø A, Nepogodiev D, Pinkney TD, White M, Laurberg S, Christensen P, Colostomy Impact Score study group (including **Øresland T**). Patient and healthcare professional perceptions of colostomy-related problems and their impact on quality of life following rectal cancer surgery. BJS Open. 2018 May 7;2(5):336-344.

Elstad JI, **Reiertsen O**. Hospitalisations during the final three years of life. Tidsskr Nor Laegeforen. 2018 May 28;138(9).

Francis NK, Curtis NJ, Conti JA, Foster JD, Bonjer HJ, Hanna GB; EAES committees (including **Ignjatovic D**). EAES classification of intraoperative adverse events in laparoscopic surgery. Surg Endosc. 2018 Sep;32(9):3822-3829.

Gaupset R, Nesgaard JM, **Kazaryan AM**, Stimec BV, Edwin B, **Ignjatovic D**. Introducing Anatomically Correct CT-Guided Laparoscopic Right Colectomy with D3 Anterior Posterior Extended Mesenterectomy: Initial Experience and Technical Pitfalls. J Laparoendosc Adv Surg Tech A. 2018 Oct;28(10):1174-1182.

Ignjatovic D, Stimec BV. Comment to Jejunal Diverticulitis Mimicking Small Bowel Perforation: Case Report and Review of the Literature. Chirurgia (Bucur). 2018 Sept-Oct;113(5):719.

Luzon JA, Andersen BT, Stimec BV, Fasel JHD, **Bakka AO**, **Kazaryan AM**, **Ignjatovic D**. Implementation of 3D printed superior mesenteric vascular models for surgical planning and/or navigation in right colectomy with extended D3 mesenterectomy: comparison of virtual and physical models to the anatomy found at surgery. Surg Endosc. Epub 2018 Jul 16.

Nesgaard JM, Stimec BV, Soulie P, Edwin B, **Bakka A**, **Ignjatovic D**. Defining minimal clearances for adequate lymphatic resection relevant to right colectomy for cancer: a post-mortem study. Surg Endosc. 2018 Sep;32(9):3806-3812.

Ommundsen N, Nesbakken A, Wyller TB, Skovlund E, **Bakka AO**, Jordhøy MS, Rostoft S. Post-discharge complications in frail older patients after surgery for colorectal cancer. Eur J Surg Oncol. 2018 Oct;44(10):1542-1547.

Ommundsen N, Wyller TB, Nesbakken A, **Bakka AO**, Jordhøy MS, Skovlund E, Rostoft S. Reply to Lawday et al. Colorectal Dis. 2018 Apr;20(4):350-351.

Sahakyan MA, Kleive D, Kazaryan AM, Aghayan DL, **Ignjatovic D**, Labori KJ, Røsok BI, Edwin B. Extended laparoscopic distal pancreatectomy for adenocarcinoma in the body and tail of the pancreas: a single-center experience. Langenbecks Arch Surg. Epub 2018 Nov 11.

Shulutko AM, Semikov VI, Osmanov EG, Gryaznov SE, Gorbacheva AV, Patalova AR, Mansurova GT, **Kazaryan AM**. Evaluation Criteria and Surgical Technique for Transoral Access to the Thyroid Gland: Experimental Study. J Invest Surg. 2018 Jan 25:1-7.

Stimec BV, Andersen BT, Benz SR, Fasel JHD, **Augestad KM**, **Ignjatovic D**. Retromesenteric course of the middle colic artery-challenges and pitfalls in D3 right colectomy for cancer. Int J Colorectal Dis. 2018 Jun;33(6):771-777.

Sunde ML, Negård A, **Øresland T**, Bakka N, Geitung JT, **Færden AE**. MRI defecography of the ileal pouch-anal anastomosis-contributes little to the understanding of functional outcome. Int J Colorectal Dis. 2018 May;33(5):609-617.

Willard CD, **Kjaestad E**, Stimec BV, Edwin B, **Ignjatovic D**; RCC Study Group. Preoperative anatomical road mapping reduces variability of operating time, estimated blood loss, and lymph node yield in right colectomy with extended D3 mesenterectomy for cancer. Int J Colorectal Dis. Epub 2018 Nov 1.

You K, Gachabayov M, Nesgaard JM, Bandovic J, **Ignjatovic D**, **Bakka A**, Bergamaschi R. D3 Extended Mesenterectomy in Right Colectomy for Cancer: A Cadaver Simulation Model. Surg Technol Int. 2018 Jun 1;32:109-113.

2015 European Society of Coloproctology Collaborating Group (including **Brun M**, **Helgeland M**, **Ignjatovic D**, **Yousefi P**, **Øresland T**). The impact of stapling technique and surgeon specialism on anastomotic failure after right-sided colorectal resection: an international multicentre, prospective audit. Colorectal Dis. Epub 2018 Jun 19.

2017 European Society of Coloproctology (ESCP) Collaborating Group (including **Banipal GS**, **Breuer R**, **Ignjatovic D**, **Moe TT**, **Øresland T**). Safety of primary anastomosis following emergency left sided colorectal resection: an international, multi-centre prospective audit. Colorectal Dis. 2018 Sep;20 Suppl 6:47-57.

2017 European Society of Coloproctology (ESCP) collaborating group (including **Banipal GS**, **Breuer R**, **Ignjatovic D**, **Moe TT**, **Øresland T**). Association of mechanical bowel preparation with oral antibiotics and anastomotic leak following left sided colorectal resection: an international, multi-centre, prospective audit. Colorectal Dis. 2018 Sep;20 Suppl 6:15-32.

2017 European Society of Coloproctology (ESCP) Collaborating Group (including **Banipal GS**, **Breuer R**, **Ignjatovic D**, **Moe TT**, **Øresland T**). The 2017 European Society of Coloproctology (ESCP) international snapshot audit of left colon, sigmoid and rectal resections - Executive Summary. Colorectal Dis. 2018 Sep;20 Suppl 6:13-14.

2017 European Society of Coloproctology (ESCP) collaborating group (including **Banipal GS**, **Breuer R**, **Ignjatovic D**, **Moe TT**, **Øresland T**). An international multicentre prospective audit of elective rectal cancer surgery; operative approach versus outcome, including transanal total mesorectal excision (TaTME). Colorectal Dis. 2018 Sep;20 Suppl 6:33-46.

2017 European Society of Coloproctology (ESCP) collaborating group (including **Banipal GS**, **Breuer R**, **Ignjatovic D**, **Moe TT**, **Øresland T**). Evaluating the incidence of pathological complete response in current international rectal cancer practice: the barriers to widespread safe deferral of surgery. Colorectal Dis. 2018 Sep;20 Suppl 6:58-68.

GlobalSurg Collaborative (including **Augestad KM**, **Banipal GS**, **Moe TT**, **Monteleone M**, **Schultz J**). Surgical site infection after gastrointestinal surgery in high-income, middle-income, and low-income countries: a prospective, international, multicentre cohort study. Lancet Infect Dis. 2018 May;18(5):516-525.

Abstracts and posters

Augestad KM, Butt K, **Ignjatovic D**. Video-basert coaching i kirurgisk utdanning. En systematisk litteraturgjennomgang og meta-analyse. The Norwegian Surgical Society Annual Meeting, Oslo, October 2018.

Furnes B, Saxe J, Forsmo HM, Dicko A, **Ignjatovic D**, Stimec B, Fawad H, Pfeffer F. Postoperative resultater og relativ overlevelse etter de 60 første åpne høyresidige hemikolektomier med D3 reseksjon og mesenterektomi. The Norwegian Surgical Society Annual Meeting, Oslo, October 2018.

Hoel AT, Staff S, Gjone H, **Teig CP**, Austrheim AI, Andersen MH, **Øresland T**, Bjørnland K. Transitional care for patients with anorectal malformations and Hirschsprung disease. The Norwegian Surgical Society Annual Meeting, Oslo, October 2018.

Lilleaas AH, Stimec BV, Edwin B, Thiis-Evensen E, **Bakka AO**, **Røkke O**, **Ignjatovic D**. Rollen til utvidet D3 mesenterektomi anterior/posterior til mesenterica superior-karene i pasienter med nevroendokrine svulster i tynntarmen. The Norwegian Surgical Society Annual Meeting, Oslo, October 2018.

Merok MA, **Naimy N**. Utprøving av FlXcision© for reseksjon av perianale fistler. The Norwegian Surgical Society Annual Meeting, Oslo, October 2018.

Næsgaard JM, Stimec BV, **Bakka AO**, Edwin B, **Ignjatovic D**. Evaluering av lymfadenektomi ved høyresidig hemicolektomi med D3-reseksjon for cancer. The Norwegian Surgical Society Annual Meeting, Oslo, October 2018.

Schultz J, **Merok MA**, **Lindam A**, **Øresland T**, **Naimy N**. Sakralnervemodulering ved analinkontinens: 1-års resultater av en singel senter kohort studie. The Norwegian Surgical Society Annual Meeting, Oslo, October 2018.

Vinge-Holmquist O, **Piroozmand K**, **Klakegg AB**, Arnø E, Sørensen V, **Langbach O**, **Røkke O**. Bedre resultater ved behandling av akutt pankreatitt siste 8 år. Gastrokirurgisk-, Billeddiagnostisk- og Intensivavdelingen, Ahus. The Norwegian Surgical Society Annual Meeting, Oslo, October 2018.

Wasmuth HH, Tranø G, **Færden AE**, **Øresland T**. Bekkenreservoarkirurgi i Norge. The Norwegian Surgical Society Annual Meeting, Oslo, October 2018.

Academic assignments

Opponent/member of adjudication committee

Opponent on the thesis: Towards a more individualised treatment of patients with gastrointestinal stromal tumour. Ivar Hompland, Oslo University Hospital, October 26. **Røkke O**.

Opponent on the thesis: Follow-up and survivorship after colorectal cancer. Ida Hovdenak Jacobsen, Aarhus University, Århus, September 7. **Øresland T**.

Invited lecturer

Minimalinvasiv kolorektalkirurgi - for pasientens eller kirurgens beste? Svenska Gastro dagarna, Falun, May 17. **Gaupset R**.

D3-studien. Vestlandske Gastroforum (VGF) høstmøte, September 22. Gaupset R.

Intra- vs ekstrakorporeal anastomose ved colonkirurgi. Ethicon kveldssymposium, October 24. Gaupset R.

Hiatuskirurgi – nett eller ikke nett? The Norwegian Surgical Society Annual Meeting, Oslo, October 26. **Gaupset R**.

"Future Vision" 3D navigation in colon cancer surgery at Ahus. The Norwegian society of thoraco-laparoscopic surgery NTLF 25 years anniversary, Drammen, May 2018. **Luzon J**.

Personalized colon cancer surgery with anatomic holographic images as an innovative visual tool for surgeons. EHiN 2018 (E-Health in Norway), Oslo, November 8. **Luzon J**.

Translation and application of condition-specific HRQoL questionaires (PFDI-20 and PFIQ-7) for women with pelvic organ prolapse and pelvic floor dysfunction in the Norwegian context. The Norwegian Incontinence and Pelvic Floor Dysfunction Research Seminar, Gardemoen, June 7. **Teig CP**.

IBD surgery, past, present and future. Norsk Gastroenterologisk årsmøte, Lillehammer, January 26-27. **Øresland T**.

S-ECCO postgraduate course, moderator. Vienna, February 15. Øresland T.

IOIBD (International org. for the study of IBD) working party on outcome measures. Participant. Rio de Janeiro, March 15-18. **Øresland T**.

Is there still a role for the continent ileostomy? The 15th Int. Coloproctology meeting Turin, April 16-18. **Øresland T**.

The 16th Nordic colorectal postgraduate course, organiser and moderator. Kristiansand, August 29-31. **Øresland T**.

Arranged meetings

TaTME. Implementering og kliniske resultater i Norge. The Norwegian Surgical Society Annual Meeting, Oslo, October 2018. **Færden AE**.

Lapconor, Train the Trainer. Stavanger, May 31-June 1. Gaupset R.

Lapconor, Cadaver course. Akershus University Hospital, May 2-3. **Gaupset R**.

Lapconor, Cadaver course. Akershus University Hospital, October 17-18. Gaupset R.

The 8th Ahus Colorectal Symposium. «Common diseases of the anus, rectum and colon».

Akershus University Hospital, January 25-26. Øresland T.

The 16th Nordic Colorectal Postgraduate course. Norsk Forening for Kolorektal kirurgi.

Kristiansand, August 29-31. Øresland T.

The 3rd IBD Nordic Conference. Malmø, October 11-12. Øresland T.

Postgraduate course in proctology. Akershus University Hospital, November 26-27. Øresland T.

Other academic activities

Main supervisor for Marie Louise Sunde, Akershus University Hospital. **Færden AE**.

Main supervisor for Jens Marius Næsgaard, Vestfold Hospital Trust. Ignjatovic D.

Main supervisor for Yngve Thorsen, Akershus University Hospital. Ignjatovic D.

Main supervisor for Javier A. Luzon, University of Oslo. Ignjatovic D.

Main supervisor for Gurpreet Singh Banipal, Akershus University Hospital. Ignjatovic D.

Main supervisor for Robin Gaupset, Akershus University Hospital. Røkke O.

Main supervisor for Yasir Malik, Akershus University Hospital. Schultz J.

Main supervisor for Johannes Schultz, Akershus University Hospital. Øresland T.

Co-supervisor for Javier A. Luzon, University of Oslo. Bakka AO.

Co-supervisor for Gurpreet Singh Banipal, Akershus University Hospital. Bakka AO.

Co-supervisor for Jens Marius Næsgaard, Vestfold Hospital Trust. Bakka AO.

Co-supervisor for Robin Gaupset, Akershus University Hospital. Eftang L.

Co-supervisor for Yasir Malik, Akershus University Hospital. Færden AE.

Co-supervisor for Robin Gaupset, Akershus University Hospital. **Ignjatovic D**.

Co-supervisor for Yasir Malik, Akershus University Hospital. **Ignjatovic D**.

Co-supervisor for Najia Azhar, Lund University. Schultz J.

Co-supervisor for Catherine Planke Teig, Akershus University Hospital. Øresland T.

Co-supervisor for Yngve Thorsen, Akershus University Hospital. Øresland T.

Co-supervisor for Marie Louise Sunde, Akershus University Hospital. Øresland T.

Co-supervisor for Mathilde Risopatron, University of Oslo. Øresland T.

Co-supervisor for Anders Telle Hoel, University of Oslo. Øresland T.

Acting Dean at Stig Palm Therkelsen's dissertation, Clinical effects and cytokine responses from

ingestion of AndoSanTM in patients with ulcerative colitis and Crohn's disease. Oslo Univerity Hospital,

March 15. **Røkke O**.

Editor of IBD Congress News. **Øresland T**.

Editorial Advisory board member Colorectal Disease. Øresland T.

Editorial board member Scandinavian Journal of Gastroenterology. **Øresland T**.

Member of Steering Committee, ALASCCA. Øresland T.

Reviewer for Diseases of the Colon & Rectum and Colorectal diseases. Ignjatovic D.

Reviewer for Br J Surgery, Scand J Gastroent, Colorectal Disease. **Schultz J**.

Reviewer for Br J Surgery, Scand J Gastroent, JCC, Colorectal Disease, Alimentary Pharmacology and

Therapeutics. **Øresland T**.

Memberships

Elected member of the International Surgical Group (ISG). Bakka AO.

Elected member of the IOIBD (International Organization for the study of IBD). Øresland T.

Chairman of the Specialist Committee for GI surgery. Færden AE.

S-ECCO consensus participant. Færden AE.

Member of the Norwegian Gastrointestinal Cancer Group – Colorectal. Færden AE.

Member of the group responsible for the revised national colorectal strategy plan. Færden AE.

Member of the Research Committee European Association of Endoscopic Surgery EAES. Ignjatovic D.

Members of the Norwegian National Registry for Anal Incontinence (NRA). Naimy N, Teig CP, Øresland T.

European Society of Coloproctology National representative. Schultz J.

Member of the Norwegian Research Network Group for Incontinence and Pelvic Floor Dysfunctions. **Teig CP**.

Chair of the S-ECCO ulcerative colitis surgical consensus group. **Øresland T**.

Elected member of The International Society for the study of IBD (IOIBD) and the Swedish SOIBD. **Øresland T**. Editorial Advisory board member Colorectal Disease. **Øresland T**.

Editorial board member Scandinavian Journal of gastroenterology. **Øresland T**.

Ongoing research projects

Scandinavian Diverticulitis Trial (www.scandiv.com)

Johannes Kurt Schultz M.D., Sheraz Yaqub M.D. Ph.D. (Oslo University Hospital), Tom Øresland Professor M.D. Ph.D., et. al.

Background: Urgent sigmoid resection for acute perforated diverticulitis with purulent peritonitis has a high morbidity and mortality. Previous, non randomized patient series have reported a better outcome for patients treated by laparoscopic peritoneal lavage.

Aim: To compare primary sigmoid resection with laparoscopic lavage as treatment for acute perforated diverticulitis.

Methods: The design is pragmatic. 21 Swedish and Norwegian hospitals participate. All patients presenting with CT-confirmed perforated diverticulitis were eligible. We intend to include 150 patients divided in the two arms. The main end-point is severe postoperative complications within 90 days.

Current status: The primary outcome and other main 90-day results have been published in JAMA in 2015. One-year results have been published in BJS in 2017. These two publications were a central part of Johannes Schultz' Ph.D thesis published in 2018 (see below). Most of the data for a long-term follow-up with a median follow-up time of 59 moth has been collected in 2018 and analysis has started. This longterm follow-up is part of a PhD project at the University of Malmö were Johannes Schultz is co-supervisor. Additionally, a spinoff project investigating all CT scans taken during the study are conducted in collaboration with Västerås Lasarett. Data collection for this project is now complete and analysis is soon completed. Another collaboration with the university of Malmö and the University of Amsterdam was started which will merge data from the SCANDIV trial and the similar Dutch Lola trial with the aim to identify factors predicting bad outcome with laparoscopic lavage.

The follow-up project SCANDIV II, conducted together with the collaborators from the SCANDIV trial, is a prospective observational study to look at all stages of perforated diverticulitis and the final version of the

protocol has been approved by the Regional Ethics Committees in Norway and Sweden. The first patients have been enrolled in SCANDIV II in Sweden in 2018. In Norway we have been working on the online CRF solution which is now up and running and inclusion will start soon.

What is the value of colonoscopy or CT colography after uncomplicated diverticulitis?

Najia Azhar M.D. (Lund University), Sheraz Yaqub M.D. Ph.D. (Oslo University Hospital), Tom Øresland Professor M.D. Ph.D., Tommy Schyman (Skåne University Hospital, Malmø), Pamela Buchwald M.D. Ph.D. (Skåne University Hospital, Malmø), Johannes Kurt Schultz M.D. Ph.D.

Background: Abdominal computed tomography (CT) has become the investigation of choice for suspected colon diverticulitis mainly to confirm the diagnosis. It might be that this CT examination also can rule out colorectal cancer (CRC) which is the feared differential diagnosis.

Aim: To evaluate the necessity of traditional colon examination after one episode with CT-confirmed acute uncomplicated diverticulitis.

Methods: Medical records of patients in Norway diagnosed with CRC within one year after hospitalization for diverticular disease between 2007 and 2010 will be reviewed to calculate the frequency of misdiagnosed CRC in patients with CT-confirmed acute diverticulitis.

Current status: The project has been approved by the Regional Ethics Committee. We have matched data from the Norwegian Patient Registry (NPR) and from the Norwegian Cancer Registry. Medical records of approximately 150 patients from more than 30 hospitals have been ordered and we have received more than 90% of the material. The project will be part of the PhD thesis of Najia Azhar in Malmø who has started analysis of the data.

Tailoring chemotherapy and surgical treatment for colon cancer to the patient and not vice versa

Ph.D. Project Yasir Malik M.D.

Main supervisor: Johannes Kurt Schultz M.D. Ph.D.

Co-Supervisors: Dejan Ignjatovic, M.D. Ph.D., Arne Engebreth Færden M.D.

The project consists of three studies:

1) Does better quality surgery have the potential to replace adjuvant chemotherapy in a selected group of Dukes C patients?

Introduction: The evidence found in favor of adjuvant chemotherapy is relatively old. Surgery has evolved since the 80's when the two previously mentioned studies were published. It is likely that this evolution of surgery (improved techniques combined with more radical lymphadenectomy) and more dedicated pathological examination of the specimen have led to a considerable stage migration. It is uncertain whether the increased lymph node harvest has had any impact on the overall survival for Stage III cancer patients and whether the role of adjuvant chemotherapy in this patient group should be reconsidered. Aim: To compare recurrence rates and survival after surgery for stage III colon cancer in patients who did/did not receive adjuvant chemotherapy. Further the impact of quality of surgery, tumor stage and vascular invasion will be assessed.

Methodology: Data for this single center cohort study is collected from electronic patient files. Dukes C patients were identified through the pathologist's code register. All patients with the code for Colon (T67) and either adenocarcinoma (M81403) or mucinous adenocarcinoma (M84803) codes treated from 31.12.2005 to 31.12.2015 were identified. All of these patients who at the same time period were registered with Lymph node (T08) and metastasis of adenocarcinoma (M81406) or mucinous adenocarcinoma (M84803) were included in the trial.

Study Status: Ethical approval for this study has been applied for but the ethical comity (REC South East) answered that ethical approval was not needed as this is a local retrospective quality control study. The study has been approved by the local data protection officer (Personvernombud) at Ahus. The study has

been started and data collection is completed. Analysis is on the way and preliminary results have been presented at the annual meeting of the Norwegian Surgical society.

2) Long-term survival rates for two cohorts: D2 vs. D3 right colectomy for cancer

Introduction: A meta-analysis conducted from 66 studies that included 1437846 patients with a median follow-up of 65 months showed that left sided primary tumor location was associated with a significantly reduced risk of death (HR, 0.82; 95% CI, 0.79-0.84; P< .001) independent of stage, race, adjuvant chemotherapy, year of study, number of participants, and quality of included studies. One reason may be a lower quality of the surgery performed in right-sided colon cancer compared to surgery for left sided tumors, due to complex anatomical relations between the right and transverse mesocolon and the root of the small bowel mesentery. The clinical trial "Safe Radical D3 Right Hemicolectomy for Cancer through Preoperative Biphasic Multi-detector Computed Tomography (MDCT) Angiography" with ethical approval: Regional ethical committee, South-East Norway (REC South East) no. 2010/3354 investigates more extensive lymphadenectomy than the standard procedure in a large patient cohort.

Aim: The aim of this study is to compare long-term survival after right colectomy with extended D3 mesenterectomy to that after conventional right hemicolectomy.

Methods: Survival of patients included in the above mentioned trial will be compared to that of a matched control group (1:2) derived from the national cancer registry, matched for preoperative tumor stage, age, gender and operation date. Patients operated in the three trial hospitals in Norway or in low volume hospitals (<30 colon cancer procedures per year) will not be considered when generating the control group.

Study Status: This study will be the first survival analysis of the ongoing clinical trial "Safe Radical D3 Right Hemicolectomy for Cancer through Preoperative Biphasic Multi-detector Computed Tomography (MDCT) Angiography" which is a multicenter cohort study including patients operated for right sided colon cancer with a new technique. This trial is approved by the ethical board (REC South East) and has already included more than 500 patients. The present study will compare survival data for the first 250 patients of this clinical trial with data for a matched cohort in the Norwegian cancer registry not operated with the new method.

3) Long-term effects of adjuvant chemotherapy on Quality of life (QoL) in recurrence free patients operated for colon cancer

Introduction: Surgery alone can cure colorectal cancer for the majority of Stage I and stage II patients. Trials from the late 80's and early 90's showed a considerable improvement in survival after adjuvant chemotherapy in stage III colon cancer. Adjuvant chemotherapy has since been standard of care for this patient group. FOLFOX (leucovorin, fluorouracil, and oxaliplatin) were introduced after the MOSAIC trial showed increased overall survival. Despite the efficacy of FOLFOX treatment for stage III colon cancer, this treatment is associated with a significant increase of cost, toxicity and changes in QoL. Common short term side effects include hair loss, mouth ulcerations, loss of appetite, nausea and vomiting, diarrhoea, immune suppression, bleeding tendency, allergic or sensitivity reactions and hand-foot syndrome whereas fatigue and neuropathy can be long term side effects. In particular, oxaliplatin-induced cumulative dosedependent neurotoxicity is a very relevant issue. Peripheral neuropathy was reported for 92.1 % of patients receiving treatments, and the incidence of grade 3 neurotoxicity 1 year after completion was estimated to be 12 % in the MOSAIC trial. Approximately 50 % of patients suffered from grade 1 or 2 neurotoxicity in the second post-treatment year.

For rectal cancer there is less support in the literature for adjuvant chemotherapy and this has not been standard in Norway until now. However, chemotherapy in combination with radiation is often used in a neoadjuvant setting for rectal cancer with the aim to reduce local recurrences.

What is the risk of intestinal dysfunction after small bowel denervation during modern surgery for right-sided colon cancer? The study concerns: alterations in bowel function; compensatory mechanisms; development of a bowel function prediction model; anatomical evidence.

Yngve Thorsen M.D., Tom Øresland Professor M.D. Ph.D. Morten Tandberg Eriksen M.D. Ph.D. (Oslo University Hospital), Dejan Ignjatovic Professor M.D. Ph.D.

Introduction: A substantial segment of the superior mesenteric nerve plexus is included in the surgical specimen in D3 right colectomy. The consequences of denervation are not entirely understood and are mostly related to bowel motility. The hypothesis behind the syndrome (postoperative diarrhea) is that s ympathetic denervation results in a stable and high-level small bowel and right/transverse colon peristaltic activity.

Methods: Patients included in the "Safe Radical D3 Right Hemicolectomy for Cancer through Preoperative Biphasic Multi-detector Computed Tomography (MDCT), a multicenter trial, are interviewed and compared with a control group operated with a traditional right hemicolectomy (Project 1). Project 2 is a clinical trial using the wireless motility capsule (Smartpill®). Project 3 represents data collected prospectively through a stool-diary lead by the patient. Project 4 is a post-mortem study.

Aim: To identify bowel function alterations (and their etiology) that occur after D3 right colectomy; this will be achieved through six articles:

Article 1: (published): Bowel function and quality of life after superior mesenteric nerve plexus transection in right colectomy with D3 extended mesenterectomy. Tech Coloproctol. 2016 Jul;20(7):445-53 27.

Article 2: (published): Detecting the non-physiological, surgically tailored ileocolic anastomosis using the wireless motility capsule. A pre- and post-operative, prospective, within-subject trial. J Neurogastroenterol Motil. 2017 Oct 30;23(4):585-591.

Article 3: (published): Bowel Motility After Injury to the Superior Mesenteric Plexus During D3 Extended Mesenterectomy. J Surg Res 2019 Jul. (Epub 2019 Feb 27).

Article 4: (submitted): The effect of vascular anatomy and gender on bowel function after right colectomy with extended D3-mesenterectomy.

Article 5: Early postoperative changes in the bowel habits after extended mesenterectomy with consecutive extrinsic denervation of the small bowel. (Based on stool-diaries the first 2 months after surgery. 45 patients included).

Article 6: What is the extent of superior mesenteric nerve plexus excision at D3 right colectomy? Which part of the plexus remains? A post-mortem study. Status: Waiting, 12 cadaver dissections planned.

Applying emerging three-dimensional (3D) visualization technologies to macro and micro anatomical datasets, for the improvement of operative planning, performance and outcomes in colon cancer surgery

Javier Luzon M.D., Arne Bakka Professor M.D. Ph.D., Bjørn Edwin Professor M.D. Ph.D. (Oslo University Hospital), Ole Jakob Elle Associate Professor Ph.D. (Oslo University Hospital), Dejan Ignjatovic Professor M.D. Ph.D.

A. Macroanatomy study:

Article 1: Implementation of 3D printed superior mesenteric vascular models for surgical planning and/ or navigation during right colectomy with extended D3 mesenterectomy. Comparison of virtual and physical models to the anatomy found at surgery.

Status: Study completed. Published as original article at the journal Surgical Endoscopy

Article 2: Augmented reality and image processing/fusion in surgery: 3D visual assistance for a safer surgical navigation of the mesenteric vasculature. CTrue project.

Status: Second version of CTrue app for Ahus with Microsoft Hololens acquired.

Accuracy and precision experiments are being performed. Data collection started.

Article 3: Semiautomatic vs manual 3D reconstruction of central mesenteric vascular models; the surgeons verdict

Status: Study completed. Manuscript submitted to a surgical journal for peer-review evaluation.

B. Microanatomy study:

Article 4: Defining the spatial 3D relations between lymphatic glands and vessels, nerves and blood vessels within the D3 area by using MicroCT imaging for the digital reconstruction of its microanatomy. **Status:** Tissue samples obtained and MicroCT scan are being performed. Currently improving staining and imaging methods.

Article 5: 3D reconstruction of histological slides: Manual segmentation and 3D volume reconstruction of microanatomy structures on histology slides. Providing architectural data on D3 extended mesenterectomy area, the lateral border of the area and watershed to the small bowel lymph. **Status:** Completed data acquision. Currently performing data analysis and manuscript design.

Assessing right colon cancer patients with metastatic central (D3) lymph nodes. Identifying the group benefiting from extended mesenterectomy and evaluation of radiological and pathological diagnostic procedures

Gurpreet Singh Banipal M.D., Dejan Ignjatovic Professor M.D. Ph.D.

Introduction: Patients suffering from right sided colon cancer with metastasis to the central lymph nodes are still in a curable phase of the disease and can be identified prior to surgery through radiology, genetic and epigenetic markers. This knowledge will enable additional treatment (chemotherapy, immunotherapy) before surgery in this patient group, as well as changes in operative technique (micro metastases and isolated cancer cells), in this way improving survival rates.

Methods: This is a reanalysis of patients included in "Safe Radical D3 Right hemicolectomy for Cancer through Preoperative Biphasic Multi-Detector Computed Tomography (MDCT) with positive nodes in the D3 volume. Article 1 represents a reanalysis of preoperative CT scans to establish spreading patterns. Article 2 is impact of surgical strategy on lymphatic dissemination patterns (isolated cancer cells, micro-metastases) and to determine if "medial to lateral" surgical access is superior to the "lateral to medial" in surgery for cure of right sided colon cancer. Article 3 is to identify cancer genes and epigenes in tumor and lymphatic nodes to identify patients who can benefit of this surgery. Article 4 is to find short and long term results.

Aim: To identify the patient group at risk of lymph node metastasis in the D3 volume of the right colon from the radiological and immunohistopathological aspect as well as to present the short and long-term outcomes of the patient group. This will be achieved through 4 articles:

Article 1. To study lymph nodes in D3 volume by preoperative CT scans, and try to establish spreading patterns in this patient group.

Article 2. To study disseminated patterns of isolated cancer cells and micro metastases relative to level of dissection and surgical technique.

Article 3. Establish better understanding of epigenetic cancer markers in this patient group, which will help in identifying group of high-risk patients in preoperative analysis.

Article 4. Determine the short- and long-term results of this patient group.

Current Status: Project is approved by regional ethical committee. Data collection is in final stages. Article 2 is expected to be published in autum 2019. This project will part of PhD thesis for Gurpreet Singh Banipal. Collection of data and analysis for the project will be done at Akershus University Hospital.

The introduction of advanced treatment principles for gastric cancer focused on the significance of chemotherapy and laparoscopic approach

Robin Gaupset M.D., Lars Eftang M.D. Ph.D., Dejan Ignjatovic Professor M.D. Ph.D., Ola Røkke Professor M.D. Ph.D.

Co-workers: Kathrin Friedrich (Dept of Pathology), Jonn Terje Geitung and Arne Borthne (Dept. of Radiology), Sutharsan Sutharalingam (Dept. Oncology), Jurathe Saltyte Benth (Department of Statistics).

Background: Gastric cancer is still one of the deadliest forms of cancer in the gastrointestinal system. Although declining in incidence in the latter years due to better hygiene and lower incidence of Helicobacter Pylori among other reasons, some 500 new cases are seen every year in Norway. The introduction of standardized operative approach, laparoscopy and chemotherapy may have had an impact on survival after treatment for this disease. Preoperative staging has improved with the development of high resolution CT.

Aim: To compare morbidity and survival before and after introduction of the above mentioned parameters. To evaluate the sensitivity and specificity of CT with regard to preoperative staging.

Methods: 185 patients operated for gastric cancer at Akershus University hospital in the period 2000 to 2016 are reviewed with regards to changes in treatment principles and impact on morbidity and survival. 50 patients in the latter period including some patients in 2017, all of who got chemotherapy preoperatively, are studied with regards to preoperative staging by CT and compared to the postoperative pathological findings. Finally several aspects of the treatments introduced will be studied with regards to side effects and quality of life.

Current status:

- The first article was published January 2018:
 - o Improved survival after implementation of multidisciplinary team meetings, perioperative chemotherapy, extended lymphnode dissection and laparoscopic surgery in the treatment of advanced gastric cancer. Journal of cancer therapy, Vol. 09 No. 02(2018)
- All data collected for the second and third article
- · Mandatory courses in Statistics and the first introductory course have been completed

Defining new explanations for bad outcome after necrotizing pancreatitis using CT-scans and "SmartPill"

Ph.D. Project under preparation. Candidate: Kourosh Piroozmand M.D.

Supervisors: Ola Røkke Professor M.D. Ph.D., Professor, Odd Langbach M.D. Ph.D.

Co-workers: Olof Vinge-Holmquist M.D., Ask Boe Klakegg M.D., Øystein Arnø M.D., Vibecke Sørensen M.D., Lars Aabakken Professor, Jurathe Saltyte-Benth Ph.D.

Introduction: Acute pancreatitis is an acute inflammation of the pancreas. 20% of the patients develop severe pancreatitis, with necrosis of pancreatic gland and/or peripancreatic tissue. Survivors are disposed for reduced quality of life. Little is known about the long term incidence and severity of these complications. The physiological cause diarrhea is also not fully understood.

Aims:

- 1) To determine if the treatment results of acute necrotizing pancreatitis
- 2) Determine function of pancreas and patients after necrotizing pancreatitis
- 3) Determine the small bowel transit time in patients after acute necrotizing pancreatitis

Material and methods: Patients admitted to Akershus University Hospital from 2000 - 2018 with acute necrotizing pancreatitis. Study 1: Compare the results of treatment of patients in the first and last period. Study 2: Follow-up of 130 surviving patients. Study 3: Study small bowel transit with the SmartPill in 20 patients surviving acute necrotizing pancreatitis compared to 73 healthy volunteers.

Current status: Data gathering and analyses.

Identification of microbial agents as a novel cause of acute pancreatitis using next-generation sequencing

Ph.D. Project under preparation. Candidate: Olof-Vinge-Holmquist M.D.

Supervisors: Ola Røkke Professor M.D. Ph.D., Odd Langbach M.D. Ph.D., Truls M Leegaard Professor Co-workers: Kourosh Piroozmand M.D., Ask Boe Klakegg M.D., Øystein Arnø M.D., Vibecke Sørensen M.D., Øyvind Kommedal Professor (Department of Microbiology, Haukeland University Hospital), Erling Bringeland (St Olavs Hospital), Rimantes Konstera M.D. (Orkdal sykehus), Jurathe Saltyte Benth Ph.D.

Introduction/Aim: Acute pancreatitis is an acute inflammation of the pancreas. In 20%, the cause of pancreatitis in unknown. 20% of the patients develop severe pancreatitis, with necrosis of pancreatic gland and/or peripancreatic tissue. The reason for this is also unknown. The present project aims to define a possible role for microorganisms as a contributing factor.

Material and methods: Identify microbes from bile-stones and bile with the next-generation sequencing technique from patients. Study 1: Compare DNA-identification of microbes from patients after acute pancreatitis operated "in house" with patients with biliary colic. Study 2: Compare DNA-identification of microbes from patients after acute pancreatitis operated 3-4 months after the attack with patients with biliary colic. Study 3: Compare DNA-identification of microbes from patients after acute necrotizing pancreatitis, acute interstitial pancreatitis and biliary colic.

Results: In a pilot study, DNA from microbes has been identified from bile stones.

Current status: Data-collection in progress. Several "Next generation technology platforms" are at present under evaluation. Pilot studies of 20 patients are currently under analyses.

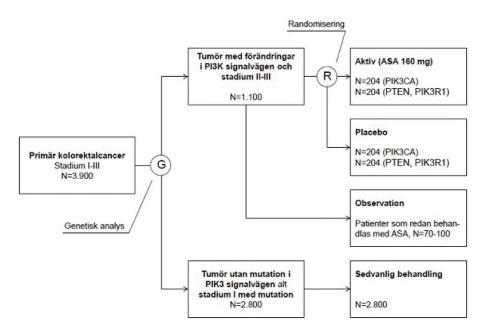


A randomized double-blind placebo-controlled study with ASA treatment in colorectal cancer patients with mutations in the PI3K signaling pathway

We are participating in the multi centre study initiated from Karolinska sjukhuset. Tom Øresland Professor M.D. Ph.D., Marianne Merok M.D. Ph.D, Nora W. Christensen M.D., Muhammad Shafique M.D., Heidi Miltvedt R.N., Merete Helgeland M.Sc.

Background: ALASCCA is a prospective, randomized, double blinded, placebo controlled, multicenter, biomarker-based study of adjuvant treatment with ASA in colorectal cancer. A total of 3,900 patients will be screened.

Objective: The primary objective of ALASCCA is to determine whether adjuvant treatment with 160 mg ASA once daily for 3 years can improve time to recurrence in patients with colorectal cancer with somatic alterations in the PI3K signaling pathway.



The study is initiated from Karolinska sjukhuset and involves centers in all Nordic countries. In Norway also Stavanger, St Olav and Tromsø is participating. Ahus is the PI for Norway.

Current status: Recruiting ongoing. Ahus has the best recruiting rate. The study expects end of recruiting by the end of 2020.

"Watch and Wait" in patients with complete clinical response (cCR) after neo-adjuvant chemoradiotherapy for primary locally advanced rectal cancer

Open population-based observational study on behalf of the Norwegian Gastro-Intestinal Cancer Group – Colorectal (NGICG-CR)

Hartwig Körner Professor M.D. Ph.D., and Jan Hallvard Træland M.D. (Stavanger University Hospital), Arne E Færden M.D. Ph.D., Stig Norderval M.D. Ph.D., and Petter Gjessing M.D. Ph.D. (University Hospital of Northern Norway, Tromsø), Hans Wasmuth M.D. Ph.D., and Gerd Tranø M.D. Ph.D. (St. Olavs Hospital), Frank Pfeffer M.D. Ph.D., and Håvard Forsmo M.D. (Haukeland University Hospital), Gro Wiedswang M.D. Ph.D., Stein Gunnar Larsen M.D. Ph.D., Marianne G. Guren M.D. Ph.D., and Ellen Viktil M.D. (Oslo University Hospital), Christian Kersten M.D., and Joakim Hauss M.D. (Sørlandet Hospital), Inger Kristin Larsen (Cancer Registry of Norway).

Background: Treatment of rectal cancer has undergone subtantial improvements during the past three decades with introduction of total mesorectal excision (TME), preoperative radiotherapy (RT) and chemoradiotherapy, improved preoperative imaging and treatment decisions in the multi-disciplinary team (MDT). Local recurrences, historically reported to be 30%, are now reported to be <5% nationwide, and relative five-year survival of rectal cancer patients has been shown to be higher as compared to colon cancer.

The introduction of preoperative CRT was accompanied by the observation that the tumour had disappeared at clinical examination 6-10 weeks after completed treatment in a subgroup of about 15-20% of the patients depending on size and T-stage of the tumour, i.e. clinical complete response (cCR). Further, Habr-Gama showed that patients with cCR could avoid surgery, and only be followed by close clinical monitoring, and introduced the concept of Watch & Wait (W&W) for patients with cCR after preoperative chemoradiotherapy. Most patients with cCR are cured, and thus avoid a major surgical procedure, but there are about 20-30% who will experience regrowth of the tumour and need surgical treatment, with comparable chance of cure for their cancer as with primary surgery. The reports from the Habr-Gama group evoked great interest in the W&W concept, and several study groups, such as the Maastricht group in the Netherlands, and the Vejle group in Denmark have published results for this concept. A recent systematic review and meta-analysis also concluded that the W&W approach appeared to be safe and resulted in comparable long-term survival as surgical treatment.

Aim: The NORWAIT trial is a national cohort study of patients with cCR after neoadjuvant treatment for rectal cancer who follow the Norwegian W&W protocol in the setting of the Norwegian Colorectal Cancer Registry. The aim of the NORWAIT trial is to estimate the rate of regrowth among patients with locally advanced rectal cancer treated with neoadjuvant radiotherapy or chemo-radiotherapy, where clinical complete response has been obtained, and thus to determine the positive predictive value of cCR in a national cohort.

Method: The current study is designed as an open prospective population-based study. All patients diagnosed and treated with radiotherapy or chemo-radiotherapy for rectal cancer in Norway will be eligible for this study. All patients will be diagnosed according to national guidelines, and treatment decisions with regard to the need for neo-adjuvant chemo-radiation therapy will be made according to national guidelines in the setting of multidisciplinary team (MDT) meetings. Patients with complete clinical respons 6-12 weeks after radiochemotherapy, and wish to participate in the study, will be included and followed closely without surgery for 8 years. Patients diagnosed with regrowth during follow-up will be scheduled for surgical resection.

Current status: Recruiting.

Geriatric intervention before surgery for colorectal cancer in frail, elderly patients

Nina Ommundsen M.D. (Akershus University Hospital/Oslo University Hospital), Siri Rostoft M.D. Ph.D. (Oslo University Hospital), Arild Nesbakken Professor M.D. Ph.D. (Oslo University Hospital), Arne Bakka Professor M.D. Ph.D., Benedicte Rønning M.D. (Oslo University Hospital), Marit S Jordhøy M.D. Ph.D. (Cancer Unit, Innlandet Hospital Trust), Torgeir Bruun Wyller Professor M.D. Ph.D. (Oslo University Hospital).

Aim: To investigate whether a preoperative geriatric assessment followed by an individualised intervention can reduce the number of postoperative complications in frail elderly patients undergoing elective surgery for colorectal cancer.

Material and methods: Randomised controlled trial including frail, elderly patients with colorectal cancer. Patients are allocated to either 1) preoperative geriatric assessment and individualised optimisation or 2) care as usual. A research assistant blinded for group allocation is recording any postoperative complications 30 days post surgery. Tumour localisation, TNM-staging, length of stay, reoperation, discharge to home/nursing home and readmission are also recorded. Three months after surgery, an assessment of living arrangements and self-assessed health is performed.

Current status: Inclusion to the study is completed. Four articles have been published.

Molecular drivers and inhibitors of colorectal cancer in inflammatory bowel diseases

Stephan Brackmann M.D. Ph.D., Tom Øresland Professor M.D. Ph.D., Solveig Norheim Andersen Professor M.D. Ph.D., Jørgen Jahnsen Professor M.D. Ph.D., Anna Frengen Dr. Scient, Morten Vatn Professor M.D. Ph.D., Hilde Nilsen Professor.

Aim: The principal objective of the project is to improve the diagnosis and the prognosis of malignancy in inflammatory bowel disease by analysing the relationship between molecular biomarkers in the mucosa, blood and faeces and genomic instability, inflammation, and pre-malignant (dysplasia) or malignant changes of the colon in a well-defined cohort of CRC in IBD including controls.

The project is part of a collaborative research network comprising several clinical divisions and departments at Akershus University Hospital (Ahus) including Gastroenterology, Surgery, Pathology, and Clinical Molecular Biology. The partners have access to unique historical retrospective CRC-IBD material complementary to the present prospective study biobank that will allow necessary proof of concept and in depth-studies. The results of the project may contribute to an improved understanding of the mechanisms involved in the development of malignancy in IBD and may help to improve surveillance strategies in these patients. The results may also give insight in factors related to the prognosis of cancer in IBD.

Current status: Recruiting.

Translation and validation of condition-specific quality of life questionnaires for women with pelvic organ prolapse in the Norwegian context

Teig Planke C, Martini A (University of Western Australia), Grotle M (Oslo and Akershus University College of Applied Sciences and Oslo University Hospital), Cvancarova S M (Department of Obstetrics and Gynecology, Akershus University Hospital), Øresland T, Kjøllesdal M (Drammens Gynekologen), Saga S (Sør-Trøndelag University College), Ellström EM (Department of Obstetrics and Gynecology, Akershus University Hospital).

Background: The goal was to translate the short versions of the Pelvic Floor Distress Inventory (PFDI-20) and Pelvic Floor Impact Questionnaire (PFIQ-7) to Norwegian and to validate them in a sample of patients with symptomatic pelvic organ prolapse (POP) and pelvic floor dysfunction (PFD).

Method, translation and cultural adaptation: The PFDI-20 and PFIQ-7 were translated from English into Norwegian using a new multistep translation and cultural adaption method. This method combined the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Group guidelines, the Delphi method and expert panel review. It involved two independent forward and backward translations and used the Delphi method (anonymous voting, controlled feedback, statistical group response) to establish a consensus on translated items in a panel of bilingual pelvic floor experts that included gynaecologists, colorectal surgeons, a urologist, a physiotherapist and a urotherapist. The translated instruments were then pilot-tested for comprehensibility, readability and equivalence through face-to-face semi-structured interviews with 20 women with POP (with or without urinary or bowel dysfunction). Minor discrepancies were identified and amended to produce Norwegian versions of the PFDI-20 and PFIQ-7 that were ready for validation.

Validation: A total of 205 Norwegian women with POP (with or without urinary or bowel dysfunction) and with Pelvic Organ Prolapse Quantification (POP-Q; stages 1–4) completed the questionnaires; 50 completed them again after 1 to 3 weeks, and 76 completed them again 6 months later. Reliability, validity and responsiveness were evaluated. Cronbach's alpha was calculated for PFDI and PFIQ-7 scores as a measurement of internal consistency. Test-retest reliability was evaluated using intra-class correlation coefficients to quantify agreement between PFDI-20 and PFIQ-7 scores, respectively. Construct validity and responsiveness were tested using a priori formulated hypotheses. The smallest detectable change, standard error of measurement, floor and ceilings effects and percentage of missing items were also reported.

Cronbach's alpha ranged from 0.66 to 0.93, and the intraclass correlation coefficients ranged from 0.85 to 0.94. Smallest Detectable Change (SDC) at the individual level constituted 15%-21% and 17%-27% of the total scores and subscales for the PFIQ-20 and PFIQ-7, respectively.

Construct validity was determined to be adequate, with 88% (7 of 8) of predefined hypotheses confirmed. Adequate responsiveness was achieved, with 100% (5 of 5) of the predefined hypotheses confirmed. No floor or ceiling effects were found in the PFDI-20 and PFIQ-7 total score distributions. Similarly, no ceiling effects were observed in any of the PFDI-20 or PFIQ-7 subscales. The UQI-7 subscales (19.5%) showed a small floor effect. Notably, major floor effects were found in the POPIQ-7 (26%) and CRAIQ-7 (47%) subscales.

Missing data at baseline reflected only 0.82% of PFDI-20 items and 1.92% of PFIQ-7 items.

Results: The median age of the sample was 61 years (range, 27-82 years). The majority who had POP were at POP-Q stage 2 or 3. Anterior compartment prolapse was the most common type of POP. Several had POP in more than one compartment. Women who were treated surgically only underwent vaginal repair. Anterior and posterior compartment repair were the most common procedures. While 172 patients (83.9%) completing the PFDI-20 reported 3 symptoms of PFD, 27 (13.2%) reported 2 PFD symptoms and 6 (2.9%) reported 1 PFD symptom.

Conclusions: The translated questionnaires provided adequate reliability, validity and good responsiveness to change. These Norwegian versions of the PFDI-20 and PFIQ-7 short versions of the Pelvic Floor Distress Inventory and Pelvic Floor Impact Questionnaire are robust instruments that will allow symptom severity and health-related quality of life to be evaluated in the Norwegian context.

Current status: One article has been published (2017) and the second one to be submitted in June, 2019.

Anorectal Malformations and Hirschsprung Disease. What are the problems, needs and expectations in young adults operated for Anorectal Malformations and Hirschsprung Disease in childhood? A Scandinavian multicenter project.

Akershus University Hospital: Tom Øresland, Catherine Planke Teig. Oslo University Hospital (RH): Kristin Bjørnland, Anders Telle Hoel. Skåne University Hospital: Pernilla Stenstrøm (Lund); Antoni Zawadzki (Malmø), Louise Tofte (Lund), Sara Johansdottir (Lund).

A study where we use qualitative methods, focus group interviews, to identify possible problems that these people might face when they transition from childhood to young adults. They will no longer be cared for by pediatric surgeons who operated on them when they were infants. The adult healthcare system has very scarce knowledge of their backgrounds and bowel function. What are their expectations and how can colorectal surgeons and the Pelvic floor center support them? What more do we have to learn, can we develop a structured care and better methods? These questions are of interest both for pediatric surgeons and for colorectal surgeons since knowledge of their lifelong bowel function and problems related to this largely is missing. We hope that this initial survey will give input for further patient driven studies.

Granted Funding

Project	Source	Amount (NOK)
CTrue project: Development of an effective 3D navigation system for colon cancer surgery Dejan Ignjatovic, Javier Luzon	Innovation funds Helse Sør-Øst (2017-2018)	750,000
A randomized double-blind placebo-controlled study with 5ASA treatment in colorectal cancer patients with mutations in the PI3K signalling pathway	Akershus University Hospital Strategic research grants	150,000
Tom Øresland, Heidi Miltvedt		
Total		900,000

Department of Anaesthesia and Intensive care

University employees:	Research fellows:
Professor II Vegard Dahl	Felix Haidl
Associate Professor Signe Søvik	Vladimir Kuklin
Lecturer Jørgen Dahlberg	

Research activity and research ambitions

All three university positions in our department are filled, as is the department's 50% research position for junior doctors. Research activity is steady, also for staff in non-academic positions. We are however ambitious and hope to increase our research activity further.

In 2018, the Department of Anaesthesiology andIntensive care participated in two European multi-centre studies, the Stress Ulcer Prophylaxis in the Intensive Care Unit (SUP-ICU) Study (http://www.sup-icu.com), published in NEJM in 2018, and the Wean-Safe study (Worldwide AssessmeNt of Separation of patients From ventilatory assistance) endorsed by ESICM, the European Society for Intensive Care Medicine. Our department has also started contributing to the IDART Study (Impairing Drugs and Alcohol as Risk Factors for Traumatic

Injuries) - a National Study on Injury Prevention. Patient inclusion is being planned for the Carbetocin Myocardium Trial (CMT) II, initiated at Oslo University Hospital, Rikshospitalet.

Academic staff in our department run Ahus-based research projects as well as projects in co-operation with research groups at the Division of Emergencies and Critical Care at Oslo University Hospital, the Centre for Medical Ethics, University of Oslo, and the Institute of Basic Medical Sciences, University of Oslo. New projects are being planned for 2019.

A continuing aim in our department is that the majority of research projects undertaken by medical students should result in published scientific work in referee-based journals. High-quality research also in smaller projects is an important tool for increasing the interest for, and ultimately the recruitment to and funding of, more demanding research projects.

Publications (peer reviewed)

Eggen EH. Første utgave av Norsk standard for barneovervåkninger er publisert. NAForum (2018), Vol 31; 4.

Haidl F, Rosseland LA, Spigset O, **Dahl V**. Effects of Adrenaline on maternal and fetal fentanyl absorption in epidural analgesia: A randomized trial. Acta Anaesthesiol Scand. 2018 Oct;62(9):1267-1273.

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Abstracts and posters

Brekke IF, **Sandemose A**, **Dahl V**. Uventet vanskelig luftvei pga asymptomatisk cystisk lesjon i laryngs. NAForum (2018) 33:39.

Dahl V, **Haidl F**, **Fjuk E**, Opøien HK, Spigset O. Opptak av peroral oksykodon umiddelbart etter keisersnitt i spinalbedøvelse. NAForum (2018) 33:46.

Gamst M, Birkeli G, Dahl V. Medisinsk simulering in situ ved postoperativ seksjon. NAForum (2018) 33:44.

Grøvlen ME, **Dahl V**. Kvinne i 50-årene med loeys-dietz syndrom presenterer med spontant inkarserert brokk. NAForum (2018) 33:38.

Hui D, **Søvik S**. Postoperativt smerteforløp etter dagkirurgisk tonsillektomi hos barn, vurdert gjennom telefonintervju av foreldre NAForum (2018) 33:50.

Orhagen BC, **Dahl V**. Bruk av gass sedasjon (anaconda ®) for pasienter med eskalerende opioidbehov i det perioperative forløp. NAForum (2018) 33:45.

Søvik S, Isachsen MS, Nordhuus KM, Tveiten CK, Eken T, Sunde K, Brurberg KG, Beitland S. Acute kidney injury in trauma patients admitted to the intensive care unit: A systematic review and meta-analysis. The 31. Annual Congress of European Society for Intensive Care Medicine, Paris, 2018.

Ongoing research projects

Pharmacokinetic interaction effects of combined fentanyl and adrenaline in epidural analgesia during childbirth

Main researchers: Vegard Dahl Professor M.D. Ph.D., Felix Haidl M.D., Signe Søvik Associate Professor M.D. Ph.D.

Co-workers: Renate Häger M.D. (Dept. of Gynaecology and Obstetrics, Ahus), Leiv Arne Rosseland Professor M.D. Ph.D., and Tore Henriksen Professor M.D. Ph.D. (Dept. of Gynaecology and Obstetrics, Oslo University Hospital).

Background: Around 50% of first-time parturients in Norway receive epidural analgesia (EDA), containing a local anaesthetic and an opioid, most frequently fentanyl. We assess whether addition of adrenaline, working as an analgesic and a vasoconstrictor in the epidural space, 1) affects maternal cardiovascular

responses during labour, 2) reduces fentanyl transfer to the fetal circulation. Fentanyl has been suspected to negatively affect early infant-mother interaction.

Methods: In a controlled, randomised, double blinded study in healthy first-time parturients, we compare effects of two different compositions of epidural analgesia (EDA) administered during labour: The Department's standard EDA, containing bupivacain, fentanyl and adrenaline versus EDA containing only bupivacain and fentanyl. Response variables are fentanyl concentration in maternal blood (time-profile) and umbilical cord blood at birth, course of labour, and fetal and maternal cardiovascular variables measured continuously by non-invasive techniques.

Current status: Data collection and analysis is completed. One paper was published in 2018, further manuscripts in preparation.

Information given to women receiving epidural analgesia for labour pain

Main researcher: Felix Haidl M.D.

Co-workers: Anne Marit Rørvik M.D., Vegard Dahl Professor M.D. Ph.D., Signe Søvik Associate Professor M.D. Ph.D.

Parturients receiving epidural analgesia at our hospital are not informed about the procedure and its possible side-effects before the epidural is requested, typically by a midwife. In an open questionnaire study we registered the amount of knowledge about epidural analgesia among parturients, where they had gathered information, and what information they ideally would have wanted. Our open recruitment resulted in a non-representative study population, heavily skewed towards well-educated, ethnically Norwegian parturients. We are now repeating and extending the study, and we will change our recruitment method to structured interviews of all eligible women. Several hospitals will participate. *Current status:* Development and validation of a new questionnaire is underway. Data collection ongoing.

Peroral oxycodone as analgetic regime in the immediate postoperative period after caesarean section Vegard Dahl Professor M.D. Ph.D., Ellen Fjuk R.N.

Introduction: All patients operated with a caesarean section in regional anaesthesia at Akershus University Hospital receive peroral, slow-release oxycodone as routine prophylactic analgesia, immediately after they are transferred to the postoperative care unit. The gastrointestinal uptake of peroral opioids may be uncertain in this period. The aim of this study is to analyse the uptake of oxycodone and register whether the individual uptake of oxycodone is related to the actual pain as expressed by a Numeric Rating Scale.

Methods: Serum analysis of oxycodone will be obtained by blood samples at regular intervals.

The parturients' level of experienced pain will be registered simultaneously.

Current status: Data collection ongoing.

Assessing competence to consent to somatic health care

Jørgen Dahlberg M.D., Reidar Pedersen M.D. Ph.D., and Reidun Førde M.D. Ph.D. (Centre for Medical Ethics, University of Oslo), Vegard Dahl Professor M.D. Ph.D.

Background: Informed consent is generally required before healthcare is provided. Such consent requires that the patient is competent. Lack of competence may be caused e.g. by reduced cognitive function. This project aims to study whether and to what extent physicians at intensive care and surgical departments assess patient competence prior to providing healthcare, and whether intervention through guidelines and education may improve lack of such assessment.

Methods: The project is a mixed method (quantitative and qualitative) interventional study on patients admitted to intensive care and surgical departments.

First, we will study whether patients showing reduced competence to consent had been assessed pursuant

to the mandatory process. We assess this by investigating patient records in a time series analysis. Then, we collect additional data through focused group interviews. Last, interventions will be implemented and new investigations of patient records will be conducted to assess effects of the intervention.

Current status: Data collection for Phase I completed, manuscript in preparation. Data collection for Phase two ongoing. Progress is in accordance with original project plan.

Effects of treatment at the Pain Treatment Centre (Smertepoliklinikken Ahus)

Danuta Polak M.D., Vegard Dahl Professor M.D. Ph.D.

Introduction: Little is known about the efficacy of the treatment given at the hospitals pain treatment centre. The aim of this study is to make a quality assessment of the different pain treatment modalities that the centre offers.

Methods: A questionnaire has been developed, aiming to register the quality of the different modalities offered. All patients will be asked to fill out this questionnaire by the end of the treatment period.

Current status: Data collection ongoing.

Effects on cerebral blood flow of volume loading and isometric muscle work in young healthy subjects Maria Skytioti M.D. (Institute of Basic Medical Sciences, University of Oslo), Signe Søvik Associate Professor M.D. Ph.D., Maja Elstad M.D. Ph.D. (Institute of Basic Medical Sciences, University of Oslo).

Background: In healthy humans, cerebral blood flow (CBF) is autoregulated against changes in blood pressure. Spontaneous fluctuations in mean arterial pressure (MAP) and CBF can be used to assess cerebral autoregulation. We hypothesized that dynamic cerebral autoregulation is affected by changes in autonomic activity, MAP, and cardiac output (CO) induced by handgrip (HG), head-down tilt (HDT), and their combination.

Methods: We recorded blood velocity by ultrasound in the internal carotid artery (ICA), HR, MAP and CO-estimates from continuous finger blood pressure, and end-tidal CO2. Instantaneous ICA beat volume (ICABV, mL) and ICA blood flow (ICABF, mL/min) were calculated. Wavelet synchronization index c (0–1) was calculated for the pairs: MAP–ICABF, CO–ICABF and HR–ICABV in the low (LF) and high (HF) frequency bands.

Results: Overall ICABF did not change between experimental states. MAP and CO were increased during HG and during HDT + HG. In the LF interval, median c for the MAP–ICABF pair (baseline: 0.23 [0.12–0.28]) and the CO–ICABF pair (baseline: 0.22 [0.15–0.28]) did not change with HG, HDT, or their combination. High c was observed for the HR–ICABV pair at the respiratory frequency, the oscillations in these variables being in inverse phase.

Conclusion: The unaltered ICABF and the maintained low synchronization between MAP and ICABF in the LF interval suggest intact dynamic cerebral autoregulation during HG, HDT, and their combination. Current status: Published in 2018.

Effects on cerebral blood flow of anaesthesia, positive pressure ventilation, and pneumoperitoneum during laparoscopic surgery

Maria Skytioti M.D. (Institute of Basic Medical Sciences, University of Oslo), Signe Søvik Associate Professor M.D. Ph.D., Maja Elstad M.D. Ph.D. (Institute of Basic Medical Sciences, University of Oslo).

Background: During surgery and anaesthesia, cerebral blood flow (CBF) will be affected by both circulatory and ventilator changes. CBF may be compromised by dehydration, haemorrhage, peripheral vasodilation, anaesthetic agents, mechanical ventilation, pneumoperito-neum, and surgical position. CBF is not easily monitored.

Aims: To assess internal carotid artery blood flow (ICA-BF) in relation to central circulatory changes in day surgery patients during anaesthesia, positive pressure ventilation, and surgical procedures known to reduce venous return to the heart.

Methods: In patients undergoing laparoscopic cholecystectomy we will measure beat-by-beat internal carotid artery blood flow (ICA-BF) by Doppler ultrasound, before anaesthesia, after induc-tion, with pneumoperito-neum, and during combined head-up-tilt (HUT) and pneumoperito-neum. Heart rate, non-invasive continuous arterial pressure, respiratory frequency, end-tidal CO2, and all medications will be recorded. Effects on cardiac stroke volume (SV), cardiac index (CI), and ICA beat volume (BV) and blood flow (BF) will be analysed with linear mixed-effects regression.

Current status: Study completed in 2018. It was included Skytioti's PhD project. A publication is under review.

Severe postpartum haemorrhage treated with surgical intervention

Signe Søvik Associate Professor M.D. Ph.D., medical students Ane Schønsberg and Joachim Goldstein (University of Oslo).

Background: Postpartum haemorrhage (PPH) is a potentially life-threatening complication to childbirth. In Norway it has been approximated that 1.1% of parturients experience severe PPH, defined as blood loss >1500 mL within 24 h of delivery. Severe PPH increases maternal mortality by a factor of 50.

Aims: In a three-year material of parturients with severe PPH treated with surgical intervention at Ahus, we will assess degree of circulatory shock upon arrival in the operating theatre, physiological and biochemical responses to general anaesthesia, fluid resuscitation, medication, and transfusion with blood products, and outcome. Specifically, we will assess treatment triggers (e.g. hypo-ten-sion, tachycardia, elevated lactate) in relation to transfusion practices, and compare obtained levels of Hb, platelets, and coagulation factors with recommended transfusion goals in national guidelines for the treatment of PPH. Obstetric risk factors for PPH, time from theatre arrival to start of surgery, duration of surgery, need for ICU treatment and length of hospital stay will be assessed.

Design: Retrospective observational study.

Methods: Manual/electronic data retrieval from patient records and curves. **Current status:** Master degrees completed 2018. Two publications are underway.

What is the optimal infusion rate of remifentanil for children undergoing adeno-tonsillectomy? Will Morton, MBChB FRCA MSc., Signe Søvik Associate Professor M.D. Ph.D.

Background: Pain after tonsillectomy is notoriously difficult to control and is long-lasting. The choice of anaesthetic agents affects the incidence of postoperative nausea and vomiting. For other surgical procedures in children and adults, the dosing of the opioid remifentanil during surgery has been shown to affect postoperative pain levels.

Aims: To assess the effects of peroperative remifentanil dosing on duration and intensity of postoperative pain and well-being, in healthy children aged 1–16 years undergoing adeno-tonsillectomy as day surgery patients.

Design: Prospective, interventional, randomised, double blinded study.

Methods: Four different remifentanil concentrations infused at fixed rate. All groups will receive same dose of the anaesthetic agent propofol and other analgesic medication. Manual/electronic data retrieval from patient records and curves. Repeated pain scoring (FLACC scale in the PO unit, POPMP scale in telephone interviews with parents) up to day 28 and then day 256 post-operatively.

Current status: Application process to regulatory bodies (REK, Norwegian Medicines Agency) started.

Evaluation of level and duration of postoperative pain in children undergoing tonsillectomy

Medical student David Hui (University of Oslo), Signe Søvik Associate Professor M.D. Ph.D.

Background: Pain after tonsillectomy is notoriously difficult to control and is long-lasting. Most children undergo this surgical procedure as day patients; thus neither their postoperative use of analgesic medication or its degree of effectiveness is followed up by the treating institution.

Aims: To assess the duration and intensity of postoperative pain in healthy children aged 1–12 years undergoing tonsillectomy as a day surgery procedure.

Design: Prospective, observational study.

Methods: Patients are recruited in the day surgery PO-unit before or immediately after tonsillectomy. The children's pain and pain behaviour are scored before hospital discharge (3-5 h postoperatively) and by telephone interviews 1, 3, 7 and 14 days later. Pain is scored by the Faces Pain Scale (handed out to parents) and by the Chambers' POPMP (Postoperative Pain Measure for Parents). Use of analgetic medication is noted.

Current status: Master degree to be completed early in 2019. Publication in manuscript.

The Influences of Pretreatment with Morphine or Ketamine on Hemodynamic, Acid-base Status, Biochemical Markers of Brain Damage and Early Survival in Rats after Asphyxial Cardiac Arrest Kuklin V, Akhatov N^{1,2}, Kondratyev T³, Baigenzhin A², Karibekov T², Shaimardanova G², Konkayeva M¹, Barlow N, Tveita T³, Konkaev A¹, Dahl V.

¹Astana Medical University, Astana, Kazakhstan, ²National Scientific Medical Center, Astana, Kazakhstan, ³Anesthesia and Critical Care Research Group, UiT The Arctic University of Norway.

Background: In different animal models of acute hypoxia, blocking of opioid or NMDA receptors have cardio- and neuroprotective effects and increase survival.

Aim: To assess effects of morphine and ketamine on hemodynamics, acid-base status, biochemical markers of brain damage, and early survival after asphyxial cardiac arrest (ACA) in rats.

Methods: Wistar rats were randomly assigned to Morphine 5 mg/kg iv (n=14), Ketamine 40 mg/kg iv (n=14), or NaCl 0,9% iv (Control, n=14), given 10 min before ACA. Asphyxia was induced by 5-min blocking of tracheostoma. Resuscitation comprised epinephrine (0.02 mg/kg, iv), thoracic compressions (180/min) and mechanical ventilation (air, 80 breaths/min). Invasive mean arterial pressure (MAP) was recorded, and blood gas samples taken at baseline and 10 min post-resuscitation. Early survival was evaluated 20 min after ACA.

Results: Pre-treatment with ketamine reduced MAP before ACA and prevented pH disturbances 10 min post-resuscitation. Early survival was 13/14 in the ketamine group vs. 10/14 and 7/14 in the morphine and control groups, respectively (P=0.034). Biochemical markers of brain damage did not differ.

Conclusion: Pre-treatment with ketamine before asphyxial cardiac arrest improved early survival. **Current status:** Manuscripts to be submitted. Long-term survival and neurological status after ACA will be studied.

Master degree study being undertaken

Is the work of Intensive Care Nurses evidence-based? A Clinical Audit of Intensive Care Nurses' function and responsibility for daily sedation interruption Christine Hardie Arstad Bjerke, Kari Sygnestveit

Background: Implementation of daily sedation interruption (DSI) is part of the Intensive Care Nurse's function and responsibility. The DSI Guideline ensures the equal and best scientific basis for treatment of all patients who benefit from DSI. The consequences of not applying the DSI Guideline could be: prolonged respiratory treatment; prolonged length of stay in the intensive care unit; and risk of complications for the patient. (Kress et.al, 2000)

Aim: The aim of this master's thesis is to verify the application of the DSI Guideline through quality control. The study of the "Clinical Guideline for Daily Sedation Interruption" encompasses the Intensive Care Nurse's direct function and responsibility towards the patient through their treatment and rehabilitation, in order to prevent complications and improve the patient's functional level. This clinical audit is evidence-based and draws from academic and empirical research, as well as patient knowledge.

Research Question: Is the work of Intensive Care Nurses evidence-based? A Clinical Audit of Intensive Care Nurses' function and responsibility for daily sedation interruption.

Methodology: The methodology is comprised of a Clinical Audit with quantitative data collection. The Thesis is based on the model for quality development at the general (macro) level, and uses clinical audit as a method for evaluating the practice (at micro level).

Results: Data from January 2016 and December 2016 shows that DSI was completed on 11 of the enrolled 59 patients, which is equivalent to only 18,64%, out of the defined standard of 100%.

Conclusion: The conclusion is that intensive care nurses haven't done what they should do. DSI is not conducted according to the guideline. This is not in line with the recommendations from the research literature. This could lead to impaired quality of care and patient safety.

The Operating Department

Publications (peer reviewed)

Willassen ET, **Jacobsen ILS**, Tveiten S. Safe Surgery Checklist, Patient Safety, Teamwork, and Responsibility-Coequal Demands? A Focus Group Study. Glob Qual Nurs Res. 2018 Mar 28;5:2333393618764070.

Abstracts and posters

Willassen ET, **Jacobsen ILS**. Safe surgery checklist, patient safety, teamwork and responsibility – coequal demands? A focus group study. 2nd Global Conference on Nursing & Healthcare, London, August 2018.

Ongoing research projects

Safe Surgery Checklist, Patient safety, Teamwork and Responsibility – coequal demands?

Inger Lise Smith Jacobsen RN, ORN, M.Sc., Elin Thove Willassen RN, ORN, M.Sc. (Oslo Met), Sidsel Tveiten Professor RN, Ph.D. (Oslo Met)

Bacground: The use of World Health Organization's (WHO's) Safe Surgery checklist is an established practice worldwide and contributes toward ensuring patient safety and collaborative teamwork. Akershus University Hospital was one of few hospitals that piloted the Safe Surgery checklist in Norway in 2009. **Aim:** The aim of this study was to elucidate operating room nurses' and operating room nursing students' experiences and opinions about execution of and compliance with checklists.

Methods: We chose a qualitative design with semistructured focus group discussions. Qualitative content analysis was conducted.

Results: Two main themes were identified; the Safe Surgery checklists have varied influence on teamwork and patient safety, and taking responsibility for executing the checks on the Safe Surgery checklist entails practical and ethical challenges.

Conclusion: The experiences and opinions of operating room nurses and their students revealed differences of practices and attitudes toward checklist compliance and the intentions of checklist procedures. These differences are related to cultural and professional distances between team members and their understanding of the Safe Surgery checklists as a tool for patient safety.

Status: One article was published in 2018.

Department of Breast and Endocrine Surgery

University employees:	Research fellows:
	Katja Vetvik (resigned 2018)
	Berit Gravdehaug
	Joel Touma
	Nazli Bahrami

The ongoing research activity in the department consists of two PhD projects. In addition, three clinicians are active and productive. Our research projects occur in collaboration with Departments of Oncology and Pathology and are a part of the hospital's Translational Breast Cancer Research Group.

Our goal is to complete the first PhD project in 2019

and the second in 2021. Activity for 2018 in addition to the research projects include organization of a biobank for breast and blood samples. The samples are collected during surgery and stored for future studies. Professor Jürgen Geisler from the department of Oncology is responsible for this collection.

Publications (peer reviewed)

Bemanian V, Noone JC, Sauer T, Touma J, Vetvik K, Søderberg-Naucler C, Lindstrøm JC, Bukholm IR, Kristensen VN, Geisler J. Somatic EP300-G211S mutations are associated with overall somatic mutational patterns and breast cancer specific survival in triple-negative breast cancer. Breast Cancer Res Treat. 2018 Nov;172(2):339-351.

McNamara KM, Guestini F, Sauer T, Touma J, Bukholm IR, Lindstrøm JC, Sasano H, Geisler J. In breast cancer subtypes steroid sulfatase (STS) is associated with less aggressive tumour characteristics. Br J Cancer. 2018 May;118(9):1208-1216.

Sauer T, Doughty RW, Orszagh V and Gravdehaug B. (2018). The Cytopathologist in the Hospital - Based Fnac Clinic: US Image Guidance is Our New Tool to an Even Better Fnac Prac-tice. M J Cyto. 2018;2(1): 007.

Other publication

Vetvik KK; Touma J, Söderberg-Naucler C, Sauer T, Rahbar A, Geisler J. Lavt hormonreseptoruttrykk (ØR/ PGR) er koblet til høygradig cytomegalovirusinfeksjon hos pasienter med brystkreft. Best Practice Onkologi/ Hematologi 2018:1-11.

Abstracts and posters

Bahrami N, Sauer T, Loeng M, **Gravdehaug B**, **Engebretsen S**, Aljabri B, Bemanian V, Lindstrøm JC, Luders T, Kristensen VN, Geisler J. The NEO-LET-EXE trial: an intra-patient cross-over study to explore the lack of cross-resistance between steroidal and nonsteroidal aromatase inhibitors. San Antonio Breast Cancer Symposium, December 4-8.

Bahrami N, Chang G, Kanaya N, Sauer T, Loeng M, **Gravdehaug B**, Chen S, Geisler J. Total estrogenic activity during neoadjuvant therapy with letrozole and exemestane: An intra-patient cross-over comparison using the AroEr tri-screen. San Antonio Breast Cancer Symposium, December 4-8.

Touma JJ, Rahbar A, Davoudi B, Lindstrom JC, Sauer T, **Bukholm IRK**, **Vetvik KK**, Soderberg-Naucler C, Geisler J. The prognostic impact of human cytomegalovirus infection in breast cancer - evaluation of recurrence and survival. American Association for Cancer Research (AACR) Annual Meeting, Chicago, USA, April 14-18.

Vaske C, **Bahrami N**, Parulkar R, Newton Y, Sauer T, Loeng M, **Gravdehaug B**, Bemanian V, Luders T, Kristensen VN, Geisler J. Time-course DNA and RNA profiling of tumors from intra-patient cross-over trial of sequential use of aromatase inhibitors. San Antonio Breast Cancer Symposium, December 4-8.

Ongoing research projects

Human Cytomegolovirus infection in Breast Cancer

Joel Touma M.D., Ph.D. student, Katja Vetvik M.D. Ph.D., Jürgen Geisler Professor (Department of Oncology), Torill Sauer Professor (Department of Pathology), Cecilia Söderberg-Nauclér Professor, and Afsar Rahbar Associate Professor (Karolinska Institutet, Sweden).

Introduction: Proteins specific for Human Cytomegalovirus (HCMV) are expressed in primary breast cancers (BC) as well as in 94 % of sentinel lymph node metastases of BC and in 98 % of brain metastases in BC patients. HCMV specific protein expression is strictly confined to tumour cells in both primary breast tumours and BC metastases while surrounding stroma cells are consistently HCMV protein negative. Earlier studies indicate that targeting HCMV in patients with glioblastoma and potentially other HCMV-positive tumours may be a feasible treatment option to improve patient outcome.

Aims: Our main goals are to evaluate the role and significance of HCMV in BC pathogenesis and to better understand the mechanisms by which CMV is involved in development and progression of the disease. In addition, we aim to explore the oncogenic and metastatic properties of the HCMV in human triple negative breast cancer.

Material and Methods: Several cohorts consisting of patients treated for BC at Ahus are used to study the scale and impact of HCMV infection for the prognostic markers and disease characteristics in addition to in vitro studies investigating the potential disease mechanisms.

Current Status: Total of 2 studies are already published. In addition, there are 4 ongoing manuscripts. Joel Touma is currently writing his thesis.

An interdisciplinary translational approach for patients with locally advanced breast cancer

Nazli Bahrami M.D., Ph.D. student, Jürgen Geisler Professor (Department of Oncology), Torill Sauer Professor (Department of Pathology), Vessela Kristensen Professor (EpiGen).

Introduction: The aromatase inhibitor letrozole (Femar®/Femara®) and the aromatase inactivator exemestane (Aromasin®) are currently used as standard care for breast cancer in all the clinical settings of the disease. A lack of cross-resistance has been demonstrated, providing the rationale for a sequential use of these compounds in the setting of metastatic breast cancer.

Aims: To study and compare the direct intra- and anti-tumor effects, and potential mechanisms of adaptation and resistance of non-steroidal aromatase inhibitor letrozole and steroidal aromatase-inactivator exemestane.

Material and methods: NEOLETEXE is a randomized, open-label, intra-patient, cross-over trial. Selected patients with locally advanced breast cancer will be randomized to therapy with either letrozole or exemestane for 2 months followed by a cross-over to the alternative drug for another 2 months following (all in all 4 months) of presurgical treatment. Open tumor biopsies and blood samples will be used to perform a comprehensive exploration of the consequences of each drug therapy. The influence on plasma and tissue steroids will be compared. In addition, whole genome and exome sequencing, epigenetics and plasma analysis (cytokines, tumor DNA fragments etc.) will be performed *Current Status:* 55 out of planned 100 patients have been enrolled in the trial so far. The last patient is expected to enter the trial in Q4- 2020. 1 study have been submitted for peer review with Nazli Bahrami as the first author. In addition, there are 3 ongoing manuscripts

Granted Funding

Project	Source	Amount (NOK)
HCMV Infections in Breast Cancer Patients	Helse Sør-Øst 2016-2019	3,000,000
Jürgen Geisler, Katja Vetvik	2010-2019	
An interdisciplinary translational approach for patients with locally advanced breast cancer	Helse Sør-Øst 2018-2021	3,000,000
Jürgen Geisler (Medical division)		



Vascular and Thoracic Surgery Research Group

Head: Associate Professor Jarlis Wesche

University employee:	Research fellows:
Associate Professor Jarlis Wesche	Mads Tønnes Helgeland
	Ai Van Thuy Ho
	Other research staff:
	Inger Helene Nådland (Research coordinator)
	Anne Rigmor Holten (Research nurse)

At the Department of Vascular and Thoracic surgery there are nine consultants, three senior residents in vascular surgery, and five are residents in general surgery. One surgeon has a doctoral thesis (Jarlis Wesche). One Master of Science has a PhD (Inger Helene Nådland) and is a research coordinator (25% position in our department). One nurse in the outpatient clinic has a 10% position as research nurse (Anne Rigmor Holten).

During 2018 we have continued the ongoing projects on hyperhidrosis and thoracoscopic sympathectomy treatment, and on endovascular treatment of abdominal aneurysms. We are about to finish the Quality of Life assessment study (the VascuQoL-6 study) in patients with peripheral atherosclerotic occlusive disease in collaboration with Østfold Hospital, Kalnes. We continued our collaboration with researchers at Oslo University Hospital in a project on "the vulnerable carotid plaque". We are participating in a new national study on Abdominal aortic aneurisms and diabetes (Abandia study), which was initiated by the Research Board of the Norwegian Society for Vascular Surgery and is coordinated from Haukeland University Hospital.

Mads T. Helgeland, M.D., a senior resident, returned from Australia spring 2018 to continue his PhD project on aspects of endovascular treatment (EVAR) of abdominal aortic aneurysms.

Ai Van Thuy Ho, M.D., is a PhD candidate. She has continued her project on "Sweat activity and cardio-vascular responses at rest and during physiological strain in healthy subjects and in hyperhidrosis patients". She has submitted two papers for her thesis (one in collaboration with researchers at Oslo University Hospital) and will finish analyzing the data for a third paper this year and has plans to finish her thesis in a year.

Anne Sofie Larsen is a consultant interventional radiologist at Østfold Hospital, Kalnes. Nils Einar Kløw, Oslo University Hospital, has been main supervisor and Jarlis Wesche has been co-supervisor for her PhD project on patients with peripheral atherosclerotic occlusive disease, recruited from Kalnes and Ahus. She defended on June 12th 2018 her thesis "Occupational radiation and additional registry outcomes in endovascular treatment of peripheral arterial disease".

Publications

Eggum R. Rapport fra NorVATS/lungekirurgisk Symposium-Ahus. Kirurgen 4/2018.

Helgeland MT. Behandling av atherosklerose i underekstremitetene-kirurgens perspektiv. Kirurgen 4/2018.

Wesche J. Karkirurgi -hvor står vi? Temaleder. Kirurgen 4/2018.

Abstracts and posters

Yousefi P, **Wesche J**. Bedre behandling av pasienter med symptomatisk carotisstenose etter carotisstudien? The Norwegian Surgical Society Annual Meeting, Oslo, October 2018.

Kerai K, Tominich K, **Eggum R**. Ortosebehandling ("Bracing") av Pectus Carinatum. The Norwegian Surgical Society Annual Meeting, Oslo, October 2018.

Thoresen Å, **Reier-Nilsen F**, **Eggum R**. Kirurgisk behandling av multiple kostafracturer. Erfaringer fra Ahus i perioden 2016-2018. The Norwegian Surgical Society Annual Meeting, Oslo, October 2018.

Haukvik JT. Rumperte aortaaneurismer ved Ahus i perioden 2012-2017. Norsk Karkirurgisk Forenings Vintermøte, Trysil, March 2018.

Academic assignments

Invited lecturer

Suturer og proteser. Postgraduate course in vascular surgical techniques. DNLF/UIO 32426, February 2018. **Wesche J**.

Lungekirurgi/VATS. LHL sykehuset. Kurs i Lungesykdommer UIO, November 2018. Eggum R.

Arranged meetings

Arranged/Faculty NorVATS, Oslo 2018. Eggum R.

Course in infrainguinal vascular surgery for residents in Vascular Surgery, Akershus University Hospital, November 6-7:

Prevalens. Risikofaktorer. ECS/ESVS Klassifikasjon og guidelines. **Helgeland M**.

Indikasjon for behandling. Behandlingsstrategi. Evidens. Helgeland M.

Kliniske symptomer ved arteriell insufficiens. Haukvik JT.

Oppfølging. Etterkontroll. Norkar. Bysting S.

Undersøkelsesmetoder makro-og mikrosirkulasjon. Nådland IH.

Karskader i underekstremitetene. Eggum R.

Pseudoaneurismer. «Bomskudd» i lyske. Reier-Nilsen F.

Akutt ischemi. Wesche J.

Indikasjon for behandling. Etiske aspekter. Olsbø F.

TEA. Profundaplastikk. Ringstripping. Femoropopliteal bypass. **Seljeskog S**.

Sårbehandling. Diabetes-behandlingsstrategier. «Akutt foot-attack». Berglund T.

Amputasjoner. Østrem F.

Other academic activities

Main supervisor for Mads Tønnes Helgeland, University of Oslo. Wesche J.

Main supervisor for Ai Van Thuy Ho, Campus Ahus, University of Oslo. Wesche J.

Co-supervisor for Anne Sofie Larsen in her thesis "Occupational radiation and additional registry outcomes in endovascular treatment of peripheral arterial disease". Østfold Hospital, Kalnes/Campus Ahus, University of Oslo, June 12. **Wesche J**.

Memberships

Member of the Quality group of the Norwegian Association for Cardiothoracic Surgery. Eggum R.

Member of the Board, the Norwegian Society for thoracolaparascopy. **Eggum R**.

Member of the Board and Web master for the Norwegian Society for Vascular Surgery. Seljeskog S.

Member of the Board, the Norwegian Society for Vascular Surgery. **Skoe ØW**.

Councilor, UEMS Division and Board of Vascular Surgery. Wesche J.

Member of the Research Board of The Norwegian Society for Vascular Surgery. Wesche J.

Member of the Examination committee (M8), The Medical Faculty, University of Oslo. Wesche J.

Member of the National Committee for a Common final Digital Exam (M8) for all Medical Faculties in Norway. **Wesche J**.

Ongoing research projects

Sweat activity and cardiovascular function at rest and during physiological strain in healthy subjects Ai Van Thuy Ho, Ph.D. student, Karin Toska M.D. Ph.D., Jarlis Wesche Associate Professor M.D. Ph.D.

Background: There is currently a lack of knowledge on the dynamics of sweat activity in healthy subjects in the thermoneutral zone, and its association with cardiovascular dynamics. Increased knowledge in this area is important in order to improve diagnosis and treatment of patients with hyperhidrosis/excessive sweat production, which is generally considered to be a subjectively perceived disease.

Aim: To investigate sweat activity and cardiovascular variables/dynamics in response to minor physiological and mental stimuli, and the reproducibility of these responses.

Methods: Thirteen healthy subjects were included in the study. Sweat activity at five skin areas were measured continuously with a skin conductance method for 30 minutes, including in a resting supine and sitting positions, followed by a period performing deep inspirations, mental challenge and exposure to a sudden sound stimulus. Cardiovascular variables such as blood pressure, heart rate, skin perfusion and radial artery blood flow were also measured simultaneously with sweat activity. Each individual was exposed to two separate days of measurements with 1-18 days between the two experimental days.

Current status: Data-analysis is finished, and a manuscript has been written and will be resubmitted in 2019.

Improved diagnosis and treatment of hyperhidrosis

Ai Van Thuy Ho, Ph.D. student, Eirik Øvensen M.D., Karin Toska M.D. Ph.D. (Oslo University Hospital), Jarlis Wesche Associate Professor M.D. Ph.D. Co-workers: Erik Fosse Professor M.D. Ph.D. (Oslo University Hospital/University of Oslo), Odd Grenager M.D., Knut Kristiansen M.D.

Background: Approximately 50 to 100 patients annually are operated on for hyperhidrosis in Norway, most of them at Akershus University Hospital. Hyperhidrosis diagnosis is based on subjective patient information. A number of treatment options are available for these patients, including surgical treatment (thoracoscopic sympathectomy). Several possible side effects of the operation are reported and, in some cases, lead to serious problems for the patients. There is thus a strong need for objective measurements of hyperhidrosis and tools to facilitate patient selection for the various treatment options.

Aim: To objectively measure sweat excretion and sympathetic physiologic responses in patients with hyperhidrosis before and after thoracoscopic sympathectomy, as well as to investigate possible side effects and cardiovascular responses to such treatment.

Methods: Patients admitted to the Department for Vascular and Thoracic Surgery for hyperhidrosis have been included. A multichannel device (i.e., a SudoLogger) was used to measure sweat activity in five different skin areas (e.g., face, palm and dorsal hand, the back, and abdomen). Measurements were obtained over a total period of 30 minutes with patients in both the supine and sitting positions, followed by a period performing deep inspirations, mental challenge and exposure to a sudden loud sound.

Current status: Data have been analyzed, a paper is being written and will be submitted in 2019.

Endovascular treatment of abdominal aortic aneurysms (EVAR) in Norway, 2000–2013

Mads Tønnes Helgeland M.D., Ph.D. student, Jarlis Wesche Associate Professor M.D. Ph.D.

Background: Abdominal aortic aneurysm is an age-related disease and one of the 10 most frequent causes of death among men. Elective repair prior to rupture provides the mainstay of treatment and is usually instituted when the aneurysm diameter reaches 55 mm or more. Since its introduction in Norway in 1995, the use of endovascular treatment of abdominal aneurysms (EVAR) has increased rapidly and now constitutes more than half of the repairs performed worldwide. For patients with aneurysm anatomy compatible with this treatment modality, EVAR provides less periprocedural morbidity and mortality, though strong evidence of long-term benefits is lacking so far.

Aim: To investigate the outcome (i.e., morbidity, 30-day mortality, survival, and secondary procedures) following EVAR in Norway in the period 2000–2013. We limit our analysis to the period following 2000, when the currently used second-generation endografts were introduced. We will investigate to what extent EVAR is used in Norway, in elderly patients, if there are regional and sex differences, and whether our practice differs from neighboring countries.

Methods: A registry study will be performed in which data are provided by the Norwegian Vascular Surgery Registry (NORKAR) and its local registries are linked to Norway's National Patient Registry (NPR) and Cause of Death Registry (DÅR). The Regional Ethics Committee has approved the study and its use of the registries.

Current status: Data from all registries were received late 2016. There has been extensive work to improve the quality of the datasets. Data analyses is ongoing and results are being analyzed and a paper will be written 2019.

Validation of a disease-specific quality of life questionnaire (VascuQoL-6) for patients with peripheral occlusive arterial disease (PAOD) in a Norwegian population

Anne Sofie Larsen M.D., Ph.D. student (Østfold Hospital, Kalnes), Camilla Larsen M.D., Inger H. Nådland M.Sc. Ph.D., Anne Rigmor Holten R.N., Jarlis Wesche Associate Professor M.D. Ph.D.

Background: Peripheral arterial occlusive disease may substantially impact the daily activities of patients with this condition. Therapy options include conservative, endovascular and open surgical treatment. It has been suggested that patient reported outcome measures such as disease-specific quality-of-life (QoL)-questionnaire should be used to measure the effect of treatment, in addition to various clinical parameters. The VascuQoL-6 is a vascular QoL-questionnaire. It is a short version of the English VascuQoL-25, and the questionnaire in Norwegian is adapted from a Swedish version.

Aim: To evaluate the VascuQol-6 questionnaire in a Norwegian population by testing against a Norwegian version of SF-36, a questionnaire for health-related QoL, as well as to evaluate results against clinical results as ankle-brachial index (ABI) and walking distance (i.e., claudication distance).

Methods: 171 patients admitted to the outpatient/inpatient clinics of Akershus University Hospital and Østfold Hospital, Kalnes due to PAOD, all of whom are claudicants or patients with chronic critical limb ischemia, have been included. Patients have completed both questionnaires. Background data on

medication, comorbidity, and tobacco smoking will be recorded as well as measurements of ABI and treadmill walking distance and status of the arteries by MR/CT angiography.

Current status: The first paper was published October 2016, and the second paper was published in 2017. Together with a previous paper on intervention for PAOD, these 2 papers comprise the PhD thesis of Anne Sofie Larsen that was defended June 12th 2018. Data for a third paper has been analyzed, a paper is written and will be submitted in 2019.

The validated Vascuquol-6 questionnaire has thereafter been implemented and is now a part of the Norwegian Vascular Registry (NORKAR).

The Norwegian Carotid Study

We have been participating in a national study on carotid surgery initiated by the Research Board of Vascular Surgery (Unikard).

Synnøve Seljeskog M.D., Jarlis Wesche Associate Professor M.D. Ph.D.

The paper was published in EJVES 2017, and showed that time from symptomatic TIA/minor stroke to carotid surgery is too long. There has been extensive work from NKKF and the Research Board of NKKF towards the Health authorities to implement this knowledge to improve the quality of such treatment on a national basis and especially to be implemented in the coming guidelines for such patients (pakkeforløp for slagpasienter).

There are also plans to apply for a continuation of the project.

The vulnerable plaque

We have been collaborating with researchers at the Department of Neurology, Nuclear medicine, Physics, and Thoracic Surgery (Oslo University Hospital) in a study on "the vulnerable carotid plaque". K Skagen M.D., K Johnsrud M.D., K Evensen M.D., H Scott M.D. Ph.D., K Krohg-Sørensen M.D. Ph.D., F Reier-Nilsen M.D., A Skretting Ph.D., JG Fjeld M.D. Ph.D., M Skjelland M.D. Ph.D., D Russell M.D. Ph.D., J Wesche Associate Professor M.D. Ph.D.

Background: Thrombo-embolic strokes due to atherosclerotic plaques at the carotid bifurcation are effectively preventable by carotid endarterectomy. In current clinical practice patient selection for carotid endarterectomy is based on the severity of luminal stenosis. However, there is increasing evidence that the degree stenosis alone is not the best predictor of stroke risk. Plaque inflammation is thought to be an important marker of plaque vulnerability and increased stroke risk. There is therefore growing interest in imaging inflammation and metabolic activity within the atherosclerotic plaques using 2-deoxy-2- [18F] fluoro-D-glucose (18F-FDG) positron emission tomography/computed tomography (PET/CT).

Aim: The aim of this study was to assess the level of agreement between 18F-FDG uptake, cerebrovascular symptoms, plaque ultrasound echogenicity and histological assessments of plaque inflammation.

Methods: Thirty-six consecutive patients with ≥70% carotid stenosis scheduled for carotid endarterectomy were included. Plaques were defined as symptomatic when associated with ipsilateral cerebral ischemic symptoms within 30 days prior to inclusion. All patients underwent a clinical neurological examination, Colour Duplex ultrasound, ¹8F-FDG PET/CT and blood tests less than 24 hours prior to endarterectomy. Plaques were assessed histologically following endarterectomy with regard to the amount of inflammation. The level of agreement between ¹8F-FDG uptake quantified by maximum standardized uptake values (Mean SUVmax and SUVmax) and target-to-background ratio (TBR), symptoms, plaque echolucency on ultrasound, and histological evidence of inflammation were assessed.

We have also started preparation for new related projects on the relationship between the vulnerable carotid plaque and the role of oral and gut bacteria, and will start inclusion of patients spring 2018. *Current status:* Papers were published in 2015 and 2016. Inclusion of patients for the gut and oral bacteria study started fall 2018 and is ongoing.



Urology Research Group *Head: Associate Professor Stig Müller*

University employee:	Research fellows:
Associate Professor Stig Müller	Karol Axcrona
	Anja Løvvik
	Tor Erik Sand
	Manuela Estop-Garanto
	Frode Nilsen

In 2018, Enhanced Recovery after Surgery (ERAS) has still been a research focus for our research group. The continous work on our prospective database has shown a reduction in length of stay and quicker recovery after cystectomy. We plan to develop an own database focussing on ERAS items that still remain a challenge in the patient pathway.

We have also focussed on the diagnostic pathway for prostate cancer patients. We have evaluated the reproducibility of multiparametric MRI and are planning several projects in this area. Our biobank of renal tumors is now utilized in a very promising study in cooperation with the Department of Oncology and EpiGen.

Publications (peer reviewed)

Aas K, Fosså SD, Kvåle R, Møller B, Myklebust TÅ, Vlatkovic L, **Müller S**, Berge V. Is time from diagnosis to radical prostatectomy associated with oncological outcomes? World J Urol. 2018 Nov 27. Epub ahead of print.

Gislefoss RE, Stenehjem JS, Hektoen HH, Andreassen BK, Langseth H, **Axcrona K**, Weiderpass E, Mondul A, Robsahm TE. Vitamin D, obesity and leptin in relation to bladder cancer incidence and survival: prospective protocol study. BMJ Open. 2018 Mar 30;8(3):e019309.

Løvf M, Zhao S, Axcrona U, Johannessen B, Bakken AC, Carm KT, Hoff AM, Myklebost O, Meza-Zepeda LA, Lie AK, **Axcrona K**, Lothe RA, Skotheim RI. Multifocal Primary Prostate Cancer Exhibits High Degree of Genomic Heterogeneity. Eur Urol. 2019 Mar;75(3):498-505. Epub 2018 Sep 1.

Müller S, Lilleaasen G, Sand TE, Løfsgaard L, Estop-Garanto M, Helgø D, Sund P, Mygland V. Poor reproducibility of PIRADS score in two multiparametric MRIs before biopsy in men with elevated PSA. World J Urol. 2018 May;36(5):687-691.

Mikropoulos C, Hutten Selkirk CG, Saya S, Bancroft E, Vertosick E, Dadaev T, Brendler C, Page E, Dias A, Evans DG, Rothwell J, Maehle L, Axcrona K, Richardson K, Eccles D, Jensen T, Osther PJ, van Asperen CJ, Vasen H, Kiemeney LA, Ringelberg J, Cybulski C, Wokolorczyk D, Hart R, Glover W, Lam J, Taylor L, Salinas M, Feliubadaló L, Oldenburg R, Cremers R, Verhaegh G, van Zelst-Stams WA, Oosterwijk JC, Cook J, Rosario DJ, Buys SS, Conner T, Domchek S, Powers J, Ausems MGEM, Teixeira MR, Maia S, Izatt L, Schmutzler R, Rhiem K, Foulkes WD, Boshari T, Davidson R, Ruijs M, Helderman-van den Enden ATJM, Andrews L, Walker L, Snape K, Henderson A, Jobson I, Lindeman GJ, Liljegren A, Harris M, Adank MA, Kirk J, Taylor A, Susman R, Chen-Shtoyerman R, Pachter N, Spigelman A, Side L, Zgajnar J, Mora J, Brewer C, Gadea N, Brady AF, Gallagher D, van Os T, Donaldson A, Stefansdottir V, Barwell J, James PA, Murphy D, Friedman E, Nicolai N, Greenhalgh L, Obeid E, Murthy V, Copakova L, McGrath J, Teo SH, Strom S, Kast K, Leongamornlert DA, Chamberlain A, Pope J, Newlin AC, Aaronson N, Ardern-Jones A, Bangma C, Castro E, Dearnaley D, Eyfjord J, Falconer A, Foster CS, Gronberg H, Hamdy FC, Johannsson O, Khoo V, Lubinski J, Grindedal EM, McKinley J, Shackleton K, Mitra AV, Moynihan C, Rennert G, Suri M, Tricker K; IMPACT study collaborators, Moss S, Kote-Jarai Z, Vickers A, Lilja H, Helfand BT, Eeles RA. Prostate-specific antigen velocity in a prospective prostate cancer screening study of men with genetic predisposition. Br J Cancer. 2018 Mar 20;118(6):e17. Epub 2018 Mar 6.

Abstracts and posters

Helgø D, Kravdal G, Moe MK. Forekomst av ulike typer nyrestein i en norsk populasjon og endringer over siste fire dekader. The Norwegian Surgical Society Annual Meeting, Oslo, October 2018.

Academic assignments

Opponent/member of adjudication committee

Opponent on the thesis: A population based study on Kidney Cancer in Norway (2008-13) - Aspects of biopsy use, surgical treatment and outcome. Karin Hjelle, University of Bergen, November 2. **Müller S**.

Invited lecturer

Any room for ERAS in other urological procedures? 6th ERAS World Congress, Stockholm, May 2018. **Müller S**.

mpMRI in Prostate Cancer – Quality and Reproducibility. Annual Meeting "Deutsche Gesellschaft für Urologie", Dresden, Germany, September 2018. **Müller S**.

Ongoing research projects

Reproducibility of multiparametric MRI in men with elevated PSA

Stig Müller Associate Professor M.D. Ph.D., Jonn Terje Geitung M.D., Clare Allen M.D. (University College Hospitals, London), Jonatan Engman M.D. (Skåne University Hospital, Malmø).

Background: Since january 2015, all men referred to our department due to elevated or other suspicion of prostate cancer undergo MRI. During the first 6 months, 126 patients were referred to another center for MR-targeted biopsies. Before these, a new MRI was performed at the other center.

Aims: Evaluate the level of agreement between two MRIs before biopsy.

Methods: The analysis of the MRI reports showed very poor level of agreement. The MRIs of the 126 patients will be reviewed in a blinded fashion by 3 independent radiologists. Collaboration with Skåne University Hospital, Malmø, and University College Hospital London.

Current status: Ongoing.

Predictors of renal function after partial nephrectomy

Veronica Elde M.D., Frode S. Nilsen M.D., Stig Müller Associate Professor M.D. Ph.D.

Background: Nephron-sparing surgery is recommended for all renal tumors up to 70 mm if technically feasible. We have a prospective database for all renal surgery.

Aims: Investigate the association of comorbidity and peroperative factors and postoperative renal function after partial nephrectomy.

Methods: Retrospective analysis of partial nephrectomies performed at our department 2012-2016. *Current status:* Completed, manuscript submitted.

Erectile Dysfunction and Urgency incontinence in the Normal Population (The Tromsø 7-study)

Stig Müller Associate Professor M.D. Ph.D., Anja Løvvik M.D., Erling Aarsæther Associate Professor M.D. Ph.D. (University Hospital North Norway), Hitendra Patel M.D. Ph.D. (University Hospital North Norway).

Background: Erectile dysfunction and Urgency Incontinence are common urological bothers and incidence data in Norway are lacking. Both erectile dysfunction and urgency incontinence are associated with other disease.

Aims: Investigate the incidence and association with other disease e.g. cardiovascular disease for erectile dysfunction and urgency incontinence.

Methods: In the seventh edition of the Tromsø Study, a large epidemiological study of Tromsø's population,

40000 subjects have been invited to participate. Standardaized questionnaires for erectile dysfunction and voiding problems were included in the study and will be analyzed with respect to demographical data and interactions with other symptoms and disease.

Current status: Data collection completed.

Molecular profiling of human renal cell cancer

Jan Oldenburg M.D. Ph.D., Glenny Cecilie Alfsen Associate Professor M.D. Ph.D., Jürgen Geisler Professor M.D. Ph.D., Daniel Heinrich M.D., Stig Müller Associate Professor M.D. Ph.D., Frode Nilsen M.D., Vahid Bemanian Ph.D., Katarina Puco M.D., Andliena Tahiri Ph.D.

Background: Metastatic Renal cell cancer (mRCC) portends a poor prognosis. Novel insights in basic tumor biology are urgently needed in order to improve treatment outcomes. Tumor kinases have become attractive targets for intervention and currently constitute the treatment basis of mRCC. This project is a collaboration between the Departments of Urology, Oncology, Pathology, Gene Technology and EPIGEN. Methods: Our department established a biobank for renal cancer in 2012. Using formaline-fixed paraffinembedded and/or fresh, frozen kidney biopsies from kidney tumors and normal kidney tissue, the project will utilize Tyrosin Kinome analysis, Next generation sequencing, Immune profiles of renal cancer and Virus infections in renal cancer.

Aims:

- 1: Corroboration of recently described different genotypes of clear-cell (cc) RCC.
- 2: Identification of pathogenetic driver lesions by comparing gene (sequence, expression, regulation) of normal, i.e. non malignant tissue, with malignant RCC from the same patient.
- 3: Assessment of the association between the kinome and gene: sequence, expression, regulation.

Current status: Ongoing.



Department of Palliative Medicine

University employee:

Olav Magnus Fredheim (NTNU)

Two of the eight senior consultants employed through 2018 (Siri Steine and Olav Fredheim) have research experience above PhD level. From January 2019 another senior consultant with PhD degree (Belal Aljabri) has been temporarily employed. One nurse (Mia Nordsveen) completed her master's degree in 2018.

From January 2014 the department has used 15-20% of a senior consultant position for research. This position has been filled by Olav Fredheim who also holds a position as professor of anaesthesiology and pain medicine at NTNU.

During 2018 one review paper with affiliation to the department was published. Three further papers

were accepted for publication and/or published online at the end of 2018. All the three latter papers were in level-2 publications. These papers will formally be reported in the annual report for 2019.

Until the autumn of 2017 only one of the staff was actively involved in research, primarily in research projects with external collaboration. During the autumn of 2017 two research projects based on data from the department of palliative medicine were initiated. A total of five of the physicians at the department are involved in these projects at a scientific level. The active involvement of more than half of the physicians in research was a milestone for the research in our department.

Publications (peer reviewed)

Fredheim O. Behandling av kreftsmerte hos pasienter i legemiddelassistert rehabilitering. Tidsskr Nor Laegeforen. 2018 Jan 22;138(2).

Ongoing and planned research projects

- Olav Fredheim is co-supervisor for one PhD-candidate performing clinical research on postanaesthetic fatigue at Sykehuset Telemark/UiO. This candidate is expected to defend his thesis in 2019. Olav Fredheim also supervises the projects of two master students at NTNU.
- Olav Fredheim conducts pharmacoepidemiological studies of analgesics in cooperation with National Institute of Public Health (FHI), NTNU and UiO. For pharmacoepidemiological research there is also cooperation with professor Per Sjøgrens' research group in Copenhagen.
- In 2017 we developed a protocol for a clinical randomized controlled study comparing intravenous and subcutaneous morphine for patient controlled analgesia in cancer pain. This protocol was used for application for Strategic research funding at AHUS, but in spite of high quality scores the project did not receive funding. We are investigating whether other sources of funding are possible.

Use of propofol for palliative sedation at Department of palliative medicine

Olav Fredheim M.D. Ph.D., Siri Steine M.D. Ph.D., Ingeborg Skulberg M.D., Morten Magelssen M.D. Ph.D. (Centre for medical Ethics, University of Oslo).

Study description: The study is a descriptive study of the clinical practice of performing palliative sedation with propofol at the department of palliative medicine. All patients having received this treatment during a four-year period were identified and included. The study has two focuses: clinical/pharmacological and decision-making/communication/ethics.

Status: Data collection for the study has been completed and a first draft of the paper has been prepare

Do not resuscitate orders and end of life decisions

Olav Fredheim Professor M.D. Ph.D., Siri Steine M.D. Ph.D., Torstein Michelet M.D., Hans van der Werff M.D.

Study description: The study is a descriptive study of the clinical practice regarding do-not-resuscitate orders and life prolonging treatments during the last days of life in patients dying at Akershus University Hospital. A death cohort of 600 patients will be studied. Focus will be on whether decisions not to start life-prolonging treatment are made at the time such treatments would be futile or whether such treatment limitations are not decided until the patient is dying.

Status: The study received NOK 50,000 from "publication money" at Surgical Division, Akershus University Hospital. Data collection has been completed and data analysis has started.

Pain classification in palliative cancer patients

Chronic non-malignant pain affects abourt 30% of the adult population, and is probably even more prevalent in palliative cancer patients. However, there is a lack of studies addressing the epidemiology and classification of non-tumor pain in palliative cancer patients. The lack of studies, probably leads to poor classification of pain in palliative cancer patients. Poor classification of pain, may lead to application of the wrong principles for pain treatment, i.e. application of the drug based principles for cancer pain when the cancer patient has chronic non-malignant pain. This project aims at performing a thorough pain evaluation and classification in outpatients referred to the department of palliative medicine.

Status: A protocol has been developed, and the project has received in January 2019 NOK 100,000 in funding from "publication money" at Surgical Division, Akershus University Hospital.



Research group for quality and patient safety Division of Surgery

Head: Anne Karin Lindahl

University employee:	Research fellows:
Professor II Anne Karin Lindahl	Hirut Mergarsa, Ethiopia (Saccade project, University of Oslo)
Professor II Vegard Dahl	Rebecka Normann (Lovisenberg diakonale høyskole)
Professor II Marie Ellstrøm-Engh	Mona Haugum (Norwegian Institute for Public Health)
Professor II Asbjørn Årøen	
Associate Professor Juha Silvola	
Associate Professor Jarlis Wesche	

Other members at Akershus University Hospital:

Ellen Catharina Deilkås	Health Services Research Unit
Astrid Marie Berg	Department of Anaesthesia and Intensive care
Hege Krippendorff	Department of Anaesthesia and Intensive care
Pernille Schjønsby	Department of Obstetrics and Gynecology
Anne Werner	Health Services Research Unit
Morten Glasø	Department of Collaboration and Health Promotion
Gunnvor Marum	Department of Quality and Patient Safety
Marie Brudvik	Department of Quality and Patient Safety
Marit Kise	Medicine and Health Sciences
Lena Bjerknes Larsen	Surgical Division

Members outside of Akershus University Hospital:

Researcher Anne-Kari Johannessen	Oslo Metropolitan University
Associate Professor Lisbeth Thoresen	Department of Medical Ethics, University of Oslo
Researcher Jon Helgeland	Norwegian Institute for Public Health
Head for department Øyvind Andresen Bjertnæs	Norwegian Institute for Public Health
Knut Magne Augestad	Helse Nord, and Department of Surgery, Columbia Presbyterian Hospital, New York, USA
Researcher Olaf Holmboe	Norwegian Institute for Public Health
Researcher Katrine Skyrud	Norwegian Institute for Public Health
Head of department Øystein Flesland	Norwegian Directorate of health

The research group was established late in 2018. There is great interest in research for quality and patient safety across the hospital, and the research group is therefore multidisciplinary. There are several ongoing projects, regarding Surgical global trigger tool, effects of emergency outreach teams,

quality indicators for surgery, patient experiences especially with surgical services, and patient safety in maternity wards in Ethiopia. Cooperation with researchers within Akershus University Hospital, University of Oslo and Oslo Metropolitan University, as well as external partners, will develop further.

Publications (peer reviewed)

Naylor AR, Ricco JB, de Borst GJ, Debus S, de Haro J, Halliday A, Hamilton G, Kakisis J, Kakkos S, Lepidi S, Markus HS, McCabe DJ, Roy J, Sillesen H, van den Berg JC, Vermassen F, Esvs Guidelines Committee, Kolh P, Chakfe N, Hinchliffe RJ, Koncar I, Lindholt JS, Vega de Ceniga M, Verzini F, Esvs Guideline Reviewers, Archie J, Bellmunt S, Chaudhuri A, Koelemay M, **Lindahl AK**, Padberg F, Venermo M. Editor's Choice - Management of Atherosclerotic Carotid and Vertebral Artery Disease: 2017 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg. 2018 Jan;55(1):3-81.

Abstracts and posters

Holmboe O, Bjertnaes \emptyset , **Lindahl AK**. Patient-reported incidents in hospital: do scores for surgical and non-surgical patients differ? Results from a national survey. Presented at the 5th Nordic conference on research for quality and patient safety, Copenhagen, August 30-31.



