RESEARCH ACTIVITY

at the Division of Ear, Nose and Throat Diseases

2021

Karolinska Institutet

KAROLINSKA Universitetssjukhuset

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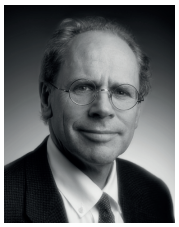

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Eva Munck Wikland, Adjunct Professor
Pär Stjärne, Adjunct Professor
Claus Bachert, Affiliated Professor
Antti Mäkitie, Affiliated Professor
Sten Hellström, Senior Professor
Dan Bagger-Sjöbäck, Professor Emeritus
Ulf Rosenhall, Professor Emeritus
Bengt Carlsöö, Professor Emeritus

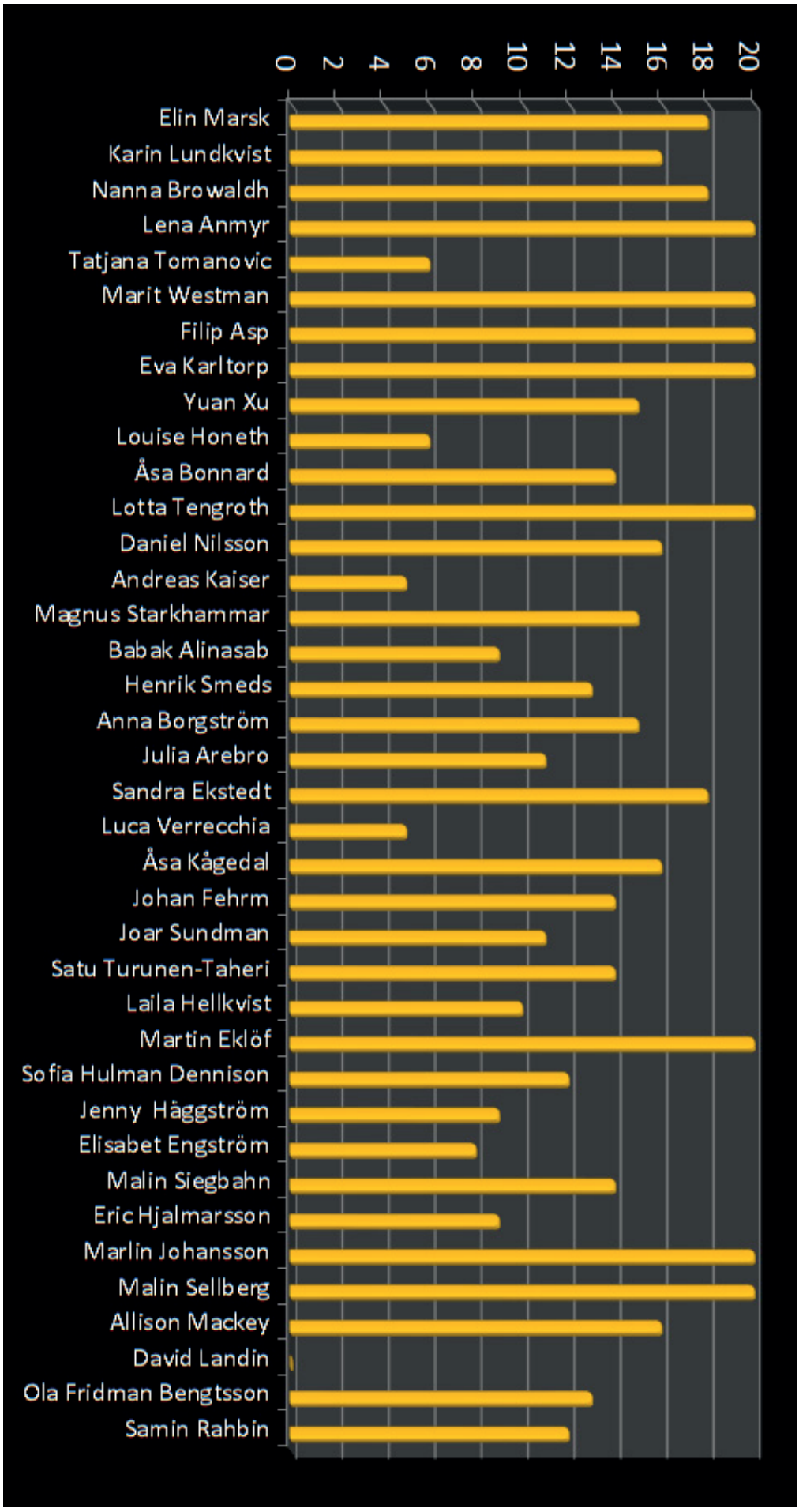
Docents

Erik Berninger
Maoli Duan
Lalle Hammarstedt Nordenvall
Linda Marklund
Riitta Möller
Inger Uhlén

Dissertations / Half time seminars 2021

Date		Name	Title
2021-03-26	Dissertation	Elisabet Engström	Neurophysiological conditions for hearing in children using hearing aids or cochlear implants: an intervention and follow-up study
2021-05-07	Dissertation	Sofia Hultman Dennison	Complications due to acute rhinosinusitis in children
2021-06-04	Dissertation	Malin Wendt	Optimizing treatment: tumor markers and sclerotherapy in head and neck lesions
2021-10-22	Half time	Samin Rahbin	Zygomaticomaxillary Complex (ZMC) Fractures - Aspects of Diagnostic Methods, Treatment and Complications

Participation at halftime seminars during 2010-10 to 2021-12-31



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Bachert, Claus ..... 14.
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Holmström, Mats ..... 42.
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Jonstam, Karin ..... 44.
Kaiser, Andreas ..... 45.
Kumlien Georén, Susanna ..... 46.
Kågedal, Åsa ..... 48.
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Olsson, Petter ..... 55.
Palmgren, Björn ..... 56.
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Stjärne, Pär ..... 58.
Sundman, Joar ..... 60.
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Verrecchia, Luca ..... 67.
von Becherath, Mathias ..... 69.
Wales, Jeremy ..... 70.
Wendt, Malin ..... 71.

Affiliated not presented in this book:
Baumgartner, Wolf-Dieter; Hultman Dennison, Sofia; Karltorp, Eva

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I. Mapping of Sinonasal cancer in Sweden.
Treatment for sinonasal malignancies, like other malignancies includes surgery, radiotherapy and chemotherapy of which surgery is the most central. What combination treatment that is most effective, however, is disputed.
Recent publications of treatment combinations has found that multimodal treatment was superior, as measured by survival. Herein there is a knowledge gap that this project will attempt to address.
The aim of this ongoing project is to both map the incidence, prevalence and relative survival of patients with sinonasal cancer. Different treatment modalities will be compared and evaluated in relation to long term survival and recurrence.

II. Isolated Orbital Floor Fractures – To operate or not to operate.
A significant BOF needs surgical treatment otherwise it may lead to double vision and aesthetic deformities such as sunken eye. It is highly important to differentiate which patients need to be operated on or which do not.
In the on going projects below, we aim to identify which patients with BOF need an operation and which do not require an operation to prevent functional and aesthetic disorders.
1. Controlled randomized studies on patients with BOF with inferior BOF with a herniation > 1mL.
2. Prospective cohort study on isolated medial BOF.

III. Zygomaticomaxillary Complex Fractures: aspects of diagnostic methods, treatment and sequelae
In zygomaticomaxillary Complex fractures, the surgeons' individual training, experience and preference influences the treatment and not systematic evidence, even though earlier studies on surgical treatment have shown that the choice of treatment have an impact on surgical outcome. As the degree and success of the reconstruction of a fractured zygoma is assessed by evaluating the contralateral, non-fractured side, the unfractured zygoma is used as a reference when planning for surgery.

In this ongoing project we aim to:
-Evaluate the long-term results of patients with ZMC fractures.
-Detect correlations between complications and to evaluate the overall management of ZMC fractures.
-To introduce a reliable treatment algorithm based on evidence based medicine.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Samin Rahbin	

Ethical permit No.

2009/331-31	2018/302-31	2019-04287-1		

Publications 2019, 2020, 2021

1. Loss of Malar Bags in Lower Eyelid In Orbital Blow Out Fracture Reconstruction Following Pre- or Retro-septal Transconjunctival Incision. Craniomaxillofacial Trauma Reconstruction. J Craniofac Surg. 2019. Accepted.

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Investigating the role of extracellular vesicle-associated miR-142 in the tumor micro-environment

Oral squamous cell carcinoma (OSCC) remains an under-studied and significant global cancer killer; dismal survival rates have not changed in decades. A better understanding of the molecular basis of OSCC progression and metastasis is needed to provide new treatment/disease management options. We aim to find new strategies in diagnosing and treting this diseaes through stydying fibroblasts in the tumor microenvironment and signalling of miRNA in extracellular vesicles

Immune signalling in the upper and lower airways in patients with COPD and chronic bronchitis

WHO have stated COPD to be the third most common cause of death worldwide. In Sweden, up to 700,000 people suffer from COPD generating a yearly coast of 15 billion SEK. Todays methods for diagnosing, treating and monotoring COPD and chronic bronchitis are insufficient. It is well known that smokers with COPD and/or chronic bronchitis suffer from repeated airway infections but the underlying mechanisms are unknown. We aim to investigate IL-26, IL-17 and other markers from Th17 helper cells in the upper airway in a attempt to see if COPD and chronic bronchitis can be monitored through markers in the upper airways.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

H15-02913 (UBC REB)				

Publications 2019, 2020,2021

1. Arebro J, Palmgren B. Post-surgical pyoderma gangrenosum and flap necrosis in a head and neck cancer patient following neck dissection. Clin Case Rep. 2020;00:1–5
2. Khan A, Huynh TMT, Vandeplas G, Joish VN, Mannent LP, Tomassen P, van Zele T, Cardell LO, Arebro J, Olze H, Forster-Ruhrmann U, Kowalski ML, Olszewska-Ziaber A, Fokkens W, van Drunen C, Mullol J, Alobid I, Hellings PW, Hox V, Toskala E, Scadding G, Lund V, Bachert C. The GALEN rhinosinusitis cohort: chronic rhinosinusitis with nasal polyps affects health-related quality of life. Rhinology. 2019 Oct 1;57(5):343-351.
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Spatial Hearing and auditory plasticity - Effects of Hearing Loss and intervention

Hearing with two ears (binaural hearing) facilitates recognition of speech in challenging listening conditions, spatial hearing, and sound localization. Horizontal sound localization is an ideal ability for the study of deficits in binaural hearing, since high accuracy is dependent on precise temporal processing and interaural comparison of acoustic signals. Hearing loss has a negative impact on sound localization, also in mild cases, for example unilateral hearing loss. We study the effects of congenital and aquired hearing loss and various interventions (e.g. auditory implants and hearing aids) on sound localization from as early as 6 months of age, using a rapid and objective technique. Our innovative method measures latency and accuracy of eye-movements towards auditory events, as an index of localization ability. The ultimate goal is to alleviate the negative impact of hearing impairment, and increase our understanding of how impaired spatial hearing affects humans, specifically during critial periods of development.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Fatima Moumèn Denanto	Marlin Johansson
	Malin Siegbahn
	Hanna Josefsson

Ethical permit No.

2016/414-16 (Gothenburg)	2015/1878-31/2	2013/4:2	2013/2248-3	2019-04696

Publications 2019, 2020, 2021

1. Johansson, M., Asp, F., Berninger, E. 2019. Children With Congenital Unilateral Sensorineural Hearing Loss: Effects of Late Hearing Aid Amplification—A Pilot Study, Ear Hear, Early Online
2. Videhult Pierre, P., Eklof, M., Smeds, H., & Asp, F. (2019). Cochlear Implantation with the CI512 and CI532 Precurved Electrode Arrays: One-Year Speech Recognition and Intraoperative Thresholds of Electrically Evoked Compound Action Potentials. Audiol Neurootol, 24(6), 299-308. https://doi.org/10.1159/000504592
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Innovative treatment approaches in CRSwNP

Chronic rhinosinusitis (CRS) with (CRSwNP) is in 85% of cases characterized by an eosinophilic type 2 inflammation. With the severity of the type 2 inflammation in CRSwNP patients, asthma comorbidity and relapse of disease become more frequent. In recent years, monoclonal antibodies (mAbs) directed towards the type 2 inflammatory response have been demonstrated to be efficacious in CRSwNP. The focus of the last year was on the granulocytes and their roles in CRSwNP as well as CRSsNP, identifying important interactions between them and inflammatory conditions. In 2021, several Phase 3 trials with biologics have been published and interpreted, and compared to surgery or each other. These trials and clinical pathway papers based on them help to define the possible responders among the CRSwNP patients, identify criteria for inclusion and for stopping rules, and recommendations for the duration of the treatments. Novel treatment strategies include dupilumab, a mAb directed to the IL-4 Receptor alpha, omalizumab, an anti-IgE mab, and mepolizumab, an anti-IL5 mab targeting the eosinophils in CRSwNP disease. Although all these approaches show clinical efficacy, the magnitudes of the effects and the responder rates are different and need to be further analyzed to increase patient selection and monitoring possibilities. Also Reboot surgery, removing the mucosal lining from the sinuses, works on cytokine expression in the newly growing mucosa, and yielded better result vs. conventional surgery up to 2 years after surgery, also allowing many patient to regain smell. At the same time, now approaches including single cell sequencing and other -omincs already now starts to revolutionize our understanding of the complex disease pathophysiology, promising a real step forward in the knowledge, but possibly also in the therapy of chronic airway diseases in the near future.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

Publications 2019, 2020, 2021

1. Jonstam K, Alsharif S, Bogaert S, Suchonos N, Holtappels G, Jae-Hyun Park J, Bachert C. Extent of inflammation in severe nasal polyposis and effect of sinus surgery on inflammation. Allergy 2021;76(3):933-936
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8. Bachert C, Maurer M, Palomares O, Busse WW. What is the contribution of IgE to nasal polyposis? J Allergy Clin Immunol 2021 Mar 20:S0091-6749(21)00472-3
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ENT-cancer

On going projects:

- Prospective study: Use of ancor in extirpation of non-palpable lymphnodes and cysts in the neck.
- The risk for regional metastasis in patients with gingival cancer in realation to tumor size, localization (maxilla/mandible), T-class and histopathology.
- PILGRIM-Microbiota study of head- and neck cancer patients with prophylactic intravenous antibiotics during/after surgery.
- Sentinelnode assisted neck dissektion in N+ oral cancer patients. Prevalence of occult metastases.

Future project:

- Prospective study: Can HPV be used as a predictor in differentiating between cystic metastasis and lateral branchial cleft cyst?
-

Sex hormones & hearing

- Longitudinal prospective study of the hearing in women with breast cancer treated with anti-Estrogens.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

2020-00448	2021-00697	2021-01265		

Publications 2019, 2020, 2021

1. Hammarstedt-Nordenvall L, Evelina J, Beckerath M, Tani E, Nordemar S, Bark R. Prevalence of cystic metastases in a consecutive cohort of surgically removed branchial cleft cysts. ACTA Otolaryngol. 2021. DOI:10.1080/00016489.2021.2016951.
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3. Vujasinovic M, Öst Å, Bark R, Brismar T, Hynning B, Lindblad M, Elbe P. Metastasis to the gastrostomy site in a patient with pharynx cancer after percutaneous endoscopic gastrostomy: a case report. Scand J Gastroenterol. 2020 Aug;55(8):1002-1004.
4. Bonnard Å, Bark R, Hederstierna C. Clinical update on sensorineural hearing loss in Turner syndrome and the X-chromosome. Am J Med Genet C Semin Med Genet. 2019 Mar;181(1):18-24.

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Digital Twins for personalised medicine

One of the greatest health care problems today is that many patients do not respond to drug treatment. This reflects the complexity of the human body, which consists of trillions of cells, each of which may express thousands of genes, in different combinations, at different time points, before and during disease. There is a wide gap between this complexity and modern health care. The Swedish Digital Twin Consortium (sdtc.se) proposes that this gap can be bridged by digital twins of individual patients. Each twin is computationally treated (computreated) with thousands of drugs, in order to find the best treatment for the patient The twins are constructed and treated by applying network tools and artificial intelligence (AI) to single cell RNA-seq (scRNA-seq) and clinical data from each patient. We have shown clinical feasibility by treating a mouse model of arthritis, and diagnostic studies of multiple diseases (all references are found in sdtc.se). Recent case reports support the clinical applicability of scRNA-guided treatment of a patients that do not respond th that did not respond to conventional treatment. However, that treatment was based on empirical analyses of the data. By contrast, our digital twin strategy is based on systematic prioritization of drugs and computreatment of the twins with those drugs, before actually treating individual patients. We are now planning to show clinical feasibility by treating individual patients. The ultimate aim is that each healthy individual should have her/his digital twin for predictive, preventive, personalised and participatory medicine

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Martin Smelik	Simon Söderholm
Samuel Schäfer	
Sandra Lilja	
Yelin Zhao	

Ethical permit No.

Publications 2019, 2020, 2021

1. Bensberg M, Rundquist O, Selimovic A, Benson M, Gustafsson M, Nestor C. TET2 as a tumor suppressor and therapeutic target in T-cell acute lymphoblastic leukemia. PNAS 2021 (in press)
2. Hellberg S, Benson M, Gustafsson M, Jenmalm M, Nestor C, Ernerudh J. CD4+ T-cell methylation changes during pregnancy significantly correlate with disease-associated methylation changes in autoimmune diseases. Epigenetics 2021 (in press)
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Hearing impairment in newborns. New objective technologies and intervention strategies during a sensitive period of development to improve subsequent communication

Our research project aims at very early diagnosis and intervention to reduce or reverse disability and thus improve the communication capacity of the hearing-impaired child. The long-term goal is to find the causes and mechanisms behind various nonsyndromic congenital sensorineural hearing losses (SNHL) and to develop future treatment options. The main research directions are:

A. Causes and mechanisms behind nonsyndromic congenital SNHL
B. Impact of early intervention during a critical period of development
C. Sound localization as a clinical tool
D. Rapid and objective ABR technique for newborns and infants

Overall aims of the research directions are: A.) To identify and precisely diagnose various forms of congenital SNHL, as determined at the level of specific anatomical structures down to the molecular level. To identify and develop future treatment options on the basis of highly specific diagnoses, as determined at birth. B.) To study the impact of relevant auditory stimulation during a sensitive period of development, and to identify the extent of that period. C.) To study the relationship between behavioural development and maturation of the central auditory pathways and the physiology of binaural interaction at the brainstem level. Development of a new rapid noninvasive and objective test for e.g. central auditory processing dysfunction from 6 months of age. Evaluation of various intervention/care strategies. D.) To develop a rapid, valid, and reliable electrophysiological technique applicable in newborns and infants for diagnostics and as a basis for fine-tuning of e.g. nonlinear hearing aids.

Part of the studies will be supervised by PhD Filip Asp and Senior Professor Sten Hellström. All the studies will be performed at the recently established Scientific Center for Advanced Pediatric Audiology (SCAPA), Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Marlin Johansson	

Ethical permit No.

2012/494-31/1; 2018/1500-31 (Approved addendum, 2020-06-10)	2014/1162-31/1; 2015/1878-21/2	2012/189-31/3; 2013/2248-3	2013/104-31/4; 2017/293-31/4	2008/1961-31; 2019-03826

Publications 2019, 2020, 2021

1. Eklöf M, Asp F, Berninger E. Sound localization latency in normal hearing and simulated unilateral hearing loss. Hear Res. 2020;395:108011.(doi):10.1016/j.heares.2020.108011. Epub 2020 Jun 11.
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3. Johansson M, Olofsson Å, Berninger E. Twin study of neonatal transient-evoked otoacoustic emissions. Hear Res. 2020;398:108108.(doi):10.1016/j.heares.2020.108108. Epub 2020 Oct 28.
4. Marlin Johansson, Åke Olofsson, Erik Berninger. Twin study of neonatal transient-evoked otoacoustic emissions, 2021 MidWinter Research Meeting, Association for Research in Otolaryngology, Virtual Meeting, USA, February 20-24, 2021.

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Cholesteatoma in Sweden and Results from the Swedish Quality Registry of Ear Surgery, SwedEar

1. Surgery for Cholesteatoma is a quite common ear procedure. The disease is accompanied with risks for severe side effects as meningitis, intracranial abscess, sinus thrombosis, hearing loss, facial palsy and dizziness if not treated. Unfortunately, the surgical procedure also have side effects due to the need for extensive surgery to eradicate the disease.
In this nationwide study, the Swedish Patient Registry will be used to map cholesteatoma surgery in Sweden in regard to incidence and prevalence, risks with surgery, factors increasing risk for disease and recurrency of disease. A combination with the Swedish Patient Registry and The Swedish Multiple Generation Register will be used to identify the frequency of familiar cholesteatoma. This sub study will be followed by a genetic study regarding families in Stockholm County with multiple family members with cholesteatoma. A longside with this, a regional follow-up study will be performed in regard to hearing, balance and quality of life after cholestatoma surgery.

2. The Swedish Quality Registry of Ear Surgery, SwedEar, is a nationwide registry collecting pre- and post-operative data in regard to ear surgery for all types of chronic otitis including cholesteatoma. Several papers based on this registry has been published showing the outcome of Myringoplasty and the risk for complications regarding tinnitus and taste disturbances related to surgery. New studies regarding the hearing results, patient satisfaction and complications after Ossiculoplasty are ongoing.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Agnes Modée	Sara Olaison, Örebro Universitetssjukhus Kvalitetsregisterkopplat projekt om ossikuloplastik

Ethical permit No.

2014/2203-31/4	2019-05190	2020-00245	2021-05727-02	2020-05935

Publications 2019, 2020, 2021

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Evaluation and surgical treatment of children with tonsil hypertrophy and sleep disordered breathing

Research in the field of pediatric obstructive sleep apnea,with evaluation of diagnostic tools and of surgical treatment. The focus has been on tonsil surgery and a randomized clinical trial comparing tonsillectomy and tonsillotomy in children with OSA. Data for long-term follow-up from this trial are now being analyzed

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
	Isabella Sjölander

Ethical permit No.

Publications 2019, 2020, 2021

1. Borgström A, Nerfeldt P, Friberg D; Postoperative pain and bleeding after adenotonsillectomy vs adenotonsillotomy in pediatric obstructive sleep apnea: an RCT; European Archives of Oto-Rhino-Laryngology, 2019 Aug (3), 1-8
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Effects on Cardiovascular Parameters in Children with Severe Obstructive Sleep Apnea before and after Adenotonsillectomy

Obstructive sleep apnea (OSA) is a common disorder and recognized as a significant cause of morbidity in children. The intermittent episodes of airway obstruction and desaturations may result in changes within the autonomic nervous system, which results in significant changes in the cardiovascular system.

In this study we will investigate cardiovascular sequelae of severe OSA in children (for example changes in heart rate, blood pressure, and cardiac morphology by echocardiography) and changes before and after treatment with adenotonsillectomy (removal of the tonsils and adenoid).

The children in the study will be 2-5 years of age with apneahypopnea index >19.9 and tonsil size 2-4.

1. Substudy 1 is a descriptive study with 25 patients with polysomnography before and after adenotonsillectomy. In connection to the polysomnography the patients will also undergo echocardiography and blood pressure measurment (24-h ambulatory blood pressure monitoring, or in some cases office (in house) blood pressure monitoring for 3-4 hours).
2. Substudy 2 is a randomised controlled study with 60-80 patients. The patients will be randomised to either adenotonsillectomy within 1-2 weeks or delayed surgery/expectancy for 4 weeks. As in substudy 1, the children will undergo echocardiography and blood pressure measurement in connection to the polysomnography pre- and postoperatively.

Primary outcome in both studies: change in blood pressure.
Secondary outcomes in both studies:changes in cardiac functions and structures

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

2019-04851				

Publications 2019, 2020, 2021

1. Sundman J, Friberg D, Bring J, Lowden A, Nagai R, Browaldh N Sleep Quality After Modified Uvulopalatopharyngoplasty: Results From the SKUP3 Randomized Controlled Trial Sleep 2018 Sep 25
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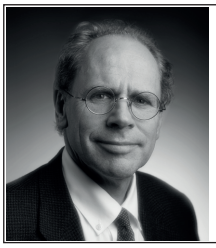

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Neutrophils, T- and B-cells in the development and progression of allergic airway and head and neck squamous cell cancer inflammation

Research in allergy immunotherapy and cancer immunology have shown that the tolerance development that takes place in both diseases, involves the same type of immune cells. It is also evident that it is dysregulation and dysfunction in these pathways that causes a significant part of the disease burden in both allergy and cancer. To simplify, these diseases represent two opposite poles in a tolerance spectrum. In allergy, the immune system overreacts causing a continues on-going local inflammation, whereas in cancer the natural defence mechanisms are circumvented and turned down in order to let malignantly transformed cells roam free and unhindered. Hence, the modern concept of treatment in both allergy and cancer aims at eradicating these illnesses by inducing permanent local tolerance in the former and by breaking the local tolerance in the latter. Notably, this can be achieved in both situations by affecting various types of T-cells. The role of B-cells is well established in similar way in allergy, whereas their role in cancer is far less researched. Furthermore, there is a long-standing notion that neutrophils play a notable role in cancer immunology (even though exactly how remains to be elucidated), whereas the potential role of these cells in allergy has been hidden behind a towering interest for the eosinophils.

The overall goal is to investigate the role of neutrophils, T-cells and B-cells in the development and progress of allergic airway inflammation and head and neck squamous cell cancer with special reference to immunological events taking place in lymph nodes.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Magnus Starkhammar	
Eric Hjalmarsson	
Krzysztof Piersiala	
Aeneas Kolev	
Carl Skröder	
Vilma Lagebro	

Ethical permit No.

2021-03633	2021-00325	2021-01265	2020-02579	2019-03518	

Publications 2019, 2020, 2021

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6. Piersiala K, Farrajota Neves da Silva P, Hjalmarsson E, Kolev A, Kågedal Å, Starkhammar M, Elliot A, Marklund L, Margolin G,

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18. Seys SF, De Bont S, ….. Cardell LO, ….. Pugin B, Hellings PW. Real-life assessment of chronic rhinosinusitis patients using mobile technology: the mySinusitisCoach project by EUFOREA 2020. Allergy (IF:13.1) 2020 May 18.
19. Westerberg J, Tideholm E, Piersiala K, Drakskog C, Georén K Mäki-Torkko, E, Cardell LO. JAK/STAT dysregulation with SOCS1 overexpression in acquired cholesteatoma-adjacent mucosa. Otol Neurotol. (IF:2.3) 2020 Nov 16.
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22. Ekstedt S, Säfholm J, Georén SK, Cardell LO. Dividing neutrophils in subsets reveals a significant role for activated neutrophils in the development of airway hyperreactivity. Clin Exp Allergy. (IF:5.0) 2019;49:285
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Hearing loss and vestibular disorders

Hearing loss and vestibular disorders are two of the common diseases in the society which affect both children and adults. We have two sub-projects in the field: 1. Vestibular disorders projects include PhD students, Niki Karpeta and Med dr Luca Verrecchia focusing on: a. Testing the diagnostic ability of VEMP and vHIT in different clinical contests such as vestibularis neuronitis and middle ear disorders b. early diagnosis of young children with vestibular disorder. Permeability of the round window membrane to aminoglicosides and corticosteroids differ between normal and hydropic ears (animal study-Med dr Pedro Marques-University of Porto Medical School, Porto, Portugal)? 2. Hearing impairment (HI) in newborns – The importantce of early diagnosis and early intervention. This project will focus on: a. To develop new objective diagnostic methods for determination of hearing thresholds, to characterize the dynamic range in young infants, and to assess whether the origin of the hearing loss is cochlear, neural or conductive. b. To establish evidence for the advantage of very early intervention with hearing aids before the age of 2-3 months and cochlear implants (before the age of 9 months) with regard to development of the central auditory pathways, and speech and language evaluated by objective electrophysiological, psychoacoustic and behavioral scientific methods. c. To identify and study predictors for early onset and progressive hearing impairments. Through continuous studies and analyses of the regional (Stockholm County Council) quality data bases Audioscreen and Audiohab the efficacy, sensitivity and specificity of the universal newborn hearing screening (UNHS).

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Niki Karpeta	Anna-Karin Strömberg

Ethical permit No.

2013/1177-31	2015/1296-31/2			

Publications 2019, 2020, 2021

1. Zhou L , Shen N , Feng M , Liu H , Duan M, Huang X. Study of age-related changes in Middle ear transfer function. Comput Methods Biomech Biomed Engin 2019 Oct;22(13):1093-1102. doi: 10.1080/10255842.2019.1632297. Epub 2019 Jul 3.
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Hereditary hemorrhagic telangiectasia, HHT, in Sweden- a registerbased study about mortality, morbidity, prevalence and treatment

HHT/Mb Osler is characterized by malformed vessels, like telangiectasia in mucosa and skin as well as arteriovenous malformation in lung, liver and brain.
HHT is an autosomal dominant disease, diagnosed by at least 3 of the 4 criteria: spontaneous nose bleedings, telangiectasia in skin and mucosa, arteriovenous malformations and heredity, where at least one close relative must have the diagnosis.
Because that the pathology affects different organs, patients get treatment within different specialities.
The disease is rare, and based on foreign studies about prevalence, approximately 1000-1500 Swedish individuals is supposed to have the disease.
Some international population-based studies have shown that these patients have an increased mortality, as well as different morbidity. One study has also seen a tendency of the disease to be under diagnosed outside the university cities, suggesting that there are several under diagnosed cases.
In Denmark, HHT patients are treated at one specific university hospital, by a single rhinologist. They have not found any increased mortality among the HHT-patients there, suggesting that adequate medical care might increase the lifespan.
In Sweden, no study about HHT has been published, and we do not know if the Swedish HHT patients have an increased mortality, what kind of treatment that is used throughout the clinics all over the country, and nothing more specific about the morbidity.
We have the opportunity to find out these questions by the unique national Swedish register, handled by the National Board of Health and Welfare, Socialstyrelsen.
The primary endpoint of the study is: Is the mortality increased in the HHT group as compared to the lifespan of the entire Swedish population.
The secondary endpoints are:

- The prevalence of HHT in Sweden?
- Specific facts about the morbidity
- Medical and surgical treatments of HHT
- Possible regional differences in the treatment of HHT in Sweden

We will get data about prevalence, medical and surgical treatment in different areas of Sweden from 2007-208 in different registers of the National Board of Health and Welfare, Socialstyrelsen As well from a specific register about causes of death in Sweden (Dödsorsaksregistret) between 2001 and 2018, and compare data with life expectancy of the Swedish population throughout these years, by comparing with data from Statistics Sweden (SCB).

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

Publications 2019, 2020, ,2021

1. Control of allergic rhinitis with MP-AzeFlu: a noninterventional study of a Swedish cohort. Stjarne P, Strand V, Theman K, Ehnhage A. Rhinology. 2019 Apr 2. [Epub ahead of print] PMID: 30938376.

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Neutrophils in airway inflammation and head and neck cancer

Neutrophils are part of the first lines of defence against invading microbes. They play an essential role in antimicrobial host defence by recognizing microorganisms through the various receptor that can be expressed on its surface. Novel subsets with different functions of already classified cells are continuously discovered. In line with this, four different neutrophil subsets have been identified based on their expression of CD16 and CD62L. The subsets reflect different stages of cell maturity and activity. My research focuses on these four subsets.

We have in the past characterised neutrophil subsets in blood before and after an inhaled allergen provocation. The fraction of CD16high/CD62Lhigh neutrophils decreased and the CD16high/CD62Ldim neutrophils increased as a result of the challenge. We have also seen functinal canges in the airways after co-cultures between segmets of airways and the subset CD16high/CD62Ldim. Theses neutrophil subsets seems to have different roles during inflammation and we are now foucusing on their role during head and necka cancer and there presents in lymph nodes.

These new findings may lead to a better understanding of the role of neutrophil subset in inflammation, and potentially to new treatments

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

Publications 2019, 2020, 2021

1. Ekstedt S, Kumlien Georén S, Cardell LO. Effects of MP-AzeFlu enhanced by activation of bitter taste receptor TAS2R. Allergy, Asthma & Clinical Immunology. 2020;16(1):45.2020
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5. Ekstedt S, Säfholm J, Kumlien Georén S, Cardell LO. Dividing neutrophils in subsets reveals a significant role for activated neutrophils in the development of airway hyperreactivity. Clin Exp Allergy. 2019 Nov

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Optimizing use of sentinel node technique in head and neck cancer

Head and neck cancer treatment is associated with difficult side-effects. The treatment and prevention of regional metastasis and recurrences is not always succesfull. The use of of sentinel node technique for head and neck cancers is increasing both as an investigation tool to find micro-metastasis and single tumour cells but also as a treatment to avoid more extensive surgery. Studies conducted in our group assess the benefits of the sentinel node techniques for different head and neck cancer subsites and different clinical cases and analyze the imunological features and of the sentinel nodes evaluating the predictiveness of different markers.

The overall aim of the studies is to assess tumour biology and interaction with the immune system, to asssess tumour spread-patterns for different tumour types and to individualize their treatment aiming to improve treatment effects and minimize their related complications.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

2017/1333-31/1	2012/49-31/2	2019/03518		

Publications 2019, 2020, 2021

1. Elliot A, Marklund L, Håkansson N, Song H, Ye W, Stjärne P, Hammarstedt-Nordenvall L. Incidence of IP and risk of malignant transformation in the Swedish population 1960-2010. Eur Arch Otorhinolaryngol. 2017 Mar;274(3):1445-1448. doi: 10.1007/s00405-016-4321-x. Epub 2016 Oct 18. PMID: 27757542; PMCID: PMC5309288.
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Assessment and activation of tympanic membrane progenitor/stem cells - clinical and laboratory studies

With this project we aim to increase knowledge about the normal healing process and to improve the treatment of tympanic membrane perforations with the ultimate goal to design a simple, out-patient procedure without the need for advanced surgery.
In laboratory studies we will identify stem cells and proliferative zones in normal human tympanic membranes as well as in tympanic membranes that has been mechanically and chemically injured. The goal is to better understand the healing mechanism of the tympanic membrane.
Plasminogen is an endogenous protein and has a role in cell migration and wound healing and has been identified as a possible drug for medical treatment of chronical tympanic membrane perforation. In a clinical trial different doses of plasminogen are injected close to the tympanic membrane in the ear canal in patients with chronic perforations and the effect on healing of the ear drum is evaluated.

Development of central auditory pathways in patients with unilateral conductive hearing loss and effects of early intervention

The main purpose of this project is to evaluate the effect on the brain in individuals with unilateral canal atresia, which is when a child is born without a developed hearing canal causing a severe conductive hearing loss. Children with hearing habilitation and untreated adults will be included in the study. An animal model will also be used for longitudinal studies to achieve information about when to expect changes in the auditory pathways of the brain. Methods used in the project are different types of audiometric testing including corneal reflection eye-tracking (a new method for evaluation of sound localization), questionnaires, diffusion MRI and resting state functional MRI.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Elnaz Sepehri	Agnes Modée
Malin Siegbahn	
Hanna Josefsson	

Ethical permit No.

2018/364	2017/2011-31	2012/1661-31/3	N191/14	N113/15

Publications 2019, 2020, 2021

1. Siegbahn M, Engmér Berglin C, Hultcrantz M, Asp F. Adults with unilateral congenital ear canal atresia - sound localization ability and recognition of speech in competing speech in unaided condition.Acta Otolaryngol. 2021 Jul;141(7):689-694.
2. Cortés Fuentes IA, Pierre PV, Berglin CE. Improving Clinical Outcomes in Cochlear Implantation Using Glucocorticoid Therapy: A Review. Ear Hear. Jan/Feb 2020;41(1):17-24.

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Surgical Treatment of Obstructive Sleep Apnea - Randomized Controlled Studies in Children and Adults

Obstructive sleep apnea (OSA) is a common disorder in both children and adults. Surgery is the primary treatment for children and an alternative for adults in selected cases.

This project consists of three RCTs and aims to evaluate:
- If surgery (uvulopalatopharyngoplasty) decreases blood pressure in adult patients with OSA.
- If adenotonsillectomy (ATE, the primary surgical treatment for pediatric OSA) is more effective than no treatment for young children with mild to moderate OSA.
- If a modified ATE is more effective for treating children with severe OSA.

Results from the project shows that:
- Surgery decreases blood pressure in adult patients with OSA.
- ATE is more effective in improving quality of life but not objective respiratory parameters in children with mild to moderate OSA
- Modified ATE is not more effective to treat children with severe OSA.

Future studies include:
- Long-term follow-ups
- Analyses of tonsillar tissue to better understand the etiology of tonsillar growth
- The effect on other cardiovascular endpoints (eg. blood lipids and systemic inflammatory markers) after surgery in adults

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

2007/449-31/3	Ö21-2007	2014/1000-31/1		

Publications 2019, 2020, 2021

1. Fehrm J, Nerfeldt P, Browaldh N, Friberg D. Effectiveness of Adenotonsillectomy vs Watchful Waiting in Young Children with Mild to Moderate Obstructive Sleep Apnea: A Randomized Clinical Trial. JAMA Otolaryngol - Head Neck Surg. 2020;146(7):647-654.
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3. Sundman J, Browaldh N, Fehrm J, Friberg D. Eight-Year Follow-up of Modified Uvulopalatopharyngoplasty in Patients With Obstructive Sleep Apnea. Laryngoscope. 2021;131(1):E307-E313.
4. Carrasco A, Sjölander I, Van Acker A, Dernstedt A, Fehrm J, Forsell M, Friberg D, Mjösberg J, Rao A. The Tonsil Lymphocyte Landscape in Pediatric Tonsil Hyperplasia and Obstructive Sleep Apnea. Front Immunol. 2021 Oct 22;12:674080.
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Hearing and Cognition, Hearing Preservation in Vestibular Schwannoma

- Hearing in the elderly and cognition, noise and, diet . Epidemiological studies where the influence of various factors on hearing function is assessed in patients, and in population databases such as H70.
- Hearing in vestibular schwannoma - Gamma knife surgery vs initial conservative treatment for vestibular schwannoma patients with preserved hearing, a prospective randomized study. PI Ass Prof Föander, Department of Neurosurgery, Karolinska.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
	Jenny Häggström

Ethical permit No.

Publications 2019, 2020, 2021

1. Haggstrom, J., et al., Prognostic Value of a Test of Central Auditory Function in Conversion from Mild Cognitive Impairment to Dementia. Audiol Neurootol, 2020: p. 1-7.
2. Tengroth, B., A. Lohmander, and C. Hederstierna, Hearing Thresholds in Young Children With Otitis Media With Effusion With and Without Cleft Palate. Cleft Palate Craniofac J, 2019: p. 1055665619889744.
3. Bonnard, A., R. Bark, and C. Hederstierna, Clinical update on sensorineural hearing loss in Turner syndrome and the X-chromosome. Am J Med Genet C Semin Med Genet, 2019. 181(1): p. 18-24.

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Obstructive Sleep Apnea in children and adults, Tonsill surgery and Subglottic stenosis

Obstructive sleep apnea: the group has performed five randomized controlled trials on surgical treatment methods and are continously focusing on the longterm outcomes. Patients are evaluated with both objective and subjective parameters such as polysomnography findings (the gold standard sleep registration), vigilans, daytime sleepiness, quality of life, blood pressure, inflammatory markers etc.

Tonsil surgery: the Swedish National Tonsill Surgery Registra is a national quality registra, were we evaluate incidence, morbitidy, symtom relief and trends over time and over the healthcare regions.

Subglottic stenosis: retrospective and prospective evaluation of the treatment methods and success at Karolinska University Hospital. Further we are analysing the measurement Oral Peak Inspiratory Flow, evaluating the normal range in an adult population.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

Publications 2019, 2020, 2021

1. Postoperative pain and bleeding after adenotonsillectomy versus adenotonsillotomy in pediatric obstructive sleep apnea: an RCT. Borgström Anna, MD; Nerfeldt Pia MD, PhD; Friberg Danielle, MD, PhD. Eur Arch Otorhinolaryngol 2019 doi.org/10.1007/s00405-019-05571-ww
2. Obstructive sleep apnea in children with Down syndrome - Prevalence and evaluation of surgical treatment. Nerfeldt Pia MD PhD, Sundelin Amalia MD. Int J Pediatr Otorhinolaryngol. 2020 Feb 26;133:109968. doi: 10.1016/j.ijporl.2020.109968.
3. Postoperative morbidity after adenotonsillectomy versus adenopharyngoplasty in young children with obstructive sleep apnea: an RCT. Johan Fehrm, MD; Pia Nerfeldt, MD, PhD; Anna Borgström, MD, PhD; Danielle Friberg, MD, PhD. Eur Arch Otorhinolaryngol 2020 Oct;277(10):2821-2827
4. Effectiveness of Adenotonsillectomy vs Watchful Waiting in Young Children With Mild to Moderate Obstructive Sleep Apnea: A Randomized Clinical Trial. Fehrm J, Nerfeldt P, Browaldh N, Friberg D. JAMA Otolaryngol Head Neck Surg. 2020 Jul 1;146(7):647-654.
5. A validation study of data in the National Tonsil Surgery Register in Sweden: high agreement with medical records ensures that data can be used to monitor clinical practices and outcomes. Lundström F, Odhagen E, Alm F, Hemlin C, Nerfeldt P, Sunnergren O. BMC Med Res Methodol. 2022 Jan 7;22(1):3. doi: 10.1186/s12874-021-01467-8.

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Radiotherapy induced tissue inflammation, treatment of salivary gland cancer and reconstructive laryngotracheal airway surgery

I) Studies on patients treated for salivary gland cancer
- To validate the sentinel node technique in salivary gland cancer
- To validate a histopathological risk model for patients with salivary gland cancer

II) Studies on radiotherapy-induced tissue inflammation. The project is a multidisciplinary collaboration between surgeons, dermatologists, pathologists and oncologists. The main area of interest is clinical outcome in patients treated for head and neck malignancies.
- The impact of irradiation on acute and long-term changes i tissues (blood vessels, fat, bone and skin) following radiotherapy treatment.
- Underlying mechanisms in human tissue and in an experimental mouse model

III) Studies on laryngotracheal airway diseases.
- Long-term outcome of reconstrutive airway surgery in pediatric and adult patients
- Psychosomatic development and life quality in children with tracheostomy

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Björn Eriksson	

Ethical permit No.

2019-05211	2008/114-31	2012/1663-32	2018/1972-31	2021-06074-02

Publications 2019, 2020, 2021

1. Gahm C, Näsman A, Papatziamos G. Segmental congenital deficiency of tracheal rings in cervical trachea managed by tracheal resection: A case report and literature review. Int J Ped Otorhinolaryngol. 2021 Sept;148
2. Osteoradionecrosis, an increasing indication for microvascular head and neck reconstruction. Danielsson D, Gahm C, Haghdoost S, Munck-Wikland E, Halle M. Int J Oral Maxillofac Surg. 2019 Jul 8. S0901-5027 (19)31185-3
3. Eriksson B, Gahm, C, Halle M. Upregulation of Plasminogen Activator Inhibitor-1 in irradiated recipient arteries and veins from free tissue transfer reconstruction" Mediators of inflammation. Oct 4;2018:4058986.
4. Haeggblom L, Ursu RG, Mirzaie L, Attoff T, Gahm C, Nordenvall LH, Näsman A. No evidence for human papillomavirus having a causal role in salivary gland tumors. Diagn Pathol. 2018 Jul 18;13(1):44.
5. Ramqvist T, Ursu RG, Haeggblom L, Mirzaie L, Gahm C, Hammarstedt-Nordenvall L, Dalianis T, Näsman A. Human Polyomaviruses Are Not Frequently Present in Cancer of the Salivary Glands. Anticancer Res. 2018 May;38(5):2871-2874.
6. Halle M, Eriksson BO, Docherty Skogh AC, Sommar P, Hammarstedt L, Gahm C. Improved Head and Neck Free Flap Outcome-Effects of a Treatment Protocol Adjustment from Pre- to Postoperative Radiotherapy. Plastic and reconstructive surgery. Global open 2017 5;3 e1253-
7. Kamali A, Gahm C, Palmgren B, Marklund L, Hammarstedt,-Nordenvall L. Regional recurrence in early stage I-II oral tongue cancer- a single institutional study and review of the litterature. Acta Oto-laryngologica 2017 137;7 755-761

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Effects of cochlear implants in elderly individuals

Ongoing project Co-supervision for Dr Sofia Hultman-Dennison, PhD project on acute rhinosinusitis in children.
Ongoing and planned: Study on effects of cochlear implants in adults with special respect to vestibular functions, hearing outcomes and cognitive abilities in the elderly. Vestibular testing before and after cochlear implantation is ongoing. Studies on the outcomes of treatment (quality of life, hearing outcomes) with cochlear implants related to age, cognition and social environment are planned. The intention is to start a PhD project (S. Mikelöv) during 2021.The main aim of the project is to establish if there are certain specific risks for impairment of vestibular function after cochlear implantation i younger and older (+70y) adults respectively. We also want to investigate the impact of social environment and cognitive functions in individuals older than 70y. Vestibular testing, questionnaires, hearing tests, technical data from implants and cognitive tests will be used for the surevey.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Sara Mikelöv (Planned project)	Sofia Hultman Dennison

Ethical permit No.

2018/1032-31				

Publications 2019, 2020, 2020

1. Dennison SH, Ask LS, Eriksson M, Granath A, Hertting O, Bennet R, Lindstrand A, Masaba P, Dimitriou P, Stjärne P. Serious complications due to acute rhinosinusitis in children up to five years old in Stockholm, Sweden - Still a challenge in the pneumococcal conjugate vaccine era. International journal of pediatric otorhinolaryngology 2019 121; 50-54

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Studier på H&N Cancer

Inflammatory changes of skin after radiotherapy-implications for treatment of head and neck cancer
Injury to the shoulder innervation after head and neck surgery-anatomical basis for new treatment strategies
Nasopharyngeal cancer in Sweden-characterization of a rare disease
Early tongue cancer- sentinel node biopsi and other predictive and progostic markers
Salivary gland tumors- the use of sentinel node to predict drainage and immunohistochemical markers to better predict aggressiveness
Oropharyngeal cancer- the value of HPV in non-tonsillar and non-base of tongue orofaryngeal cancer

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Evelina Gille	Björn Eriksson
	Rasmus Blomkvist
	David Landin

Ethical permit No.

Publications 2019, 2020, 2021

1. Ilmarinen T, Hammarstedt-Nordenvall L, Bäck L, Mäkitie A. Enteral tube feeding of head and neck cancer patients undergoing definitive chemoradiotherapy in the Nordic Countries: Survey of the Scandinavian Society for Head and Neck Oncology. Eur Arch Otorhinolaryngol. 2021 Sep;278(9):3489-3496. doi: 10.1007/s00405-020-06545-z. Epub 2021 Jan 2.PMID: 33389006
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The FACE study - a randomized double-blinded placebo-controlled multicenter trial for evaluation of cortisone treatment in children with acute facial nerve palsy

Background: Acute facial nerve palsy occur in 15-20/100 000 children/year in Sweden. The facial nerve palsy may be associated to Borrelia infection or idiopathic. About 20 % of these children get a persistent impairment of the facial nerve with problems with excesive tear secretion, pronounication, drooling on top of social/cosmetic problems due to assymmetry in the face. Studies on cortisone treatment to adult patients with acute facial nerve palsy have shown beneficial effects, but no studies with strong quality have been performed in children. The overall purpose is to assess the utility of cortisone treatment to children with acute facial nerve palsy in a well-designed RCT.

Material/methods: We now perform a double-blind randomized doulbe blinded placebo-controlled multicenter trial on children with acute facial nerve palsy. Patients are being recruited consecutively at 18 study centers in Sweden during 2019-2023 and a total of 500 patients will be included. Prednisolone 1 mg/kg x 1 perorally in 10 days will be evaluated vs placebo. Clinical data, including clincial outcome (House-Brackmann, Sunnybrook, FaCE scale and FDI) will be documented up until the 12-months follow-up.

The primary outcome is defined as total recovery of the facial nerve palsy, measured with the House-Brackmann scale (grade 1) at 12-months follow-up.

Clincal relevance: If the total recovery rate is significantly improved in the prednisolone group as compared to the placebo group, prednisolone treatment will be introduced in clinical practice for children with acute facial nerve palsy in order to reduce the risk of persistent impairement and disability. National and international guidelines will be pubished for evidens-based treatment of children with acute facial nerve palsy.

The study protocol is published at ClincialTrials.gov NCT03781700

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Sofia Karlsson	
Sigurdur Arnason	

Ethical permit No.

2017/554				

Publications 2019, 2020, 2021

1. Karlsson S, Arnason S, Nermin Hadziosmanovic N, Laestadius A , Hultcrantz M, Marsk E, Skogman BH. The facial nerve palsy and cortisone evaluation (FACE) study in children: protocol for a randomized, placebo-controlled, multicenter trial, in a Borrelia burgdorferi endemic area. BMC Pediatrics. 2021; 21:220 (doi.org/10.1186/s12887-021-02571-w)
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3. Appelgren D, Enocsson H, Skogman BH, Nordberg M, Perander L, Nyman D, Nyberg C, Knopf J, Munoz LE, Sjowall C, Sjowall J. Neutrophil Extracellular Traps (NETs) in the Cerebrospinal Fluid Samples from Children and Adults with Central Nervous System Infections. Cells. 2019;9(1).

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Allergy vaccination- novel strategies and biomarkers for outcome

Allergic rhinitis deprives quality of life, work capacity and social activities and costs the Swedish society about 1.3 billion SEK annually. Allergen-specific immunotherapy (AIT) gives a significant symptom reduction and also improves the course of the disease. Conventional AIT involves more than 50 subcutaneous injections at hospital or daily sublingual tablets, during 3-4 years. The long treatment duration, problems with side-effects and lack of allergology specialists limits the use; only a minority of the patients eligible for AIT gets the treatment.

Intralymphatic immunotherapy (ILIT) is an emerging form of AIT, which requires only 3 ultrasound guided lymph node injections during a period of 12 weeks. The overall aims for this project are to optimize the ILIT treatment protocol and explore the immunological mechanisms behind tolerance induction in ILIT as well as in conventional AIT. We will investigate if using a lower dose of allergen than previously tested, will be equally or more efficient. In addition, we will investigate if concomitant medication can enhance the treatment effect. In the search for biomarkers for treatment outcome, immune cells sampled from the blood, lymph nodes and nasal mucosa will be characterized, mainly using flow cytometry.

If the treatment protocol in ILIT can be optimized, more patients with allergic rhinitis could benefit from the treatment, to a lower cost for the health care system.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

2009/714	2021-03633			

Publications 2019, 2020, 2021

1. A preseason booster prolongs the increase of allergen specific IgG4 levels, after basic allergen intralymphatic immunotherapy, against grass pollen seasonal allergy. Weinfeld D, Westin U, Hellkvist L, Mellqvist U-H, Jacobsson I, Cardell L-O. Allergy Asthma Clin Immunol. 2020 Apr 28;16:31. doi: 10.1186/s13223-020-00427-z. eCollection 2020.
2. High dose pollen intralymphatic immunotherapy: Two RDBPC trials question the benefit of dose increase. Hellkvist L, Hjalmarsson E, Weinfeld D, Dahl Å, Karlsson A, Lundkvist K, Westman M, Kumlien Georén S, Winqvist O, Westin U, Cardell LO. Allergy. 2021; 00:1-14

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Ear and Hearing

The ear and hearing research focuses on three avenues.

1. To study quality and benefit of audiological rehabilitation for patients with severe-to-profound hearing loss with or without vision impairment. The study also aims at invesgating the type of audiological rehabilitation received by patients and whether it is necessary to improve rehabilitation efforts, for example, in terms of a gender perspective. Other questions regard e.g. do all patients which qualify for CI-implantation get a CI. An important basis for the studies is the national Quality Register for severe-to-profound hearing loss.
2. To supervise the development and establishment of a "Scientific Center for Advanced Pediatric Audiology". The hearing research at Karolinska dominates by studies on children. This field has an enormous potential to become a national and international frontline research area.
3. To study plasminogen, a preinflammatory protein, and its involvement in healing of wounds. One project concerns healing of tympanic membrane perforations but also chronic wounds, like diabetic foot ulcers. The study is performered at Umeå Univ in collaboration with international bioscience companies.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
	Niki Karpeta
	Fatima Moumén Denanto

Ethical permit No.

2012/057	2014/2101-31			

Publications 2019, 2020, 2021

1. Tong B, Niu K, Ku W, Xie W, Dai Q, Hellström S, Duan M. Comparison of Therapeutic Results with/without Additional Hyperbaric Oxygen Therapy in Idiopathic Sudden Sensorineural Hearing Loss: A Randomized Prospective Study. Audiol Neurootol. 2021;26(1):11-16.
2. Tong B, Wang Q, Dai Q, Hellstrom S, Duan M. Efficacy of Various Corticosteroid Treatment Modalities for the Initial Treatment of Idiopathic Sudden Hearing Loss: A Prospective Randomized Controlled Trial. Audiol Neurootol. 2021;26(1):45-52. Publications 2018, 2019, 2020,2021
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Evaluation of treatment of subglottical stenosis carried out retrospectively from 1998 and prospectively on the ENTdepartment at Karolinska university hospital

Retrospective (from 1998) and prospective evaluation on the patients with subglottical stenosis treated at the ENT-department, Karolinska University hospital. Main treatment in the past has been a surgical reduction of the stenosis in combination with local peroperative dilation and sometimes treatment with locally applied cortison and Mitomycin. Beside operation endoscopically (or in some few cases end-to-end anastomosis) in full anaestethic mode we can now offer the patient local cortison injection with the help of a local anestethic setting at our outpatient department. This treatment contains repeated injections direct into the stenotic areawith 1 month between each injection

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

2021-02110				

Publications 2019, 2020, 2021

1. Lundström N, Henriksson G, Börjesson O, Jonsson Fagerlund M, Petersson J.Lundström N, et al. Among authors: henriksson g. Circulatory Collapse due to Hyperinflation in a Patient with Tracheobronchomalacia: A Case Report and Brief Review. Case Rep Crit Care. 2019 Jan 29;2019:2921819. doi: 10.1155/2019/2921819. eCollec tion 2019.Case Rep Crit Care. 2019. PMID: 30838137

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Reconstruction of vocal fold scarring with mesenchymal stem cells

This projects aims to find a treatment for severe voice disorders caused by vocal fold scar. This may be the result of surgery cancer treatment severe inflammation of congenital disorders affecting voice. At present effective treatment is lacking. In a series of animal experiments since 2004 we have shown positive effects, regeneration and prevention of scar formation after injection of human mesenchymal stem cells, MSC (and embryonic stem cells).
From 2012 an ongoin study in cooperation with Professor Katarina LeBlanc at KI is including and treating patients with severe hoaseness and scarring of the vocal folds.The patients are recruited from Karolinska and other parts of Sweden. Vocal folds are dissected and scar tissue is reduced/removed followed by a local injection of autologous MSCs. At present 16 patients are treated. Preliminary results at 1 year follow up for the patients shown clearly improved vocal fold function without side effedts.
At present a clinical trial approved by EPM and Swedish Product Agency (Läkemedelsverket) is ongoing, We are recruiting up to 15 patients with severe dysphonia and voca fold scarring which are treated with an autologous MSC product injected into the operated scarred vocal folds

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Emma Malmström	Erik Bergström Börlin

Ethical permit No.

2019-06160	2020-04565	2021-00933	2021-03904	

Publications 2019, 2020, 2021

1. Nagubothu S.R., Davies L.C., Sugars R., Tudzarovski N., Törnqvist Andrén A., Bottai M, Hertegård S. and Le Blanc K. Mesenchymal stromal cells modulate tissue repair responses after local injection within scarred vocal folds. Laryngoscope. 2019 Mar 5. doi: 10.1002/lary.27885. [Epub ahead of print]
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3. Sveinsson O, Udd B, Svenningsson P, Gassner C, Engström C, Laffita-Mesa J, Solders G, Hertegård S, Savitcheva I, Jung HH, Tolnay M, Frey BM, Paucar M. Involuntary movements, vocalizations and cognitive decline. Parkinsonism Relat Disord. 2019 May 29. pii: S1353-8020(19)30250-0. doi:10.1016/j.parkreldis. 2019.05.029. [Epub ahead of print] No abstract available. PMID: 31153763
4. Hertegård S., Nagubothu S.R., Malmström E., LeBlanc K. Treatment of Vocal Fold Scarring with Autologous Bone Marrow Derived Human Mesenchymal Stromal Cells- First Phase I/II Human Clinical Study. Stem Cell Research and Therapy. 2020 Mar 20;11(1):128. doi: 10.1186/s13287-020-01632-8. DOI:10.1186/s13287-020-01632-8. SCRT-D-20-00039R22020
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Nasal Aspects on Unilateral Cleft,- Lip-and Palate and Obstructive Sleep Apnea

Cleft lip and palate has functional and aesthetical impact on the face and upper airways. Patients were examined 20-40 years after primary surgery. A control group was examined in the same way. Objective evaluation of nasal form and function was performed as well as studies of QoL and voice function with blinded evaluation.
The impact of chronic rhino sinusitis on sleep and obstructive sleep apnea is analyzed as well as vice versa. Variables for a poor outcome in CPAP treatment are also analyzed.
Hereditary Hemorrhagic Telangiectasia in Sweden. A register based study of prevalence, morbidity and mortality is analyzed.
Chronic rhinosinusitis in adolescence: prevalence, clinical characteristics and inflammatory markers.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
	Karin Åberg

Ethical permit No.

2012/1472-31	2014/448	2013/397	2020/6950	

Publications 2019, 2020, 2021

1. Bjermer L, Westman M, Holmström M, Wickman MC The complex pathophysiology of allergic rhinitis: scientific rationale for the development of an alternative treatment option. Allergy Asthma Clin Immunol. 2019 Apr 16;15:24.
2. Bengtsson C, Jonsson L, Holmström M, Hellgren J, Franklin K, Gíslason T, Holm M, Johannessen A, Jõgi R, Schlünssen V, Janson C, Lindberg E Incident Chronic Rhinosinusitis Is Associated With Impaired Sleep Quality: Results of the RHINE Study.J Clin Sleep Med. 2019 May 24. pii: jc-18-00575. [Epub ahead of print]
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6. Hultman-Dennison S, Granath A, Holmström M, Stjärne P, Hertting O Bacterial cultures, virus detection, allergy sensitization and immunoglobulins in children with complications to acute bacterial rhinosinusitis – a prospective study. Submitted
7. Morén S, Lindestad P-Å, Stålhammar L, Holmström M, Mani, M. Speech in Adults Treated for Unilateral Cleft Lip and Palate as Rated by Naïve Listeners, Speech-Language Pathologists and Patients. Submitted

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Aging, cognition and central auditory function

The main topic of this project is about relationships between aging, cognitive decline, and central auditory function (CAD).
The goal is to establish an assessment method by which CAD can be verified in patients with cognitive impairment, thereby allowing for prevention of accelerated cognitive decline and hearing rehabilitation adapted to cognitive level.
The hypothesis is that combined measures of CAD and cognitive function will accurately identify persons with both hearing impairment and cognitive deficits.
In the first longitudinal study (Häggström et al., 2018), it has been demonstrated that central auditory function, as measured with the Dichotic Digit Test (DDT), suggested that DDT may reflect on ongoing process resulting in dementia.
In the second study (Häggström et al., 2020), the objective was to evaluate the predictive capacity of the DDT in conversion from mild cognitive impairment (MCI) to dementia. It has been suggested that DDT as a central auditory test may be suitable when evaluating cognitive decline.
In the next study the correlation betwen the DDT and morphological changes in the corpus callosum on existing MRI images is planed to be investigated, in order to further evaluate the diagnostic validity of the DDT.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Jenny Häggström	

Ethical permit No.

2005/914-3	2014/2087-31-2	2018/1291-32		

Publications 2019, 2020, 2021

1. Häggström J, Rosenhall U, Hederstierna C, Östberg P, Idrizbegovic E. A Longitudinal Study of Peripheral and Central Auditory Function in Alzheimer's Disease and in Mild Cognitive Impairment. Dement Geriatr Cogn Dis Extra. 2018 Oct 22;8(3):393-401. doi: 10.1159/000493340. eCollection 2018 Sep-Dec.
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Implementation of monoclonal antibodies in chronic rhinosinusitis treatment

The last couple of years novel treatments to treat chronic rhinosinusitis have evolved, monoclonal antibodies targeting the type 2 immune response, especially effective in nasal polyp patients. Last year the first monoclonal antibody was approved for treatment of nasal polyps, Dupixent, targeting the IL-4, IL-13 immunological pathway. These treatments are expensive, for long-term use and some nasal polyp patients does not respond at all; we do not know why. We are initiating a research project that hopefully will help us to understand why some patients are responders and others are non-responders, and to identify easy to access clinical or biomarkers to guide us in the decision to initiate this treatment.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

Publications 2019, 2020. 2021

1. Dupilumab reduces local type 2 pro-inflammatory biomarkers in chronic rhinosinusitis with nasal polyposis. Jonstam K, Swanson BN, Mannent L, Cardell LO, Tian N, Wang Y, et al. Allergy 2019
2. Endoscopic Sinus Surgery for Type-2 CRS wNP: An Endotype-Based Retrospective Study. Alsharif S, Jonstam K, van Zele T, Gevaert P, Holtappels G, Bachert C. Laryngoscope 2019.
3. Endotypes of chronic rhinosinusitis: Impact on management. Cardell LO, Stjärne P, Jonstam K, Bachert C. J Allergy Clin Immunol 2020
4. Extent of inflammation in severe nasal polyposis and effect of sinus surgery on inflammation. Jonstam K, Alsharif S, Bogaert S, Suchonos N, Holtappels G, Jae-Hyun Park J, et al. Allergy 2020.
5. Type 2 Inflammatory Shift in Chronic Rhinosinusitis During 2007-2018 in Belgium. Jonstam K, Delemarre T, Holtappels G, Cardell LO, Westamn M, Bachert C. Laryngoscope 2020.

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Auditory Organotypic Cultures and Progenitor Cell Implantation

Concluded PhD project during 2018. Researchactivity presently composed of reviewer work. Looking for clinically relevant projects in neurotology

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

C100115/15				

Publications 2019, 2020, 2021

1. Kaiser A, Kale A, Novozhilova E, Olivius P. 2019.The Effects of Matrigel on the Survival and Differentiation of a Human Neural Progenitor Dissociated Sphere Culture. The Anatomical Record. DOI: 10.1002/ar.24131

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Immune responses in airway inflammatory diseases and head- and neckcancer.

*Chronic inflammation is considered to play an important role in the development of HNSCC. Moreover, the degree of the inflammatory response seen in these tumors has reported to have prognostic value in different histopathological malignancy grading systems . The overall goal of this research is to gain a better understanding of innate immunity and inflammation in head and neck cancers and to stress the possibility for using inflammatory markers as base for novel approaches to prediction.

*Intralymphatic allergen specific immunotherapy (ILIT) is an emerging form of Allergy ImmunoTherapy that uses a novel route of delivery with shorter duration, good compliance (3 injections over 8 weeks) and only mild side effects. It uses the same allergen-based vaccine as in Sub Cutan Immuno Therapy (SCIT) but in lower concentration. We aim to investigate the lymph node specific immune response in both ILIT and SCIT.

*Chronic rhinosinusitis s/w polyps and asthma exacerbations have lately been thought to have underlying infectious basis, and the innate immunity is thought to have a great importance. We aim to outline the interplay between the innate and adaptive immune response and different subgroups of neutrophils role for the development of the diseases.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
	Eric Hjalmarsson
	Magnus Starkhammar
	Krzysztof Piersiala
	Vilma Lagebro

Ethical permit No.

Publications 2019, 2020, 2021

1. Piersiala K, Farrajota Neves da Silva P, Hjalmarsson E, Kolev A, Kågedal Å, Starkhammar M, Elliot A, Marklund L, Margolin G, Munck-Wikland E, Kumlien Georén S, Cardell LO. CD4+ and CD8+ T cells in sentinel nodes exhibit distinct pattern of PD-1, CD69, and HLA-DR expression compared to tumor tissue in oral squamous cell carcinoma. Cancer science 2021 112;3 1048-1059
2. Hellkvist L, Hjalmarsson E, Weinfeld D, Dahl Å, Karlsson A, Westman M, Lundkvist K, Winqvist O, Georén SK, Westin U, Cardell LO. High dose pollen intralymphatic immunotherapy: Two RDBPC trials question the benefit of dose increase. Allergy 2021 ;
3. Westerberg J, Tideholm E, Piersiala K, Drakskog C, Kumlien Georén S, Mäki-Torkko E, Cardell LO. JAK/STAT Dysregulation With SOCS1 Overexpression in Acquired Cholesteatoma-Adjacent Mucosa. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology 2021 42;1 e94-e100
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5. Ma JJ, Tibbitt CA, Georen SK, Christian M, Murrell B, Cardell LO, Bachert C, Coquet JM. Single-cell analysis pinpoints distinct populations of cytotoxic CD4(+) T cells and an IL-10(+)CD109(+) T(H)2 cell population in nasal polyps. SCIENCE IMMUNOLOGY 2021 6;62

6. Larsson O, Sunnergren O, Bachert C, Kumlien Georén S, Cardell LO. The SP-TLR axis, which locally primes the nasal mucosa, is impeded in patients with allergic rhinitis. Clinical and translational allergy 2021 11;1 e12009-
7. Kagedal A, Hjalmarsson E, da Silva PFN, Piersiala K, Georen SK, Margolin G, Munck-Wikland E, Winqvist O, Hayry V, Cardell LO. Activation of T helper cells in sentinel node predicts poor prognosis in oral squamous cell carcinoma. SCIENTIFIC REPORTS 2020 10;1 22352-
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9. Ekstedt S, Larsson O, Kumlien Georén S, Cardell LO. CD16high CD62Ldim neutrophils induce nerve-mediated airway hyperreactivity. Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology 2020 50;6 756-759
10. Ekstedt S, Georen SK, Cardell LO. Effects of MP-AzeFlu enhanced by activation of bitter taste receptor TAS2R. All Asthma Clin Immun 2020 16;1 45-
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Sentinel Node detection in patients with Sinonasal Tumours

Sinonasal malignancies are rare but have a high mortality and the post treatment morbidity is severe with mutilating surgery and radiotherapy. The lymphatic drainage from the nasal cavity and the paranasal sinuses are not well studied. With sentinel node procedure and flow cytometry technique for early detection of metastases and new immunological biomarkers we hope to gain knowledge for better treatment both in terms of limiting the field of radiotherapy and improve the possibilities for immune therapy.

Immune response in COVID 19 patients

COVID 19 patients presents with a high immune response. In our study we examine the immune response in blood with flow cytometry and main focus on neutrophils, with an aim to predict the severity of the disease

Immune Respons and Tumour Cell Detection in Head and Neck Cancer

Metastases in lymph nodes are an important factor for outcome in oral cancer patients. The development of the new immune therapies has changed the field of cancer medicine and it is important to define the selection of patients for these new treatments. The overall goal of this research is to study the immune response in tumour tissue, lymph nodes and blood in patients with oral cancer. We use sentinel node technique to find the draining lymph node where we detect tumour cells with flow cytometry and identify immunological biomarkers.

Ethical permit No.

2011/717-31-1	2013/1943-3-4	2015/1650-31-2	2018/811-32		

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Optimizing treatment for head and neck tumors

Treatment of head and neck tumors consists surgery, radiotherapy and chemotherapy, used as single treatment or combined in advanced tumors. Today treatment is standardized and mainly based on TNM-status although the tumors vary in aggressiveness and sensitivity to treatment. Complications to treatmet is loss of nerve function, pain, stifness, swallowing problems, dryeness of mouth wich have major impact of th quality of life. A number of molecular markers have been evaluated for predictive value at head and neck tumors. However, few studies have been performed specifically for each subgroup of tumors although these differ considerably in terms of treatment response and prognosis. Therefore, the overall iam of all studies is to optimize and individualize the tratment for patients with head and neck tumors. We evaluate the predictive value of a number of markers in order to be able to select patients for surgery or oncologic treatment, and also be able to better select type and intensity of oncologic treatment and also the extent of surgery, both on the tumor site and the neck.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
David Landin	Aeneas Kolev
Rasmus Blomkvist	

Ethical permit No.

2017/1333-31/1	2012/49-31/2	2019/03518		

Publications 2019, 2020, 2021

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Bells palsy during pregnancy and puerperium

- **Surgical intervention in patients with peripheral facial palsy**
- **Facial nerve palsy in children; treatment and clinical outcome**

Bell's palsy is an acute peripheral facial nerve palsy with unknown etiology that can affect both adults and children. There is a higher incidence among pregnant women and in the puerperium. The disease can cause severe disfigurement of the face, impair the ability to eat, drink and speak, and seriously affect the patient's quality of life. Many patients need surgical interventions.

In our work, we study different aspects of Bell's palsy in both adults (especially among pregnant women) and children. Surgical interventions with nerve transfers and neurotomy on adults with severe facial plays is studied and different neurofysiologiscal tests are described. A multi-center randomised, clinical trial is performed on children with acute facial palsy to study the effect of prednisolone on the facial outcome.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Lovisa Lansing	Rebecka Ohm
	Sigurdur Arnason
	Evelina Gille
	Emma Malmström

Ethical permit No.

Publications 2019, 2020, 2021

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Head and neck cancer

We study predictive and prognostic markers in head and neck cancer aiming at indivdualize and optimize treatment for our patients.
Daniel studies ”Osteoradionecrosis (ORN) - risk factors and reconstructive outcome” including biomarkers for increased risk for ORN, proportion of ORN in reconstructive surgery, quality of life after reconstruction and brachytherapy and risk for ORN.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Daniel Danielsson	Krzysztof Piersiala
	David Landin
	Vilma Lagebro

Ethical permit No.

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Prognostic Markers, Treatment Outcome, and New Therapeutical Modalities in Head and Neck Cancer

1. Identification of biomarkers that predict HNSCC treatment outcome.
This collaborative project aims to identify markers that predict treatment response and can be analyzed in a tissue biopsy from a suspected tumor and/or in the patient's blood sample or saliva or possibly in exhaled breath. The ultimate goal is to find combinations of markers, which could guide clinicians to provide cancer patients with a more adequate, individualized, and effective treatment.

2. The Nordic Head and Neck Cancer (HNC) Study: management and outcome of various subsites of head and cancer in the Nordic countries. Our aim is to evaluate current treatment outcome of HNC in the Nordic countries and to form a recommendation for a unified treatment protocol for this entity to be used in this area. The secondary aim is to find prognostic markers for clinical use by using multi-institutional series of HNC patients and available samples.

Ethical permit No.

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Undergraduate students' clinical learning environment and lifelong learning

Undergraduate students' clinical learning environment (CLE).
It is widely acknowledged that CLE impacts students' professional development and their ability to achieve the learning outcomes. This project aims to identify and provide an in-depth understanding of students' perception of the clinical learning environment and the relationship to self-reported health-related quality of life across four different undergraduate programs. The first study assessed the CLE by the Undergraduate Clinical Education Environment Measure (UCEEM) and showed signifigant differences between the programs with physiotherapy students rating highest and medical students lowest their CLE. Th eporjecst has been progressed with two new qualitative studies.

The other research path concerns undergraduate students scientific development and attitudes to lifelong learning. Ethical application is to be submitted in the begiining of the this year and two new studies are to be started in 2022.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Malin Sellberg	

Ethical permit No.

2017/38-31/4	2013/2212-31/4	2010/1100-31/1	2010/1606-31/5	2010/1100-31/1	2011/493-32	

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Upper airway disease; treatments and health economy

Research interests include the epidemiology of rhinitis and nasal polyposis, the medical and surgical management of nasal polyposis and more recently, immunotherapy and biologic treatments of upper airway disease, inluding health economy

Ethical permit No.

2016/2158-31/2				

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Laryngeal cancer at the Karolinska University Hospital 2000-2020

In this project, we want to investigate laryngeal cancer treatment strategies and outcome in patients treated at the Karolinska University Hospital 2000-2020. Furthermore, we want to see if we can find good predictors to better select those patients whose tumors should receive radiotherapy (read radiation sensitive) and those where surgery becomes the primary choice. We also want to see if we can streamline care and follow-up without affecting the quality of care.

The research project preliminarily consists of several sub-projects, all with the aim of highlighting the characteristics and treatment outcomes of laryngeal cancer:

1. A descriptive retrospective study with the purpose to acquire data on the management and outcome of laryngeal squamous cell cancer for patients treated at the Karolinska University Hospital 2000-2020.
2. To specifically evaluate treatment and outcome for large cancers of the larynx, i.e. T3 and T4 tumours. We will specifically analyse x-rays and control the tumors for size, extension of growt and destruction of cartillage.
3. To evaluate the treatment of T3, T4 laryngeal cancer with the Bayesian network model based on observation data. We will analyse 18 variables on aproximately 300 Swedish and Finnish patients.

In the research group we also have collaboration with Prof. Mäkitie from Helsinki, Finland. Thus, we aim to compare data on the management and outcome for laryngeal cancer patient in Sweden and Finland.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
	Rasmus Blomkvist

Ethical permit No.

2019-04829				

Publications 2019, 2020, 2021

1. A descriptive study highlighting the differences in the treatment protocol for oral tongue cancer in Sweden and Finland. Mäkitie A, Kamali A, Mroueh R, Lindford A, Koivunen P, Autio T, Lassus P, Halle M, Bäck L, Palmgren B, Hammarstedt-Nordenvall L.Mäkitie A, et al. Acta Otolaryngol. 2020 Feb;140(2):188-194. doi: 10.1080/00016489.2019.1699663. Epub 2019 Dec 18.Acta Otolaryngol. 2020. PMID: 31852347
2. Postsurgical pyoderma gangrenosum and flap necrosis in a head and neck cancer patient following neck dissection. Arebro J, Palmgren B.Arebro J, et al. Clin Case Rep. 2020 Apr 8;8(7):1121-1125. doi: 10.1002/ccr3.2828. eCollection 2020 Jul.Clin Case Rep. 2020. PMID: 32695340

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Cochlear Implantation in Children with Cochlear Malformation

Cochlear implantation makes hearing restoration possible in patients with severe to profound hearing loss. Our research today focus on clinical studies of cochlear implantation in children with cochlear malformations. During the last years we have examined the effects of cochlear implant surgery on children with x-linked (DFNX2) inner ear malformation. We describe surgical techniques necessary for safe cochlear implantation, and further show that implantation permits hearing restoration and the development of spoken language in these children. Further analysis of hearing and language outcomes, cognition and mental health revealed poorer outcome in hearing, language and mental health and lower executive functional level, as compared to a control group. Genetic analysis confirmed mutations in the POU3F4 gene on the X-chromosome. X-linked malformation deafness has been considered non-syndromic. However, we have shown that these children exhibit signs of neuro-developmental problems consistent with attention deficit and hyperactivity, which is likely related to the POU3F4 mutation. Additionally, during the last years the group has focused on refinement of the classification of inner ear malformations on CT and MRI, including the vestibular system.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Kaijsa Edholm	Eleonor Koro (Umeå)
	Jonas Frodlund

Ethical permit No.

2014/2068-31/2				

Publications 2019, 2020, 2021

1. Cochlear Implantation with the CI512 and CI532 Precurved Electrode Arrays: One-Year Speech Recognition and Intraoperative Thresholds of Electrically Evoked Compound Action Potentials. Videhult Pierre P, Eklöf M, Smeds H, Asp F. Audiol Neurootol. 2019;24(6):299-308.
2. X-linked Malformation Deafness: Neurodevelopmental Symptoms Are Common in Children With IP3 Malformation and Mutation in POU3F4. Smeds H, Wales J, Karltorp E, Anderlid BM, Henricson C, Asp F, Anmyr L, Lagerstedt-Robinson K, Löfkvist U. Ear Hear. 2021 Jun 15;43(1):53-69.
3. Wideband tympanometry in ears with superior canal dehiscence before and after surgical correction. Velikoselskii A, Papatziamos G, Smeds H, Verrecchia L. Int J Audiol. 2021 Aug 21:1-6.

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Clinical studies on upper airway inflammation, skullbase and sinonasal tumors and treatment of facial fractures.

Inflammation in the upper respiratory tract ; mechanistic mapping and evaluation of medical and surgical intervention . The project contains two parts:
• Studies of mechanisms in pregnancy rhinitis and its effect on the pregnant woman's quality of life.
• Epidiologic studies om acute rhinosinusitis in children.
The overall objective is to understand the basic epidemiology and mechanisms and but also to improve the treatment of these patient groups. Zygomatic and orbital blow out fractures ; diagnosis and evaluation of treatment The project includes both retrospective studies as prospective randomized trials and aims to improve the management of patients with facial fractures . Some questions that we want to highlight :
•To what extent does the change in orbital volume upon an orbital fracture influence patient's symptoms and what other factors are important for the development of sequelae
•What is the significance of fixation of facial fractures in relation to adequate fracture reduction
Studies of sinonasal tumors and pituitary adenomas: We have created an interdisciplinary network that aims to study sinonasal tumors and pituitary adenomas . The network, which covers most aspects from "bench to bedside ", has all prerequisites to get powerful synergies both in terms of basic knowledge about the tumor pathophysiology and epidemiology as well as the implementation of new discoveries in clinical work. .

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Ola Fridman Bengtsson	

Ethical permit No.

2012/4931	2012/89131	2012/4:8		

Publications 2019, 2020, 2021

1. Hultman Dennison S, Hertting O, Bennet R, Eriksson M, Holmström M, Schollin Ask L, Lindstrand A, Dimitriou P, Stjärne P, Granath A. A Swedish population-based study of complications due to acute rhinosinusitis in children 5-18 years old. Int J Pediatr Otorhinolaryngol. 2021 Nov;150:110866. doi: 10.1016/j.ijporl.2021.110866. Epub 2021 Aug 5.
2. Lundström J, Stjärne P. Förlorat luktsinne – möjligt tidigt tecken på covid-19. Lakartidningen. 2020 Apr 8;117:F3P9
3. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, Toppila-Salmi S, Bernal-Sprekelsen M, Mullol J, Alobid I, Terezinha Anselmo-Lima W, Bachert C, Baroody F, von Buchwald C, Cervin A, Cohen N, Constantinidis J, De Gabory L, Desrosiers M, Diamant Z, Douglas RG, Gevaert PH, Hafner A, Harvey RJ, Joos GF, Kalogjera L, Knill A, Kocks JH, Landis BN, Limpens J, Lebeer S, Lourenco O, Matricardi PM, Meco C, O Mahony L, Philpott CM, Ryan D, Schlosser R, Senior B, Smith TL, Teeling T, Tomazic PV, Wang DY, Wang D, Zhang L, Agius AM, Ahlstrom-Emanuelsson C, Alabri R, Albu S, Alhabash S, Aleksic A, Aloulah M, Al-Qudah M, Alsaleh S, Baban MA, Baudoin T, Balvers T, Battaglia T, Bedoya JD, Beule A, Bofares KM, Braverman I, Brozek-Madry E, Richard B, Callejas C, Carrie S, Caulley L, Chussi D, de Corso E, Coste A, Lal D, El Hadi U, Elfarouk A, Eloy PH, Farrokhi S, Felisati G, Ferrari MD, Fishchuk R, Grayson W, Goncalves PM, Grdinic B, Grgic V, Hamizan AW, Heinichen JV, Husain S, Ping TI, Ivaska J, Jakimovska F, Jovancevic L, Kakande E, Kamel R, Karpischenko S, Kariyawasam HH, Kjeldsen A, Klimek L, Kim SW, Letort JJ, Lopatin A, Mahdjoubi A, Netkovski J, Nyenbue Tshipukane D, Obando-Valverde A, Okano M, Onerci M, Ong YK, Orlandi R, Ouennoughy K, Ozkan M, Peric A, Plzak J, Prokopakis E, Prepageran N, Psaltis A, Pugin B, Raftopulos M, Rombaux P, Sahtout S, Sarafoleanu CC, Searyoh K, Rhee CS, Shi J, Shkoukani M, Shukuryan AK, Sicak M, Smyth D, Snidvongs K, Soklic Kosak T, Stjarne P. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Rhinology. 2020 Feb 20;58(Suppl S29):1-464. doi: 10.4193/Rhin20.600. PubMed PMID: 32077450.

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Tonsillectomy vs Uvulopalatopharyngoplasty in Adults with Obstructive Sleep Apnea The TEAMUP Randomized Controlled Trial

Background: Uvulopalatopharyngoplasty with tonsillectomy (UPPP) is a common surgical treatment for selected adults with Obstructive Sleep Apnea (OSA). Tonsillectomy (TE) alone is a less invasive alternative. The aim of this study was to investigate whether UPPP is more effective than TE in improving nocturnal respiration and daytime sleepiness.

Methods: Randomized controlled trial (RCT) of adults with medium or large tonsils and moderate to severe OSA who received either TE or UPPP. Outcomes were the differences between the groups in changes of apnea-hypopnea index (AHI) and Epworth Sleepiness scale (ESS), from baseline to the 6-month follow-up.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

2015/755-31/2				

Publications 2019, 2020, 2021

1. Niessl, J., Sekine, T., Lange, J., Konya, V., Forkel, M., Maric, J., Rao, A., Mazzurana, L., Kokkinou, E., Weigel, W., Llewellyn-Lacey, S., Hodcroft, E. B., Karlsson, A. C., Fehrm, J., Sundman, J., Price, D. A., Mjösberg, J., Friberg, D., & Buggert, M. (2021). Identification of resident memory CD8+ T cells with functional specificity for SARS-CoV-2 in unexposed oropharyngeal lymphoid tissue. Science Immunology
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Hearing in children with cleft palate

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

2012/2213-31	2012/46-31/2			

Publications 2019, 2020, 2021

1. Tengroth, B., Lohmander, A., & Hederstierna, C. (2019). Hearing Thresholds in Young Children With Otitis Media With Effusion With and Without Cleft Palate. Cleft Palate Craniofac J, doi:10.1177/1055665619889744
2. Lohmander, A. Westberg, L. R. Olsson, S. Tengroth, B. Flynn, T. (2020). Canonical Babbling and Early Consonant Development Related to Hearing in Children With Otitis Media With Effusion With or Without Cleft Palate. Cleft Palate Craniofac J, 2020 Oct 21, doi:10.1177/1055665620966198

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Hearing and speech with bilateral implants

The research focus on language development in children who have undergone surgery with cochlear implants, on the development of both language and other development in these subjects. There is new material, non-analyzed subgroups and other aspects to use to deepen the research field and knowledge. The research will elucidate the language development in subjects operated with cochlear implants and bone anchored hearing aids.
Language understanding and development, localization of sound is focus.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
	Fatima Moumén Denanto

Ethical permit No.

2013/104-31/	2013/1127-31/2	2013/104-31/4		

Publications 2019, 2020, 2021

1. Cochlear implants before 9 months of age led to more natural spoken language development without increased surgical risks. Karltorp E, Eklöf M, Östlund E, Asp F, Tideholm B, Löfkvist U. Acta Paediatr. 2019 Jul 27.
2. Psychometric properties of the Swedish version of the Glasgow Benefit Inventory in otosclerosis subjects.
3. Redfors YD, Jönsson R, Tideholm B, Finizia C.Laryngoscope Investig Otolaryngol. 2019 Nov 27;4(6):673-677. doi: 10.1002/lio2.320. eCollection 2019 Dec.

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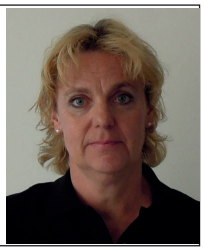

Treatment with dupilumab versus omalizumab in chronic rhinosinusitis with nasal polyps (CRSwNP)

Severe chronic rhinosinusitis with nasal polyps (CRSwNP) is a serious chronic inflammatory disease, including loss of smell, nasal congestion and nasal discharge. Many of them have astma. It is predominantly driven by type 2 inflammation in 50-80 % of patients. First line treatment for CRSwNP is intranasal corticosteroid in combination with nasal irrigations. In some patients addition of systemic corticosteroids is needed. When medical management fails surgery is indicated. In many patients there are a high rates of recurrence and revision surgery is needed.
Two biologics are approved for treatment of severe CRSwNP – omalizumab and dupilumab.
Therefore, the purpose of this multi-center study is to compare the efficacy and safety of dupilumab versus omalizumab in patients with severe CRSwNP and comorbid asthma.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

Publications 2019, 2020, 2021

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Effect of different treatments on symptoms in Menieres disease- retrospective study

The aim of the study is to evaluate different treatments for the symptoms of the Menieres disease. Treatment protocol for Meniere's disease is adjusted continuously, which should be evaluated.
Publication in the Lancet from 2016 Patel M, et al have shown that Intra tympanal steroid injections have less toxic effect on hair cells than gentamicin and have better properties in preserving hearing, although the effect in vertigo control does not differ. A recommendation was made for the treatment of Meniere's disease during the 21st IFOS Congress in Paris, in June 2017. International consensus (ICON) on treatment of Meniere's disease. Treatment with intra tympanal steroid injections would be before chemical destruction with gentamicin. We will evaluate different variables in hearing and balance function from questionnaires and journal data, for example. the frequency of dizziness, severity of dizziness, general effect on balance function, hearing loss between different groups of patients with Meniere's disease who were treated in different ways.

Tests used to dg and follow up the effect of different treatments also need to be analyzed and adjusted.
Meniere disease is the syndrome of endolymphatic hydrops. With the milestone achievement of endolymphatic hydrops imaging, today the pathology can be ascertained. ''HYDROPS'' (Hybrid of the reverse image of the positive endolymph signal and native image of the positive perilymph signal) was introduced in Karolinska University Hospital in November 2019 and in collaboration with Neuroradiology department we have started with clinical use of visualization the endolymphatic hydrops to ascertain the Meniere diagnosis in living patients.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

2021-06481-02				

Publications 2019, 2020, 2021

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EUscreen- H2020-SC1-2016-RTD. Implementation of cost-optimized childhood vision and hearing screening programs in middle-income countries in Europe.

The EU-funded EUSCREEN project (2017-2021) aimed to make vision and hearing screening available for all children in Europe by comparing the current screening programmes and by developing an online-available, cost-effectiveness model to assist with the introduction of a screening programme, taking the local circumstances in any given country into account. In a large survey, representatives of 41 countries in Europe and 5 countries outside Europe were asked to provide detailed data on the demography, the existing screening system, its coverage and attendance, screening tests used, follow-up, diagnosis, treatment, benefits and adverse effects of screening. Through this collaborative effort, the data set regarding vision and hearing screening is the largest ever collected. A cost-effectiveness model for vision and hearing screening has been developed to the point that users all over the world can enter their choice of screening programme. As a complimentary resource to the cost-effectiveness model, the EUSCREEN Manual for Implementation or Modification of Child Vision and Hearing Screening Programmes was written.

How effective is screening for the early detection of all children with hearing impairment?

The purpose of this research project is to improve the detection pathways for children with HI that are not currently detected through NHS in Sweden. Answers to these questions will help guide policy on how to improve pathways and protocol for detecting children with HI as early as possible. The results of the present study will ultimately determine how to improve HI detection pathways for children with HI. Using registry data not previously published, we will determine the predictive clinical attributes for late detection, retrospectively investigate the screening results and parameters to improve sensitivity and analyse the effectiveness of pathways to detection after NHS.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Allison Mackey	

Ethical permit No.

2010/1456 32	2020/07203			

Publications 2019, 2020, 2021

1. Mackey AR, Bussé AML, Hoeve HLJ, Goedegebure A, Carr G, Simonsz HJ, Uhlén IM, EUS€REEN Foundation. Assessment of hearing screening programmes across 47 countries or regions II: coverage, referral, follow-up and detection rates from newborn hearing screening International journal of audiology 2021 60:11 831-840 View in Web of Science
2. Bussé AML, Mackey AR, Carr G, Hoeve HLJ, Uhlén IM, Goedegebure A, Simonsz HJ, EUS€REEN Foundation. Assessment of hearing screening programmes across 47 countries or regions III: provision of childhood hearing screening after the newborn period International journal of audiology 2021 60:11 841-848 View in Web of Science
3. Bussé AML, Mackey AR, Hoeve HLJ, Goedegebure A, Carr G, Uhlén IM, Simonsz HJ, EUS€REEN Foundation. Assessment of hearing screening programmes across 47 countries or regions I: provision of newborn hearing screening International journal of audiology 2021 60:11 821-830 View in Web of Science
4. Engström E, Kallioinen P, Nakeva von Mentzer C, Lindgren M, Sahlén B, Lyxell B, Ors M, Uhlén I. Auditory event-related potentials and mismatch negativity in children with hearing loss using hearing aids or cochlear implants - A three-year follow-up study International journal of pediatric otorhinolaryngology 2021 140: 110519- View in Web of Science

5. Verkleij ML, Heijnsdijk EAM, Bussé AML, Carr G, Goedegebure A, Mackey AR, Qirjazi B, Uhlén IM, Sloot F, Hoeve HLJ, de Koning HJ, Country-Committees Joint-Partnership of EUSCREEN Study Consortium. Cost-Effectiveness of Neonatal Hearing Screening Programs: A Micro-Simulation Modeling Analysis Ear and hearing 2021 42:4 909-916 View in Web of Science
6. Cederroth CR, Lugo A, Edvall NK, Lazar A, Lopez-Escamez JA, Bulla J, Uhlen I, Hoare DJ, Baguley DM, Canlon B, Gallus S. Association between Hyperacusis and Tinnitus JOURNAL OF CLINICAL MEDICINE 2020 9:8 View in Web of Science
7. Engström E, Kallioinen P, Lindgren M, Nakeva von Mentzer C, Sahlén B, Lyxell B, Uhlén I. Computer assisted reading intervention for children with hearing impairment using cochlear implants: Effects on auditory event-related potentials and mismatch negativity International journal of pediatric otorhinolaryngology 2020 137: 110229- View in Web of Science
8. Uhlen I, Mackey A, Rosenhall U. Prevalence of childhood hearing impairment in the County of Stockholm - a 40-year perspective from Sweden and other high-income countries INTERNATIONAL JOURNAL OF AUDIOLOGY 2020 59:11 866-873 View in Web of Science
9. Lugo A, Edvall NK, Lazar A, Mehraei G, Lopez-Escamez JA, Bulla J, Uhlen I, Canlon B, Gallus S, Cederroth CR. Relationship between headaches and tinnitus in a Swedish study SCIENTIFIC REPORTS 2020 10:1 8494- View in Web of Science
10. Niu K, Brandström A, Skenbäck S, Duan M, Uhlén I. Risk factors and etiology of childhood hearing loss: a cohort review of 296 subjects Acta oto-laryngologica 2020 140:8 668-674 View in Web of Science
11. Trpchevska N, Bulla J, Prada Hellberg M, Edvall NK, Lazar A, Mehraei G, Uhlen I, Schlee W, Canlon B, Gallus S, Lopez-Escamez JA, Cederroth CR. Sex-Dependent Aggregation of Tinnitus in Swedish Families Journal of clinical medicine 2020 9:12 View in Web of Science 1 / 2
12. Engström E, Kallioinen P, Nakeva von Mentzer C, Lindgren M, Ors M, Sahlén B, Lyxell B, Uhlén I. Computer-assisted reading intervention for children with sensorineural hearing loss using hearing aids: Effects on auditory event-related potentials and mismatch negativity International journal of pediatric otorhinolaryngology 2019 117: 17-25 View in Web of Science

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Objective balance testing in children

This project, linked to the doctoral eduction of MD Niki Karpeta, aims to validate a modern pediatric objective balance testing in clinical practice. An ongoing validation study is about the balance screening of newborns with vestibular evoked miogenic potentials (VEMP), along with the universal hearing screening program. An observational study deals with the testining of vestibular function in CI recipients grown up to teenage. A third study will test the vestibular function in schoolaged children complaining about vertigo. A fourth study concerns the validation of a swedish version of the Pediatric Vestibular Symptom Questionnaire, developed by the King´s College, London. This project is supported by SCAPA (https://ki.se/clintec/om-scapa), a research organisation at CLINTEC for advanced clinical research in pediatric audiology and neurotology, which I lead togheter with assoc. professor Erik Berninger and M. Sc. CS, PhD Filip Asp

New methods for a better diagnosis of dizziness by bone conducted stimulation

The project represents my post-doctoral studies, as guest researcher at the Department of Electrical Engineering, Chalmers University of Technology. Supervised by full professor Bo Håkansson and assoc professor Sabine Reinfeldt, I´m testing the clinical use of a new bone transducer prototype, the Ortofon B250. In a first study we present a new hearing test based on bone conducted stimulation at malleolus by B250 as a screening test for superior canal dehiscence syndrome (SCDS). We are also investigating the role of B250 in easing and promoting the clinical balance testing by VEMP. Finally we will introduce this device in VEMP testing for children.

Advancements in superior canal dehiscence diagnostics

With this research line I will continue my doctoral studies in SCDS diagnostics. In a study we have shown the utility of wideband tympanometry in revealing the ears´ admittance normalization after SCDS surgery. In a recent case report we discussed the risk SCDS overdiagnosis by balance testing.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
	Niki Karpeta

Ethical permit No.

2019-05214	2019-02019	2013/1177-31		

Publications 2019, 2020, 2021

1. Verrecchia L, Edholm K, Pekkari M. Asymptomatic superior semicircular canal dehiscence. J Laryngol Otol. 2021 Oct 27:1-4.
2. Velikoselskii A, Papatziamos G, Smeds H, Verrecchia L. Wideband tympanometry in ears with superior canal dehiscence before and after surgical correction. Int J Audiol. 2021 Aug 21:1-6.
3. Lazar A, Löfkvist U, Verrecchia L, Karltorp E. Identical twins affected by congenital cytomegalovirus infections showed different audio-vestibular profiles. Acta Paediatr. 2021 Jan;110(1):30-35.
4. Verrecchia L, Galle Barrett K, Karltorp E. The feasibility, validity and reliability of a child friendly vestibular assessment in infants and children candidates to cochlear implant. Int J Pediatr Otorhinolaryngol. 2020 Aug;135:110093.

5. Wibble T, Engström J, Verrecchia L, Pansell T. The effects of meclizine on motion sickness revisited. Br J Clin Pharmacol. 2020 Aug;86(8):1510-1518.
6. Verrecchia L, Karpeta N, Westin M, Johansson A, Aldenklint S, Brantberg K, Duan M. Methodological aspects of testing vestibular evoked myogenic potentials in infants at universal hearing screening program. Sci Rep. 2019 Nov 21;9(1):17225.
7. Skott H, Muntean-Firanescu C, Samuelsson K, Verrecchia L, Svenningsson P, Malmgren H, Cananau C, Espay AJ, Press R, Solders G, Paucar M. The cerebellar phenotype of Charcot-Marie-Tooth neuropathy type 4C. Cerebellum Ataxias. 2019 Jul 15;6:9.
8. Verrecchia L, Brantberg K, Tawfique Z, Maoli D. Diagnostic Accuracy of Ocular Vestibular Evoked Myogenic Potentials for Superior Canal Dehiscence Syndrome in a Large Cohort of Dizzy Patients. Ear Hear. 2019 Mar/Apr;40(2):287-294.
9. Verrecchia L, Glad K, Frisk R, Duan M. Vestibular myogenic potentials evoked by air-conducted stimuli at safe acoustic intensity levels retain optimal diagnostic properties for superior canal dehiscence syndrome. Acta Otolaryngol. 2019 Jan;139(1):11-17.

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Diagnostics and treatment of Head and Neck Cancer

Several projects:

- Tracheal Stenosis - Increased specificity and sensitivity of diagnosis and evaluation of treatment. Can outpatient corticosteroid injections in tracheal stenosis patients extend the procedure free intervall for patients with recurrent stenosis.
- Oral cancer - Can ultrasound increase the survival of patients when used during resection. Is ultrasound superior to other diagnostic procedures in measuring the depth of invasion and thereby increse the diagnostic accuracy. Can NBI (Narrow band imaging) improve the decisionmaking in resections of oral cancers.
- Citrculating cell free HPV-DNA as a marker of recurrence of oropharyngeal cancer.
- Can sentinel node biopsies be used in salivary gland cancers? Can it be used in node positive necks?

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
	Eleftherios Ntouniadakis
	Olof Nilsson
	Anna Oldaeus Almeren

Ethical permit No.

2019-0323	2018-104	2020-05509	2016-275	2016-193

Publications 2019, 2020, 2021

1. Kristiansson S, Reizenstein J, von Beckerath M, Landstrom F. Long-term follow-up in patients treated with electrochemotherapy for non-melanoma skin cancer in the head and neck area. Acta Otolaryngol. 2019 Feb;139(2):195-200. PubMed PMID: 30734631. Epub 2019/02/09.
2. Ntouniadakis E, Brus O, von Beckerath M. Dyspnea Index: An upper airway obstruction instrument; translation and validation in Swedish. Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery. 2021 Mar;46(2):380-7. PubMed PMID: 33277799. Pubmed Central PMCID: PMC7986702. Epub 2020/12/06.
3. von Beckerath M, Svensson J, Landström F. Feasibility of an inexperienced examiner using trans-cervical ultrasound in the diagnosis of peritonsillar abscesses. Acta Oto-Laryngologica. 2021:1-4.
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6. Prevalence of cystic metastases in a consecutive cohort of surgically removed branchial cleft cysts. Acta Otolaryngol. 2021 Dec 28:1-6. PubMed PMID: 34962438. Epub 2021/12/29.

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1. Temporal bone malformation.
Children with temporal bone malformations often present with a significant progressive hearing loss. Cochlea implantation is often needed to improve speech understanding and for the patient to develop the ability to communicate. We are investigating large vestibular aqueduct, and incomplete partition types 2 and 3 malformations. We are assessing new methods in radiological diagnosis, implantation technique, hearing and related neurological factors.

2. Intraoperative assessment of the ossicular chain.
Ossicular fixation in the middle ear is one cause of conductive hearing loss where there is no reliable objective system to assess this. We are developing a system (MIVIB) utilising laser vibrometry to assess the movement of the ossicular chain to determine which operation and which prosthesis will give the best hearing result.

3. Bilateral bone anchored hearing solutions.
Bone-anchored hearing solutions are often implanted unilaterally. We are assessing whether patients have an imporved ability to localise sound and hear when background noise is present if they are provided with bilateral BAHS.

4. Tracheostomy in the era of Covid-19.
The pandemic led to an unprecedented amount of patients requiring tracheostomy. We analyse the immediate, short- and long-term complications of this technique when performed by otolaryngologists or intensivists.

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*
Clara Svenberg Lind (intended)	Kaijsa Edholm
	Fatima Moumen Denanto

Ethical permit No.

2020-02779	2018/1032-31	2014/2068-31/2		

Publicatiions 2019, 2020, 2021

1. Wales, J., Smeds, H., Karltorp, E., Anderlid, B.M., Henricson, C., Asp, F., Anmyr, L., Lagerstedt-Robinson, K., Löfkvist, U. X-linked Malformation Deafness: Neurodevelopmental Symptoms Are Common in Children With IP3 Malformation and Mutation in POU3F4. Ear and hearing 2021;():-
2. Globalsurg Collaborative, Covidsurg Collaborative. Effects of pre-operative isolation on postoperative pulmonary complications after elective surgery: an international prospective cohort study. Anaesthesia 2021;76(11):1454-1464.
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4. Covidsurg Collaborative Globalsurg Collaborative. SARS-CoV-2 vaccination modelling for safe surgery to save lives: data from an international prospective cohort study. The British journal of surgery 2021;108(9):1056-1063
5. Globalsurg Collaborative, Covidsurg Collaborative. Timing of surgery following SARS-CoV-2 infection: an international prospective cohort study. Anaesthesia 2021;76(6):748-758
6. Wales, J., Alinasab, B., Fridman Bengtsson, O. A superficial nasal dermoid cyst excised through a novel horizontal zig-zag incision in a 49-year old man. Acta Otolaryngologica Case reports. 2020; 5:28-32.
7. Wales, J., Gladine, K., Silvola, J., Muyshondt, P., Topsakal, V., Van De Heyning, P., Dirckx, J., von Unge, M. Evaluation of artificial fixation of the incus and malleus with minimally invasive intraoperative laser vibrometry (MIVIB) in a temporal bone model. Otol. Neurotol. 2020; 41:45-51.

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Studies on laryngotracheal airway diseases

Long-term outcome of reconstructive airway surgery in pediatric and adult patients
- Pediatric tracheostomy - mortality, morbidity and long-term outcome
- Psychosomatic development and quality of life in pediatric patients with tracheostomy

Supervision of PhD-students:

Main Supervisor	*Co-supervisor*

Ethical permit No.

2020-02779	2018/1032-31	2014/2068-31/2		

Publicatiions 2019, 2020, 2021

1. Wendt M, Hammarstedt L, Dalianis T, Landin D, Munck-Wikland E, Näsman A, Marklund L. Long-term survival and recurrence in oropharyngeal squamous cell carcinoma, in relation to HPV and p16-status. Cancers 2021 May 23;13(11):2553.
2. Wendt M, Papatziamos G, Munck-Wikland E and Marklund L. Sclerotherapy with OK 432 on ranula – a prospective, randomised, double-blinded placebo-controlled study.
3. ACTA Otolaryngol. 2021; 27:1-6

PhD-students

Arnason, Sigurdur ..... 74.
Blomkvist, Rasmus ..... 75.
Dahlby Skoog, Malin ..... 76.
Danielsson, Daniel ..... 77.
Eriksson, Björn ..... 78.
Fridman Bengtsson, Ola ..... 79.
Gille, Evelina ..... 80.
Hjalmarsson, Eric ..... 81.
Häggström, Jenny ..... 82.
Johansson, Marlin ..... 83.
Josefsson, Hanna ..... 84.
Karlsson, Sofia ..... 85.
Karpeta, Niki ..... 86.
Kolev, Aeneas ..... 87.
Lagebro, Vilma ..... 88.
Landin, David ..... 89.
Lansing, Lovisa ..... 90.
Mackey, Allison ..... 91.
Malmström, Emma ..... 92.
Modée, Agnes ..... 93.
Moumen Denanto, Fatima ..... 94.
Ohm, Rebecka ..... 95.
Piersiala, Krzysztof ..... 96.
Rahbin, Samin ..... 98.
Sellberg, Malin ..... 99.
Sepehri, Elnaz ..... 100.
Siegbahn, Malin ..... 101.
Skröder, Carl ..... 102.
Starkhammar, Magnus ..... 103.
Turunen-Taheri, Satu ..... 104.
Åberg, Karin ..... 105.

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Main supervisor Barbro Hedin Skogman
Co-supervisor Malou Hultcrantz, Åsa Laestadius, Elin Marsk
Registered 2019-09-27
Halftime seminar
Planed dissertation

Facial nerve palsy in children; treatment and clinical outcome

I. Peripheral facial nerve palsy in children in a Borrelia high endemic area: epidemiology and evaluation of clinical recovery. A retrospective follow-up. To identify the incidence, etiology and prognosis of acute peripheral facial nerve palsy (FNP) in children in the Stockholm area. A retrospective study identifying children from 0-17 years of age visiting a pediatric emergency department for acute FNP during a one-year period from 2014-2015 (77 patients).

II. Efficacy of cortisone vs. placebo in children with idiopathic facial nerve palsy and Lyme neuroborreliosis facial nerve palsy. Participation in the FACE study (Facial nerve palsy And Cortisone Evaluation in children), a multicenter randomized placebo-controlled study on the efficacy of cortisone treatment in children with acute facial nerve palsy. For inclusion the cause of FNP will be either Lyme neuroborreliosis (LNB) or idiopathic facial palsy. Children with LNB will be treated with antibiotics according to present guidelines in combination with the treatment provided in the study (cortisone vs. placebo). Follow-up will take place via telephone and with follow-up visits at 1 and 12 months. Subjects will be graded according to the House-Brackmann and the Sunnybrook facial grading scales and specific standardized facial palsy questionnaires.

III. Long term outcome and neurophysiologic findings in idiopathic facial nerve palsy in a pediatric population. This study will aim to highlight the long-term prognosis of 50 children affected by idiopathic facial nerve palsy. The aim is to follow-up the children with idiopathic facial palsy and record subjective, objective and neurophysiological findings.

IV. Detection of brain damage markers S-100B and NSE in serum in children with Lyme neuroborreliosis for evaluation as prognostic marker for clinical outcome. The brain damage markers S-100 B and NSE (Neuron-specific enolase) will be analyzed in serum in children with LNB and in a non-neuroinflammatory group.

Ethical permit No.

2016/1937-31/4 (Stockholm)	2017/554 (Uppsala)	2010/106 (Uppsala)	

Publications/manuscripts 2019, 2020, 2021

1. Arnason, S, Hultcrantz, M, Nilsson, A, Laestadius, Å. Peripheral facial nerve palsy in children in a Borrelia high-endemic area, a retrospective follow-up study. Acta Paediatr. 2020; 109: 1229– 1235. https://doi.org/10.1111/apa.15063
2. Karlsson, Arnason, S., Hadziosmanovic, N., Laestadius, Å., Hultcrantz, M., Marsk, E., and Skogman, B. H. (2021). The facial nerve palsy and cortisone evaluation (FACE) study in children: protocol for a randomized, placebo-controlled, multicenter trial, in a Borrelia burgdorferi endemic area. BMC Pediatrics, 21(1), 220–220. https://doi.org/10.1186/s12887-021-02571-w

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Registered 2021-02-16
Halftime seminar
Planed dissertation

Predictive markers for laryngeal cancer

Cancer of the vocal cords, laryngeal cancer, is one of the most common tumor types in the head and neck region with approximately 180 new cases each year in Sweden. Whereas the survival rate for small tumors (T1) is relatively good, more advanced disease (T2-T4) is associated with poor outcome and has not improved significantly in recent decades. In Sweden and in Stockholm according to national guidelines, patients with T2 and T3 laryngeal cancer are treated with radiotherapy (RT) or chemoradiotherapy (CRT) to preserve the patient's larynx, while patients with T4-tumors are treated surgically with laryngectomy, i.e. resection of the entire larynx and upper trachea often in combination with adjuvant RT/CRT. Our own data and other studies show that there is poorer survival for patients with T3 compared with T4 laryngeal cancer. It is clear that many patients with tumors classified as T3 are undertreated. The question is how to identify which laryngeal tumors that are in need of extended treatment to avoid recurrence and death from laryngeal cancer.

All our sub-studies in this research project aim to identify clinically useful markers and methods that can help us to optimize the choice of treatment strategy for patients with advanced laryngeal cancer.

Ethical permit No.

2019-04829			

Publications/manuscripts 2019, 2020, 2021

1.

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Co-supervisor Eva Karltorp, Björn Lyxell, Tamara Kalandadze
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Halftime seminar
Planned dissertation

Long term effects of early age at cochlear implantation on metaphor comprehension and executive functions in Swedish teenagers

Early age at cochlear implantation has positive effects on early spoken language for congenitally deaf children, but there is need for more research on the long-term effects of early implantation to explain the large variability in outcomes seen in this group. The research regarding long term effects of cochlear implantation on higher linguistic skills, such as metaphor comprehension, is scarce. Executive functions are higher cognitive functions including working memory, attention shifting and inhibitory control. Executive functions develop in close relationship with linguistic skills.

The aim of this project, as part of a multidisciplinary follow up program, is to investigate long term effects of early cochlear implantation on the development of executive functions and metaphor comprehension. We are also interested in the possible relationship between executive functions and the higher linguistic skill of metaphor comprehension. The cohort is estimated to be around 100 individuals between 13 and 18 years old, fitted with CI before 30 months of age at the Hearing Implantation Center at Karolinska university hospital. There will also be a normal hearing control group matched for age, sex and socioeconomic status. Children from multilingual as well as monolingual homes will be included.

Metaphor comprehension will be measured using a multiple-choice task. Linguistic skills (vocabulary and reading) will be assessed with standardized tests. Executive functions will be assessed by task performance and the BRIEF questionnaire.

Data collection is planned to start in january 2022

Ethical permit No.

Publications/manuscripts 2019, 2020, 2021

1. Löfkvist, U., Bäckström, K., Dahly-Skoog, M., Gunnarsson, S., Persson, M., Lohmander, A. (2019). Babbling and consonant production in children with hearing impairment who use hearing aids or cochlear implants – a pilot study. Logopedics Phoniatrics Vocology, Nov 29:1-9. doi: 10.1080/14015439.2019.1695929

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Co-supervisor Siamak Haghdoost
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Halftime seminar 2020-06-17
Planned dissertation

Osteoradionecrosis - Riskfactors and reconstructive outcome

Irradiation, surgery and chemotherapy are the three main treatment modalities for head and neck cancer patients. Irradiation, especially in combination with chemotherapy, is associated with considerable side effects.
Osteoradionecrosis, ORN, is a late and often severe side effect to irradiation. It is defined as necrotic bone exposed through a mucosal and/or skin defect without tumor recurrence and with a duration of more than three months.
There is no exact definition of the pathophysiology of ORN but the current thesis include:

1. Direct damage to local micro vessels causing vascular necrosis in the irradiated area.
2. Production of ROS(reactive oxygen species) that gives an irreversible damage to osteoblasts, -cytes, -clasts.
3. Cytokine mediated dysregulation of fibroblasts and collagen metabolism leading to fibrotic tissue. ORN is for the individual patient a severe condition affecting daily life. Symptoms include trismus, pain, im- paired nutritional capacity and infection not seldom associated with oro-cutanous fistula. ORN is seldom reversible and will progress over time leading to pathological fractures and need for extensive reconstruc- tive surgical intervention including free tissue transfer. This treatment is costly to both patient and society.

Radiation therapy is dose dependant but individual differences exists. The incidence of ORN in the head and neck ara is reported to 3-8%.

Aim of our studies:

1. Possible markers for individual radiosensitivity; oxidative stress response, genetic and protein level
2. Osteoradionecrosis impact on indications for exstensive maxillomandibular reconstruction
3. Quality of life comparative study for ORN patients before and after extensive reconstrucitve surgery with free tissue transfer.
4. Impact of Brachy therapy in onset of ORN in patients treated for cancer of the tounge

Ethical permit No.

2006/1413-32	2016/1578-32	2016/277-32	2016/506-31	

Publications/manuscripts 2019, 2020, 2021

1. Osteoradionecrosis, an increasing indication for microvascular head and neck reconstruction. Danielsson D, Gahm C, Haghdoost S, Munck-Wikland E, Halle M. Int J Oral Maxillofac Surg. 2020 Jan;49(1):1-6. doi: 10.1016/j.ijom.2019.06.009. Epub 2019 Jul 8. PMID: 31296436
2. Quality of life after microvascular mandibular reconstruction for osteoradionecrosis-A prospective study. Danielsson D, Munck-Wikland E, Hagel E, Halle M. Head Neck. 2019 Jul;41(7):2225-2230. doi: 10.1002/hed.25681. Epub 2019 Feb 5. PMID: 30721560

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Registered 2018-01-29
Halftime seminar
Planned dissertation

Inflammatory changes of skin after radiotherapy

An increasing number of long-term cancer survivors have a reduced quality of life due to sequelae from previous radiotherapy. Fibrosis of soft tissue leads to cosmetic as well as functional difficulties, e.g. stiffness, dysphagia and hoarseness. Exposure to ionizing radiation in the head and neck area and thorax also predispose to stroke or heart disease.

Our hypothesis is that radiotherapy leads to dysregulation of the innate and adaptive immune system, resulting in chronic inflammation, and deposition of extracellular matrix. A decrease in the size and number of blood vessels leads to a perpetual and worsening hypoxia of the tissue, which further exacerbates the problem.

We collect skin samples from previously irradiated patients undergoing surgery in the ENT unit and will compare these samples to a murine radiation model using immunohistochemistry, immunofluorescence and gene expression analysis. Through a better understanding of the biology causing these changes, we hope to ameliorate the morbidity of future cancer survivors.

Ethical permit No.

2015/696-32	2008/814-31	2012/1663-32	2008/484-31/2	2006/834-31/1

Publications/manuscripts 2019, 2020, 2021

1. Martin Halle, Bjorn O Eriksson, Ann-Charlott Docherty Skogh, Pehr Sommar, Lalle Hammarstedt, Caroline Gahm. Improved Head and Neck Free Flap Outcome-Effects of a Treatment Protocol Adjustment from Pre- to Postoperative Radiotherapy Plast Reconstr Surg Glob Open. 2017 Mar 30;5(3):e1253. eCollection 2017 Mar. PMID: 28458967 PMCID: PMC5404438 DOI: 10.1097/GOX.0000000000001253
2.
3. Bjorn O Eriksson, Caroline Gahm, Martin Halle. Upregulation of Plasminogen Activator Inhibitor-1 in Irradiated Recipient Arteries and Veins from Free Tissue Transfer Reconstruction in Cancer Patients. Mediators Inflamm. 2018 Oct 4;2018:4058986. eCollection 2018. PMID: 30402041 PMCID: PMC6193344DOI: 10.1155/2018/4058986

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Halftime seminar 2021-01-22
Planed dissertation

Pituitary tumors; clinical aspects of treatment and expression of Galanin,- and pattern recognition receptors

Pituitary adenomas are classified into hormone secreting or clinically inactive. Symptoms arise either due to hormononal effects or local compression, usually the optic chiasm.
Treatment for these adenomas are either medical och surgical dependent on characteristics of the tumor. Sometimes radiation can be used for surgically unacessible locations.
My thesis aims to evaluate treatment in Karolinska University Hospital during the time period 2005-17, focusing on cure rates in ACTH and GH producing adenomas and complications within the group as a whole. This manuscript is due for submission.
We have also evaluated different treatment strategies in periopoperative cortison substitution and published on this topic 2019.
Since 2012 we have collected tissue from pituitary adenomas and pituitaries from 11 organ donors as a base for our receptor studies.
Our aim is that these 2 studies are to be completed during 2022. One study will evaluate prevalence of Galaninreceptors, especially type 3, which in previous materials have been indicated as a marker for pituitary adenomas as opposed to normal pituitary tissue.
The fourth study will investigate a new inflammatory marker, called TSLP (Thymic Stromal Lymphopoetin) and which has been described in inflammatory airway disease, but not yet been studied in pituitary adenomas. We will also look at neuropeptide Y, pattern recognition receptors and TGFbeta.

Ethical permit No.

2012/1689-31/4 (2019-01941)	2012/891-31/2			

Publications/manuscripts 2019, 2020, 2021

1. Evaluations of different treatment strategies in transsphenoidal pituitary surgery,Acta Neurochirurgica (2019) 161:1715–1721. https://doi.org/10.1007/s00701-019-03885-6
2. Acta Neurochirurgica (2019) 161:1715–1721 ”Cure rate, complications and overall survival in transsphenoidal pituitary surgery at Karolinska University Hospital, manuscript.

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Planned dissertation

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Lalle Hammarstedt Nordenvall
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2020-05-25

Studies on Nasopharyngeal Cancer – a characterization of a rare disease

I: To describe the pattern of recurrence in patients treated for nasopharyngeal cancer in Stockholm. Hypothesis: Local recurrences occur outside target volume. Retrospective single institution study. Data from medical records and target volume, will be correlated to recurrence and place of recurrence, ie outside or inside target volume. Pattern of failure will teach us more on how to design treatment models in this disease. If recurrences occur outside treatment volume that might be an indication to improve treatment planning.

II: A register-based cohort study of Nasopharyngeal Carcinoma in Sweden, using SweHNCR: outcome, fai lure rate and site of failure Hyphothesis: Local regional failure is more common than distant failure Data from Swedish Head and Neck Cancer Registry (SweHNCR). All patients in Sweden diagnosed with Nasopharyngeal carcinoma, histology codes for Squamous cell carcinoma, Lymfoepithelioma or undiffe rentiated carcinoma will be included. This study will describe the pattern of failure in Sweden and thus indirectly characterize the disease as resembling either the endemic type or the non-endemic type.

III: To describe the distribution of the different histopathological subgroups and to assess the viral correla tion. Hypothesis: The overall viral correlation is higher than in Finland The Stockholm cohort will be used to assess viral association. Data on how the distribution of viral correla tion is in Sweden will be of importance when addressing treatment options.

IV:To describe the risk profile for second primary in patients with NPC. Hypothesis: Patients treated for NPC carries a higher risk for second primary than the general population. A register-based study will be performed to characterize the population at risk for the disease. Linkage to multi-generation registry will be used in this regard, will be used to assess risk of second primary

Ethical permit No.

2019-01933					

Publications/manuscripts 2019, 2020, 2021

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Planned dissertation

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2019-12-17

Intralymphatic Allergy Vaccination; immuneresponse and tollerance

Intra lymphatic immunotherapy is proposed as a faster and safer alternative to conventional allergy therapy. We have confirmed the safety of ILIT with 1000 SQ-U/ml, and also shown that concomitant ILIT with birch and grass allergen reduce symptoms during the following pollen season. In a follow up study the clinical response could also be detected 5-6 years after the initial ILIT treatment. An ILIT study with increased allergen dos >1000SQ-U /ml have also been conducted. This ILIT treatment protocol did not improve the clinial outcome for the patients and can not be recommended.
In patients treated with active ILIT we have detected an increased activation of T-cells in the allergen injected lymph nodes. Remarkably, the increased activation was also detected at the follow up 5-6 years after the ILIT injections. More in depth analyzis of the T-cells in lymph nodes could not be performed due to the smal samle size. In blood the levels of CD4+CD25++ (Treg) and CD4+CCR5+ (Th1) was increased in patients treated with active ILIT. Tregs are known to indrease during ILIT and can influnce the immune response by blocking T-cell and antigen presenting cell activation, thus promoting allergen tollerance. Further, the increased levels of CD4+CCR5+ (Th1) may also be a sign of tollerance induction. A specific type of allergen specific Th1 T-cells can only be detected in non-allergic individuals. This subset of T-cells may be key to better detect responders to ILIT.
Immunological findings realated to B-cells was incresaed levels of allergen specific IgG4 and reduced levels of allergen specific IgE. IgG4 block the biological function of IgE and have been shown to closely relate to clinical response. Interestingly, increased levels of IgG4 in blood do not automaticly result in a clinical response.
We belive that more focus on immunological changes in nasal mucosa is key to better understand how ILIT induce allergen tollerance.

Ethical permit No.

2012/1018-31/2	2013/1422-31/1	2015/2257-31/1	2018/697-31	2016/823-31-2	

Publications/manuscripts 2019, 2020, 2021

1. Hellkvist L, Hjalmarsson E, Weinfeld D, Dahl Å, Karlsson A, Westman M, Lundkvist K, Winqvist O, Georén SK, Westin U, Cardell LO. High dose pollen intralymphatic immunotherapy: Two RDBPC trials question the benefit of dose increase. Allergy. 2021 Aug 11. doi: 10.1111/all.15042. Epub ahead of print. PMID: 34379802.

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Main supevisor Esma Idrizbegovic
Co-supervisor Christina Hederstierna, Per Östberg, Nenad Bogdanovic
Registered 2016-11-14
Halftime seminar 2019-05-20
Planned dissertation

Hearing, cognition and aging

Huvudsyfte är att belysa central hörselfunktion, hur vi kan mäta den, och dess relation till kognitiv svikt. Mer specifikt att öka förståelsen hur hjärnförändringar vid demens och kognitiv svikt påverkar central hörselfunktion. Antalet äldre ökar stadigt i befolkningen tack vare att vi lever allt längre. Med stigande ålder ökar också risken av att drabbas av kognitiv svikt, demens och hörselnedsättning. En form av hörselnedsättning hos främst äldre är s.k. central auditory processing dysfunction, (CAPD). Dessa personer har svårigheter att uppfatta vad som sägs i störande ljudmiljöer med bakgrundsbuller eller när flera personer talar samtidigt, och de har inte optimal nytta av hörapparatanvändning. Den centrala hörselstörningen beror på försämrad funktion i de delar av centrala nervsystemet som ansvarar för bearbetningen av ljudstimuli. CAPD har påvisats hos patienter med lindrig kognitiv störning och Alzheimers sjukdom genom dikotiska lyssningstest. I delarbete 1 följdes tre grupper av individer med varierande kognitiv funktion med perifera och centrala hörseltestunder efter fem år. I delarbete 2 tittade vi på kognitiv utveckling hos en grupp individer med mild kognitiv störning (MCI) och jämförde kognitivt utfall under 5 år med resultat på dikotiska tester med siffror (DDT) vid baseline. I delarbete 3 korreleras resultat på DDT till deltagarnas biomarkörer i cerebrospinalvätska. I delarbete 4 kommer vi att undersöka hur förändringar i corpus callosum, som förbinder de båda hjärnhalvorna, korrelerar till resultat på DDT hos personer med Alzheimers sjukdom (AD), MCI och subjektiv minnesstörning (SMC). DDT förutsätter en intakt förbindelse mellan hjärnhalvorna via corpus callosum.

Ethical permit No.

2005/914-31	2014/2087-31/2	2018/1291-32		

Publications/manuscripts 2019, 2020, 2021

1. Prognostic value of a test of central auditory function, the dichotic digits test, in conversion from mild cognitive impairment to dementia, submitted 2019

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Main supevisor	Erik Berninger
Co-supervisor	Filip Asp, Sten Hellström, Kamilla Angelo
Registered	2016-11-03
Halftime seminar	2020-09-11
Planned dissertation	Planned for end 2022

Children with Congenital Unilateral Sensorineural Hearing Loss: The effect of Auditory Stimulation in the Impaired Ear During Development

The overall aim is to study the causes and mechanisms underlying congenital unilateral sensorineural hearing loss (uSNHL) and the effects of intervention.

The first publication was a pilot study of hearing aid outcomes in school-aged children with congenital uNSHL. The children demonstrated both hearing aid benefit and dis-benefit. The statistically significant benefit was found in one-to-one communication, based on child and parent questionnaires. Hearing aid dis-benefit was found for sound localization measured with eye-tracking in sound field. Neither significant hearing aid benefit nor dis-benefit existed for speech understanding in background noise/speech (sound field and questionnaires) or reverberation (questionnaires). A close relationship between neural maturation and aided sound localization was also found, indicating that hearing aids may be more efficient if fitted earlier in development, before the brain adapts to asymmetrical hearing.

In the second publication we studied heredity of transient evoked otoacoustic emissions (TEOAEs), that are recorded as part of the universal neonatal hearing-screening program. We found that the TEOAEs at birth are largely inherited, perhaps more than for young adult twins. Additionally, we found that sex and ear differences existed at birth, and that the twin testosterone transfer hypothesis, that female twins with male co-twins would have masculinized TEOAEs, was not supported for neonatal twins.

We have invited 20 neonates with congenital uSNHL born in Region Stockholm to study etiology, early hearing, speech-language and communication development, and the outcomes of very early hearing aid intervention longitudinally. The manuscript with focus on etiology has being finalized and sent for review.

Ethical permit No.

2015/1878-31/2	2018/1500-31	2019–03826		

Publications/manuscripts 2019, 2020, 2021

1. Johansson, M., Asp, F., Berninger, E. 2020. Children With Congenital Unilateral Sensorineural Hearing Loss: Effects of Late Hearing Aid Amplification-A Pilot Study. Ear and Hearing 41, 55-66. doi:10.1097/aud.0000000000000730.
2. Johansson, M., Olofsson, Å., & Berninger, E. (2020). Twin study of neonatal transient-evoked otoacoustic emissions. Hearing Research, 398, 108108. doi:10.1016/j.heares.2020.108108.
3. Johansson, M., Karltorp, E., Edholm, K., Drott, M. & Berninger, E. (2021). Etiology of congenital unilateral sensorineural hearing loss—a prospective study of affected mechanisms in neonates. Submitted Manuscript.

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Planned dissertation

Effects of Early Intervention on the Development of Binaural Hearing in Children with Unilateral Aural Atresia

Individuals with unilateral hearing loss are known to have difficulties in situations requiring binaural processing of sounds, such as listening in noisy environments and localizing sound. This project focuses on children born with unilateral aural atresia causing a conductive hearing loss on the affected side. We aim to study the effect of habilitation with bone conduction devices (BCD) on audiological outcomes such as sound localisation ability (SLA) and speech recognition (SCS), surgical outcomes and the degree of patient satisfaction.

Study 1: Horizontal Sound Localization Ability and Speech Perception in Competing Speech in Children with Unilateral Aural Atresia Using Percutaneous BCD.
Children age 5-10 years with BCD is recruited for testing of PTA, SCS and SLA using corneal eye tracking.

Study 2: Evaluation of Bone Anchored Hearing Systems, Audiology and Fixture Mechanics.
Children with congenital conductive hearing loss suited for implantation with percutaneous BCD using a titanium fixture are included in this study that evaluates a new type of titanium screw, BHX. In collaboration with Oticon Medical.

Study 3: A Retrospective Chart Study of BCD Usage in Children with Aural Atresia at Karolinska University Hospital.
A retrospective chart review of children with aural atresia treated with percutaneous BCD at Karolinska University Hospital.

Study 4: Patient Satisfaction and Long-Term Usage of Percutaneous BCD
Subjects aged 0-18 operated with percutaneous BCD at Karolinska University Hospital 2010-2020 are asked to fill out a questionnaire regarding usage of their implant, and reasons for possible non-usage.

Study 5: BHAMBI, Binaural Hearing in children with unilateral Atresia using active Middle ear or Bone conduction Implants
Subjects aged 5-18 eligible for implantation with an aMEI or an active transcutaneous BCD. Per- and postoperative surgical complications are registered. Subjects will participate in standard clinical audiometry, SLA and SCS.

Ethical permit No.

2012/1661-313	2018/864-31	2021-02984		

Publications/manuscripts 2019, 2020, 2021

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Planned dissertation

Corticosteroid treatment in children with acute facial nerve palsy

My project is based on the Facial nerve palsy And Cortisone Evaluation (FACE) study in children. It is a randomized, placebo-controlled, double-blind, multicentre trial aiming to determine the efficacy of prednisolone treatment in children with acute facial nerve palsy.

Twenty percent of children acquiring an acute facial nerve palsy will not regain full facial function. Symptoms that these children report are, for example, pronunciation problems, drooling and tearing eye in addition to social and psychological consequences of having facial asymmetry. The aim of our study is to determine if prednisolone treatment will improve the outcome for children with acute facial nerve palsy as previously have been shown in adults.

The FACE study includes children with idiopathic facial nerve palsy as well as children with facial nerve palsy associated with Lyme neuroborreliosis. Enrolment takes place at 12 paediatric departments in Sweden and a total of 500 children will be randomized to either prednisolone 1mg/kg/day (maximum 50 mg/day) or placebo per orally for 10 days. The treatment procedure is double-blinded.

Our primary outcome is complete recovery (defined as House-Barackmann grade 1) at 12-months follow-up. In addition to determining the efficacy of prednisolone in children's acute facial nerve palsy, we will also evaluate the agreement between physician-assessed facial grading and self-/proxy-reported disability and quality of life. Furthermore, we will investigate factors of importance for predicting complete recovery in an early phase of the disease.

Inclusion in the FACE study is ongoing since May 2019 and is expected to continue throughout 2022.

Ethical permit No.

2017/554	2019-01546			

Publications/manuscripts 2019, 2020, 2021

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Halftime seminar
Planned dissertation

Developing of objective balance tests in newborns and young children

Balance and vestibular disorders in adults are well studied, but in children are not well determined. Although motor and balance function is still under development throughout childhood, the vestibular function is present at birth and becomes fully integrated in puberty. A vestibular assessment in infants and children is increasingly required in clinical practice especially in those undergoing cochlear implantation as well as in children with neurological diagnoses with delayed motor skills. This knowledge will play a significant role in early rehabilitation and motor development of these children.
Video Impulse test (vHIT) and Vestibular Evoked Myogenic Potentials (VEMP)have been identified as two potential methods methods of high feasibility in children . The methods are harmless , quick and easy to perform.A test protocol of both has been adopted in the Audiological Department of Karolinska University Hospital in order to access the vestibular function in these underrepresented patient groups.

Ethical permit No.

2015/1296-31/2				

Publications/manuscripts 2019, 2020, 2021

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Halftime seminar
Planned dissertation

Immunological response in sentinel node and flow cytometric detection of satellitosis and micro metastasis

For a few years sentinel node technology has been used in our clinic in the diagnostics of oral cancer. A first sub-study aims to describe and follow up the patients where the technique has been used. The topographic location of the sentinel node is interesting because it sometimes does not match the established views of how transmission routes look like in oral cancer.

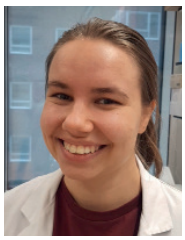
Our research group has also developed a method to detect squamous cell carcinoma in lymph nodes using flow cytometry. Markers for epithelial cells are detected and have been shown to respond well to the presence of metastases. In a previous project, lymph nodes from neck dissections performed on patients with oral cancer were analyzed with flow cytometry based on the presence of micro metastases. In my second sub-study, I do a follow up on these patients to see if there is a correlation between the incidence of micro metastases and recurrence.

A third sub-study investigates whether it is possible to detect cancer cells in muscle tissue with the same technology. During surgical resection of the tumor in patients with tongue cancer, biopsies are taken from the wound surface. The biopsies are analyzed by flow cytometry to see if it is possible to detect small foci of cancer cells. Patients are followed up to see if these findings correlate with histology and recurence.
Patients with oral cancer have been shown to differ in sentinel node immunological activity. In a fourth sub-study, we investigate what the immunological response looks like in the sentinel node in tonsil cancer. At the clinic, a prototype has been developed that connects the gamma probe with an ultrasound probe. Then, one can locate the sentinel node with ultrasound and perform fine-needle aspiration. The sample is analyzed with standard cytology and immunological analyzes. Patients are then monitored to see if the immunological response can be correlated with cytological presence of cancer cells, treatment response and recurrence

Ethical permit No.

2019-03518	2021-01265			

Publications/manuscripts 2019, 2020, 2021



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Sentinel node B-cells and their interaction with host's immune system in head and neck cancer

Many patients with head and neck squamous cell cancer (HNSCC) present regional spread to the cervical lymph nodes (LN), while distant metastases are rare. Nodal involvement is the most important factor adversely affecting both the treatment and outcome. The treatment involves surgical removal of primary tumour, and removal of LN from one or more anatomical regions of the neck. However, extensive neck dissection is not without risks for severe complications. We want to provide an improved perioperative staging, so that only patients diagnosed with metastasis or unfavorable immunological features in sentinel node will receive a full neck dissection. Our preliminary results, clearly indicate that patients with low T-cells activation in LN have significantly higher risk of recurrence and death. Moreover, the development of new cancer treatments, especially immune checkpoint inhibitors (CPI), have changed the field of oncology. However, less than 20% of patients with HNSCC treated with CPI responds to this treatment. This is why, in order to fully benefit from this paradigm shift we have to improve the way we select patients for various treatment alternatives. The overall goal is to provide a better outcome prognostic marker as well as introduce an improved selection of patients who need more rigorous follow-up and those who would benefit from CPI. The overall aims are firstly to provide a detailed characterization of different B cellular components of a lymph node. Secondly, to comprehensively investigate the humoral immune response against various tumour-associated antigens (TAAs) and lastly, to explore the mechanism of B cell cellular interactions and B cell mediated immune suppression in patients with oral cancer

Ethical permit No.

2019-03518	2021-01265			

Publications/manuscripts 2019, 2020, 2021

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Halftime seminar		2020-12-11
Planned dissertation		2022-06-03

Clinical use of prognostic markers in Head- and Neck Cancer

Numerous reports in recent decades have shown that, in addition to smoking and alcohol, human papilloma virus (HPV) is also associated with the development of oropharyngeal squamous cell carcinoma , predominantly in the tonsils and base of the tongue. In addition, patients with HPV-positive oropharyngeal SCC have a better clinical response to therapy than patients with HPV-negative oropharyngeal cancer. In hypopharyngeal cancer, which have a bad prognosis overall, HPV is less present, but still HPV-positive tumors have better clinical response to oncologic treatment.

Aim of the first study is to clarify the presence of HPV in all types of lumps of the neck, we didn't find HPV 16 or HPV 18 in any benign neck masses, published in 2016. In the second study we tested brancial cleft cysts for HPV, all cysts turned out to be HPV-negative. The third study investigate the use of other markers than HPV in hypopharyngeal cancer

In the fourth study we paln to investigate if the FDG uptake on PET-CT correlates with viable tumours in neck disscition.

Ethical permit No.

Publications/manuscripts 2019, 2020, 2021

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Planned dissertation

Bell's palsy in pregnancy and puerperium

To examine the incidence of Bell's palsy among pregnant women in Stockholm during a 10-years period, to find risk factors for developing Bell's palsy during pregnancy and the puerperium (first 6 weeks post partum), to see how these women heal compared to non pregnant women with Bells palsy and how the disease affects the patient's quality of life.

Ethical permit No.

2015/2349-31/1				

Publications/manuscripts 2019, 2020, 2021

1.

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Halftime seminar	2020-09-21
Planned dissertation	

Perspectives on screening strategies for early detection of childhood hearing impairment

The benefits of early detection of hearing impairment are well understood. Yet, the diversity in screening strategies across countries makes it challenging for policymakers to choose a protocol that is optimal for their country or region. Three methods are used to explain and evaluate various screening strategies. First, a comprehensive questionnaire gathered information on hearing screening programmes across countries, primarily in Europe. Second, a systematic literature review was performed on newborn hearing screening (NHS) programmes and protocols and their performance. Finally, a registry-based study is underway in Region Stockholm.

The following are some conclusions from the studies.

- Countries with NHS that use only OAE screening on all infants (including NICU infants) had lower health care expenditure compared to countries that use more complex protocols, i.e., having a separate protocol for NICU infants, and using automated-ABR screening.
- There was a widespread lack of data available on the performance of screening across the participating countries, suggesting that many programmes do not monitor or evaluate the of quality of their screening programme.
- Among programmes with data on NHS, loss to follow-up between screening steps and from screening to diagnostic assessment was a common barrier to effective screening.
- Factors that reduced referral rate from NHS were: using aABR in the protocol, screening at least 3 days after birth, and reattempting the screen before referring.
- Loss to follow-up rates were related to the organisation and management of the NHS programme
- A small proportion of participating countries provide hearing screening from 3 to 7 years of age.
- The lack of certainty to the cost-effectiveness of hearing screening at preschool age is perpetuated by the fact that the fact that data are mostly not available on the outcomes of screening

Ethical permit No.

2020-07302				

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2012-05-24

Effects on breast-feeding and development of hard palate in children with ankyglossia (tongue tie). Comparative measurements with alginate imprints of the hard palate, oral scanner, neonatal tongue screening test and TABBY (tongue assessment tool for tongue-tie in breastfed babies)

Hypothesis: A restriction of the mobility of the tongue affects the hard palate and gives a high palate.
Aim: The main purpose is to be able to determine with greater certainty which children who have a restricted tongue due to a tongue-tie, would benefit the most from a frenotomy .
Normally when nose-breathing, the muscle Buccinator and the periorbital muscles give an external pressure to the maxilla which the tongue counteracts hence giving a normal development of the hard palate. But when mouth-breathing occur, ie. nasal congestion or low muscle tone, the middle face becomes elongated with a narrowing of the maxilla and often a narrowing upwards of the hard palate. This event has also been suggested to happen, when tongue mobility is restricted and do not reach the hard palate. To clarify if there is any correlation between a tongue-tie and a high palate, we want to examine 25 newborn, full-term children who have undergone a normal pregnancy and birth at BB Danderyds Hospital. The hard palate is assessed in correlation with the appearance and function of the tongue, but also if there are any problems like breastfeeding, reflux, lip blisters, weight gain, ability to take a pacifier and baby bottle.

Study plan
Visit 1: at 3 days of age, casting of the hard palate with alginate imprint and the use of an intraoral scanner. Visual and palpable inspection of the tongue using Neonatal tongue screening test and TABBY tongue assessment (tool for tongue-tie in breastfed babies). Interview with the breastfeeding parent regarding breastfeeding.
Visit 2: at 6 weeks of age with telephone interview about breastfeeding, reflux, weight gain, whether the parents have received / need breastfeeding support and whether the child has had the tongue band fixed with a frenotomy. 3:
Visit 3: follow-up at 6 months of age with new alginate casting and intraoral scanning, examination of tongue as at visit 1, and answer the study's standard questionnaire.

Ethical permit No.

Publications/manuscripts 2019, 2020, 2021

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2021-11-02

Adverse events in cholesteatoma surgery - risk, contributing factors and quality of life

Cholesteatoma, the growth of squamous cell epithelium into the middle ear may cause complications such as hearing loss, infections, bon destruction and facial palsy. The treatment is surgical, and surgery is performed in an area defined by the facial nerve, the sigmoid dura, the middle fossa dura plate, the labyrinth, the temporomandibular joint and the posterior wall of the ear canal. Sensitive structures that may be affected during surgery.

The aim of the thesis is analyzing different aspects of adverse events and effects on quality of life after cholesteatoma surgery as well as risk factors for the disease. This will be studied both nationally in a registry based study and locally in retrospective as well as prospective studies.

Ethical permit No.

2020-05935	2019-05190	2020-00245		

Publications/manuscripts 2019, 2020, 2021

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Registered	2020-04-20
Halftime seminar	
Planned dissertation	2025

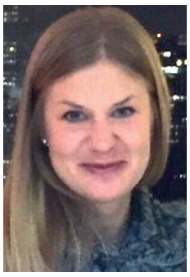
Bilateral bone anchored hearing devices

Binaural hearing is important for everyday listening tasks. The ability to localize sound and understanding speech in a noisy environment is dependent on the difference in time and level at which the sound reaches the two ears. In bone conducted sound this ability is affected due to the properties of the skull and surrounding tissue. In my doctoral project we study wether a bilateral fitting of bone conduction hearing devices (BAHS) gives a better hearing compared to one device in terms of sound localization accuracy and speech understanding in spatially separated competing speech. In addition, self-perceived benefit and quality of life will be assessed. Normal hearing subjects as well as patients with bilateral conductive/mixed hearing loss that are using one BAHS will be assessed and tested with bilateral fitting compared to unilateral BAHS.

Ethical permit No.

2019-04696				

Publications/manuscripts 2019, 2020, 2021



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Halftime seminar
Planned dissertation

Surgical interventions in peripheral facial palsy; assessment of regained function and quality of life

Persistent sequele of peripheral facial palsy imposes a great reduction in quality of life. The acute phase of the disease is well known, but the prevalence of long term sequele is unknown. We are mapping the prevalence in a large Stockholm based cohort.

A common sequele is synkinesis, ie mass muscle movement as a result of defect nerve healing. The gold standard treatment is physiotherapy and repeated Botox injections. If this treatment is unsatisfactory, no evidence based treatment is currently available. We will evaluate highly selective neurectomy as a treatment option.

Ethical permit No.

2019-00421	2021-00246			

Publications/manuscripts 2019, 2020, 2021

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Halftime seminar
Planned dissertation

Sentinel node B-cells and their role in tumour specific immune suppression in head and neck cancer

For decades, cancer research was focused on finding external pharmaceutical agents bearing the ability to recognize and destroy cancer cells in cases of metastatic disease. A very recent clinical discovery of immune checkpoint inhibitors (CPI) proved that the human immune system in appropriate conditions has the capability to eradicate on its own even metastatic cancer disease. However, still only a small fraction of patients shows a positive durable response to CPI treatment.
The contribution of different immune cell subsets, especially T cells, in CPI mediated regained anti-tumour immune response is well established. In contrast to T cells, the anti-tumour contribution of B cells has been scarcely investigated. B-cells are often overlooked even though they are important players in a fully-integrated immune response and constitute a substantial fraction of lymphocytes draining tumour tissue. We hypothesise that by better understanding of B-cell mediated anti-tumour response, we can identify new biomarkers predicting survival, response to standard anti-cancer treatment, CPI therapy or even develop new immune therapy targets. At the same time, giving the foundation to personalized immunotherapy approach in advanced HNSCC, we intend to test drugs sensitivity, including CPI agents, on primary tumour cells culture in the presence of lymphocytes derived from neck lymphatic system of affected patients.

Ethical permit No.

2019-03518				

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21. Jackowska J, Wojnowski W, Hashimoto A, Małaczyńska B, Piersiala K, Świdziński P, Wiskirska-Woźnica B, Wierzbicka M. Voice improvement in patients with recurrent respiratory papillomatosis after combined treatment with cidofovir and CO2 laser surgery. Lasers in medical science 2019 34;7 1433-1440

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Co-supervisor Ola Sunnergren, Hatef Darabi, Pär Stjärne
Registered 2020-08-18
Halftime seminar 2021-10-22
Planned dissertation

Zygomaticomaxillary Complex Fractures: Aspects of Diagnostic Methods, Treatments and Complications

Zygomaticomaxillary Complex (ZMC) fractures are one of the most common types of facial fractures and frequently managed at Karolinska University Hospital (KUH). Functional complixations (e.g. trismus, double vision or impaired sensation) and cosmetic complications (e.g. ocular dystopia or a sunken/broadened cheek) are common and managed either by conservative or surgical treatment. Although the body of literature offers a wide range of suggestions and algorithms for managing ZMC fractures, it is still largely the surgeons' individual training, experience and preference that influence the choice of treatment instead of systematic evidence.

Overall aim of the project:

- To describe a new complication following orbital floor reconstructions.
- To evaluate long-term results of patients with ZMC fractures managed at KUH and to gain an overview of the most common functional and cosmetic complications.
- To introduce the volume difference along the external surface (VDAES) as a novel method of assessing zygomatic bone asymmetry.

Ethical permit No.

2017/960-31/1	2018-302/31			

Publications/manuscripts 2019, 2020, 2021

1. Rahbin S, Toufani T, Al-Khabbaz AM, Lindblom J, Sunnergren O, Darabi H, Qureshi A R, Alinasab B: The Volume Difference Along the External Surface of the Zygomatic Bone: A Novel Method of Measuring Zygomatic Bone Asymmetry. J Craniofac Surg. (article in press)
2. S Rahbin, M Kjellberg, M Söderlind & A Ekborn: Well-planned rather than rushed extraction of airway foreign body in 532 g preterm neonate. Acta Oto-Laryngologica Case Reports. 6:1, 85-87. DOI: 10.1080/23772484.2021.2002153 (2021).
3. Rahbin, S; Liakos, A; Alinasab, B: Loss of Malar Bags in Lower Eyelid in Orbital Blow Out Fracture Reconstruction Following Pre- or Retro-Septal Transconjunctival Incision. J Craniofac Surg. May/Jun 2020;31(3):769-771. DOI: 10.1097/SCS.0000000000006103 (2020).

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Halftime seminar 2020-10-16
Planned dissertation 2022-06-14

Students' and supervisors perception and experience of the clinical learning environment, a cross-sectional study

The clinical learning environment (CLE) influences students' achievement of learning outcomes and the development of their professional behaviors. The CLEs are not always optimal for learning because of clinical productivity expectations and a lack of support from supervisors. Our first study highlighted that clinical supervisors find it hard to provide feedback to students. Measuring students experiences of first longer clinical placement, our second study showed significant differences between four programs at Karolinska Institutet, with physiotherapy and speech pathology students giving the highest scores, nursing students lower and medical students the lowest. Our third study aim to, due to previous high ratings, explore physiotherapy students' experiences of supervision during their first clinical placement. Our fourth study aims to investigate experiences of first longer clinical placement among medical students.

Ethical permit No.

2016/1425-31	2017/38-31/4			

Publications/manuscripts 2019, 2020, 2021

1. Sellberg M, Skavberg Roaldsen K, Nygren-Bonnier M, Halvarsson A. 2020. Clinical supervisors' experience of giving feedback to students during clinical integrated learning. Physiotherapy theory and practice, 1-10.
2. Sellberg M, Palmgren P J, Möller R. 2021. A cross-sectional study of clinical learning environments across four undergraduate programs using the undergraduate clinical education environment measure. BMC Medical Education, 21(1), 1-13.
3. Sellberg M, Halvarsson A, PT, Nygren-Bonnier M, Palmgren P J, Möller R, Relationships Matter: A Qualitative Study of Physiotherapy Students' Experiences of Their First Clinical Placement (manuscript)

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Halftime seminar
Planned dissertation

Assessment and activation of tympanic membrane progenitor/stem cells- clinical and laboratory studies

This PhD-project aims to map the occurrence and activation of regenerative zones in the human ear drum.

In laboratory studies we try to identify stem cells and proliferative zones in normal human tympanic membranes as well as in tympanic membranes that has been mechanically and chemically injured. The goal is to better understand the healing mechanism.

Plasminogen is an endogenous protein and has a role in cell migration and wound healing and has been identified as a possible drug for medical treatment of chronic tympanic membrane perforation. In a clinical trial different doses of plasminogen are injected close to the tympanic membrane in the ear canal in patients with chronic perforations and the effect on healing of the ear drum is evaluated.

With this project we aim to increase knowledge about the normal healing process and to improve the treatment of tympanic membrane perforations with the ultimate goal to design a simple, out-patient procedure without the need for advanced surgery.

Ethical permit No.

2018/364	2017/2011-31			

Publications/manuscripts 2019, 2020, 2021

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Halftime seminar 2019-10-11
Planned dissertation

Growing up with one ear: Central auditory structure and function in unilateral hearing loss

Ear canal atresia causes profound conductive hearing loss of the affected ear. Unilateral hearing loss in This project investigates the status of the auditory brain structures in adults with unilateral congenital conductive hearing impairment in ear atresia. MRI has been used to evaluate the auditory structures as compared to age and gender matched controls.

Part of the project examines experience of unilateral hearing loss and ability to localize sound source, as well as discriminate speech in a cocktail party setting. A group of subjects with congenital unilateral atresia was tested and found that level of hearing on the atretic ear was important for the ability to localize sound source. A group of subjects with single-sided deafness has also been tested with a sound localization task to evaluate if experience of unilateral hearing is important for the ability to localize.

Ethical permit No.

2012/1661-31/3	T453-17/414-16			

Publications/manuscripts 2019, 2020, 2021

1. Adults with congenital unilateral ear canal atresia -sound localization ability and recognition of speech in competing speech. Siegbahn M, Engnér-Berglin C, Hultcrantz M, Asp F. Acta Oto-Laryngologica 2021 Jul;141(7):689-694.

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Registered 2020-05-14
Halftime seminar
Planned dissertation

Behandling av allergisk rinit med systemiska steroider samt hälsoekonomiska aspekter

Kortison tabletter används som behandling av allergisk rinit när sedvanlig lokalbehandling inte ger tillräcklig symtomlindring. Användningen av metylprednisolon som behandling mot allergisk rinit förekommer relativt frekvent i Sverige, framförallt i primärvården. Många allergispecialister avråder dock från denna depotbehandling då den inte går att avbryta om komplikationer uppstår.

Primär hypotes: En intramuskulär injektion av 80 mg (2 ml) metylprednisolon ger en betydande större symptomlindring än 2 ml intramuskulär injektion av placebo (NaCl).
20 mg Prednisolon ger betydande symtomlindring jämfört med 20 mg Kestine.
Sekundära hypotes: En intramuskulär injektion av 80 mg metylprednisolon ger ingen påverkan på Cortisol, ACTH eller benomsättningsproven CTX/C1NP.
20 mg Prednisolon ger ingen påverkan på Cortisol, ACTH eller benomsättningsproven CTX/C1NP.

I injektionsstudien kan man vid jämförelse av total nasal symptome score (TNSS), medical score (MS) och combined symptome and medical score (CSMS) kunde man se en signifikant skillnad med lägre poäng i gruppen behandlad med metylprednisolon. Skillnaden var dock så liten att den inte bedöms ha någon klinisk relevans. Vid analys av Quality of life formulär (SNOT-22 och RQLQ) kunde man inte se någon signifikant skillnad mellan grupperna.
I tablettstudien sågs ingen skillnad i TNSS, MS, CSMS, SNOT-22 eller RQLQ mellan grupperna.

Ethical permit No.

2016/2158	2017/947	2018/11		

Publications/manuscripts 2019, 2020, 2021

1. HealthSWEDE: Costs with sublingual immunotherapy - a questionnaire study. Petter Olsson, Carl Skröder, Lars Ahlbeck, Frida Hjalte, Karl-Olof Welin, Ulla Westin, Morgan Andersson, Cecilia Ahlström-Emanuelsson & Lars-Olaf Cardell. Allergy, Asthma & Clinical Immunology volume 17, Article number: 55 (2021). Manuscript
2. It is advisable to be hesitant in the use of prednisolone tablets as treatment of pollen induced allergic rhinitis - Databearbetning. Carl Skröder, Laila Hellkvist, Ulla Westin, Pernilla Sahlstrand-Johnsson, Åslög Dahl, Leif Bjermer, Lars Olaf Cardell
3. Is the effect of methylprednisolone treating pollen induced allergic rhinitis mainly due to a placebo effect? - manus klart för inskick. Carl Skröder, Laila Hellkvist, Åslög Dahl, Leif Bjermer, Ulla Westin, Lars Olaf Cardell

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Registered 2008-02-18
Halftime seminar 2014-05-19
Planned dissertation

Airway hyperresponsiveness in conjunction with stimulation of viral recognizing Toll-like receptors.

Viral respiratory tract infections are a common cause for acute exacerbations of asthma and rhinitis. During an airway infection, individuals with asthma suffer from longer lasting illness and more severe respiratory symptoms, such as airway hyperresponsiveness, compared to healthy persons. The mechanisms behind these phenomena are not fully understood and new ways of treatment are required.
Toll-like receptors (TLRs) are pattern recognition receptors wich can identify viruses in the airway and by that evoke an inflammatory reponse. TLRs are found located in different cell types implicated in the pathogenesis of asthma, as in airway epithelial cells, in smooth muscle cells or in leukocytes. TLRs may be an important link between viral infections and asthma exacerbations.

The aim of this project is to study the effects on airway reactivity and inflammatory patterns in connection with stimulation of viral recognizing TLRs.

Ethical permit No.

N152/06	N152/11	N348/11	N44/12	N41/14	N143/14

Publications/manuscripts 2018, 2019, 2021

1.

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Registered		2015-03-24
Halftime seminar		2019-04-19
Planned dissertation		2021-11-11

Adult patients with severe to profound hearing loss. A register-based and interview study.

In Sweden, roughly 25,000 individuals in the adult population have severe-to-profound hearing impairment. This patient group often needs extended audiological rehabilitation. The general aim of the thesis was to explore and describe patients with severe-to-profound hearing loss and/or patients with dual sensory loss. The specific focus studied was dual sensory loss in Paper I and Paper V, audiological rehabilitation in Papers I-V, cochlear implants (CI) in Paper III, and mental fatigue Paper IV. The five papers are based on data from the quality register for severe-to-profound hearing loss, a pilot clinical study, and an interview study. Paper I compared patients with dual sensory loss to patients with severe-to-profound hearing loss only and found a significant negative effect on QoL parameters among the dual sensory loss group. In Paper II, data on 4,286 patients with severe-to-profound hearing loss were studied. The results revealed that only 40.5% received extended rehabilitation. Hearing loss seemed to have a significantly more negative impact on daily life of women than of men. In Paper III comparisons with patients rehabilitated with or without CI were investigated. The study found that only 8.5% had CI, despite most fulfilled the criteria for CI. The various reasons were studied, and the most common were related to hearing (management with hearing aids) and unknown reasons for not receiving CI. Paper IV indicated that most patients in the study population with severe mental fatigue had normal hearing or mild-to-moderate hearing loss, and severe mental fatigue was associated with severe tinnitus. Paper V demonstrated experiences of disabilities in daily life in patient with dual sensory loss. The results revealed that patients did notthink of their dual sensory loss as a combination, but rather as separate disabilities. Isolation and the ability to control one's own daily life emerged as the main themes.

Ethical permit No.

2012/057	2014/2101-31			

Publications/manuscripts 2019, 2020, 2021

1. Turunen-Taheri, S., Skagerstrand, Å., Hellström, S., & Carlsson, P-I. (2017). Patients with severe-to-profound hearing impairment and simultaneous severe vision impairmen: a quality-of-life study. Acta Oto-Laryngologica, 137:3, 279-285.
2. Turunen-Taheri, S., Carlsson, P-I., Johnson, A-C, & Hellström, S. (2019). Severe-to-profound hearing impairment: demographic data, gender differences and benefits of audiological rehabilitation. Disability and Rehabilitation, 41:23, 2766-2774 (online 12 June 2018).
3. Turunen-Taheri, S., Edén M., Hellström, S., & Carlsson, P-I. (2019). Rehabilitation of adult patients with severe-to-profound hearing impairment – why not cochlear implants? Acta Oto-Laryngologica, 139 (7): 604-611.
4. Turunen-Taheri, S., Carlsson, P-I., Ternevall, E., & Hellström, S. Mental fatigue in patients with hearing loss and/or tinnitus ongoing audiological rehabilitation – a pilot study. Manuscript submitted 2021.
5. Turunen-Taheri, S., Hagerman-Sirelius, A., Hellström, S., Skjönsberg, Å., & Backenroth G. Combined severe-to-profound hearing and vision impairment – experiences of daily life and need of support, an interview study. Manuscript.

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Planned dissertation

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2017-12-21

Predictors of upper airway symptoms in the BAMSE birth cohort

Background: Rhinitis and rhinosinusitis are inflammatory diseases in the upper airways, often associated with asthma. Allergic rhinitis (AR) is an IgE-mediated disease. It is one of the most costly diseases to the society. Sensitization is a strong risk factor for later development of AR and, in some cases, asthma. During the last decade, there has been a rapid increase in knowledge about specific allergen proteins (allergen components). This has primarily been used within food allergy to be able to separate life threatening allergies from cross reactions (component resolved diagnostics).
Chronic rhinosinusitis (CRS) is a multifactorial inflammatory disease in the upper airways, with several different endotypes. The prevalence is somewhat uncertain since the diagnosis is difficult to ensure via questionnaires.
To be able to estimate prognosis and decide on treatment for these diseases, there is a need for prognostic biomarkers.

Aim: The overall aim of this project is to identify early prognostic factors for upper airway disease and to increase the understanding of the relationship between symptoms from the upper and lower airways.

Methods: We use data from the population based birth cohort BAMSE (Barn Allergi Miljö Stockholm Epidemiologi) consisting of 4089 children. The children were included at the age of 2 months and have been followed repeatedly by questionnaires. At 4, 8 and 16 years of age clinical examinations were performed, including blood samples for specific IgE. The follow-up at 24 years of age is finished last year. We have also performed a subgroup study of the 24-year-olds with CRS symptoms a. The data from this study is beeing/has been processed and the article is under progress.

Ethical permit No.

93:189	98:175	2007/1634-31	2010/1474-31/3	2016/1380-31/2

Publications/manuscripts 2019, 2020, 2021

1. Westman M, Åberg K, Apostolovic D, Lupinek C, Gattinger P, Mitterman I, Andersson N, Melèn E, Bergström A, Antò J M, Bousquet J, Valenta R, Wickman M, van Hage M. Longitudinal assessment of sensitization to grass pollen allergen molecules in a birth cohort – the importance of Phl p 4 for diagnosis and prediction of grass pollen allergy. JACI April 2020

Appendix 1

Checklista för ansvarig forskare/prövare: Uppstart av klinisk studie

Datum: 2021-11-04

Denna checklista är ett internt dokument som kan användas som stöd inför uppstart av forskningsprojekt på patienter och forskningspersoner som bedrivs vid Karolinska Universitetssjukhuset.

Det är en övergripande checklista med syfte att underlätta planeringen av olika typer av studier, såväl kliniska läkemedelsprövningar som mindre omfattande analyser av patientmaterial.

Dokumentet är tänkt att användas som en mall och kan anpassas utifrån specifika studier och verksamhetens interna rutiner. Alla delar av checklistan är därmed inte applicerbar på alla studier Checklistan upprättas för varje studie och förvaras hos ansvarig forskare. En kopia lämnas till verksamhetschefen där studiens huvudsakligen bedrivs i samband med att studien påbörjas.

Titel på forskningsprojektet/studien	Karolinska diarie nr
Tema/Funktion/Medicinsk enhet	Ansvarig verksamhetschef
Ansvarig forskare/prövare	Ansvarig Forskningssjuksköterska/forskningskoordinator
Sponsor för studien	

Id.	Karolinska Universitetssjukhusets databas för kliniska studier	Kommentar	Utfört
1.1	Alla studier som bedrivs inom Karolinska Universitetssjukhusets verksamhetsområde och där Karolinska Universitetssjukhuset står med på etikprövningsansökan ska registreras i databasen. Databas för kliniska studier (karolinska.se)		
Id.	**Ansökningar och godkännanden**	**Kommentar**	**Utfört**
2.1	DIARIENUMMER K Diarienummer:_____ Ansök om diarienummer för studien via Registrator.karolinska@regionstockholm.se Karolinska Universitetssjukhuset är en myndighet och omfattas därför av de regler och lagar som rör offentlighetsprincipen. Detta innebär bland annat att vi ska diarieföra eller registrera de flesta av våra handlingar. Alla avtal som Karolinska Universitetssjukhuset ingår med extern part ska enligt lag diarieföras.		
2.2	ANSVARSINTYG Ansvarsintygen utgör sjukhusinterna dokument och ska aldrig hanteras av extern part. Tillämpligt ansvarsintyg ska alltid vara upprättat innan uppstart av studien. **Ansvarsintyg K/KI** är avsett att användas för studier som kräver ett etikgodkännande och ska genomföras i samverkan mellan Karolinska Universitetssjukhuset och Karolinska Institutet. Samverkan avses när ansvarig forskare är knuten till både Karolinska Universitetssjukhuset och Karolinska Institutet Intyg om ansvarsfördelning K/KI (2018-06-25) **Ansvarsintyg K** är avsett att användas för studier som kräver ett etikgodkännande och som ska genomföras på fler än en Medicinsk enhet (ME) på Karolinska Universitetssjukhuset. Ansvarsintyg inom Karolinska Universitetssjukhuset (21-02-12)		

2.3	ETIKPRÖVNINGMYNDIGHETEN (EPM) inkl. strålskydd, ansökan och godkännande Diarienummer:_____ Ansökt datum:_____ Godkänt datum:_____ Ändringsansökan datum:_____ Viktig information och instruktion om hur och vad som ska inkluderas i etikprövningsansökan finns på https://etikprovningsmyndigheten.se/ Om studien godkänts med villkor måste dessa uppfyllas innan studien startar. För kliniska läkemedelsprövningar: Väsentliga ändringar till EPM (ändringsansökan) behöver även skickas till Läkemedelsverket. Undantag: Byte av ansvarig forskare (PI) vid ett center eller tillägg av center skall skickas till EPM, men behöver inte skickas in till LV om amendment inte omfattar något utöver detta. Informationen om byte av PI skickas då till LV vid nästa väsentliga amendment. Notera: Om studien inkluderar humana prover kan ett rådgivande möte bokas med Stockholms medicinska biobank (SMB) för diskussion innan inskick till EPM (se nedan under sektion 1.5 BIOBANK). Om **kompensation till forskningspersonerna** förekommer ska detta vara godkänt av Etikprövningsmyndigheten Notera: För medicintekniska kliniska prövningar används ett samlat förfarande där alla ansökningshandlingar skickas till LV som fördelar delar av dokumentationen till EPM. Specifika blanketter skall dock laddas ner från EPM på följande länk: https://etikprovningsmyndigheten.se/medicintekniska-produkter/		
2.4	LÄKEMEDELSVERKET, anmälan/ansökan och godkännande Diarienummer:_____ EudraCTnummer:_____ För medicinteknisk produkt Eudamed nummer:_____ Ansökt datum:_____ Godkänt datum:_____ Amendment: _____ Viktig information och instruktion om hur och vad som ska inkluderas i ansökan för klinisk läkemedelsprövning finns på: https://www.lakemedelsverket.se/sv/tillstand-godkannande-och-kontroll/klinisk-provning/lakemedel-for-manniskor/ansoka-om-klinisk-provning		

	Viktig information och instruktion om hur och vad som ska inkluderas i anmälan/ansökan om medicinteknisk klinisk prövning finns på: https://www.lakemedelsverket.se/sv/tillstand-godkannande-och-kontroll/klinisk-provning/medicinteknik/ansokan-eller-anmalan		
2.5	BIOBANK, ansökan och godkännande Diarienummer:_____ Ansökt datum:_____ Godkänt datum:_____ MTA Godkänt datum:_____ Biobanksavtal upprättas där extra forskningsprover tas inom studien. I Biobankslagen finns undantagsregel för prover som analyseras **inom 6 månader** efter provtagningsdatum **och destrueras** i direkt anslutning till analys. OBS! Båda villkoren måste vara uppfyllda. Är det aktuellt med undantagsregeln så skall detta beskrivas i ansökan till EPM under punkten 14.1.5. Multicenterbiobanksavtal (N1) upprättas vanligen för alla nya prover om det är fler center som medverkar i Sverige och kompletteras samtidigt med lokal biobank för varje site (L1 och L1a) om uttag från befintligt prov behövs. Kontakta SMB biobankstockholm.se vid frågor om hur biobanksansökan ska skrivas. Ett MTA (Material Transfer Agreement) behöver upprättas då biobanksprov med tillhörande provkod överförs från en huvudman till en annan. MTA information (biobanksverige.se) Ansökningsblanketter finns på www.biobanksverige.se/forskning och skickas elektroniskt till biobankstockholm.karolinska@regionstockholm.se samt i pappersform. Se Biobankens hemsida för information om hur många exemplar dokumenten skall upprättas i.		

2.6	GDPR **Anmälan av personuppgiftsbehandling vid Karolinska Universitetssjukhuset** Karolinska Universitetssjukhuset är skyldig att föra ett register över de personuppgiftsbehandlingar som utförs under sjukhusets ansvar. Varje personuppgiftsbehandling (t.ex. forskningsstudier, kvalitetsregister mm.) måste anmälas till detta register. Från och med 2021-10-01 ska samtliga personuppgiftsbehandlingar anmälas i Privacy Records (Draftit). Information om hur man registrerar i Privacy Records finns på inuti: Personuppgiftsbehandling (GDPR) – För dig som är forskare (karolinska.se) Inför vissa personuppgiftsbehandlingar behöver det upprättas en konsekvensbedömning/DPIA gällande personuppgiftsbehandlingen. Så är fallet när det rör sig om behandling av känsliga personuppgifter, när man behandlar personuppgifter i stor omfattning, när man använder ny teknik eller nya organisatoriska lösningar. Mall för DPIA finns här: Sjukhusgemensamma dokument (sll.se) **PUB-avtal (Personuppgiftsbiträdesavtal)** Enligt dataskyddsförordningen ska personuppgiftsansvariga och personuppgiftsbiträden reglera sina relationer genom ett skriftligt avtal. När sjukhuset låter en extern part hantera personuppgifter för sjukhusets räkning skall därför ett PUB-avtal upprättas. Information finns på https://www.datainspektionen.se/lagar--regler/dataskyddsforordningen/personuppgiftsansvariga-och-personuppgiftsbitraden/personuppgiftsbitradesavtal/ Mall för PUB-avtal finns på: https://inuti.karolinska.se/verksamheter/sjukhusovergripande/rattskansli/sjukhus--och-myndighetsjuridik/personuppgiftsbehandling-gdpr/personuppgiftsbehandling-gdpr--for-dig-som-ar-forskare/ Utlämnande av patientdata för forskningsändamål: Om data utlämnas till en annan part för egna forskningsändamål skall en Begäran om utlämnande av patientdata upprättas. På inuti finns en beskrivning och kontaktuppgifter		

	Utlämnande av patientdata för forskningsändamål (karolinska.se) Om sponsor finns i ett land utanför EU kan man på Integritetsmyndighetens hemsida hitta information om landet är godkänt för utlämning av uppgifter. Om landet inte finns med så behöver FoU-juristerna kontaktas innan studieavtal signeras		
2.7	REGISTRERING I OFFENTLIG DATABAS. Varje forskningsstudie som omfattar människor ska enligt Helsingforsdeklarationen registreras i en offentligt tillgänglig databas innan den första forskningspersonen rekryteras. *(Ref: Helsingforsdeklarationen, 35).* Registrering kan göras i t.ex. ClinicalTrials.gov. Kontakta Katarina Risbecker Sektionschef sektion forskningsstöd (katarina.risbeckeregionstockholm.se) för att få inlogg i clinicaltrials.gov På WHO:s hemsida finns exempel på andra offentliga databaser. https://www.who.int/clinical-trials-registry-platform/network/primary-registries OBS! Finansiärer och/eller tidskrifter kan ha särskilda krav på var registreringen ska ske.		
Id	Avtal och Ekonomi	Kommentar	Utfört
3.1	AVTAL Alla avtal som skrivs med extern part behöver inför avtalssignering granskas av jurist på Karolinska Universitetssjukhuset. Kontakta FoU jurist via email: forskningsavtal.karolinska@regionstockholm.se Kliniska studieavtal signeras enligt gällande arbets-och delegationsordning (Sjukhusgemensamma dokument (sll.se) med nedan förtydligande: **PI & Verksamhetschef (VC):** Det är viktigt att PI och VC är införstådda i vad avtalet omfattar. PI och VC signerar som indikator på ”läst och förstått” / ”read and understood”, vilket bekräftar att de ansvarar för genomförande av projektet / studien i enlighet med avtalet.		

	Temachef (TC/Funktionschef (FC)) signerar forskningsavtal upp till 5 MSEK under förutsättning att avtalet är granskat juridiskt, säkerställt att det är ekonomiskt kostnadstäckande och att PI/ VC läst och förstått, dvs vetenskapligt granskat avtalet. Även CDA/NDA avtal innefattas i denna punkt. **Sjukhusdirektören signerar forskningsavtal värda 5 MSEK och över** under förutsättning att avtalet är signerat av TC/FC, vilket då innebär att avtalet är: Juridiskt granskat av avtalsjurist eller i vissa fall av erfaren personal på kliniska studieverksamheten på temat/funktionen. Ekonomiskt granskat av PI och VC och/eller personal på kliniska studieverksamheten. Stöd för detta finns också centralt på sektion forskningsstöd (Se rubrik Ekonomiskt avtal). Vetenskapligt granskat av PI som ska efterleva avtalet och av VC som stöttar projektet. Sjukhusdirektören signerar alla EU-finansierade projekt eftersom dessa bedöms vara av särskild risk.		
3.2	EKONOMISKT AVTAL Studiens kostnader och tidsåtgång beräknas av enhet/sektionsschef eller av VC utsedd person. Därefter upprättas **ett** ekonomiskt avtal mellan Karolinska Universitetssjukhuset och sponsor. Detta avtal ska vara underskrivet och **klart innan** start av studie. Karolinska Universitetssjukhusets original skickas till registrator på Karolinska Universitetssjukhuset. Kopior på alla ekonomiska avtal för studien förvaras i prövarpärmen eller på annan avsedd plats (se punkt prövarpärm). För hjälp med underlagsmall för avtal och stöd för kostnadsberäkning och avtalsprocess kontakta sektionschef för sektion forskningsstöd: katarina.risbecker@regionstockholm.se Forskningsprislista gällande timpriser samt slutenvårdpriser finns att ladda ner från inuti http://inuti.karolinska.se/Inuti/Verksamheter/Centrala-staber/FoU/Kliniska-studier/		
3.3	INTERNA AVTAL Interna avtal mellan Karolinska Universitetssjukhusets verksamheter signeras av VC alternativt chef för klinisk studieenhet om budgetansvar för verksamheten åligger denne. Interna avtal / överenskommelser är inte juridiskt bindande i samma bemärkelse som externa avtal. Det kan vara av stort värde för ansvariga inom verksamheten och forskningsprojektet att ha en process på plats där ansvariga chefer i verksamheten är informerade om och tar ansvar för genomförande av kliniska studier.		

3.4	APOTEKET Ett avtal ska upprättas med apoteket när prövningsläkemedel ska användas. Avtal upprättas i de flesta fall direkt mellan sponsor och apoteket. Kopia av apoteksavtalet tillhandahålls av sponsor och förvaras i prövarpärmen. I de all Karolinska Universitetssjukhuset är sponsor/tecknar avtal med apoteksfunktion skall ApoEx anlitas. Email adress: klinprov.stockholm@apoex.se		
3.5	BILD OCH FUNKTION (BoF) Ett internavtal kan behöva upprättas med BoF för studiespecifika undersökningar tex CT/MR/PET, ultraljud mfl. Kontakta till BoF Enheten för kliniska studier (EKS) rtg.klinprov.karolinska@regionstockholm.se För barnstudier kontaktas FOBarnradiologikliniskastudier.karolinska@regionstockholm.se Röntgen återkommer med ett internavtal som signeras enligt gällande arbets-och delegationsordning.		
3.6	PATOLOGEN I vissa studier behöver ett avtal upprättas med patologen t.ex. när arkiverat tumörmaterial ska skickas för analys . Det kan då också behövas en ansvarig patolog för studien. Det finns två sorters avtal, biobanksavtal (skickas till puc.samordning.karolinska@regionstockholm.se) och kostnadsavtal (skickas till studiecenter på MDK) efter det att Patologen har tagit fram en offert på projektet. Projekt som omfattar humanvävnad insamlad inom Sverige ska ha ett biobanksavtal upprättat innan kostnadsavtal upprättas. I prövarpärmen ska det finnas instruktion för hur man beställer, hanterar och vart (lokalt/centralt lab) patologmaterial skickas.		

3.7	PROVTAGNING/STUDIECENTER lab Beroende på studiens upplägg kan avtal behövas, såsom vid provtagning utöver klinisk rutin, prover som ej finns i sortimentet m.m. Kontaktuppgifter: studiecenterlab.karolinska@regionstockholm.se Studiecenter återkommer med internavtal för signering enligt gällande arbets-och delegationsordning.		
3.8	ÖGON Om ögonundersökning ska utföras kan Stockholms ögonklinik användas. Skicka e-post med en kort sammanfattning om studien, vilka undersökningar som är aktuella och när undersökningarna ska utföras. Bifoga information från forskningsplanen/protokollet som beskriver vad som ska undersökas (flödesschema) till; kundcenter@stockholmsogonklinik.se för upprättande av internavtal		
3.9	FYSLAB Ett avtal ska upprättas om studiespecifika EKG ska utföras. För barnstudier kontaktas barnkardiologen.		

Appendix 2

Lägga till ett nytt e-postkonto i Outlook

Outlook för Microsoft 365 Outlook för Microsoft 365 för Mac Outlook 2021 Fler...

Håll kontakten och schemat

Du kan vara organiserad och hålla tidsplaneringen med Outlook – din livsorganisatör.

Prova 1 månad utan kostnad

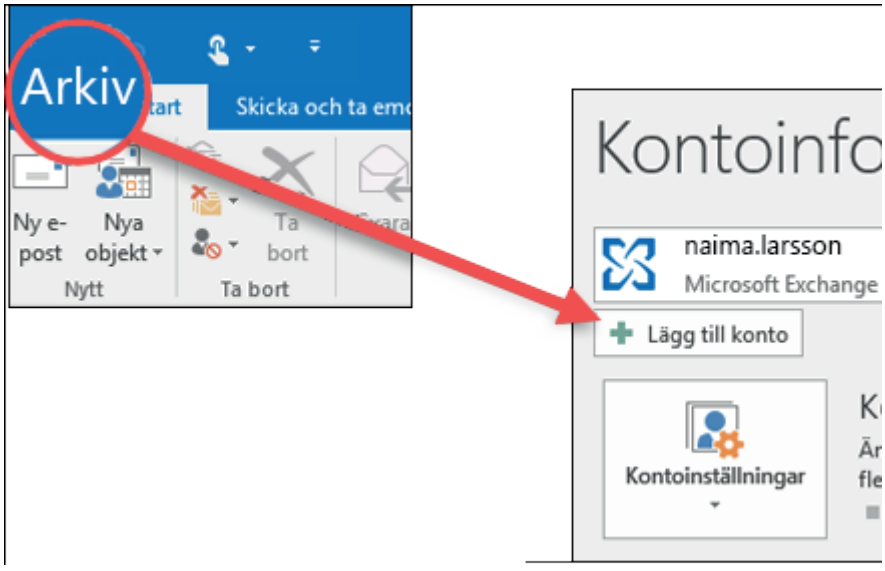
Det finns många olika typer av e-postkonton som du kan lägga till i Outlook, bland annat Microsoft 365, Gmail-, Yahoo-, iCloud- och Exchange-konton.

Vissa tredjepartsleverantörer av e-post, till exempel Gmail, Yahoo och iCloud, kräver att du ändrar vissa inställningar på respektive webbplats innan du kan lägga till dessa konton i Outlook.

Outlook för PCOutlook för MacMobil e-post

De här stegen är desamma oavsett om du lägger till ditt första e-postkonto eller andra e-postkonton i Outlook.

1. Välj **Arkiv** > **Lägg till konto**.



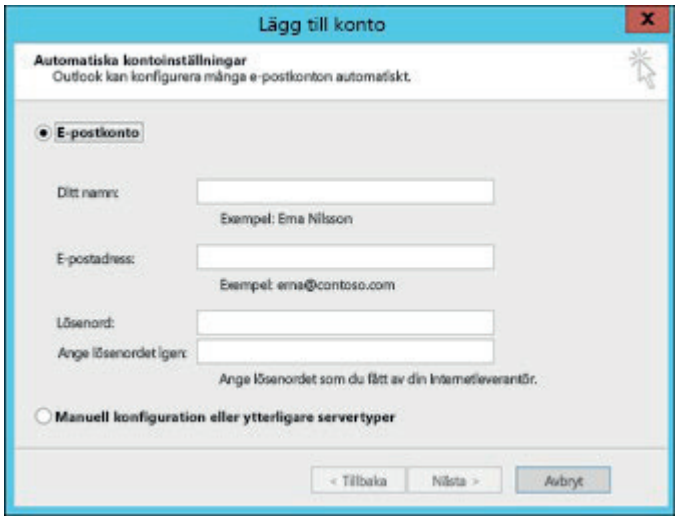
2. Vad som visas därnäst beror på vilken version av Outlook du har.

   För Outlook för Microsoft 365 och Outlook 2016

   För Outlook 2013 och Outlook 2010

Källa: https://support.microsoft.com/sv-se/office/l%C3%A4gga-till-ett-nytt-e-postkonto-i-outlook-6e27792a-9267-4aa4-8bb6-c84ef146101b

Ange din e-postadress och klicka på **Anslut**.



Ange namn, e-postadress och lösenord och klicka på **Nästa**.

3. Ange lösenordet igen om du uppmanas till det och välj sedan **OK** > **Slutför** för att börja använda ditt e-postkonto i Outlook.

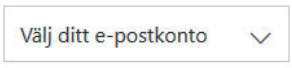
Outlook accepterar inte mitt lösenord

Om Outlook inte accepterar ditt lösenord och du vet att du använder rätt lösenord för e-postkontot, kanske du har ett e-postkonto som kräver ytterligare säkerhetsfunktioner.

Gmail-, Yahoo-, iCloud-, Outlook.com- och AOL-konton använder alla tvåfaktorautentisering för att verifiera att du är den person som försöker komma åt ditt e-postkonto.

För att lägga till ditt e-postkonto i Outlook behöver du ett applösenord, även kallat ett programlösenord. Det är ett annat lösenord än ditt vanliga lösenord för e-postkontot. Du vet att du behöver ett applösenord om du ser följande meddelande: *Tvåfaktorautentisering har ställts in för ditt konto. Logga in med ditt lösenord för programmet.*

Stegen för att hämta ett applösenord är olika för varje e-postleverantör. Välj din leverantör i listrutan för att få anvisningar.



Har du problem med att lägga till ditt e-postkonto? Använd avancerade inställningar.

Du kan behöva lägga till ditt e-postkonto manuellt. Välj någon av de avancerade metoderna nedan:

Använda avancerade inställningar för att lägga till ett POP- eller IMAP-konto i Outlook för Windows

Du kan använda Outlooks avancerade inställningar om du behöver ange specifika värden för namn på inkommande och utgående server, portnummer eller SSL-inställningar. Du kan använda de här anvisningarna för att lägga till ett POP- eller IMAP-konto i Outlook.

1. Öppna Outlook och välj **Arkiv** > **Lägg till konto**.
2. På nästa sida anger du din e-postadress och väljer **Avancerade alternativ**. Markera sedan kryssrutan för **Jag vill konfigurera mitt konto manuellt** och välj **Anslut**.
3. Välj din kontotyp. Oftast när du måste använda det här alternativet väljer du **IMAP**.
4. Sidan **Kontoinställningar** bör vara förifylld med de flesta av de kontoinställningar som du behöver. Men om du måste leta reda på inställningarna läser du avsnittet Inställningar för POP- och IMAP-konto. Ange inställningar för inkommande och utgående server och välj **Nästa**.
5. Ange ditt lösenord och välj sedan **Anslut**.

Använda avancerade inställningar för att lägga till ett IMAP-konto från tredje part i Outlook för Windows

Om du använder en MAPI-tredjepartsleverantör laddar du ned och konfigurerar leverantörens MAPI-e-postprogram som föreslås av leverantörsföretaget.

1. Öppna Outlook och välj **Arkiv** > **Lägg till konto**.
2. På nästa sida anger du din e-postadress och väljer **Avancerade alternativ**. Markera sedan kryssrutan för **Jag vill konfigurera mitt konto manuellt** och välj **Anslut**.
3. På sidan **Avancerad konfiguration** väljer du **Annan**.
4. Välj vilken typ av server som du vill ansluta till i listan på skärmen **Annan**.
   Obs! Alternativet **Annan** och din kontotyp som visas under det visas bara om du har installerat och konfigurerat MAPI-leverantören korrekt.
5. Klicka på **Anslut**.
6. Det MAPI-leverantörsprogram för tredje part som är installerat på datorn bör startas.
7. Slutför kontokonfigurationen genom att följa MAPI-leverantörens instruktioner.

Vill du uppdatera inställningar för ett befintligt e-postkonto i Outlook?

Om du redan har skapat ett e-postkonto och vill uppdatera befintliga inställningar på grund av ett aktuellt problem går du till Ändra eller uppdatera inställningar för e-postkonto i Outlook för Windows.

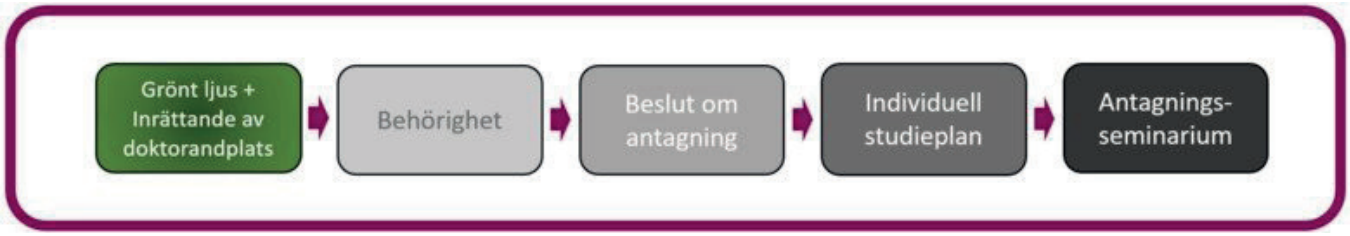
Se även

Ändra eller uppdatera inställningar för e-postkonto i Outlook för Windows

POP- och IMAP-e-postinställningar för Outlook

Appendix 3

Admission process at CLINTEC (In Swedish)



Rekrytering:
Alla doktorandplatser vid KI ska utlysas genom annonsering, förutom i de fall då undantag från kravet på utlysning medges https://ki.se/medarbetare/antagning-till-forskarutbildning
Vid inlämnandet av grönt ljus ansökan skall även Appendix 1-3 bifogas och Inrättande av doktorandplats.

Doktorandplatser ska:
- annonseras via KIs rekryteringssystem Varbi med den annonsmall som finns i systemet.
- annonseras under lämplig tidpunkt och ansökningstiden rekommenderas att vara tre veckor eller längre.
- annons ska finnas på svenska och/eller engelska.

Flödesschema där undantag för annonsering föreligger

Steg 1	Beredningsmöte inför antagning	Blankett: Inrättande av doktorandplats Blankett: Finansieringsplan Blankett: Grönt ljus ansökan, Blankett: Appendix 1-3 Lämnas in enligt resp. inlämningsdag med deadline för inlämnandet av ansökan till enhetschef, se schema. Alla dokument lämnas in enkelsidiga! Resp. enhetschef inbjuds som föredragande av ansökan till ett beredningsmöte. Rekommenderar att de sökande går igenom ansökan med sin enhetschef innan mötet. Godkänd/avslagen ansökan meddelas enhetschef för vidarebefordran till den sökande.
Steg 2	Bedömning av behörighet	Efter att steg 1 är avklarad. Får den sökande epost från LADOK-administratören med vidare instruktioner och länk till Varbi, där den blivande doktoranden skall ansökan om behörighet till forskarutbildningen vid KI. Föreligger behörighet skickas ett behörighetsutlåtande via epost till kandidat och handledare, vilket skrivs ut och bifogas ”Beslut om antagning”

Steg 3	Beslut om antagning	Efter att steg 1-2 är klara lämnas nedanstående blanketter med bilagor in till LADOK-administratören inför beslut av studierektorn och prefekt. Blankett: Beslut om antagning till utbildning på forskarnivå
Steg 4	Individuell studieplan	Fr o m 1 februari 2021 lanserades digital individuell studieplan (ISP). Samtliga institutioner ska börja använda digital ISP för doktorander antagna från 1 februari 2021. Huvudhandledare tilldelas behörighet till den digitala ISP via epost från LADOK-administratören. Huvudhandledare skapar här en ny ISP till sin doktorand. Mer information om hur du skapar en ny ISP inkl. manualer finns på KIs hemsida ”Create, write and submit ISP”
Steg 5	Antagningsseminarium	Doktoranden kommer att bjudas till ett antagningsseminarium vid CLINTEC, tillsammans med sin huvudhandledare, för att presentera sitt projekt under 5 minuter. Presentationen (max 4 bilder utan animeringar (ppt)) skickas till LADOK-administratören senast två dagar innan seminariet. Presentationen skall framföras på engelska. Kommer presentationen att ske via länk (ZOOM) delar doktoranden sin presentation via länken

Vid eventuella frågor, kontakta LADOK-administratören

Agneta Wittlock
forskarutbildning@clintec.ki.se
08-585 87353