

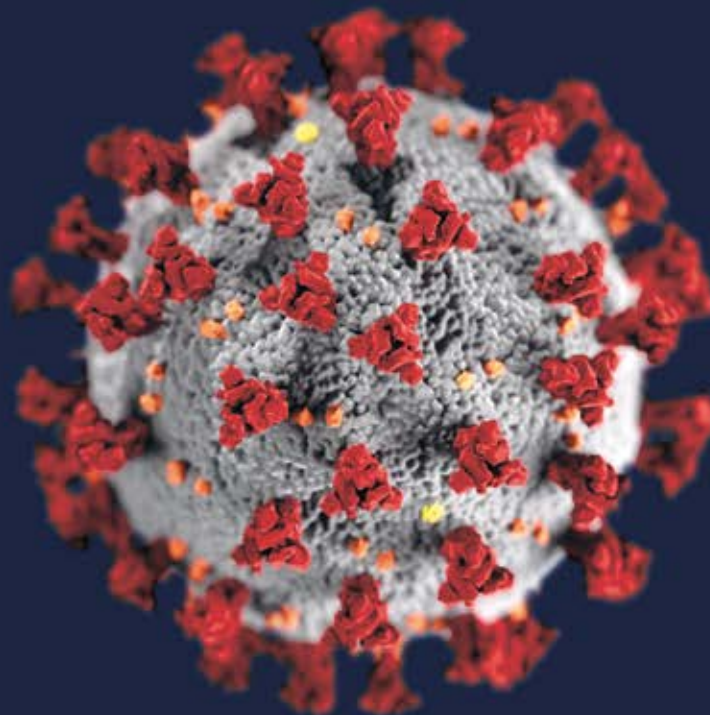


Rigshospitalet



Department of Clinical Physiology, Nuclear Medicine & PET

Annual Report 2020





Rigshospitalet

King Frederik V founded Rigshospitalet in 1757. Today it has app. 1,250 beds and 12,000 employees. Research at Rigshospitalet is published in more than 2,000 peer review papers per year, including >200 higher academic theses (PhD and Doctor of Medical Science). Rigshospitalet is part of The Capital Region of Denmark and is a Copenhagen University Hospital.

University of Copenhagen

The University of Copenhagen was founded in 1479. The Faculty of Health and Medical Sciences has 10,000 students, including medicine and bioengineering in collaboration with The Technical University of Denmark, DTU. The University of Copenhagen is member of IARU, the International Alliance of Research Universities and LERU, League of the European Research Universities. www.ku.dk



Rigshospitalet



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Preface

2020 was a tough year. The Corona pandemic in 2020 influenced the Department of Clinical Physiology, Nuclear Medicine and PET from the first lockdown March 12, 2020 and throughout the rest of the year. We did a tremendous effort, and thanks to this dedication we managed.

We had to reorganize the department to overcome the challenges. We would like to express a warm thank you to all staff members, young and old from all groups for a fantastic effort and your positive engagement for the sake of our patients and their safety – and the safety of the staff. We examined and treated all patients referred to

us, we were serious in our approach to preventive measures and we spent extra time cleaning all scanners, equipment and rooms between every patient. We avoided spread of the disease among the staff, but some employees inevitably were infected by their family members with the SARS COVID-2 virus disease.

The staff has been very diligent in wearing masks and taking all precautionary measures, and so far it has been a success story. Patients referred to lung function tests, lung diffusion capacity measurements and lung scintigraphy with SPECT/CT for ventilation and perfusion were

a special challenge, as these investigations are heavily aerosol producing. A warm thank you to all involved.

We had extra expenditures due to all the precautionary measures including masks, gear, washing of scanners between each patient etc.

We still have the old Agfa RIS/PACS ICT system, and as reported in previous annual reports we waste a lot of time every day due to lack of stability, performance and problems with the speech function. The Capital Region of Denmark has promised a new system to all the

hospitals in the region, and we have initialized the process, and look forward to a busy 2021 with the acquisition of a new, modern, well-functioning, state-of-the-art system.

All patients have, despite the challenges, been treated with state-of-the-art quality in a professional, dignified and friendly atmosphere. For that we would like to express a warm thank you to all staff members.

The highlight of the year was the new PET/MRI scanner donated by the John and Birthe Meyer Foundation. We got new additional rooms in the Finsen Building, and they have been designed to accommodate the new scanner. The section will be completed in 2021. We look forward to the privilege of doing patient studies, research and education with the new super equipment. Thank you very much to the John and Birthe Meyer Foundation for all the generosity.

Another very positive development in the hospital was the opening of the new North Wing in September 2020. A very beautiful, modern hospital with single rooms for all patients and a modern patient- and staff-friendly design.

Research is a key activity and focus area of our department, and we have a comprehensive research program directed towards innovative solutions to solve unmet clinical needs. We have special focus on implementation of personalized medicine in collaboration with other research groups here and internationally. AI, artificial intelligence, is a new important research area with the young research group CAAI, Clinically Applied Artificial Intelligence. To all our research groups: A sincere thank you for the dedicated, impressive and important work. The high research output with publications and patents is mostly based

on research done in previous years. During this Corona-year we have tried to protect the research projects, but of course the situation has led to some postponements.

Due to prohibition of larger meetings and travel, conferences were changed to e-learning and webinars, and the educational situation had to adapt very quickly to these new conditions. We have learned a lot through e-learning.

New Center Director Helle Konradsen, MD, DMSc, started March 1, 2020. Thank you to Helle and to Vice Director Lene Ørnstrup Christensen for help, support and collaboration throughout the year.

Thank you to the Department of Radiology, Head of Department Ilse Vejborg, who changed to Head of Department of Breast Cancer Screening. We would like to say thank you to Ilse for the fine collaboration throughout the years. The same thank you to Chief Radiographer Johnny Madelung, who is in charge, together with the new Acting Head of Department Martin Lundsgaard Hansen, MD, PhD, whom we would like to express a warm welcome to.

Our Chief Nuclear Medicine Technologist Linda M. Kragh retired October 2020 after more than 50 years as medicine technologist and more than 30 years as our Chief Nuclear Medicine Technologist. From Rigshospitalet a warm thank you to Linda for the tremendous effort all those years and the very best wishes for a happy life further on.

The new Chief Nuclear Medicine Technologist, Ida Kjær Robsøe started October 2020, and the department is privileged by having Ida as new leader.

Professor Andreas Kjær stepped down as professor in charge of research and was replaced by Professor Jann Mortensen. Thank you to Andreas Kjær for the great effort for our research throughout the many years, and a warm welcome to Jann Mortensen. Thank you very much to Jann for taking over.

Head of Department, Professor Liselotte Højgaard was from Autumn 2019 until March 2020 also Acting Head of Department of Pathology. This extraordinary period ended March 12, the day where the Corona lockdown began.

The Department of Clinical Physiology, Nuclear Medicine and PET leadership tried in 2020 to balance the many challenges and demands due to the Corona-pandemic and secure that all patients, relatives and staff were sailed safely through the rough seas and troubled waters.

Our aim is to deliver the best patient treatment and the best research and education. Thank you to all staff members, collaborators and international colleagues for making this possible – also in the Corona year.

Liselotte Højgaard, MD DMSc
Professor, Head of Department

Linda M. Kragh
Chief Nuclear Medicine Technologist

Ida Kjær Robsøe, MPG
Chief Nuclear Medicine Technologist



Mission and objectives

We strive to provide the best for each and every patient:

- ▶ Clinical physiology and nuclear medicine patient investigations and treatment
- ▶ Research at the highest international level
- ▶ Undergraduate and postgraduate education
- ▶ Good patient experiences through state-of-the-art quality, high patient security and focus on the wellbeing of each patient
- ▶ The best possible everyday worklife for all staff members



Chief Nuclear Medicine Technologist Linda M. Kragh - retirement

October 2020 Linda M. Kragh, our Chief Nuclear Medicine Technologist for more than 30 years decided to retire. In 2019 Linda had celebrated her 40 Years Anniversary as nuclear medicine technologist, and she had received the prestigious annual award: “Technologist of the year 2019” from Rigshospitalet. Due to the Corona pandemic the retirement party had to be quite small, but the “Thank you very much to Linda” for a marvelous job done was huge. Linda has been an icebreaker for the professional development of the nuclear medicine technologists in Denmark, and she has been a much loved and respected leader of our department. From all of us a warm thank you for all the effort. Linda is a role model for all of us - always with a smile and in great shape.

New Chief Nuclear Medicine Technologist Ida Kjær Robsøe, MPG

October 2020 Chief Nuclear Medicine Technologist Ida Kjær Robsøe, MPG took the helm. We are privileged by having Ida as new dedicated and competent leader. Ida was previously Chief Nuclear Medicine Technologist in Herning and Køge, and from March 2020 as staff technologist here. We look forward to the future with new exiting developments.





Professor Andreas Kjær stepped down as research leader

Andreas Kjær has been professor in charge of research for the department for long. June 2020 he decided to step down from this function to concentrate on his new prestigious Lundbeck Professorship. Andreas has throughout the years developed research in our department very successfully in collaboration with the other 4 professors and all research groups and clinical scientists. From all of us – thank you very much for the dedicated effort and fine job done. Molecular imaging is a cornerstone for the development of nuclear medicine.



Professor Jann Mortensen new research leader

Professor Jann Mortensen is our new professor in charge of research. Apart from his own research program in lung physiology, Jann has 10 years of experience in the Ethical Committee, so the qualifications for the job as research leader are in place. A warm welcome to Jann, and a big thank you for taking over.



Head of Department, Professor, MD DMSc Liselotte Højgaard

The Corona pandemic 2020

Denmark experienced the first day of “lockdown” due to the emerging Corona pandemic March 12, 2020. The number of patients with COVID-19 disease in the hospital was still low, but preparations to receive many patients were initiated immediately. Protection gear was now mandatory, but still insufficiently available. Many precautions including extra disinfection of hands and use of masks were initiated. Administrative staff should work from home, but we have only few of those, and we all had to adapt and work in a different way at the hospital or at home.

The first wave of the Corona pandemic in Denmark lasted until late Spring 2020. We experienced a moderate decrease in number of patients referred to us. Rigshospitalet is a tertiary university hospital for patients in need of highly specialized treatment: patients with serious diseases as cancer, heart

diseases, transplantations and small newborn children with congenital diseases in need of surgery.

Especially the diagnosis of patients with COVID-19 disease was a challenge, as they imply procedures with aerosol production, such as lung function tests, lung diffusion capacity measurements and lung scintigraphy with SPECT/CT for perfusion and ventilation images. For these studies extra precautions had to be initialized. In the beginning it was a bit frightening for the staff with these very sick patients and the unknown risks from the new contagious disease, but we quickly calmed down and got used to it.

The department managed to avoid spread of disease from patients and among the staff, although some few staff members got the disease from their family and children.

We worked a lot, and the new situation was a bit scary, but dedication and an impressive effort was delivered from everyone in the department. Over Summer and early Autumn, we kept all the restrictions, and worked hard with both the usual patients, the waiting lists and the increasing number of COVID-19 patients and post COVID-19 patients with lung diseases.

It was a tough period where we reduced the waiting list and at the same time had all the Corona measures with facial masks, the special protection gear and the extra time we had to use between every patient in the scanner rooms. (Between every patient we had to clean the scanner and all equipment extra compared to our usual standard and all protection gear had to be changed. It takes extra 15 min between patients and with an annual number of 130,000 patients it adds up). The staff



did a fantastic job taking care of patients plus these extra preventive measures and overtime was frequent.

A CT scan of the lungs in patients with COVID-19 pneumonia is almost pathognomonic for the diagnosis. Many patients with the disease also experience smaller or more widespread clotting in the lungs, and the number of patients referred to lung perfusion- and ventilation scintigraphy with SPECT/CT was increased. Post COVID-19 disease is frequent even in young, previously healthy patients. These patients develop a fibrosis-like condition with reduced lung diffusion capacity lasting for months. As the number of patients grew, the number of post COVID-19 cases increased in parallel, and the lung function test rooms were opened extra in the evening every day to accommodate the rise in patient referrals.



In late autumn 2020 the second wave of the Corona pandemic in Denmark developed, and it lasted until February 2021.

The situation in the department necessitated a new way of organizing patient studies, but also research and education had to be rearranged. Clinical research could be maintained in most patients, but some protocols had to be postponed. Education had to be changed, and small and large meetings, gatherings and conferences were changed to Teams, Zoom, Skype, or e-learning. Or even cancelled. We therefore introduced a weekly Webinar arranged by Staff Specialist Camilla Bardram Johnbeck, MD, PhD, Senior Registrar Per Krakow Cramon, MD, PhD, Computer Scientist Sune Keller, MSc, PhD and collaborators. The Webinars were available for all staff members and shared also outside the hospital. The education

for specialists in clinical physiology and nuclear medicine was unchanged with the national courses uninterrupted, but otherwise most of conferences and meetings both in Denmark and internationally were either cancelled or changed to e-learning and web-conferences. It has been a very quick transformation, and all the good things with e-learning, Webinars, Team-meetings will be kept also post Corona.

In December 2020 the hospital leadership and the Capital Region of Copenhagen expressed a warm thank you to all of us who worked hard to secure that the patients were diagnosed and treated during the Corona year 2020. It was nice with this recognition and appreciation.



Professor Jann Mortensen and Associate Professor Ronan Berg

Lung studies

Rigshospitalet was the first to develop simultaneous V/Q SPECT/CT for diagnosis of pulmonary embolism. The high diagnostic performance of V/Q SPECT/CT is a benefit to the many patients that we study before and after lung transplantation, lung volume reduction, lung cancer, and for work-up of pulmonary embolism and pulmonary hypertension.

Radioaerosol inhalation and subsequent bronchoscintigraphy was developed by us to assess mucociliary clearance in patients with lung diseases e.g. recurrent lung infections. We use it for diagnosing primary ciliary dyskinesia and to assess if mucus transport can be increased by intervention e.g. physiotherapy or salt inhalation.

Lung function tests such as spirometry, body plethysmography and diffusion capacity are routinely performed for diagnosis and monitoring in patients with COPD and emphysema, many

types of cancer and hematologic diseases, before thoracic surgery and radiation treatment, and pulmonary hypertension. If needed, we have now added measurements of respiratory muscle strength, small airways disease with impulse oscillometry (IOS) or multiple breath nitrogen washout (MBN2W), and dual tracer diffusion capacity (using both carbon monoxide [CO] and nitric oxide [NO] as tracers) to our standard panel of lung function tests.

All of these clinical physiological and nuclear medicine lung studies are both used in the daily clinical routine and in clinical research. Two examples are given below.

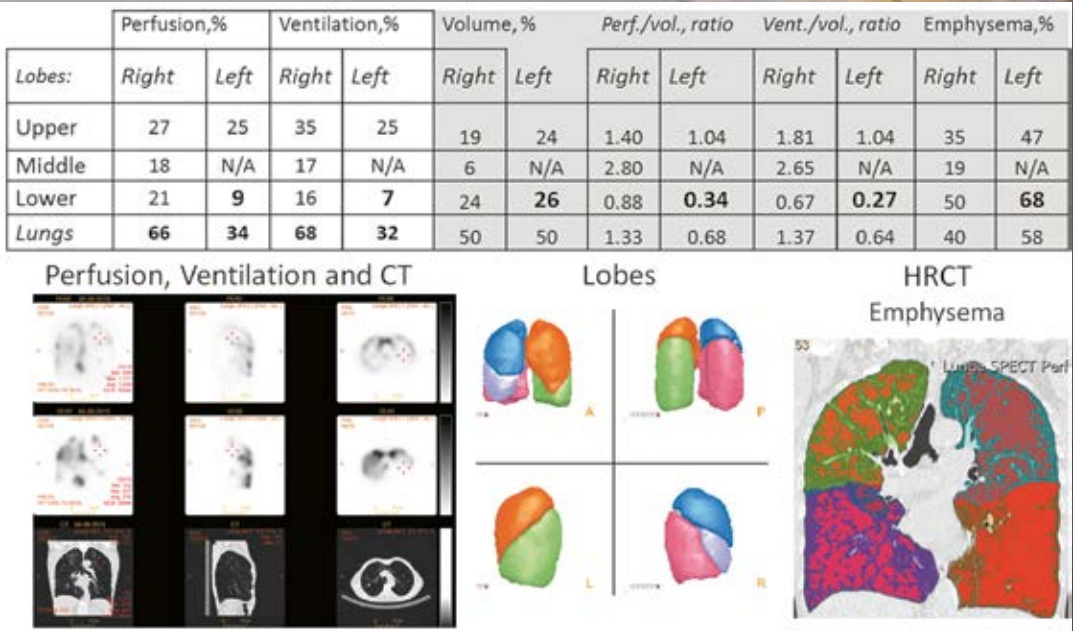
In the SECURE study, we investigate the extent of airway and lung complications 3-12 months after COVID-19 with multiple lung function test and V/Q SPECT/CT and high-resolution CT (HRCT) in collaboration with the Department of Infectious

Diseases and other departments at Rigshospitalet. Preliminarily, we often find a reduced diffusion capacity with interstitial changes, and sequela after pulmonary thromboembolism. Yet, it remains to be determined if these changes are reversible after 12 months.

Lung volume reduction surgery is an efficient and approved treatment for selected emphysema patients. In Denmark it is centralized at Rigshospitalet. Our responsibility is to assess the degree of lung function impairment and hyperinflation, the degree of emphysema, as well as each lung lobes' perfusion, ventilation and volume before and after treatment. Our studies are mandatory for decision making on the multi-disciplinary meetings for the assessment of whether the treatment can be offered, and which lobe is the best target for treatment.



Report of V/Q SPECT/HRCT in a patient assessed for lung volume reduction. Suggestion for target: Left Lower Lobe. Upper table shows the relative perfusion, ventilation, lung volume and degree of emphysema in each lobe.



Lung studies





Chief Nuclear Medicine Technologist, MPG Ida Kjær Robsøe

Newsletter

Our first Newsletter was launched in November 2020. Ida Kjær Robsøe, our Chief Nuclear Medicine Technologist launched it as one of her first innovative moves to enhance information and communication across the entire department.

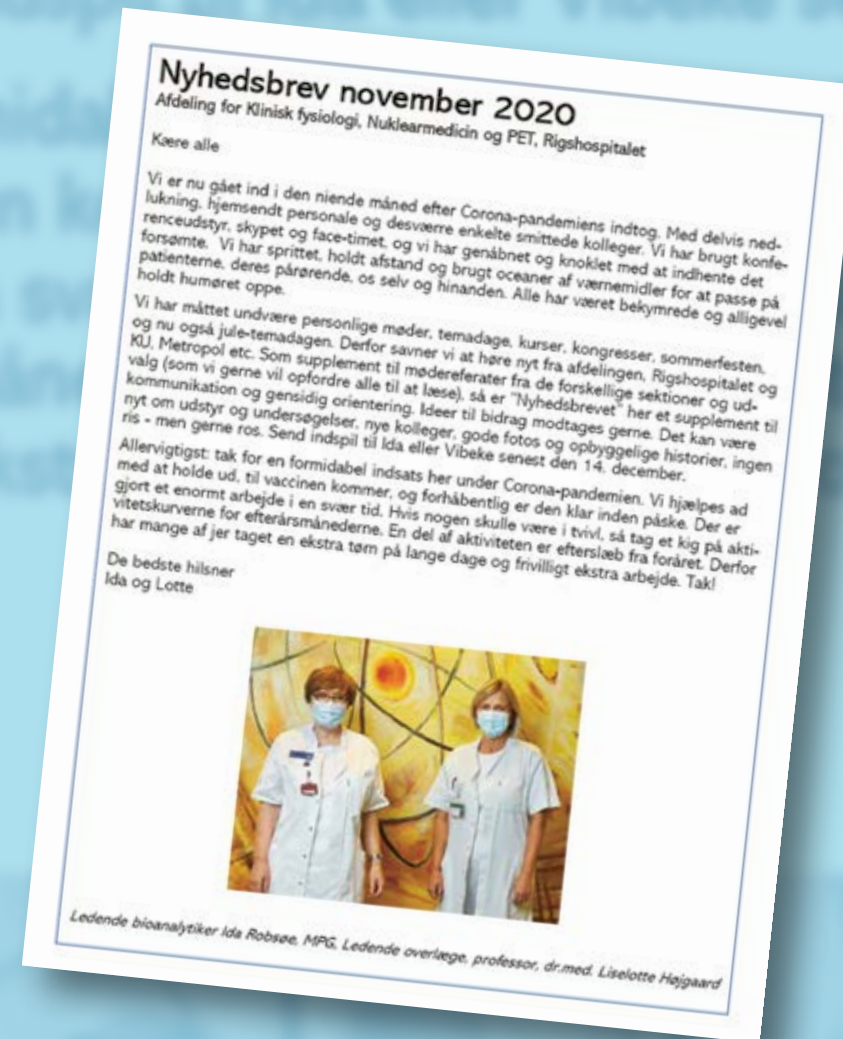
The majority of the department's physical meetings and personal contacts had to be reduced to a minimum due to the Corona-pandemic, and meetings were replaced by digital solutions. We were therefore challenged regarding communication and information across the various sections of the department. Despite "minutes of meetings" from the sections, several employees expressed a desire for more knowledge about news and changes also in other sections.

We therefore decided to publish an occasional informal newsletter that picks up on both minor and major news, information and changes. The quality of both clinical patient studies, research and development depends on good collaboration and coherence across all sections of the department.

The Newsletters include presentations of new employees, information about retirements, students writing bachelor projects and other staff-related updates. In a large organization, there are constantly tasks and responsibilities that change hands, new tasks that are delegated, working groups that are appointed, etc. The aim of the Newsletter was to increase cohesion and

sense of a common denominator among the many teams and groups of the department. We also use the Newsletter to present new equipment, new surveys and changes that optimize workflow and organization.

It is our hope that the Newsletter, combined with meeting minutes, intranet and local meetings, will contribute positively, so that all employees feel as an integral and valued member of the department. We also use the Newsletter to invite staff to come forward with constructive ideas and initiatives.





Chief Nuclear Medicine Technologists Linda M. Kragh and Ida Kjør Robsøe

Nuclear medicine technologists, radiographers, nurses and laboratory technicians

2020 was a challenging year for the nuclear medicine technologists, radiographers, nurses and laboratory technicians. Regarding the patient investigations we were all influenced by the lockdown of the Danish society in early March 2020. Many studies were postponed, and patients were worried and cautious about the dangerous and in those days unknown virus. (Just as we were).

Our daily work with drug manufacturing and patient examinations require the physical attendance of all our staff members, and we are grateful for the dedication and discipline shown in the past year. Despite difficulties in society with the closure of schools, kindergartens, etc.,

the staff has in the finest way accomplished all tasks and hopefully also the work-life balance. We are full of admiration for the collegial efforts made to provide patients and relatives with the best possible quality and service.

Teaching and education

Despite the difficulties, we decided that the Corona-crisis must not stop us. From the summer of 2020, the professional teams have held workshops and internal teaching. This has been possible with a special focus on hygiene and distance. Training on Teams by our specialists has proven to work well. Thank you to the teachers involved. We are all looking forward to the days when it will be possible again to attend

qualifying CT courses, isotope courses, conferences and meeting etc., but we are also proud that we have managed to keep the professional flag high this year in spite of the difficulties.

Our Teaching Nuclear Medicine Technologists Mia Hjorth Albers and Annette Foldager have experienced very special challenges from the start of the lock down. In a very short time, they have transformed themselves, the students and the clinic into a completely new way of teaching. We appreciate their great effort as well as the clinical supervisors’ great efforts in bringing the next generation of nuclear medicine technologists and radiographers through to their exams.



Management

The daily operation of the sections is led by the four Staff Nuclear Medicine Technologists in collaboration with the sections’ Chief Consultant or Chief Chemist. They have together as a team very central roles both in the respective sections and for cooperation and coherence throughout the whole department. They have managed to steer the sections safely through the COVID-19 problems while meeting the usual challenges of training, new equipment, conversions etc.

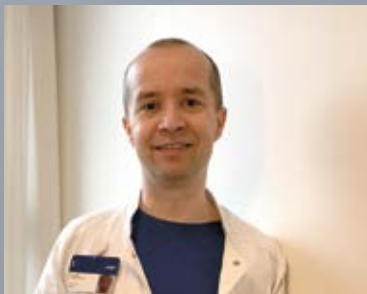
In the KF Section we have had a “change of guard” at the position. Our two Nuclear Medicine Technologists Cejlan Zulfovska and Mariam Hassan took care of the tasks when the

position became vacant, and from December 1, 2020 we were pleased to announce that Mariam Hassan has taken over in the KF Section as staff nuclear medicine technologist.

To ensure continuity and leadership there is also now a deputy for the staff nuclear medicine technologist in all sections. In the Radiochemistry Section, Nuclear Medicine Technologist Tina Wikke Hallund in 2020 took over as Staff Nuclear Medicine Technologist Anne Sørensen’s deputy.

Regarding leadership and management, we prioritize education and professional development for leaders, and we are pleased that Staff Nuclear Medicine Technologist Maria Helene

Pejtersen in the PET Scanner Section and Staff Nuclear Medicine Technologist Helle Møllegaard Dahl in the Glostrup Section have both completed the Capital Region of Denmark’s management training in 2020.



Consultant Rasmus Sejersten Ripa

Team structure

In January 2019 it was decided to divide the entire department into a number of teams. The primary aim was to support the clinical and professional development within the department.

Each team was based in a clinical area (e.g. a lung team). In addition, we created teams with a more cross-cutting function (e.g. a research team and an education team). In total, we created 18 teams. For each team, a team leader was appointed.

We have a long tradition of holding 4 annual meetings with all senior staff incl. all consultants – called “large management meeting”. Over the years, these meetings had evolved to have mainly an administrative content.

With the introduction of the team structure, it was important for us also to ensure communication and cooperation between the individual teams. We therefore changed the “large management meeting” to focus primarily on the teams.

At the meeting, each team leader presents a brief status from the team under the following headings:

- What is the status of the team clinically-professionally?*
- What is the status of the research within the team?*
- Plans or desires for development within the team?*

That way, all senior staff will be up to date with status across the entire department. At the same time, the meeting provides an opportunity to

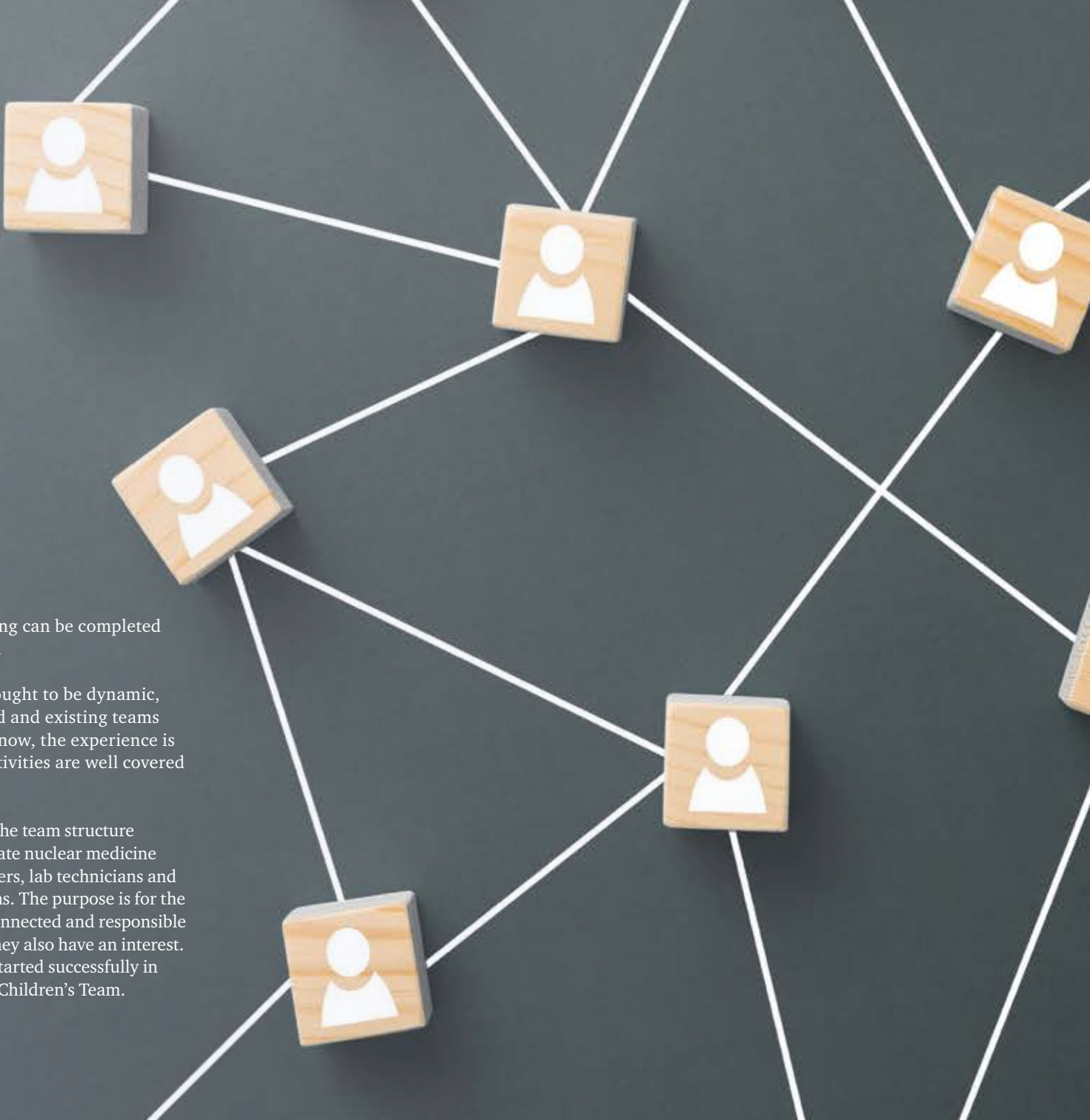
discuss plans or desires for development among all senior staff.

In the last year, physical meetings have been very limited, but still the team structure has proved its worth. We have been able to have a continuous development using the flexibility of a team structure with a short chain of command, where the team leader is closely involved in the daily clinical work. The Corona restriction has also challenged our internal education of the staff. In this special situation we have delegated the educational responsibility to the individual teams. Using this approach each team leader can focus the education on the most important clinical topics and include the relevant staff only. We have found that even

hands-on practical training can be completed using online supervision.

The team structure is thought to be dynamic, new teams can be created and existing teams can be disbanded. Right now, the experience is that the department’s activities are well covered with the existing teams.

Next year, the work with the team structure will primarily be to associate nuclear medicine technologists, radiographers, lab technicians and nurses to the various teams. The purpose is for the staff to feel particularly connected and responsible within an area in which they also have an interest. This process has already started successfully in several teams such as the Children’s Team.





Chief Nuclear Medicine Technologist, MPG Ida Kjær Robsøe

Work environment

Efforts in the work environment area have primarily been focused on handling COVID-19. Both in relation to patients, relatives and staff. It quickly became clear that in 2020 a good and safe work environment would mean, that we would have to introduce some new routines which in other contexts would be perceived as work environment inhibiting.

Protective equipment

Fortunately, our employees are trained to think and act with hygiene in mind and we have used hand washing and disinfection with ethanol between all patient-related tasks for long. We had to get used to the fact that this also had to include other items as keyboards, pens, tables, door handles, etc. Everything was disinfected again and again. Where possible, we set up transparent acrylic screens to create physical barriers between patient and staff, e.g. at the patient receptions. Before COVID-19, we used protective equipment

such as coatings, masks, etc. for particularly vulnerable patients or patients with known infectious diseases. We initially extended this to all patients due to the high-risk of aerosol infection transmission. As the COVID-19 infection spread in the community, we introduced these protective devices for all procedures. Many have experienced skin problems due to the frequent use of hand disinfection with alcohol and the permanent use of masks. We have tried to alleviate this by changing workflows and by purchasing different types of protective equipment. However, delivery difficulties and the escalating need for the use of protective equipment have unfortunately meant that some of our employees are still suffering from skin problems and discomfort.

Distance

We are now used to the everyday life with physical distance between patients, relatives and

colleagues. The number of chairs and tables in waiting areas, staff rooms and meeting rooms had to be reduced, and as the pandemic progressed, we had to reduce the number of people allowed in all rooms. Meeting activities were reduced and transformed to digital meetings on Teams, Zoom, Skype, Webinars etc. All unnecessary assemblies had to be avoided.

Testing

In connection with Rigshospitalet's COVID-19 clinics for testing of patients and staff, assistance was provided over the summer. In a hurry, several of the department's staff volunteered for this work. We would like to thank the employees who made this extra effort in the tents, so that we all had the opportunity for a quick test and not least; a quick answer. It has been of great importance for both patient flow and the working environment that we have had such easy access.

Vaccines

End of 2020 we received the long-awaited message that a vaccine was close to approval and release for the elderly, vulnerable and hospital frontline staff. Before the Christmas holidays, our frontline staff signed up for the vaccination list. We owe a big thank you to the work environment representatives and to all staff members who have followed all restrictions to the letter. We have so far experienced no infections between colleagues in the department. The good habits and responsiveness to the health authorities' recommendations have brought us through 2020 with an almost normal service for patients and clinicians.

We are full of admiration for the efforts made - extra work, collegiality, patience and flexibility.



Highlights 2020



A warm welcome to Professor Jann Mortensen as our new professor in charge of research.



In October our new Chief Nuclear Medicine Technologist, Ida Kjær Robsøe started. We are pleased and privileged to welcome Ida in the department.



The department was privileged by a new PET/MRI scanner donated from The John and Birthe Meyer Foundation. Thank you very much to The John and Birthe Meyer Foundation for all the generosity.



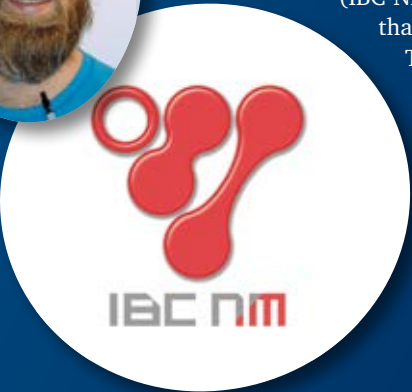
Professor, Head of Department Liselotte Højgaard was appointed Member of the ERC Scientific Council.



Our Head of Dept. Professor Liselotte Højgaard had a busy winter, as she was also Acting Head of Dept. of Pathology, from November 2019 to March 2020.



Professor Andreas Kjær obtained a Lundbeck Professorship from the Lundbeck Foundation.



In October 2020, we implemented the state-of-the art Nuclear Medicine Management System (IBC-NM) in the KF Section. A warm thank you to Nuclear Medicine Technologist Kim Ryder Jensen and the other expert nuclear medicine technologists who contributed with implementation.



The new North Wing was opened in September 2020. A very beautiful, modern hospital with single rooms for all patients and a modern patient- and staff-friendly design.



Consultant Lotte Hahn Enevoldsen and Staff Nuclear Medicine Technologist Mariam Hassan

The KF Section

The KF Section offers a variety of nuclear medicine and clinical physiological examinations of both routine patients and for many research investigations in a broad spectrum of disciplines. In addition to nuclear medicine diagnostics our section also comprises radionuclide therapy of patients with neuroendocrine tumors (¹⁷⁷Lu-DO-TATATE), patients with castration resistant prostate cancer and symptomatic bone metastases (²²³Ra), and patients with benign thyroid diseases (¹³¹I-Iodine).

We participate in various weekly and monthly multidisciplinary team conferences discussing neuroendocrine tumors, thyroid diseases, adrenal diseases, cardiac diseases, lung diseases and pediatric oncology with our clinical colleagues. In 2020 the demand for lung function testing and lung scintigraphies increased due to referral of

patients with either ongoing or post COVID-19 infection. In order to meet this need, our section was expanded with an extra examination room for lung function testing, and our lung scintigraphy capacity was upgraded with an extra SPECT/CT scanner.

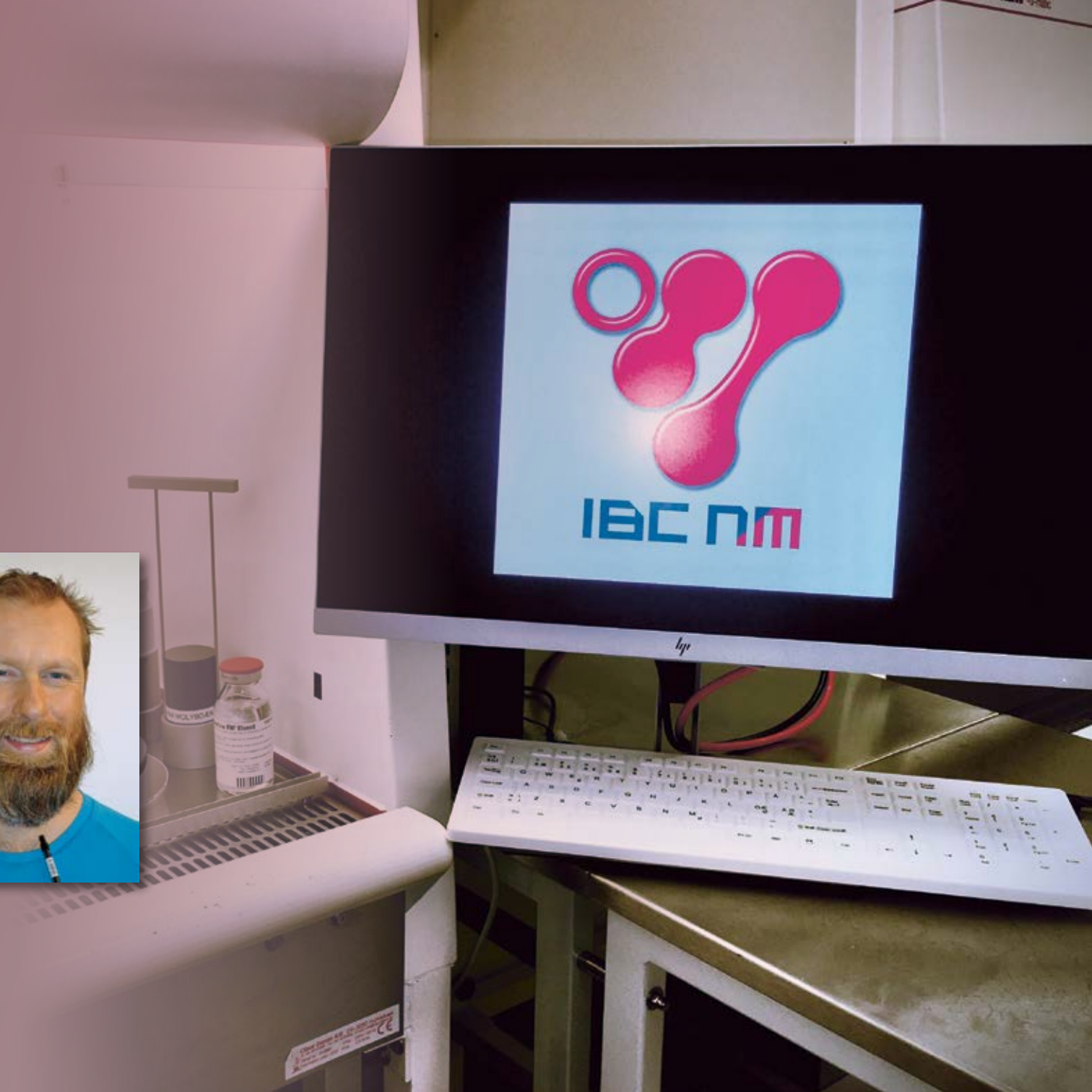
With the installation of the new SPECT/CT scanner, there has been a lot of rebuilding and rearrangement to create space. In addition, we created a larger and better preparation room for the extraction of radioactive isotopes.

IBC-NM
In October 2020, we implemented the state-of-the art Nuclear Medicine Management System (IBC-NM) in our Radiopharmacy. The preparation process in the laboratory is controlled and linked to the patient’s activity, with name and CPR

number. The system is integrated with RIS (HL7 and DICOM), and thereby data is transferred securely between the two systems.

IBC-NM also provides the opportunity of stock control of the Mo/Tc generator as well as all the other radioactive isotopes and tracers used in the section. With the simultaneous upgrade of the dose calibrators, quality controls are also gathered in the database.

Many thanks to Nuclear Medicine Technologist Kim Ryder Jensen for dedicated management of the process and thank you to the other expert nuclear medicine technologists who contributed with implementation and troubleshooting in the first weeks.





Nuclear Medicine Staff Technologist Maria Pejtersen and Consultant Annika Loft Jakobsen

The PET-Scanner Section

PET/CT has a natural place in the complex world of personalized medicine for patients suffering from oncological or inflammatory diseases not only in helping to diagnose, stage and depict the right patients for the right treatment, but also to monitor their treatment. We work in close collaboration with clinical colleagues as well as researchers from different fields.

Our dedicated team of nuclear medicine physicians, radiologists, technologists and radiographers are involved in research protocols and clinical trials testing new treatments as well as new PET tracers. This is an important and inspirational part of the daily work with patients which improves our knowledge to their diseases. As a result of this work, we have implemented new indications and scanning procedures.

We have developed the clinical use of FDG PET/CT for radiotherapy planning in collaboration with the Department of Radiotherapy by participating in research protocols, and we are expanding use of other tracers for this purpose as well.

In our daily clinical life, ¹⁸F-FDG PET/CT is the work horse investigation for a vast amount of indications, but use of other oncological tracers such as ⁶⁸Ga- and ¹⁸F-PSMA for prostate cancer patients as well as ⁶⁸Ga-Dotatoc and ⁶⁴Cu-Dotatate for patients with neuroendocrine tumors and ⁶⁸Ga-PSMA for prostate cancer patients is increasing.

FDG PET/CT also plays an increasing role in the management of patients with inflammatory and infectious diseases in diagnosing as well as treat-

ment monitoring – an exciting area to exploit in the clinical every-day work as well as in research.

At the moment we are in a phase of implementing new digital PET/CT scanners with increased sensitivity and improved image quality at higher scan speed. This will able us to increase throughput to meet the increasing demand from the clinical departments.

Artificial intelligence for improving image quality in combination with radiation dose reduction and shorter scan time opens new possibilities including increased patient comfort. The possibility of reducing the radiation doses to the staff is also an important issue that always should have the highest concern.





Consultant Lotte Hahn Enevoldsen and Staff Nuclear Medicine Technologist Helle Møllegård Dahl

The Glostrup Section

Offering a variety of nuclear medicine and clinical physiological examinations The Glostrup Section examines patients hospitalized at the Glostrup location of Rigshospitalet as well as patients from the Glostrup outpatient clinics and patients from general practice in the surrounding area.

In close collaboration with our colleagues in the PET Section we examine patients referred from both Glostrup and Blegdamsvej with wholebody ^{18}F -FDG PET/CT scans as well as dedicated brain scans.

Bone scintigraphy for rheumatologic diseases and evaluation of spine surgery with various

prostheses are performed in patients referred from Center for Rheumatology and Spine Diseases, Rigshospitalet.

We assist in diagnosing secondary hypertension with Captopril renography and Doppler ultrasound of renal arteries receiving patients from the Capital Region of Denmark and the Region of Sealand. Diagnostic ultrasound is also used together with thyroid scintigraphy in patients with thyroid diseases. In patients with stroke, we perform ultrasound examination of the arteries supplying the brain, diagnosing eventual plaques in and stenosis of the vessels.

Using the tilt test, we examine patients with episodes of syncope or unexplained dizziness. Other physiological examinations offered are testing of lung function, distal blood pressure measurements on the extremities evaluating patients with claudicatio or ulcers, as well as 24-hour measurement of systemic blood pressure for diagnosis and evaluation of hypertension in adults and children.

In 2020, we have focused on reorganizing several examination rooms, to optimize patient experience during the examination and the ergonomics of the staff.





Consultant Philip Hasbak

Nuclear cardiology

Rigshospitalet was the first hospital in Scandinavia and one of the first in Europe to introduce Rubidium-PET. A cardiac Rubidium-PET test can provide information about blood flow to the heart muscle at rest and during stress, assess damage to the heart muscle from a prior heart attack, and provide information about the pumping function of the heart.

At Rigshospitalet there is a special need to provide cardiac PET every day, since a large proportion of our patients with ischemic heart disease need an acute or sub-acute work-up that requires quick decision making as to coronary revascularization strategy. Patients with unstable angina or non-STEMI should be revascularized with percutaneous coronary intervention (PCI)

within 3 days after admission or with coronary artery bypass graft surgery (CABG) within 5-7 days according to The Danish National Board of Health. Non-invasive assessment of myocardial function is an important domain of cardiac Rubidium-PET.

Traditionally, cardiac PET images have been visually interpreted, using uptake as a measure of function. This approach, however, takes only a fraction of the full PET information into account. The application of tracer kinetic modelling to dynamically measured data is able to extract objective measures of perfusion and/or metabolism, depending on the tracer. While such true cardiac quantification has been troublesome and time-consuming in the past, our new cardiac

tools now makes this state-of-the-art technology readily available. Further, we offer CT coronary angiography (CTCA) which is useful for planning many invasive cardiac procedures, particularly complex PCI procedures including chronic total occlusions (CTOs) and bifurcation stenting.

Furthermore, we offer Fluorodeoxyglucose (FDG) positron emission tomography (PET) for cardiac viability imaging and for cardiac sarcoid detection and Tc-pyrophosphate imaging to assess the presence of amyloid in the heart.

Research-wise we have a close, good and productive cooperation with various clinical departments.





Chief of Pediatric Nuclear Medicine, Consultant, PhD Lise Borgwardt

Pediatric nuclear medicine

In 2020 we performed more than 3,000 pediatric nuclear medicine investigations. It is a special focus area for our department to perform children’s investigations at the highest level of excellence, and at the same time make it a positive experience for both the child and the parents.

This year we have been continuing the cooperation of the organizational work on preparing our new Children’s Hospital Copenhagen. The project is very visionary and contains a large Diagnostic Unit where Pediatric Nuclear Medicine, among other diagnostic specialties, will be located. We plan to develop an integration of the diagnostic specialties in multidisciplinary team conferences 24/7, where the individual child is being discussed in a synergistic continuous diagnostic process with the purpose of accelerated personalized diagnostics and

treatment. The Children’s Hospital Copenhagen will be finished 2025 and this year we started building it.

We already have a children’s unit integrated in our department with a children-friendly PET/128SliceCT, SPECT/CT, EDTA Clearance room and a renography room. PET/MRI scans are performed in the PET Scanner Section. In each scanner-room in the children’s unit, high quality projectors are showing films at the ceiling to secure and entertain the child during the scan. In the waiting area the children have the opportunity to watch the animated decorations, use apps or watch films at the tablets giving, when entering the unit, or play in the toy corner.

Our multidisciplinary pediatric hematology- and oncology conferences are presented as a

web-based nuclear medical platform combined with videoconference including districts outside the capital. Our collaborators are very pleased with the possibilities and the advantages in the diagnostic evaluation of the children.

Research in pediatric nuclear medicine and PET is necessary, as we have an increasing number of medical doctors, PhD students and technicians involved in the field. The department undertakes many pediatric investigations, including participation in an array of prospective studies. These research protocols, using of PET and SPECT, are carried out in cooperation with clinical departments, particularly within oncology and infections with FDG PET, kidney parenchyma studies and studies of the function of the hepato-biliary system. In this area we conduct research protocols

in children with acute- and chronic liver diseases, incl. translational piglet studies and the two PhDs in the field was started this year. Furthermore, we have conducted protocols in pediatric non-oncological PET/MRI and our data from the Pediatric PET/MRI protocol for children with CNS tumors are being analyzed. We started up AI-projects in pediatric oncological diseases.

In 2020 we continued participating in randomized clinical trials for experimental immunotherapy for children with cancer as a part of the Nordic Center for these treatments. We are part of the EpSSG in the Radiology Committee, participating in conducting the new European protocol. Also targeted radionuclide therapy for cancer in children is currently an area of intense interest.





Consultant Johan Löfgren

RIS/PACS

As the last hospital in the Capital Region, Rigshospitalet in the beginning of 2018 implemented the new AGFA RIS/PACS system. A huge project initially started in 2009 where the radiology, clinical physiology and nuclear medicine departments in the region, after a joint requirement analysis, agreed on shifting to a common RIS/PACS system.

Ever since the system was installed, we've had huge problems with performance and stability, including client crashes and speech recognition. Few, but alarming reports of patient mix-up, have also been registered. The extra expenditure for our budget and the negative influence on our daily workflow have been major.

The regional IT department in collaboration with the RIS/PACS vendor has used large resources to try to fix the problems without any major success. Two major updates in 2020 were implemented with some initial problems but no noticeable improvement has been reported from users.

Thanks to our Head of Department, Professor Liselotte Højgaard, and 'Sundhedsfagligt Råd' (the Speciality Counsel) for both radiology and clinical physiology and nuclear medicine in the Capital Region, there has finally been taken a political decision to start the process to buy a new RIS/PACS system. All imaging departments in the region understand that it means a lot

of hard work but it's the only way to a future professional RIS/PACS system and patient safe operation.

We all hope for a brighter future where IT is a tool we can trust and use as help and support in our everyday work and help us take clinical physiology and nuclear medicine to the next level with research, artificial intelligence, big data, advanced visualization and personalized medicine.





Chief Physicist Thomas Levin Klausen

The Physicist and Technology Group

The Physicist and Technology Group (physicists, engineers and computer scientists) is involved in many aspects of the work in the department. Our primary responsibility is to enhance, daily and on location, radiation safety and patient dosimetry. We are also responsible for optimization and maintenance of all our scanners (see Equipment), handling and storing of patient data and to conduct and facilitate clinical research in the department.

Artificial intelligence (AI) is a quickly evolving field and is already of great importance for the clinical setup, patient diagnosis and treatment. At our department we have formed a program for Clinically Applied Artificial Intelligence (CAAI) with the sole purpose of bringing AI into clinical routine. The group is led by Computer Scientists Claes Nøhr Ladefoged and Flemming Littrup

Andersen, and further comprises 8 pre-graduate students, 6 PhD students, 2 postdocs and with links to various departments at Rigshospitalet, primarily Cluster for Molecular Imaging, Department of Radiology, Department of Oncology and Department of Pediatrics.

CAAI currently runs several projects spanning from bachelor to PhD level with a strong focus on pre-graduate supervision of computer scientist and engineer students. The primary research areas, defined in close dialogue with the clinicians, have been directed towards data domain translation i.e. converting MRI to synthetic CT images, lesion segmentation and noise reduction of image data.

Studies are ongoing to show feasibility for using synthetic-CT-derived dose plans for radiotherapy

in head and neck cancer and cervical cancer (supported by European Union’s Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement) with application to the PET/MRI as a one-stop shop for dose planning.

In the area of image segmentation, we have currently implemented automatic segmentation of PE2I brain images that visualizes availability of the dopamine transporter in the striatum. Another project has focused on multiple sclerosis (MS) using MRI Flair images to implement white matter lesion segmentation.

Noise reduction, which in medical imaging translates to lower radioactivity dose or shorter scanning time both to great benefit for the patients, received a 2.5 million grant from

Danske Regioner, and several projects have been started within this area covering a number of organs. An example of reduced scan time for patients with Hodgkin’s lymphoma is showed in figure 1.

We are also continually developing our MRI capabilities regarding both PET/MRI and stand-alone MRI functional scans. This year we have had three bachelor students, two master students and one PhD student combining AI with quantitative MRI imaging to develop new clinical tools to evaluate the physiology of abdominal organs and muscle tissue. This includes the ability to measure tissue perfusion and oxygenation in organs such as the kidneys and the liver as well as in muscle tissue.

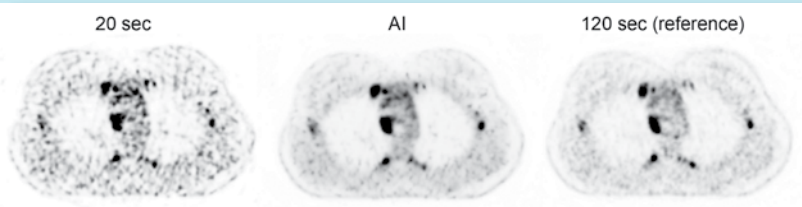
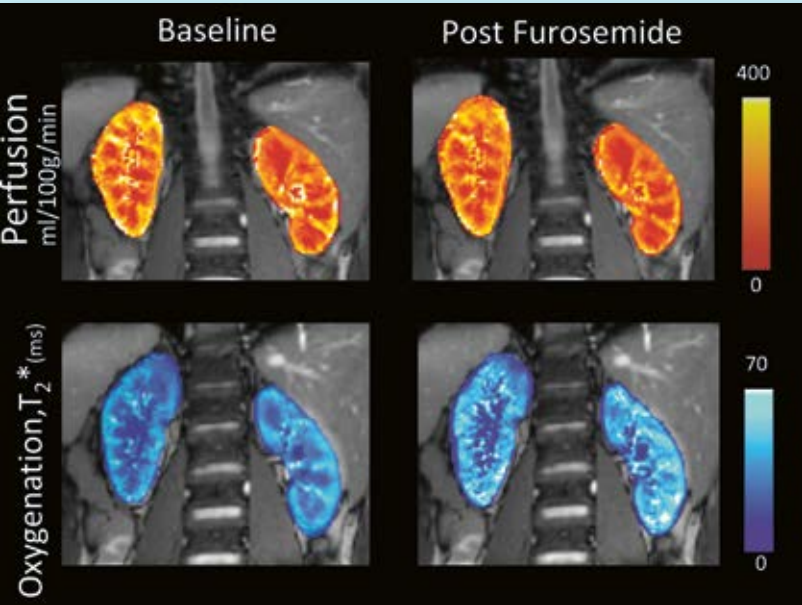
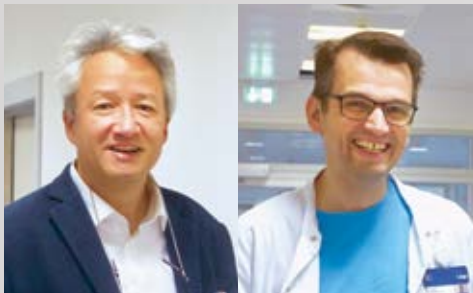


Figure 1. FDG-PET Imaging of patient with Hodgkin’s lymphoma in single breath hold (6 x 20 sec). Note that the AI image based on the 20 sec. scan is “identical” to the 120 sec scan

Figure 2. Kidney T2* and perfusion maps before and after the administration of a diuretic. The increases of T2* in the medulla without significant changes in perfusion indicates a decrease in metabolism after the administration of furosemide. This is an example of how differing physiological information measured via MRI or PET/MRI can provide more complete information describing the underlying physiological process.





Professor, Consultant, dr.med. Ian Law and Consultant Otto Mølby Henriksen

Neuro PET

In the Neuro PET group, we continuously strive to improve the use and availability of PET and hybrid imaging in routine clinical brain imaging, and to further explore hybrid imaging of brain physiology in both the diseased and healthy brain. Collaborating with international and clinical research partners, a number of clinical and basic science projects explore the use of the most recent development in radiopharmaceuticals and MRI.

The glucose analog 2-[¹⁸F]Fluoro-2-deoxy-D-glucose (2-[¹⁸F]FDG) showing the functional integrity of the brain remains the backbone of clinical imaging of dementia and epilepsy. In the workout in neurodegeneration we further provide imaging with [¹¹C]-PIB for evaluation of cerebral amyloid in Alzheimer’s disease, and [¹⁸F]FE-PE2I for assessment of Parkinsonism. We are increasingly serving regional and extra regional memory

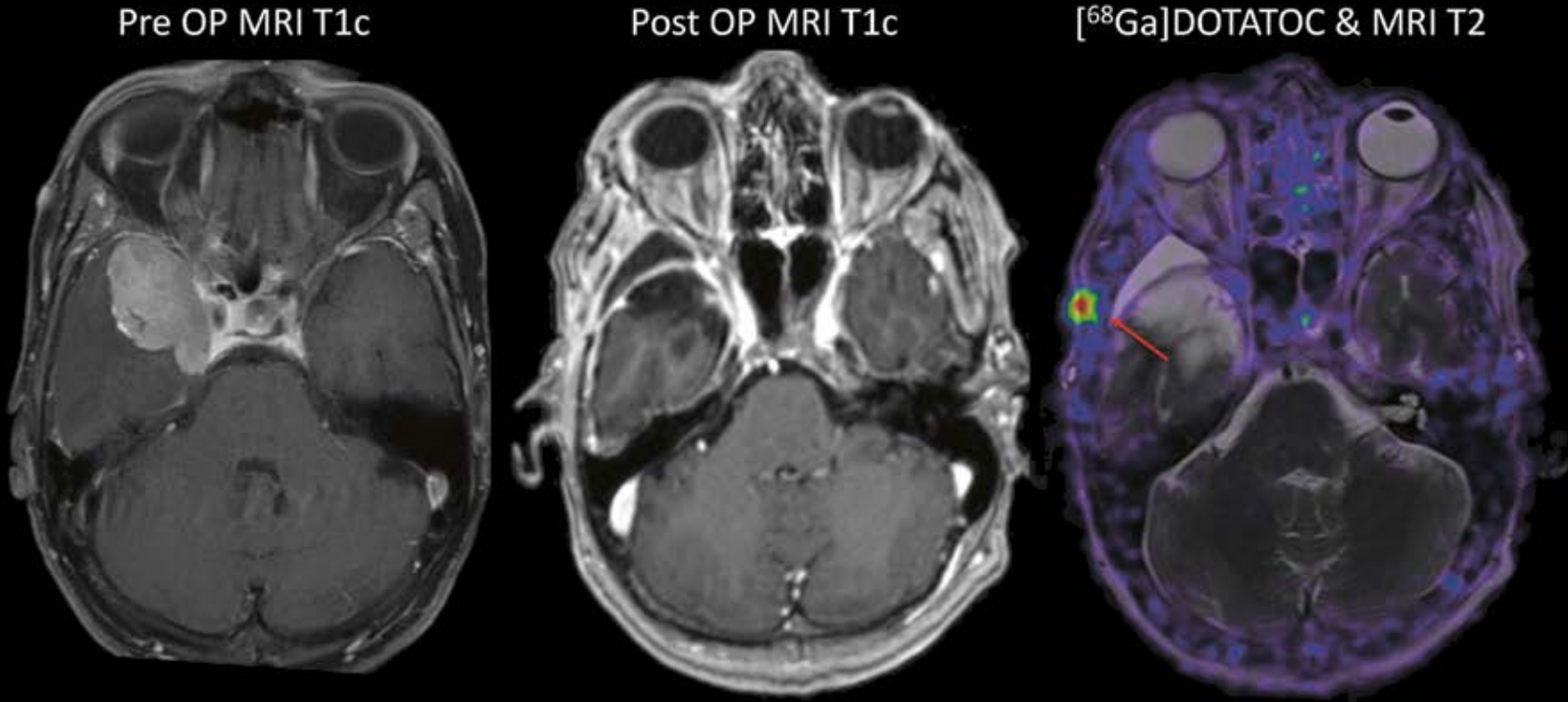
and movement disorder clinics with imaging in this field. We use [¹⁵O]H₂O for quantification of cerebral blood flow reserve in patients with carotid occlusions and chronic ischemia.

For brain tumors we supplement MRI with PET images using the amino acid analogue [¹⁸F]Flouro-Ethyl-Tyrosine ([¹⁸F]FET) for gliomas, and the somatostatin II receptor ligand [⁶⁸Ga]DOTA-TOC for meningiomas. The latter has expanded particularly in the identification of post-operative tumor remnants, not identifiable on MRI (Figure 1)

Our Siemens hybrid PET/MRI scanners allow a comprehensive structural and functional evaluation of brain pathologies within a single imaging session, and is not only a powerful research tool, but now also fully implemented in routine clinical

investigations of patients with dementia and brain tumors and in increasing use. This also allows us to evaluate the potential of various novel MRI techniques as supplements or alternatives to PET in patients referred for routine PET/MRI.

With the increasing demand of Neuro PET examinations and increasing analytical complexity of in particular PET/MRI studies, we have implemented post-processing pipelines providing fully automated reports with standardized analyses of PET and MRI data supporting clinical interpretation and reporting. Reports are used routinely for hippocampal volumetric measurements showing reduction in Alzheimer’s disease, for identifying signs of parkinsonism using [¹⁸F]FE-PE2I, and for identifying reduced cerebrovascular reserve using [¹⁵O]H₂O.



► **Figure 1. Example of use of the PET radiotracer [⁶⁸Ga]DOTATOC for detection of unrecognized meningioma remnants on MRI.** A patient with an atypical WHO grade II meningioma in the right temporal lobe before (left) and after resection (center) with no tumor remnant on MRI is referred for [⁶⁸Ga]DOTATOC PET radiotherapy planning. PET finds a solitary nodular focus (red arrow) in the subcutaneous tissue later confirmed to be meningioma tissue on extirpation (right).



Professor, Consultant Henrik BW Larsson

MRI imaging of renal perfusion and oxygenation

Renal cortical and medullary perfusion are closely regulated by neural, endocrine and paracrine factors. Inappropriately low perfusion with localized hypoxia is believed to be the initiating factor in major population diseases such as chronic kidney disease and hypertension. Renal parenchymal perfusion and oxygenation is not easy to measure in humans, but Functional Magnetic Resonance Imaging (fMRI) may provide insight into these important parameters. In collaboration with Sir Peter Mansfield Unit, Nottingham, we carried out two sets of experiments to verify whether fMRI could detect changes in medullary perfusion and oxygenation. We choose handgrip exercise, which we expected to reduce cortical perfusion via increased renal sympatic nerve activity, and furosemide, a loop diuretic, known to reduce oxygen consumption in the renal medulla by uncoupling the energy dependent sodium reabsorption.

Handgrip exercise elicited a marked decrease in total renal blood flow, as measured with phase-encoded velocity fMRI, and a decrease tissue perfusion in both cortex and medulla, measured with arterial spin labelling fMRI, using magnetic inverted water protons as a tracer of local perfusion (Figure 1). By using deoxy-hemoglobin T2* sensitivity fMRI, we could further show a reduced oxygenation in the cortex, while oxygenetion unexpectedly increased in the medulla. We ascribed this to a reduction of filtered sodium and hence reduced reabsorptive workload (1).

Furosemide increased medullary oxygenation as anticipated (Figure 2), but caused no change of total renal flow, cortical or medullary perfusion.

These results confirm that we are in a unique position to launch studies of major population

diseases such as hypertension and chronic kidney disease. Besides uncovering details about the pathophysiology, the aim is also to monitor the effects of medical interventions. We have initiated a collaboration with the research team at Steno Diabetic Center, headed by professor Peter Rossing, studying the effect of inhibition of sodium-glucose transport protein 2 with Dapagliflozin, an SGLT2 inhibitor, in type 1 diabetes with nephropathy. Preliminary results suggest that the beneficial effects of SGLT2 inhibitors may partly be ascribed to effects on renal cortical and medullary perfusion and oxygenation. Further studies of various pharmacological substances including the gut hormone GLP-1 are in progress. It is our belief that these studies will lead to new understanding of the pathophysiology of kidney related diseases.

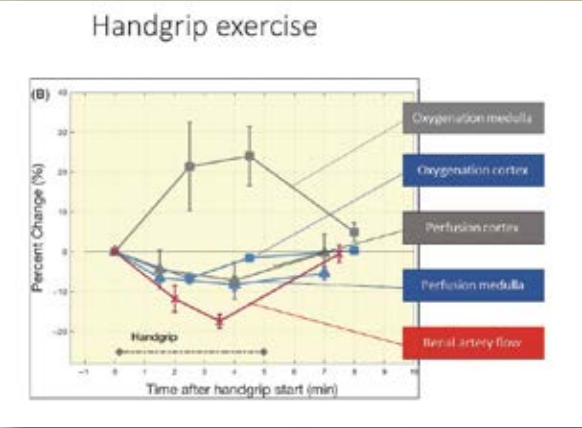


Figure 1. Changes of renal blood flow, cortical perfusion and oxygenation during 5 min. sessions of hand grip exercise. Renal blood flow is reduced by 20%. Cortical and medullary perfusion and cortical oxygenation decreases, while medullary oxygenation unexpectedly increases.

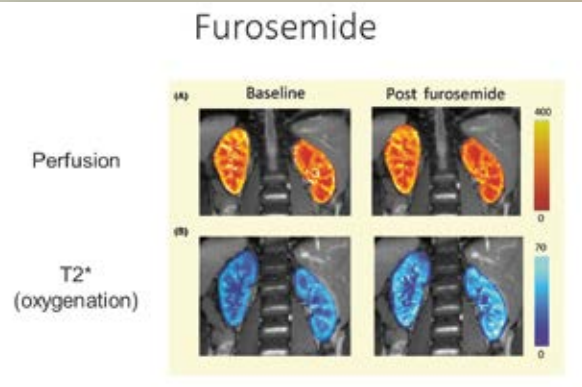


Figure 2. Cortical and medullary perfusion and oxygenation before and after injection of furosemide. Basal perfusion and oxygenation are low in the medulla. After furosemide, medullary oxygenation increases (bottom right: medullary areas turn light blue) while perfusion unchanged.





Consultant Johan Löfgren and Physicist Thomas Lund Andersen

PET/MRI

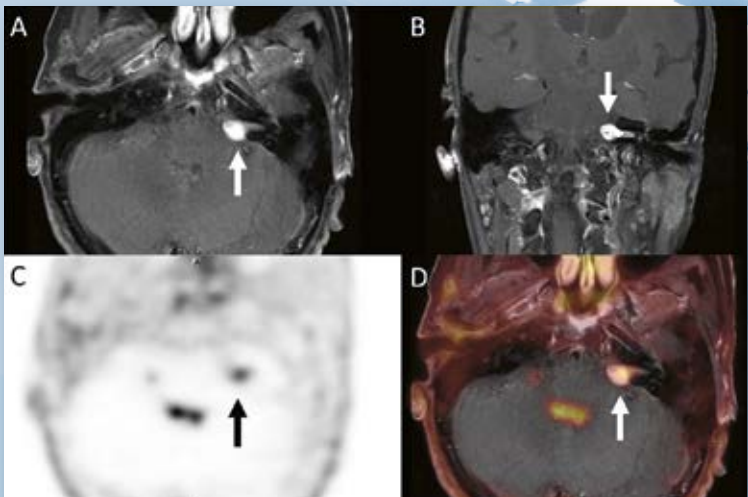
In the end of 2020, in the midst of the Corona pandemic, our second integrated PET/MRI system, a state-of-the-art Siemens Biograph mMRI, was successfully installed doubling the current capacity and further underlining the Department of Clinical Physiology, Nuclear Medicine & PET at Rigshospitalet as one the world leading sites of PET/MRI with two concurrent PET/MRI installations.

PET/MRI offers a unique simultaneous combination of molecular imaging with anatomic and functional MRI. These capabilities are being exploited in clinical, translational and basic research, as well as for clinical examinations. The types of PET/MRI examinations performed in the department range from clinical dementia exams is including static ¹⁸F-FDG PET and anatomic MRI with a duration of 20 minutes to dynamic PET acquisitions with kinetic modeling and physiologic

MRI measurements which may last 1-2 hours. In 2020 the number of examinations performed was approximately 880, out of which approximately 80% were clinical.

Clinical PET/MRI is undertaken primarily of patients with dementia, primarily Alzheimer’s disease, patients with brain tumors examined with ¹⁸F-FET PET and pediatric patients. Here, the simultaneous PET and MRI acquisition reduces the overall scan time and provides all indicated imaging within one session. Such a ‘one-stop-shop’ examination provides a valuable logistic advantage for patients and relatives as well as for the diagnostic reading and minimizes PET/MRI misalignment. Since 2019 we have been using an Artificial Intelligence-based PET attenuation correction developed in the department in clinical routine for ¹⁸F-FDG PET brain examinations.

► **Figure 1.** Images from a project studying ⁶⁸Ga-NODAGA-E[c(RGDyK)]₂ uptake in sporadic Vestibular Schwannoma to predict the growth potential. A) Transverse contrast enhanced T1-weighted fat-suppressed Turbo spin echo MRI showing a left-sided vestibular schwannoma (arrow). B) Coronal contrast enhanced T1-weighted fat-suppressed Turbo spin echo MRI. C) Transverse ⁶⁸Ga-NODAGA-E[c(RGDyK)]₂-PET. D) PET/MRI fused image [H C Reeberg Sass et al.].



To further expand the clinical use of PET/MRI, a large number of ongoing clinical research studies explore the utilization of PET and MRI in a synergistic fashion to improve patient management. Due to the Corona pandemic we unfortunately have had to pause many of our research projects and focusing on mitigating the spread of COVID-19 by thorough hygiene procedures and reducing the pressure on the scanners and staff.

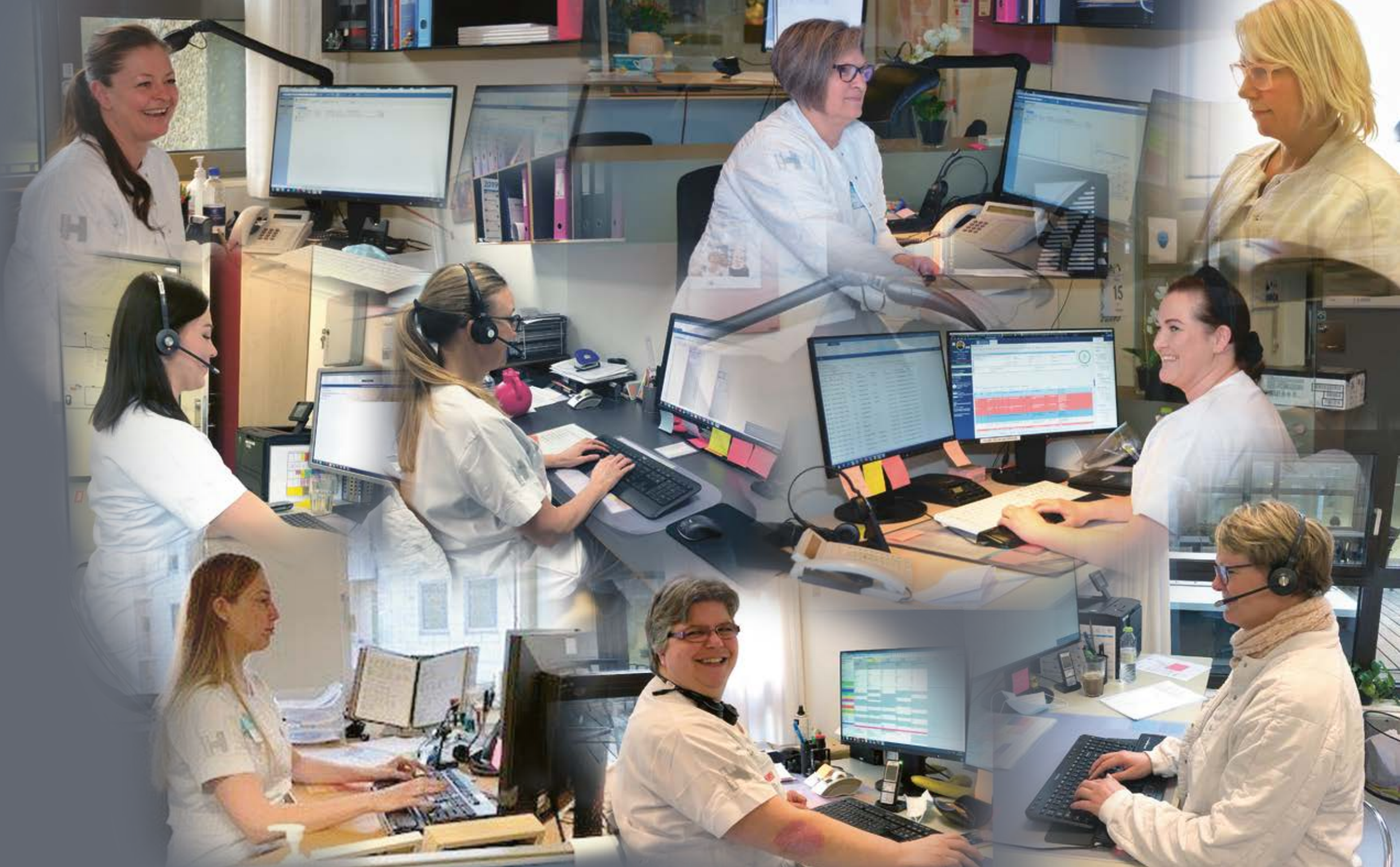
Indications investigated include lung cancer, head and neck cancer, gynecological cancer, neuro-oncology, dementia, pediatric oncology, and vascular inflammation. Finally, a number of clinical and pre-clinical research studies examine the utilization of combined PET and MRI to characterize the biology of disease (Figure 1).

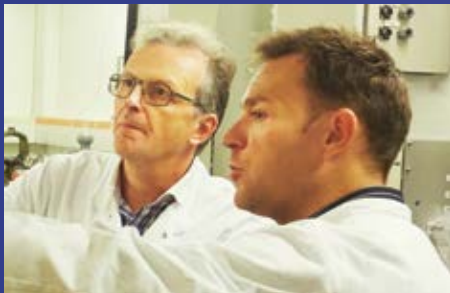
Medical secretaries

In the department we have highly competent medical secretaries important for referral of patients, organisation of the flow of patients through the department, writing the reports and sending them to the clinical departments. They do a dedicated effort. The medical secretaries master the complicated booking and secure that the waiting lists, the patient control examinations and research scans can be done in spite of a high workload and

a year with challenges due to the Corona pandemic. A dedicated thank you to Camilla Kuhre Vildrik Bendtzon, Frederikke Hurup Henriksen, Gudrun Semitoje, Helle Højen Jensen, Lone Kjærshøj Vindt, Marianne Stahlfest, Mette Fabiansen, Nina Bjørling and Tina Vikmann Nielsen.

We would like to say a warm thank you to everyone for the high quality and performance.





Cyclotron Chief Holger J. Jensen and Deputy Cyclotron Chief Jesper Jørgensen

The Cyclotron Section

During the last 10 years we have experienced a relative stable number of productions at our two cyclotrons of $1,250 \pm 90$ productions per year (Figure 1). In 2020 we had in total 1,325 successful productions (570 and 755 for our Scanditronix MC32 and Siemens RDS Eclipse cyclotrons respectively) giving an average success rate of $99,4 \pm 0,5\%$ since 2011. Despite of the COVID-19 situation we have not seen a drop in our productions. As in the previous years we managed to keep the average radiation dose to the employee in The Cyclotron- and Radiochemistry Section at a low level (Figure 2).

Figure 3 shows the development in the controlled release via our chimney of low radioactive waste gas produced in our Cyclotron- and Radiochemis-

try Section since 2011. Our permission from the authorities (SIS) allows us to release 10 TBq per year. In 2020 we ended at the very save side with a release of only 8,7% of this limit.

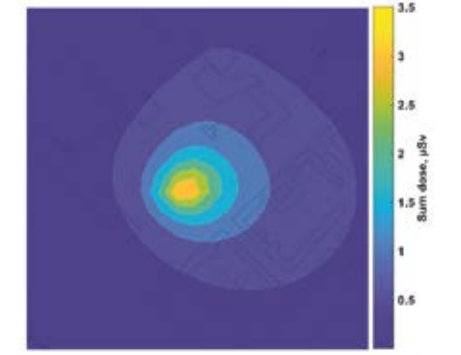
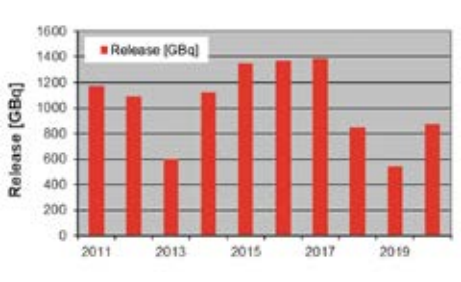
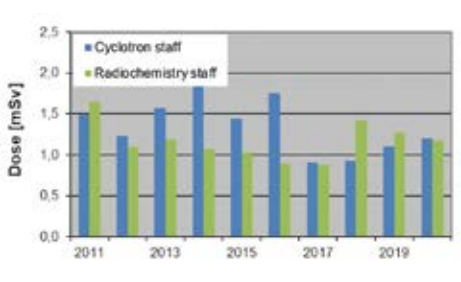
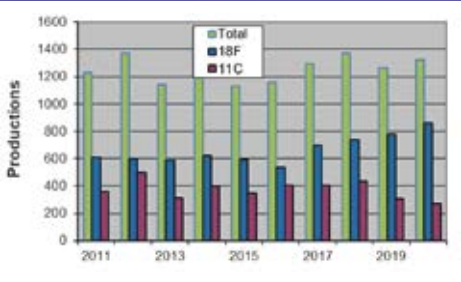
The authorities require the chimney designed, so no one in the general public can receive a radiation dose from our activities higher than $100 \mu\text{Sv}$ /year (or approximately 40 times lower than the average background dose in Denmark). Figure 4 shows the estimated total dose distribution from the release last year illustrated for a 400x400 meter grid in the neighbourhood of the chimney. The example is given for a height of 20 m, where we have the highest concentrations. The highest possible dose level is seen to be below $3,5 \mu\text{Sv}$ and far from the release limit.

► **Figure 1.** Development in ^{18}F , ^{11}C and the total number of productions since 2011.

► **Figure 2.** Average received dose per year for employees in The Cyclotron- and Radiochemistry Section since 2011.

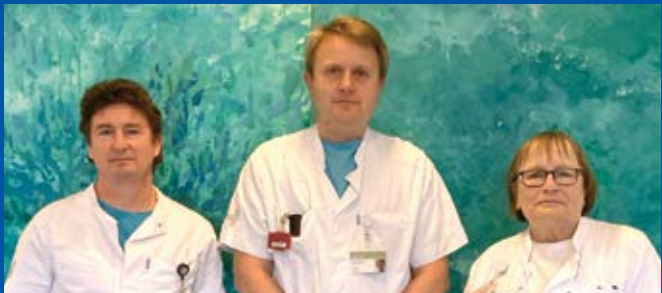
► **Figure 3.** Development in release of radioactive gas via our new chimney and filter system since 2011.

► **Figure 4.** Total dose distribution in the neighbourhood of the chimney for a total release of 0,87 TBq last year. Values are shown at a height of 20 m above ground level.



▼ **Figure 5.** The new AGA unit with 24 channels for high precision current measurements.





Chief Radiochemist Nic Gillings, Chief Production Manager Jacob Madsen and Staff Nuclear Medicine Technologist Anne Sørensen

The Radiochemistry Section

Production for clinical and research PET investigations in humans

Production of [^{18}F]FDG and krypton-81m generators along with [^{18}F]FET, [^{18}F]FE-PE2I, [^{11}C]PIB and ^{68}Ga -labelled ligands continued on a similar level compared to previous years. Following validation and approval from The Danish Medicines Agency, the production of [^{18}F]FE-PE2I was transferred to a new cassette based synthesis module in December 2020, resulting in significantly higher radiochemical yields and a more stable production with up to 20 GBq per batch. [^{18}F]FE-PE2I is produced 3 times a week for use at Rigshospitalet and Bispebjerg Hospital. We continued to produce the uPAR imaging agent, [^{68}Ga]Ga-NOTA-AE105 and our angiogenesis tracer, [^{68}Ga]Ga-NOD-AGA-E[c(RGDyK)]₂ in 2020. Both are being

evaluated in phase II clinical trials. There were 1,081 batches released for human use in 2020 comprising of 12 different radiopharmaceuticals (see figure).

There was a slight reduction in released batches compared to 2019 which was mainly due to the suspension of research projects during the Corona virus lockdown. When possible, production of neuroreceptor PET radioligands for human use for various research projects conducted by The Neurobiology Research Unit at Rigshospitalet, continued as in previous years. In particular, we received approval for human use of the synaptic density tracer, [^{11}C]UCB-J in spring 2020 and this is now being used in various research projects.

Radiopharmaceutical development

Oncology

A revised production method for [^{68}Ga]Ga-PSMA-11 for prostate cancer imaging was validated in 2020 and an application for human use has been submitted.

We are currently optimizing the production of meta- [^{18}F]fluorobenzyl guanidine (mFBG) for use in pediatric patients (neuroendocrine tumors). An application for human use will be submitted in 2021.

Miscellaneous

A new system for production of O-15 water developed by the Danish company MedTrace Pharma A/S was installed in 2019 and the production process



Radiopharmaceutical	Batches	Usage/Target
[¹⁸ F]FDG	336	Oncology/glucose metabolism
Krypton-81m generator	146	Lung ventilation
[¹¹ C]PIB	66	Alzheimer's Disease/β-amyloid plaques
[¹⁸ F]FE-PE2I	131	Neurology/dopamine transporter ligand
[¹⁸ F]FET	54	Oncology/amino acid transport
[⁶⁸ Ga]Ga-DOTATOC	184	Neuroendocrine tumours/somatostatin receptors
[⁶⁸ Ga]Ga-NODAGA-E[c(RGDyK)] ₂	93	Oncology/angiogenesis imaging
[⁶⁸ Ga]Ga-NOTA-AE105	12	Oncology/uPAR imaging
[⁶⁸ Ga]Ga-DOTATATE	13	Neuroendocrine tumours/somatostatin receptors (clinical trial)
[¹¹ C]UCB-J	23	Brain research/synaptic density marker
[¹¹ C]SB207145	15	Brain Research/5-HT ₄ receptors
[¹¹ C]Cimbi-36	8	Brain Research/5-HT _{2A} receptors
Total	1,081	

was validated in 2020. An application for human use has been submitted.

The production of [^{99m}Tc]technetium galactosyl human serum albumin ([^{99m}Tc]GSA), a radiopharmaceutical for the non-invasive assessment of liver function in a clinical setting is currently being developed and will be validated in 2021.

Quality Assurance

In 2020 we received funding to purchase a laboratory information management system (LIMS) which has been developed by LabLogic in the United Kingdom and is used in many PET centers throughout the world. This is an electronic system which will allow all production and quality control data to be automatically captured in a database, thus making the whole process more or less paperless. The system will be installed, validated and implemented in stages during the course of

2021 and, although this will be a major undertaking, it will ultimately result in a more efficient and standardized production system and eliminate manual transcription errors.

Laboratory technicians and technologists

Laboratory Technician Sonja Lærke has been appointed as QC-specialist and will be responsible for various tasks regarding validation and maintenance of the QC-systems and methods. Technologist Tina Wikke Hallund has been appointed radiation safety officer and deputy for Staff Technologist Anne Sørensen.

Education in radiopharmaceutical chemistry

The teaching program in radiopharmaceutical chemistry led by Associate Professor Matthias Herth, which was initiated in 2016 at the Faculty of Health and Medical Sciences, University of Copenhagen, continued in a similar format in 2020,

with several members of The Radiochemistry Section involved in lecturing and practical exercises. In addition, Matthias supervises a number of students focused on radiopharmaceutical research.

Radiopharmaceutical research and PhD projects

- ▶ Troels Elmer Jeppesen is employed as a post-doc and works on methods for rapid fluorine-18 labelling of peptides and labelling of optimised ligands for uPAR.
- ▶ Camilla Christensen was on maternity leave for the most of 2020 and will continue her PhD studies in 2021.
- ▶ Klas Bratteby submitted his PhD thesis in December 2020. This includes an investigation of ¹⁸F-fluorination methods for base sensitive labelling precursors which resulted in improved methods for the radiosynthesis of [¹⁸F]FE-PE2I and ¹⁸F-labelled tetrazines.





Senior Physicist Søren Holm



DANISH HEALTH
AUTHORITY
Radiation Protection



SIS inspection in December 2020

The EU Council Directive 2013/59/Euratom laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation – colloquially known as the BSS-directive – was approved by the Council on December 5, 2013. The implementation into Danish national law was prepared and overseen by the national competent authorities, the National Institute of Radiation Protection (in Danish known as SIS), a section under the Danish Health Authorities, within the deadline of February 6, 2018. During this process and after, our department has had the possibility and pleasure to give constructive criticism to drafts of the legislative texts. The final result of relevance for us consists of a law:

- ▶ “Act on Ionising Radiation and Radiation Protection” (“Strålebeskyttelsesloven” in Danish), and three associated executive orders:
- ▶ BEK669: Executive Order on Ionising Radiation and Radiation Protection
- ▶ BEK670: Executive Order on Use of Radioactive Substances
- ▶ BEK671: Executive Order on Use of Radiation Generators

Following the publication of these orders, SIS has increased the focus on safety assessments as a tool to improve radiation safety. The department already has a well established documen-

tation system (D4) where all procedures are described, but more details have been added. To further enhance our safety focus, all department teams (like brain team, heart team, oncology team, pediatric team etc) have performed assessments of their specific work. What could possibly go wrong, and what have we done to prevent that happening?

In accordance with the Council directive, SIS is also responsible for inspection and control to ensure compliance with national law and, thereby, with the directive.

As a nuclear medicine department, working with and handling ionizing radiation we were chosen for SIS inspection in December 2020. The original plan was an on-site visit scheduled for 3 full days, including inspection, interviews and survey of the department’s quality assurance system.

Due to COVID-19 the visit was, in close dialogue with SIS, converted into a virtual 2 days meeting. In advance, SIS had been granted electronic access to the full documentation in the D4 system. During the meeting, a total of 15 staff members were interviewed, including radiation protection officers, medical physics experts and

clinically responsible practitioners. The inspection and interviews were conducted in a professional and warm atmosphere leading to many good inputs and discussions. In the final written report from SIS there were only few minor and fair annotations easy to implement in quality assurance system and daily work. A physical inspection of the department’s premises will be performed once the COVID-19 situation has been normalized to allow visitors.





Professor, Consultant Jann Mortensen and Consultant Peter Oturai

Education

Our department contributes to the activities of the Faculty of Health Sciences at the University of Copenhagen for medical students, human biology students and medicine & technology students in collaboration with DTU in various subjects, e.g. nuclear medicine, clinical physiology and medical technology. Also, nuclear medicine technologist students and radiographer students receive parts of their education at our department.

Regarding postgraduate education, seven educational positions for young physicians training to become specialists in clinical physiology and nuclear medicine are held by the facilities in our department. Other roles in the specialist education of physicians are related to the dedicated courses in oncology, and cardiological-, pulmonary-,

endocrine pathophysiology- and molecular imaging as well as courses in methodology such as MRI, hybride imaging, and kinetics. Courses held and arranged by our professors, consultants and physcists. Furthermore, we contribute to the specialist education of physicians from other specialities such as urology, nephrology, radiology, oncology, haematology, pulmonology and thoracic surgery. A high number of PhD students are associated with the research activities in the department.

Colleagues and students from Denmark and abroad, have visited the department for educational and research purposes for periods ranging from weeks to months, and we deliver training programmes to staff from other nuclear medicine and radiological departments in Denmark and the Nordic countries.

The department’s educational activities have been accredited by the Accreditation of Nuclear Medicine Training Center’s Committee, the Section of Nuclear Medicine of the European Union of Medical Specialists (UEMS) and The Danish Health Authorities.

Consultant Peter Oturai is responsible for the postgraduate education of physicians in the department, and Professor Jann Mortensen, Professor Ian law and Professor Henrik Larsson are responsible for the undergraduate education of medical students. Professor Liselotte Højgaard is responsible for under- and postgraduate education for bioengineers.





Chief Physicist Thomas Levin Klausen

Equipment

Equipment	Product	Purchase year
Gamma cameras	Mie-Scinttron	2004
	DDD Solo	2020
	Mediso N-TH45-D	2008
	DDD SoloMobile	2012
	DDD NephroCam System	2016
SPECT-cameras	Mediso Nucline X-Ring-R/HR	2009
	Symbia Evon	2017
SPECT/CT cameras	Siemens SymbiaT2	2006
	GE Discovery 670	2010
	Siemens Symbia 16-slice CT	2011
	Siemens Symbia Intevo Bold 16 slice CT	2017
PET scanner	Siemens Symbia Intevo Bold 16 slice CT	2020
	HRRT Siemens/CTI	2007
PET/CT scanner	Siemens Biograph TrueV 64-slice CT	2009
	Siemens Vision (64)	2010
	Siemens Biograph mCT (64)	2011
	Siemens Vision (64)	2019
	Siemens Vision (64)	2019
	Siemens mCT-S (128)	2013
	Siemens mCT-S (64)	2016

Equipment	Product	Purchase year
PET/MR scanner	Siemens mMR	2011
	Siemens mMR	2020
Lung function	GE SPINlab MR Hyperpolarizer	2014
	Jaeger Masterscreen w/bodybox	2005
	Jæger Masterscreen w/bodybox	2019
	Jaeger PFT pro w/bodybox	2007/13
DXA scanner	GE Lunar Prodigy	2004
	GE Lunar Prodigy	2005
	GE Lunar Prodigy	2011
	GE Lunar iDXA	2014
Whole body counter	WBC w/Nal counting chamber	1977
	WBC w/plast counting chamber	1978
Cyclotrons	Scanditronix 32 MeV	1991
	RDS Eclipse cyclotron, CTI	2005
At Cluster for Molecular Imaging, Panum	Provivo/ ADAC mobile gamma camera	1990
	Siemens Micro-PET Focus 120	2006
	Phosphor Imager Perkin Elmer cyclone	2007
	Bruker preclinical MRI PharmaScan 7T	2013
	Siemens preclinical PET/CT Inveon	2013
	PX Inc. preclinical RT X-RAD 320	2013
	Mediso nanoScan SPECT/CT	2015



*The most grateful thank you
to the John and Birthe Meyer
Foundation*

New PET/MRI scanner

In 2019 we received a very generous donation from The John and Birthe Meyer Foundation of a state-of-the-art full integrated PET/MRI system leading to a doubling of our PET/MRI capacity and strengthening The Department of Clinical Physiology, Nuclear Medicine & PET's position as one of the world leading sites of PET/MRI.

Despite strict regulations due to COVID-19 throughout 2020, the new scanner has been installed and it is used for patient studies. We are still working on the surrounding facilities supporting the function of the scanner, and we look forward to presenting the scanner fall 2021, when the mist of COVID-19 has hopefully lifted.

1991 Scanditronix 32 MeV,

1991 GE4096 PET Scanner

1993 NMR Spectrometer

1993 PET Advance Scanner

2001 PET/CT Scanner

2005 PET/CT Scanner

2005 Cyclotron 2

2007 HRRT Scanner

2009 Radiochemistry Synthesizer

2011 PET/MR Scanner

2017 PET/CT Scanner

2019 PET/MRI Scanner

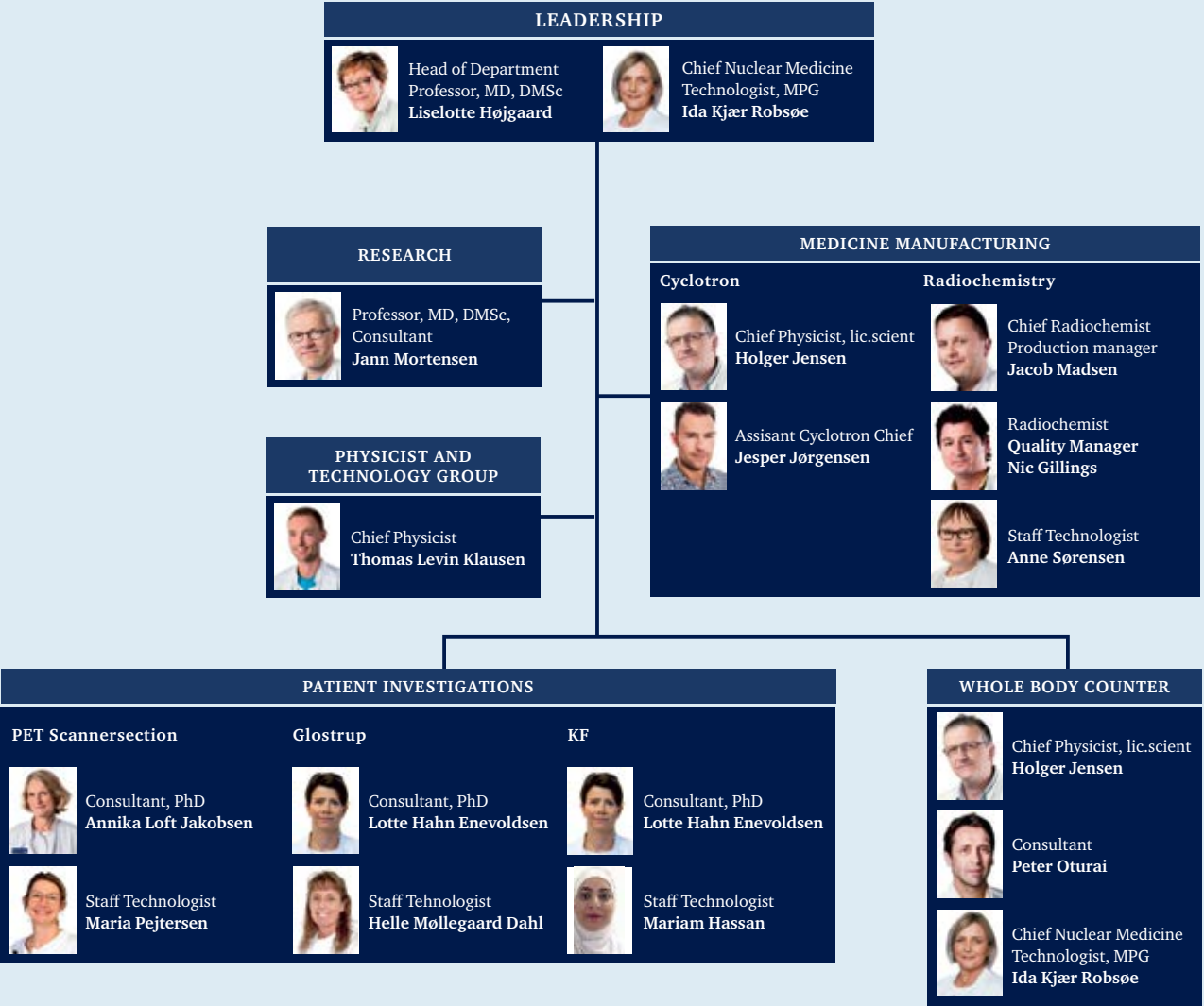
Organisation and staff

Abrahamsen, Nynne Hejdemann, Technologist.
Afzai, Remshah, Technologist.
Agner, Elissaveta Castella, Radiographer.
Ahangari, Sahar, Research Fellow.
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Al-Atabi, Susan, Technologist.
Albers, Mia C. Hjorth, Teaching Technologist.
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Department of Clinical Physiology, Nuclear Medicine & PET



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Nielsen, Kasper With, Animal Technologist.
Nielsen, Marcus Kristian, Student.
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Okkels, Charlotte Holmgaard, Technologist.
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Ripa, Rasmus Sejersten, MD, DMSc, Consultant.
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Rønn, Vibeke, Chief Secretary, PA.
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Stillits, Andreas, Student.

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Svejstrup, Waldemar, Student.
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Tolstrup, Britt Maria Jæger, Radiographer.
Tornvig, Cecilie Maja, Technologist.
Uhrenholdt, Lukas, Student.
Ullersted, Eva, Service Assistant.
Urhammer, Gitte Marie, Technologist.
Uzer, Sefika, Technologist.
Vandel, Julius Scheel, Student.
Varpe, Elden Varpe, Technologist.
Veseli, Antigona, Technologist.
Vestergaard, Mark Bitsch, PhD Student.
Vijayakumar, Gidega, Student.
Viknes, Vitusha, Student.
Vindt, Lone Kjærshøj, Medical Secretary.
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Wieslander, Bente Krogsgaard, MD, Consultant.
Wiinberg, Martin, Student.
Wiinholt, Mette Neiegaard, Msc. Human Biology, Technologist.
Willumsen, Ida Vigdís, Student.
Wittekind, Anne-Mette Nielsen, QA Pharmacist.
Zare, Soheil Naser, Radiographer.

Studies

Peripheral vessels	
Systolic blood pressure, fingers	4
Systolic blood pressure, ancle and toes	292
Systolic blood pressure, ancle-brachial index after treadmill	105
Doppler ultrasound of the carotides	340
Doppler ultrasound of the carotides	3,854
Doppler ultrasound of abdominal vessels	
24 hours blood pressure measurement	294
Total	4,889

Blood and lymph system	
Sentinel node scintigr. tumor drainage, ^{99m} Tc-Nanocolloid	244
Sentinel node scintigr. tumor drainage, head/neck SPECT, ^{99m} Tc-Nanocolloid	167
Spleen scintigraphy, ^{99m} Tc-erythrocyte, heated	10
Erythrocyt volume, ^{99m} Tc-erythrocytter	52
Plasma volume, ¹²⁵ I-HSA	52
Peritumoral injection of ^{99m} Tc-Nanocolloid for sentinel node	535
Total	1,060

CNS and peripheral nervous system	
CT scanning of cerebrum	439
CT scanning of cerebrum	2
Regional cerebral blood flow, ^{99m} Tc- HMPAO, pharm.prov.	13
Cerebral metabolism, ¹⁸ F-FDG	7
Cerebral metabolism, ¹⁸ F-FDG	1,637
Cerebral receptor, ¹⁸ F-PE2I	343
Cisternography ^{99m} Tc-DTPA	1
Cerebral neuroreceptor, ¹⁸ F-FET	303
Cerebral receptor, ¹¹ C-PIB	111
Cerebral receptor, ⁶⁸ Ga-Dotatoc	71
Cerebral blood flow, ^{99m} Tc- HMPAO	12
Regional cerebral receptor, ¹⁸ F-Florbetapir	6
MR scanning of cerebrum with and without contrast	2,001
MR scanning of hippocampus (MR-HCV)	401
Total	5,347

Other diagnostic procedures	
Image fusion (PET, SPECT, MRI, CT or planar)	14,250
Scintigraphy after ¹⁷⁷ Lu- Dotatate therapy	158
Whole body, contamination measurement	101
White blood cell scintigraphy, ^{99m} Tc-white blood cell	9
White blood cell scintigraphy, ^{99m} Tc-white blood cell, SPECT	4
Neuroendokrine receptors, WB, ¹⁸ F-DOPA	1
PET tumor scanning, ⁶⁸ Ga-Dotatoc	565
PET tumor scanning, ⁶⁴ Cu-Dotatate	186
PET scanning ¹⁸ F-NaF	3
PET scanning, ¹⁸ F-FDG	6,787
PET tumor scanning, ⁶⁸ Ga-PSMA	26
PET tumor scanning, ¹⁸ F- PSMA	7
CT head/neck SPECT/CT	276
CT lower and upper extremities SPECT/CT	25
CT abdomen SPECT/CT	316
CT pelvis SPECT/CT	43
CT pelvis SPECT/CT	116
CT wb PET/CT	1,924
CT wb PET/CT with contrast	6,504
CT wb SPET/CT	110
CT wb SPET/CT	14
CT wb SPET/CT	200
CT thorax SPECT/CT	632
CT thorax SPECT/CT	1
CT thorax PET/CT breathhold	38
CT thorax SPECT/CT	98
MR wb PET/MR	97
MR wb PET/MR	12
PET thorax PET/CT breathhold	37
Other investigations, incl. ¹¹ C-different tracers (NRU)	247
Supplementary/repeated imaging	2,552
Second opinions external	1,575
Extra tumor delineation	324
Total	37,238

Endocrine organs	
Adrenal marrow scintigraphy, ¹²³ I-MIBG	48
Tumorscintigraphy, ¹²³ I-Iodide	1
Iodine uptake test, ¹³¹ I-Iodide	25
Iodine uptake test, ¹³¹ I-Iodide	12
Parathyroid scintigraphy, ^{99m} Tc-Stamisis, SPECT	67
Thyroid scintigraphy, ¹²³ I-Iodide	67
Thyroid scintigraphy, ^{99m} Tc-Per technetat	1,048
Thyroid ultrasound	1,117
Thyroid, fine needle aspiration biopsy	135
Parathyroid fine needle aspiration biopsy	2
Parathyroid ultrasound	1
Total	2,523

Gastric intestinal tract, liver, biliary tract and pancreas	
Bleeding scintigraphy (abdomen) ^{99m} Tc-erytrocytter	3
Biliary tract scintigraphy, ^{99m} Tc-Mebrofenin	60
Meckels diverticle scintigraphy, ^{99m} Tc-Per technetat	1
Salivary gland scintigraphy ^{99m} Tc-Per technetat	16
Doppler ultrasound of splanchnic blood flow	425
Doppler ultrasound of splanchnic blood flow	2
Total	507

Heart and cardiovascular system	
Analysis of heart rate variability	275
Tilt table test	278
Isotope cardiography, LVEF, ^{99m} Tc-HSA	1,424
Myocardial calcium score	834
PET myocardial perfusion, ⁸² Rb, rest	1,184
PET myocardial metabolism, ¹⁸ F-FDG	173
PET myocardial perfusion, ⁸² Rb, pharmacological stress	1,092
Myocardial perf. scintigr. gated, ^{99m} Tc-MIBI, stress	2
Myocardial perf. scintigr. gated, ^{99m} Tc-MIBI, rest	1
Myocardial scintigraphy, ^{99m} Tc-PYP	78
Myocardial ¹²³ I- MIBG, sympaticus activity	2
Total	5,343

Bone and joint	
DXA, body composition	530
Bone scintigraphy, ^{99m} Tc-HDP, whole body, static	1,144
Bone scintigraphy, ^{99m} Tc-HDP, SPECT	733
Bone scintigraphy, ^{99m} Tc-HDP, 2 phased	56
Bone scintigraphy, ^{99m} Tc-HDP, regional, static	36
Osteodens. dual X-ray absorptiometri (DXA), columna lumb.	3,753
Osteodensitometri, dual X-ray absorptiometri collum fem.	3,753
Osteodens. dual X-ray absorptiometri (DXA), columna lumb.	77
Osteodens. dual X-ray absorptiometri (DXA), lat.spine	240
Osteodensitometri, dual X-ray absorptiometri collum fem.	6
Osteodensitometri, dual X-ray absorptiometri collum fem.	3
Osteodensitometri, dual X-ray absorptiometri collum fem.	9
Osteodens. dual X-ray absorptiometri (DXA), radius	142
Osteodens. dual X-ray absorptiometri (DXA), radius	3
Osteodens. dual X-ray absorptiometri (DXA), radius	5
MR scanning columna cervicalis	120
MR scanning columna thoracalis	80
MR scanning columna lumbalis	4
Total	10,694

Respiratory organs	
Lung perfusion scintigraphy, SPECT, ^{99m} Tc-MAA	508
Lung ventilation scintigraphy, SPECT, ^{81m} Kr-gas	458
Lung function test, spirometry w/reversibility	141
Lung function test, spirometry w/reversibility	4
Lung function test, diffusion capacity (CO)	3,734
Lung function test, diffusion capacity (NO/CO)	70
Lung function test, whole body plethysmography	2,364
Lung function test, whole body plethysmography	1
Lung function test, whole body plethysmography w/reversibility	318
Lung function test, spirometry	3
Lung function test, spirometry	946
Lung function test, spirometry w/reversibility	4
Lung ventilation scintigraphy, regional, ^{81m} Kr-gas	255
Lung ventilation scintigraphy, ^{81m} Kr-gas	6
Lung ventilation scintigraphy, SPECT ^{99m} Tc-Technegas	48
Max. insp. abd exspir. muscle pressure	92
Mucociliary clearance, ^{99m} Tc-Venticolloid	6
Total	8,958

Studies

Kidneys and urinary tract	
Glomerular filtration, ⁵¹ Cr-EDTA	3
Glomerular filtration, ^{99m} Tc-DTPA	2,341
Renal scintigraphy, ^{99m} Tc-DMSA	21
Renography, ^{99m} Tc-MAG 3	2,338
Renography, ^{99m} Tc-MAG 3, ACE-inhibitor	136
Renography, ^{99m} Tc-MAG, diuresis	16
Renography, ^{99m} Tc-MAG 3, dual head	6
Doppler ultrasound of renal blood flow	400
Ultrasound kidneys	399
Ultrasound of retroperitoneum	19
MR-scaning of kidneys	162
Total	5,841

Radiotherapy	
Treatment with ¹³¹ I, benign thyroid	64
Isotope treatment with ¹⁷⁷ Lu-Dotatate	139
Isotope treatment with ²²³ Ra-Dichlorid	114
Isotope treatment with ¹⁷⁷ Lu-PSMA	11
Total	328

In vitro analyses	
Affinity studies	408
Flow cytometry analyses	52,438
Gene expression analyses	7,616
Immunohistochemistry	2,380
Phage display	39
Plasma and protein analyses	22,858
Total	85,739

Animal studies

Pigs	
⁶⁸ Ga-RGD	4
MR	4

Rats	
¹⁸ F-FDG	9
⁸² Rubidium	10
^{99m} Tc SPECT	9

MR	210
CT images for fusion	28
Ultrasound	24

Mice	
¹⁸ F-FDG	97
¹⁸ F-tetrazine	32
¹⁸ F-tryptophan	4
¹⁹ F-FES	40
⁶⁴ Cu	30
⁶⁴ Cu-liposomes	48
⁶⁴ Cu-NOTA-IgG2b.F(ab)ʹ2	8
⁶⁸ Ga-NOTA-nanoparticles	20
⁶⁸ Ga-sdAb	15
⁶⁸ Ga-xx	120
⁸⁹ Zr-Herceptin	50
¹¹¹ In-Tetrazine	143
Bioluminescence (luciferin)	975
Fluorescence (BODIPY)	4
Fluorescence (Cy5.5)	345
Fluorescence (ICG-AE105)	105
Fluorescence (IRDye800-AE105)	56
Fluorescensce (PARPi-FL)	12
MR	2,860
CT images for fusion	607
Ultrasound	569
Photothermal therapy	72
Radiotherapy, externally	1,464
Radionuclide therapy (α and β emitters)	391

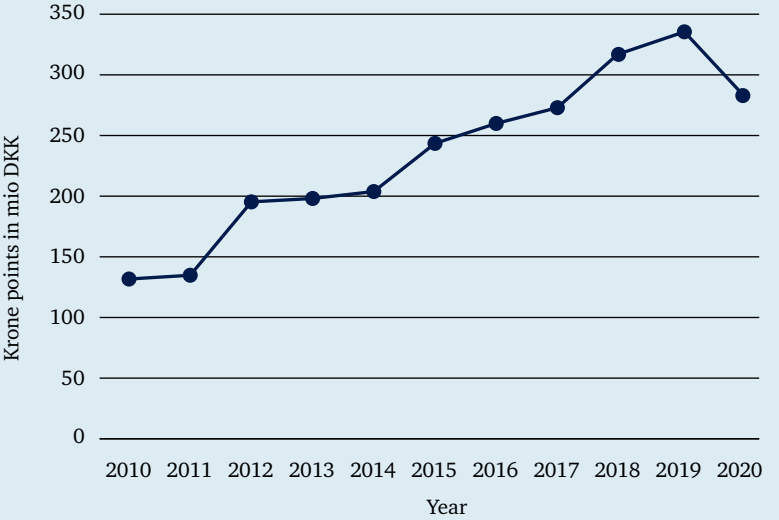
Rabbits	
¹⁸ F-FDG	35
¹⁸ F-NaF	22
⁶⁴ Cu-DOTATATE	17
⁸² Rubidium	9
CT images for fusion	66

Total	8,514
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Total number of studies176,981

Finance

Turnover



The increase in activities measured in krone point* rose from 131.7 mio DKK in 2010 to 287.3 mio DKK in 2020.

* Krone point: Price for each patient investigation multiplied with number of investigations, summarized for all patient studies performed during the year.

Balance 2020	(DKK mio)
Expenditure	96
Income	15

Publications

Theses

Doctoral thesis

Berg, Ronan MG. ”Cerebral Haemodynamic Function in Experimental and Clinical Sepsis” Doctoral thesis, Faculty of Health and Medical Sciences, University of Copenhagen. Defended Sept. 7, 2020

PhD theses

Zarnani, Kiyana. “Healthy Ageing, ”Beyond A Bigger Brain”, Faculty of Health, University of Copenhagen. Defended Jan. 28, 2020.

Puig, Oriol. ”Multimodal measurements of cerebral blood flow using a hybrid PET/MRI system”. Faculty of Health, University of Copenhagen. Defended Febr. 6, 2020.

Haddock, Bryan Thomas. “Acute physiological responses to muscle loading assessed with PET and MRI - a comparison of Free Flow versus Blood Flow Restricted Exercise”. Faculty of Health, University of Copenhagen. Defended April 27, 2020.

Gjerum, Le. “Optimizing ¹⁸F-FDG-PET in the diagnosis of dementia disorders”. Faculty of Health, University of Copenhagen. Defended Sept. 1, 2020.

Juhl K. “Development and validation of a uPAR targeted optical probe in preclinical cancer models”. Faculty of Health, University of Copenhagen. Defended Sept. 22, 2020.

Younis, Samaira. “MRI investigations of the brain stem in migraine patients”. Faculty of Health, University of Copenhagen. Defended Sept. 28, 2020.

Bashir, Asma: ”Estimation of proliferation in meningioma using ⁶⁸Ga-DOTATOC PET/MRI and ¹⁸F FLT PET/CT”. Faculty of Health, University of Copenhagen. Defended Oct. 8, 2020.

Sass, Hjalte Christian Reeberg. “Growth of Vestibular Schwannomas - molecular factors and improvement of treatment”. Faculty of Health, University of Copenhagen. Defended Nov. 19, 2020.

Patents

Kjaer A (with co-inventors). ⁶⁸Ga-and ⁶⁴Cu-NODAGA-E[c(RGDyK)]₂ for use as PET tracers in the imaging of angiogenesis in humans. US Patent App. 16/762,873. September 10, 2020.

Kjaer A (with co-inventors). ⁶⁸Ga-and ⁶⁴Cu-NODAGA-E[c(RGDyK)]₂ for use as PET tracers in the imaging of angiogenesis in humans. EP Patent App. EP-3706809. September 16, 2020.

Publications

Alcazar J, Kamper RS, Aagaard P, Haddock B, Prescott E, Ara I, Suetta C. Relation between leg extension power and 30-s sit-to-stand muscle power in older adults: validation and translation to functional performance. Sci Rep. 2020 Oct; 10(1):16337.

Alcazar J, Aagaard P, Haddock B, Kamper RS, Hansen SK, Prescott E, Alegre, LM, Frandsen U, Suetta C. Age- and Sex-Specific Changes in Lower-Limb Muscle Power Throughout the Lifespan. J Gerontol A Biol Sci Med Sci. 2020 Jun 18;75(7):1369–78.

Ambrosen KS, Skjerbæk MW, Foldager J, Axelsen MC, Bak N, Arvastson L, Christensen SR, Johansen LB, Raghava JM, Oranje B, Rostrup E, Nielsen MØ, Osler M, Fagerlund B, Pantelis

C, Kinon BJ, Glenthøj BY, Hansen LK, Ebdrup BH. A machine-learning framework for robust and reliable prediction of short- and long-term treatment response in initially antipsychotic-naïve schizophrenia patients based on multimodal neuropsychiatric data. Transl Psychiatry. 2020 Aug 10;10(1):276.

Andersen HG, Raghava JM, Svarer C, Wulff S, Johansen LB, Antonsen PK, Nielsen MØ, Rostrup E, Vernon AC, Jensen LT, Pinborg LH, Glenthøj BY, Ebdrup BH. Striatal Volume Increase After Six Weeks of Selective Dopamine D2/3 Receptor Blockade in First-Episode, Antipsychotic-Naïve Schizophrenia Patients. Front Neurosci. 2020 May 20;14:484.

Andersen KF, Someh NS, Loft A, Brittain JM. Primary Cardiac Intimal Sarcoma Visualized on 2-[18F]FDG PET/CT. Diagnostics (Basel). 2020 Sep18;10(9):718.

Asferg CL, Andersen UB, Linneberg A, Hedley PL, Christiansen M, Goetze JP, Jeppesen JL. Serum B-type natriuretic peptide does not increase with higher systolic blood pressure in obese men despite evidence of blood pressure-related increases in left ventricular mass and filling pressure. Peptides. 2020 Dec;134:170390.

Asmar A, Cramon PK, Asmar M, Simonsen L, Sorensen CM, Madsbad S, Moro C, Hartmann B, Rehfeld JF, Holst JJ, Hovind P, Jensen BL, Bülow J. Increased oral sodium chloride intake in humans amplifies selectively postprandial GLP-1 but not GIP, CCK, and gastrin in plasma. Physiol Rep. 2020 Aug;8(15):e14519.

Back TA, Jennbacken K, Hagberg Thulin M, Lindegren S, Jensen H, Olafsen T, Yazaki PJ, Palm S, Albertsson P, Damber JE, Wu AM, Welen K.

Targeted alpha therapy with astatine-211-labeled anti-PSCA A11 minibody shows antitumor efficacy in prostate cancer xenografts and bone microtumors. EJNMMI Res. 2020;10:10.

Baekdal J, Krogh J, Klose M, Holmager P, Langer SW, Oturai P, Kjaer A, Federspiel B, Hilsted L, Rehfeld JF, Knigge U, Andreassen M. Limited Diagnostic Utility of Chromogranin A Measurements in Workup of Neuroendocrine Tumors. Diagnostics (Basel). 2020;10(11):881.

Bailey DM, Rose GA, Berg RMG, Davies RG, Appadurai IR, Lewis MH, Williams IM. Authors’ response to Cardiorespiratory fitness in patients undergoing elective open surgery for abdominal aortic aneurysm: does it really fail to predict short-term postoperative mortality? Annals of the Royal College of Surgeons of England. 2020; 102(8):644-645.

Bailey DM, Rose GA, Berg RMG, Davies RG, Appadurai IR, Lewis MH, Williams IM. Cardiorespiratory fitness fails to predict short-term postoperative mortality in patients undergoing elective open surgery for abdominal aortic aneurysm. Annals of the Royal College of Surgeons of England. 2020;102(7):536-539.

Baltzersen OB, Meltzer HY, Frokjaer VG, Raghava JM, Baandrup L, Fagerlund B, Larsson HBW, Fibiger HC, Glenthøj BY, Knudsen GM, Ebdrup BH. Identification of a Serotonin 2A Receptor Subtype of Schizophrenia Spectrum Disorders With Pimavanserin: The Sub-Sero Proof-of-Concept Trial Protocol. Front Pharmacol. 2020 Apr 30;11:591.

Barloese MCJ, Beske RP, Petersen AS, Haddock B, Lund N, Jensen RH. Episodic and chronic cluster headache: differences in family history, traumatic head injury, and chronorisk. Headache. 2020;60(3):515-25.

Bashir A, Binderup T, Vestergaard MB, Broholm H, Marner L, Ziebell M, Fugleholm K, Kjær A, Law I. In vivo imaging of cell proliferation in meningioma using 3’-deoxy-3’-[18F]fluorothymidine PET/MRI. Eur J Nucl Med Mol Imaging. 2020;47:1496-1509.

Bashir A, Broholm H, Clasen-Linde E, Vestergaard MB, Law I. Pearls and Pitfalls in Interpretation of ⁶⁸Ga-DOTATOC PET Imaging. Clin Nucl Med. 2020;45:e279-e280.

Bashir A, Vestergaard MB, Binderup T, Broholm H, Marner L, Ziebell M, Fugleholm K, Mathiesen T, Kjær A, Law I. Pharmacokinetic analysis of [⁶⁸Ga]Ga-DOTA-TOC PET in meningiomas for assessment of in vivo somatostatin receptor subtype 2. Eur J Nucl Med Mol Imaging. 2020;47:2577-2588.

Bashir A, Vestergaard MB, Marner L, Larsen VA, Ziebell M, Fugleholm K, Law I. PET imaging of meningioma with ¹⁸F-FLT: a predictor of tumour progression. Brain. 2020 Dec 5;143(11):3308-3317.

Berg RMG, Ronit A, Rørvig SB, Plovsing RR. Atypical lymphocytes in bronchoalveolar lavage fluid from patients with COVID-19 ARDS. Pathology - Research & Practice. 2020;216(12):153242.

Berg RMG, Space is in the air. Physiology News. 2020;117:5.

Berg RMG, Stetoskopi af lunger – back to basics. Udførelse, beskrivelse og tolkning. Månedsskrift for Almen Praksis. 2020;8:526-534.

Berg RMG, Turan J. Physiologist among the stars: A conversation with Jim Pawelczyk. Physiology News. 2020;117:10-11.

Binderup T, Knigge U, Johnbeck CB, Loft A, Berthelsen AK, Oturai P, Mortensen J, Federspiel B, Langer SW, Kjaer A. ¹⁸F-FDG-PET is superior to WHO grading as prognostic tool in neuroendocrine neoplasms and useful in guiding peptide receptor radionuclide therapy: a prospective 10-year follow-up study of 166 patients. J Nucl Med. 2020 Oct 16: jnumed. 120.244798.

Bojesen KB, Ebdrup BH, Jessen K, Sigvard A, Tangmose K, Edden RAE, Larsson HBW, Rostrup E, Broberg BV, Glenthøj BY. Treatment response after 6 and 26 weeks is related to baseline glutamate and GABA levels in antipsychotic-naïve patients with psychosis. Psychol Med. 2020 Oct;50(13):2182-2193.

Bratteby K, Torkelsson E, L'Estrade ET, Peterson K, Shalgunov V, Xiong M, Leffler H, Zetterberg FR, Olsson TG, Gillings N, Nilsson UJ, Herth MM, Erlandsson M. In Vivo Veritas: ¹⁸F-Radiolabeled Glycomimetics Allow Insights into the Pharmacological Fate of Galectin-3 Inhibitors. J Med Chem. 2020 Jan 23;63(2):747-755.

Byrne C, Kjaer A, Forman JL, Hasbak P. Reproducibility of LVEF, LV volumes, and LV mass between Rubidium-82 PET/CT scans in young healthy volunteers using two commercially available software packages. J Nucl Cardiol. 2020;27:1237-1245.

Publications

Børresen B, Hansen AE, Fliedner FP, Henriksen JR, Elema DR, Brandt-Larsen M, Kristensen LK, Kristensen AT, Andresen TL, Kjær A. Noninvasive Molecular Imaging of the Enhanced Permeability and Retention Effect by ⁶⁴Cu-Liposomes: In vivo Correlations with ⁶⁸Ga-RGD, Fluid Pressure, Diffusivity and ¹⁸F-FDG. *Int J Nanomedicine*. 2020 Nov 2;15:8571-8581.

Carlsen EA, Johnbeck CB, Binderup T, Loft M, Pfeifer A, Mortensen J, Oturai P, Loft A, Berthelsen AK, Langer SW, Knigge U, Kjaer A. ⁶⁴Cu-DOTATATE PET/CT and Prediction of Overall and Progression-Free Survival in Patients with Neuroendocrine Neoplasms. *J Nucl Med*. 2020;61(10):1491-1497.

Chételat G, Arbizu J, Barthel H, Garibotto V, Law I, Morbelli S, van de Giessen E, Agosta F, Barkhof F, Brooks DJ, Carrillo MC, Dubois B, Fjell AM, Frisoni GB, Hansson O, Herholz K, Hutton BF, Jack CR, Lammertsma AA, Landau SM, Minoshima S, Nobili F, Nordberg A, Ossenkoppele R, Oyen WJG, Perani D, Rabinovici GD, Scheltens P, Villemagne VL, Zetterberg H, Drzezga A. Amyloid-PET and ¹⁸F-FDG-PET in the diagnostic investigation of Alzheimer’s disease and other dementias. *Lancet Neurol*. 2020;19:951-962.

Christensen C, Kristensen LK, Alfsen MZ, Nielsen CH, Kjaer A. Quantitative PET imaging of PD-L1 expression in xenograft and syngeneic tumour models using a site-specifically labelled PD-L1 antibody. *Eur J Nucl Med Mol Imaging*. 2020; 47:1302-1313.

Christensen TN, Langer SW, Villumsen KE, Johannesen HH, Löfgren J, Keller SH, Hansen AE, Kjaer A, Fischer BM. ¹⁸F-fluorothymidine (FLT)-PET and diffusion-weighted MRI for early response evaluation in patients with small cell lung cancer: a pilot study. *European Journal of Hybrid Imaging*. 2020;4(1):2.

Clausen AS, Østergaard DE, Holmberg P, Henriksen JR, Tham J, Damborg PP, Jensen AI, Kjaer A, Hansen AE, Andresen TL. Quantitative determination of ⁶⁴Cu-liposome accumulation at inflammatory and infectious sites: Potential for future theranostic system. *J Control Release*. 2020;327:737-746.

Clausen MM, Vogelius IR, Kjær A, Bentzen SM. Multiple Testing, Cut-Point Optimization, and Signs of Publication Bias in Prognostic FDG-PET Imaging Studies of Head and Neck and Lung Cancer: A Review and Meta-Analysis. *Diagnostics (Basel)*. 2020 Dec 1;10(12):1030.

Clausen, AS, Ørbæk M, Pedersen RR, Jensen PO, Lebech A-M, Kjaer A. ⁶⁴Cu-DOTATATE Positron Emission Tomography (PET) of Borrelia Burgdorferi Infection: In Vivo Imaging of Macrophages in Experimental Model of Lyme Arthritis. *Diagnostics (MDPI)*, 2020;10:790.

Cramer SP, Vestergaard MB, Lindberg U, Larsson HBW. Physical and Physiological Principles of Perfusion and Permeability. *Quantitative Magnetic Resonance Imaging*. 2020, 1(11):269-294. Academic Press

Dahl RH, Taudorf S, Bailey DM, Møller K, Berg RMG. A method for modelling the oxyhaemoglobin dissociation curve at the level of the cerebral capillary in humans. *Experimental Physiology*. 2020;105(7):1063-1070.

Dejanovic D, Amtoft AG. Dejanovic D, Extensive Subcutaneous Foreign Body Granulomas Associated With “Skin Popping” Demonstrated on ¹⁸F-FDG PET/CT. *Clin Nucl Med*. 2020 May;45(5):e241-e242.

Dekkers IA, de Boer A, Sharma K, Cox EF, Lamb HJ, Buckley DL, Bane O, Morris DM, Prasad PV, Semple SIK, Gillis KA, Hockings P, Buchanan C, Wolf M, Laustsen C, Leiner T, Haddock B, Hoogduin JM, Pullens P, Sourbron S. Consensus-based technical recommendations for clinical translation of renal T1 and T2 mapping MRI. *MAGMA*. 2020 Feb;33(1): 163-76.

Delpassand ES, Ranganathan D, Wagh N, Shafie A, Gaber A, Abbasi A, Kjaer A, Tworowska I, Nunez R. ⁶⁴Cu-DOTATATE PET/CT for Imaging Patients with Known or Suspected Somatostatin Receptor-Positive Neuroendocrine Tumors: Results of the First US Prospective, Reader-Blinded Clinical Trial. *J Nucl Med*. 2020;61:890-896.

Donat CK, Hansen HH, Hansen HD, Mease RC, Horti AG, Pomper MG, L’Estrade ET, Herth MM, Peters D, Knudsen GM, Mikkelsen JD. In Vitro and In Vivo Characterization of Dibenzothiophene Derivatives [125I]Iodo-ASEM and [18F]ASEM as Radiotracers of Homo- and Heteromeric α 7 Nicotinic Acetylcholine Receptors. *Molecules*. 2020 Mar 20;25(6).

Donovan LL, Magnussen JH, Dyssegaard A, Lehel S, Hooker JM, Knudsen GM, Hansen HD. Imaging HDACs In Vivo: Cross-Validation of the [11C] Martinostat Radioligand in the Pig Brain. *Mol Imaging Biol*. 2020 Jun;22(3):569-577.

Edem PE, Jørgensen JT, Nørregaard K, Rossin R, Yazdani A, Valliant JF, Robillard M, Herth MM, Kjaer A. Evaluation of a ⁶⁸Ga-Labeled DOTA-Tetrazine as a PET Alternative to ¹¹¹In-SPECT Pretargeted Imaging. *Molecules*. 2020;25:463.

Einarsdóttir HS, Berg RMG, Borgwardt L. Interrater Reliability of ^{99m}Tc-DMSA Scintigraphy Performed as Planar Scan vs. SPECT/Low Dose CT for Diagnosing Renal Scarring in Children. *Diagnostics (Basel)*. 2020 Dec 17;10(12):1101.

Espersen C, Borgwardt L, Larsen PN, Andersen TB, Stenholt L, Petersen LJ. Nuclear imaging methods for the prediction of postoperative morbidity and mortality in patients undergoing localized, liver-directed treatments: a systematic review. *EJNMMI Res*. 2020 Sep 4;10(1):101.

Fagerlund B, Pantelis C, Jepsen JRM, Raghava JM, Rostrup E, Thomas MB, Nielsen MØ, Bojesen K, Jensen KG, Stentebjerg-Decara M, Klauber DG, Rudå D, Ebdrup BH, Jessen K, Sigvard A, Tangmose K, Jeppesen P, Correll CU, Fink-Jensen A, Pagsberg AK, Glenthøj BY. Differential effects of age at illness onset on verbal memory functions in antipsychotic-naïve schizophrenia patients aged 12-43 years. *Psychol Med*. 2020 Mar 11:1-11.

Filikci Z, Gustafsson MAK, Henriksen OM, Marner L, Høgh P. C9ORF72 hexanucleotide repeat expansion with Alzheimer’s disease-like clinical phenotype: A case report with results from neuropsychology, CSF, FDG-PET, and PiB-PET. *Clin Case Rep*. 2020 Oct 27;8(12):3416-3420.

Flidner FP, Engel TB, El-Ali HH, Hansen AE, Kjaer A. Diffusion weighted magnetic resonance imaging (DW-MRI) as a non-invasive, tissue cellularity marker to monitor cancer treatment response. *BMC Cancer*. 2020;20:134.

Froeding LP, Høgdall C, Kristensen E, Zobbe V, Niemann I, Ørtoft G, Thrano V, Mathiesen O, Mortensen J, Schnack TH. Recurrence and survival rates in node negative patients after sentinel node biopsy for early-stage vulva cancer - A nationwide study. *Gynecol Oncol*. 2020 Jan;156(1):124-130.

Gbyl K, Rostrup E, Raghava JM, Andersen C, Rosenberg R, Larsson HBW, Videbech P. Volume of hippocampal subregions and clinical improvement following electroconvulsive therapy in patients with depression. *Prog Neuropsychopharmacol Biol Psychiatry* 2020;104:110048.

Ghanizada H, Al-Karagholi MA, Arnglim N, Mørch-Rasmussen M, Metcalf-Clausen M, Larsson HBW, Amin FM, Ashina M. Investigation of sumatriptan and ketorolac trometamol in the human experimental model of headache. *J Headache Pain*. 2020 Feb 24;21(1):19.

Giovannella M, Andresen B, Andersen JB, El-Mahdaoui S, Contini D, Spinelli L, Torricelli A, Greisen G, Durduran T, Weigel UM, Law I. Validation of diffuse correlation spectroscopy against ¹⁵O-water PET for regional cerebral blood flow measurement in neonatal piglets. *J Cereb Blood Flow Metab*, 2020;40:2055-2065.

Gjerum L, Frederiksen KS, Henriksen OM, Law I, Bruun M, Simonsen AH, Mecocci P, Baroni M, Dottorini ME, Koikkalainen J, Lötjönen J, Hasselbalch SG. Evaluating 2-[¹⁸F]FDG-PET in differential diagnosis of dementia using a data-driven decision model. *Neuroimage Clin*. 2020;27:102267.

Gjerum L, Frederiksen KS, Henriksen OM, Law I, Anderberg L, Andersen BB, Bjerregaard E, Hejl AM, Høgh P, Hasselbalch SG. A visual rating scale for cingulate island sign on ¹⁸F-FDG-PET to differentiate dementia with Lewy bodies and Alzheimer’s disease. *J Neurol Sci*. 2020;410:116645.

Gramkow MH, Gjerum L, Koikkalainen J, Lötjönen J, Law I, Hasselbalch SG, Waldemar G, Frederiksen KS. Prognostic value of complementary biomarkers of neurodegeneration in a mixed memory clinic cohort. *Peer J*. 2020;8:e9498.

Gudbergsson JM, Christensen E, Kostrikov S, Moos T, Duroux M, Kjaer A, Johnsen KB, Andresen TL. Conventional treatment of glioblastoma reveals persistent CD44+ subpopulations. *Neurobiol*. 2020;57(9):3943-3955.

Haddock B, Hansen SK, Lindberg U, Nielsen JL, Frandsen U, Aagaard P, Larsson HBW, Suetta C. Physiological responses of human skeletal muscle to acute blood flow restricted exercise assessed by multimodal MRI. *J Appl Physiol* (1985). 2020 Oct 1;129(4):748-759.

Hansen AE, Henriksen JR, Jølcck RI, Flidner FP, Bruun LM, Scherman J, Jensen AI, Munck Af Rosenschöld P, Moorman L, Kurbegovic S, de Blanck SR, Larsen KR, Clementsen PF, Christensen AN, Clausen MH, Wang W, Kempen P, Christensen M, Viby NE, Persson G, Larsen R, Conradsen K, McEvoy FJ, Kjaer A, Eriksen T, Andresen TL. Multimodal soft tissue markers for bridging high-resolution diagnostic imaging with therapeutic intervention. *Sci. Adv*. 2020 Aug;19;6(34):

Hansen HD, Lindberg U, Ozenne B, Fisher PM, Johansen A, Svarer C, Keller SH, Hansen AE, Knudsen GM. Visual stimuli induce serotonin release in occipital cortex: A simultaneous positron emission tomography/magnetic resonance imaging study. *Hum Brain Mapp*. 2020 Aug 19;41(16):4753-4763.

Hansen SL, de Nijs R, Mortensen J, Berg RMG. Ventilation–perfusion SPECT versus CTPA in young

Publications

adult females with suspected pulmonary embolism. Eur Respir J. 2020 Jun 11;55(6): 2000448.

Hedsund C, Wilcke TR, Berg RMG. Defining “stable chronic hypercapnia” in patients with COPD: the physiological perspective. Eur Respir J. 2020;55(2):902172.

Henriksen OM, Holm S, Marner L, Law I. Effect of blood glucose and body weight on image quality in brain [18F]FDG PET imaging. Nucl Med Commun. 2020 Dec;41(12):1265-1274.

Hoel H, Ueland T, Knudsen A, Kjaer A, Michelsen AE, Sagen EL, Halvorsen B, Yndestad A, Nielsen SD, Aukrust P, Lebech AM, Troseid M. Soluble Markers of Interleukin 1 Activation as Predictors of First-Time Myocardial Infarction in HIV-Infected Individuals. J Infect Dis. 2020;221:506-509.

Holle SLK, Andersen MH, Klein CF, Bruun NE, Tønder N, Haarmark C, Loft A, Høilund-Carslen PF, Bundgaard H, Iversen KK. Clinical usefulness of FDG-PET/CT for identification of abnormal extra-cardiac foci in patients with infective endocarditis. Int J Cardiovasc Imaging. 2020 May;36(5):939-946.

Hornum M, Iversen M, Oturai P, Andersen MJ, Zemtsovski M, Bredahl P, Bjarnason NH, Christensen KB, Carlsen J, Møller CH, Feldt-Rasmussen B, Perch M. Felodipine and renal function in lung transplantation: A randomized placebo-controlled trial. J Heart Lung Transplant. 2020;39(6):541-550.

Hougaard A, Younis S, Iljazi A, Haanes KA, Lindberg U, Vestergaard MB, Amin FM, Sugimoto K, Kruse LS, Ayata C, Ashina M. Cerebrovascular effects of endothelin-1 investigated using high-resolution magnetic resonance imaging in healthy volunteers. J Cereb Blood Flow Metab. 2020 Aug;40(8):1685-1694.

Hvedstrup J, Amin FM, Hougaard A, Ashina H, Christensen CE, Larsson HBW, Ashina M, Schytz HW. Volume of the rectus capitis posterior minor muscle in migraine patients: a cross-sectional structural MRI study. J Headache Pain. 2020 May 27;21(1):57.

Hvistendahl M, Naimi RM, Enevoldsen LH, Madsen JL, Stefan Fuglsang S, Jeppesen PB. Effect of glepaglutide, a long-acting glucagon-like peptide 2 analog, on gastrointestinal transit time and motility in patients with short bowel syndrome: findings from a randomized trial. JPEN J Parenter Enteral Nutr. 2020 Nov;44(8):1535-1544.

Højfeldt G, Bülow J, Agergaard J, Asmar A, Schjerling P, Simonsen L, Bülow J, van Hall G, Holm L. Impact of habituated dietary protein intake on fasting and postprandial whole-body protein turnover and splanchnic amino acid metabolism in elderly men: a randomized, controlled, crossover trial. Am J Clin Nutr. 2020 Dec 10;112(6):1468-1484.

Ingvarsen SZ, Gårdsvoll H, van Putten S, Nørregaard KS, Krigslund O, Meilstrup JA, Tran C, Jürgensen HJ, Melander MC, Nielsen CH, Kjaer A, Bugge TH, Engelholm LH, Behrendt N. Tumor cell MT1-MMP is dispensable for osteosarcoma tumor growth, bone degradation and lung metastasis. Sci Rep. 2020 Nov 5;10(1):19138.

Knudsen GM, Ganz M, Appelhoff S, Boellaard R, Bormans G, Carson RE, Catana C, Doudet D, Gee AD, Greve DN, Gunn RN, Halldin C, Herscovitch P, Huang H, Keller SH, Lammertsma AA, Lanzenberger R, Liow JS, Lohith TG, Lubberink M, Lyoo CH, Mann JJ, Matheson GJ, Nichols TE, Nørgaard M, Ogden T, Parsey R, Pike VW, Price J, Rizzo G, Rosa-Neto P, Schain M, Scott PJ, Searle G, Slifstein M, Suhara T, Talbot PS, Thomas A, Veronese M, Wong DF, Yaqub M, Zanderigo F, Zoghbi S, Innis RB. Guidelines for the content and format of PET brain data in publications and archives: A consensus paper. J Cereb Blood Flow Metab. 2020 Aug;40(8):1576-1585.

Kramer V, Dyssegaard A, Flores J, Soza-Ried C, Rösch F, Knudsen GM, Amaral H, Herth MM. Characterization of the serotonin 2A receptor selective PET tracer (R)-[18F]MH.MZ in the human brain. Eur J Nucl Med Mol Imaging. 2020 Feb;47(2):355-365.

Kristensen AW, Berg RMG, Greve AM, Dahl RH, Perch M, Mortensen J. Survival in patients with scintigraphic evidence of pulmonary thromboembolism 12 weeks after double lung transplantation. J Heart Lung Transplant. 2020 Jul;39(7):719-721.

Kristensen AW, Greve AM, Dahl RH, Perch M, Mortensen J, Berg RMG. Evidence of unilateral diaphragmatic paralysis on lung scintigraphy after double lung transplantation: impact on lung function and survival. Scand J Clin Lab Invest. 2020 Oct;80(6):454-455.

Kristensen LK, Christensen C, Alfsen MZ, Cold S, Nielsen CH, Kjaer A. Monitoring CD8a+ T Cell Responses to Radiotherapy and CTLA-4 Blockade Using [64Cu]NOTA-CD8a PET Imaging. Mol Imaging Biol. 2020;22:1021-1030.

Ladefoged CN, Andersen FL, Højgaard L. Kunstig intelligens til klinisk billediagnostik. Ugeskr Laeger. 2020 Mar 23;182(13).

Ladefoged CN, Hansen AE, Henriksen OM, Bruun FJ, Eikenes L, Øen SK, Karlberg A, Højgaard L, Law I, Andersen FL. AI-driven attenuation correction for brain PET/MRI: Clinical evaluation of a dementia cohort and importance of the training group size. Neuroimage. 2020 Nov 15;222:117221.

Laursen AH, Elming MB, Ripa RS, Hasbak P, Kjær A, Køber L, Marott JL, Thune JJ, Hutchings M. Rubidium-82 positron emission tomography for detection of acute doxorubicin-induced cardiac effects in lymphoma patients. J Nucl Cardiol. 2020 Oct;27(5):1698-1707.

Laursen AH, Ripa RS, Hasbak P, Kjær A, Elming MB, Køber L, Hutchings M, Thune JJ. 123I-MIBG for detection of subacute doxorubicin-induced cardiotoxicity in patients with malignant lymphoma. J Nucl Cardiol. 2020 Jun;27(3):931-939.

Law I, Paulson OB. Hjernens fysiologi. In: Paulson OB, Sørensen PS, Waldemar G, Sørensen JCH, Sellebjerg F, editors. Klinisk neurologi og neurokirurgi, 7. Udgave, FADL's forlag, 2020, Chapter 9, p. 195-216.

Lawaetz Schultz HH, Møller CH, Møller-Sørensen H, Mortensen J, Lund TK, Andersen CB, Perch M, Carlsen J, Iversen M. Variation in Time to Peak Values for Different Lung Function Parameters After Double Lung Transplantation. Transplant Proc. 2020 Jan-Feb;52(1):295-301.

L'Estrade ET, Erlandsson M, Edgar FG, Ohlsson T, Knudsen GM, Herth MM. Towards selective CNS PET Imaging of the 5-HT7 Receptor System: Past, Present and Future. Neuropharmacology. 2020 Aug 1;172:107830.

L'Estrade ET, Shalgunov V, Edgar FG, Strebl-Bantillo MG, Xiong M, Crestey F, Neelamegam R, Dyssegaard A, Lehel S, Erlandsson M, Ohlsson T, Hooker JM, Knudsen GM, Herth MM, Hansen HD. Radiosynthesis and preclinical evaluation of [11C]Cimbi-701 - Towards the imaging of cerebral 5-HT7 receptors. J Labelled Comp Radiopharm. 2020 Feb;63(2):46-55.

Lindegren S, Albertsson P, Bäck T, Jensen H, Palm S, Aneheim E. Realizing Clinical Trials with Astatine-211: The Chemistry Infrastructure. Cancer Biotherapy and Radiopharmaceuticals 2020;35(2):425-436.

Lobatto ME, Binderup T, Robson PM, Giesen LFP, Calcagno C, Witjes J, Fay F, Baxter S, Wessel CH, Eldib M, Bini J, Carlin SD, Stroes ESG, Storm G, Kjaer A, Lewis JS, Reiner T, Fayad ZA, Mulder WJM, Pérez-Medina C. Multimodal Positron Emission Tomography Imaging to Quantify Uptake of 89Zr-Labeled Liposomes in the Atherosclerotic Vessel Wall. Bioconjug Chem. 2020;31:360-368.

Loft M, Carlsen EA, Johnbeck CB, Johannesen HH, Binderup T, Pfeifer A, Mortensen J, Oturai P, Loft A, Kerthelsen AK, Langer SW, Knigge U, Kjaer A. 64Cu-DOTATATE PET in Patients With Neuroendocrine Neoplasms: Prospective, Head-to-Head Comparison of Imaging at 1 Hour and 3 Hours Post-Injection. J Nucl Med. 2020;May 22:73-80.

Madsen MK, Fisher PM, Stenbæk DS, Kristiansen S, Burmester D, Lehel S, Páleníček T, Kuchař M, Svarer C, Ozenne B, Knudsen GM. A single psilocybin dose is associated with long-term increased mindfulness, preceded by a proportional change in neocortical 5-HT2A receptor binding. Eur Neuropsychopharmacol. 2020 Apr;33:71-80.

Mandrup CM, Roland CB, Egelund J, Nyberg M, Enevoldsen LH, Kjaer A, Clemmensen A, Christensen AN, Suetta C, Frikke-Schmidt R, Utoft BB, Kirstensen JM, Wojtaszewski JFP, Hellsten Y, Stallknecht B. Effects of High-Intensity Exercise Training on Adipose Tissue Mass, Glucose Uptake and Protein Content in Pre- and Post-menopausal Women. Frontiers in Sports and Active living. 2020 June; (2):60.

Mirian C, Duun-Henriksen AK, Juratli T, Sahm F, Spiegl-Kreinecker S, Peyre M, Biczok A, Tonn JC, Goutagny S, Bertero L, Maier AD, Møller Pedersen M, Law I, Broholm H, Cahill DP, Brastianos P, Poulsgaard L, Fugleholm K, Ziebell M, Munch T, Mathiesen T. Poor prognosis associated with TERT gene alterations in meningioma is independent of the WHO classification: an individual patient data meta-analysis. J Neurol Neurosurg Psychiatry. 2020;91:378-387.

Morbelli S, Ekmekcioglu O, Barthel H, Albert NL, Boellaard R, Cecchin D, Guedj E, Lammertsma AA, Law I, Penuelas I, Semah F, Traub-Weidinger T, van de Giessen E, Varrone A, Garibotto V, EANM NC. COVID-19 and the brain: impact on nuclear medicine in neurology. Eur J Nucl Med Mol Imaging. 2020;47:2487-2492.

Morbelli S, Esposito G, Arbizu J, Barthel H, Boellaard R, Bohnen NI, Brooks DJ, Darcourt J, Dickson JC, Douglas D, Drzezga A, Dubroff J, Ekmekcioglu O, Garibotto V, Herscovitch P, Kuo P, Lammertsma A, Pappata S, Peñuelas I, Seibyl J, Semah F, Tossici-Bolt L, Van de Giessen E, Van Laere K, Varrone A, Wanner M, Zubal G, Law I. EANM practice guideline/SNMMI procedure standard for dopaminergic imaging in Parkinsonian syndromes 1.0. Eur J Nucl Med Mol Imaging. 2020;47:1885-1912.

Munkholm M., Mortensen J. (2020) Reference Equations for Simultaneously Measured DLCO and DLNO: How Are Reference Equations Influenced by Age, Sex, and Anthropometric Variables? In: Yamaguchi K. (eds) Structure-Function Relationships in Various Respiratory Systems. Respiratory Disease Series: Diagnostic Tools and Disease Managements. Springer, Singapore. https://doi.org/10.1007/978-981-15-5596-1_14.

Nielsen BR, Andersen HE, Haddock B, Hovind P, Schwarz P, Suetta C. Prevalence of muscle dysfunction concomitant with osteoporosis in a home-dwelling Danish population aged 65-93 years - The Copenhagen Sarcopenia Study. *Exp Gerontol.* 2020 Sep;138:110974.

Nielsen K, Binderup T, Langer SW, Kjaer A, Knigge P, Grondahl V, Melchior L, Federspiel B, Knigge U. P53, Somatostatin receptor 2a and Chromogranin A immunostaining as prognostic markers in high grade gastroenteropancreatic neuroendocrine neoplasms. *BMC Cancer.* 2020;20:27.

Nygård L, Ahlborn LB, Persson GF, Chandrananda D, Langer JW, Fischer BM, Langer SW, Gabrielaite M, Kjær A, Rosenfeld N, Mouliere F, Østrup O, Vogelius IR, Bentzen SM. Circulating cell free DNA during definitive chemo-radiotherapy in non-small cell lung cancer patients - initial observations. *PLoS One.* 2020 Apr 8;15(4):e0231884.

Olin A, Hansen AE, Rasmussen JH, Ladefoged CN, Berthelsen AK, Håkansson K, Vogelius IR, Specht L, Gothelf AB, Kjaer A, Fischer BM & Andersen FL. Feasibility of multiparametric PET/MRI as a one-stop-shop for radiotherapy planning of head and neck cancer patients. *Int J Radiat Oncol Biol Phys.* 2020;108(5):1329-1338.

Pedersbæk D, Krogager L, Albertsen CH, Ringgaard L, Hansen AE, Jønsson K, Larsen JB, Kjær A, Andresen TL, Simonsen JB. Effect of apoA-I PEGylation on the Biological Fate of Biomimetic High-Density Lipoproteins. *ACS Omega.* 2020;6:871-880.

Puig O, Henriksen OM, Vestergaard MB, Hansen AE, Andersen FL, Ladefoged CN, Rostrup E, Larsson HB, Lindberg U, Law I. Comparison of simultaneous arterial spin labeling MRI and ¹⁵O-H₂O PET measurements of regional cerebral blood flow in rest and altered perfusion states. *J Cereb Blood Flow Metab.* 2020 Aug;40(8):1621-1633.

Rasmussen JH, Olin A, Lelkaitis G, Hansen AE, Andersen FL, Johannesen HH, Kjær A, Vogelius IR, Specht L, Bentzen SM, Wessel I, von Buchwald C, Fischer BM. Does multiparametric imaging with ¹⁸F-FDG-PET/MRI capture spatial variation in immunohistochemical cancer biomarkers in head and neck squamous cell carcinoma? *Br J Cancer.* 2020 Jul;123(1):46-53.

Rasmussen LJH, Schultz M, Iversen K, Eugen-Olsen J, Helms M, David K, Kjaer A, Lebech A, Kronborg G. Soluble urokinase plasminogen activator receptor (suPAR) is lower in disease-free patients but cannot rule out incident disease in patients with suspected cancer. *Clin Biochem.* 2020; 84:32-37.

Rasmussen T, de Nijs R, Kjær Olsen LK, Kamper AL, Evi Bang L, Frimodt-Møller M, Kelbæk H, Schwartz Sørensen S, Kjær A, Feldt-Rasmussen B, Hastrup Svendsen J, Hasbak P. Renal ¹²³I-MIBG Uptake before and after Live-Donor Kidney Transplantation. *Diagnostics (Basel).* 2020 Oct 9;10(10):802.

Reichkender MH, Berg RMG, de Nijs R, Nørgaard H, Schmidt IM, Borgwardt L. Planar scan vs. SPECT/low-dose CT for estimating split renal function by ^{99m}Tc-DMSA scintigraphy in children. *Eur J Nucl Med Mol Imaging.* 2020 Mar;47(3):729-733.

Ringgaard L, Melander F, Eliassen R, Henriksen JR, Jølck RI, Engel TB, Bak M, Flidner FP, Kristensen K, Elema DR, Kjaer A, Hansen AE, Andresen TL. Tumor repolarization by an advanced liposomal drug delivery system provides a potent new approach for chemo-immunotherapy. *Sci Adv.* 2020 Sep 4;6(36):

Risør LM, Loft A, Berthelsen AK, Loft FC, Madsen AR, Vogelius IR, Kjaer A, Friberg J. FDG-PET/CT in the surveillance of head and neck cancer following radiotherapy. *Eur Arch Otorhinolaryngol* 2020;277:539-547.

Ronit A, Berg RMG, Bay JT, Haugaard AK, Ahlström MG, Burgdorf KS, Ullum H, Rørvig SB, Tjelle K, Foss NB, Benfield T, Marquart HV, Plovsing RR. Compartmental immunophenotyping in COVID-19 ARDS: A case series. *Journal of Allergy and Clinical Immunology.* 2020;147(1):81-91.

Shalgunov V, Xiong M, L'Estrade ET, Raval NR, Andersen IV, Edgar FG, Speth NR, Baerentzen SL, Hansen HD, Donovan LL, Nasser A, Peitersen ST, Kjaer A, Knudsen GM, Syvänen S, Palner M, Herth MM. Blocking of efflux transporters in rats improves translational validation of brain radioligands. *EJNMMI Res.* 2020 Oct 19;10(1):124.

Simón M, Jørgensen JT, Norregaard K, Kjaer A. F-FDG positron emission tomography and diffusion-weighted magnetic resonance imaging for response evaluation of nanoparticle-mediated photothermal therapy. *Sci Rep.* 2020;10:7595.

Skougaard K, Østrup O, Guldbrandsen K, Sørensen B, Meldgaard P, Saghir Z, Gørtz P, Lonsdale MN, Frank MS, Gerke O, Rychwicka-Kielek BA, Persson G, Land LH, Schytte T, Bodtger U, Skuladottir H, Søgaard J, Nielsen SS, Rasmussen TR and Fischer BM. Surveillance with PET/CT and liquid biopsies of stage I-III lung cancer patients after completion of definitive therapy; a Randomized controlled trial (SUPE_R). *Clin Lung Cancer.* 2020 Nov 21:e61-e64.

Slipsager JM, Glimberg SL, Søgaard J, Paulsen RR, Johannesen HH, Martens PC, Seth A, Marner L, Henriksen OM, Olesen OV, Højgaard L. Quantifying the Financial Savings of Motion Correction in Brain MRI: A Model-Based Estimate of the Costs Arising from Patient Head Motion and Potential Savings from Implementation of Motion Correction. *J Magn Reson Imaging.* 2020 Sep;52(3):731-738.

Stéen EJJ, Jørgensen JT, Johann K, Nørregaard K, Sohr B, Svatunek D, Birke A, Shalgunov V, Edem PE, Rossin R, Seidl C, Schmid F, Robillard MS, Kristensen JL, Mikula H, Barz M, Kjaer A, Herth MM. Trans-Cyclooctene-Functionalized PeptoBrushes with Improved Reaction Kinetics of the Tetrazine Ligation for Pretargeted Nuclear Imaging. *ACS Nano.* 2020;14:568-584.

Svane MS, Johannesen HH, Martinussen C, Bojsen-Møller KN, Hansen ML, Hansen AE, Deacon CF, Hartmann B, Keller SH, Klausen TL, Loft A, Kjaer A, Madsbad S, Löfgren J, Holst JJ, Wewer Albrechtsen NJ. No effects of a 6-week intervention with a glucagon-like peptide-1 receptor agonist on pancreatic volume and oedema in obese men without diabetes. *Diabetes Obes Metab.* 2020 Oct;22(10):1837-1846.

Svane MS, Johannesen HH, Martinussen C, Bojsen-Møller KN, ML Hansen ML Hansen AE, Deacon CF, Hartmann B, Keller SH, Klausen TL, Loft A, Kjaer A, Madsbad S, Löfgren J, Holst JJ, Albrechtsen NJW. Diabetes, Obesity and Metabolism 2020/10; Cover Image, Volume 22, Issue 10.

Thorlacius-Ussing G, Nielsen JE, Law I, Hansen HV, Birgitte Bo A. Mania triggered by levodopa treatment in a patient with frontotemporal dementia caused by A C9orf72 repeat expansion: A case report. *Clin Neurol Neurosurg.* 2020;198:106147.

van Koningsbruggen-Rietschel S, Davies JC, Pressler T, Fischer R, MacGregor G, Donaldson SH, Smerud K, Meland N, Mortensen J, Fosbøl MØ, Downey DG, Myrset AH, Flaten H, Rye PD. Inhaled dry powder alginate oligosaccharide in cystic fibrosis: a randomised, double-blind, placebo-controlled, crossover phase 2b study. *ERJ Open Res.* 2020 Oct 19;6(4):00132-2020.

Vestergaard MB, Jensen ML, Arngrim N, Lindberg U, Larsson HB. Higher physiological vulnerability to hypoxic exposure with advancing age in the human brain. *J Cereb Blood Flow Metab.* 2020 Feb;40(2):341-353.

Wang W, Flidner FP, Hansen AE, Eliassen R, Melander F, Kjaer A, Andresen TL, Jensen AI, Henriksen JR. Preclinical evaluation of cationic DOTA-triarginine-lipid conjugates for theranostic liquid brachytherapy. *Nanotheranostics.* 2020;4:142-155.

Wenneberg C, Glenthøj BY, Glenthøj LB, Fagerlund B, Krakauer K, Kristensen TD, Hjorthøj C, Edden RAE, Broberg BV, Bojesen KB, Rostrup E, Nordentoft M. Baseline measures of cerebral glutamate and GABA levels in individuals at ultra-high risk for psychosis: Implications for clinical outcome after 12 months. *Eur Psychiatry.* 2020 Aug 7;63(1):e83.

Wenneberg C, Nordentoft M, Rostrup E, Glenthøj LB, Bojesen KB, Fagerlund B, Hjorthøj C, Krakauer K, Kristensen TD, Schwartz C, Edden RAE, Broberg BV, Glenthøj BY. Cerebral Glutamate and Gamma-Aminobutyric Acid Levels in Individuals at Ultra-high Risk for Psychosis and the Association with Clinical Symptoms and Cognition. *Biol Psychiatry Cogn Neurosci Neuroimaging.* 2020 Jun;5(6):569-579.

Wulff S, Nielsen MØ, Rostrup E, Svarer C, Jensen LT, Pinborg L, Glenthøj BY. The relation between dopamine D2 receptor blockade and the brain reward system: a longitudinal study of first-episode schizophrenia patients. *Psychol Med.* 2020 Jan;50(2):220-228.

Younis S, Hougaard A, Christensen CE, Vestergaard MB, Petersen ET, Boer VO, Paulson OB, Ashina M, Marsman A, Larsson HBW. Feasibility of Glutamate and GABA Detection in Pons and Thalamus at 3T and 7T by Proton Magnetic Resonance Spectroscopy. *Front Neurosci.* 2020 Oct 23;14:559314.

Zhang DG, Amin FM, Guo S, Vestergaard MB, Hougaard A, Ashina M. Plasma Glucose Levels Increase During Spontaneous Attacks of Migraine With and Without Aura. *Headache.* 2020 Apr;60(4):655-664.

Zobel EH, Christensen RH, Winther SA, Hasbak P, Hansen CS, von Scholten BJ, Holmvang L, Kjaer A, Rossing P, Hansen TW. Relation of cardiac adipose tissue to coronary calcification and myocardial microvascular function in type 1 and type 2 diabetes. *Cardiovasc Diabetol.* 2020;19:16.

Doctoral Thesis

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Cerebral Haemodynamic Function in Experimental and Clinical Sepsis

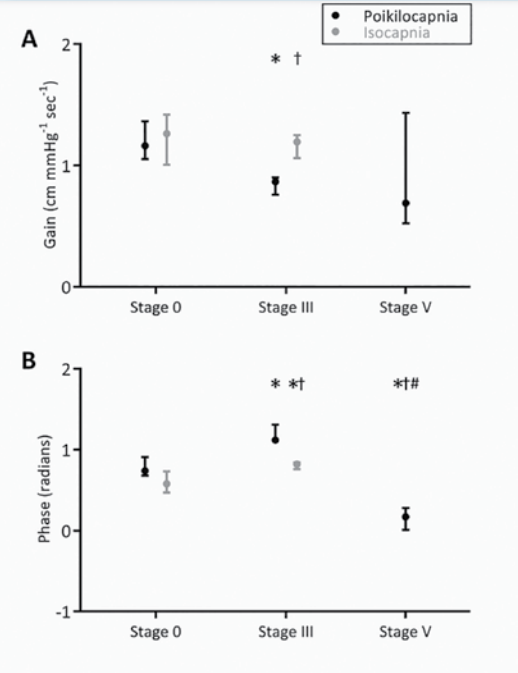
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Abstract
The thesis is based on eight original articles and a review, the scope of which were to elucidate the cerebral pathophysiology of sepsis. Based on studies in healthy volunteers and critically ill septic patients, changes in arterial carbon dioxide and core temperature were found to affect cerebral vasomotor tone in a manner that exerts neuroprotection through multiple mechanisms during the early stages of sepsis. During more advanced stages of disease, these mechanisms fail, thus predisposing to cerebral ischemia and thus encephalopathy and permanent cognitive decline.



Dynamic cerebral autoregulation in healthy volunteers at baseline (stage 0), after intravenous lipopolysaccharide (LPS) infusion (stage III) and in critically ill patients with sepsis (stage V). In an experimental model of early sepsis (LPS infusion, stage III), cerebral autoregulation becomes more efficient (reduced gain) and faster (increased phase) due to hyperventilation. In critically ill patients with sepsis, the ability of cerebral autoregulation to respond to changes in blood pressure is maintained (unaffected gain), but the autoregulatory response becomes slower (decreased phase). *Significantly different from stage 0; †significantly different from stage III during poikilocapnia; #significantly different from stage III during isocapnia.



PhD Thesis

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Healthy Ageing, Beyond A Bigger Brain

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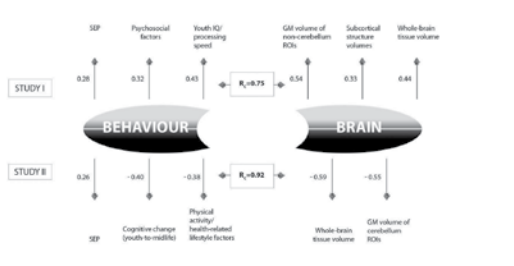
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Abstract
This PhD provides a reliable procedure for identifying correlates of healthy ageing trajectories. Using the 1953 Danish Male Birth Cohort (N=193) multifaceted dataset we report a link between (cross-sectional and longitudinal) broad-brush and specific brain and behavioural measures and how they may be influenced by multiple potential age-related modifiers. Future studies that continue to value the importance of social, biological and environmental differences in health outcome will undoubtedly aid the discovering of early intervention targets and clinical diagnoses which may in turn improve the quality of years in our increasingly ageing population.

Fig. 9: Summary of CCA results from Study 1 and Study 2. In study 1 (top) CCA identified a single statistically significant mode of population covariation ($R_c = 0.75$, permuted $P_{corrected} = 0.01$) linking higher cognitive performance, positive early-



life social factors, and psychosocial factors to larger brain volume of several brain structures, overall brain volume, and microstructural properties of some white matter tracts. In study 2 (bottom) CCA identified a single statistically significant mode of population covariation ($R_c = 0.92$, permuted $P_{corrected} = 0.001$) linking longitudinal change in behaviour to change in brain structure. Specifically, the CCA-mode identified indicates that participants demonstrating cognitive decline across specific cognitive domains are also those showing longitudinal declines in whole brain tissue volume over the two-repeated late-midlife assessments and that this is related to demographic, health-related lifestyle factors. Values between each top-contributing observed measure and each CCA-mode represents canonical structure correlations derived from post-hoc correlation analyses.



PhD Thesis

Oriol Puig

Multimodal measurements of cerebral blood flow using a hybrid PET/MRI system



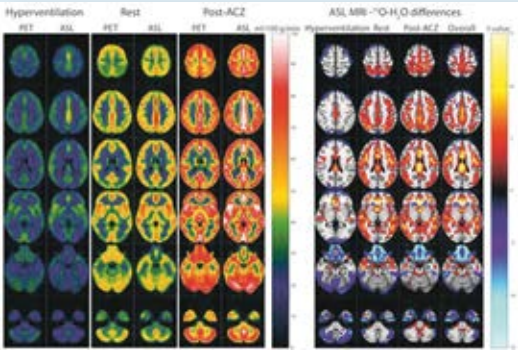
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Abstract
Magnetic resonance imaging techniques such as arterial spin labelling and phase contrast mapping provide cheap, non-invasive and fast approaches for measuring regional and global cerebral blood flow (CBF), respectively. However, the accuracy of these methods in comparison to the clinical reference method, ¹⁵O-H₂O-PET, was not well established. This project compares, for the first time, advanced MRI techniques for fully quantitative global and regional cerebral blood flow with simultaneously acquired ¹⁵O-H₂O-PET in different perfusion states.

Additionally, an MRI and deep learning-based method for attenuation correction of PET images was evaluated and compared to the best performing MRI-based attenuation correction method and the reference standard for PET attenuation correction, the computed tomography, in dynamic ¹⁵O-H₂O-PET studies.



Average perfusion maps by ¹⁵O-H₂O PET and ASL MRI in the three perfusion states (6 left columns) and z-score maps showing the magnitude of the difference between techniques (z-score) in the regions where the difference is significant.

PhD Thesis

Bryan Haddock, MSc Physicist

Acute physiological responses to muscle loading assessed with PET and MRI - a comparison of Free Flow versus Blood Flow Restricted Exercise

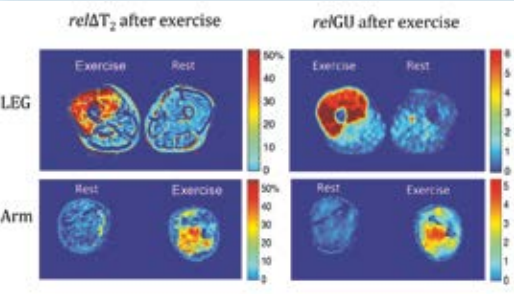


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Abstract
One of the most striking biological adaptations is the growth of skeletal muscle in response to exercise. Physiological stressors believed to trigger anabolic pathways towards muscle growth are metabolic stress and structures in muscle sensitive to tension. Accentuating metabolic stress and cell swelling using partial blood flow restriction (BFR) have been shown to increase muscle mass and strength. This dissertation develops 3D mapping of metabolic stress in muscle tissue using MRI. It concludes that BFR accentuates metabolic stress and cell swelling. Collectively, quantitative MRI represents a promising tool to decode important mechanisms of muscle maintenance and for optimizing effective rehabilitative training.



Example of post exercise arm and leg muscle relΔT₂ and relGU of one subject from study I.

PhD Thesis

Le Gjerum

Optimizing ¹⁸F-FDG-PET in the diagnosis of dementia disorders

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Sept. 1, 2020, University of Copenhagen.

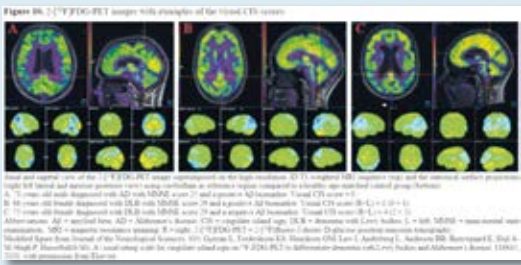
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Abstract
Study I: Comparison of the added clinical value of CSF and 2-[18F]FDG-PET in patients with suspected AD. CSF biomarkers per-formed better than 2-[18F] FDG-PET in classifying AD patients.

Study II: Development of a visual rating scale for cingulate island sign on 2-[18F]FDG-PET. The visual rating scale for cingulate island sign was able to significantly differenti-ate patients with DLB from patients with AD.

Study III: Evaluation of 2-[18F]FDG-PET biomarkers and other diagnostic tests in a data-driven decision model. The addition of 2-[18F]FDG-PET biomarkers to the other diagnostic tests improved the classification accuracy for FTD and DLB.



PhD Thesis

Karina Juhl

Development and validation of a uPAR targeted opti-cal probe in preclinical cancer models

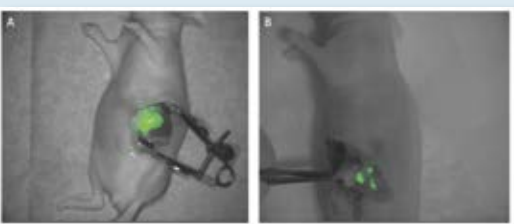
Defended
September 22, 2020, University of Copenhagen

Supervisor
Professor Andreas Kjær, Department of Clinical Physiology, Nuclear Medicine & PET, Righospitalet.
Professor Niels Kroman, Department og Clinical Medicine, Herlev-Gentofte Hospital and Danish Cancer Society.

Assesors
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Consultant Carsten Palnæs Hansen, Department of Surgical Gastroeneterology. Rigshospitalet, Denmark.
Professor John Y.K. Lee, Department of Neurosur-gery, University of Pennsylvania, USA.

Abstract
The success of surgery is dependent on achieving radical resection without compromising healthy adja-cent tissue. However, in up to 50% of the patients positive margins are found (cancer tissue left behind). This calls for better guidance during surgery. A new technique, fluorescence guided surgery (FGS) with targeted optical probes, has shown great potential in guiding the surgeons to better delineate tumors.

The aim of this thesis was therefore to develop and demonstrate in vivo the efficacy of a uPAR-targeted optical probe. The optical probe showed clear accu-mulation in a preclinical tumor model. Compared to standard surgery using white light, FGS showed supe-rior performance in an orthotopic metastatic human xenograft pancreatic cancer model. The probe is currently entering clinical testing.



Fluorescent imaging of orthotopic pancreatic mouse models injected with ICG-Glu-Glu-AE105 using the clinically approved camera Fluobeam®800. A: depicts a primary pancreatic tumour, clearly delineated by the fluorescent signal. B: shows small metastases in the peritoneal cavity developed after removal of the primary tumour. Small tumour deposits in the mm range was clearly visible

PhD Thesis

Samaira Younis

MRI investigations of the brain stem in migraine patients

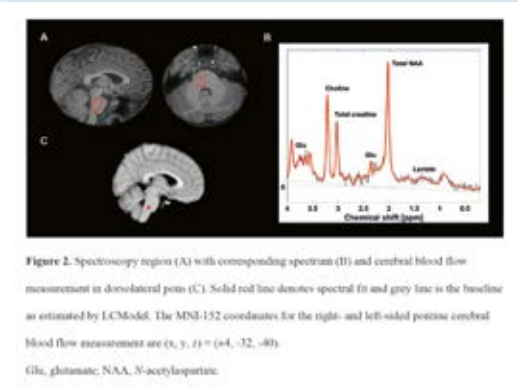


Defended
September 28, 2020, University of Copenhagen.

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Associate Professor Jan Hoffmann, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

Abstract
Despite years of research, the origin of migraine attacks remains a conundrum. One indication is abnormal neuronal activation in the pons during migraine attacks. Evidence suggest that increased glutamate levels in the pons might be associated with pontine hyperactivity, providing a possible mechanism of attack initiation. We developed and applied a human migraine model of pontine investi-gations during attacks. While pontine CBF was increased during attacks, there was no corresponding change in glutamate levels. Interestingly, we found increased total creatine levels, suggesting possible altered energy metabolism in pons during the headache phase of attacks. Collec-tively, pons may, in fact, be a structure of relevance to migraine pathophysiology, and future research is warranted to clarify its specific role and underlying mechanism.



PhD Thesis

Asma Bashir

Evaluation of [⁶⁸Ga]Ga-DOTA-TOC PET/CT and [¹⁸F]FLT PET/MRI in meningioma in relation to tumor resection and tumor growth



Defended,
Nov. 19, 2020 University of Copenhagen.

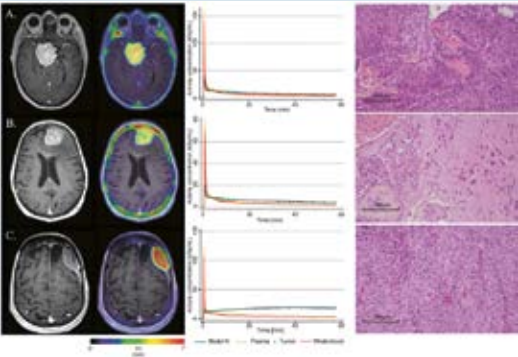
Supervisors
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Consultant Kåre Fugleholm Buch, Department of Neurosurgery, Rigshospitalet.
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Jörg-Christian Tonn, MD, DMSc, Department of Neurosurgery, University Hospital of Ludwig Maximilian

Abstract
Meningiomas are the most important neuro-oncologic entities requiring reliable imaging modalities.

Meningiomas express somatostatin-receptor subtype 2 (SSTR2), enabling a PET-based imaging with the somatostatin-receptor ligand, DOTA-D-Phy1-Tyr3-octreotide with gallium-68 ([⁶⁸Ga]Ga-DOTA-TOC). We demonstrated a strong association between [⁶⁸Ga] Ga-DOTA-TOC PET-metrics and SSTR2 in meningioma tissue that provided subsequently additional information in patients with MRI-based gross-total resection by detecting tracer-avid lesions, which were later confirmed as residual meningiomas.

3'-deoxy-3'-[¹⁸F]fluorothymidine ([¹⁸F]FLT) is a promising PET-tracer in characterizing malignancies. The results showed that [¹⁸F]FLT uptake was significantly correlated with proliferative biomarkers e.g. Ki-67 index and acted as the independent predictor for disease progression of asymptomatic meningiomas.

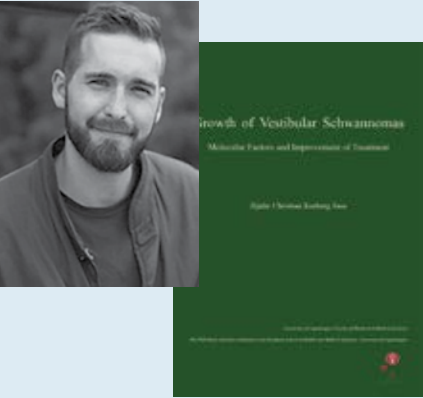


Axial sections of static PET imaging with ¹⁸F-FLT fused to MRI with kinetic modelling and subsequent histology

PhD Thesis

Hjalte Sass

Growth of Vestibular Schwannomas - molecular factors and improvement of treatment



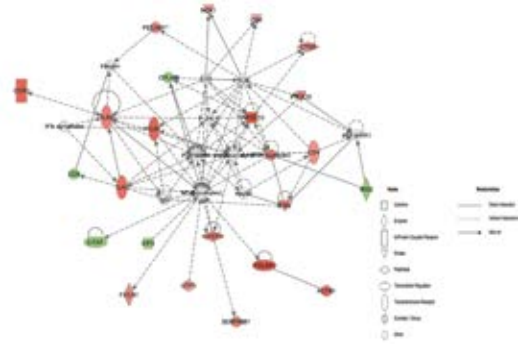
Defended
Nov.19, 2020, University of Copenhagen.

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Assessors
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Professor Simon KW Lloyd, ENT Surgery, University of Manchester, UK.
Associate Professor Dan Dupont Hougaard, Department . of Otorhinoloaryngology, Aalborg University Hospital, DK.

Abstract
Vestibular schwannomas (VS) are benign tumors located at the vestibular nerve, originating from the surrounding Schwann cells. The majority of newly diagnosed patients enter a watchful waiting regime with yearly MRI scans.

Presently, no clinical prognostic markers to determine the future growth of a VS exist. Through basic science studies, we found three cellular processes responsible for the growth rate of VS (pro-angiogenetic, cytoskeleton remodeling and pro-inflammatory factors). Future studies will show if these may serve as prognostic markers. In addition, we found a significant increase in the preservation of serviceable hearing when using a newly developed intraoperative neuromonitoring method.



Network 1 included 24 of the 109 differentially expressed genes (19 up-regulated and 5 down-regulated) (P-score =42). The network included 35 nodes and involved IFN alpha/beta-, Interferon alpha-, PI3K-, NF- κ B-, Jnk- and P38 MAPK-associated signaling pathways.



Academic and other activities

Andreas Kjær, Professor, Consultant, ERC advanced grantee, is member of the Oncology Committee of the European Association of Nuclear Medicine (EANM), member of the advisory board of the European Neuroendocrine Tumor Society (ENETS) and board member of the Cancer Research Foundation at University of Copenhagen. Past President of the Scandinavian Society of Clinical Physiology and Nuclear Medicine (SSCPNM) and member of the Scientific Committee of the Danish Cancer Society. Founding Editor-in-Chief of Diagnostics (Basel) and International Associate Editor of Journal of Nuclear Medicine (JNM). Leader of multi partner project for development of compounds to visualize aggressive cancer, funded by the Innovation Fund Denmark. Coordinator of an H2020 project on click-chemistry for PET. Head of the Cluster for Molecular Imaging and Director of the PhD Program for Medical & Molecular Imaging at the Faculty of Health and Medical Sciences, University of Copenhagen. Co-chair of the Lundbeck Foundation Danish American Research Exchange (DARE) Program. Co-chair of Clinical Academic Group – Image-Guided Cancer Surgery. Member of the Industrial Researcher Committee, Innovation Fund Denmark. Member of the Academy of Technical Sciences (ATV).

Anne-Mette N. Wittekind, MSc. Pharm., Deputy Qualified Person, is member of Dansk Standard.

Annika Loft Jakobsen, Consultant, MD, PhD, is involved in a various number of clinical research

protocols, teaching at national and international courses pre- and postgraduate for medical doctors, technologists, radiographers and nurses and is invited speaker at national and international meetings and congresses. She is supervisor and opponent for several PhD students and responsible for the specialist course in oncology for nuclear medicine physicians. She is member of the “European Organization for Research and Treatment of Cancer” (EORTC). Member of European Association of Nuclear Medicine (EANM) and member of BIR, Danish Society of Oncological Radiology and Danish Society of Clinical Physiology and Nuclear Medicine. Member of Regional Working Groups for implementation of clinical guidelines for: lymphoma, malignant melanoma, lung cancer, cancer of unknown primary, and suspicion of severe disease. Member of National Working Groups for lymphoma (Chair of the Diagnostic Imaging Group under Danish Lymphoma Group (DLG)). Member of the National PET/CT Group. Board member of DGCG (Danish Gynecological Cancer Group).

Birgitte Hanel, Biomedical Scientist, DMSc. Member of the committee, Dansk Lungefunktions Standard. Member of the Spirometry Committee, ERS. Teaching in specialist course in “Clinical Respiratory Physiology” for nuclear medicine physicians and respiratory physicians. Teaching in course of spirometry and quality control organized by PLO. Board member of the Foundation of Biomedical Laboratory Scientists.

Bryan Haddock, MPE, PhD, Member of both the Danish Society for Clinical Physiology and Nuclear Medicine (DSKFNM) and the Danish Society for Medical Physics (DSMF). Supervisor for several master- and bachelor students.

Camilla Bardram Johnbeck, MD, PhD, Staff Specialist, Chairman of the board of Young Doctors in Nuclear Medicine in Denmark (YNK), member of the board in Danish Society of Clinical Physiology and Nuclear Medicine (DSKFNM) and member of the European Neuroendocrine Tumor Society (ENETS).

Claes Nøhr Ladefoged, Postdoc, MSc, PhD, co-supervisor for PhD and MSc students in the department. Co-head of the research group Clinically Applied Artificial Intelligence (CAAI). Responsible for PET/MRI attenuation correction.

Elisabeth Albrecht-Beste, Clinical Associate Professor, Consultant, member of Danish Society of Radiology, chair of post-graduate education committee of Danish Society of Radiology, chair of the Regional Advisory Board in postgraduate education in radiology and member of the Danish Society of Oncoradiology.

Flemming Littrup Andersen, Head of IT, MSc, PhD, Associate Professor at Department of Clinical Medicine, Copenhagen University, is involved in a number of clinical and pre-clinical research protocols, supervisor for several PhD, master and bachelor students and involved in both pre- and postgraduate

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Helle Hjorth Johannesen, Consultant, is member of Danish Society of Radiology, member of Danish Society of Oncoradiology and member of Danish Society of Medical Magnetic Resonans Imaging.

Helle Juhl Simonsen, Research MR Technologist, Biomedical Laboratory Scientist. Board member in ISMRM White Matter Study Group as SMRT representative, member of the Global Relation Committee, MR Safety Committee and Nominations Committee in International Society for Magnetic Resonance in Medicine (ISMRM)/Section for MR Technologists (SMRT). Board member of the Danish Society for Magnetic Resonance, member and service responsible. Member of RegionH’s MR safety committee, MR safety education group and MR contrast group.

Henrik B.W. Larsson, MD, DMSc, Consultant, Head of Functional Imaging Unit. Professor in Clinical and Comparative Physiology, Institute of Clinical Medicine, The Faculty of Health and Medical Science, University of Copenhagen, Denmark. Responsible for specialist course in tracer kinetic theory, math and statistic for nuclear medicine physicians. Responsible for specialist course in functional

imaging (MRI, PET-MRI, UL) for nuclear medicine physicians. Member of the Danish Multiple Sclerosis Research Council.

Julie Bjerglund Andersen, MD, PhD, Senior Registrar Board, member in Society for Junior Phycisians in Nuclear Medicine, a part of the Danish Society of Nuclear Medicine and Clinical Physiology. Coordinator for postgraduate education in junior doctors, Glostrup Section. Finishing specialty training in Nuclear Medicine 1. June 2021.

Ian Law, Professor, Consultant, is Senior member of the Neuroimaging Comittee, European Association of Nuclear Medicine (EANM), Member of the “PET Response Assessment in Neurooncology (RANO) working group” under the European Association of Nuclear Medicine (EANM), European Association of Neuro- oncology (EANO), and Society of Neurooncology (SNO). Member of the Danish Neurooncology group (DNOG) and the European Organisation for Research and Treatment of Cancer. (EORTC) Brain Tumour Group. Responsible for the specialist training course in the central nervous system for nuclear medicine physicians.

Jann Mortensen, Clinical Professor, Consultant, is responsible for the specialist course in “Clinical Respiratory Physiology” for nuclear medicine physicians and respiratory physicians. Responsible physician for Nuclear Medicine in the Faroe Islands, member of the steering committee of “Dansk Lungecancer Gruppe” (Danish Lung

Cancer Group), the subcommittees for “Dansk Diagnostisk Lungecancer Gruppe” (Danish Diagnostic Lung Cancer Group) and “Lungecancer Screeningsgruppen” (Screening of Lung Cancer Group), member of the steering committee and the quality subcommittee for creating Danish reference values for lung function, and member of the steering committee of the Danish spirometry course.

Johan Löfgren, Consultant, teaches at specialist courses for oncologists, endocrinologists, radiologists and nuclear medicine specialists. Member of the Diagnostic Imaging Group under Danish Lymphoma Group. Involved in clinical research protocols with special focus on PET/MRI and is an invited speaker at national and international meetings and congresses. Involved as a clinical expert in RIS/PACS and HIS on a local and regional level.

Kim Francis Andersen, Consultant, is Chairman of the Danish Sarcoma Group (DSG). He is involved in various clinical research protocols. He teaches at specialist courses for medical doctors and is supervisor for students at the Medicine and Technology programme (Biomedical Engineering), Technical University of Denmark (DTU).

Linda M. Kragh, Chief Nuclear Medicine Technologist, member of Sundhedsfagligt Råd i Klinisk Fysiologi og Nuklearmedicin i Region H, SFR, (the Speciality Advisory Committee in Clinical Physiology and Nuclear Medicine in the Capital Region), member of the DRG Committee of

Academic and other activities

DSKFNM, and member of Uddannelsesudvalget på Radiografuddannelsen at Metropol (the Speciality Council for the Education of Radiographers at Metropol).

Lise Borgwardt, Consultant, PhD. Chief of Pediatric Nuclear Medicine at Rigshospitalet, Senior Advisor of the Paediatric Committee under EANM, Scientific Committee member of the EANM, Boardmember of DAPHO for Diagnostic Imaging, Boardmember of BørneRigets Project Steering Group, Member of Radiology Committee EpSSG, Member of NM Committee SIOPEN, member of the Paediatric Imaging Harmonization Group EANM/ SNM, member of the Tumourboard for Paediatric Solid Tumours at Rigshospitalet, Chair of Danish Association of Paediatric Nuclear Medicine, Chair of the Paediatric Focus Group at the Department of Clinical Physiology, Nuclear Medicine and PET and member of the Process Group for the development of the Children’s Hospital at Rigshospitalet. Involved in clinical research protocols, supervisor for PhD students, teaching at national and international courses pre- and postgraduate for medical doctors, and invited speaker at national and international meetings and congresses.

Liselotte Højgaard, Professor, Head of Department, member of the Board, Die Robert Bosch Stiftung, Germany. Member of the Board of Directors, The Novo Nordisk Foundation. Member of the ERC Scientific Council. She represents the University of Copenhagen, Rigshospitalet in the

Medicine and Technology Bioengineer program, the Technical University of Denmark (DTU), where she is also adj. professor. Elected member of the Royal Danish Academy of Sciences and Letters, elected member of ATV, “the Danish Academy of Technical Sciences”, member of the Olav Thon Foundation, Science Advisory Board, member of the Board of the Crown Prince Frederik and Crown Princess Mary’s Foundation and member of the Board of Arvid Nilsson’s Foundation and Chair of Tagea Brandt’s prize.

Malene Fischer, Associate Professor of Research, Consultant, is supervisor for several PhD, master and bachelor students and involved in both pre- and postgraduate teaching. Member of the European Association of Nuclear Medicine (EANM), European Society of Hybrid Imaging (ESHI) where she is treasurer and member of the board, the Danish Society of Clinical Physiology and Nuclear Medicine (DSKFNM) and the Danish Society of Clinical Oncology. Affiliated to the Centre of Excellence for Personalized Medicine of Infectious Complications in Immune Deficiency (PERSIMUNE). Work package leader in the HYBRID Network; a collaboration for research and training of young researchers in the field of hybrid imaging, funded as a Marie Skłodowska-Curie Innovative Training Network under EU Horizon 2020. MF is a member of the ”Hybrid, Molecular and Translational Imaging” committee for the European Conference of Radiology 2022. Since June 2018 holding a joined position as Senior Clinical Lecturer and honorary

Consultant at the PET Centre, Guy’s & St Thomas Hospital, Kings College London in UK.

Maria Helene Pejtersen, Staff Nuclear Medicine Technologist, is member of the Symposiagroup for Technologists at Rigshospitalet.

Nic Gillings, MPhil, PhD, Chief Radiochemist, Qualified Person (QP) is vice chair of the EANM Radiopharmacy Committee, member of the editorial board of EJNMMI Radiopharmacy and Chemistry, member of the Society of Radiopharmaceutical Sciences and member of the Royal Society of Chemistry. He also acts as coordinator for the joint supplier audit program for all manufacturers of PET radiopharmaceuticals in Denmark and Southern Sweden.

Otto Mølby Henriksen, Consultant, PhD, is member of the DRG Committee in Danish Society for Clinical Physiology and Nuclear Medicine (DSKFNM) and member of the Danish Epilepsy Surgery Team. He is co-supervisor of two PhD students and teaches at PhD courses as well as pregraduate courses for Medicine and Technology Bioengineers.

Peter Oturai, Consultant, is responsible for the postgraduate education of physicians in the department. He is head of the Doctors Clinical Physiology and Nuclear Medicine (CPNM) Training Committee affiliated to DSKFNM. He is responsible for the specialist course in Endocrine Pathophysiology for CPNM physicians in Denmark.

Rasmus Sejersten Ripa, Consultant, DMSc, Supervisor for several PhD students. Member of the Danish Health Authority’s Committee for Heart Disease. Board member of the Society for Theoretical and Applied Therapy and member of American Society of Nuclear Cardiology. Editorial Board Member “Diagnostics”, Section editor “Frontiers in Endocrinology”.

Robin de Nijs, MSc, PDEng, PhD, Medical Physicist, is member of the Danish Society for Medical Physics and lecturer at the Technical University of Denmark, Copenhagen University and for the association of physics teachers. Supervisor for under- and postgraduate students in a.o. Medicine & Technology and Medical Physics. Associated Medical Physics Expert for the SPECT brain scan section of the Neurobiology Research Unit at Copenhagen University Hospital.

Ronan M.G. Berg, MD, DMSc, Staff Specialist and Associate Professor of respiratory physiology at the University of Copenhagen, Visiting Professor at the University of South Wales, UK, scientific co-editor at the journal Physiology News (London, UK). Member of several scientific societies including the Physiological Society (UK) and the Danish Society of Medical Philosophy, Ethics and Methodology. He has previously received the prestigious Pfizer Prize from the Physiological Society for his contributions to the physiological sciences. He teaches physiology, nuclear medicine

and medical ethics at both pre- and postgraduate levels, and handles scientific supervision on bachelor, master, and PhD levels both in Denmark and in the UK.

Sune Høgild Keller, Computer Scientist, PhD, is involved in various clinical and preclinical research protocols and scientific development in PET/CT, PET/MR and neuro-PET (HRRT). He teaches at a variety of courses for medical doctors, PhD students, technologists and MSc students. He is supervisor for students at the Medicine and Technology program (Biomedical Engineering), Technical University of Denmark (DTU) and co-supervises PhD students in biomedical engineering and computer science.

Søren Holm, Senior Physicist, is chair of the EANM Radiation Protection committee. He is a delegate for the Danish Medical Physics Society (DSMF) to the European and International organizations for Medical Physics (EFOMP and IOMP), assessor for EFOMP’s Examination Board (EBB), member of an IAEA advisory group concerned with QA/QC of non-imaging nuclear medicine equipment and member of ICRP Task Group 117 for radiation protection in PET and PET/CT. He is member of Sundhedsfagligt Råd i Klinisk Fysiologi og Nuklearmedicin in the Capital Region, (the Specialty Advisory Committee (SFR) in Clinical Physiology and Nuclear Medicine) and external lecturer at University of Copenhagen.

Thomas Levin Klausen, Chief Physicist, MSc, Specialist Medical Physicist, member of the Danish Society for Medical Physics (DSMF) and the Danish Society of Clinical Physiology and Nuclear Medicine (DSKFNM). Responsible Physicist for Nuclear Medicine at the Faroe Islands.

Thomas Lund Andersen, MSc, PhD., Medical Physicist, is member of the Danish Society for Medical Physics (DSMF) and the Danish Society for Medical Magnetic Resonance (DSMMR). Involved in various clinical and preclinical research protocols and the scientific development of PET/MRI.

Ulrik B. Andersen, Consultant, Co-supervisor for PhD students in the department. Member of European Society of Hypertension and acknowledged hypertension specialist by this society. Expert in vascular ultrasound and responsible for the specialist course in vascular ultrasound for nuclear medicine physicians in Denmark. Member of the Danish Society of Clinical Physiology and Nuclear Medicine, Danish Society of Cardiology and Danish Society of Diagnostic Ultrasound.



Professor Jann Mortensen and Associate Professor Ronan Berg

Research

The COVID-19 pandemic was a world-changing event that had a major impact on scientific communities and the conduct of science everywhere, including our department which houses several research groups. But science is agile and indeed driven by change, and at a time like this science is more important than ever. So despite the irrefutable challenges that we have all had to face, and due to the dedication of our many scientists on all levels, we have maintained our comprehensive research program directed at developing innovative solutions to solve unmet clinical needs. Our research program is built on our strong in-house competencies as well as on strategic collaborations with leading international and national research groups with complementary competencies and capabilities. Even though many of our scientists with medical backgrounds were reallocated to clinical duties at other departments

during 2020, we and our collaborators have been involved in COVID-19 studies on the mechanisms and fundamental pathophysiology, diagnostics, prognostication, and rebalitation of COVID-19 studies across all our current major research themes which are highlighted below.

New tracers

Several projects aimed at developing new PET tracers for non-invasive tissue characterization and phenotyping are ongoing. These novel tracers will be used both for diagnosing, staging and risk stratification as well as for therapy planning and monitoring. Tracers developed and already taken first-in-humans at our department include ⁶⁴Cu-DOTATATE, ⁶⁴Cu-DOTA-AE105, ⁶⁸Ga-NOTA-AE105, ⁶⁸Ga-NODAGA-RGD₂ and ¹⁸F-ASIS. Some of these tracers have now moved into phase II clinical trials to investigate and establish their

clinical utility and where they may be of particular value to patients. Accordingly, ⁶⁸Ga-NOTA-AE105, a PET tracer targeting uPAR, which is a marker of cancer aggressiveness and metastatic potential has been tested in three completed and six ongoing phase II trials in various cancers. Likewise, ⁶⁸Ga-NODAGA-RGD₂, an angiogenesis PET tracer, is currently tested in Phase II clinical trials both within cancer and cardiovascular disease. To facilitate development and clinical translation of new PET tracers, we have over the years built a comprehensive platform for validation of novel tracers, including facilities for cell work, molecular biology (proteomics and genomics), histology, biomarker measurements and predictive relevant animal models. We have other promising new PET tracers in our developmental pipeline and expect a continuous translation of the best of these into clinical use over the coming years.

PET/MRI

Being one of the first departments to install a combined PET/MRI scanner, we have established a comprehensive research program on PET/MRI with focus on the added value of combining molecular imaging with PET and multiparametric MRI. A large number of clinical trials have been finalized or are ongoing with this purpose. The ambition is to improve tissue characterization and response monitoring ability in cancer treatment, pediatric studies, brain studies and atherosclerotic plaque characterization. Focus of MRI includes the use of diffusion weighted images (DWI) / apparent diffusion coefficient (ADC) and magnetic resonance spectroscopy (MRS) especially with the use of hyperpolarized molecules. With access to matching preclinical PET and 7T MRI, we can work translational in developing and evaluating new methods. As an example, the use of PET/MRI for radiation therapy planning and response monitoring is being evaluated both preclinically and clinically.

HyperPET

Our department was the first to install a dynamic nuclear polarized (DNP) for hyperpolarization of ¹³C-labeled compounds next to a PET/MRI scanner. We have used this set-up for development of and research in the combination of hyperpolarized ¹³C-MRS and PET, a combination we named *hyperPET*. So far, we have focused on the use of hyperPET for tissue characterization in cancer,

cardiovascular disease and inflammation/infection. Using ¹³C-pyruvate, we have continued our studies of the Warburg effect and its relation to glucose uptake as measured by FDG. Recently, we also combined ¹³C-pyruvate with a non-FDG PET tracer, i.e. the angiogenesis tracer ⁶⁸Ga-NODA-GA-RGD₂. In addition, we studied non-pyruvate ¹³C-compounds, e.g. ¹³C-fumarate which is an indicator of necrosis. Based on our results obtained so far, hyperPET is superior in cancer phenotyping and response monitoring, and has the potential for future clinical use.

Clinical PET/CT in oncology

A large number of prospective clinical protocols aimed at evaluating the diagnostic and prognostic value of PET/CT using various tracers, including those developed in-house, are currently undertaken. The studies are performed in cancers, both in children and adults. Head-to-head comparison of new PET tracers and established imaging methods is also an area of interest. Currently, the use of PET/CT for the planning of radiation therapy (“dose-painting”) and the use of respiratory gating are also being evaluated. Many of these studies also include PET/MRI to study the added value compared to PET/CT.

Pediatric nuclear medicine investigations

The department undertakes many pediatric investigations, and is involved in a wide array of pro-

spective clinical trials using both PET and SPECT in collaboration with clinical pediatric departments. These ongoing studies particularly focus on diagnostics and treatment of pediatric cancers and infections with FDG-PET, as well as functional assessments of the hepato-biliary system and renal function. Also, targeted radionuclide therapy for cancer in children is currently an area of intense interest. Finally, the use of PET/MRI in children to save radiation dose is studied.

Neuro-PET

Over the past year, the research focus has mainly been on clinical method development in brain tumors and dementia classification, as well as non-invasive assessments of the molecular characteristics and growth of meningioma, and the detection of small tumor remnants after treatment. Furthermore, we have been engaged in tumor perfusion mapping using predominantly PET/MRI. In cooperation with the Neurobiology Research Unit and Centre for Integrated Molecular Brain Imaging, neuroreceptor ligands in the serotonergic system have been developed and used for research in neurobiology.

Functional MRI

We have conducted several functional MRI-based studies on tissue perfusion, flow in large vessels, oxygen consumption, integrity of the blood brain barrier, vascular reactivity, functional brain

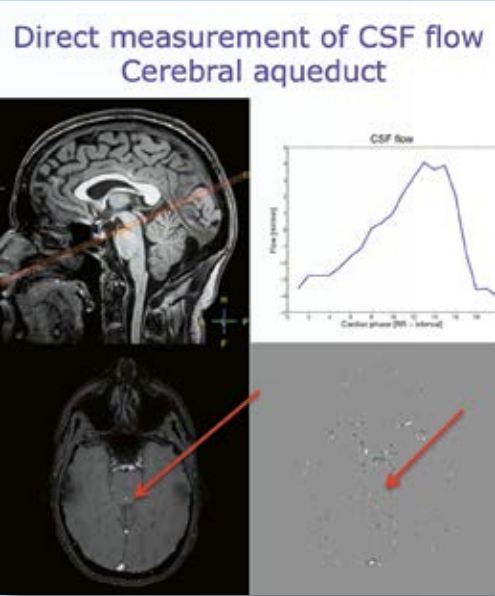


Figure 1. The figure shows an example of measuring the flow in the cerebral aqueduct. Upper left: A sagittal slice showing the slice position for flow measurement, shown lower left. Lower right: One velocity encoded frame out of 20 -same slice position as lower left - gray scale represents velocity, where uniform gray corresponds to zero velocity. Upper right: instantaneous flow as function of cardiac cycle. Flow changes from caudal (negative) to cranial direction (positive). Integrated net flow is in caudal direction.

centers, brain networks and metabolites such as lactate, glutamate and GABA (**Figure 1**). These studies provide important information in our research focusing on brain degenerative, inflammatory and cancer diseases. Many of these studies are undertaken in close collaboration with clinical departments within neurology and psychiatry. A particular area of interest is development of new methods and clinical application of new functional and molecular MRI methods. Methods are aimed at obtaining information on tissue physiology, organ perfusion, and molecular biology. Currently we are in the process of applying these functional methods to the kidney, liver and heart enabling us to open up new avenues into the study of hypertension, renal failure, diabetes mellitus and obesity.

Atherosclerosis

Non-invasive visualization of atherosclerosis and prediction of plaque vulnerability in atherosclerosis using PET/MRI and PET/CT is intensively studied both preclinically and in clinical studies. The quantification of low-grade vascular inflammation has become a focus area and is now used in several clinical trials on cardiovascular risk and mode-of-action studies of different therapies, like GLP-1 antagonists. In addition, patient groups at risk are studied and special focus is on the value of new specific

PET tracers, e.g. for the study of macrophage activation by ⁶⁴Cu-DOTATATE. Clinically, our ambition is to provide image-based risk stratification to select patients that will benefit from vascular surgery. We continue to refine and develop vascular imaging using novel PET tracers.

Nuclear cardiology

Taking advantage of the ability to quantify myocardial perfusion in absolute terms and myocardial flow reserve by ⁸²Rb PET, we study these parameters in various cardiovascular diseases. This includes studies on how interventions as stem cell therapy, gene therapy and pharmacological treatment affect myocardial perfusion and integrated vasomotor function. The development of ischaemic heart diseases is studied in selected groups of patients, e.g. patients with diabetes. In addition we study the value of new specific PET tracers, e.g. for the study of myocardial angiogenesis by ⁶⁸Ga-NODAGA-E[c(RGDyK)]₂. On basis of this, better screening algorithms for early detection of ischaemic heart disease are developed.

Lung studies

A large number of studies using lung function testing and lung scintigraphy (VQ-SPECT/CT) in different patient groups are ongoing, e.g. studies in COVID-19, lung transplantation and lung volume reduction treatment of emphy-

sema, thus taken advantage of the superior diagnostic performance of VQ-SPECT/CT compared to CT alone as previously demonstrated by us. We have also conducted studies on the pulmonary immunology of COVID-19, as well as several studies on mucociliary clearance, a method pioneered at the department, of the nose and lungs. Finally, we are participating in a large study collecting data for a lung function test reference database.

Studies of muscle function

With the use of methods from clinical physiology, nuclear medicine, MRI and molecular analyses, muscle function, bone density, and body composition have been studied with a current focus on the effects of exercise, immobilization, and aging. Data collected on the same parameters form a population-based study, that serves as a reference database and which may elucidate markers to predict aging-related diseases.

Immune cell tracking

At present, a particular focus is on development of new imaging tools for non-invasive visualization of the immune response and for tracking immune cells. These methods will be used in studies of inflammation, infection, rejection and in particular immune oncology. Our department is a key participant in the PERSIMUNE program funded by the Danish National

Research Foundation. Currently, special attention and support from the PERSIMUNE program is given to development and use of new PET ligands for specific imaging of the immune response, e.g. CD4, CD8 and macrophage imaging. Within immune oncology, these tracers will serve to better understand the mechanisms behind immune responses in cancer and as a tool to select patients eligible and likely to respond to specific immunotherapies.

Radionuclide therapy and theranostics

An ever increasing attention is directed towards development and use of targeted radionuclide therapy using both beta- or alpha-emitting specific ligands targeting relevant cancer characteristics. The department takes part in research within this area by testing new ligands and producing relevant therapeutic isotopes. Most notably, we also in-house develop new theranostics based on promising imaging ligands, which are then labeled with beta- or alpha emitting radionuclides. Cancers that are currently being targeted clinically include glioblastomas, neuroendocrine tumors, prostate and colorectal cancer. Development of therapeutic radioligands is largely based on imaging with the same ligand as the therapy (theranostics). The concept of a tracer that visualizes the target prior to starting therapy is also known as companion diagnostics.

Image guided surgery

Image-guided cancer surgery using optical probes is a relatively new concept. In collaboration with several surgical departments, we develop our most promising PET ligands targeting cancer specific targets into near-infrared (NIR) optical probes. These are used for intraoperative delineation of cancer to better ensure negative (free of cancer cells) surgical margins and to spare critical functional tissue, e.g. during brain surgery. The technology of image-guided cancer surgery is expected to lead to better patient outcome, including overall survival and improved quality of life. Within this field, the department participates in the Clinical Academic Group – Imaging-Guided Cancer Surgery (CAG-IGCS). We expect the optical methods to work in synergy with PET, as a preoperative PET will predict whether use of optical imaging of the same target is feasible. We expect the optical technologies to become enablers of performing semi-automated robotic in the future.

Whole body counting

Together with external collaborators, we apply whole body counting for precise measurements of body composition. Moreover, studies on the absorption of certain minerals from the gastrointestinal tract are undertaken.

Clinically applied artificial intelligence

We study how to exploit artificial intelligence in medical imaging (**Figure 2**). These studies cover most of the imaging modalities and disease areas in the department, e.g. oncology, brain, cardiovascular and radiation therapy. Examples of studies performed includes generation of synthetic CT from MRI scans for PET attenuation correction and RT dose planning, noise reduction applied to reduction of radiotracer doses, or outcome prediction, segmentation, and classification in order to support image reading including artificial intelligence-driven image derived biomarkers.

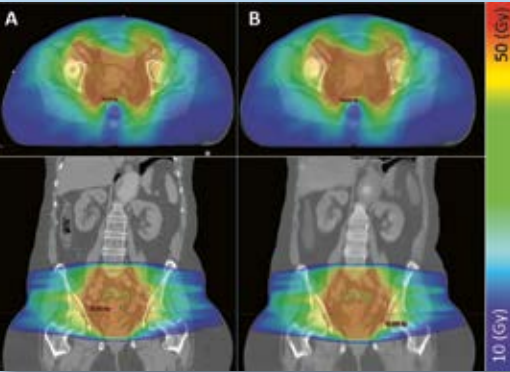


Figure 2. A) Dose plan calculated from CT-image. B) Dose plan calculated from PET/MR derived synthetic CT using AI.



Professor Andreas Kjær

Cluster for Molecular Imaging

The paradigm of precision medicine, i.e. tailoring therapy to the disease characteristics of the individual patient, has caused a need for diagnosing at the molecular level. Standard molecular biology methods rely on tissue sampling for in vitro and ex vivo analyses and are prone to samples not being representative. In contrast, molecular imaging allows for non-invasive studies at whole-body level and elegantly circumvents sampling error. Due to the unsurpassed sensitivity of PET and the possibility to quantify tracer uptake, the technology holds great promise for molecular imaging of phenotypic characteristics as a basis for practicing personalized medicine. Among characteristics, which can be visualized are the hallmarks of cancer, e.g. cancer aggressiveness, angiogenesis, and interaction with the immune system. We predict that such PET ligands will be game changing within many diseases including cancer and cardiovascular disease. Moreover, successful PET imaging ligands may be “modified” into tar-

geted radionuclide therapies if labeled with α - or β -emitting isotopes or into optical imaging ligands for guiding surgery.

At present, our translational molecular imaging and theranostics research program focuses on development and application of new molecular imaging and therapeutic ligands to support precision medicine.

Cluster for Molecular Imaging was established in 2003 at the University of Copenhagen (Panum Institute) and started out as a specialized facility for molecular imaging in animals using PET, SPECT, CT, MRI and optical imaging. Over the years, it was further developed into a comprehensive translational platform to support the development of new PET tracers and radionuclide therapies. Testing in animal models forms the basis for ligand selection and translation into clinical use. We currently have a broad pipeline of PET tracers and radionuclide

therapies in pre-clinical development and expect several of these candidates to be taken into clinical testing and human use over the next years.

Development of predictive animal models, e.g. orthotopically implanted human xenograft tumors as well as metastatic cancer models is a core competence. Most recently, through collaborations, we added models of diffusely infiltrating glioblastomas as well as models for testing ability of new ligands to cross the blood-brain-barrier.

With the increasing use of immunotherapies, in particular checkpoint inhibitors that support the immune system to fight cancers, we have established numerous models of syngeneic cancer animal models. The goal is to unfold the immense potential of immunotherapies that are currently hampered by low response rates. For this purpose, we have focus on development of immune cell tracking with imaging ligands, e.g. targeting



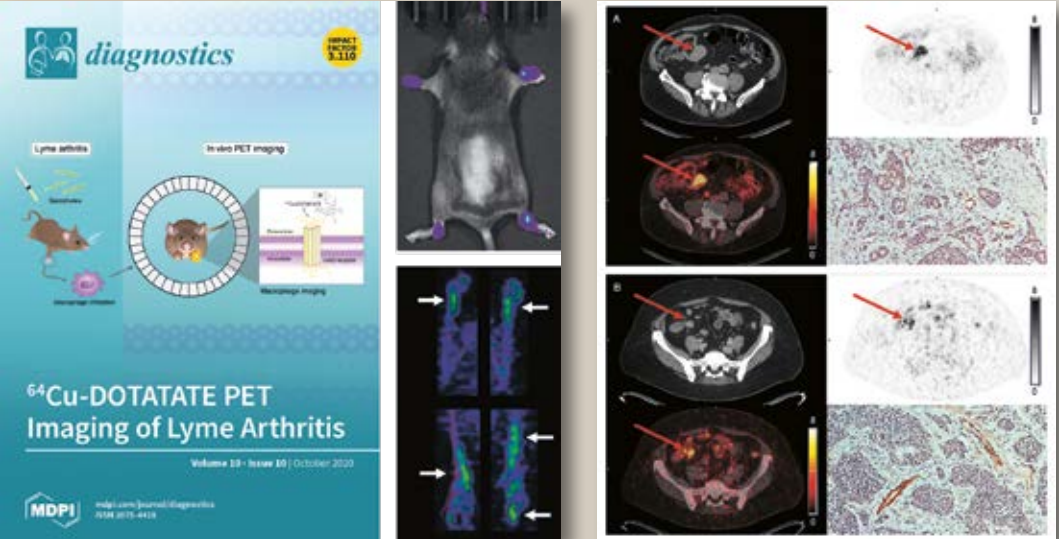


Figure 1. Use of macrophage imaging in infectious arthritis. In vivo bioluminescence imaging *B. burgdorferi* infection (upper right) and ^{64}Cu -DOTATATE macrophage imaging (lower right) in a *B. burgdorferi*-infected mouse. Note the clear accumulation of bacteria (spirochetes) in the joints as well as local macrophage response in same locations. The method holds promise for use in monitoring of disease activity in patients with Lyme borreliosis. The study made it to the front page of the October issue of *Diagnostics* (left). (Clausen AS et al. *Diagnostics* 2020).

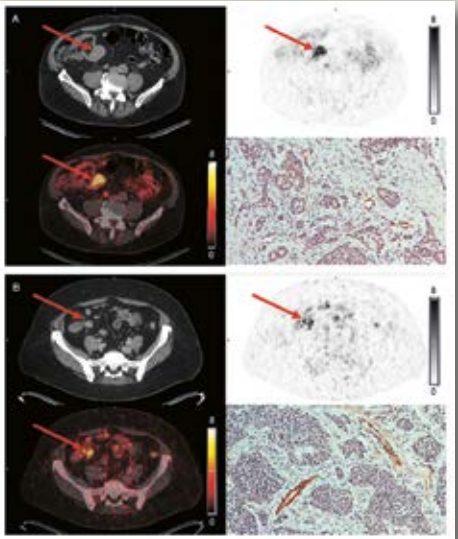


Figure 2. Angiogenesis PET imaging in a neuroendocrine tumor patient using our in-house developed radiotracer. (A) Representative transverse CT, PET and co-registered PET/CT images of primary tumor lesion (red arrows) with a high uptake of ^{68}Ga -NODAGA- $\text{E}[\text{c}(\text{RGDyK})]_2$ in a small intestinal primary tumor. Lower right image reveals high intensity immunohistochemistry staining of $\alpha_5\beta_3$ integrin (images provided by Clausen M, Carlsen EA et al.).

T-cells (CD4) or cytotoxic T-cells (CD8). With this platform, we have been able to predict the response to checkpoint inhibitor blockade in various cancer models and are convinced that this technology may serve for identify likely responders to immunotherapy. In addition, we have demonstrated how “priming” with radiotherapy increased the T-cell (CD8) infiltration of tumors and improved survival after use of checkpoint inhibitors.

PET tracers that track immune cells may also be used outside immune oncology, e.g. in inflammation and infection. Accordingly, we recently demonstrated how imaging of CD4 T-cells could be used to visualize collagen arthritis in an experimental model of human rheumatoid arthritis. Also, imaging of macrophages using a somatostatin receptor binding ligand could demonstrate active infectious Lyme arthritis (Figure 1).

We have established animal models of atherosclerosis, myocardial infarction and heart failure, with reduced or with preserved ejection fraction, for the study of cardiovascular disease and the effect of intervention with novel therapies, e.g. stem cell and GLP-1 therapy. Many of the models include advanced surgical procedures. We apply various PET tracers for the study of different aspects of cardiovascular disease and for prediction of outcome that may be used for tailoring therapies.

One area of interest has been imaging of angiogenesis, which is important both in cancer (Figure 2) and cardiovascular disease and is likely to become

game changing in management and personalization of angiogenesis-modifying therapies. In cancer, the goal is to inhibit angiogenesis whereas the goal in cardiovascular disease in general is to stimulate neoangiogenesis, e.g. by stem cells following myocardial infarction.

Another focus area has been targeting uPAR, a marker of cancer aggressiveness that can both be used for prognostication but potentially also as a target for radionuclide therapy. We have studied the uPAR-PET tracer in various cancers and most recently demonstrated that uptake in prostate cancer correlates with Gleason score.

Optical imaging has recently gained momentum as it can be used for guidance in cancer surgery. We have developed some of our promising ligands used for PET into optical probes. Accordingly, the peptide used for uPAR binding in PET has demonstrated ability to delineate tumor margins in several orthotopic xenograft tumors models, e.g. glioblastoma and pancreatic cancer.

Finally, an increasing focus is currently on developing new radionuclide therapies. Using small animal SPECT, it is possible to visualize, e.g. ^{177}Lu -labeled radionuclide therapy ligands to investigate biodistribution and binding to tumors. In addition, we are approved by the authorities to perform animal experiments using α -emitting therapy, which is more effective due to the high linear energy transfer (LET). Efficacy of these therapies are tested in relevant, predictive human tumor models.





Professor Jann Mortensen and Chief Physicist Thomas Levin Klausen

Collaboration with The National Hospital of the Faroe Islands

Landssjúkrahúsið was founded in 1924 in Tórshavn. It was originally named Dronning Alexandrines Hospital after the Danish Queen. In the 1960's the hospital was expanded and officially declared the National Hospital of the Faroe Islands. Recently it merged with the two smaller hospitals in Klaksvík and Tvøroyri into one hospital system with joint leadership. The National Hospital of the Faroe Islands serves The Faroe Islands population of 52,000.

The National Hospital has 900 employees and 160 beds. The 9,500 in-patients and 115,000 out-

patients visits annually are taken care of by 29 medical specialities, of which 9 are via consultant collaborations, including collaboration in clinical physiology and nuclear medicine with our department at Rigshospitalet.

Second opinion on scintigraphies and lung function measurements is provided via a direct telemedicine connection. The responsible physician and physicist for Nuclear Medicine in Tórshavn is Professor, Consultant Jann Mortensen, DMSc and Chief Physicist Thomas Levin Klausen.

In 2020, the Department of Clinical Physiology and Nuclear Medicine in Tórshavn performed around 1,300 patient examinations even though it was a COVID-19 year: 477 scintigraphies of lungs, bones, thyroid, kidneys and renographies with the department's old 2-headed Skylight camera; 232 lung function tests (spirometry, body plethysmography and diffusion capacity for CO) were performed with the Jaeger whole body plethysmograph; and 587 routine and research DXA studies (BMD and body composition) were performed with The Norland DXA 840 scanner.



Neurobiology Research Unit

We appreciate the excellent collaboration with Professor Gitte Moos Knudsen, Head of the Neurobiology Research Unit (NRU) at Rigshospitalet, University of Copenhagen and also Director of the Lundbeck Foundation's Center for Integrated Molecular Brain Imaging (CIMBI) and Innovation Fund Denmark Center for Experimental Medicine NeuroPharmacology (NeuroPharm). The research focus of NRU is neurobiology, physiology and pathophysiology, molecular imaging and neuroreceptor ligands with focus on the serotonergic system.

nru.dk | cimbi.dk | neuropharm.eu





Bioengineer in Medicine and Technology

In cooperation with the Technical University of Denmark (DTU) and the University of Copenhagen (KU), the department represented by Professor Liselotte Højgaard is involved in the Bioengineer program in Medicine and Technology at bachelor and master level. You can read more about the program at dtu.dk/bme.

At present several of the bioengineers are seconded to the department as PhD students, and we have numerous students working with bachelor and master reports in collaboration with DTU.



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Going green

