Rigshospitalet

Department of Clinical Physiology and Nuclear Medicine

Annual Report 2022

Rigshospitalet · University of Copenhagen

Rigshospitalet
King Frederik V founded Rigshospitalet in 1757. Today it has app. 1,100 beds and 13,000 employees. Research at Rigshospitalet is published in more than 3,500 peer review papers per year, including >100 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

REGION Rigshospitalet

DTU

UNIVERSITY OF COPENHAGEN

Contents

Preface

2022 was the third year with Corona. In winter the Omicron wave swept across the country and patients and staff were sick. In spring it vanished again.

May 10th we celebrated a happy event unveiling the portrait of Birthe Meyer. Birthe attended with her daughter Gitte Meyer Brandt, and sons Jens and Henrik Meyer, all from The John and Birthe Meyer Foundation, our patrons through the last 30 years.

The same evening a dramatic accident happened: A leaked water hose poured 30 tons of water on PET scanners in the Finsen building. The accident caused a mess and it has taken us more than half a year to repair. We managed to keep up patient flow and research due to an impressive and dedicated effort from our PET staff and help by other sections of the department. It has been a tremendous effort from everyone.
A BIG THANK YOU.

June 21st we received a donation 19.5 mio.kr. from The John and Birthe Meyer Foundation for a new cyclotron. We are immensely grateful.
A BIG THANK YOU.

We could participate in meetings and conferences again when Corona disappeared. Many participated in ESTRO in Copenhagen in May, EANM in Barcelona in October, DSKFNM in Elsinore in September and several other national and international meetings. It was a joy to learn and to share new knowledge with colleagues and gather news from abroad.

In 2022 we continued wasting time with the old Agfa RIS/PACS, but fortunately The Capital Region of Denmark promised a new system to all the hospitals in the region. We participated in the procurement and preparations of a new system, which will be from SECTRA, and implemented in Bispebjerg Hospital, May 2023, and Rigshospitalet November 2023 – if all goes well. Thank you to the many experts from the department working with this.

Patients and research are key activities with a comprehensive research program directed towards innovative solutions to solve unmet clinical needs in collaboration with other research groups here and internationally. To all our research groups: A sincere thank you for the dedicated, impressive and important work.

Thank you very much to Center Director Helle Konradsen, MD, DMSc, and Vice Director Lene Ørnstrup Christensen for help, support and collaboration throughout the year. Thank you to the Department of Radiology, Head of Department Martin Lundsgaard Hansen, and Chief Radiographer Johnny Madelung, for an excellent collaboration throughout the year

We would like to praise the great achievements of our staff from the youngest newly arrived technologist to the most senior professor. We are all "clinician scientist" working in one big interdisciplinary team effort, where everyone is engaged and striving towards the best patient treatment, research, innovation, education – in a positive and friendly working environment.

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 – in this Corona year 3.

Liselotte Højgaard, MD DMSc
Professor, Head of Department

Ida Kjær Robsøe, MPG
Chief Nuclear Medicine Technologist

Mission and objectives

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

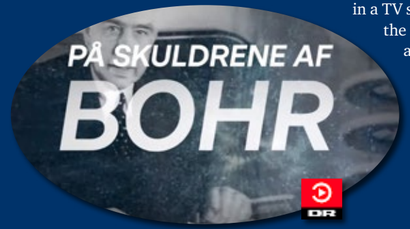
- Clinical physiology and nuclear medicine patient investigations and treatment
- Research at the highest international level
- Undergraduate and postgraduate education
- Good patient experiences through state-of-the-art quality, high patient security and focus on the wellbeing of each patient
- The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

Highlights 2022

Prof. Malene Fischer, Inaugural lecture, September 2nd 2022.

ESTRO Honorary Membership May 2022 to Prof. Liselotte Højgaard as an acknowledgement of exceptional contribution to Radiotherapy and Oncology.

Annette Foldager, 40 years anniversary November 2022.



Our department was portrayed in a TV series celebrating the 100 years anniversary of Niles Bohr's Nobel Prize.

On 26th of January Dr. Stig Præstekjær Cramer received a grant of 75.000 kr from the Torben Fog and Erik Triers Foundation as a recognition of his important scientific contribution to research on the blood-brain barrier's influence on multiple sclerosis.

Dr. Peter Oturai, Chief Physician and leader of education in our department was honored by The "Scintillator Prize" from DSKFNM, The Danish Society of Clinical Physiology and Nuclear Medicine, for his excellent effort for education of NM physicians. He is also a musician, and entertained the whole congress with his orchestra.

Prof. Henrik Bo Wiberg Larsson received 5,5 mio kr from Sygeforsikringen "danmark" (Health Insurance "denmark") for a new project regarding MRI and brain damage after trauma -post commotio syndrome.

Educational day of the Year , June 17th 2022 with lectures at Rigshospitalet followed by summer party at Dyrehavsbakken.

Prof. Jann Mortensen, 25 years anniversary November 2022.

DSKFNM 40 years anniversary meeting took place September 2022. A new Danish textbook on clinical nuclear medicine was launched on the occasion.

EANM annual congress, Barcelona, October 2022. After years with Corona it was finally possible to participate in scientific meetings and congresses again. Posters and oral presentations from our department covered many aspects of nuclear medicine.

Inaugural lecture

On 2nd September 2022 professor Malene Fischer gave her inaugural lecture in auditorium 2 at Rigshospitalet. The lecture gave an elegant overview of the broader development of hybrid imaging in oncology as well as examples of Malene Fischer's research and the impact this have had, especially on patients with lung cancer. The lecture was followed by a well-attended reception.

Malene Fischer returns from a position as senior lecturer at the School of Biomedical Engineering and Imaging Sciences at Kings College London and honorary consultant at The PET Centre at Guy's & St Thomas Hospital in London. In her role as professor, Malene Fischer will be responsible for oncology PET research, PET/MR, implementation of Quadra PET/CT as well as leading her research group CRHIC (Clinical Research on Hybrid Imaging in Cancer). CRHIC works to improve treatment of patients with cancer thru improved diagnosis and tissue characterization.

Nuclear medicine technologists, radiographers, nurses, and laboratory technicians

Chief Nuclear Medicine Technologist, MPG Ida Kjær Robsøe

First of all a warm thank you, to all our technologists, radiographers, nurses and laboratory technologists. Every day they welcome patients, and act with a high professionalism in both communication and technical procedures when carrying out clinical examinations, taking into considerations the individual patients' needs.

You have all done a great job, and several of you have had the opportunity to participate in meetings and congresses for the last 12 months. Some of you contributing with presentations and posters:

Anne Viktoria Setterberg, Caroline Rena Lind Hansen, Eunice Sanchez Saxtoft, Christina Schulz, Lume Rexhepi, Astrid Lysemose, Susan Al-Atabi Stensgaard, Vibeke Jensen, Susanne Svalling, and Kristin Varpe have all presented posters or oral presentations at EANM, DSFNM and the Technologist´s Symposia 2022.

Thank you for your great contribution and for representing us so well.

We successfully started an in-house PET-course dedicated to experienced technologists, nurses and radiographers. We are fortunate to having local physicists, chemists and MD teaching us. It is our aim to expand with more topics for experienced staff in 2023.

This year we were pleased to congratulate Annette Foldager on her 40 years anniversary as technologist and clinical teacher in the department. Annette joined us in 1992 and is highly valued for her many years at Glostrup Hospital and especially for her dedicated contribution to clinical training and education

KF section

Head of Section, Consultant Lotte Hahn Enevoldsen and Nuclear Medicine Staff Technologist Mariam Hassan

The KF Section at Blegdamsvej offers a broad variety of nuclear medicine examinations. Among these are SPECT/CT and scintigraphy for various oncological, pulmological, endocrine and nephrourological diseases. Other frequent investigations are PET/CT for cardiac, neuroendocrine, and pediatric diseases. Furthermore, DXA-scan for bone mineral density, lung function test and DTPA-clearance for GFR measurement are performed in our department. Diagnostic ultrasound is used in estimating LVEF in patients receiving potentially cardiotoxic chemotherapy and as an adjunct in patients having thyroid diseases.

We continually focus on study quality and patient-friendly procedures. State-of-the-art nuclear medicine investigations are made possible by implementing new studies, new indication areas and acquisition of new equipment.

In addition to nuclear medicine diagnostics, our section also perform radionuclide therapy for patients with neuroendocrine tumours (177Lu-DOTATATE), patients with castration resistant prostate cancer and symptomatic bone metastases (Radium-223), and patients with benign thyroid diseases (Iodine-131).

Furthermore, we participate in various weekly and monthly multidisciplinary team conferences discussing neuroendocrine tumors, thyroid diseases, adrenal diseases, cardiac diseases, and lung diseases with our clinical colleagues.

In November, there were weeks where we received technecium-99m generators that provided only small quantities of activity and weeks where we received none at all. This greatly reduced our ability to provide examinations using nuclear medicine. Fortunately, we were able to compensate to some degree by performing a larger number of physiological examinations and PET scans.

Glostrup section

Head of Section, Consultant Lotte Hahn Enevoldsen and Nuclear Medicine Staff Technogist Charlotte Okkels

Offering a variety of nuclear medicine and clinical physiological examinations 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 Scanner Section we examine patients referred from both Glostrup and the PET Scanner Section with wholebody ^{18}F-FDG PET/CT scans as well as dedicated brain scans for Parkinson's disease.

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 diagnose renal artery stenoses in adults and children with Doppler ultrasound of renal arteries, receiving patients from the Capital Region of Denmark and the Region of Sealand, and participate in the multidisciplinary conferences on invasive treatment of renovascular disease in Eastern Denmark.

Diagnostic ultrasound is also used together with thyroid scintigraphy in patients with thyroid diseases.

We perform subacute examinations of the carotid arteries with Doppler ultrasound for plaques and stenoses in all patients entering the hospital with stroke or transitory ischemia as part of the National Stroke Prevention Program.

In cooperation with the Geriatric Falls Clinics we perform tilt table tests, 24-hour blood pressure measurements and DXA-scans for bone density, body composition and screening for sarcopenia.

We also perform tilt table tests to investigate autonomous neural dysfunction and unexplained syncopes.

Other physiological examinations offered are testing of lung function, blood pressure measurements on the extremities in patients with claudication or ulcers, as well as 24-hour measurement of systemic blood pressure for diagnosis and evaluation of hypertension in adults and children.

PET scanner section

Head of Section, Consultant Annika Loft Jakobsen and Nuclear Medicine Staff Technologist Maria Pejtersen

PET/CT has found its' natural place in the work around patients suffering from oncological or inflammatory diseases in helping to diagnose, stage and depict the right patients for the right treatment as well as monitoring their treatment.

Our new digital PET/CT scanners and the total body Quadra PET/CT with increased sensitivity and improved image quality at high scan speed enables us to increase throughput in order to meet the increasing demand from the clinical departments without compromising the high diagnostic quality of our images.

^{18}F-FDG PET/CT is the workhorse investigation for a vast amount of indications, but use of ^{68}Ga-PSMA-11 for prostate cancer patients is increasing and we have implemented 3'-[^{18}F]fluoro-3'-deoxy-thymidin (^{18}F-FLT) for discriminating radiation therapy induced inflammation from residual malignant disease in lung cancer patients. We also offer ^{18}F-FDG PET/CT for radiotherapy planning.

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 improving our knowledge to their diseases.

Cardiac investigations

Consultant Philip Hasbak

Our nuclear cardiology laboratory performs a variety of non-invasive cardiovascular imaging studies:

- ^{82}Rb-PET to assess myocardial perfusion for the presence of ischemia and scar and to evaluate the pumping function of the heart.
- Viability imaging using ^{18}F-FDG is used to assess how much heart muscle has been damaged by a heart attack or heart disease.
- ^{18}F-FDG, ^{68}Ga-DOTATOC and ^{99m}Tc-pyrophosphate are used to evaluate infiltrative cardiac disease (sarcoidosis/amyloidosis)
- In cardio-oncology patients receiving cardiotoxic cancer treatment three-dimensional (3D) echocardiography is our preferred echocardiography modality for the assessment of LVEF and cardiac volumes, but multigated acquisition nuclear imaging (MUGA) is still available for the assessment of LVEF in selected patients.

At Rigshospitalet there is a need to provide cardiac PET every day, because 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 revascularisation strategy. Patients with unstable angina or non-STEMI should be revascularised 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.

Lung investigations

Professor Jann Mortensen and Associate Professor Ronan Berg

Lung function tests such as dynamic spirometry, body plethysmography and diffusion capacity, bronchodilator test, and mannitol provocation test, and respiratory muscle strength are routinely performed at the Department. We are currently evaluating the use of impulse oscillometry (IOS) and the forced oscillation technique (FOT) for the assessment of respiratory mechanics and small airways disease.

In terms of imaging, we were the first to implement simultaneous ventilation-perfusion (V/P) scintigraphy as SPECT/CT for the diagnosis of pulmonary embolism. The high diagnostic performance of V/P SPECT/CT combined with a relatively low radiation dose is a benefit to the many patients that we study before and after lung volume reduction, lung transplantation, lung cancer, and for the 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.

In 2022, we published the first paper from the SECURe, in which we showed that the decline in pulmonary diffusion capacity observed after COVID-19 is caused by a fibrosis-like condition in the lungs rather than persisting pulmonary thromboembolic disease. Among our ongoing studies, we are currently developing the use of dual tracer diffusion capacity measurements during acute exercise and during postural changes as clinical indices of alveolar-capillary reserve in chronic lung disease. We have recently reported that this method has an excellent test-retest reliability in healthy volunteers and are currently evaluating it in patients with chronic obstructive lung disease and also after COVID-19. Such measures may potentially help us provide in-depth physiological and imaging-based phenotyping of patients, with the goal of optimizing prognostic stratification and guiding treatment.

Pediatric nuclear medicine

Consultant Lise Borgwardt and Consultant Kim Francis Andersen

The year 2022 was another busy year in terms of the number of pediatric nuclear medicine investigations performed. We strive for examinations with the highest level of excellence, while maintaining an environment facilitating the best possible experience for children and their parents.

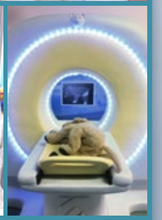
The vast majority of pediatric PET investigations are now performed on our LArge Field Of View (LAFOV) PET/CT-scanner, the Biograph Vision Quadra. The combination of ultra-high sensitivity and a long axial field of view, allows for reduced injections and/or shorter PET scan time of children. This does not only have a huge impact on radiation exposure, but also results in better cooperation with children and their parents – and importantly – it leads to a marked reduction in the need for general anaesthesia/sedation during the investigations. Hours of dedicated research and involvement in quality assurance projects throughout the year – including the application of AI – has led to optimized imaging protocols and all the other facets related to pediatric PET imaging.

We have started performing [18F]mFBG LAFOV PET/CT-scanning of children with neuroblastoma in a prospective trial comparing [123I]mIBG with [18F]mFBG and the images are of a fantastic quality. Preliminary results demonstrate that more neuroblastoma localisations were detected on [18F]mFBG LAFOV PET/CT compared to [123I]mIBG scintigraphy with SPECT/CT. The clinical benefit of [18F]mFBG LAFOV PET/CT is a one day protocol, much shorter scan time and avoidance of general anaesthesia/sedation in most children. [18F]mFBG LAFOV PET/CT shows promise for future staging and response assessment in neuroblastoma in children.

This year we continued treating children and adolescents for relapsed or retractory cancers with intrathecal radio-immunotherapy in a close collaboration with the team of paediatric oncology, performed in our unit for radionuclide treatments at our department and we also started up new protocolized treatments in children.

Copenhagen Children's Hospital is being build, and will be finished in 2025. This year it was named Mary Elizabeth's Hospital - Rigshospitalet for Children, Teens and Expecting Families after Her Royal Highness Crown Princess Mary. We will have a Diagnostic Unit with an integration of the diagnostic specialties in a 24/7 MultiDisicplinary Team (MDT), a professional forum for discussing the changing diagnosis and treatment of the individual child.

The Pediatric Nuclear Medicine Team is highly involved in international collaborations and organizations. Currently, team members are holding the positions as Chair of the Imaging Committee of EpSSG, SIOP Europe Steering Committee member of the Imaging Working Group and Leader of the Imaging & Radiomics Group, European Osteosarcoma Consortium - FOSTER (Fight Osteosarcoma through European Research). They are also involved in numerous other pediatric related national and international consortiums and research networks (SNITCH, DAPHO, DSG, SSG, EEC, DAPNM, EANM, SNMMI).



SUPER COOL SIBLINGS

In April 2022 Sandra Meinich Juhl aka the Teddy Bear Doctor (Bamselægen, from a Danish children's TV show), visited the department for the event Super Cool Siblings (Super Seje Søskende). The focus of the day was celebrating the siblings of children with chronic illness treated at Rigshospitalet. There were age-appropriate activities for 5-18 year-old siblings, and the youngest children could scan their teddy bear in a scanner in our department. The event aimed at supporting the families with chronically ill children. Parents were invited to participate in workshops and parent forums, encouraging a supportive network of parents of children with chronic illness to be established. The day was a huge success thanks to the dedicated work of everyone involved.

RIS/PACS

Consultant Johan Löfgren

The Capital Region of Copenhagen (RegionH) has had huge problems with our current RIS/PACS system since the first installation. Problems include slow performance, lack of stability, client crashes, speech recognition errors and few but alarming reports of patient mix-ups. The extra expenditure to our budget and negative influence on our daily workflow has been major.

Thanks to our Head of Department, Professor Liselotte Højgaard, and *Sundhedsfaglig råd* (the Speciality Counsel) for both radiology and clinical physiology and nuclear medicine in The Capital Region of Denmark, a political decision was made in 2022 to accelerate the implementation of a new RIS/PACS system.

The Capital Region of Denmark chose the Swedish RIS/PACS vendor Sectra after a tendering process, including negotiations and clarifications with three qualified vendors. Sectra is a company with more than 30 years' experience in RIS/PACS systems, a good reputation and a large customer base worldwide and in the Nordic countries. Jens Gordon, CEO of the Capital Region of Denmark, signed the contract May 3rd 2022, and the implementation process began.

The regional IT department and the hospitals' Imaging Departments work, in close collaboration with Sectra, to get set for a quick rollout, which will start with the regional breast cancer screening clinics in May 2023. The schedule is tight, and the plan is that all Imaging Departments will have switched over to the new RIS/PACS system before the summer of 2024. Rigshospitalet is planned to go live in November 2023.

Many experts from the Imaging Departments are spending a lot of time and effort to secure well-functioning workflows and integrations, including migration and transition from the current system. I have had the privilege of co-chair this "Clinical Working Group" with Dr. Thomas Axelsen, chief physician from the Radiology department at Rigshospitalet.

Implementing a new RIS/PACS system obviously involves a lot of hard work including training all staff, however, it is necessary for ensuring a stable future-proof RIS/PACS system and patient safe operation. We believe our new RIS/PACS system will give us a brighter future, because it will support us in our everyday work and help us take clinical physiology and nuclear medicine to the next level when it comes to research, artificial intelligence, big data, advanced visualization and personalized medicine.

Medical isotope shortage November 2022

In November 2022 Europe faced a serious shortage in the production of isotopes, including Tc-99m, the isotope used for bone scintigraphy, renography, thyroid scintigraphy, sentinel node studies etc.

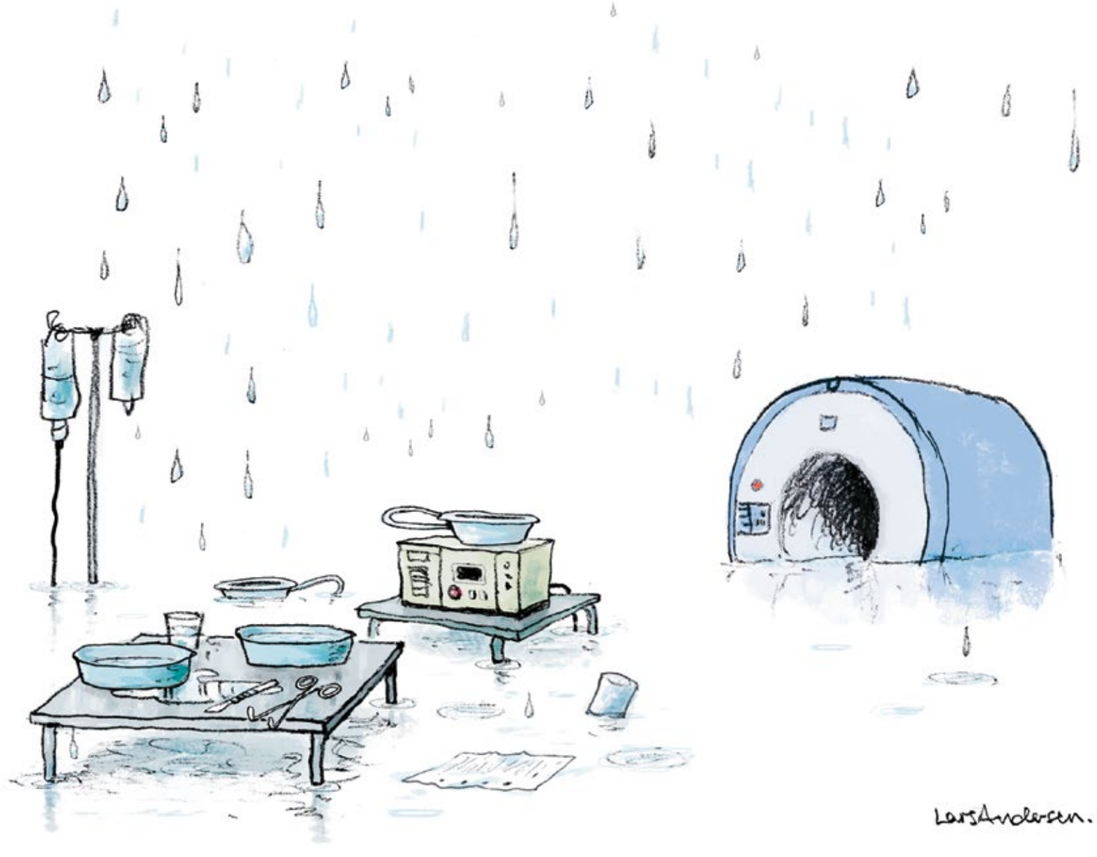
The reactors in Holland and Belgium were out of order, and so was the South Africa production line. The whole of Europe experienced a serious shortage with implications for patient investigations.

The clinicians were helpful, and the departments of nuclear medicine collaborated to secure the most optimal use of the few droplets available.

Water damages

In May 2022 a large water damage affected the PET/CT scanners in The Finsen Building. The whole section was flooded, and two PET/CT scanners were out of order for long periods, one of them almost half a year. A water hose exploded in the evening of May 10th and 30 tons of water poured out over the scanner section during that night creating havoc. It took us more than half a year to repair. The PET Section has been in a state of emergency for half a year because patients were still taken care of during this period. We owe everyone in the PET section A BIG THANK YOU for the dedicated effort during this very tough time.

In 2017 and 2018 we also experienced large water damages in the department, and extensive renovation was carried out in the 60 year old building after this. At that time we wrote: “Now all seems renovated, and we will hopefully never experience anything like this again”. Standing where we are, beginning of 2023, we are very careful about what we say now– but we do hope that this incidence in May is the last in this unfortunate series of large water damages. We have pledged the management for preventive measures– and hope to get this soon.



The Physicist and Technology Group

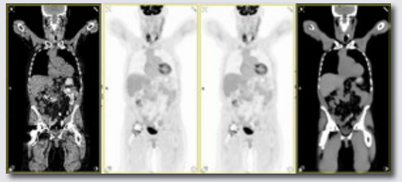


Figure 2: *Left: PET/CT images using lowdose CT. Right: AI generated PET/CT images using the synthetic CT.*

Figure 1: *Siemens Quadra PET/CT scan of a patient with malignant melanoma, left in deep inspiration breath hold, right in free breathing.*

Chief Physicist Thomas Levin Klausen

The Physicist and Technology Group (physicists, engineers and computer scientists) is involved in many aspects of the work in the clinic. 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 conducting and facilitating clinical research in the department.

With the installation of the new total body PET scanner: Siemens Vision Quadra, the focus has been to facility advanced analysis capabilities as well as data handling. Scanning protocols have been devised for ultra-low dose PET scanning using 1/10th of the normal activity. This allow for routine scanning of sensitive pediatrics, pregnant woman and healthy controls. Pipelines for whole body data analysis in the field of kinetic modeling has been setup for the Quadra including a clinical implementation of perfusion images using ^{15}O-water and image derived input function for the descending aorta using AI. Also, in close corporation with department of oncology, we have implemented a setup for PET scanning the whole body in deep inspiration breathhold. DIBH is critical for avoiding side effect of heart, vessels and lung tissue during radiation therapy and it is today our standard procedure for malignant melanoma patients, see Figure 1.

Artificial intelligence is a quickly evolving field and is already of great importance for the clinical setup, patient diagnosis and treatment. Our AI research group, clinically applied artificial intelligence (CAAI) led by Computer Scientists Flemming Littrup Andersen and Claes Ladefoged, defines the primary research areas in close dialogue with the clinicians. This includes data domain translation, synthetic images generation, lesion segmentation, and general noise reduction of image data.

Lately, studies has been targeting synthetic imaging using deep learning to produce clinical useful PET and CT image data, as an example, we synthesize CT for attenuation correction directly from the PET emission data as illustrated in Figure 2. By combination synthetic CT with ultra-low dose PET scanning on the Siemens Vision Quadra, PET/CT scanning with radiation dose below 0.5 mSv has become feasible.

Kidney T2* and perfusion maps before and after the administration of a diuretic. The increases of T_2* 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.

The Physicist and Technology Group continually develops our abilities to process functional data from CT, SPECT, PET and MRI scans for not only clinical scans, but for internal and external research projects as well. Here for example, we developed the necessary tools using AI and signal processing to evaluate the levels of lipids in the kidneys of patients from Steno Diabetes Centre using magnetic resonance spectroscopy.

Neuro PET

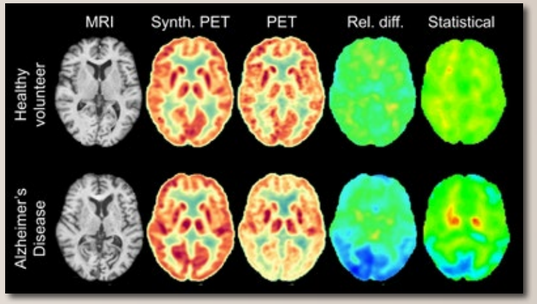


Figure: *Deep learning generation of synthetic baseline for analysis of ^{18}F-FDG PET. Upper row healthy subject and lower row patients with Alzheimer's disease. Based on structural scan (MRI) a synthetic PET showing the expected tracer distribution is generated using deep learning. The actual PET image is compared with the synthetic image, and a map showing relative difference is calculated. For comparison the vendor supplied statistical analysis of PET compared to a normal database is shown.*

Professor, Consultant Ian Law and Consultant Otto Mølby Henriksen

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.

The glucose analog 2-[^{18}F]fluoro-2-deoxy-D-glucose (^{18}F-FDG) showing the functional integrity of the brain remains the backbone of clinical imaging of dementia and epilepsy. In the workout if neurodegeneration we further provide imaging with ^{11}C-PIB for evaluation of cerebral amyloid in Alzheimers's disease, and ^{18}F-FE-PE2I for assessment of Parkinsonism. We use [^{15}O]H_2O 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 [^{18}F]fluoroethyl-tyrosine (^{18}F-FET) for gliomas, and the somatostatin II receptor ligand ^{68}Ga-DOTATOC for meningiomas.

Our hybrid PET/MR scanners allows a comprehensive structural and functional evaluation of brain pathologies within a single imaging session, and is a powerful tool both for research and for routine clinical investigations of patients with dementia and brain tumors. The total body PET/CT system allows us to perform short scan sessions in patients, mainly children, and to obtain image derived input function from aorta allowing kinetic modelling of brain PET data without the need for arterial cannulation.

With the increasing demand of neuro PET examinations and increasing analytical complexity of in particular PET/MR studies, we have implemented post-processing pipelines providing fully automated reports with standardized analyses of PET and MRI data supporting clinical interpretation and reporting. In collaboration with our AI group deep learning methods for generation of synthetic CT for attenuation in PET/MR has now been fully implemented in clinical routine, and methods for individualized analysis of ^{18}F-FDG PET are investigated (Figure 1).

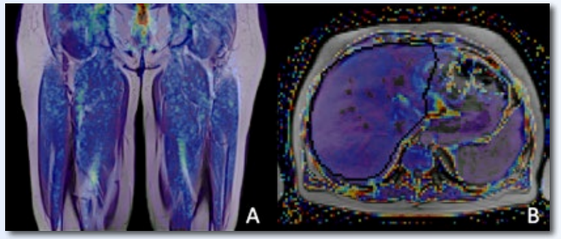


Figure 1: *Images from selected projects ranging from inflammatory processes in larger muscle groups to fatty livers. A) coronal T1-weighted MRI fused with ^{18}F-FDG for the examination of myositis in the lower extremities C) transverse T1-weighted scan fused with a fat fraction map to examine liver fat content and distribution*

PET/ MRI

Physicist Thomas Lund Andersen and Professor, Consultant Malene Fischer

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Functional Magnetic Resonance Imaging

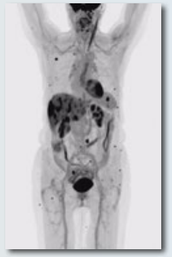
Professor, Consultant Henrik BW Larsson

Three large projects were finalised in 2022: The Copsych project focusing on brain physiology in relation to psycho-pathology in 10 year-old children; the Metropolite study focusing on healthy aging in men born in 1953, and finally the study of general anaesthesia on brain function in healthy volunteers. Evaluation of this data is in progress. The Functional Imaging Unit (FIU) in collaboration with partners have published a total of 18 studies in peer-reviewed journals. Some highlights are: In a study of patients with cerebrovascular disease we found evidence for an uneven capillary perfusion pattern as especially seen in these patients is linked to reduced oxygen delivery to the brain. This is a hot topic and highly debated in the neuro-science literature (J Cereb Blood Flow Metab. 2022;11). In the Metropolite study, lower cognitive ability was associated with reduced vascular reactivity to a visual stimulation, thus linking cognition with blood vessel functionality (Geroscience 2022;44, p1904). Furthermore, in the Metropolite cohort we could not find any link between reduced cognitive function and blood brain barrier (BBB) leakage in the hippocampus area, as claimed by other studies. However, the subgroup with Diabetes Mellitus (DM) showed generally higher BBB leakage compared to non-DM subjects (Geroscience 2022). An artificial intelligence system for automatic Multiple Sclerosis (MS) lesion delineation has been developed based on thousands of MR images from MS patients (Clin Neuroradiol 2022;32, p643). This method will make classification and follow-up studies much easier and faster in future studies of MS patients.

In 2023 three new studies will be initiated and three new PhD students will be recruited: The REPCON project focusing on patients with post-concussion syndrome, long-lasting symptom after concussion, funded by sygeforsikringen 'danmark', a project focusing on B-cell lymphoma and brain involvement funded by The Danish Cancer Foundation, and finally a project focusing on brain pathophysiology in progressive MS patients in order to better understand the pathophysiology, funded by The Danish MS Society.

QUADRA

Professor, Consultant Malene Fischer



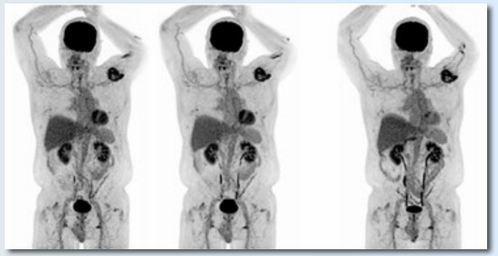


Figure 1: *PET scan from the Quadra of a 64-year-old female with melanoma relapse. The high sensitivity enables detection of multiple small lesions.*

Figure 2: *Ultra-low dose PET after injection of 28 MBq. The two PET scans to the left are reconstructed after 10 respectively 20 mins acquisition time. The PET scan to the left is standard PET acquisition after injection of 300 MBq (same patient).*

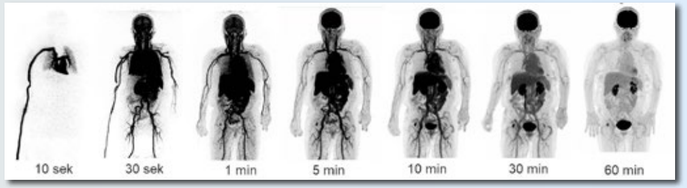


Figure 3: *Dynamic whole body FDG-PET scan performed on the Quadra.*

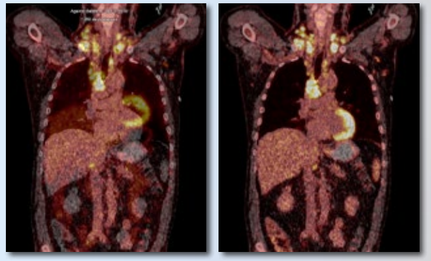


Figure 4: *PET/CT performed for radiotherapy planning in a patient with lymphoma. The fused scan to the right was performed with both PET and CT in DIBH, illustrating the potential for improved matching between PET and CT. This is especially important for radiotherapy planning.*

With more than 2000 patients scanned, 2022 has been the year where our total body PET/CT scanner, Quadra, has proven its worth. The implementation of the Quadra PET/CT have been done by a multidisciplinary team consisting of nuclear medicine physicians, radiologists, physicist, technologists, radiographers and computer scientists led by professor Malene Fischer and Data Manager Flemming Andersen. Early research on total body PET/CT systems promised significantly improved sensitivity and we have not been disappointed. Our experience from reading PET/CT scans performed on the Quadra, as well as a systematic evaluation of image quality confirms the improved sensitivity and signal-to-noise ratio. The image quality provided by the Quadra PET/CT is second to none and has opened up possibilities to significantly decrease scanning time or decrease radiation dose to the patient while maintaining high image quality. We are now utilizing this by offering faster scans with lower radiation dose to pediatric patient, ultra-low dose PET for pregnant patients and in research performed on otherwise healthy individuals. Projects with dynamic PET acquisition of different tracers exploits the high sensitivity and total body coverage unique for the Quadra and whole-body deep inspiration breath-hold PET has been introduced for radiotherapy planning.

The Birthe Meyer portrait

The Birthe Meyer portrait was revealed May 2022 by Rikke Raben, the sculptor of the portrait. The John and Birthe Meyer Foundation has generously donated to the equipment of the Department of Clinical Physiology and Nuclear Medicine throughout the years. We are extremely grateful for these contributions!

Radiochemistry

Chief Radiochemist Nic Gillings, Chief Radiochemist, Production Manager Jacob Madsen and Nuclear Medicine Staff Technologist Tina Wikke Hallund

Highlights
In 2022 we received approval from The Danish Medicines Agency for production of [^{18}F]mFBG for imaging neuroblastoma in paediatric patients. This PET-tracer has proven to be extremely advantageous for small children, where a very short scanning time allows this to be performed without sedation or general anaesthesia.

For the first time, scans of hyperpolarised ^{13}C-pyruvate in patients were performed in 2022 using a PET/MR scanner as part of a clinical trial. This is planned to continue in 2023.

Production for clinical and research PET investigations in humans
In addition to [^{18}F]mFBG, 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. We also continued to produce the uPAR imaging agent, [^{68}Ga]Ga-NOTA-AE105 and our angiogenesis tracer, [^{68}Ga]Ga-NODAGA-E[c(RG-DyK)]$_2$ in 2022. Both are being evaluated in phase II clinical trials. Production of neuroreceptor PET radioligands for human use ([^{11}C]UCB-J, [^{11}C]SB207145 and [^{11}C]Cimbi-36) for various research projects, conducted by The Neurobiology Research Unit at Rigshospitalet, continued as in previous years. In total there were 1040 batches released for human use in 2022 comprising 16 different radiopharmaceuticals.

Radiopharmaceutical development
Optimisation of 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, was finalised in 2022 and the production process will be validated prior to application for approval for human use. [^{89}Zr]Zr-S2-Trastuzumab has been developed by Camilla Christiansen as part of her PhD project. This is a monoclonal antibody with high affinity for HER2, which is overexpressed in breast cancer. The optimisation and validation of analytical methods was finalised in 2022 and process validation will commence in 2023.

In 2022 we started working on the implementation of three new radiopharmaceuticals:

- [^{68}Ga]satoreotide trizoxetan - for use in an investigator initiated clinical trial investigating imaging of somatostatin positive tumours (small cell lung cancer).
- [^{68}Ga]Ga-FAPI-46 - a fibroblast activation protein inhibitor for use in an investigator initiated clinical trial for imaging of pancreatic and gastroesophageal cancer.
- [^{18}F]sorbitol – for investigation of bacterial infections.

We expect to commence final validation and production of all five of the above-mentioned radiopharmaceuticals in 2023.

Quality Assurance
We are currently in the process of implementing a laboratory information management system (LIMS) which has been developed by LabLogic in the United Kingdom and is used in many PET centres throughout the world. This is an electronic system that allows all production and quality control data to be automatically captured in a database, thus making the whole process more or less paperless. The system is now fully installed and optimised, and the final validation will be performed in early 2023.

Radiopharmaceuticals produced for human use in 2022 ▸

Radiopharmaceutical	Batches	Usage/Target
Krypton-81m generator	150	Lung ventilation
[^{18}F]FDG	327	Oncology/glucose metabolism
[^{18}F]FE-PE2I	138	Neurology/dopamine transporter ligand
[^{18}F]FET	52	Oncology/amino acid transport
[^{18}F]mFBG	10	Oncology/neuroblastoma
[^{18}F]FLT	5	Oncology/cell proliferation
[^{11}C]PIB	79	Alzheimer's Disease/β-amyloid plaques
[^{11}C]UCB-J	56	Brain research/synaptic density marker
[^{11}C]SB207145	43	Brain research/5-HT$_4$ receptors
[^{11}C]Cimbi-36	3	Brain research/5-HT$_{2A}$ receptors
[^{68}Ga]Ga-DOTATOC (SOMA kit TOC)	96	Neuroendocrine tumours/somatostatin receptors
[^{68}Ga]Ga-DOTATATE	13	Neuroendocrine tumours/somatostatin receptors (clinical trial)
[^{68}Ga]Ga-NODAGA-E[c(RGDyK)]$_2$	5	Oncology/angiogenesis imaging (clinical trial)
[^{68}Ga]Ga-NOTA-AE105	14	Oncology/uPAR imaging (clinical trial)
[^{68}Ga]Ga-PSMA-11	28	Oncology/prostate specific membrane antigen ligand
[^{15}O]Water	15	Cerebral blood flow
Total	1,034	

Cyclotrons

Cyclotron Chief Holger J. Jensen

We have experienced a relative stable number of productions at our two cyclotrons of 1242±84 productions per year in the last 10 years (Figure 1). In 2022 we had a total of 1205 successful productions (610 and 595 for our Scanditronix MC32 and CTI/Siemens RDS Eclipse cyclotrons respectively) giving an average success rate of 99,5±0,4% since 2013. In 2022 the number of ^{211}At customers increased from only 2 to 7 and the number of productions is expected to increase significantly in 2023. ^{211}At is used for targeted radionuclide therapy and our department is one of the leading producers in Europe. We managed to keep the average radiation dose to the employee in the Cyclotron- and Radiochemistry unit at a low and constant level (Figure 2) in the previous years.

Figure 3 shows the development in the controlled release via our chimney of low radioactive waste gas produced in the Cyclotron- and Radiochemistry unit since 2013. Our permission from the authorities (SIS) allows us to release 10 TBq per year. In 2022 we ended with a release of only 9 % of this limit.

In 2022 we received funding from The John and Birthe Meyer Foundation for a new cyclotron. The new cyclotron is replacing the CTI/Siemens cyclotron, thus, securing the isotope production for the coming decades. The plan is that it will be installed in 2024 releasing the Scanditronix MC32 cyclotron from part of its routine production load so this machine can focus on production of more difficult and unique isotopes.

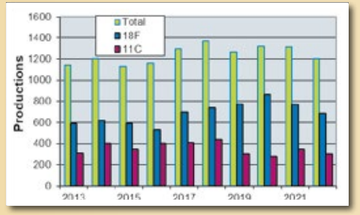


Figure 1: *Development in 18F, 11C and the total number of productions since 2013.*

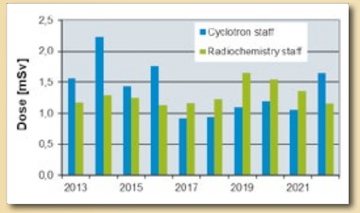


Figure 2: *Average received dose per year for employee in the cyclotron- and radiochemistry unit since 2013.*

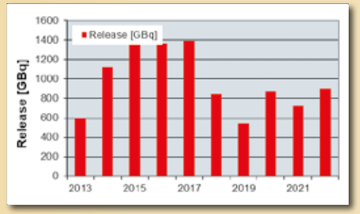
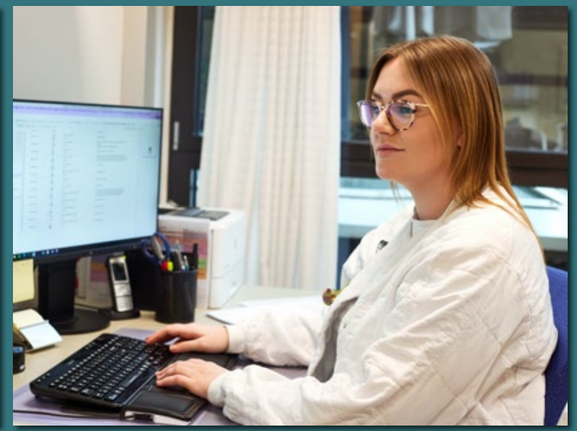


Figure 3: *Development in release of radioactive gas via our new chimney and filter system since 2013.*

Medical secretaries

We have highly competent medical secretaries responsible for referral of patients, organisation of the flow of patients through the department, writing reports and sending them to the clinical departments. They make a dedicated effort. The medical secretaries manage patient bookings, waiting lists, the patient control examinations, and research scans to a high standard. A dedicated thank you to Marianne Stahlfest, Mette Fabiansen and Helle Højen Jensen in the KF Section, Gitte Hass and Sevil Durmus in the Glostrup Section and Tina Vikmann Nielsen, Gudrun Semitoje and Frederikke Hurup Henriksen in the PET Scanner Section. Welcome to Katja Petrea Pedersen who started in the PET Scanner Section in November.

We would like to say a warm thank you to everyone for the professional and great performance.



Education

Consultant Peter Oturai

The department contributes to many of the pre-graduate 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. Nuclear medicine technologist students and radiographer students and medical secretaries/SAK-students receive parts of their education at our department.

Seven positions for physicians training to become specialists in clinical physiology and nuclear medicine are held by the department. Courses held by our physicians and physicists are dedicated courses in oncology, pulmonary-, and endocrine-pathophysiology and molecular imaging as well as courses in methodology such as MR, hybrid imaging, and kinetics. 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, visit the department for educational and research purposes for periods ranging from weeks to months.

The department's educational activities have been accredited by the Accreditation of Nuclear Medicine Training Centres Committee of 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. Professor Jann Mortensen, Professor Ian law, Professor Henrik Larsson, Professor. Malene Fischer and associate professor Ronan Berg are responsible for the undergraduate education of medical students in the department and the medical faculty. Professor Liselotte Højgaard is responsible for under- and postgraduate education for bioengineers.

Clinical teachers, Mia Hjorth Ahlers, Torben Kirk Lehnskov and Anette Foldager

Technologist students and staff training
Our department contributes with many activities for our technologist students, biomedical laboratory scientist and radiographers, at the University College Copenhagen. In 2022, 35 students have received clinical training and education.

In august 2022 a student enrolled in an unique program at the department in collaboration with University College Copenhagen. The focus of this program is "research and development", and the student will write an article instead of a bachelor thesis. She has already validated new equipment for lung function test and will soon commence the implementation in the clinic. It is a very rewarding process for the student and the department.

We started our trainee program in 2022. Our two trainees will rotate between our three sections and will have their first shift in April 2023. We hope this will strengthen relations and interprofessional teamwork in our organization.

Last, but not least, it is now possible for a staff member to become "specialist in clinical physiology and nuclear medicine". This new education was approved by the board of Danish Society for Clinical Physiology and Nuclear Medicine and is available to departments across the country.

Medical secreatary Tutor Tina Vikmann Nielsen

Medical Secreataries and SAK students
SAK stands for "Health Administrative Coordinator", and is an education for aspiring medical secretaries. The department currently take onboard SAK students for 10-week internships.

Equipment

Chief Physicist Thomas Levin Klausen

Equipment	Product	Purchase year
Gamma cameras	DDD NephroCam System	2016
	DDD Solo	2020
	Mediso N-TH45-D	2008
	DDD SoloMobile	2012
	DDD NephroCam System	2019
	Symbia Evon	2017
SPECT/CT cameras	GE Discovery 670	2010
	GE StarGuide	2022
	Siemens Intevo Bold 16 slice CT	2017
	Siemens Intevo Bold 16 slice CT	2020
	Siemens Symbia 16-slice CT	2011
PET scanner	HRRT Siemens/CTI	2007
PET/CT scanner	Siemens Quadra	2009
	Siemens Vision (128)	2010
	Siemens Vision (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
	GE SPINlab MR Hyperpolarizer	2014
Lung function	Jaeger Masterscreen w/bodybox	2005
	Jaeger Masterscreen w/bodybox	2019
	Jaeger PFT pro w/bodybox	2007/13
	Jaeger Vyntus One PFT w/bodybox	2021
DXA scanner	GE Lunar Prodigy	2004
	GE Lunar Prodigy	2005
	GE Lunar Prodigy	2011
	GE Lunar iDXA	2014
Whole body counter	WBC w/NaI counting chamber	1977
	WBC w/plast counting chamber	1978
Cyclotrons	Scanditronix 32 MeV	1991
	RDS Eclipse cyclotron, CTI	2005

Organisation and staff

Abrahamsen, Nynne Hejdemann, Technologist.
Afzai, Remshah, Technologist.
Agner, Elissaveta Castella, Radiographer.
Ahangari, Sahar, PhD student.
Ahlberg, Sofie, Technologist.
Ahmadi, Amir, Radiographer.
Albers, Mia C. Hjorth, Clinical Teacher.
Albrecht-Beste, Elisabeth, Consultant.
Aleksyniene, Ramune, Radiologist.
Alexandrova, Alzhbeta, Technologist.
Ali, Mahvish Tayyab, Technologist.
Anderberg, Lasse, Research Assistant.
Andersen, Amanda Øster, MD, PhD student.
Andersen, Ditte Lindbjerg, Radiographer.
Andersen, Flemming Littrup, Computer Scientist, MSc, PhD.
Andersen, Jane, Technologist.
Andersen, Julie Bjerglund, PhD, Staff Specialist.
Andersen, Kim Francis, Consultant.
Andersen, Thomas Lund, Physicist, PhD
Andersen, Ulrik Bjørn, Consultant.
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Azizi, Nadia, Radiographer.
Bach, Mathias Jacobsen, Student Assistant.
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Cold, Sigrid, MSc, PhD student.
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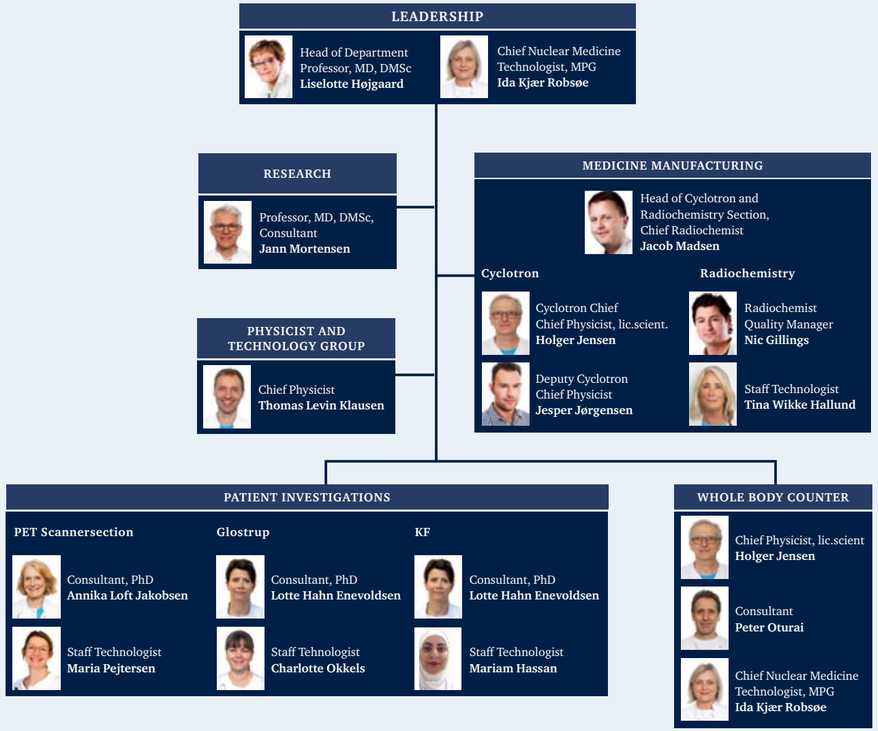
Gustafsson, Thea Waidtløv, Senior Registrar.
Haddock, Bryan Thomas, Chief Physicist, PhD.
Hag, Anne Mette Fisker, MSc, PhD, Postdoc, Research Coordinator.
Halberg, Simon Thor Weber, Radiograper.

Department of Clinical Physiology and Nuclear Medicine



Organisation and staff

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Jørgensen, Dea Lie, Bioanalytiker.
Jørgensen, Jesper Tranekjær MSc, PhD, Assistant Professor.
Jørgensen, Jesper, MSc, Deputy Cyclotron Chief
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Jørgensen, Philip, Technologist.
Jørgensen, Rasmus, Student Assistant.
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Larsen, Kristina, Technologist.
Larsen, Naja Jean, Student Assistant.
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Madsen, Johanne Straarup, MD, PhD student.
Madsen, Karine, Consultant.
Markova, Elena, Consultant.
Martín, Marina Simón, MSc, PhD Student.
Michaelsdóttir, Thórunn, Registrar.
Montgomery, Maria Elkjær, Student Assistant.
Mortensen, Jann, DMSc, Professor, Consultant.
Mortensen, Julie van Krimpen, Student Assistant.
Moustapha, Amani, Technologist.
Müller, Asger Raza, Radiographer.
Müller, Felix, Registrar.
Møller, Mine Creutzberg, Technologist.
Månsson, Anna, Veterinary Technician.
Nielsen, Betina Sølvi, Technologist.
Nielsen, Cille Wehlast, Student Assistant.
Nielsen, Cora Schaumann, Technologist.
Nielsen, Marcus Kristian, Student Assistant.
Nielsen, Signe Maja Halstrøm, Radiographer.
Nielsen, Susanne Weile, Technologist.
Nielsen, Tina Vikmann, Medical Secretary.
Nijs, Robin de, Specialist Medical Physicist.
Okkels, Charlotte Holmgaard, Staff specialist.
Olin, Anders Beck. PhD, Postdoc, Engineer.
Olsen, Høgni Janus Barnason, Student Assistant.
Oturai, Peter Sandor, Consultant.
Oueiti, Ghena Nasser, Technologist.
Ovesen, Karen Rosbjerg, Student Assistant.
Pedersen, Cecilie Høeg, MSc, PhD Student.
Pedersen, Karl-Emil, Technologist.
Pedersen, Katja Petrea Gissemann, Medical Secretary
Pedersen, Rune Ploegstra, Student Assistant.
Pejtersen, Maria Helene, Staff Technologist.
Pedersen, Nanna Overbeck, Student Assistant.
Philipsen, Frederik Ersø, Student Assistant.
Poulsen, Constance Eline Grandjean, MSc, PhD Student.
Qvist, Katrine, MSc, Technologist.
Raghava, Jayachandra Mitta, Postdoc.
Rasmussen, Thomas, MD, PhD, Postdoc.
Reichkendler, Michala, Staff Specialist.
Rexhepi, Lume, Technologist.
Riedel, Casper Schwartz, Registrar.
Ripa, Rasmus Sejersten, MD, DMSc, Consultant.
Risør, Louise Madeleine, MD, PhD Student.
Robsøe, Ida Kjær, Chief Nuclear Medicine Technologist, MPG.
Ryssel, Heidi, MD, PhD Student.
Sandholdt, Michele Windtberg, Technologist.
Saribayir, Sirin, Technologist.
Saxtoft, Eunice, Technologist, Clinical Instructor.
Schulze, Christina, Technologist.
Sell, Danna Kamstrup, MSc, PhD Student.
Semitoje, Gudrun, Medical Secretary.
Sergi-Lindell, Elin, Technologist.
Setterberg, Victoria, Technologist.
Shalgunov, Vladimir, Chemist.
Simonsen, Helle Juhl, Research MR Technologist.
Sinik, Edita, Technologist.
Símon, Marina Martín, MSc, PhD, Postdoc.
Sinkjær, Anders Wilgaard, MSc, PhD student.
Sjöstedt, Sannia, Senior Registrar.
Sloth, Ane Beth, MSc, PhD Student.
Solanellas, Pere G, Student Assistant.
Soldath, Patrick, MD, PhD Student.
Sommer, Niyan, Technologist.
Stahlfest, Marianne, Medical Secretary.
Stensgaard, Susan Al-Atabi, Technologist.
Stavnsbjerg, Camilla, MSc, PhD, Postdoc.
Stillits, Andreas, Student Assistant.
Svalling, Susanne, Technologist, Deputy Staff Technologist.
Svendsen, Nini Hvidtfeldt, Technologist.
Sørensen, Louise Sørup Lendorf, Deputy Staff Technologist.
Sørensen, Maja Støvring, Technologist.
Teilmann, Laura Marie, Student Assistant.
Thomsen, Frederikke, Technologist.
Topsøe-Jensen, Morten, Technologist.
Treiberg, Tuule, MSc, PhD Student.
Trollesborg, Alma, Service Assistant.
Urhammer, Gitte Marie, Technologist.
Uzer, Sefika, Technologist.
Vandel, Julius Scheel, Student Assistant.
Varpe, Kristin, Technologist.
Veseli, Antigona, Technologist.
Vestergaard, Mark Bitsch, PhD Student.
Weihrauch, Per, Cyclotron Technician.
Wiinholt, Mette Neiegaard, MSc, Technologist.
Willumsen, Ida Vigdís, Student Assistant.
Wittekind, Anne-Mette Nielsen, QA Pharmacist.

Studies 2022

Radiotherapy	
Treatment with ^{131}I, benign thyroid	84
Treatment with ^{177}Lu-DOTATATE	137
Treatment with ^{223}Ra-Dichlorid	70
Treatment with ^{177}Lu-PSMA-617	7
Total	**298**

Peripheral vessels	
Systolic blood pressure, fingers	3
Systolic blood pressure, ancle and toes	364
Systolic blood pressure, ancle-brachial index after treadmill	106
Doppler ultrasound of the carotides	4310
24 hours blood pressure measurement	343
Total	**5,126**

Blood and lymph system	
Sentinel node scintigraphy,	170
Sentinel node scintigraphy, head/neck SPECT,	182
Spleen scintigraphy,	4
Erythrocyt volume,	15
Plasma volume,	19
Peritumoral injection of	0
Total	**390**

CNS and peripheral nervous system	
CT scanning of cerebrum	588
Regional cerebral blood flow, ^{15}O-H_2O, farm pro	18
Cerebral metabolism,	1,684
Cerebral transporter ligand, ^{18}F-FE-PE2I	362
Cisternography,	2
Cerebral amino acid transport,	267
Cerebral amyloid ligand,	172
Cerebral receptor,	197
Cerebral blood flow,	0
Regional amyloid ligand, ^{18}F-Florbetapir	0
MR scanning of cerebrum with and without contrast	1,043
MR scanning of hippocampus (MR-HCV)	778
Total	**5,111**

Other diagnostic procedures	
Image fusion (PET, SPECT, MRI, CT or planar)	15,372
Scintigraphy after	70
Whole body, contamination measurement	50
Neuroendokrine receptors, WB,	0
PET tumor scanning,	40
PET tumor scanning,	797
PET scanning	62
PET scanning,	7,224
PET tumor scanning,	44
PET tumor scanning,	0
CT head/neck SPECT/CT	291
CT lower and upper extremities SPECT/CT	30
CT abdomen SPECT/CT	283
CT pelvis SPECT/CT	164
CT wb PET/CT	1,921
CT wb PET/CT with contrast	6,518
CT wb SPET/CT	287
CT thorax SPECT/CT	658
CT thorax PET/CT breathhold	21
MR wb PET/MR	170
PET thorax PET/CT breathhold	21
Other investigations, incl, ^{11}C-different tracers (NRU)	152
Supplementary/repeated imaging	2,574
Second opinions external PET, PET/CT, SPECT/CT, CT and MR	1,700
Extra tumor delineation	335
Total	**38,784**

Endocrine organs	
Adrenal marrow scintigraphy,	33
Iodine uptake test,	26
Parathyroid scintigraphy,	70
Thyroid scintigraphy,	71
Thyroid scintigraphy,	1,044
Thyroid ultrasound	1,123
Thyroid, fine needle aspiration biopsy	89
Total	**2,456**

Gastric intestinal tract, liver, biliary tract and pancreas	
Bleeding scintigraphy (abdomen)	0
Biliary tract scintigraphy,	98
Liver perfusion, ICG	32
Meckels diverticle scintigraphy,	1
Salivary gland scintigraphy,	5
Doppler ultrasound of splanchnic blood flow	601
Total	**737**

Heart and cardiovascular system	
Analysis of heart rate variability	249
Tilt table test	263
Isotope cardiography, LVEF,	1,026
Myocardial calcium score	794
PET myocardial perfusion,	1,154
PET myocardial metabolism,	257
PET myocardial perfusion,	1,025
Myocardial perf, scintigr, gated,	2
Myocardial perf, scintigr, gated,	2
Myocardial scintigraphy,	134
Myocardial	0
CT heart, with contrast	61
Transtorakal ekkokardiografi	167
Transtorakal ultralydsdiagnostik, fokuseret	492
Total	**5,626**

Bone and joint	
DXA, body composition	751
Bone scintigraphy,	1,053
Bone scintigraphy,	741
Bone scintigraphy,	36
Bone scintigraphy,	28
Osteodensitometri (DXA), columna lumbalis	5,135
Osteodensitometri (DXA) collum femoris	5,135
Osteodensitometri (DXA), lateral spine	332
Osteodensitometri (DXA), radius	326
MR scanning columna cervicalis	0
MR scanning columna thoracalis	0
MR scanning columna lumbalis	0
Total	**13,537**

Respiratory organs	
Lung perfusion scintigraphy, SPECT,	551
Lung ventilation scintigraphy, SPECT,	458
Lung function test, spirometry w/reversibility	89
Lung function test, fysiol/farm prov,	20
Lung function test, diffusion capacity (CO)	4,237
Lung function test, diffusion capacity (NO/CO)	33
Lung function test, whole body plethysmography	3,280
Lung function test, whole body plethysmography w/reversibility	334
Lung function test, spirometry	336
Lung ventilation scintigraphy, regional, ^{81m}Kr-gas	274
Lung ventilation scintigraphy, SPECT ^{99m}Tc-Technegas	83
Max, insp, abd exspir, muscle pressure	33
Mucociliary clearance,	12
Total	**8,622**

Kidneys and urinary tract	
Glomerular filtration,	1,922
Renal scintigraphy,	20
Renography,	1,997
Renography,	40
Renography,	6
Renography,	10
Doppler ultrasound of renal blood flow	582
Ultrasound of kidneys	582
Ultrasound of retroperitoneum	24
Total	**5,183**

In vitro analyses	
Affinity studies	57
Flow cytometry analyses	738
Gene expression analyses	2,976
Immunohistochemistry	945
Phage display	263
Plasma and protein analyses	13,375
Total	**18,354**

Animal studies	
Mice	
^{18}F-tetrazine	16
^{64}Cu-xx-uPAR	42
^{64}Cu-DOTA-AE105	109
^{177}Lu-DOTA-TATE	30
MR	1,312
CT images for fusion	197
Radiotherapy, externally	850
Total	**2,556**

Total number of studies **106,780**

Publications 2022

PhD thesis

Ahangari S. Multi-parametric PET/MRI imaging for radiotherapy planning in patients with cervical cancer. July 1st, 2022, University of Copenhagen.

Christensen, T. N. Prognostic evaluation and relapse detection with FLT-PET and FDG-PET/CT in patients with lung cancer. May 24th, 2022, University of Copenhagen.

Fosbøl, M. Ø. Molecular imaging in prostate cancer; from initial risk stratification to prognostication in patients with advanced disease. February 8th, 2022 University of Copenhagen.

Martin, M.S. Photothermal therapy in combinatorial strategies for cancer treatment. September 23rd, 2022, University of Copenhagen.

Olsen M.H. The mean flow index: the Emperor's new clothes? - a critical investigation of reliability and validity of a measure for dynamic cerebral autoregulation. June 3rd, 2022, University of Copenhagen.

Risom E.C. Preoperative pulmonary function and outcome after cardiac surgery. June 17th, 2022, University of Copenhagen.

Patents

Kjaer A (with co-inventors). Novel tetrazine compounds for in vivo imaging. US Patent App. 17/297,924. April 21, 2022

Kjaer A (with co-inventors). Positron emitting radionuclide labeled peptides for human uPAR PET imaging. US Patent App. 17/697,485. June 30, 2022

Kjaer A (with co-inventors). 18F-labeled novel tetrazines imaging probes for pretargeting in PET imaging. US Patent App. 17/612,144. August 11, 2022.

Kjaer A (with co-inventors). A urokinase plasminogen activator receptor-targeting peptide. US Patent App. 17/625,973. December 22, 2022.

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PhD thesis

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Multi-parametric PET/MRI imaging for radiotherapy planning in patients with cervical cancer.

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Supervisors:
Prof. Barbara Malene Fischer, Prof. Adam Espe Hansen, Assoc. Prof. Flemming Littrup Andersen & Prof. Andreas Kjær

Tine Nøhr Christensen

Prognostic evaluation and relapse detection with FLT-PET and FDG-PET/CT in patients with lung cancer.

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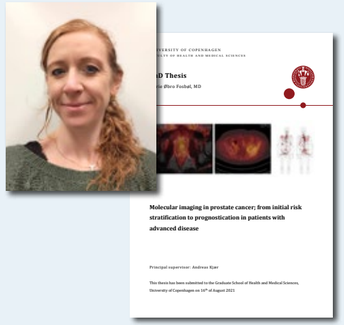

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Molecular imaging in prostate cancer; from initial risk stratification to prognostication in patients with advanced disease.

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Photothermal therapy in combinatorial strategies for cancer treatment.

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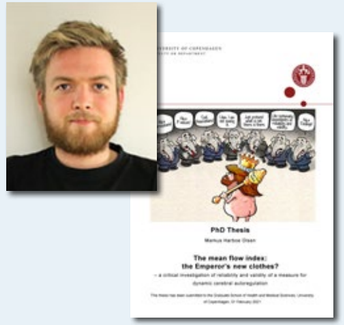
Supervisors:
Prof. Andreas Kjær & Ass Prof. Jesper Tranekjær Jørgensen



Markus Harboe Olsen

The mean flow index: the Emperor's new clothes? - a critical investigation of reliability and validity of a measure for dynamic cerebral autoregulation.

Defended June 3rd, 2022,
University of Copenhagen.

Supervisors:
Prof. Kirsten Møller, Ass. Prof. Ronan Berg, & Søren Bache.

Emilie Claudi Risom

Preoperative pulmonary function and outcome after cardiac surgery.

Defended June 17th, 2022,
University of Copenhagen.

Supervisors:
Prof. Hanne Berg Ravn, Katrine Bredahl Buggeskov, Prof. Jann Mortensen & Prof. René Horsleben Petersen.

Academic and other activities

Andreas Kjær, Professor, Consultant, ERC advanced grantee, is advisory board member of the European Neuroendocrine Tumor Society (ENETS). Founding Editor-in-Chief of Diagnostics (Basel) and International Assoc. Editor of the J Nucl Med. Head of the Cluster for Molecular Imaging and Director of the PhD Program for Medical & Molecular Imaging at 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). Currently holds a Lundbeck Foundation Professorship.

Anne-Mette N. Wittekind, MSc. Pharm., Deputy Qualified Person, is member of Danish Standards.

Annika Loft Jakobsen, Section Leader, Consultant, MD, Ph.D. Member of the "European Organization for Research and Treatment of Cancer" (EORTC), European Association of Nuclear Medicine (EANM), Danish Society of Oncological Radiology and Danish Society of Clinical Physiology and Nuclear Medicine. Member of the National PET/CT Group. Board member of DLG (Danish Lymphoma Group). Member of National Working Groups for lymphoma (Chair of Diagnostic Imaging Group in DLG), and cervical -, esophageal - and pharyngeal/laryngeal cancer. Member of Danish Advisory Board on Cancer in Pregnancy.

Birgitte Hanel, Biomedical Scientist, DMSc. Member of the editor committee, Danish Lung Function Standard (Dansk Lungefunktionsstandard). Member of the Spirometry Committee, ERS. Teaching "Clinical Respiratory Physiology", a specialist course for Nuclear Medicine Physicians and Respiratory Physicians. Teaching course of spirometry and quality control organized by PLO. Board member of the Foundation of Biomedical Laboratory Scientist.

Bryan Haddock, MPE, PhD, Board member of both the Danish Society for Clinical Physiology and Nuclear Medicine (DSKFNM) and the Danish Society for Medical Physics (DSMF).

Camilla Bardram Johnbeck, MD, PhD, Staff specialist at Rigshospitalet is 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-head of research group Clinically Applied Artificial Intelligence (CAAI) with supervision of PhD and MSc students.

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

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 teaching. Joint head of the research program CAAI for Clinically Applied Artificial Intelligence at the department. Member of the HYBRID Network; a collaboration for research and training of young researchers in the field of hybrid imaging, funded as a Marie Sklodowska-Curie Innovative Training Network under EU Horizon 2020. Member of PREFERENCE, a network for collaboration and training within the EU at research sites and private partners for long axial field-of-view PET scanners.

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, member of International Society for Magnetic Resonance in Medicine (ISMRM)/Section for MR Technologist (SMRT) MR safety committee. 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. Member of the National MR safety group developing Danish guidelines for MRI safety.

Henrik B.W. Larsson, Professor, Consultant, DMSc, 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.

Ian Law, Professor, Consultant, Member of the "PET Response Assessment in Neurooncology (RANO) working group". Board member of Danish Neurooncology group (DNOG), Member of Neurooncology and Imaging (EORTC), 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 "Clinical Respiratory Physiology" for nuclear medicine physicians and respiratory physicians. Physician responsible for Nuclear Medicine in the Faroe Islands. Member of the board for Danish Research Center for Lung Cancer (Dansk Forskningscenter for Lungekræft), Danish Lung Cancer Group (Dansk Lungecancer Gruppe), Screening of Lung Cancer Group (Lungecancer Screeningsgruppen), and the Danish Lung Function Standard (Dansk Lungefunktionsstandard).

Johan Löfgren, Consultant, is involved in clinical research protocols and teaches at specialist courses. Regional clinical expert in RIS/PACS and HIS.

Julie Bjerglund Andersen, Staff Specialist, PhD. Board member in Society for Junior Physisians in Nuclear Medicine, a part of the Danish Society of Nuclear Medicine and Clinical Physiology. Staff representative for Junior Physisians in the Department.

Kim Francis Andersen, Consultant, Team Leader Pediatric PET. He is Chairman of the Danish Sarcoma Group (DSG) and the Imaging Subcommittee of Scandinavian Sarcoma Group (SSG), Co-leader of the Imaging & Radiomics Group in FOSTER (European Osteosarcoma Consortium), as well as member of the Euro Ewing Consortium (EEC - INTER-EWING-1 imaging group) and the Danish Pediatric Hematology Oncology Group (DAPHO - solid tumor subgroup). He is involved in various clinical research protocols, including the role as co-investigator in SNITCH (Sarcoma Network Improving Trajectories, Cure rates & Health). He teaches at specialist courses for medical doctors.

Lise Borgwardt, Senior Consultant, Ph.D.Process Leader for Organizational Structure for Diagnostic Unit at Mary Elizabeth Hospital (Copenhagen Children's Hospital), representative for Diagnostic Center in The Project Steering Committee of Mary Elizabeth Hospital (Copenhagen Children's Hospital), chair of Imaging Committee of EpSSG, board member of SIOP Europe Imaging Working Group, PET/MR taskgroup of Pediatric Council SNMMI, Senior Advisor of the Paediatric Committee of EANM, member of the Paediatric Imaging Harmonization Group EANM/SNMMI. 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, Professor of Hybrid Imaging, 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 member of the board. MF is chair of the "Hybrid, Molecular and Translational Imaging" committee for the European Conference of Radiology 2023. MF is board member of "Overlægeforeningen", member of the Committee for Education and the Committee for Research under the Danish Medical Association, member of National Committee for the Education of Doctors and the AC Committee for Education and Research (Akademikernes Centralorganisation). Since June 2018 Senior Clinical Lecturer at the PET Centre, Guy's & St Thomas Hospital, Kings College London in UK.

Maria Helene Pejtersen, Staff Nuclear Medicine Technologist.

Academic and other activities

Nic Gillings, MPhil, PhD, Chief Radiochemist, Qualified Person (QP) is a 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 a consortium of manufacturers of PET radiopharmaceuticals in Denmark and 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 teaches at PhD courses as well as pre- and postgraduate courses.

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.

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.

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 Engineer the Future at pre-university educations. 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, and Deputy Editor-in-Chief at the journal Experimental Physiology (Physiological Society, London, UK. 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.

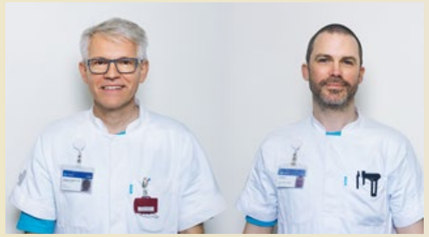
Sune Høgild Keller, Computer Scientist, PhD, is involved in various clinical and preclinical research protocols and scientific development in PET/CT, PET/MR and neuro-PET (HRRT). He teaches at a variety of courses for medical doctors, PhD students, technologists and MSc students. He is supervisor for 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, chair of the EANM Radiation Protection committee, a delegate for the Danish medical physics society (DSMF) to the European and International Organisations for Medical Physics (EFOMP and IOMP), member of an IAEA advisory group, and member of ICRP task group 117 for radiation protection in PET and PET/CT. He is a member of the Specialty Advisory Committee (SFR) in Clinical Physiology and Nuclear Medicine in The Capital Region of Denmark.

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, Assoc. Professor at Copenhagen University, Medical Physicist. Member of the Danish Society of Medical Physics (DSMF) and part of the scientific committee for the Nordic Association of Clinical Physics and European Conference of Medical Physics. Supervisor for PhD, MSc and BSc students.

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. Fields of expertise: Vascular ultrasound and renovascular hypertension.



Research

Professor Jann Mortensen and Associate Professor Ronan Berg

The year 2022 was characterized by rebuilding after the COVID-19 pandemic. Our dedicated scientists managed to maintain our comprehensive research program focusing on developing innovative solutions to clinical needs throughout the pandemic. After practically all COVID-19 restrictions were withdrawn in 2022, we managed to use the unique experience of conducting advanced studies during the challenging circumstances of a pandemic, thus, developing our research program further. We continually use our reseach efforts and the outputs have really blossomed. The new Total Body PET/CT scanner installed ultimo 2021, has improved our clinical service and has now become an integral part of many research studies in the department. Studies across all our current major research themes are highlighted below.

New tracers

Several projects aiming at developing new PET tracers for non-invasive tissue characterization and phenotyping are ongoing. Novel tracers developed, including [^{64}Cu]Cu-DOTATATE, [^{64}Cu]Cu-DOTA-AE105, [^{68}Ga]Ga-NOTA-AE105, [^{68}Ga]Ga-NODAGA-RGD$_2$, [^{18}F]ASIS, will be used both for diagnosing, staging and risk stratification as well as for therapy planning and monitoring. These tracers have already been taken first-in-humans at the department in phase I clinical trials and some of them 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.

Clinical PET/CT

The department is among the largest clinical PET-facilities in Europe and have strong clinically embedded research. This includes a large number of prospective clinical protocols aimed at evaluating the diagnostic and prognostic value of PET/CT in different clinical scenarios, from phase 1 and 2 trials testing new tracers to larger studies aiming at clinical implementation.

PET/MRI

Being one of the first departments to install a combined PET/MRI scanner in 2011/2012 and a second one in 2020, we have established a comprehensive research program on PET/MRI focusing on the added value of combining molecular imaging with PET and multiparametric MRI. Many 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.

HyperPET

We were the first to install a dynamic nuclear polarized (DNP) for hyperpolarization of ^{13}C-labeled compounds next to a PET/MRI scanner. We have used this set-up for development of and research in the combination of hyperpolarized ^{13}C-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.

Functional MRI

We currently have a major focus on the brain's glycolysis and lactate production, and have indeed contributed to a new understanding of the

brain's metabolism, where oxygen consumption is related to the steady on-going energy 'household' while transient increases in local neural activity relies on a fast but less efficient energy production from lactate-producing glycolysis. This links neural activity and metabolism directly and gives new perspective for improving or ameliorating cognitive decline during aging, mild cognitive decline and neurodegenerative diseases as Alzheimer's dementia.

Neuro-PET

The research focus has mainly been on clinical method development in brain tumors, 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. The Total Body PET/CT system has been implemented for use in pediatric neurooncology and non-invasive estimation of cerebral perfusion for assessment of cerebrovascular disease.

Nuclear cardiology

We are conducting studies on how innovative treatment interventions, systemic diseases, and drug abuses affect myocardial perfusion and integrated vasomotor function by taking advantage of the ability to quantify myocardial perfusion in absolute terms by ^{82}Rb PET. In addition, we study the value of new specific PET tracers, e.g. angiogenesis by [^{68}Ga]Ga-NODAGA-E[c(RGDyK)]$_2$ and inflammation by [^{64}Cu]Cu-DOTATATE.

Atherosclerosis

Non-invasive visualization of atherosclerosis and prediction of plaque vulnerability using PET/MRI and PET/CT are studied both preclinically and clinically. We focus on low-grade vascular inflammation in 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 [^{64}Cu]Cu-DOTATATE.

Lung studies

We perform studies on lung sequelae after COVID-19 and effects of rehabilitation efforts after COVID-19 using either aeroboc training or inspiratory muscle training. Lung function testing and VQ-SPECT/CT studies are ongoing especially in lung transplantation, and lung volume reduction treatment of emphysema, as well as studies on rehabilitation strategies that specifically target the lungs. In addition, studies on radioaerosol deposition and mucociliary clearance are conducted.

Pediatric nuclear medicine investigations

We are involved in many prospective clinical trials on PET and SPECT in collaboration with clinical pediatric departments. Most of our pediatric PET investigations are now performed on our new Total Body PET/CT-scanner, and a lot of work have been invested in terms of research and quality assurance projects, including the application of AI, in order to optimize imaging protocols. Recently, we have initiated a prospective study directly comparing the diagnostic value of the new [^{18}F]mFBG tracer on Total Body PET/CT with [^{123}I]mIBG SPECT/CT in children with neuro-blastoma. Preliminary results demonstrate that more neuroblastoma localisations are detected on [^{18}F]mFBG PET/CT, thus, the new tracer shows promise for future staging and response assessment in neuroblastoma in children.

Radionuclide therapy and theranostics

We develop new theranostics in-house based on new imaging ligands, which are then labeled with beta or alpha emitting radionuclides. Cancers that are currently being targeted and treated with radionuclides clinically include glioblastomas, neuroendocrine tumors and prostate cancer.

Image guided surgery

In collaboration with several surgical departments, we develop our most promising PET ligands targeting cancer specific targets for intraoperative delineation of cancer. The technology is expected to lead to better patient outcome, including overall survival and improved quality of life.

Immune cell tracking

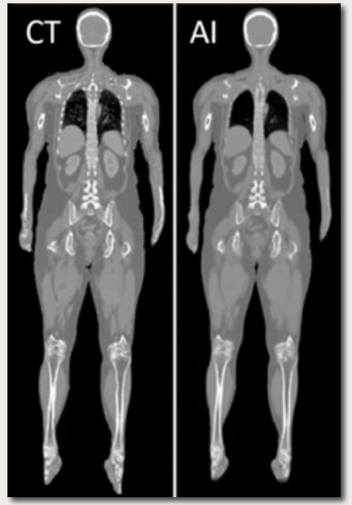
A particular focus is on development of new imaging tools for non-invasive visualization of the immune response and for tracking immune cells. These methods will be used in studies of inflammation, infection, rejection and in particular immune oncology

Whole body counting

In collaboration with external partners, we apply whole body counting for precise measurements of body composition.

Clinically applied artificial intelligence

We study how to exploit artificial intelligence in medical imaging. These studies cover most of the imaging modalities and disease areas, and enable the generation of synthetic CT from MR scans, radiotherapy dose planning, noise reduction, and improved or outcome prediction.



Whole body CT and corresponding synthetic CT generated by AI for use in PET attenuation correction. Ahangari S, et al 2022.

Cluster for Molecular Imaging

Professor Andreas Kjær

Precision medicine, i.e. tailoring therapy according to the disease characteristics of the individual patient, has led to a need for diagnosing at the molecular level. Molecular imaging allows for non-invasive studies at the whole-body level and elegantly circumvents *sampling error,* and due to the unsurpassed sensitivity and quantitative nature of PET, the technology is a preferred method for non-invasive, image-based phenotyping of disease. Among characteristics, which can be visualized are the *hallmarks of cancer*, e.g. cancer aggressiveness, angiogenesis, and interaction with the immune system. We foresee that such PET ligands will become game-changing within many diseases including cancer and cardiovascular disease. Moreover, successful PET imaging ligands can be "modified" into radioligand therapy 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 the development and application of new molecular imaging and therapeutic ligands to support *precision medicine*.

Cluster for Molecular Imaging, established in 2003 at the University of Copenhagen (Panum Institute), is a highly specialized facility for molecular imaging in animals using PET, SPECT, CT, MRI and optical imaging and has further developed into a comprehensive translational platform to support the discovery and development of new PET tracers and radionuclide therapies. Testing in relevant animal models forms the basis for ligand selection and translation into clinical use. The development of *predictive animal models* across disease entities, e.g. orthotopically implanted patient-derived xenograft (PDX) tumors as well as metastatic cancer models has become a core competence.

We currently hold 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.

Immunotherapies, in particular checkpoint inhibitors that support the immune system to fight cancers, are increasingly being used. How-

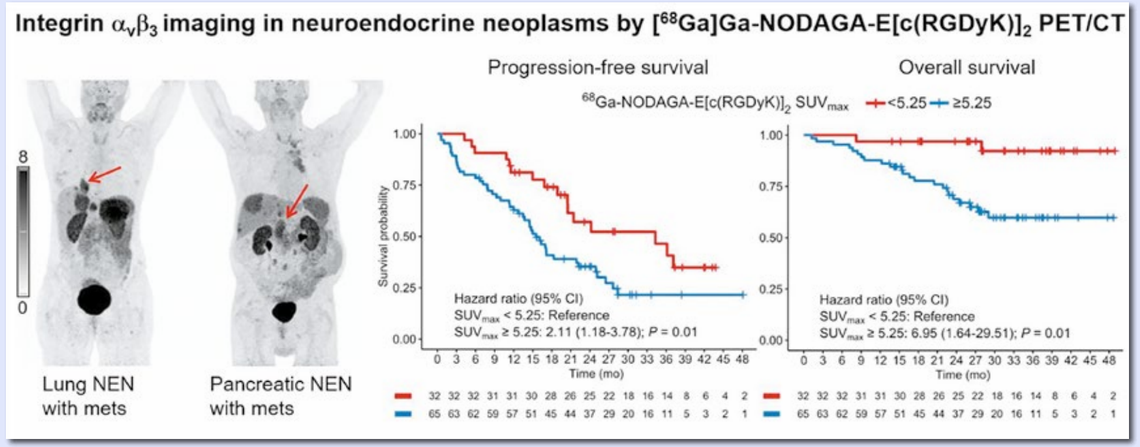


Figure 1: *Examples of two patients with metastatic neuroendocrine tumors. Red arrows point at the primary tumors. Angiogenesis-PET was performed using our in-house developed PET tracer 68Ga-NODAGA-E[c(RGDyK]2. Kaplan-Meier plots demonstrate the prognostic value of uptake of the tracer (images provided by Carlsen EA et al.).*

ever, the response rates are still relatively low. To unfold the potential, we have a focus on development of *immune cell imaging* ligands, e.g. targeting T-cells (CD4/CD8). With this platform, we have demonstrated that we are able to predict the response to checkpoint inhibitor blockade in various cancer models and we anticipate that this technology may serve for identifying likely responders to immunotherapy. In addition, we have studied how "priming" with radiotherapy increased the T-cell 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*.

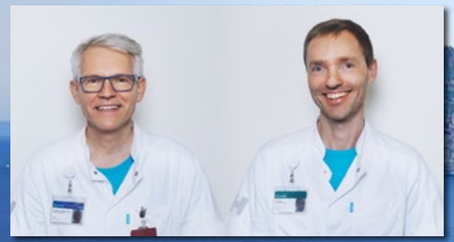
We have established relevant animal models of atherosclerosis, myocardial infarction and heart failure, with reduced or with preserved ejection fraction. These models are used for studies of *cardiovascular disease* and the effect of intervention with novel therapies, e.g. stem cell and GLP-1 therapy.

A particular focus is the targeting of uPAR, a marker of *cancer aggressiveness* that can both be used for prognostication but also as a target for radionuclide therapy. More than 400 patients have been studied in phase phase I/II studies across various cancer types. In general, uPAR has been demonstrated to be highly prognostic and a promising target for radioligand therapy.

Our interest of imaging of *angiogenesis*, which is important both in cancer and cardiovascular disease, has continued. We believe angiogenesis PET may 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. Several Phase II studies have recently been concluded (Figure 1) or are underway.

Optical imaging has recently gained traction for guidance in cancer surgery. We have developed promising ligands used for PET, into optical probes. Accordingly, the peptide used for uPAR binding in PET has demonstrated the ability to delineate tumor margins in several orthotopic xenograft tumors models. Most recently, our first uPAR-targeting ligand has been tested successfully in more than 50 brain, lung and oral cancer patients.

Finally, an increasing focus is currently on developing new *radionuclide therapies*. 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). The efficacy of several such therapies is currently being tested in relevant, predictive human tumor models.



Collaboration with The National Hospital of the Faroe Islands

Professor Jann Mortensen and Chief Physicist Thomas Levin Klausen

The National Hospital of the Faroe Islands, Sjúkrahúsverkið, consist of the two smaller hospitals in Klaksvík and Tvøroyri and the larger central hospital, Landssjúkrahúsið, in Tórshavn. The National Hospital serves the Faroe Islands population of ca. 54,300. The National hospital has 900 employees and 120 beds. There are 29 medical specialities, of which nine are consultant collaborations, including collaboration in Clinical Physiology and Nuclear Medicine with our department at Rigshospitalet.

Reporting of the scintigraphies and lung function test is provided via a direct telemedicine connection. The responsible physician and physicist for Nuclear Medicine in Tórshavn is Consultant, professor, DMSc Jann Mortensen and Head Physicist Thomas Levin Klausen.

In 2022, Department of Clinical Physiology and Nuclear Medicine in Tórshavn performed 1219 (1388 in 2021) patient examinations comprising:

- 368 (499 in 2021) lung-, bone-, thyroid-, kidney scintigraphy's and renographies acquired with the old Skylight camera from 2006 – which had technical problems for three months during which 22 urgent scintigraphy's instead were performed at Rigshospitalet;
- 271 (260 in 2021) lung function test (spirometry, body plethysmography and CO diffusion capacity) performed on the Jaeger whole body plethysmograph;
- 580 (629 in 2021) routine and research DXA studies (BMD and body composition) performed on The Norland DXA 840 scanner.

Collaboration with the Large Animal Teaching Hospital

UNIVERSITY OF COPENHAGEN

Head of Hospital Susanne Nautrup Olsen and Associate Professor Lene Buelund

Skeletal bone-phase scintigraphy has been available as a diagnostic tool at the Large Animal Teaching Hospital, University of Copenhagen since 2012. Scintigraphies are performed in a wide variety of the equine patients admitted to the hospital. It is used to confirm or reject the suspicion of fracture or fissure in horses with severe lameness, where the use of radiography and ultrasound has not been sufficient to reach a diagnosis. Especially pelvic stress fractures are difficult to diagnose using other imaging modalities because of the size of the animal (approx. 600 kg), the large muscles covering the bones and the complex 3-dimensional anatomy.

Another frequent patient category is the sport horse performing poorly or showing multiple limb lameness. In this patient category scintigraphy can help the clinician localize areas for further investigation or treatment.

The scintigraphic examination can include areas like the front limbs, the pelvis or the hindlimbs if a specific fracture is suspected or the entire skeleton of the animal in the poorly performing horse.

The Large Animal Teaching Hospital performs bone-phase scintigraphy on approximately 50 patients a year. The patients are a mixture of in-house orthopedic cases and cases referred from private practice mainly in Zealand and the southern parts of Sweden.

The average activity is 6,4 GBq (technetium-99m pertechnetate) for the typical equine patient with a body weight of 6-700 kg. The activity is injected via an intravenous catheter in the jugular vein and the imaging is performed after a two hour absorption period on the standing sedated animal in a specially designed room where the gamma camera can be moved around the horse.

We have been very satisfied with the collaboration with Rigshospitalet and the consistent and precise deliveries which are crucial for making our scintigraphy service possible. In the future we hope to expand our service to PET scans which is recently introduced and developed in special equine clinics in the USA. We hope to be able to be one of the first equine hospitals in Europe to offer PET scans as a diagnostic tool.

Neurobiology Research Unit

We appreciate the great collaboration with Professor Gitte Moos Knudsen, Head of the Neurobiology Research Unit (NRU) at Rigshospitalet, University of Copenhagen, the Lundbeck Foundation thematic research alliance 'BrainDrugs' as well as the Innovation Fund Denmark Center for Experimental Medicine NeuroPharmacology (NeuroPharm). The research focus of NRU is neurobiology, neuropharmacology, functional and molecular neuroimaging.

nru.dk | braindrugs.eu | 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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Vibeke Rønn
1956-2022

†

Our Head Medical secretary through almost 20 years, Mrs. Vibeke Rønn, sadly passed away suddenly and unexpectedly in the summer of 2022. The Department would like to express our gratitude for Vibeke's dedicated, professional and excellent effort. Our sincere condolences to Vibeke's family and friends.

Vibeke was editor of our annual report for many years. This edition 2022 is dedicated to Vibeke.

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Going green