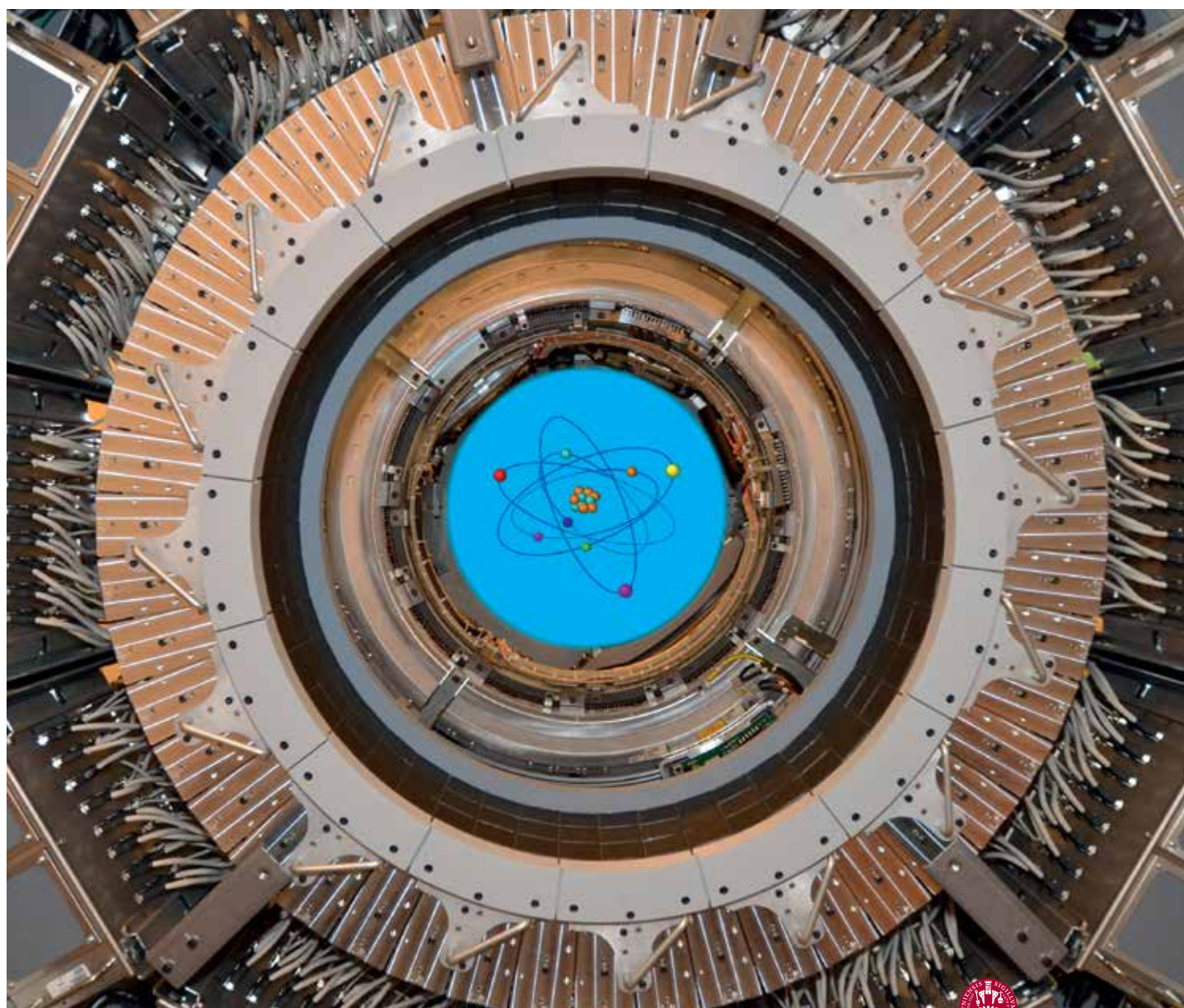


Department of Clinical Physiology, Nuclear Medicine & PET

Annual Report 2012



Rigshospitalet

King Frederik V founded Rigshospitalet in 1757. Today, it has 1,200 beds, 8,500 employees and an annual budget of 5 billion DKK. Research at Rigshospitalet is published in more than 2,000 peer review papers per year, including around 90 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 Sciences has 4,000 students and 10 bachelor- and master educations, 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. www.ku.dk

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Preface

Department of Clinical Physiology, Nuclear Medicine & PET had a another record year in 2012 with 60,851 patient investigations; a significant rise compared to the years previously. The research programmes are the basis for patient studies with implementation of research results in clinical practice as soon as an appropriate level of evidence has been reached. The research programmes last year resulted in 106 peer review publications and 3 theses (PhD and Doctor of Medical Science): strong papers which pushed the boundaries of nuclear medicine. It is the aim of our department that all our patients should receive the best and most appropriate investigation and be treated in a dignified and friendly atmosphere.

A warm thank you to Professor Andreas Kjær who is head of the research in the department and a warm thank you to all the researchers and the staff teaming up to make research the basis for the best patient diagnosis and treatment throughout all activities in the department. A warm thank you to Professor Gitte Moos Knudsen and her team at CIMBI for the enthusiastic and productive collaboration in neurobiology and research (www.cimbi.dk).

We would like to convey our most sincere thank you to all staff members for a fine job done in 2012 with patients, research and education in an enthusiastic, positive and nice atmosphere with trust, communication and interdisciplinarity. The department should be a nice place to work, and in line with that we were one of the best departments in the hospital in the last questionnaire "Trivsel OP" asking how the staff perceived the daily work. In 2012 we focused on improving quality of day life in the department for the staff members, including new light installations, practical devices, new tables with automatic height adjustment. The PET Section implemented a successful LEAN project improving efficiency and working conditions at the same time. The waiting lists have been reduced, and the production has gone up after a successful project led by the Heads of Section Dr Annika Loft Jakobsen and Deputy Chief Nuclear Medicine Technologist Kate Pedersen, and most important the enthusiastic team comprising the total staff in PET. Thank you to every one in the PET Section for the great effort with the LEAN project.

In 2012 we started to use the new PET/MR scanner donated by The John and Birthe Meyer Foundation. It is a "magic machine" for research and at present we have 14 research projects approved by the local Ethical Committee running on the scanner. It is occupied from morning till late afternoon. You can read more in the dedicated section about the PET/MR scanner.



Linda M. Kragh and Liselotte Højgaard

In the Nuclear Medicine Section the treatment with ^{177}Lu -Dotatate in patients with neuroendocrine tumors continued to grow with now more than 200 treatments given in total. Clinical Physiology, Nuclear Medicine & PET is a *Global Excellence* department, and the neuroendocrine program was again accredited by the European Neuroendocrine Tumor Society (ENETS).

Thank you to our directors at the Center of Diagnostics, Rigshospitalet, Center Director, Dr. Bettina Lundgren and Leading Chief Technologist Karin Nørgaard and their team for positive and helpful collaboration. Our department has kept the budget now for the last 13 years; we regard that as a positive and major mutual achievement.

Thank you to the Board of Directors, Rigshospitalet: Torben Stentoft, Chief Executive Officer, Jannik Hilsted, Chief Medical Officer and Helen Bernt Andersen, Chief Nursing Officer for being helpful in many ways throughout the year.

Thank you to the Department of Radiation Therapy for collaboration on research and patient treatment: Professor Svend Aage Engelholm, Chief Nurse Kirsten Amsinck and Chief Physicist Jens Peter Bangsgaard.

Thank you to the Department of Radiology for collaboration on patients and research; we look forward to a continued positive collaboration with the new Head of Department Ilse Vejborg and Chief Radiographer Johnny Madelung. Thank you to Ole Bergsten for valuable help with advice and equipment.

Internationally the EMRC, the European Medical Research Councils, with the office at ESF in Strasbourg are thanked warmly for the great effort for strengthening medical research in Europe and globally as seen on the last page of this report. Thank you to all members and to Professor Kirsten Steinhausen, Mrs. Janet Latzel and the whole team at EMRC.

Our aim is to deliver the best patient treatment and the best research and education. Without all your great effort it would not have been possible. Thank you to all staff, collaborators and international colleagues.

Liselotte Højgaard
Professor, Head of Department

Linda M. Kragh
Chief Technologist



Mission and objectives

The mission of Rigshospitalet is to be the leading hospital in Denmark for patients in need of highly specialized treatment.

The general objectives are:

- » to be at the forefront of highly specialized diagnostic treatment and nursing
- » to carry out research and development at an advanced international level
- » to educate staff in the health services to a highly specialized level
- » to contribute with professional advice and exchange of knowledge and expertise to the wider healthcare community
- » to be characterized by openness and human respect

The objectives of the Department of Clinical Physiology, Nuclear Medicine & PET are:

- » to provide optimal clinical physiology and nuclear medicine for patient investigation
- » to carry out research at the highest international level in clinical physiology and nuclear medicine with special emphasis on molecular imaging, isotopes and radiopharmaceuticals
- » to deliver undergraduate and postgraduate education for all relevant professionals within the relevant expert clinical fields, nationally and internationally
- » to provide a good patient experience and ensure the wellbeing of the staff

The staff have participated in very many congresses, symposias, meetings and workshops with invited lectures, oral presentations, abstracts and posters. We have a comprehensive program for all staff members at the department, and frequent visits from Danish and international research groups.

In 2012 more than 300 groups and individuals visited the department.

Organisation and staff



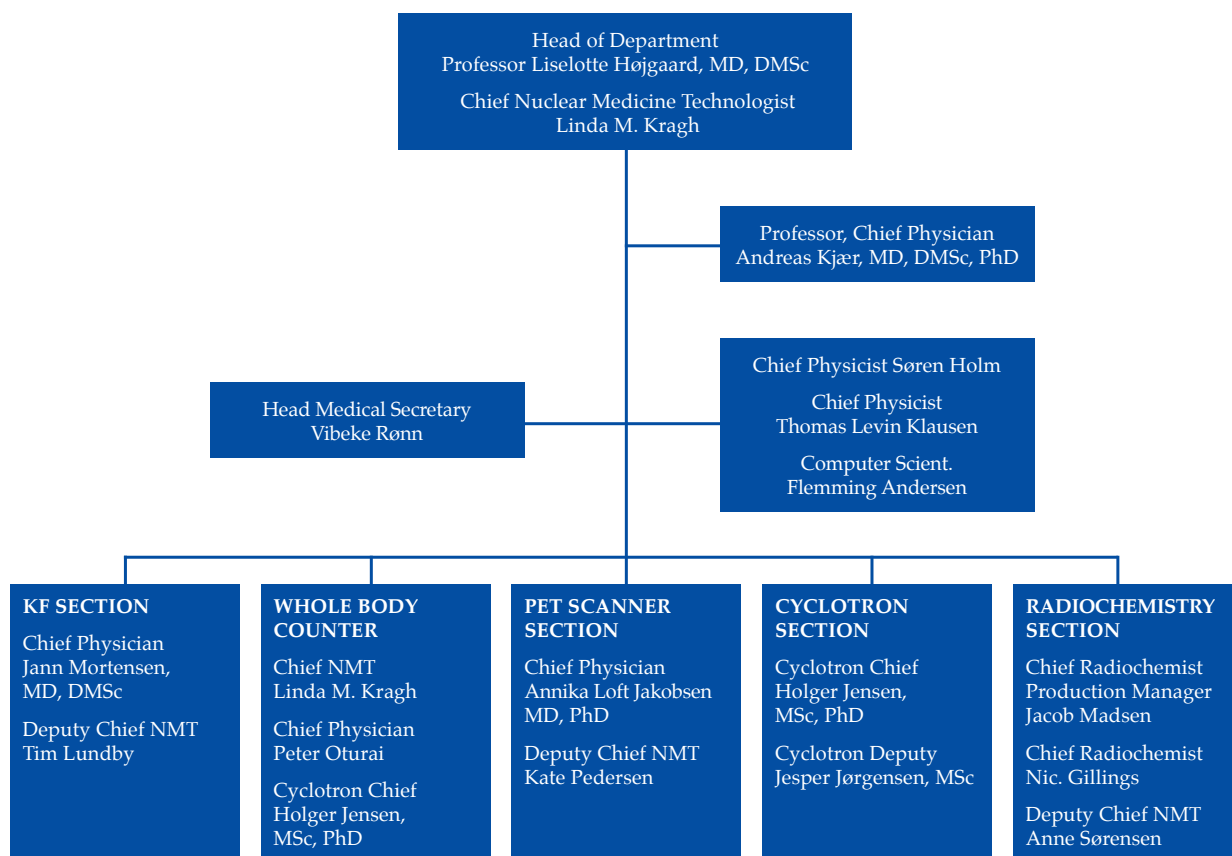
Department of Clinical Physiology, Nuclear Medicine & PET is part of The Diagnostic Center headed by Bettina Lundgren, Director, MD, DMSc and Karin Nørgaard, Vicedirector.

Physicians

Andersen, Kim Francis, Senior Registrar. Benzon, Eric von, MD, Chief Physician. Berthelsen, Anne Kiil, MD, Chief Physician. Borgwardt, Lise, MD, PhD, Chief Physician. Christensen, Charlotte Birk, MD, Senior Registrar. Costa, Junia, MD, Senior Registrar. Fischer, Barbara Malene, MD, DMSc, PhD, Senior Registrar. Hansen, Tine Willum, MD, Senior Registrar. Hasbak, Philip, MD, Chief Physician. Henriksen, Otto Mølby, Senior Registrar. Hesse, Birger, MD, DMSc, Chief Physician. Højgaard, Liselotte, MD, DMSc, Head of Department, Professor. Jakobsen, Annika Loft, MD, PhD, Chief Physician. Johannesen, Helle Hjorth, Chief Physician. Jørgensen, Louise, Registrar. Kjær, Andreas, MD, DMSc, PhD, MBA, Chief Physician, Professor. Korsholm, Kirsten, MD, Registrar. Law, Ian, MD, PhD, Chief Physician. Löfgren, Johan, MD, Chief Physician. Markova, Elena, MD, Chief Physician. Marner, Lisbeth, MD, Registrar. Mladenovic, Maja, MD, Registrar. Mortensen, Jann, MD, DMSc, Chief Physician, Ass. Professor. Mørup, Peter, Senior Registrar. Oturai, Peter, MD, Chief Physician. Rask, Charlotte Krogh, Senior Registrar.

PhD students, postdocs & clinical assistants

Andersen, Julie Bjerglund, MD, PhD Student. Andersen, Valdemar Lykke, Pharmacist, PhD Student, Cimbi Researcher. Binderup, Tina, MSc, PhD Human Biology, postdoc. Bodholt, Rasmus Poul, Research Fellow. Christensen, Thomas Emil, PhD Student. Clausen, Malene, MD, PhD Student. Clemmensen, Andreas Ettrup, Engineer, Research Fellow. da Cunha-Bang, Sophie MD, PhD Student, NRU Researcher.



Department of Clinical Physiology, Nuclear Medicine & PET is part of The Diagnostic Center headed by Bettina Lundgren, Director, MD, DMSc and Karin Nørgaard, Vicedirector.

Erlandsson, Maria, MSc, PhD, Chemist. Ettrup, Anders, MSc Human Biology, PhD, NRU Researcher. Fisher, Patrick, PhD, NRU Researcher. Frøkjær, Vibe, MD, PhD, NRU Researcher. Ghotbi, Adam Ali, MD, PhD Student. Grüner Julie Marie, MD, PhD Student. Hag, Anne Mette Fisker, MSc Human Biology, PhD Student. Haahr, Mette, MD, PhD Student, NRU Researcher. Hansen, Hanne Demant, PhD Student, NRU Researcher. Hansen, Martin, MSc, PhD Student. Herth, Matthias, PhD, Cimbi Researcher. Hollensen, Christian, PhD Student. Jensen, Mette Munk, MSc Human Biology, PhD student. Johnbeck, Camilla Bardram, MD, PhD Student. Jørgensen, Jesper Tranekær, MSc Human Biology, PhD student. Kaijer, Michelle Nymann, Technologist. Knudsen, Jesper Andreas, MD, PhD Student. Li, Fan, MSc Med Tech, PhD Student. MacMahon, Brenda MD, PhD Student, NRU Researcher. Marthin, June, MD, PhD Student. Nedergaard, Mette Kjølhede, MD, PhD Student. Nielsen, Anna Pors, MD, Research Assistant, NRU Researcher. Nielsen, Carsten Haagen, MSc Med Tech, PhD Student. Nielsen, Kristina Rue, MD, PhD Student. Olesen, Oline Vinter, MSc Med Tech, PhD Student. Persson, Morten, MSc Pharm, PhD Student. Pedersen, Sune Folke, MSc Human Biology, PhD Student. Pfeifer, Andreas, MD, PhD Student. Ripa, Rasmus S, MD, DMSc, Post.Doc. Schjøth-Eskesen, Christina, MSc Chem, PhD Student. Skovgaard, Dorthie, MD, PhD, Post.Doc. Thorsteinsson, Kristina, MD, Research Fellow. Zornhagen, Kamilla Westarp, DVM, PhD Student.

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Highlights 2012



Professor Andreas Kjær introduced first-in-man use of the PET-tracer ^{64}Cu -DOTATATE.



Barbara Malene Bjerregaard Fischer, MD PhD defended her Doctoral Thesis at the University of Copenhagen Medical Faculty. The defence took place in the old auditorium in the Medical Museion, previously The Royal Academy of Surgery, founded 1785.



The John and Birthe Meyer Foundation donated 35 mill. DKK to the first PET/MR scanner in the Nordic Countries. In 2012 we started to use the machine for a variety of research programmes, and it is indeed a "magic machine".

The Capital Region of Copenhagen donated 12 mill. for a hyperpolarization equipment to produce ^{13}C -Pyruvate for advanced metabolic MRI research on the PET/MR machinery. It will be one of the first machines world wide with this function added.





From June 2012 the department initiated the use of Rubidium Cardiac PET studies for research and routine investigations of complicated cardiac patients before.



Professor Liselotte Højgaard was in the end of 2012 appointed Chairman of the Board of the Danish National Research Foundation, "Danmarks Grundforskningsfond", and will take over after Professor Klaus Bock 1st of January 2013

Professor Liselotte Højgaard was President of the Copenhagen Research Forum I and II with feed back from 600 excellent European researchers to the European Commission and European governments on how to structure the new "Horizon 2020", the EU Frame Work Programme for research 2014-2020, with a budget 70 bio €. The Capital Region of Denmark, The Technical University of Denmark and University of Copenhagen were hosting the Copenhagen Research Forum, and the recommendations for optimal implementation of "Horizon 2020" were published in the reports (<http://www.crf2012.org/>). Feed back was delivered to the Ministers of Health and the Ministers of Research in Europe at the Informal Council of Ministers meetings in spring 2012, when Denmark had the presidency of EU.



PET/MRI

The integrated PET/MR system was installed in December 2011 and the first scanings were performed in February 2012. The system allows simultaneous acquisition from both modalities and both partial- and wholebody examinations can be done, and different PET-tracers can be applied. The pie plots illustrate the distribution of the production on the scanner in 2012, with a total of 294 combined PET/MR exams.

Work on the PET/MR scanner comprises both clinical research protocols, aimed at unravelling the best diagnostic use of the system, and basic research. Current research topics include metastatic bone lesions, head-neck cancers for radiotherapy planning, gynecological cancers, dementia imaging, characterization of brain tumors, neuroendocrine tumors and atherosclerosis/plaque imaging in the head-neck region. Also cardiac imaging, sarcoma and lung cancer imaging are pursued, as well as pediatric imaging. 9 research protocols were running at the end of 2012.

The novel hardware combination of PET and MRI scanners gives rise to new challenges and opportunities for reconstruction of PET images and fusion of PET and MRI image data. In PET/MRI, PET artifacts can arise from e.g. truncation of MRI images, effects of magnetic susceptibility, metal, the small MR signal from bone and MR image distortions. A large effort has been devoted to monitoring of images and reducing artifacts. Likewise, the simultaneous acquisition of PET and MR images is pursued for motion tracking and correction of PET data. In addition, cutting edge functional MRI methods like dynamic contrastenhanced perfusion and functional brain mapping are being implemented.

The efforts to do research and to realize the full diagnostic potential of PET/MRI are done in a multidisciplinary team, comprising physicists, medical doctors and technologists, with the noteworthy addition in 2012 of visiting professor Thomas Beyer. In addition, we are collaborating with the Martinos center at MGH, Boston, on motion correction and PET reconstruction, and with the neurobiology research unit (NRU). Accepted publications 2012: 5 (4 peerreviewed); presented conference abstracts: 7.

A photograph of a PET/MRI scanner in a clinical setting. The scanner is a large, white, cylindrical machine with a patient bed extending from the center. To the left, there is a computer monitor on a stand. The room has white walls and a blue carpet.

Thank you very much to The John and Birthe Meyer Foundation for the generous donation



Fig 1. ^{18}F -NaF-PET/MR . 51-year-old female patient treated for locally advanced breastcancer. Scanned for bone metastases. ^{18}F -NaF-avid lesions can easily be correlated to MR findings and vice versa.

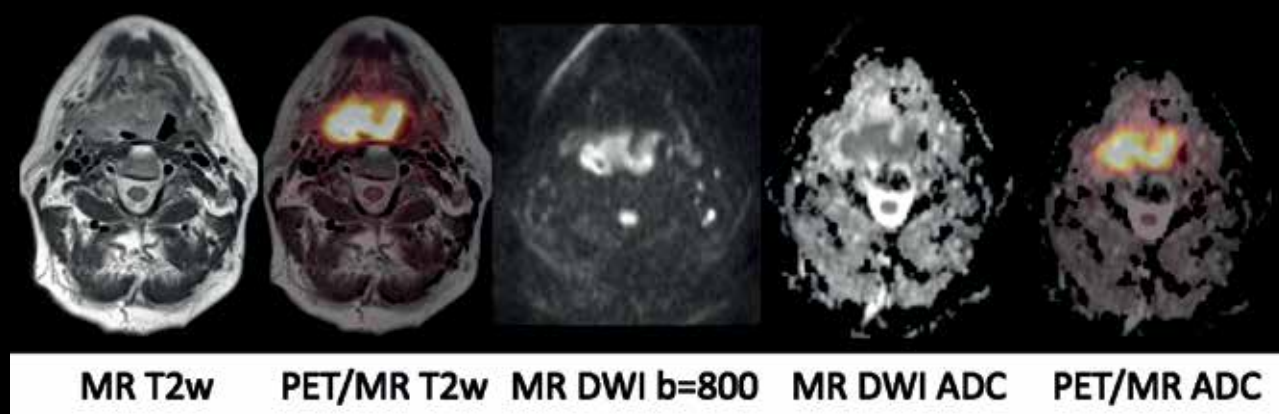


Fig 2. ^{18}F -FDG PET/MR . 72-year old male with newly diagnosed squamous cell carcinoma involving the right tonsil and tongue base region. There is good agreement between the FDG-avid tumor and the diffusion weighted images.

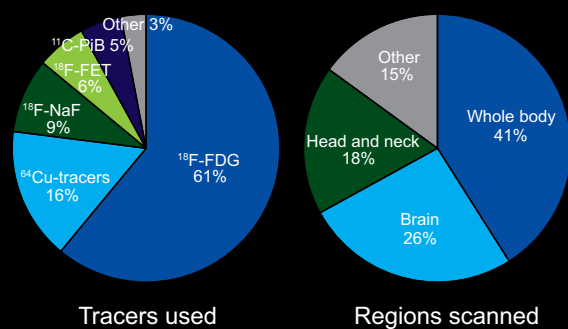


Fig 3. Distribution of the production on the PET/MR scanner in 2012.

Radionuclide therapy

¹³¹I-iodine and ¹⁷⁷Lu-DOTATATE



Jann Mortensen and Peter Oturai

For many years the department has successfully treated patients with benign thyroid diseases – goiter and hyperthyroidism – with ¹³¹I-iodine. Then Zevalin (with Yttrium-90) was introduced for treatment of non-Hodgkin lymphoma.

Since May 2009 we have provided treatment with ¹⁷⁷Lu-DOTATATE in Denmark to patients with neuroendocrine tumor (NET) metastases. Until the end of 2012, 76 patients have been given a total of 246 treatments. Being one of the two highly specialised centers using this treatment modality in Denmark we work in close collaboration with the Departments of Gastro Surgery, Oncology, Radiology, Pathology and Endocrinology at Rigshospitalet.

The NET-Center at Rigshospitalet has been accredited as *Center of Excellence* by the European Neuroendocrine Tumor Society (eNETS).

¹⁷⁷Lu-DOTATATE is synthesized and labelled at the Hevesy Laboratory at Risø, DTU.

¹⁷⁷Lu-DOTATATE is administered in our dedicated facilities in the department and the patients stay overnight at the surgical ward.

The rationale for the treatment is, that the radio labelled somatostatin analogue binds to neuroendocrine tumors expressing somatostatin receptors, especially subtype 2. The emitted beta-particles from the ¹⁷⁷Lu-isotope destroy the tumor cells. In addition the emission of gamma photons from ¹⁷⁷Lu allows for scintigraphic imaging and dosimetry.

The indications for ¹⁷⁷Lu-DOTATATE therapy are inoperable patients with neuroendocrine tumors that either show progression or cannot tolerate standard treatment. A prerequisite is somatostatin receptor imaging (usually an ¹¹¹In-octreotide scan) demonstrating a high density of somatostatin receptors in the tumors.

Our experience of the clinical effect is comparable to what we expect from the literature, i.e. some measurable effect in the majority of the patients, and relatively few side-effects.



Nuclear medicine 2012

The majority of the patient examinations in the nuclear medicine section of our department are related to the diagnosis and monitoring of cancer patients. Hybrid SPECT/CT scans of neuroendocrine tumors, sentinel node scintigraphy for oral cancer, breast cancer, malignant melanoma, penile and vulva cancer, bone scans for primary and secondary malignant tumors, MUGA and ^{51}Cr -EDTA clearance measurements for monitoring side effects in chemotherapy treated patients are some examples. Early 2012 we performed the first diagnostic contrast enhanced CT investigations on our Siemens Symbia SPECT/CT scanner, which was the first time in Denmark on this hybrid scanner type. Yet, we have performed contrast enhanced CT investigations on our Philips Precedence SPECT/CT scanners since 2006.

The somatostatin receptor ligand ^{111}In -Octreotide imaging, most often combined with CT scans of diagnostic quality, is an important endocrine nuclear medicine imaging modality and is being increasingly used for evaluation and monitoring of therapy in patients with inoperable tumors. Weekly receptor targeted radionuclide therapy against neuroendocrine tumors, initiated 2009, is a routine function in our department. Read more about ^{177}Lu -DOTATATE therapy on page 14.

During 2012 we acquired a mobile single-head gamma camera (Solo-Mobile, DDDiagnostics) which will be used for routine and research studies in- and outside our department. The gamma camera equipment for routine nuclear medicine imaging and research studies now comprise three hybrid SPECT/CT cameras, one dual-head gamma camera and four single-head cameras.

Radioisotope leakage monitoring procedures are used during isolated limb perfusion with melphalan and tumor necrosis alpha for recurrent melanoma and soft-tissue sarcoma.

Since February 2012 our new DEXA-scanner has been extensively used for bone mineral density and whole body composition investigations – for both routine patients and research projects.

Frequent indications for lung physiology measurements are control after chemotherapy,



Peter Oturai and Jann Mortensen

pre- and postoperative evaluation of endo-bronchial stents in COPD, transplantation and lung cancer, and radio-aerosol mucociliary clearance investigations for the diagnosis of primary ciliary dyskinesia. For lung function testing we have two Jaeger body plethysmographs.

Diagnostic ultrasound is used for thyroid patients having thyroid scintigraphy performed.

In 2012 we have had weekly and monthly conferences dealing with neuroendocrine tumors, pediatric oncology, thyroid, pulmonary, cardiac, adrenal and orthodontic diseases.



Pediatric nuclear medicine

Each year we perform 1600 pediatric nuclear medicine investigations, thereof 300 PET scans, mainly for the large pediatric departments at the hospital. It is a special focus area for our department to perform these investigations at the highest level of excellence, and at the same time make it a positive experience for both the child and its parents. The department is a member of the EANM Pediatric Committee and the Pediatric Imaging Harmonization SNM/EANM.





Lise Borgwardt

In the beginning of this year our new PET/MRI scanner was installed. It has been an interesting year developing the pediatric area of PET/MRI with challenges, but also a lot of very rewarding scans, really showing the reason for this new hybrid modality, especially in children.

This year we have also been focusing on dose reduction in pediatric imaging. Both by implementing PET/MR in the diagnostic work-up of children, but also working on dose reduction in CT protocols and NM dose evaluation in the department and also as part of the Pediatric Imaging Harmonization SNM/EANM. In the process we invited Dr. Helen Nadel, Head of Division of Nuclear Medicine, BC Children's Hospital, Canada and one of the main forces in the Image Gently Campaign. She gave some very interesting talks both at our hospital and at our conference in radiology in Copenhagen.

We are now performing FET PET scanning of pediatric CNS tumors primarily for evaluation and monitoring. It has been implemented in our department by Dr. Ian Law. At EANM 2012 in Milano our group gave a CME talk by Lise Borgwardt on isotope imaging in pediatric brain tumors, also presenting our experiences with FET PET in children.

Our multidisciplinary pediatric haematology and oncology conferences have this year successfully developed into a form being able to present a web-based nuclear medical platform combined with videoconference including districts outside the capital. Our collaborators are very pleased by the new possibilities and the advantages in the diagnostic evaluation of the children.

Research in pediatric nuclear medicine and PET is necessary, as we have an increasing amount of medical doctors, students and technicians involved in the field and we conduct research protocols in children primarily with PET/MRI in order to develop this interesting area.

The work in the Pediatric Committee this year has been very interesting and inspiring, and we are looking forward to next years work in the committee.

Cyclotron Unit



Holger J. Jensen

In 2012 we experienced, as in the previous years, an increase in our productions of radioactive isotopes and ended up with in total 1368 successful productions (582 and 786 for our Scanditronix MC32 and Siemens RDS Eclipse cyclotrons respectively) or 11.4% more than in 2011. During the last 7 years we have experienced an increase of 10% per year in average as seen in figure 1. The major increase this year came from ^{11}C , which increased with 39%. All other productions stayed at a constant level. Looking at the development in the produced ^{18}F activity, we have increased the activity by 16% per year in average since 2006. Despite of we are handling larger and larger activities we have managed to keep the doses to the employees in the Cyclotron- and Radiochemistry Unit under control during the last few years as seen in figure 2.

The year was relatively quiet without any major technical problems for the two cyclotrons and due to the high flexibility of running two cyclotrons we succeeded to have less than 0.3% cancelled productions in 2012. But if 2012 was quiet with respect to technical problems it was very busy with respect to new and ongoing projects:

- » A Bachelor of Science project in cyclotron physics on ion source improvements (both experimentally and theoretically) were performed successfully by Martin R. Henriksen from NBI. As a result we have been able to increase the yield from the ion source by up to 50%. The development is still ongoing.
- » A Master of Science project in cyclotron physics on the development of a new $^{62}\text{Zn}/^{62}\text{Cu}$ generator as a source of ^{62}Cu (97.4% β^+) for PET radiopharmaceuticals were started in September 2012 by Thorkil K. Værge from NBI. The short half-life of ^{62}Cu (9,74 min) makes the use of ^{62}Cu very limited, when produced directly in a cyclotron. But with the 9.13h half-life of ^{62}Zn the generator can be used for more than one day and can potentially at the same time be distributed to many hospitals in Denmark and Sweden. The nuclear fusion reaction used for producing ^{62}Zn requires relative high beam energy of something like 32 MeV. This is much higher than the available energies for typical medical cyclotrons and therefore ideal for our Scanditronix MC32 cyclotron.
- » In 2012 we started several upgrade projects for our Scanditronix MC32 cyclotron. The projects are all in progress and are expected to be finished in 2013, but will anyway be listed here:

- a) A new ^{18}F target has been developed together with our colleagues in Uppsala and Lund. With the new target we expect to become able to increase the maximum beam current at the target from the present 30 to 50-60 μA and therefore doubling the ^{18}F production capacity.
 - b) The high-vacuum pumps have been modified in various ways (better cooling of the baffles and better oil) to reduce the back streaming of oil into the vacuum chamber and consequently give a better beam.
 - c) In order to improve the vacuum of the central region we have started a process of constructing new parts for the central region, which gives a better conductivity. This development is done together with the company HRS from Kalundborg. In this ongoing work we also attempt to improve the electrical fields in the central region and obtain a better (axial) focusing of the beam for the first few critical orbits.
 - d) The original *Siemens Simatic* S5 and CP521 based control system from 1992 was replaced by a S7 and IGSS based SCADA system. In 2013 all I/O boards for the more than 1000 digital and analogue signals will be changed. The update, which still needs to be validated, gives us a modern software- and hardware platform and an up to date system with modern features of easy handling of alarms and coding of new logic, the possibility of logging parameters and making various reports and graphs. The upgrade plays an important part in our many future plans for the MC32 cyclotron.
 - e) The last project to be mentioned here is our plans for replacing major parts of the electronics in the RF system. The system is more than 20 years old and it is getting more and more difficult to find spare parts for this subsystem. Consequently a new project were started in 2012, where we together with *Axcon Aps* carried out a detailed pre-investigation of the system in order to establish the necessary knowledge to design new electronic boards and to estimate the cost for a total replacement. Money for this project has been applied for via different channels.
- » In 2012 we also got money for upgrading our stack monitoring system (PAMS) in order to solve problems of saturation in the counting system in connection with high releases of activity. This project is done together with the company *CANBERRA* from Belgium.
- » In 2012 we hosted the *Siemens European Cyclotron Users* meeting with participants from all over Europe, US and South Africa.

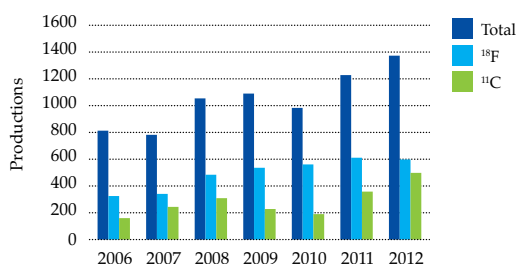


Figure 1 Development in total number of productions, ^{18}F and ^{11}C productions since 2006.

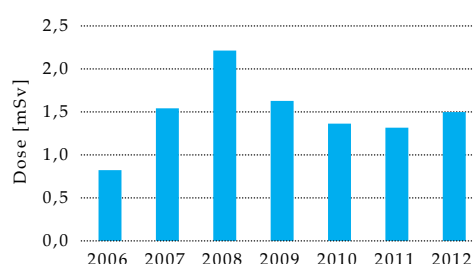


Figure 2 Average received doses for employee in the Cyclotron and Radiochemistry Unit since 2006.

Radiochemistry

Highlights

In May 2012 we started using our new hotlab for routine ^{18}F -FDG production and dispensing, and in June we came through an inspection by The Danish Medicines and Health Authority relatively unscathed. Another highlight was the establishment of a new GMP hotlab with 2 hotcells which will expand the capacity for production of new tracers for human use in the coming years. The greatest highlight of 2012 for the Radiochemistry Section came near the end of the year when, after a lengthy approval process, the first ever ^{11}C -Cimbi-36 human scan was performed. This was the start of a clinical trial of this novel radiopharmaceutical developed *in-house* for 5-HT_{2A} neuroreceptor imaging. The clinical trial will continue throughout 2013.

Production for clinical and research PET in humans

Production of ^{18}F -FDG and krypton-81m generators was on a level with last year whilst production of the newly established tracers increased dramatically in 2012 (see figure). The brain tumor tracer ^{18}F -FET, the cell proliferation tracer ^{18}F -FLT and the neuroendocrine tumor tracer ^{68}Ga -DOTATOC are now produced on a regular basis for both clinical and research applications in humans. Production of the Alzheimer tracer, ^{11}C -PIB also increased compared with previous years as did production of neuroreceptor ligands for brain research. Excluding ^{18}F -FDG and krypton-81m generators, the number of radiopharmaceutical productions for human use increased by 85% compared with 2011.

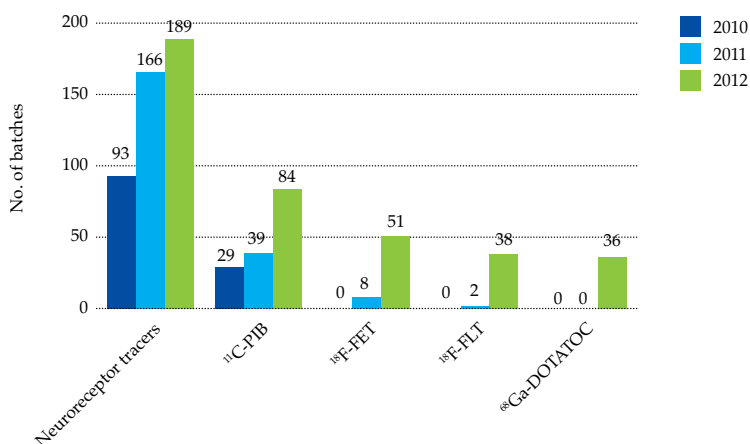
Radiopharmaceutical Development

Oncology — In 2012 the monomer and dimer of cyclic RGD-peptides were radiolabelled with ^{68}Ga and ^{64}Cu for evaluation of their *in vivo* properties in mice. Regular production of ^{18}F -Annexin V for animal studies was continued and, in parallel, more specific labelling approaches were pursued. Another ongoing project involves development of a new tracer for uPAR imaging. Among several candidates, ^{64}Cu -DOTA-AE105 seems to have appealing properties and its potential will be further investigated. A new project focusing on radiolabelling of the inactivated form of rFVIIa (factor seven) was initiated. The first candidate labelled with ^{18}F -SFB seems to have promising properties. As a part of a PhD project, efforts will be made to develop new candidates labelled with various radionuclides. Another ongoing PhD project involves development of labelled peptides for imaging the mutated epidermal growth factor tyrosine kinase receptor (EGFRVIII).



Neurobiology — Collaboration with The Neurobiology Research Unit, Rigshospitalet and the Department of Medicinal Chemistry at PHARMA (University of Copenhagen) under CIMBI (Centre for Integrated Molecular Brain Imaging) continued in 2012. New development focused mainly on 5-HT₇ antagonists and fluorine-18 analogues of ¹¹C-Cimbi-36 (5-HT_{2a} agonist). There were 31 pig scans performed for evaluation of new compounds in 2012. Also validation of a 5-HT_{1b} agonist ligand was commenced and an application for human use will be submitted early in 2013.

Increased production of PET radiopharmaceuticals 2010-2012





New GMP hotlab



¹⁸F-FDG production and dispensing laboratory

Radiopharmaceutical	Usage/target
¹⁸ F-FDG	Oncology / Glucose metabolism
Krypton-81m generator	Lung ventilation
¹⁸ F-FLT	Oncology / cell proliferation tracer
¹⁸ F-FET	Oncology / amino acid transport
⁶⁸ Ga-DOTATOC	Neuroendocrine tumors / Somatostatin receptors
¹¹ C-PIB	Alzheimers Disease / β -amyloid plaques
¹⁸ F-Altanserin	Brain Research / 5-HT _{2a} receptors
¹¹ C-Cimbi-36	Brain Research / 5-HT _{2a} receptors
¹¹ C-CUMI-101	Brain Research / 5-HT _{1a} receptors
¹¹ C-DASB	Brain Research / serotonin transporter
¹¹ C-Flumazenil	Brain Research / central benzodiazepine receptors
¹¹ C-SB207145	Brain Research / 5-HT ₄ receptors
¹⁵ O-water	Cerebral blood flow
¹³ N-ammomia	Cardiology / cadiac blood flow

Radiopharmaceuticals for human use produced at Rigshospitalet

PET/CT scanning in oncology



Annika Loft Jakobsen and Anne Kiil Berthelsen

Positron emission tomography is now well established in oncology and plays a major role in the diagnostic work-up for many patients due to the high sensitivity and specificity for diagnosis and treatment response monitoring.

Our CT scans of PET/CT are performed as high quality diagnostic scans with the use of oral and intravenous contrast media. The PET- and the CT scans are initially interpreted separately followed by a joint interpretation of the fused images and a final, combined conclusion taking both examinations into account. This provides the clinician with a more precise PET result, a better CT result and also a more useful conclusion. The CT result improves in quality because PET can help depicting small tumors that could easily have been overlooked even by a trained radiologist's eye. The PET positive foci are more precisely determined as correct or false positive with the help of the CT information. Finally, the combined PET/CT conclusion is superior to both scan results alone. Furthermore, the patient is spared from an extra CT examination at The Department of Radiology as well as an extra radiation dose.

The indications in oncology are mainly diagnosis, staging, therapy monitoring and detection of recurrent disease in patients with a variety of malignant diagnoses. As a routine, we have included a supplementary CT of the lungs with breath hold technique to improve the diagnostic quality. Approximately 50% of our patients participate in clinical research protocols. Our main topics are gynecology, malignant lymphoma, neuroendocrine tumors and lung cancer. We have 17 weekly multidisciplinary team conferences, where our PET/CT scan results are discussed with the clinical experts.

FDG is still the main tracer in oncology, but we also use ^{18}F -NaF, ^{18}F -FET, ^{18}F -FLT and ^{68}Ga -DOTATOC in clinical studies as well as in research protocols.

Working with PET/CT for many years now, we are convinced of the usefulness of PET/CT in the everyday clinical work. However, clinical trials are still necessary to verify the usefulness of the method, refine the scanning protocols and to develop new indications.



PET/CT scanning in radiation therapy



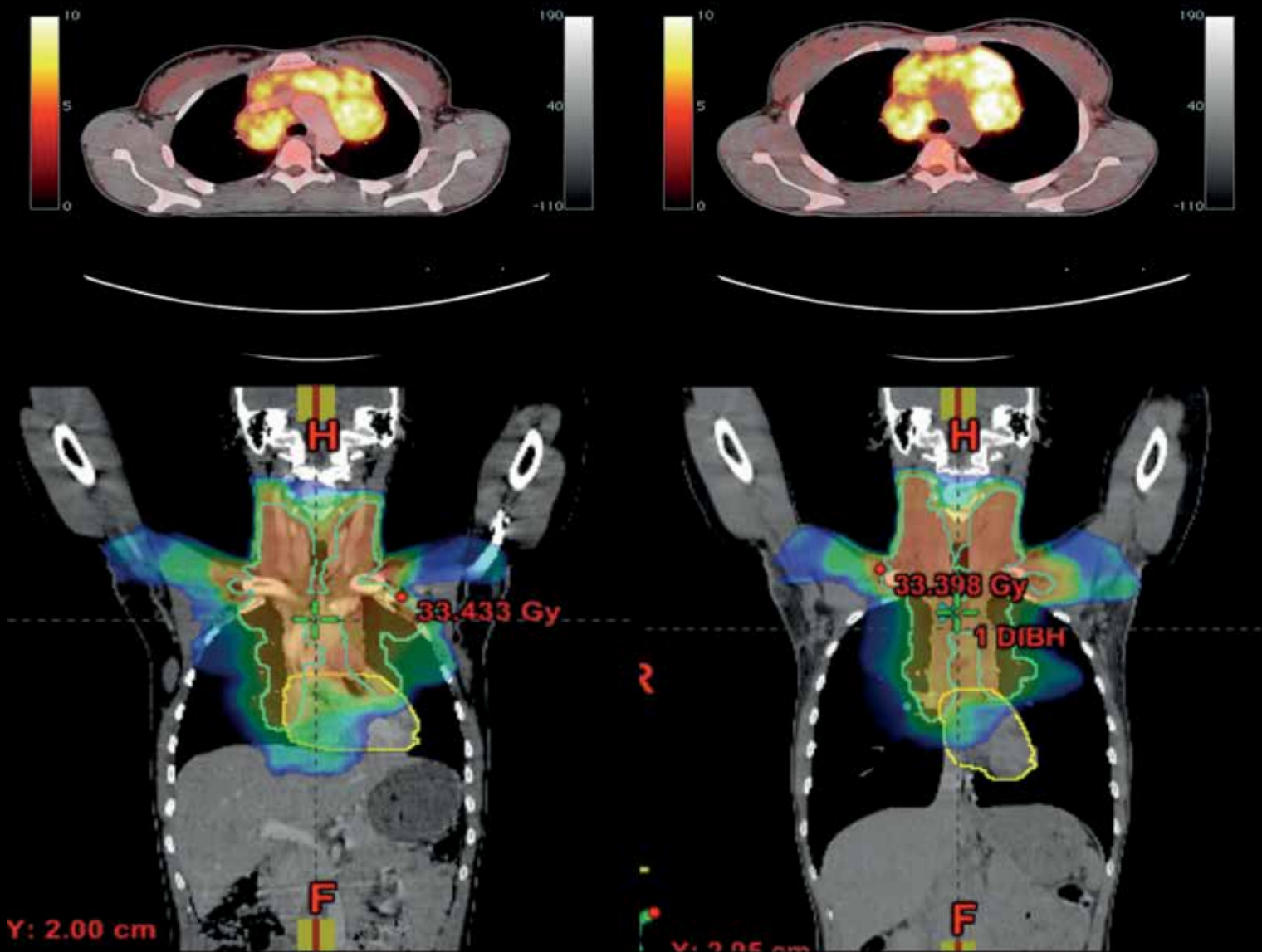
Annika Loft Jakobsen and Anne Kiil Berthelsen

PET/CT in radiotherapy planning of cancer patients is now a daily routine in our department. We perform 1500 PET/CT scans for radiotherapy every year for patients with brain, cervix-, head & neck-, lung-, oesophageus-, cardia-, rectum- and anal cancer as well as malignant lymphoma and mesothelioma.

The demanding collaboration between mould technicians, nuclear medicine physicians and technologists, radiologists and radiology technologists, radiation oncologists, physicists, and dosimetrists must be emphasized.

The advantages are numerous: The anatomical localisation and the metabolic activity of the tumor are defined, especially when the tumor density in CT images is difficult to differentiate from that of the surrounding normal tissue, and the tissue heterogeneity can then be taken into account when choosing radiation technique and energy, and only one scan is necessary. All our PET/CT scanners have the possibility of performing PET/CT scans for radiotherapy planning. The nuclear medicine specialist delineates the viable tumors depicted by PET on the fused PET/CT images after interpretation together with the radiologist. We rely on visual analysis more than fixed threshold levels. The regions are exported to the radiation dose planning system together with the CT scan, and the information is incorporated in the treatment planning.

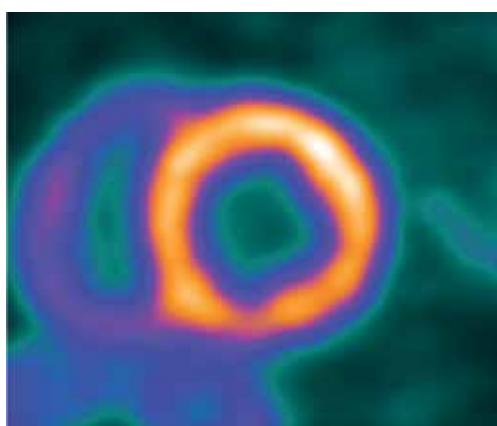
Research in this field is necessary. We are now finalizing our study using breathhold PET in lymphoma of the mediastinum. The preliminary results are so encouraging, that we expect to implement the method in our routine management of lymphoma patients with mediastinal involvement in the nearest future. We are involved in numerous research protocols, local as well as multicenter.



A: Standard PET/CT with free shallow breathing of a patient with malignant lymphoma involving the mediastinum. The image below shows the radiation dose plan based on the PET/CT.

B: Breath hold PET/CT of the same patient as in A. Notice the changes in configuration of the tumor volume and the heart due to inflation of the lungs hereby reducing the radiation dose to the heart and lungs.

^{82}Ru -PET/CT advances heart imaging at Rigshospitalet



Rigshospitalet is the first hospital in Scandinavia and one of the first in Europe to diagnose ischemic heart disease using a new type of advanced imaging system. The system, called Rubidium PET/CT Scanning, combines positron emission tomography (PET) with computed tomography (CT) angiography. In half an hour, this noninvasive imaging technology helps us make a precise diagnosis, which is the first step for providing excellent patient care.

What is exciting about this system is that we can obtain information about the heart's anatomy and function in the same setting. This complementary information makes it possible to interpret the data much more intelligently and quickly determine what kind of treatment will most benefit a patient, whether it is medical therapy, angioplasty or surgery.

Rubidium PET acquires images by detecting the radioactive tracer rubidium. The CT part of the combined imaging system uses rotating X-ray beams to visualize potential coronary artery stenosis. The combined system measures blood flow in precise, numerical terms and yields images of coronary arteries comparable to those seen in the invasive technique cardiac catheterization.

In addition, when combined with another tracer called ^{18}F -FDG, that assesses sugar molecules which the heart burns as its main fuel, rubidium PET/CT produces a clear picture of viable areas of heart muscle and differentiates them from those that are scarred. This distinction can help us decide whether bypass surgery or angioplasty would make it possible for patients with reduced heart function to improve the left ventricular function after surgery.

A rubidium-based PET/CT scanner is much less expensive to operate than PET/CT systems that use another tracer, ammonia, which provide similar measurements and images. The annual cost of rubidium is less compared to the yearly expense to operate a cyclotron to produce the ammonia tracer.



Philip Hasbak

PET imaging has been around for years. It is used extensively to diagnose various cancers. The cardiac community has been slow to adopt PET imaging because it is more expensive than another commonly used imaging system called Single Photon Emission Computed Tomography (SPECT).

Many hospitals, including Rigshospitalet, use SPECT imaging during treadmill and pharmacological stress tests to determine whether a patient needs angioplasty to unblock a clogged coronary artery. These SPECT studies usually take 2 days to complete. SPECT is useful for detecting advanced heart disease, but because SPECT images are not as detailed as PET images. SPECT may not show blood flow restrictions that could signal early stages of heart disease. SPECT images, show blood flow only in relative terms, as coloured areas on a screen. PET shows the true, underlying disease in numerical, quantitative terms. So whether the study is done in UK, USA or in Denmark, we should all get the same quantitative numbers and not simply rely on the expertise of the interpreter at a particular institution.

A major advantage of PET over SPECT comes when testing obese patients. Large body size impairs the ability of photons, the particles of light that come from the radioactive tracer, to register correctly on the SPECT imaging camera. This could result in a false positive reading and an incorrect diagnosis. These images may suggest that there is impaired blood flow in the heart muscle, when in fact the image is not as clear because of the fatty tissue lying over the heart.

This is definitely an important advance in imaging for cardiovascular disease. It is new and we are still evaluating its use for particular types of patients, but it may become a one-stop solution for the early diagnosis of heart disease. The PET/CT combination improves the ability to do research, because it is noninvasive.

PET/CT scanning can establish baseline blood flow measurements. Individuals who are studied today and are told to change their eating habits, increase their exercise, and take medications to reduce their risk for coronary artery disease, can be scanned a year later to see what has happened. This type of imaging could help us get ahead of heart disease, and possibly reverse the process of atherosclerosis earlier. PET/CT scans can furthermore be useful in tailoring medication dosages to treat heart disease by comparing baseline images to scans after medical therapy.

PET scanning of the brain

In 2012 we doubled the clinical PET scans performed to more than 1200 examinations divided between 2/3 neurodegenerative diseases and 1/3 neurooncology. This testifies the high diagnostic value of the method and the integration of the technique into the routine clinical workflow. Approximately 40% of the patients participate in clinical research protocols.

The integrated PET/MR scanner was taken into use in early 2012 and represents an exciting development for the neurological patient. MR is characterized by a superior soft tissue contrast relative to CT and is in high demand in most neurological conditions. This may add even further value to the PET scans enabling a high level of integration between the structural and the function evaluation of our patients in a fast and comfortable manner. The technique can deliver the outmost in diagnostic quality in a single visit, which can be expected to increase compliance from patient and clinician and benefit both the clinical routine and research. The results so far are very encouraging, but we are still optimizing the technique.

For the patients with neurodegenerative disease we have designed a salient 20 min PET/MR workflow in cooperation with the Department of Neuroradiology that can deliver high quality cerebral MR images. With high sensitivity we may rule out a number of competing dementia causing conditions, such as brain tumor, ischemia, inflammation, and haemorrhage. At the same time we can identify functional neuronal injury and suggest possible subclassifications of dementia using ^{18}F -FDG or identify cortical amyloid uptake using ^{11}C -PIB, a necessary risk factor for Alzheimers disease. A promising additional imaging biomarker that is under development is hippocampal volume measures based on segmented structural MR imaging that may add additional confidence for the clinician in the dementia diagnosis (fig 1).

In 2012 it was our privilege to participate in 3 randomized clinical treatment trials for Alzheimers disease in collaboration with the Memory Disorders Research Group. These trials are given a high priority as they give access to a potential treatment for a serious progressive condition. Further they enable us to evaluate new tracer technology before they introduced nationally, e.g. alternative brain amyloid tracers.

For the brain tumor patient the perspective is integrated multimodality diagnostic imaging in primary diagnosis, preoperative planning, post-operative evaluation of residual



Ian Law

tumor tissue, radiation treatment planning, treatment monitoring, and detection of tumor recurrence. PET/MR using the aminoacid analogue, ^{18}F -Flouro-Ethyl-Tyrosine (FET) and tissue perfusion measurements using advanced MRI can efficiently supplement the traditional structural MR data to give a unified tissue characterization (fig 2). We collaborate intensely with The Functional Imaging Unit, Glostrup hospital, in the integration of advanced MR into PET/MR for the benefit of these patients.

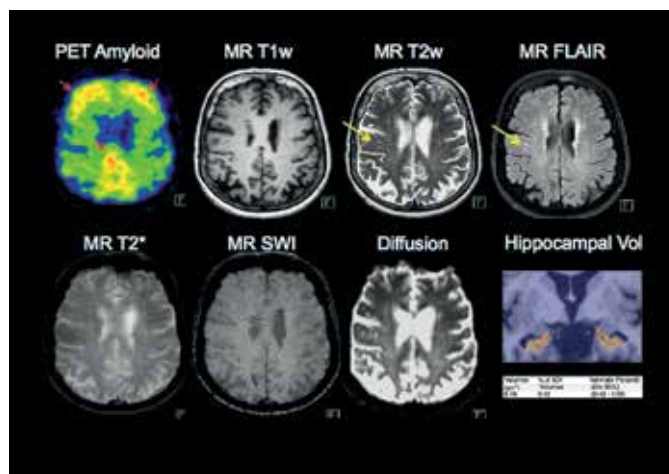


Fig 1. 72 year old female patient suspected of Alzheimers Disease. Simultaneous PET/MRI acquisition shows significant cortical amyloid binding, an essential risk factor for Alzheimers Disease (red arrows). Clinical MRI shows discrete white matter lesions (yellow arrows) presumably older ischemic changes (T2w, FLAIR, Diffusion). There are no microbleedings (T2, SWI). The hippocampal volume is significantly reduced. The combinations of clinical presentation, increased amyloid binding and structural, neuronal damage would categorize the biomarker probability of Alzheimers disease as high.*

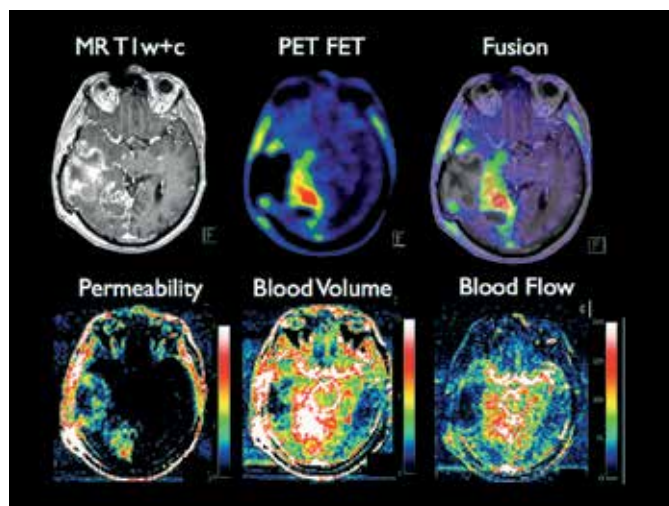
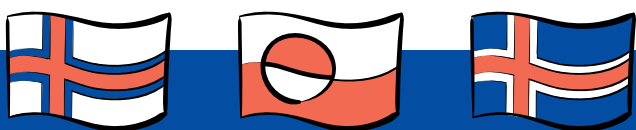


Fig 2. Patient with malignant high grade tumor PET/MR scanned postoperatively using PET FET and advanced MR measurement of permeability, blood volume and blood flow to identify viable tumor tissue.

Collaboration with Landssygehuset, Faroe Islands and Greenland - Iceland



The Department of Clinical Physiology, Nuclear Medicine & PET, Rigshospitalet has a close collaboration with Landssygehuset in Tórshavn, Faroe Islands.

The hospital has a staff of 850 and 170 beds. The 8,000 in-patients and 60,000 out-patients annually are taken care of by 29 specialities, of which 9 are via consultant collaborations, including collaboration with the Department of Clinical Physiology and Nuclear Medicine, Rigshospitalet.

The Department of Clinical Physiology and Nuclear Medicine in Tórshavn performed more than 500 scintigraphies of lungs, bones, thyroid, kidneys, sentinel nodes and renography in 2012. The department is equipped with a one 2-headed Skylight camera, a Norland DXA scanner and a Jaeger whole body plethysmograph. Second opinion on scintigraphy and lung function measurements is provided via a direct telemedicine connection. The responsible physician and physicist for Nuclear Medicine in Tórshavn is Consultant, DMSc Jann Mortensen and Physicist Thomas Levin Klausen.

Chief Nuclear Medicine Technologist Linda M. Kragh at Rigshospitalet, made a 2-day successful audit of the facilities in September 2012 in accordance to the National guidelines.

Rigshospitalet receives the patients from Greenland who need highly specialized treatment. In our PET Center we also investigate patients from Iceland.



Jann Mortensen and Thomas Levin Klausen



Academic and other activities

Andreas Kjær, Chief Physician, is the President of the Scandinavian Society of Clinical Physiology and Nuclear Medicine (SSCPNM), member of the Scientific Committee of the Danish Cancer Society, Editor-in-Chief of Open Neuroendocrinology Journal as well as for Diagnostics. Leader of the project Molecular Imaging for Testing of New Drugs funded by the Danish National Advanced Technology Foundation, Leader of a project on new PET tracers funded by the Strategic Research Council and Partner of the Danish Chinese Center for Proteases and Cancer funded by the National Natural Science Foundation of China and the Danish National Research Foundation, National Center Director and partner of EATRIS (the European Advanced Translational Research Infrastructure in Medicine) under the EU 7FP, and Head of the Cluster for Molecular Imaging and Director of the Postgraduate School for Medical & Molecular Imaging at the Faculty of Health Sciences, University of Copenhagen.

Anne Kiil Berthelsen, Chief Physician, is a member of the International Lymphoma Radiation Oncology Group, Steering Committee (ILROG), "European Organisation for Research and Treatment of Cancer Lymphoma Group" (EORTC), the Danish Radiology Society, the Danish and the Nordic Society of Gynaecological Oncology, British institute of Radiology (BIR), Billedagnostisk udvalg Ukendt Primær tumor (DAHANCA), National PET/CT Group, the Danish Society of Clinical Oncology and the Danish Society of Magnetic Imaging.

Annika Loft Jacobsen, Chief Physician, is involved in teaching at many different national and international courses pre- and post graduate for medical doctors, technologists, radiographers and nurses. She is supervisor for several PhD students. Responsible for the specialist course in oncology for nuclear medicine physicians. She is a member of the "European Organisation for Research and Treatment of Cancer" (EORTC), the Functional Imaging Group. Member of the EANM, AMI, BIR, Danish Society of Oncological Radiology and Danish Society of Clinical Physiology and Nuclear Medicine. Member of Regional Working Groups for implementation of clinical guidelines for:

colorectal liver metastases, lymphoma, malignant melanoma, cancer of unknown primary, prostate, penile and testicular cancer, and unknown primary cancer. Member of National Working Groups for Lymphoma (Chair of the Diagnostic Imaging Group under Danish Lymphoma Group (DLG)) and pharyngeal/laryngeal cancer. Member of the Steering Group for Danish Liver and Biliary Cancer, DAPROCA (Danish Prostate Cancer Group) and board member of DGCG (Danish Gynecological Cancer Group).

Camilla Sloth Knudsen, Nuclear Medicine Technologist, is member of the Board of LSB (Laboratoriemedicins Selskab for Bioanalytikere).

Jacob Madsen, Chief Production Manager, is member of the Board of DSKFNM (Danish Society of Clinical Physiology and Nuclear Medicine).

Jann Mortensen, Clinical associate professor, Chief physician, is a member (vicepresident) of the board of "Dansk Selskab for Klinisk Fysiologi og Nuklearmedicin, DSKFNM" (Danish Society of Clinical Physiology and Nuclear Medicine) and the steering committee of "Dansk Lungecancer Gruppe" (Danish Lung Cancer Group). He is member of "Den Regionale Videnskabetiske Komite for Hovedstaden" (regional ethics committee). He is member of the subcommittees for "Dansk Diagnostisk Lungecancer Gruppe" (Danish Diagnostic Lung Cancer Group) and "Lungecancer Screeningsgruppen" (Screening of Lung Cancer Group). Member of the supplementary training committee of the DSKFNM and representative for DSKFNM in "Lægevidenskabelige Selskaber" (Organization of Danish Medical Societies). Member of the National Working Group for defining clinical guidelines for Lung Cancer workup and the Regional Working Group for implementation of clinical guidelines for Breast Cancer workup and the Working Group for Creating Danish Reference Values For Lung Function. He is responsible for the specialist course in "Clinical Respiratory Physiology" for nuclear medicine physicians and respiratory physicians. Member of the editorial board of The Turkish Journal of Medical Sciences (Türkiye Klinikleri).

Kate Pedersen, Deputy Chief Technologist, is member of "Fagligt Udvalg for Ledende og Afdelingsbioanalytikere" in the Capital Region under Dbio and member of the University Hospital Rigshospitalets Technologist Symposium.

Linda Kragh, Chief Nuclear Medicine Technologist, is member of "Sundhedsfagligt Råd i Klinisk Fysiologi og Nuklearmedicin i Region H", SFR, (the Speciality Advisory Committee in Clinical Physiology and Nuclear Medicine in the Capital Region), member of Uddannelsesrådet for Bioanalytiker-uddannelsen i Region H, (the Speciality Council for the Education of Technologists in the Capital Region).

Lise Borgwardt, Chief Physician, is a member at the Pediatric Committee under EANM, member of the tumorboard for Pediatric Solid Tumors at Rigshospitalet, member of the Pediatric Imaging Harmonization Group, Chair of the Pediatric Network Group at Rigshospitalet and Chair of the Pediatric Focus Group at the Department of Clinical Physiology, Nuclear Medicine and PET.

Liselotte Højgaard, Professor, Head of Department, was Chair of the Standing Committee of the European Medical Research Councils (EMRC) at the European Science Foundation, Strasbourg, 2006-2012. She is Member of Conseil d'Administration, INSERM, L'Institut National de la Sante et de la Recherches Medicales, Frankrig. Chair of EC FP7 Science Advisory Board in Health Research, 2010-2012. Member of the ESS European Spallation Source, Preparatory Group, University of Copenhagen. 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. Member of ATV "The Danish Academy of Technical Sciences". Member of the advisory boards: Wonderful Copenhagen, Medico-Innovation, Rikshospitalet & University of Oslo, Faculty of Science, University of Lund and DKFZ, Das Deutsche Krebsforschungs Zentrum, member of WHO Research Committee and member of the board of Arvid Nilssons Foundation and Tagea Brandt's prize. Editor of The Oncologist. From 1th of January 2013. Liselotte Højgaard is appointed Chairman of the board of the Danish National Research Foundation.

Malene Fischer, Senior Registrar, is Head of YNK (Yngre Nuklearmedicineres Klub), Member of the Board of DSKFNM (Danish Society of Clinical Physiology and Nuclear Medicine) and Young EANM Delegate.

Marianne Federspiel, Nuclear Medicine Technologist, is member of EANM Technologists Committee.

Nic Gillings, Chief Radiochemist, is member of the Editorial Board of ISRN Molecular Imaging.

Peter Oturai, Chief Physician, is responsible for the postgraduate education in the department. He is Danish delegate, representing Danish Society for Clinical Physiology and Nuclear Medicine (DSKFNM), in the European Union of Medical Specialists (UEMS). He is a member of the UEMS - Accreditation of Nuclear Medicine Training Centers Committee, member of the board of the Danish Endocrine Society (DES), member of the board of the Danish Thyroid Association (DTS), and member of the Danish Thyroid Cancer Guideline Group. Member of the Doctors Clinical Physiology and Nuclear Medicine Training Committee of the DSKFNM. He is responsible for the specialist course in Endocrine Pathophysiology for nuclear medicine physicians in Denmark.

Philip Hasbak, Chief Physician, is a Nucleus Member of Cardiac Imaging, Danish Society of Cardiology, Co-author in the Writing Committee of the position statement on strategies for preintervention diagnosis and imaging in patients with recent onset chest pain or discomfort of suspected cardiac origin, Nucleus Member of National Pathways for Lifethreatening Cardiac diseases and Nucleus Member of Library Subscriptions in Denmark.

Robin de Nijs, MSc, PDeng, PhD, Specialist Medical Physicist, is member of European Association of Nuclear Medicine's Network of Excellence for Brainimaging, participant in EANM's Network of Excellence for Dopamine Transporter Imaging and member of the Danish Society for Medical Physics.

Søren Holm, Chief Physicist, is President of the Danish Society for Medical Physics (DSMF), a delegate for the DSMF at the European Federation of Organisations in Medical Physics (EFOMP), a board member of the Nordic Society for Radiation Protection (NSFS), a member of an IAEA advisory group concerned with QA/QC and image artefacts affecting quantitation in PET/CT, a member of Sundhedsfagligt Råd i Klinisk Fysiologi og Nuklearmedicin in the Capital Region, the Specialty Advisory Committee (SFR) in Clinical Physiology and Nuclear Medicine, and an external lecturer at Copenhagen University.

Tim Lundby, Deputy Chief Technologist, is member of "Lederrådet i Danske Bioanalytikere".

Patient investigations 2012

CNS and peripheral nervous system

Regional cerebral blood flow, DIAMOX, ^{15}O -H ₂ O	7
Regional cerebral metabolism, ^{18}F -FDG	624
Regional cerebral receptor, ^{11}C -PIB	149
Regional cerebral receptor, ^{18}F -FET	512
Regional cerebral metabolism, ^{18}F -Altanserin	12
Regional cerebral receptor, ^{11}C -DASB	135
Regional cerebral receptor, ^{11}C -SB	31
Regional cerebral receptor, ^{18}F -Florbetaben	10
Regional cerebral receptor, ^{18}F -Florbetapir	13
Regional cerebral receptor, ^{18}F -PIB	2
Regional cerebral receptor, ^{18}F -FLT	100
Regional cerebral receptor, ^{11}C -CIMBI	30
Regional cerebral receptor, ^{68}Ga -Dotatoc	2
CT-scanning of cerebrum	41
MR-scanning of cerebrum	101
Total	1,782

Respiratory organs

Lung function test, whole body plethysmography	1,749
Lung function test, whole body plethysmography w / reversibility	146
Lung function test, spirometry,	1,567
Lung function test, spirometry w / reversibility	115
Lung function test, spirometry, physiological provocation	6
Lung function test, diffusion capacity (CO)	3,510
Max. insp. abd expir. muscle pressure	20
Lung perfusion scintigraphy, $^{99\text{mTc}}$ -MAA	45
Lung perfusion scintigraphy, regional,	104
Lung perfusion scintigraphy, SPECT, $^{99\text{mTc}}$ -MAA	224
Lung ventilation scintigraphy, SPECT, $^{81\text{mKr}}$ -gas	272
Lung ventilation scintigraphy, $^{81\text{mKr}}$ -gas	44
Lung ventilation scintigraphy, regional, $^{81\text{mKr}}$ -gas	221
Lung ventilation scintigraphy, $^{99\text{mTc}}$ -Technegas	1
Lung ventilation scintigraphy, regional	8
Lung ventilation scintigraphy, SPECT $^{99\text{mTc}}$ -Technegas	30
Pulmonal clearance, $^{99\text{mTc}}$ -DTPA	5
Mucociliary clearance, $^{99\text{mTc}}$ -Venticolloid	36
Total	8,103

Heart and cardiovascular system

Isotope cardiography, first pass, $^{99\text{mTc}}$ -HSA	12
Isotope cardiography, LVEF, $^{99\text{mTc}}$ -HSA	1,603
Isotope cardiography, LVEF, $^{99\text{mTc}}$ -erythrocyter	0
Myocardial perf. scintigr. gated, $^{99\text{mTc}}$ -MIBI, pharmacol. stress, dipy.	14
Myocardial perf. scintigr. gated, $^{99\text{mTc}}$ -MIBI, pharmacol. stress, adeno.	100
Myocardial perf. scintigr. gated, $^{99\text{mTc}}$ -MIBI, physiological stress	69

Myocardial perf. scintigr. gated, $^{99\text{mTc}}$ -MIBI, NTG	191
Myocardial perf. scintigr. gated, $^{99\text{mTc}}$ -MIBG, Sympaticus activity	40
Myocardial Calcium score	279
PET myocardial perfusion, ^{13}N -NH ₃	44
PET myocardial perfusion, ^{13}N -NH ₃ , pharmacology, stress	19
PET myocardial metabolism, ^{18}F -FDG	77
PET myocardial perfusion, ^{82}Rb	164
PET myocardial perfusion, ^{82}Rb , pharmacology.	116
Stress, adeno	
Exercise electrocardiography	79
Electrocardiography	5
Total	2,812

Peripheral vessels

Isolated limb perfusion leakage monitoring, $^{99\text{mTc}}$ -erythrocyt	17
Total	17

Gastrointestinal tract, liver, biliary tract and pancreas

Salivary gland scintigraphy $^{99\text{mTc}}$ -Pertechnetat	60
Bleeding scintigraphy (abdomen), $^{99\text{mTc}}$ -erythrocyt	3
Bleeding scintigraphy (abdomen), $^{99\text{mTc}}$ -HSA	1
Biliary tract scintigraphy, $^{99\text{mTc}}$ -Mebrofenin	18
Meckels diverticulum scintigraphy, $^{99\text{mTc}}$ -Pertechnetat	4
Total	86

Kidneys and urinary tract

Glomerular filtration, ^{51}Cr -EDTA, several samples	202
Glomerular filtration, ^{51}Cr -EDTA, one sample	4,524
Renal scintigraphy, $^{99\text{mTc}}$ -DMSA	20
Renography, $^{99\text{mTc}}$ -MAG, diuresis	42
Renography, $^{99\text{mTc}}$ -MAG 3, Graft	1,924
Renography, $^{99\text{mTc}}$ -MAG 3, ACE-inhibitor	82
Renography, $^{99\text{mTc}}$ -MAG 3, Graft	13
Renography, $^{99\text{mTc}}$ -MAG 3, Dual head	3
Renography, $^{99\text{mTc}}$ -DTPA	1
^{131}I -Hippuran clearance	57
$^{99\text{mTc}}$ -DTPA clearance	84
Total	6,952

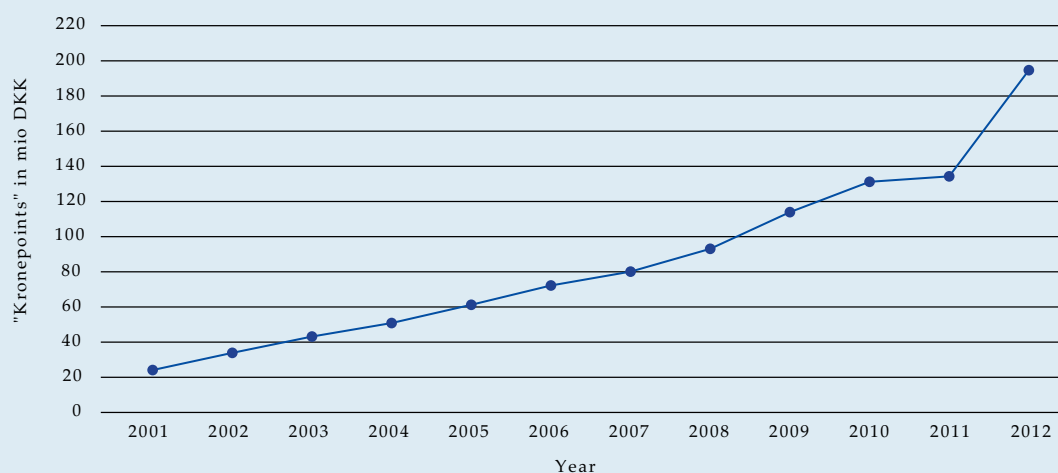
Bone and joint

Bone scintigraphy, $^{99\text{mTc}}$ -HDP, regional, static	63
Bone scintigraphy, $^{99\text{mTc}}$ -HDP, whole body, static	863
Bone scintigraphy, $^{99\text{mTc}}$ -HDP, SPECT	253
Bone marrow, $^{99\text{mTc}}$ -Nanocolloid	3
Bone scintigraphy, ^{18}F -Fluorid, whole body, static	25
Osteodens. dual X-ray absorptiometri (DXA), columna lumb.	1,012

Osteodens. dual X-ray absorptiometri (DXA), lat.spine	23	CT therapy scanning, brain	138
Osteodens. dual X-ray absorptiometri (DXA), radius	88	Second opinions external PET, PET /CT, SPECT /CT, CT and MR investigations	779
Osteodensitometri, dual X-ray absorptiometri, collum fem.	1,995	Extra tumor delineation	104
DXA, body composition	127	Other investigations	17
Total	4,452	Supplementary / repeated imaging	2,946
Endocrine organs		Total	22,262
Thyroid scintigraphy, ^{99m} Tc-Pertechnetat	529	Radiotherapy	
Thyroid scintigraphy, ^{99m} Tc-Pertechnetat, SPECT	1	Treatment with ¹³¹ I, benign thyroid	75
Thyroid, ultrasound	450	Isotope treatment with Zevalin ⁹⁰ Yttrium	0
Parathyroid scintigraphy, ^{99m} Tc-MIBI/ Stamisis	61	Isotope treatment with ¹⁷⁷ Lu-Dotatate	59
SPECT + CT		Total	134
Tumorscintigraphy, ¹²³ I-jodid	15	Total number of patient investigations	
Adrenal marrow scintigraphy, ¹²³ I-MIBG	47		60,851
Scintigraphy after ¹⁷⁷ Lu- Dotatate therapy	96	Animal Studies	
Total	1,199		
Blood and lymph system		Dogs	
Erythrocyt volume, ^{99m} Tc-erythrocytter	8	¹⁸ F-FDG	7
Plasma volume, ¹²⁵ I-HSA	6	⁶⁴ Cu-liposomer	7
Lymph scintigraphy, extremities, ^{99m} Tc-HSA, leakage	2	Rats	
Lymph scintigraphy, extremities, ^{99m} Tc-Nanocolloid, stases	1	¹⁸ F-Annexin	14
Sentinel node, tumor drainage, ^{99m} Tc-Nanocolloid	145	¹⁸ F-FDG	76
Sentinel node scintigr. tumor drainage, c. mammae, ^{99m} Tc-Nanocolloid	31	⁸² Rubidium	14
Sentinel node scintigr. tumor drainage, mel. malign., ^{99m} Tc-Nanocolloid	103	Mice	
Sentinel node scintigr. tumor drainage, c. penis, ^{99m} Tc-Nanocolloid	14	¹⁷⁷ Lu-DOTATATE	30
Sentinel node scintigr. tumor drainage, c. vulvae, ^{99m} Tc-Nanocolloid	24	¹⁸ F-Annexin	10
Sentinel node, peroperative with gamma probe, ^{99m} Tc-Nanocolloid	2	¹⁸ F-FDG	381
Peritumoral injection of ^{99m} Tc-Nanocolloid for sentinel node	655	¹⁸ F-FET	229
Spleen scintigraphy, ^{99m} Tc-erythrocyte, heated	3	¹⁸ F-FLT	126
Total	994	¹⁸ F-NaF	8
In vitro analysis		⁶⁴ Cu-ATSM	80
Plasma analysis	3,364	⁶⁴ CuCl ₂	40
Gene expression analysis	8,444	⁶⁴ Cu-liposomer	239
Immunohistochemistry	250	¹⁷⁷ Lu-liposomer	44
Total	12,058	⁶⁴ Cu-miceller	169
Other diagnostic procedures		⁶⁴ Cu-RGD	104
Tumor scintigraphy, ¹¹¹ In-Octreotide	378	⁶⁴ DOTATATE	16
PET tumor scanning, ¹⁸ F-FDG	4,382	⁶⁸ Ga-RGD	118
PET infection scanning, ¹⁸ F-FDG	78	Au-gel cytokin	112
PET tumor scanning, ⁶⁸ Ga-Dotatoc	45	Nano-gold particles	222
PET tumor scintigraphy, ⁶⁴ Cu-Dotatate	44	Optical imaging	240
White blood cell scintigraphy, ^{99m} Tc-white blood cell	150	Pigs	
White blood cell scintigraphy, ¹¹¹ In-white blood cell	106	¹⁵ O-H ₂ O	1
MR, Columna	116	¹¹ C-NS (NRU)	7
Whole body, contamination measurement	47	¹¹ C-CIMBI717 (NRU)	4
Image fusion (PET, SPECT, MRI, CT or planar)	7,445	¹¹ C-CIMBI712 (NRU)	4
Diagnostic CT	4,784	¹¹ C-VLA32 (NRU)	4
CT therapy scanning, wb	703	¹¹ C-PF5 (NRU)	2
		¹¹ C-PF (NRU)	3
		¹¹ C-AZ (NRU)	1
		¹¹ C PF30 (NRU)	2
		¹⁸ F-CM320 (NRU)	1
		¹¹ C-775 (NRU)	2
		¹¹ C-BA10 (NRU)	4

Finance

Turnover



The increase in activities measured in "krone points" rose from 43.5 million in 2003 to 195 million in 2012.

"Krone points": price for each patient investigation multiplied with number of investigations, summarized for all patient studies performed during the year.

Balance 2012

Expenditure (DKK mio.)

Running costs	23.6
Staff	50.8
In total	74.4

Receipts	21.6
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Publications 2012

Theses

Fischer BM, Doctoral thesis, University of Copenhagen: PET/CT scanning for diagnosing and staging patients with non-small cell lung cancer. Ugeskrift for Læger, 2012. Defended on 14th of December 2012 at Medicinsk Museion, Copenhagen.

Due AK, PhD thesis, University of Copenhagen: Recurrence location after definitive (chemo)radiation therapy for head and neck squamous cell carcinoma in relation to clinical target volumes and ¹⁸F-FDG uptake. Own publishing, 2012. Defended on 12th of October 2012, Tejlumbygningen, Rigshospitalet.

Hollensen C, PhD thesis, Technical University of Denmark: Planning and Evaluation of Radio-Therapeutic Treatment of Head-and-Neck Cancer Using PET/CT. Own publishing, 2012. Defended on 23th of November 2012, the Technical University of Denmark.

Scientific publications

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As in previous annual reports we have listed scientific papers only and not the many abstracts and proceedings from the department.

Research

A strong focus on research is a cornerstone of the department. We have an extensive research program and collaborate with several national and international partners. Our research focuses on development of new tracers for PET, *theranostics*, clinical evaluation of new diagnostic methods, and on the use of methods from clinical physiology and nuclear medicine to study pathophysiology. Translational research in the area of molecular imaging is given special attention in order to accelerate translation of new tracers into clinical use in patients. Some current major research areas are mentioned below.

New tracers

A series of projects are aimed at development of new, specific tracers for non-invasive tissue characterization are currently undertaken. These tracers are to be used for the diagnosis of different cancer types as well as for planning and monitoring of therapy. The projects, translational in nature, are carried out in collaboration with other departments and laboratories both nationally and internationally to obtain the necessary expertise in molecular biology, chemistry, radiochemistry, cancer biology and imaging. Examples of a new tracers developed at the department and now used in patients with neuroendocrine tumors is ^{64}Cu -DOTATATE. In addition we develop new peptide-based PET tracers for imaging of the invasive phenotype and targeted nanoparticles for PET. We have developed a comprehensive platform for validation of new tracers including cell laboratory, molecular biology (proteomics and genomics), histology and biomarker laboratory facilities at the department.

PET/MRI

With installment of the first integrated PET/MRI scanner in the Nordic Countries, we have developed an extensive research program with focus on the added value of combining PET and MRI. A large number of clinical trials as well as projects on method development are currently undertaken with focus on the combined use of the modalities for improved tissue characterization and response monitoring in cancer treatment, pediatric studies, brain studies and atherosclerotic plaque characterization. Focus on MRI includes the use of diffusion weighted images (DWI)/apparent diffusion coefficient (ADC) and magnetic resonance spectroscopy (MRS).



Andreas Kjær

Clinical PET/CT

A large number of prospective protocols are performed to evaluate the diagnostic and prognostic value of PET/CT with different tracers in various forms of cancer in children and adults. Head-to-head comparison studies of new PET tracers and established imaging methods are also performed. The use of PET/CT for the planning of radiation therapy (“dose-painting”) and the use of respiratory gating are also currently being evaluated. Many of these studies now include PET/MRI to the study of added value compared to PET/CT.

Pediatric nuclear medicine investigations

The department conducts many pediatric investigations. Several research protocols with the use of PET and SPECT are carried out in cooperation with clinical departments, particularly within oncology. The use of PET/MRI in children to save radiation dose is also the subject of investigations.



Neuro PET

With the use of PET/CT, including HRRT, studies on brain tumors are undertaken. Studies of brain perfusion using PET or DCE-CT are also performed. In addition, imaging of dementia with new tracers and brain tumors with FET is studied. PET/MRI is now integrated into many of these studies. In cooperation with Neurobiology Research Unit and Centre for Integrated Molecular Brain Imaging, neuroreceptor ligands have been developed and used for research in neurobiology. The focus has mainly been on the serotonergic system.

Atherosclerosis

With the use of PET/CT and PET/MRI we can non-invasively visualize atherosclerosis and probably predict vulnerability of atherosclerotic plaques. With this technique, several studies in different groups of patients at risk and with the use of new PET tracers are currently undertaken. The goal is to develop an image-based algorithm for identification of patients at risk that will benefit from surgery.

Nuclear cardiology

With the introduction and use of ^{82}Rb PET coronary flow regulation is studied quantitatively in connection with a variety of cardiovascular diseases and the influence of interventions including gene therapy, pharmacological treatment and exercise. With the use of SPECT/CT or PET/CT the development of ischaemic heart diseases is studied in selected groups of patients. On basis of this, screening algorithms for detection of ischaemic heart disease are evaluated. Some of the studies are combined with PET tracers characterizing other aspects of the myocardium and its viability. Several of the studies are performed using PET/MRI for additional information.

Lung studies

Research using lung function testing and lung scintigraphy in different patient groups, e.g. lung transplantation and endobronchial stenting for emphysema, are undertaken. The value of combined use of SPECT/CT for diagnosing pulmonary embolism has recently been evaluated. The value of biomarkers in combination with imaging is also studied. In addition, evaluation of the different ventilation tracers for assessment of ventilation inhomogeneity is undertaken. Research is also being conducted into mucociliary clearance, a method pioneered at the department, of the nose and lungs.

Radionuclide treatment and theranostics

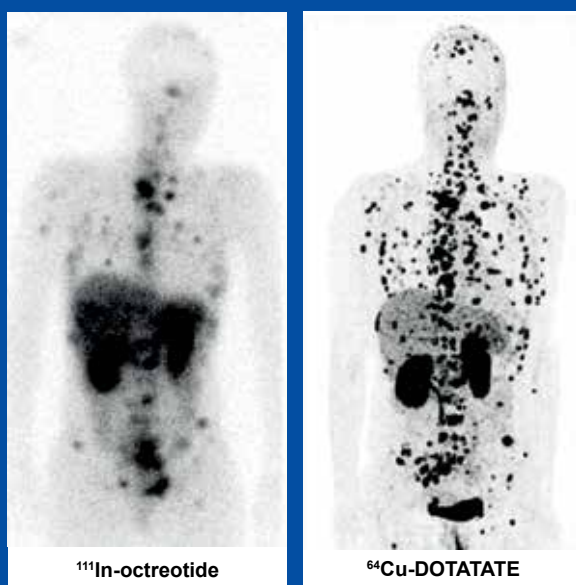
Localized radiation therapy using specific ligands binding to certain cancer forms has recently been implemented. The department takes part in research within this area by testing new ligands and producing relevant isotopes. We also develop new theranostics based on promising imaging ligands labeled with beta or alpha emitting radionuclides. Cancers that are currently being targeted clinically include neuroendocrine tumors and ovarian cancer. Treatment with radionuclides will in part be based on imaging using new tracers for molecular profiling or the same ligand as the therapy (theranostics) for better outcome and fewer side effects.

Whole body counting

Together with external partners, whole body counting is used for exact measurements of body composition in a series of studies. In addition we are investigating absorption of certain minerals from the gastrointestinal tract.

^{64}Cu -DOTATATE:

First-in-humans study of a new PET tracer for neuroendocrine tumors



Comparison of ^{111}In -DTPA-octreotide and our new PET tracer ^{64}Cu -DOTATATE in the same patient with multiple bone and soft-tissue metastases.

One of the focus areas of research at the Department is development of new PET tracers for cancer using our translational capabilities. In 2012 we published data on one such new tracer that we successfully have taken all the way into clinical use.

For neuroendocrine tumors, somatostatin receptor imaging is an important diagnostic tool. Currently SPECT, using the tracer ^{111}In -DTPA-octreotide, is considered gold standard. However, PET is superior to SPECT with regard to sensitivity and spatial resolution and accordingly ^{68}Ga -labeled PET tracers have been introduced for somatostatin receptor imaging. However, due to the high positron energy and short half-life of ^{68}Ga only modest spatial resolution is obtained and delayed imaging is not possible. Therefore, we have worked on development of a new PET tracer based on the positron emitter ^{64}Cu , which has low-energy and an intermediate-half-life of 13 hours. In 2012 we published the first-in-humans study using ^{64}Cu -DOATATE in patients with neuroendocrine tumors. The study showed in a head-to-head comparison with ^{111}In -DTPA-octreotide an excellent imaging quality, reduced radiation burden and increased lesion detection rate. Until now we have performed more than 200 PET scans with ^{64}Cu -DOTATATE.

Our department is part of the European Neuroendocrine Tumor Society (ENETS) accredited Center of Excellence at Rigshospitalet and has been awarded Global Excellence by the Capital Region of Denmark. The development and testing of the tracer has involved several partners of the ENETS Centre at Rigshospitalet as well as the Hevesy Laboratory at Risø, DTU.

Cluster for Molecular Imaging



Andreas Kjær

The change in paradigm towards individualized, tailored therapy has led to a need for diagnosing at the molecular level. Molecular biology methods need tissue sampling for in vitro analysis. In contrast, molecular imaging allows for non-invasive studies at the molecular level in intact organisms. With PET it is possible to label bio-molecules with radioactive isotopes. This method can be used for non-invasive visualization of tumor specific receptors and tissue characteristics such as angiogenesis and ability to metastasize. Especially within cancer biology the technique is expected to lead to a break-through in diagnosing and treatment. Among the different techniques for molecular imaging, the nuclear medicine based technologies have the greatest translational potential since methods developed in animal models may directly be transferred and used in humans. In addition, successful imaging ligands may be developed into radionuclide therapy, such an imaging-therapy pair is known as theranostics.

Our current molecular imaging and theranostics research program is aimed at through use of molecular biology and imaging techniques in both animals and humans to develop, evaluate and use non-invasive molecular imaging for human tissue characterization. Major applications of these tracers are expected to be: 1) planning of individualized, tailored therapy, 2) testing of new drug candidates and 3) basis for development of radionuclide therapy (theranostics).

The development of new molecular imaging tracers for PET is a very complex process that involves many steps from definition of target to final use of the tracer in patients.

Major steps involved in PET tracer development and translation into patients

- » Selection of key-processes involved in the pathophysiology of the disease
- » Definition of relevant molecular targets of the key-processes
- » Design of specific ligands
- » Radioactive labelling of ligands
- » Test of imaging ligands in relevant animal models
- » Use of imaging data for therapy planning and monitoring of response
- » Use for diagnosing, therapy planning and monitoring in patients
- » Use for testing of new drugs

Through formation of Cluster for Molecular Imaging at the Faculty of Health Sciences, University of Copenhagen (headed by Professor Andreas Kjær) a core facility at the Panum Institute for molecular imaging in animals with PET, SPECT, CT and MRI (2013) has been established. This has improved our translational capacity since we are now able to test new tracers and radionuclide therapies in animal models prior to clinical use. In accordance with this we have currently several new tracers in pre-clinical testing in animal models that already have or soon will become available for human use. A strong focus has recently been on the use of clinically relevant animal cancer models, which include orthotopic human xenograft tumors as well as metastatic cancer models using human cancer cell lines. Furthermore, we have also introduced and developed animal models of cardiovascular diseases including atherosclerosis, myocardial infarction and takotsubo.

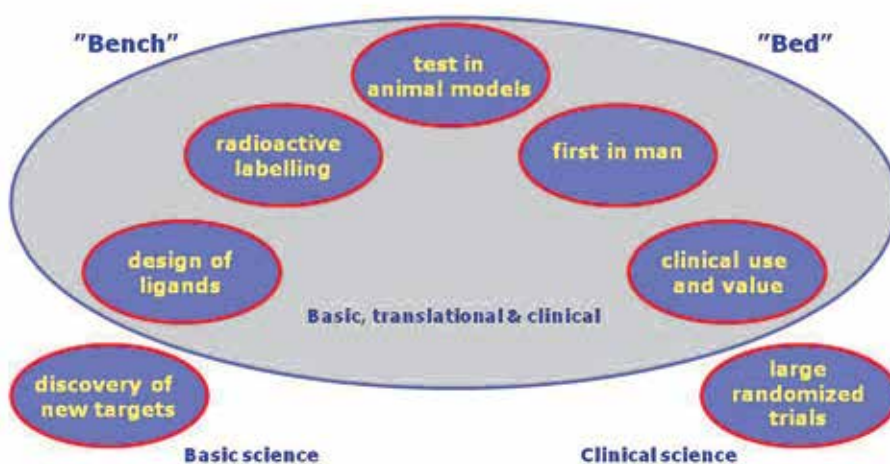
Cluster for Molecular Imaging is imaging partner in the European Advanced Translational Infrastructure in Medicine (EATRIS) under EU 7FP.

Currently the main focus of the translational research in tracers for non-invasive tissue characterization is on the use in cancer and cardiovascular disease and new targeted radionuclide therapies for cancer. However, several other applications are also foreseen.

Some tissue characteristics currently targeted for imaging:

- » Cancer specific receptors (several projects)
- » Glycolytic activity
- » Cell proliferation
- » Amino acid transport
- » Hypoxia
- » Apoptosis
- » Angiogenesis
- » Invasive phenotype

Translation into patients: From new targets to randomized trials



The “translational bridge” with our key competences highlighted in grey

Danish Chinese scientific collaborations

The Department has continued its collaborations with hospitals and research institutions in China. The Danish-Chinese collaborations are focused on development of new molecular imaging probes for cancer and their use and evaluation of anti-cancer therapies, including Traditional Chinese Medicine (TCM).

As part of our research collaboration with Shuguang University Hospital in Shanghai Dr Wenhai Wang from the Department of Oncology, served as visiting scientist at our department, where she was part of a project using PET to detect anti-cancer effects of TCM.

Professor Andreas Kjær is partner in one of the Danish-Chinese Research Centers funded by the Danish National Research Foundation (Danmarks Grundforskningsfond) and the National Natural Science Foundation of China. Recently, the funding of the Center was extended for 2012-2014. The main focus of the Centre is to perform high level research leading to new molecular imaging ligands and tailored therapies. Our current focus is on new PET imaging ligands to identify the invasive cancer phenotype and to translate one or more of these into clinical use. In addition to Rigshospitalet, the partners are Aarhus University, Chinese Academy of Sciences, Fuzhou and Soochow University, Suzhou.



*Danish-Chinese Centre for Proteases and Cancer
The Danish National Research Foundation and
The National Natural Science Foundation of China*

Danish Indian scientific collaborations

We have initiated collaboration with Professor Abhijit De from the Advanced Centre for Treatment, Research and Education in Cancer (ACTREC) of the Tata Memorial Centre and Hospital in Navi Mumbai. Tata Memorial Hospital is the largest cancer hospital in Asia. The collaboration is focused on basic, translational and clinical studies to develop new, cost-effective methods for tumor-targeted treatment of patients using radionuclides. As part of this collaboration Professor Andreas Kjaer served as faculty of the International Conference in Radiation Biology 2012 held in Mumbai, India.



Professor Andreas Kjaer gave a lecture on the use of PET for evaluation of therapies in cancer and chaired a session on molecular imaging at the 2012 ICRB conference held in Mumbai, India. Professor Abhijit De (right) of ACTREC was one of the main organizers of the meeting.

Young investigator prizes

PhD student Carsten Haagen Nielsen

PhD Day, Faculty of Health Sciences, University of Copenhagen, May 2012.

PhD Student of the Year.

PhD student Camilla Bardram Johnbeck

Society for Nuclear Medicine (SNM), Annual Meeting, Miami Beach, USA, June 2012.

Nuclear Oncology Council, Young Investigator Award.

PhD student Sune Folke Pedersen

European Atherosclerosis Society, 80th EAS Congress, Milan, Italy, May 2012.

Best Poster Award.



National Advanced Technology Foundation

With 2012 the project on molecular imaging with PET supported by the Danish National Advanced Technology Foundation (Højteknologifonden) had reached its major goals. At a ceremony held at the Royal Theatre Professor Andreas Kjær received a diploma of successful completion on behalf of all partners. The diploma was handed over by Chairman of the Board Jørgen Mads Clausen from Danfoss A/S and Vice Chairman Professor Klaus Bock.

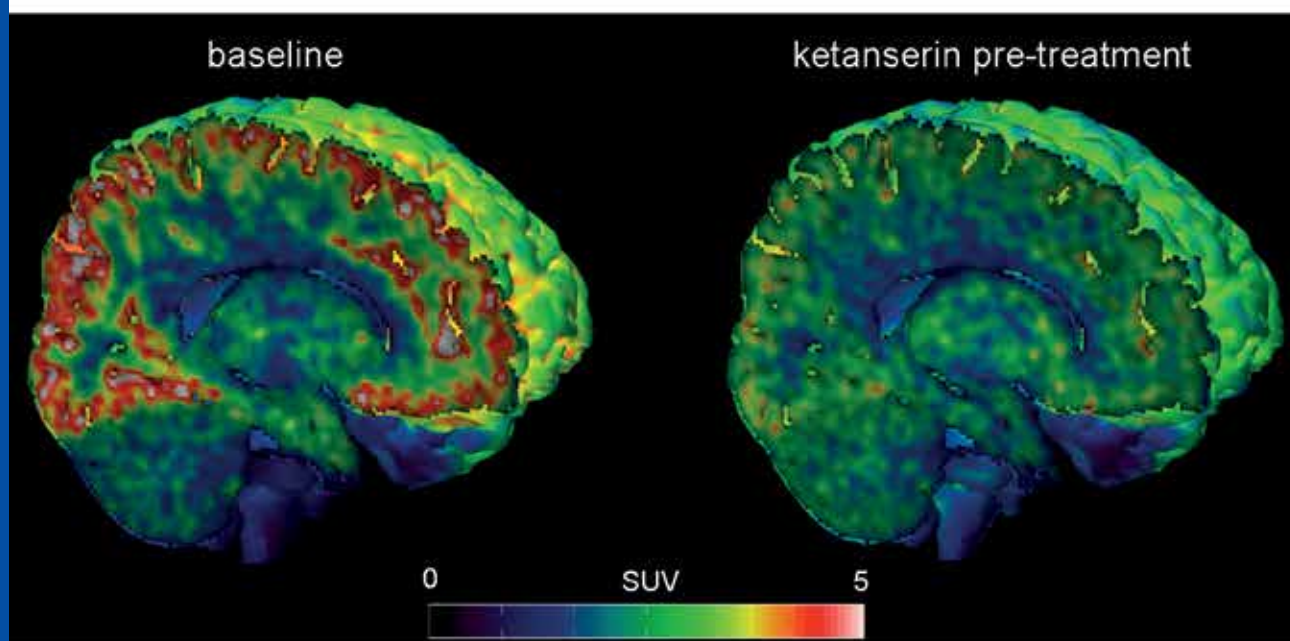


CIMBI

Center for Integrated Molecular Brain Imaging,
University of Copenhagen, Rigshospitalet



We are proud to contribute and collaborate with Professor Gitte Moos Knudsen, Chair of the Neurobiology Research Unit at Rigshospitalet, University of Copenhagen and also Director of the CIMBI, Center for Integrated Molecular Brain Imaging, funded by the Lundbeck Foundation. The focus of the research program is on neurobiology, physiology and pathophysiology, molecular imaging and neuroreceptor ligands with focus on the serotonergic system. Gitte Moos Knudsen and her research team are highly appreciated and we appreciate the excellent collaboration.



Education

In March 2012 the Department of Clinical Physiology, Nuclear Medicine & PET was appointed “Best Education Department of the Year 2011 at Rigshospitalet”. This recognition was based on the evaluation of physicians having had part of their postgraduate education at the department.

For all staff members educational activities are part of their daily functions. The department is highly active in education at different levels of various health related professionals. Regarding undergraduate education, the department contributes to the activities of the Faculty of Health Sciences at the University of Copenhagen for medical students, human biology students in collaboration with DTU in various subjects, e.g. physiology, nuclear medicine and medical technology. Nuclear medicine technologist students and radiographer students receive part of their education from the department.





Jann Mortensen and Peter Oturai

In *postgraduate education*, the department plays an active role in the specialist education of physicians in clinical physiology and nuclear medicine in different ways. The dedicated courses in oncology-, cardiology-, lung-, endocrinology- and pathophysiology are all held at our department and arranged by chief physicians, and the department has four educational positions for young physicians training to become specialists in clinical physiology and nuclear medicine. Furthermore, we contribute to the specialist education of physicians from other specialities such as urology, nephrology, radiology, oncology, haematology and thoracic surgery. A high number of PhD students are associated with the research activities in the department.

The department delivers extensive training programmes to staff from other nuclear medicine and radiological departments in Denmark and the Nordic countries.

A high number of study visits to our department from physicians and students for periods ranging from a few weeks to six months, from both Denmark and abroad, have been arranged.

The departments educational activities have been accredited by the *Danish National Board of Health* and by the *Accreditation of Nuclear Medicine Training Centres Committee of the Section of Nuclear Medicine of the European Union of Medical Specialists (UEMS)*.

Chief Physician Peter Oturai is responsible for the postgraduate education of physicians in the department. Clinical Associate Professor Jann Mortensen is responsible for the undergraduate education of medical students. Professor Liselotte Højgaard is responsible for under- and postgraduate education for bioengineers.

Nuclear medicine technologists

In our department we have 39 nuclear medicine technologists, radiographers and laboratory technicians (NMT's), who are allocated to the KF Section, the PET Section and the Radiochemistry Section. Their tasks are varied and dependent on the section they are allocated. In 2012 all the NMT's did a marvelous job and were crucial for our achievements. The most important was to keep the waiting list very short, as recommended by our politicians and decision makers, in spite of a further increase in patient studies 2012 with 9%, to now >60,000 studies annually. At the same time research and education has been on a high international level and with active engagement from all staff members.

The Danish National Board of Health, the Medicinal Inspection Section, was visiting us in November 2012. We were graced with a very positive report. Due to the positive result, the frequency of future inspections will be with fewer visits, as a sign of our high quality level. The Diagnostic Center's Employee Committee was also visiting our department, and the members were very impressed by the department, as we have one of the finest scores in the official questionnaire from the Capital Region of Copenhagen about staff satisfaction.

We have succeeded because we try to exploit all hours from early to late. The Cyclotron and Radiochemistry team starts at 3 AM, the team taking care of quality control of the new Rubidium generator for PET heart studies start at 6 AM, all to assure that the isotopes are ready for patient studies at 8 AM. Patient investigations are continued until 7-8 PM.

In the PET Scanner Section we obtained two new staff positions due to the introduction of the new radiopharmaceutical ^{18}F -FET for PET brain scanning in tumor patients. In 2012 we did 512 of these patient studies, and it is now implemented as part of the routine. The year 2012 was very active with scientific presentations nationally and internationally and the publication of our book "PET CT Radiotherapy Planning" a guide for technologists made by EANM.

Camilla Sloth Knudsen obtained the prize for best presentation at the LSB Congress with the talk "PET scanning of the brain". Investigations in children are also an area with special focus, and this year Mariam Hassan and Elisabeth Abrahamsson gave a

successful lecture for the Department of Children Oncology 5044. Thank you to all of you for the great effort.

February our first DXA scanner was up and running. Here at Rigshospitalet DXA has been a modality used locally by several clinical departments, but to assure that all clinicians could refer patients to DXA scans we obtained DXA here in our department also. Christina Bojesen and Ceylan Zulfovskaja were in charge of the implementation. We expected 800 investigations the first year, however the actual number was well above 1000. The DXA scanner is used for routine investigations, but already many research projects are running on the scanner, including on Saturdays and Sundays, where our NMT's are in charge. Another major achievement for the department was, that the Siemens Symbia T16 SPECT/CT was used for diagnostic CT with i.v. contrast, (for the first time in the Nordic countries).

The labelling of white blood cells in the ALECAT project (white blood cells primed to target specific brain receptors) with ^{99m}Tc -HMPAO or ^{111}In -Tropolone is difficult, and initially we had a varied labelling percentage. Our Deputy Chief Nuclear Medicine Technologist Tim Lundby has optimized the procedure, and now we successfully use the ^{111}In -Tropolone methodology.

In July we introduced ^{82}Ru -scanning of the myocardium, using PET technology. The investigation is performed as a collaboration between the PET Scanner Section, Anna Ljunggren, Elin Lindell and the KF Section, Camilla Christensen and Lasse Hansen. The new methodology was well functioning already from day one, which was only possible because the summer vacation planning for the implementation group was made, so that all four were here in June. The Rubidium generator needs a quality control every day, taking 1½ hours before use. We therefore start this QC work already at 6.30 to secure that we are ready for patient studies at 8.00.



Tim Lundby, Kate Pedersen and Anne Sørensen

The PET/MR scanner is now implemented in the department. MR is a new diagnostic investigation for our nuclear medicine technologists, and we have an expert MR Radiographer Jákup Poulsen, who has been in charge of the implementation together with Nuclear Medicine Technologist Karin Stahr. They both participated in the PET/MR Workshop in Tübingen last Spring. It is planned to involve further nuclear medicine technologists in the PET/MR team.

In the PET Scanner Section we have started to investigate patients with ^{11}C -PIB for the diagnosis of dementia. It is a challenging task to take care of these patients as they might get lost on their way from the reception area to the scanner. Our staff has done a marvelous job in taking care of these fragile patients.

In the Radiochemistry Section we have had a rising production, and we have established new clean room facilities. We have a large production of ^{18}F -FDG, and we use Theodorico from Comcer for the daily dispensing of ^{18}F -FDG for our own use and for hospitals in Eastern Denmark.

Education

In 2012 Metropol Copenhagen has taken charge of the dedicated CT course, (80 hours for our nuclear medicine technologists) and this implies that participation will give ECTS points in the future.

UDDX is an educational laboratory – a project initiated by the Capital Region of Copenhagen and the European Social Fund with funding 12.5 and 25 mio DKK of a total budget 50 mio. The project will run over 3 years, from January 2012 to October 2014. Diagnostic Center participates in the project, and the first project was a portfolio for nuclear medicine technologist students. Our Nuclear Medicine Technologist Educational Supervisor Mia Hjorth Alberts was project leader. The portfolio is a study diary with reflections written by the students, and their log book etc. is shared by student and supervisor.

Deputy Chief Nuclear Medicine Technologist Tim Lundby is external censor, participating in the education as nuclear medicine technologist.

In June we had the traditional biannual Summer Day for the whole department and our Head of Department Professor Liselotte Højgaard and Linda M. Kragh gave a “state of the art presentation” about the department, our visions and our future strategy. Professor Andreas Kjær presented the research plan, and we heard updates about PET brain scanning and PET/MR. We are now a large department and few people know all the different sections. Therefore we had planned visits in all parts of the department. It was a great success with show cases in all the different sections and also nice food and drink (home made cookies, home made ice cream and a professional coffee shop on a bicycle). The Cluster for Molecular Imaging at the Panum Institute was specially attractive, as only few people from PET and KF have been there before. Our November Educational Day had “high lights” from all sections and the serious debate was in the afternoon followed by the Christmas Party in the evening.

The year 2012 was busy with many extroverted activities for the nuclear medicine technologists/radiographers:

Congresses

- » *Molecular Imaging in Radiation Oncology (MIRO).*
Lecture: The multimodality approach for therapy treatment planning with PET/CT
Marianne Federspiel og Elisabeth Abrahamsson

- » *Society of Nuclear Med (SNM) Miami, June 2012*
Lecture: Pediatric PET/CT for Radiotherapy Planning
Marianne Federspiel and Elisabeth Abrahamsson
Lecture (invited) Optimizing procedures for pediatric PET/CT patients and the family
Marianne Federspiel, Elisabeth Abrahamsson

- » *EANM congress in Milano September 2012*
Education session/lecture: Radiopharmaceutical Tracer - from first step to first patient
Louise Sørensen, Tina Wikke and Sonja Pedersen Lærke
Education session/lecture: Positioning and Immobilization of Lung Cancer Patients
Elisabeth Abrahamsson
Poster: Optimizing scan positioning of patients undergoing ^{18}F -FDG brain PET for Neurostat analysis, Karin Stahr, Bente Dall
Poster: ^{18}F -FET PET for Brain Tumors
Anna Ljunggren, Camilla Sloth Knudsen
Poster: Data collection procedures for bone marrow dosimetry in peptide receptor radionuclide therapy with ^{177}Lu -DOTATATE on neuroendocrine tumors"
Mette Frederiksen

- » *Laboratoriemedicinsk Selskab for Bioanalytikere, LSB*
(Society of Laboratory medicines for technologist)
Lecture: Biomarkører som sporstoffer til PET/CT scanning
Camilla Sloth Knudsen
Selected as best lecture

Symposium

- » *The Symposium for Technologists at the University Hospital Rigshospitalet, May 2012*
Poster: "Hvad kan helkropstællerne på Rigshospitalet?" (What can whole body counters on Rigshospitalet do?)
Susanne Svalling
Lecture: ^{18}F -FET PET scanning til hjernetumorer (^{18}F -FET PET scanning for brain tumors)
Camilla Sloth Knudsen

Others

- » *LIFE - festauditoriet 01.02.2012*
Lecture: Billeddiagnostik af mennesket og dets bedste ven. (Imaging of man and his best friend)
Elisabeth Abrahamsson

Education

» *Metropolitan University College, Copenhagen:*

CT-course in Nuclear Medicine (CT teorikursus i klinisk fysiologi og nuklearmedicin),
(80 Hours)

Nuclear Medicine Technologist: Joo Yerst, Elida Sinik, Stine Holm and Dorte Nielsen

Lederkommunikation der virker, hvordan motiverer jeg mine medarbejdere? (Chief
communication that works; how to motivate my employees) (one day)

Deputy Chief Technologist Tim Lundby

EANM in Wien: Basic Technologist learning course on PET/CT, (Weekend course).

Nuclear Medicine Technologist Stine Holm and Euginice Saxtoft

Gentofte Hospital: Nuklearmedicinsk Apparatur- og Isotopkursus, (two days)

Stine Holm og Euginice Saxtoft

Deputy Chief Technologist Anne Sørensen has completed a leadership course

The radiochemical technologists have participated in different GMP courses

Tübingen PET/MR Workshop

Nuclear Medicine Technologist Karin Stahr, and Radiographer Jákup Poulsen

Many nuclear medicine technologists have participated in different one day courses

Publications

» *EANM - Part 3, A Technologist Guide: PET/CT Radiotherapy Planning*

Marianne Federspiel, editor, Susanne Svalling, Karin Stahr and Elisabeth

Abrahamsson has written chapters in the book

» *Article: in "Radiografen" og "Bioanalytikerens"*

Medical Laboratory and Radiography; Faggrænserne flyder. (Demarcations/ disciplinary
boundaries flowing)

Kate Pedersen, Marianne Federspiel og Elisabeth Abrahamsson

LEAN in PET



In 2012 we initiated a LEAN project on the PET/CT scanner site in order to reduce time waste and increase time for research. Doctors, technologists, radiographers and secretaries were all involved in analysing our shared workflow with focus on optimized patient workflow. We were fortunate to have external assistance from experienced LEAN experts who guided us through the process.

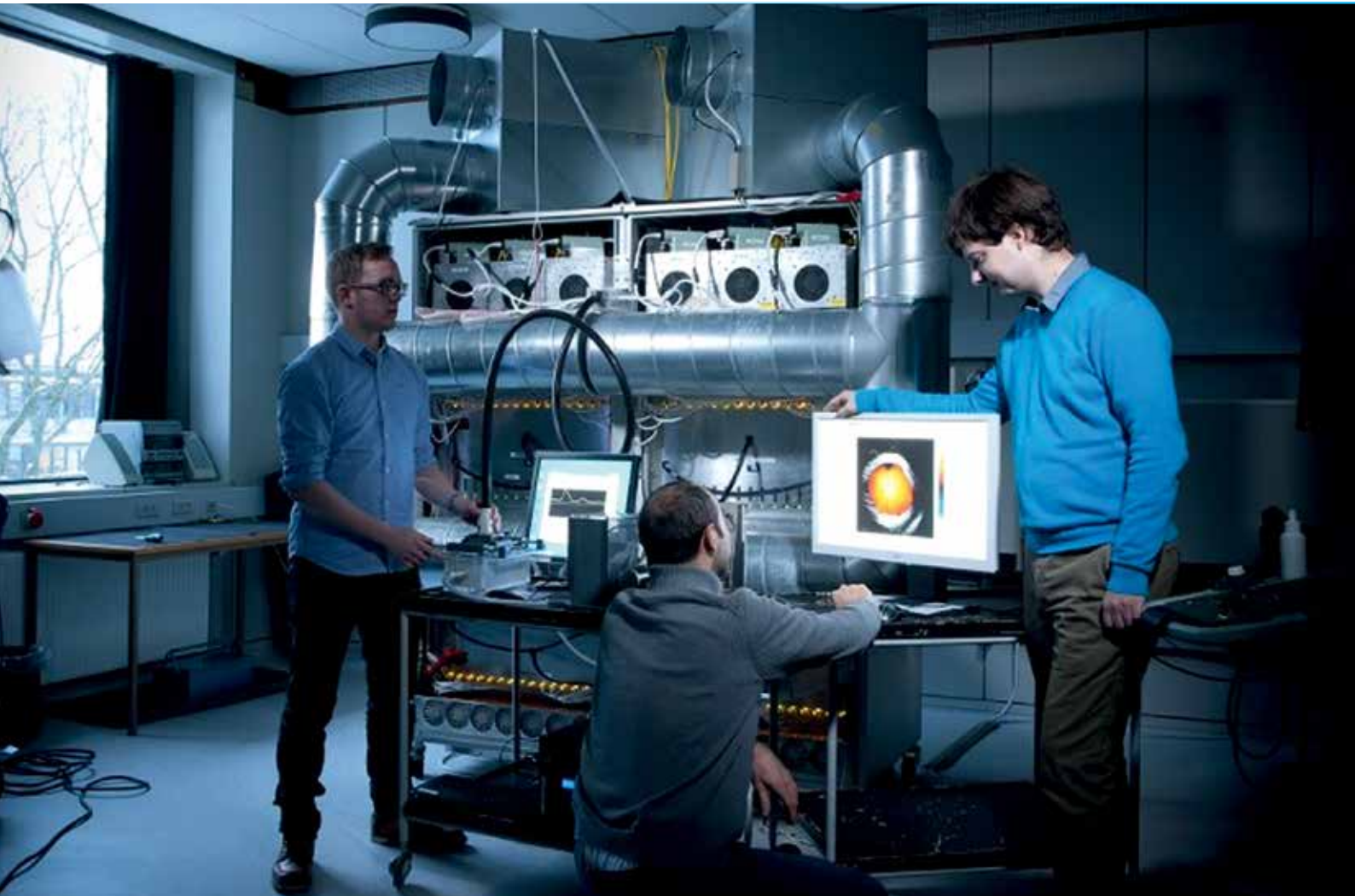
The LEAN project was performed in collaboration with Diagnostic Center and an external consultant from Implement. Deputy Chief Nuclear Medicine Technologist Kate Pedersen and Consultant Annika Loft Jakobsen, MD PhD were project leaders. Every one participated in the project with great enthusiasm, and when we reported about this positive and enthusiastic participation in the Diagnostic Centers Employee Committee, all were puzzled, and asked how we could do that. The explanation was, according to the staff, that the leadership of the department listens to the staff. Through the LEAN project we have optimized our meetings, so that they are performed standing before the LEAN board.

Patients are now given oral contrast media after they have had the injection of ^{18}F -FDG intravenously, when they are lying and waiting in the dedicated waiting area, and they don't have to move from lying down to sitting up in a chair. Thereby unnecessary steps are avoided making it easier for the nuclear medicine technologists and simpler for patients. More beds are required for patients, and more beds have been bought, so that the PET scanners will not have to wait for patients but the other way around.

The project was rather time consuming, but nevertheless it was a success with good results in terms of reducing time waste. Many eye-openers were revealed and many timesaving procedures were implemented. It was fruitful to discuss the workflow with representatives from all staff groups.

We see it now as if the work with LEAN just has started and we are all eager to continue analyzing our different workflows to find more areas where we can save time and work even smarter.

MSc in Medicine and Technology





Liselotte Højgaard

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 MSc program in Medicine and Technology. It is a five year bioengineering degree at bachelor and master's level. The first master graduated in 2008. Since the launch of the program in 2003 more than 200 students have applied for the 60 available places each year. You can read more about the program at www.medicin-ing.dk.

At present 4 of these bioengineers are seconded to the Department as PhD students and we have numerous students working with bachelor and master reports in collaboration with DTU, IMM (Institute for Mathematical Modelling), Professor Rasmus Larsen and DTU, Electro with Professor Jørgen Arendt Jensen and our department here at Rigshospitalet. In 2010 the course was subject to accreditation with a positive result. A warm thank you to Professor Jørgen Arendt Jensen, Associate Professor Kaj-Åge Henneberg, Reader Jens E. Wilhelm, DTU and Associate Professor Bente Stallknecht, University of Copenhagen, for their great effort and our great collaboration both on education and research.



PET and PET hybrid systems

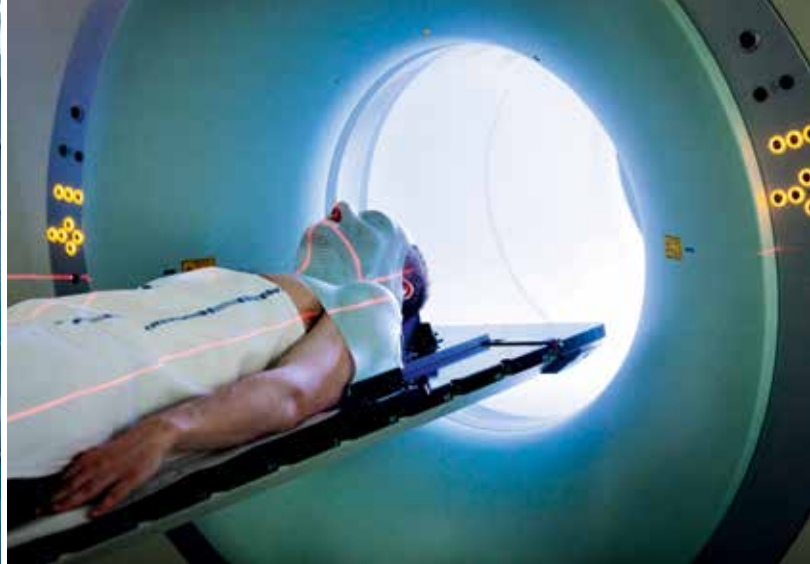
The PET and Cyclotron Unit has one dedicated, stand-alone brain PET scanner, four combined PET/CT scanners and one PET/MR scanner in the hospital itself (Finsen building). We are also involved in the experimental work with PET and CT at Cluster for Molecular Imaging at the Faculty of Health Sciences at the University of Copenhagen.

In the Cluster for Molecular Imaging, we operate two research scanners for PET and CT of small animals. The PET is a Focus 120 with resolution well below 2 mm, and the CT is a microCAT II, with an ultimate 15 μ resolution. The durable GE 4096 PET scanner from 1991 was finally moved out to make room for an upcoming MR-installation.

In the hospital, brain research continues on the HRRT (High Resolution Research Tomograph). Originally intended - as the name indicates - mainly for research, the HRRT has however also become a clinically useful instrument. Designed in cooperation by several research groups in Europe and USA, and built by CTI in Knoxville, Tennessee (now owned by Siemens) the HRRT project has a more than 10 year long history that finally resulted in the building of one series of 18 instruments; the Copenhagen installation is among the last of these, but nevertheless at the front in application. Our computer scientists work actively to improve the software and in this respect provide support to the HRRT User group worldwide.

The majority of studies in the PET Section continue to be FDG whole-body scans for cancer diagnosis, staging, planning and follow-up, but recently a significant number of FET, FLT and ^{11}C -PIB have been added. All these scans are routinely performed with the use of combined PET and CT. In this combination, most CT scans are performed as a full diagnostic quality CT (including contrast media). With the last achievement in 2011, we now have 4 highly modern scanners with rather similar specifications, which provides an important flexibility in patient scheduling.

In 2011, we acquired the second Siemens mCT with 64 slice CT, which is identical to the scanner installed in 2010. Both have the potential of performing Time-of-Flight PET. This feature slightly improves image quality (or reduces scantime), in particular in larger patients, or patients that have to be scanned with "arms down". One scanner is running in a unique well-functioning collaboration with the Department of Radiotherapy, and it is



extensively used for therapy planning, for which purpose its large opening (78 cm) is an important design improvement over the previous generation of systems.

The remaining two PET/CT scanners are Siemens Biographs, one with 40 and one with 64 slice CT, acquired in 2007 and 2009. These are installed in the new part of the Finsen building, sharing patient preparation facilities and with one common, large control room.

The fully integrated PET/MR scanner (Siemens mMR) was installed by the end of 2011 and was among the first in the world to become operational in early 2012. Previous attempts to combine the two modalities have either been limited in use (brain “insert” only) or not fully integrated (two separate gantrys). In the mMR, a new amplifier principle in the PET detectors makes them insensitive to the magnetic field, and small enough to allow the PET scanner’s detector ring to be placed inside the 3-tesla MR-magnet between the gradient coils and the RF transmitter. The receiver coils have been redesigned to minimize absorption of the PET-photons. This makes it possible to perform truly simultaneous measurements of PET or MR. The combined scanner is anticipated to improve the diagnostic power (in particular soft tissue differentiation) but also has the potential of reducing radiation exposure, which is particularly important in children’s examination. A lot of work has been performed from the physics group on the issues of attenuation correction and artefact suppression in order to support the clinical research protocols starting up.



Søren Holm and Thomas Levin Klausen

Equipment 2012

Equipment	Product	Purchase year
Gamma cameras	Mie-Scinttron	2004
	Mediso N-TH45-D	2008
	DDD SoloMobile	2012
SPECT cameras	Philips ADAC Skylight	2002
	Mediso Nucline X-Ring-R/HR	2009
SPECT/CT cameras	Philips, Precedence 16-slice CT	2006
	Philips, Precedence 16-slice CT	2008
	Siemens Symbia 16-slice CT	2011
PET scanners	HRRT Siemens/CTI	2007
PET/CT scanners	Siemens Biograph TrueV 40-slice CT	2007
	Siemens Biograph TrueV 64-slice CT	2009
	Siemens mCT-S (64)	2010
	Siemens mCT-S (64)	2011
PET/MR scanner	Siemens mMR	2011
Lung function	Jaeger Masterscreen w/bodybox	2005
	Jaeger PFT pro w/bodybox	2007
DXA scanner	GE Lunar Prodigy	2011
Whole body counter	WBC w/Nal counting chamber	1977
	WBC w/plast counting chamber	1978
Cyclotrons	Scanditronix 32 MeV	1991
	RDS Eclipse cyclotron, CTI	2005
Cluster for Molecular Imaging	Provivo/ ADAC mobile gamma camera	1990
	PET scanner GE 4096	1991
	SPECT Mediso Nucline X-Ring/R	2004
	Siemens Micro-PET Focus 120	2006
	Micro-CT Siemens Micro-CAT II	2006
	Phosphor Imager Perkin Elmer cyclone	2007

Accreditation

Rigshospitalet and our department have been accredited succesfully by:

- » Center of Excellence by the European Neuroendocrine Tumor Society
- » Certified by SIS, National Institute of Radiation Protection, The Danish National Board of Health
- » Danish Medicines Agency
- » The Danish National Board of Health, MD Specialist education
- » EURATOM, The European Atomic Energy Community
- » Joint Commission International, the International American accreditation board
- » Section of Nuclear Medicine of the European Union of Medical Specialists (UEMS)
"Accreditation of Nuclear Medicine Training Centers Committee", MD Specialist Education.
- » European Association of Nuclear Medicine.
- » The Specialty Advisory Committee (SFR) in Clinical Physiology and Nuclear Medicine



Program Certified
by Joint Commission International

European Medical Research Councils



Professor Liselotte Højgaard

The European Medical Research Councils (EMRC) was the membership organisation of all the European medical research councils – for the EU member states as well as other European countries. The Chair of the Committee for the European Medical Research Councils was Professor Liselotte Højgaard from Rigshospitalet, University of Copenhagen, Denmark, 2006-2012. The Standing Committee was composed of delegates with a high scientific profile in biomedical sciences nominated by their ESF Member Organisations and also observers from the European Commission, The Wellcome Trust, WHO-Europe, Australia, Canada, Israel, New Zealand and USA. From 2013 EMRC was changed to Science Europe, located in Bruxelles. Liselotte Højgaard has successfully completed her 3 + 3 years terms as Chair of EMRC.

From 2010-2012 Liselotte Højgaard was appointed Chair of The European Commission Science Advisory Board for Frame Work Program 7 in Health. This secured coordination between the national funders and the Frame Work Program. A warm thank you to Dr. Ruxandra Draghia-Akli and her team at the EC DG Research Health for a very fine collaboration.

A warm thank you to the EMRC Unit at ESF in Strasbourg for all the work done in 2012. It has been a tough year 2012 due to the changes in ESF. A warm thank you to the whole unit, specialty Unit Coordinator Janet Latzel, Science Officer Professor Dr Kirsten Steinhausen and former Head of Unit Dr Stephane Berghmans. A warm thank you to the Core Group and Plenary Group of EMRC making it worth the effort. Professor Richard Frackowiak, the new Head of Science Europe Medicine, was in Copenhagen August 2012 to assure and facilitate a positive hand-over from EMRC to Science Europe. In Strasbourg the research activities and programs will close in 2015 and Professor Stig Slørdahl has taken over as Chair of the Research Evaluation Committee following EMRC.

It has been a privilege to be “a servant of science” as chair of EMRC for the last 6 years, and the best of wishes to my successors. Take good care of the European biomedical research policy.

EMRC Publications



Personalised Medicine for the European Citizen (iPM)
Forward Look Report
ISBN: 978-2-918428-90-9
December 2012



Open Access in Biomedical Research
Science Policy Briefing No. 47 (DRAFT)
ISBN: 978-2-918428-78-7
October 2012



Implementation of Medical Research in Clinical Practice
ESF Science Policy Briefing No. 45
ISBN: 978-2-918428-78-7
September 2012



Medical Research Education in Europe
Science Policy Briefing No. 46
ISBN: 978-2-918428-79-4
September 2012



Pan-European Clinical Trials (ECT)
EUROCORES Final Report
ISBN: 978-2-918428-80-0
September 2012



Success Stories about Human Stem Cell Research in Europe
September 2012



EMRC Newsletter No. 20
Newsletter
May 2012



Researching Complex Interventions for Nursing (REFLECTION)
Research Networking Programme
January 2012



EMRC Newsletter No. 21
Newsletter
December 2012

Professor Liselotte Højgaard is membre de Conseil d'Administration de l'INSERM, L'Institute Nationale de la Sante et de la Recherches Medicale, France.



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