

Annual Report 2006

DEPARTMENT OF CLINICAL PHYSIOLOGY AND NUCLEAR MEDICINE & PET AND CYCLOTRON UNIT





Rigshospitalet, Copenhagen University Hospital

Rigshospitalet, Copenhagen University Hospital, was founded in 1757. At present it has 1.500 beds, 17.000 employees and a budget of approximately ½ billion Euros. The research production is more than 1.000 publications per year, including approximately 50 higher academic degrees (PhD and doctoral of medical science).

From the 1st January 2007 Rigshospitalet is part of Region Hovedstaden.

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Preface

The highlight of 2006 was the opening of the new advanced Philips Presence SPECT/CT scanner together with the opening of the Cluster for Molecular Imaging at the Panum Institute. We had a fine day at the opening symposium with a guest lecture by Professor Richard Wahl, Johns Hopkins, US. In January 2006 Professor Andreas Kjær received the August Krogh Prize, one of the most prestigious Danish honours in the field of medicine. The number of patient investigations increased approximately 10% in 2006: primarily cancer patients with complicated cases. For both sentinel node investigations, parathyroid scintigraphies and octreotid scintigraphies it is now routine to carry out SPECT with CT to optimize the usability of the studies. This new procedure is highly appreciated by our referring clinicians. An increasing number of patients given chemotherapy were referred to renal clearance studies monitoring renal function and MUGA studies to monitor cardiac function.

We performed more than 20 renal clearance studies daily, and fortunately, the department was rebuilt, with a new large room for the renal clearance studies and an adjacent friendly patient waiting room. To make this happen, reconstruction and new rooms were necessary also at KF 4012, where we got a new staff room and new rooms for interpretation of patient investigations. When the department here in the south wing of Rigshospitalet was opened more than 30 years ago, the department performed 2.000 investigations annually, on a bit more space than today. At present we have more than 20.000 patient investigations annually on fewer square meters than 30 years ago. So lack of space is indeed one of our critical bottle necks.

In The PET and Cyclotron Unit more than 3.000 PET and PET/CT scans were performed in 2006 including approximately 500 PET/CT for planning of radiotherapy with IMRT (Intensity Modulated Radiation Therapy). Thank you for the the positive and rewarding collaboration with the Department of Radiotherapy, headed by Dr. Svend Aage Engelholm, Chief Physicist Håkan Nyström and Kirsten Amsing, Leading Staff Nurse. Also many thanks to the Department of Radiology for at good collaboration on the CT and MRI scans.

In the PET and Cyclotron Unit the production of FDG has increased and we now deliver FDG daily to our own PET and PET/CT scans and to Bispebjerg Hospital, Herlev Hospital, Hillerød Hospital, Lund University Hospital and also The Sahlgrenska Hospital in Gothenburg. The Cyclotron starts at 03:30 am in the morning and the FDG is ready at 08:00 am. The number of new tracers being developed in the cyclotron and radiochemistry unit has increased and the new production laboratories have been introduced in the daily routine. Every Tuesday night we produce ^{211}At – an alpha emitter for studies with monoclonal antibody radio treatment for micrometastasis from ovarian carcinoma for use in Gothenburg.

In 2006 the research comprised 60 peer review publications. The focus area is molecular imaging: primarily clinical research on PET and PET/CT, development of new radioisotopes and ligands, pediatric nuclear medicine including PET, labelling of stemcells and neuro-PET in collaboration with The Neurobiology Research Unit and Professor Gitte Moos Knudsen. Further, we research in nuclear cardiology and neuroendocrinology, lung function investigations and treatment with radionuclides, as well as research in the Whole Body

Counter in collaboration with Faculty of Life Science, University of Copenhagen. Cluster for Molecular Imaging is headed by Professor Andreas Kjær and situated at the Panum Institute in proximity with the animal facilities. The Cluster has a gamma camera, a PET camera and a micro-SPECT camera, a micro-PET camera and a micro-CT scanner together with labs for molecular imaging.

In 2006 the department staff participated in national and international meetings and congresses as invited lecturers, and many were the oral presentations, abstracts and posters, chairmanships and activities given around the world. More than 70 international research groups and individuals have visited the department in 2006 and we had frequent longer visits from Denmark and the other Nordic countries for mutual education.

The contributions of the staff have been very high in 2006 for patient studies, isotope production, research & development and education, both in Clinical Physiology & Nuclear Medicine and in the PET & Cyclotron Unit.

A warm thank you to all staff members and all external collaborators for their contributions in 2006 – for the sake of better patient care and progress in research & development.

A very positive experience in 2006 was a morning with an old gentleman referred for an acute lung investigation, waiting in his bed outside the SPECT/CT scanner. One of our Nuclear Medicine Technologists came with a chair for his accompanying wife, and his comment was: "Yes, here you can feel it at once, they are very helpful and nice".

Liselotte Højgaard & Linda M. Kragh





Mission and Objectives

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

General objectives:

- To be in the lead within highly specialized diagnostics treatment and nursing
- To carry out research and development at an advanced international level
- To educate staff in the health services on an highly specialized level
- To contribute with professional advice and exchange of knowledge and expertise with the surrounding world
- To be characterized by openness and human respect

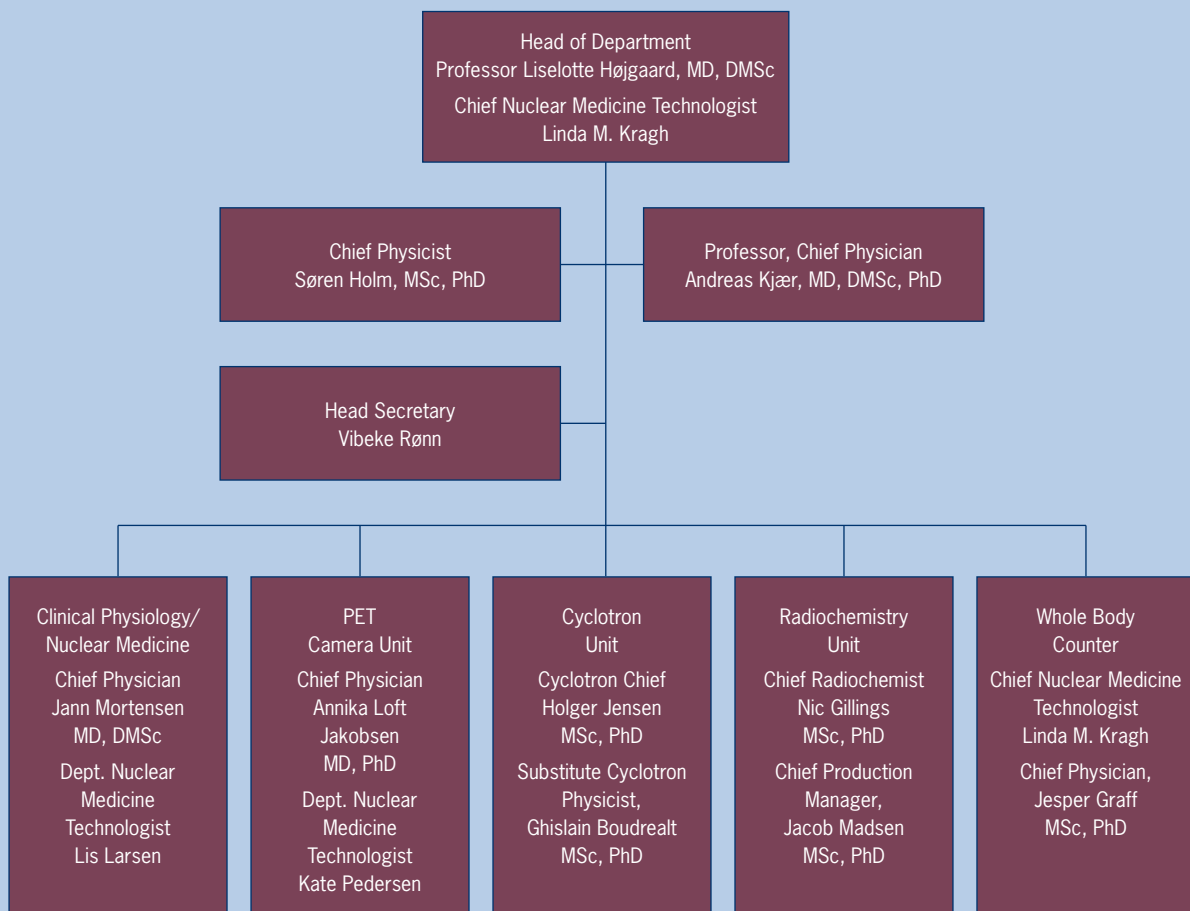
The objectives of The Department of Clinical Physiology and Nuclear Medicine & PET and Cyclotron Unit are:

- To carry out clinical patient investigations in clinical physiology and nuclear medicine, including PET – at the most advanced international level and dedicated to patients in need of highly specialized treatment.
- To conduct research and development in nuclear medicine, including PET and clinical physiology at a high international level
- To develop and test new radioactive isotopes and to produce radioactive isotopes and medicinal products for clinical purposes and research
- To participate in education and the spreading of knowledge in a national and international setting within the expert fields of the clinic
- To develop diagnostic strategies for clinical patient investigations in collaboration with clinicians in accordance with the principles of evidence-based medicine
- To be an attractive and positive place of work with emphasis on teamwork, competence and a positive atmosphere

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

In 2006 more than 100 groups individuals visited the department.

Organisation and Staff



Department of Clinical Physiology and Nuclear Medicine & PET and Cyclotron Unit is part of the Diagnostic Center, headed by Mogens Sandbjerg Hansen, Director, MD, DMSc and Karin Nørregaard, Vicedirector.



Physicians

- Berthelsen, Anne Kiil, MD, Chief Physician
- Doetsch, Anne-Marie, MD, Senior Registrar
- Graff, Jesper, MD, DMSc, PhD, Chief Physician
- Gutte, Henrik, MD, Registrar
- Jakobsen, Annika Loft, MD, PhD, Chief Physician
- Hesse, Birger, MD, DMSc, Chief Physician
- Hoving, Peter, MD, DMSc., Registrar
- Højgaard, Liselotte, MD, DMSc, Head of Department, Professor
- Høyer, Alice Outzen, Consultant
- Kjær, Andreas, MD, DMSc, PhD, MBA, Chief Physician, Professor
- Kupers, Ron, MD, Associate Professor
- Law, Ian, MD, PhD, Staff Physician
- Lyttkens, Kerstin, MD, Chief Physician
- Markova, Elena, MD, Staff Physician
- Marving, Jens, MD, Staff Physician
- Mehlsen, Anne-Birgitte, MD, Senior Registrar
- Mortensen, Jann, MD, DMSc, Chief Physician
- Pedersen, Dorthe Skovgaard, MD
- Ormstrup, Tina, MD, Staff Physician
- Pedersen, Anne-Birgitte, MD, Senior Registrar
- Pfeifer, Andreas, MD, Registrar

PhD students

- Binderup, Tina, Human Biologist
- Borgwardt, Lise, MD, PhD, Registrar, Clinical Assistant
- Chakera, Anette H., MD, Ph.D. Student
- Fischer, Barbara Malene, MD, Registrar, Clinical Assistant
- Hansen, Charlotte Lund, MSc, Chemist
- Hutchings, Martin, MD, Registrar, Clinical Assistant
- Jørgensen, Emilie Arnth, Human Biologist
- Kristoffersen, Ulrik Sloth, MD, Clinical Assistant
- Pedersen, Dorthe, MD, Ph.D. Student
- Pedersen, Minna W., MSc, Research Assistant
- Stavngaard, Trine, MD, Ph.D, Clinical Assistant
- Søndergaard, Kåre, MSc, Ph.D. Student, Chemist
- Tagil, Kristina, MD, Clinical Assistant
- Vogelsang, Thomas Wiis, MSc, Research Assistant

Physicists, Chemists

- Andersen, Peter Andreas, MSc, PhD, Physicist
- Boudreal, Gislain, MSc, PhD, Substitute Cyclotron Physicist
- Brandt, Malene, PhD, Chemist
- Gillings, Nicolas, MSc, PhD, Chief Radio Chemist
- Golrokhian, Diana, Physicist
- Holm, Søren, MSc, PhD, Chief Physicist
- Jensen, Holger J., MSc, PhD, Cyclotron Chief Physicist
- Madsen, Jacob, MSc, PhD, Chief Production Manager, Chemist
- Szabolcs, Lehel, MSc, PhD, Chemist

Engineers, Technicians, Computer Scientists

- Andersen, Flemming, MSc, PhD, Computer Scientist
- Christensen, Jan Damgaard, Engineer Assistant
- Drennan, David, Cyclotron Technician
- Dähnhardt, Andreas, Computer Scientist
- Jensen, Ole, Engineer Assistant
- Jensen, Per Hovalt, Civil Engineer
- Kuhlmann, Per, Cyclotron Technician
- Steffensen, Anders H., Engineer Assistant
- Wehrauch, Per, Cyclotron Technician

NM Technologists, Radiographers and Nurses

- Abrahamsson, Elisabeth, Radiographer
- Andersson, Katarina, NM Technologist
- Banerup, Tony, NM Technologist
- Bøhm, Mette, NM Technologist
- Christensen, Pia, NM Technologist
- Cortsen, Annette, NM Technologist
- Dall, Bente, NM Technologist
- Dondera, Brita, NM Technologist
- Elkington, Sakeena, NM Technologist
- Federspiel, Marianne, NM Technologist
- Frommelt, Louise B., NM Technologist
- Gudmundsson, Sven, NM Technologist
- Heiberg, Therese, NM Technologist
- Hovgaard, Beinta, NM Technologist
- Høybye, Lene, NM Technologist
- Jensen, Martin Ravn, NM Technologist
- Jørgensen, Hanne, NM Technologist
- Jørgensen, Mette Møller, NM Technologist
- Kernchen, Ulla, Staff Nurse
- Kragh, Linda M., Chief NM Technologist

- Korftsen, Julie, NM Technologist
- Larsen, Lis, Department NM Technologist
- Linnet, Solveig, NM Technologist
- Lundby, Tim, NM Technologist
- Myschetzky, Rebecca, NM Technologist
- Nielsen, Majbritt Lykke, NM Technologist
- Nielsen, Merete Søndersø, NM Technologist
- Nilausen, Mia, NM Technologist
- Pedersen, Kate, Department NM Technologist
- Pejtersen, Maria H., NM Technologist
- Petersen, Tina Wikke, NM Technologist
- Ramadani, Lutjeta, NM Technologist
- Stahr, Karin, NM Technologist
- Svalling, Susanne, NM Technologist
- Sørensen, Anne, NM Technologist
- Sørensen, Louise Sørup, NM Technologist
- Velgaard, Susanne, NM Technologist

Secretaries

- Christensen, Eva, Medical Secretary
- Damborg, Anne-Marie, Quality Co-ordinator
- Forstrøm, Ulla, Assistant Secretary
- Marquardsen, Joan, Medical Secretary
- Myltoft, Mette, Medical Secretary
- Petersen, Tina Wikmann, Secretary
- Runge, Gitte, Medical Secretary
- Rydahl, Maybritt, Medical Secretary
- Rønn, Vibeke, Head Secretary
- Semitoje, Gudrun, Medical Secretary

Students, Assistants

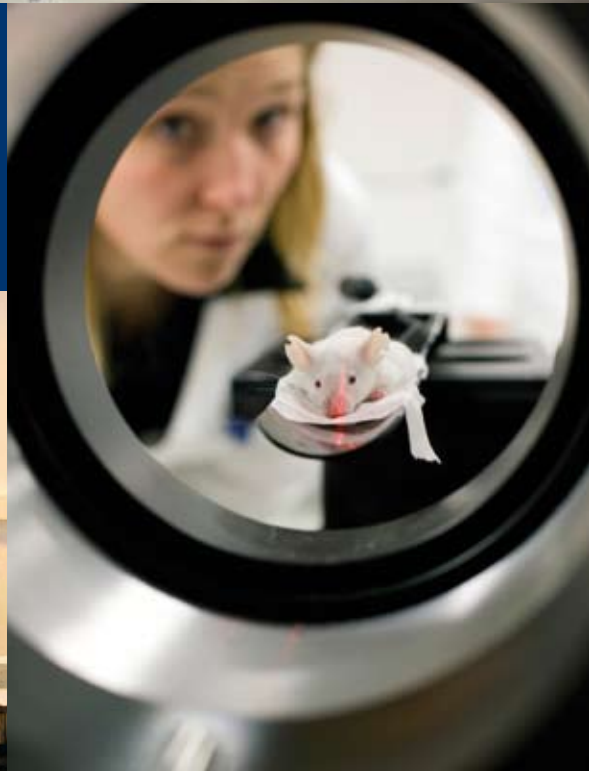
- Boota, Sobia Aniki Aslam, Assistant
- Christiansen, Maria, Assistant
- Dalbjerg, Christian, Student
- Fonsleet, Jesper, Student
- Gudmundsson, Marie, Assistant
- Jørgensen, Jesper, Student
- Kamstrup, Andreas, Student
- Naert, Arne, Student
- Nielsen, Carsten Haagen, Student
- Nielsen, Lea Allingham, Student
- Pappense, Meike, Student
- Pinholt, Rasmus, Student
- Toft-Petersen, Rasmus, Student

Highlight of the year 2006



Cluster for Molecular Imaging

Opening of the Cluster for Molecular Imaging, headed by Professor Andreas Kjær, with focus on translation from basic science to clinical research in medicine. Micro PET/CT financed by the foundation "A.P. Møller & Hustru Chastine Mc-Kinney Møllers Fond til almene Formaal".





SPECT/CT opening 2006

Opening of the new SPECT/CT scanner with 64-slice CT June 2006, with invited guest lecture by Professor Richard Wahl, The Johns Hopkins, US. The scanner is financed by the "Cancer Programme under the Ministry of Health".



Nuclear Medicine



The Department of Clinical Physiology and Nuclear Medicine has six gamma cameras for routine clinical imaging and human research studies, including two hybrid SPECT/CT cameras, one with a 16 slice CT-scanner (Precedence) and one with a one slice low-dose CT-scanner (Hawkeye), two dual-head gamma cameras and two single-head cameras. In addition two mobile cameras are used for studies in experimental animals in "Cluster for Molecular Imaging". Furthermore, we have two Jaeger body plethysmographs used for lung function testing. More than half of our examinations are related to the diagnosis and monitoring of cancer patients.

There has been an increase in the numbers of hybrid SPECT/CT scans, especially for imaging of neuroendocrine tumours, pulmonary embolism and sentinel nodes. The somatostatin receptor ligand ^{111}In Octreotide imaging is the most important endocrine nuclear medicine imaging modality and is increasingly used for evaluation and monitoring of radionuclide therapy of inoperable patients. Treatment of benign hyperthyroid disease and euthyroid goitre has increased, and pre-treatment with rhTSH is regularly included. State-of-the-art 3-D physiologic and anatomical hybrid imaging using both perfusion and ^{81}mKr ventilation SPECT together with pulmonary CT angiography have been

applied for the diagnosis of pulmonary embolism. Other frequent indications for lung physiology measurements in children and adults are control after chemotherapy and transplantation or preoperative evaluation. There has been an increase in radioaerosol mucociliary clearance examinations for the diagnosis of primary ciliary dyskinesia.

Radioisotope leakage monitoring procedures during isolated limb perfusion with melphalan and tumour necrosis alpha for recurrent melanoma and soft-tissue sarcoma have increased in numbers. The use of the sentinel node technique increases rapidly, leading to optimized surgery of breast cancer, melanoma, oral cancer and other cancers.

Research studies in nuclear cardiology include myocardial perfusion imaging and ^{111}In labelling of stem cells in the evaluation of the effect and homing of stem cells in severe coronary disease. Immuno-scintigraphic imaging with a dual isotope technique has been tested in mice and rabbits. The department has been much involved in comprehensive European, nuclear cardiology guidelines. Studies have tested, both in vitro and in vivo, ^{123}I , ^{131}I as well as $^{99\text{m}}\text{Tc}$ -labelled, recombinant rFVII (Novo-Seven) for the development of a new radiopharmaceutical to localize acute gastrointestinal bleeding lesions.

Jann Mortensen

Pediatric Nuclear Medicine



Each year we perform 1.200 pediatric nuclear medicine investigations mainly for the large pediatric clinics at the hospital. It is a special focus area for our clinic to perform these investigations on the highest level of excellence, and at the same time make it a positive experience for both the child and the parents. The clinic is member of the Pediatric Nuclear Medicine Network, the international telemedicine expert network for second opinion and exchange of ideas.

The clinic has been performing children PET scans as a focus area since 1999 and has now performed close to 800 children PET scans. Since our introduction of PET/CT in 2001 and the second PET/CT scanner in 2005, most of the whole body studies have been performed as PET/CT, though only a relevant number as high resolution CT scans.

The brain PET studies are performed as PET alone and then afterwards co-registered to MRI with The Siemens Fusion Registration System, to benefit from the high resolution of MRI.

Our technicians from the pediatric focus group, Marianne Federspiel and Elisabeth Abrahamsson were represented at the CME for technicians, EANM 2006 in Athens, where they gave a very successful talk on how to perform children PET scans.

In November we had a visit from The Pediatrics Committee under EANM presented by the Head of Committee Dr. Lorenzo Biassoni, Hospital for Sick Children, Great Ormond St. London and Senior member Dr. Thomas Lynch, Belfast. The aim of the visit was to discuss and develop PET/CT in children, and to discuss relevant indications of children PET scans.

We had some very interesting days in their company.

Research in pediatric nuclear medicine including PET is necessary, and we conduct research protocols in children with lymphomas, sarcomas, epilepsy, Mb. Fabry and brain tumours to further develop this important area.

Lise Borgwardt

Cyclotron Unit



In 2006, as in the previous years, the total number of productions increased. At the Scanditronix and the CTI/Siemens cyclotrons 476 and 337 successful irradiations was made. This corresponds to an increase of 14% relative to 2005. The total success rate for our two cyclotrons was 98.0% this year. The small decrease relative to last year (98.6) was mainly due to RF- and target problems. A major part of our routine ^{18}F productions for FDG and Al-tanserin was in 2006 moved to the new CTI/Siemens cyclotron. This gave more available beam time at the Scanditronix

cyclotron for production of the unique isotopes, which only can be produced at this cyclotron.

In order to strengthen our research program on ^{11}C labelled radio pharmaceuticals, we this year invested in a new ^{11}C target for the CTI/Siemens cyclotron. The new target is able to produce 60-70 GBq $[^{11}\text{C}]\text{-CO}_2$ in a 40 minutes irradiation at a beam current of 60 μA . The target was installed in the spring and has given stable yields through out the whole year.

Holger J. Jensen

Radiochemistry



Routine Production

In 2006 production of [^{18}F]FDG continued in a similar manner to 2005, with one or two syntheses each day. Our reliability was further increased with a synthesis failure rate of only 1.2%. Odense University Hospital was added as a customer in early 2006 and will receive FDG from us and the new Hevesy Laboratory at Risø National Laboratory until they are granted their own marketing authorization. Of the 256 batches of [^{18}F]FDG produced in 2006 (see Figure) the average batch size was 59 GBq at end of synthesis.

Production of krypton generators continued according to the well-established delivery schedule on Mondays, Wednesdays and Fridays, amounting to production of 694 generators in 2006.

Research Production

Production of labelled neuroreceptor ligands for use in research projects by the Neurobiology Research Unit at Rigshospitalet increased steadily in 2006. At present both [^{18}F]altanserin and [^{11}C]DASB are produced on a regular basis. In addition the 5-HT₄ antagonist [^{11}C]SB207145 was produced for initial testing in humans.

A number of experiments were performed in 2006 in order to optimize the measurement of plasma metabolites from this ligand and a method for blocking plasma esterases was developed. Now these problems are overcome, further human and pig studies will resume in 2007. The benzodiazepine tracer [^{11}C]flumazenil was validated and approved for human use in 2006. Use of this tracer will commence in 2007, for both clinical and research use. As in previous years we continued to produce [^{13}N]ammonia for cardiac blood flow measurements and [^{15}O]water for cerebral blood flow measurements.

Oncology Research and Development Charlotte Lund Hansen continues her PhD project on development of labeled peptides for imaging the epidermal growth factor tyrosine kinase receptor. This project is conducted in collaboration with The Department of Radiation Biology at Rigshospitalet and The Chemistry Department at the Royal Veterinary and Agricultural University in Denmark (KVL). Charlotte is spending 6 months at the PET center in Orsay near Paris and will return to the department in April 2007. Production of the promising hypoxia tracer [^{64}Cu]ATSM is now set up and ready for

validation. The Hevesy Laboratory at Risø supplies copper-64. Animal studies using microPET will be performed at the Cluster for Molecular Imaging at The Panum Institute before an application for human use is submitted to The Danish Medicines Agency.

Neurobiology Research and Development Collaboration with The Neurobiology Research Unit, Rigshospitalet and the Department of Medicinal Chemistry at the Danish University of Pharmaceutical Sciences under CIMBI (Centre for Integrated Brain Imaging) continued in 2006. The main focus is on the development of serotonin agonist ligands for PET. A post-doc is employed at Danish University of Pharmaceutical Sciences and a PhD Student will be employed in early 2007.

Pain Research and Development

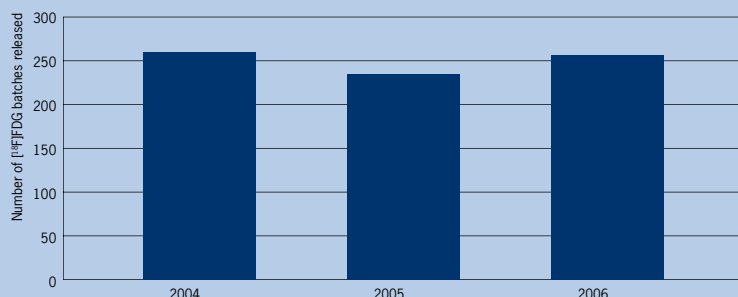
[^{11}C]Carfenanil, an opioid receptor ligand and [^{11}C]FLB457, a very potent dopamine D₂ receptor ligand are currently under process validation and permission for use in humans will be sought in early 2007. These tracers will be used by senior researcher Ron Kupers in his pain research using PET imaging together with Henrik Kehlet from the Section for Surgical Pathophysiology at Rigshospitalet. The research will focus on furthering the understanding of chronic post-operative pain processes.

Cluster for Molecular Imaging

A number of new PET tracers will be introduced in the coming year, which will be used initially for animal research using microPET at The Panum Institute. These will include tracers for measurement of apoptosis, histamine and muscarinic receptors.

Nic Gillings & Jacob Madsen

[^{18}F]FDG PRODUCTION 2004-2006



PET and PET/CT Scanners



The PET and Cyclotron Unit is currently running one stand-alone PET scanner and two combined PET/CT scanners in the hospital. We are also involved in the experimental work at Cluster for Molecular Imaging at the Faculty of Health Sciences at the University of Copenhagen.

Our first PET/CT scanner is a GE Discovery LS, where the PET is almost identical to the Advance PET scanner that we have had since 1993. The Discovery LS was installed in the autumn of 2001 as the second in Europe. In the combined PET/CT examination, the CT scan is used both as a full diagnostic quality CT (including contrast media) and for attenuation correction of the PET images. Our second PET/CT, installed in 2005, is a Siemens Biograph Hirez, with 16 slice CT. It is run in collaboration with the Department of Radiotherapy, and it is extensively used for therapy planning. One major advantage of the Biograph is that the patient opening in this new generation of scanners has been widened to

70 cm (vs. 60 cm before). This is particularly important for patients that are being prepared for therapy, because it ensures that there is enough room for the necessary "fixation" devices that are used to guarantee that the position of the patient is known and can be transferred to the linear accelerators with great precision.

The PET Advance scanner still performs most of the brain scans, including the receptor research. It also does the ammonia heart perfusion studies, but less wholebody PET. The reason is straightforward: A combined PET/CT wholebody scan on either of the two PET/CT scanners takes only half the time of a PET wholebody on the Advance PET scanner, and this, of course, is of benefit to the individual patient as well as to the capacity of the department. We have a large and still increasing number of patients referred for PET and PET/CT scans. When the PET Centre started, PET scanning was looked upon primarily as a research tool, but today all the scanners are used

from early morning till late afternoon for clinical patient studies and, occasionally, on weekend days too. Therefore, a third PET/CT scanner is planned for installation in the new, extended radiotherapy building in 2007.

In the Cluster for Molecular Imaging, we maintain the old 4096 PET scanner (suitable for larger animals, e.g., pigs), and this year we installed 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 mi-croCAT II, with an ultimate 15μ resolution.

Søren Holm



PET/CT and Oncology



At this institution, we are fortunate to have a GE Advance dedicated PET scanner and two PET/CT scanners, a GE Discovery LS installed in December 2001, and a Siemens Biograph Hi-Rez PET/CT scanner with 16-slice CT installed in January 2005. The main work frame is within Oncology, with more than 90% of our patients suffering from a malignant disease or being suspected of having an undiscovered cancer.

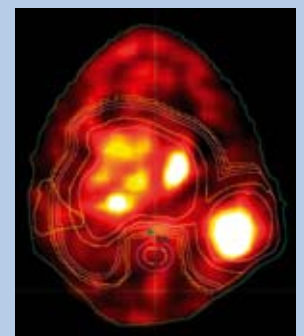
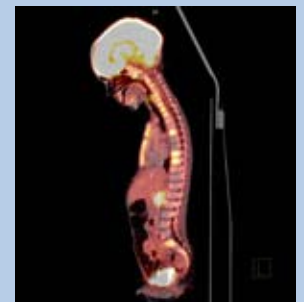
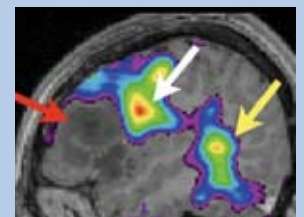
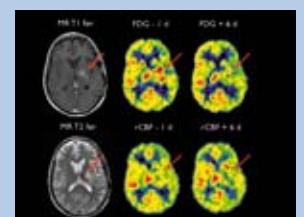
The CT scans are routinely performed as high quality diagnostic scans using oral and intravenous contrast media. Concerning the risk of contrast-induced artefacts, we have conducted a study, which confirmed our clinical observations, that the artefacts, if any, do not have any impact on the interpretation of the scans. The combined PET/CT conclusion is superior to both scan results alone and the patient is spared from an extra CT examination.

We cooperate closely with The Department of Radiotherapy on the use of PET/CT for the treatment planning of cancer. The advantages are numerous: the anatomical localisation and the metabolic activity of the tumor are defined, and the tissue heterogeneity can then be taken into account when choosing radiation technique and energy, and only one scan is necessary. Research in this field is necessary, and we conduct trials with nasopharyngeal cancer, mesothelioma and lymphoma, including IMRT (Intensity Modulated Radiotherapy). After finishing a clinical trial with PET/CT for staging and planning of Radiotherapy for cervical cancer, PET/CT has now been implemented as the first investigation for newly diagnosed patients, followed by a clinical examination and a laparoscopic confirmation of PET/CT findings, and for patients in need of Radiotherapy, the PET/CT results are included in the therapy planning.

Respiratory movements are a challenge for radiotherapy, since the tumor as well as surrounding normal tissue move. Traditionally, the radiation fields are enlarged in order to ensure that the tumor is constantly inside the target area. This means that more normal tissue is radiated upon concordantly. The respiratory movements also seem to blur the PET/CT images and hereby decrease the signal from small tumors. Lung metastases are often quite small, less than 5 mm in diameter, which makes them difficult to identify on a PET scan. We are investigating the usefulness of respiratory gating in two different settings, one on each scanner.

New modalities require clinical trials to verify the usefulness of the method. At present, we investigate the clinical diagnostic value of PET/CT for cervical, ovarian and lung cancer and childhood malignant lymphoma in prospective controlled trials.

Annika Loft Jakobsen & Anne Kiil Berthelsen



Patient Investigations

CNS and peripheral nervous system

Regional cerebral bloodflow, rest, 0-15-H2O	4
Regional cerebral bloodflow, physiological, 0-15-H2O	236
Regional cerebral metabolism, F-18 FDG	121
Regional cerebral metabolism, F-18 Altanserin	51
Regional cerebral receptor, stat., C-11-DASB	39
Regional cerebral receptor, stat., F-11-SB	5
Total	456

Respiratory organs

Lung function test, whole body plethysmography	921
Lung function test, whole body plethysmography w/reversibility	89
Lung function test, spirometry, WLHLB +WL1LB	897
Lung function test, spirometry w/reversibility	67
Lung function test, spirometry, pharmacological provocation	3
Lung function test, diffusionscapacity (CO)	1.921
Lung function test, peak flow w/reversibility	1
Lung perfusion scintigraphy, Tc-99m-MAA	190
Lung perfusion scintigraphy, regional, Tc-99m-MAA	140
Lung ventilation scintigraphy, Kr-81m	182
Lung ventilation scintigraphy, Tc-99m-DTPA	1
Lung ventilation scintigraphy, regional, Kr-81m	180
Mucociliary clearance, Tc-99m-venticolloid	51
Ciliary test	89
Total	4.732

Heart and cardiovascular system

Isotope cardiography, first pass, Tc-99m, HSA	103
Isotope cardiography, first pass, Tc-99m, ery	1
Isotope cardiography, LVEF, Tc-99m-HSA	974
Isotope cardiography, LVEF + vol, Tc-99m-ery	10
Isotope cardiography, LVEF + vol., Tc-99m-HSA	32
Myocardial perfusion scintigr., Tc-99m-MIBI, pharmacol. stress, adeno.	4
Myocardial perfusion scintigr., gated, Tc-99m-MIBI, pharmacol. stress, dipy.	15
Myocardial perfusion scintigr., gated, Tc-99m-MIBI, pharmacol. stress, dobut.	9
Myocardial perfusion scintigr., gated, Tc-99m-MIBI, pharmacol. stress, adeno.	138
Myocardial perfusion scintigr., gated, Tc-99m-MIBI, physiological stress	34
Myocardial perfusion scintigr., Tc-99m-MIBI, NTG	5
Myocardial perfusion scintigr., gated, Tc-99m-MIBI, NTG	165
Myocardial perfusion scintigr., gated, Tc-99m, MIBI	12
PET Myocardial perfusion, N-13-NH3	51
PET Myocardial perfusion, N-NH3, pharmacol. stress, dipy.	46
PET myocardial perfusion, N-13-NH3, cold press, phys. stress	11
PET myocardial metabolism, F-18 FDG	3
Exercise electrocardiography	15
Total	1.628

Peripheral vessels

Isolated limb perfusion leakage monitoring, chemotherapy	29
Total	29

Gastrin intestinal tract, including liver, biliary tract and pancreas

Salivary gland scintigraphy, Tc-99m	2
Bleeding scintigraphy (abdomen), Tc-99m-erythrocyt	3
Bleeding scintigraphy (abdomen), Tc-99m-human serumalb.	1
Gastrooesophageal reflux Tc-99m-Nanocoll	1
Biliary tract scintigraphy, Tc-99m-Mebrofenin	18
Meckels diverticulum scintigraphy, Tc-99m	4
Schillings test I	9
Total	38

Kidneys and urinary tract

Glomerular filtration, Cr-51-EDTA, several samples	206
Glomerular filtration, Cr-51-EDTA, one sample	3.274
Renal scintigraphy, Tc-99m-DMSA	16
Renography, Tc-99m-MAG3, diureses	14
Renography, Tc-99m-MAG3, Dual head	2
Renography, Tc-99m-MAG3, ph	1.614
Renography, Tc-99m-MAG3, graft	6
Renography, Tc-99m-MAG3, ACE-inhibitor	120
Renography, Tc-99m-DTPA	17
Total	5.269

Bone and joint

Bone scintigraphy, Tc-99m-HDP, regional, static	126
Bone scintigraphy, Tc-99m-HDP, whole body, static	789
Bone scintigraphy, Tc-99m-HDP, SPECT	33
Total	948

Endocrine organs

Thyreoide scintigraphy, Tc-99m	446
Thyreoide scintigraphy, I-123 jodid	1
Thyreoide perchoral washout, I-123-jodid	1
Thyreoide scintigraphy, I-123 jodid, residual tissue and up-take	1
Parathyreoide scintigraphy, Tc-99m-MIBI, SPECT + CT	77
Wholebody scintigraphy, diagnostic I-123-jodid	4
Wholebody scintigraphy, postoperative I-123-jodid	5
Adrenal marrow scintigraphy, I-123-MIBG	37
Whole body scintigraphy after I-131-therapy	68
Total	640

Blood and lymph system

Erythrocyt volume, Tc-99m-ery	17
Plasma volume, I-125, S-albumin	16

Finance

Lymph scintigraphy, extremities, Tc-99m-HAS	2
Lymph scintigraphy, extremities, Tc-99m-nanocolloid, stases	1
Sentinal node, tumor drainage, Tc-99m-nanocolloid	29
Sentinal node scintigr., tumor drainage, mamma c., Tc-99m-nanocolloid	105
Sentinal node scintigr., tumor drainage, malign. mel., Tc-99m-nanocolloid	116
Sentinal node scintigr., tumor drainage, penile c., Tc-99m-nanocolloid	5
Sentinal node scintigr., tumor drainage, vulva c., Tc-99m-nanocolloid	10
Peritumoral injection of Tc-99m-nanocolloid	346
Spleen scintigraphy, w/Tc-99m-erythrocyte, heated	6
Total	653

In vitro analysis

Plasma thyreoglobulin	852
Total	852

Other diagnostic procedures

Aprotinin scintigraphy, Tc-99m	31
Tumorscintigraphy, I-123-jodid	6
Tumor scintigraphy, In-111-Octreotide	151
PET tumor scanning, F-18 FDG	2.607
PET infection scanning, F-18 FDG	39
White blood cell scintigraphy, In-111	100
Whole body counting, K-40	10
Whole body counting, Ca-47, in meal	80
Whole body counting, radiation measurement	1
Image fusion (PET, SPECT, MRI, CT or planar), PET and KF-section	2.136
Diagnostic CT, PET	1.913
Diagnostic CT, KF	26
CT-therapy scanning	454
Total	7.554

Radiotherapy

Treatment with I-131, benign thyreoid	57
Investigation without specification	2
Cilie investigatin, in collaboration with ward 5003, RH	89
Total	148

Total number of patient investigations: 22.947

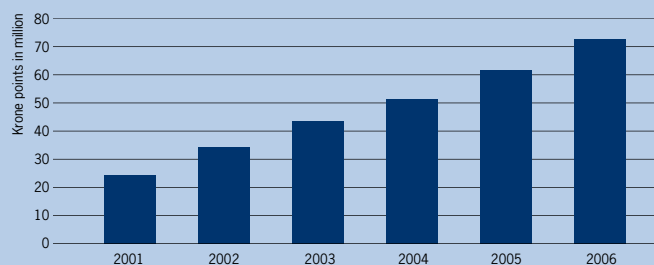
BALANCE 2006

Expenditure

Running costs	DKK 10.1 million
Staff	DKK 29.6 million
In total	DKK 39.7 million

Receipts	DKK 14.3 million
Net sum	DKK 25.4 million

TURNOVER DURING THE LAST SIX YEARS



Research



Our research focuses on development of new tracers for PET and nuclear medicine, clinical evaluation of new diagnostic methods as well as the use of methods from clinical physiology and nuclear medicine to study pathophysiology. At present, special attention is given to translational research in the area of molecular imaging.

We conduct extensive research based on the principles behind molecular imaging.

Major research areas at present are:

Development of new tracers

A series of projects aimed at development of new, specific tracers for non-invasive tissue characterization to be used for the diagnosis of different cancer types as well as for planning and monitoring of therapy are currently undertaken. These projects, most of which are translational in nature, are carried out in collaboration with other departments and laboratories, since they are dependent on expertise in molecular biology, chemistry, radiochemistry, cancer biology and imaging. In collaboration with a pharmaceutical company, a new method for diagnosing bleeding has been patented and currently awaits testing in human subjects.

Clinical PET & PET/CT

A series of prospective protocols evaluate the diagnostic and prognostic value of PET and PET/CT in different cancer forms in children and adults. Furthermore, the use of PET/CT for the planning of radiation therapy (IMRT) and the use of respiratory gating are evaluated.

Labelling of stem cells

In cooperation with stem cells researchers from cardiology, we have successfully labelled human stem cells and been able to track the cells in vivo with nuclear medicine techniques. Experiments in patients are planned in the near future.

Pediatric nuclear medicine investigations

The department conducts many paediatric investigations. Especially within oncology, several research protocols with the use of PET and SPECT are carried out in cooperation with clinical departments.

Neuro PET

In cooperation with Neurobiology Research Unit & Center for Integrated Molecular Brain Imaging, Professor Gitte Moos Knudsen and Professor Olaf B. Paulson, a series of neuro receptor ligands have been developed and used for research in neurobiology. The focus has mainly been on the serotonergic system.

Nuclear cardiology and neuroendocrinology

With the use of PET, coronary flow-regulation is studied in connection with gene therapy and pharmacological interventions in a variety of disease states. With the use of SPECT/CT the development of ischemic heart diseases is studied in selected groups of patients. A study using SPECT/CT in patients with suspected lung embolism is currently performed to study the impact on right ventricular cardiac function as assessed with gated multi-slice CT.

Lung studies

Research especially focusing on mucociliary clearance and evaluation of the use of hyperpolarized helium MRI is conducted. The latter is evaluated together with lung function tests, lung scintigraphy and CT. The added value of combined use of SPECT/CT for diagnosing acute lung embolism is currently studied. Animal experiments studying deposit characteristics and lung transplanted patients are other examples of current lung research.

Radionuclide treatment

Localized radiation therapy using specific ligands binding to certain cancer forms are currently being implemented. The department takes part in the research within this area through tests of new ligands and production of certain isotopes. Currently targeted cancer forms are certain types of lymphoma, neuroendocrine tumors as well as ovarian cancer. Treatment will in part be based on imaging using new tracers for molecular profiling.

Whole Body Counting

Together with external partners, whole body counting is used for exact measurements of body composition in a series of studies. Furthermore, absorption of certain minerals from the gastrointestinal tract is evaluated.

The department conducts research in collaboration with several national and international research partners.

Andreas Kjær

Cluster for Molecular Imaging

The change in paradigm towards individualized, tailored therapy has led to an increasing need for diagnosing at the cellular and molecular level. Most of the molecular biology methods used today need tissue sampling for in vitro analysis. In contrast, molecular imaging diagnosing at the cellular and molecular level is performed non-invasively in the living, intact organism.

With PET it is possible to label a whole new group of biomolecules with radioactive isotopes to be used for visualization of e.g. metabolism, receptors and gene-expression. Especially within cancer biology – but not limited to this - these techniques are expected to lead to a breakthrough in diagnosing and treatment. Of the different methods for molecular imaging only the nuclear medicine based techniques are of a true translational nature, i.e. methods developed in animal models may directly be transferred to and used in humans. Tailored therapy requires a thorough characterization of tissue, e.g. tumor and metastases. Ideally this could be obtained non-invasively using PET.

Our current molecular imaging 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 in order to plan individualized, tailored therapy. Development of new molecular imaging tracers for PET is a complex process that involves many steps from definition of target to final use of the tracer in patients.

Main steps involved in tracer development and use

- 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 labeling of ligands
- test of imaging ligands in animal models
- use of imaging data for therapy planning (e.g. IMRT or radionuclide therapy) and monitoring of response
- use for diagnosing, therapy planning and monitoring in patients

Through formation of Cluster for Molecular Imaging at the Faculty of Health Sciences, University of Copenhagen (headed by Professor Andreas Kjær) it has been possible to establish a core facility at the Panum Institute for molecular imaging in animals

with PET, SPECT and CT. This has improved our translational capacity since we are now able to test new tracers in animal models prior to clinical use.

Currently the main focus of the translational research is non-invasive tissue characterization in cancer and cardiovascular diseases models to study pathophysiology and to develop the diagnostic tools for selection, planning and monitoring of tailored therapy.

Some tissue characteristics currently targeted for imaging

- Hypoxia
- Angiogenesis
- Apoptosis
- Cell proliferation
- Glycolytic activity
- Receptor expression

PET scan using ^{18}F -FDG to visualize glycolytic activity of implanted tumor in nude mouse. Image is fused with CT scan (image provided by T. Binderup, MSc). Together with scans of other molecular characteristics, images are used for planning of radionuclide treatment.

Andreas Kjær



Publications 2006

PhD thesis

Bering S. The effect of *Lactobacillus plantarum* 299v and lactic acid on iron bioavailability - In vitro and human studies (ph.d.-afhandling). Frederiksberg, Samfundslitteratur Grafik: 2006:1-68. Forsvaret den 1. juni 2006 ved Københavns Universitet, Det Biomedicinske Fakultet.

Fischer BM. PET/CT imaging in small cell lung cancer (ph.d.-afhandling). Eget forlag; 2006:1-54. Forsvaret den 4. december 2006 ved Københavns Universitet. Det Sundhedsvidenskabelige Fakultet.

Olsen MW. Evaluation and modulation of angiogenesis and tumor physiology (ph.d.-afhandling). Eget forlag; 2006:1-93. Forsvaret den 10. januar 2006 ved Københavns Universitet. Det Sundhedsvidenskabelige Fakultet.

Søndergaard K. Synthesis, binding studies and PET studies of 2-substituted pormorphines (ph.d.-afhandling). HCØ Tryk: 2006:1-88. Danmarks Farmaceutiske Universitet.

Scientific publications

Andersen AB, Law I, Ostrowski SR, Lebech AM, Hoyer-Hansen G, Hojgaard L, et al. Self-reported fatigue common among optimally treated HIV patients: no correlation with cerebral FDG-PET scanning abnormalities. *Neuroimmunomodulation* 2006;13(2):69-75.

Andersen PB, Blinkenberg M, Lassen U, Kosteljanetz M, Wagner A, Poulsen HS, et al. A prospective PET study of patients with glioblastoma multiforme. *Acta Neurol Scand* 2006 Jun;113(6):412-8.

Balslev D, Nielsen FA, Lund TE, Law I, Paulson OB. Similar brain networks for detecting visuo-motor and visuo-proprioceptive synchrony. *Neuroimage* 2006 May 15;31(1):308-12.

Bilde A, Von BC, Mortensen J, Marving J, Hamilton TM, Kirkegaard J, et al. The role of SPECT-CT in the lymphoscintigraphic identification of sentinel nodes in patients with oral cancer. *Acta Otolaryngol* 2006 Oct;126(10):1096-103.

Bindslev L, Haack-Sorensen M, Bisgaard K, Kragh L, Mortensen S, Hesse B, et al. Labelling of human mesenchymal stem cells with indium-111 for SPECT imaging: effect on cell proliferation and differentiation. *Eur J Nucl Med Mol Imaging* 2006 Oct;33(10):1171-7.

Bonnema SJ, Bennedbaek FN, Veje A, Marving J, Hegedus L. Continuous methimazole therapy and its effect on the cure rate of hyperthyroidism using radioactive iodine: an evaluation by a randomized trial. *J Clin Endocrinol Metab* 2006 Aug;91(8):2946-51.

Chakera AH, Drzewiecki KT, Ingvar C, Steiniche T, Hesse B. Sentinel node imaging. *Curr Med Imag Rev* 2006;2:341-6.

Choure AJ, Garcia MJ, Hesse B, Sevensma M, Maly G, Greenberg NL, et al. In vivo analysis of the anatomical relationship of coronary sinus to mitral annulus and left circumflex coronary artery using cardiac multidetector computed tomography: implications for percutaneous coronary sinus mitral annuloplasty. *J Am Coll Cardiol* 2006 Nov 21;48(10):1938-45.

Christensen CB, Gutte H. Månedens billede: osteoidt osteom. *Ugeskr Laeger* 2006 Oct 23;168(43):3731.

Dumcke CE, Graff J, Rasmussen SP, Madsen JL, Møller S. Myokardieskintografi: Klinisk anvendelse og konsekvens på en ikke invasiv kardiologisk afdeling. *Ugeskr Laeger* 2006 Nov 6;168(45):3906-10.

Fischer BM, Mortensen J, Langer SW, Loft A, Berthelsen AK, Petersen BL, et al. A prospective study of PET/CT in initial staging of small-cell lung cancer: comparison with CT, bone scintigraphy and bone marrow analysis. *Ann Oncol* 2006 Oct 23.

Fischer BM, Olsen MW, Ley CD, Klausen TL, Mortensen J, Hojgaard L, et al. How few cancer cells can be detected by positron emission tomography? A frequent question addressed by an in vitro study. *Eur J Nucl Med Mol Imaging* 2006 Jun;33(6):697-702.

Fischer BM, Mortensen J, Langer SW, Loft A, Berthelsen AK, Daugaard G, et al. PET/CT imaging in response evaluation of patients with small cell lung cancer. *Lung Cancer* 2006 Oct;54(1):41-9.

Fischer BM, Mortensen J. The future in diagnosis and staging of lung cancer: positron emission tomography. *Respiration* 2006;73(3):267-76.

Fumal A, Laureys S, Di CL, Boly M, Bohotin V, Vandenheede M, et al. Orbitofrontal cortex involvement in chronic analgesic-overuse headache evolving from episodic migraine. *Brain* 2006 Feb;129(Pt 2):543-50.

Gerlach C, Law I, Paulson OB. Shape configuration and category-specificity. *Neuropsychologia* 2006;44(7):1247-60.

Hallund J, Tetens I, Bugel S, Tholstrup T, Ferrari M, Teerlink T, et al. Daily consumption for six weeks of a lignan complex isolated from flaxseed does not affect endothelial function in healthy postmenopausal women. *J Nutr* 2006 Sep;136(9):2314-8.

Haugbol S, Pinborg LH, Regeur L, Hansen ES, Bolwig TG, Nielsen FA, et al. Cerebral 5-HT_{2A} receptor binding is increased in patients with Tourette's syndrome. *Int J Neuropsychopharmacol* 2006 Feb 28;1-8.

Haugbol S, Pinborg LH, Arfan HM, Frokjaer VM, Madsen J, Dyrby TB, et al. Reproducibility of 5-HT_{2A} receptor measurements and sample size estimations with [¹⁸F]altanserin PET using a bolus/infusion approach. *Eur J Nucl Med Mol Imaging* 2006 Dec 29.

Hesse B, Murphy RT, Myles J, Huang J, Sabik EM. Images in cardiovascular medicine. A left atrial appendage thrombus mimicking atrial myxoma. *Circulation* 2006 Mar 21;113(11):e456-e457.

Hesse B, Murphy RT, Sigurdsson G, Nassif M, Greenberg NL, Gring C, et al. Use of tissue Doppler imaging to guide tube current modulation in cardiac multidetector computed tomographic angiography. *Am J Cardiol* 2006 Sep 1;98(5):603-7.

- Hojgaard L. Betydning af centraliseret behandling: forskning og udvikling. *Ugeskr Laeger* 2006 Apr 10;168(15):1517-9.
- Hojgaard L, Hansen MS. Centraliseret diagnostik. *Ugeskr Laeger* 2006 Apr 10;168(15):1560-2.
- Horn J, Lock-Andersen J, Sjostrand H, Loft A. Routine use of FDG-PET scans in melanoma patients with positive sentinel node biopsy. *Eur J Nucl Med Mol Imaging* 2006 Aug;33(8):887-92.
- Hoyer M, Roed H, Traberg HA, Ohlhuis L, Petersen J, Nellemann H, et al. Phase II study on stereotactic body radiotherapy of colorectal metastases. *Acta Oncol* 2006;45(7):823-30.
- Hoyer M, Roed H, Hansen AT, Ohlhuis L, Petersen J, Nellemann H, et al. Prospective study on stereotactic radiotherapy of limited-stage non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2006 Nov 15;66(4 Suppl):S128-S135.
- Hutchings M, Loft A, Hansen M, Ralfkiaer E, Specht L. Different histopathological subtypes of Hodgkin lymphoma show significantly different levels of FDG uptake. *Hematol Oncol* 2006 Sep;24(3):146-50.
- Hutchings M, Loft A, Hansen M, Pedersen LM, Buhl T, Jurlander J, et al. FDG-PET after two cycles of chemotherapy predicts treatment failure and progression-free survival in Hodgkin lymphoma. *Blood* 2006 Jan 1;107(1):52-9.
- Hutchings M, Loft A, Hansen M, Pedersen LM, Berthelsen AK, Keiding S, et al. Positron emission tomography with or without computed tomography in the primary staging of Hodgkin's lymphoma. *Haematologica* 2006 Apr;91(4):482-9.
- Hvas AM, Buhl H, Laursen NB, Hesse B, Berglund L, Nexø E. The effect of recombinant human intrinsic factor on the uptake of vitamin B12 in patients with evident vitamin B12 deficiency. *Haematologica* 2006 Jun;91(6):805-8.
- Jorgensen EA, Vogelsang TW, Knigge U, Watanabe T, Warberg J, Kjaer A. Increased susceptibility to diet-induced obesity in histamine-deficient mice. *Neuroendocrinology* 2006;83(5-6):289-94.
- Kalliokoski KK, Langberg H, Ryberg AK, Scheede-Bergdahl C, Doessing S, Kjaer A, et al. Nitric oxide and prostaglandins influence local skeletal muscle blood flow during exercise in humans: coupling between local substrate uptake and blood flow. *Am J Physiol Regul Integr Comp Physiol* 2006 Sep;291(3):R803-R809.
- Kjaer A. Molecular imaging of cancer using PET and SPECT. *Adv Exp Med Biol* 2006;587:277-84.
- Kjaer A, Lebech AM, Gerstoft J, Hesse B, Petersen CL. Right ventricular volume and mass determined by cine magnetic resonance imaging in HIV patients with possible right ventricular dysfunction. *Angiology* 2006 May;57(3):341-6.
- Kjaergaard J, Petersen CL, Kjaer A, Schadt BK, Oh JK, Hassager C. Evaluation of right ventricular volume and function by 2D and 3D echocardiography compared to MRI. *Eur J Echocardiogr* 2006 Dec;7(6):430-8.
- Kristensen MB, Hels O, Morberg CM, Marving J, Bugel S, Tetens I. Total zinc absorption in young women, but not fractional zinc absorption, differs between vegetarian and meat-based diets with equal phytic acid content. *Br J Nutr* 2006 May;95(5):963-7.
- Kristoffersen US, Hesse B, Rasmussen AK, Kjaer A. Radioiodine therapy in hyperthyroid disease: poorer outcome in patients with high 24 hours radioiodine uptake. *Clin Physiol Funct Imaging* 2006 May;26(3):167-70.
- Kupers R, Kehlet H. Brain imaging of clinical pain states: a critical review and strategies for future studies. *Lancet Neurol* 2006 Dec;5(12):1033-44.
- Kupers R. Functional imaging of allodynia in complex regional pain syndrome. *Neurology* 2006 Oct 24;67(8):1526.
- Kupers R. Neuroimaging of pain. In: Cervero F, Jensen TS, editors. *Handbook of Clinical Neurology: Pain*. Amsterdam: Elsevier; 2006. p. 481-501.
- Kupers R, Pappens M. PET studies. In: Stafleu vL, editor. *Brain imaging of pain: PET studies*. Bohn: Pijn Info; 2006. p. 69-78.
- Kupers R, Fumal A, de Noordhout AM, Gjedde A, Schoenen J, Ptito M. Transcranial magnetic stimulation of the visual cortex induces somatotopically organized qualia in blind subjects. *Proc Natl Acad Sci U S A* 2006 Aug 29;103(35):13256-60.
- Lenstrup M, Kjaergaard J, Petersen CL, Kjaer A, Hassager C. Evaluation of left ventricular mass measured by 3D echocardiography using magnetic resonance imaging as gold standard. *Scand J Clin Lab Invest* 2006;66(8):647-57.
- Lossl K, Andersen AN, Loft A, Freiesleben NL, Bangsbo S, Andersen CY. Androgen priming using aromatase inhibitor and hCG during early-follicular-phase GnRH antagonist down-regulation in modified antagonist protocols. *Hum Reprod* 2006 Oct;21(10):2593-600.
- Madsen JL, Fuglsang S, Graff J. Effect of intravenous infusion of glyceryl trinitrate on gastric and small intestinal motor function in healthy humans. *Aliment Pharmacol Ther* 2006 Apr 15;23(8):1251-7.
- Marcassa C, Bischof DA, Cuocolo A, Hesse B, Kaufmann P, Knuuti J, et al. The regulatory background of nuclear cardiology in Europe: a survey by the European Council of Nuclear Cardiology. *Eur J Nucl Med Mol Imaging* 2006 Dec;33(12):1508-12.
- Nguyen TQ, Tarnow L, Andersen S, Hovind P, Parving HH, Goldschmeding R, et al. Urinary connective tissue growth factor excretion correlates with clinical markers of renal disease in a large population of type 1 diabetic patients with diabetic nephropathy. *Diabetes Care* 2006 Jan;29(1):83-8.

As in previous annual reports we have chosen only to list scientific papers, and not the many abstracts and proceedings etc. from the department.

Oelfke U, Tucking T, Nill S, Seeber A, Hesse B, Huber P, et al. Linac-integrated kV-cone beam CT: technical features and first applications. *Med Dosim* 2006;31(1):62-70.

Persson F, Rossing P, Hovind P, Stehouwer CD, Schalkwijk C, Tarnow L, et al. Irbesartan treatment reduces biomarkers of inflammatory activity in patients with type 2 diabetes and microalbuminuria: an IRMA 2 substudy. *Diabetes* 2006 Dec;55(12):3550-5.

Rappeport ED, Hansen CP, Kjaer A, Knigge U. Multidetector computed tomography and neuroendocrine pancreaticoduodenal tumors. *Acta Radiol* 2006 Apr;47(3):248-56.

Ripa RS, Wang Y, Goetze JP, Jorgensen E, Johnsen HE, Tagil K, et al. Circulating angiogenic cytokines and stem cells in patients with severe chronic ischemic heart disease - Indicators of myocardial ischemic burden? *Int J Cardiol* 2006 Dec 5.

Ripa RS, Wang Y, Jorgensen E, Johnsen HE, Hesse B, Kastrup J. Intramyocardial injection of vascular endothelial growth factor-A165 plasmid followed by granulocyte-colony stimulating factor to induce angiogenesis in patients with severe chronic ischaemic heart disease. *Eur Heart J* 2006 Aug;27(15):1785-92.

Scheuer KH, Nielsen JE, Krabbe K, Paulson OB, Law I. Motor activation in SPG4-linked hereditary spastic paraplegia. *J Neurol Sci* 2006 May 15;244(1-2):31-9.
Schou M, Gustafsson F, Nielsen PH, Madsen LH, Kjaer A, Hildebrandt PR. Unexplained week-to-week variation in BNP and NT-proBNP is low in chronic heart failure patients during steady state. *Eur J Heart Fail* 2006 Jul 6.

Squiers L, Bright MA, Rutten LJ, Atienza AA, Treiman K, Moser RP, et al. Awareness of the National Cancer Institute's Cancer Information Service: results from the Health Information National Trends Survey (HINTS). *J Health Commun* 2006;11 Suppl 1:117-33.

Tarnow L, Gall MA, Hansen BV, Hovind P, Parving HH. Plasma N-terminal pro-B-type natriuretic peptide and mortality in type 2 diabetes. *Diabetologia* 2006 Oct;49(10):2256-62.

Tuunanen H, Engblom E, Naum A, Nagren K, Hesse B, Airaksinen KE, et al. Free fatty acid depletion acutely decreases cardiac work and efficiency in cardiomyopathic heart failure. *Circulation* 2006 Nov 14;114(20):2130-7.

Ulrich JN, Hesse B, Schuele S, Vlassak I, Sita CA, Jaber WA. Single-vessel versus

multivessel territory acute ischemic stroke: value of transesophageal echocardiography in the differentiation of embolic stroke. *J Am Soc Echocardiogr* 2006 Sep;19(9):1165-9.

Viswanath K, Breen N, Meissner H, Moser RP, Hesse B, Steele WR, et al. Cancer knowledge and disparities in the information age. *J Health Commun* 2006;11 Suppl 1:1-17.

Vogelsang TW, Yoshiga CC, Hojgaard M, Kjaer A, Warberg J, Secher NH, et al. The plasma atrial natriuretic peptide response to arm and leg exercise in humans: effect of posture. *Exp Physiol* 2006 Jul;91(4):765-71.

Watanabe H, Sakoh M, Andersen F, Rodell A, Sorensen JC, Ostergaard L, et al. Statistical mapping of effects of middle cerebral artery occlusion (MCAO) on blood flow and oxygen consumption in porcine brain. *J Neurosci Methods* 2006 Nov 25.

Witting N, Kupers RC, Svensson P, Jensen TS. A PET activation study of brush-evoked allodynia in patients with nerve injury pain. *Pain* 2006 Jan;120(1-2):145-54.

Scientific awards

Professor, overlæge, dr.med., ph.d., MBA
Andreas Kjær. August Krogh Prize 2006.

Cimbi

Center for Integrated Molecular Brain Imaging
University of Copenhagen, Rigshospitalet

In cooperation with the Neurobiology Research Unit, Professor Gitte Moos Knudsen and Professor Olaf B. Paulson, a series of neuroreceptor ligands are developed and used for research in neurobiology. The focus has mainly been on the serotonergic system. In 2005 Gitte Moos Knudsen received a grant from the Lundbeck Foundation and established CIMBI; "Center for Integrated Molecular Brain Imaging", where we are proud to collaborate on the PET studies.

Professor Gitte Moos Knudsen



MSc in Medicine and Technology

In cooperation with the Technical University of Denmark (DTU) and the University of Copenhagen (KU), the department represented by Professor Liselotte Højgaard has been involved in planning of the new programme, MSc in Medicine and Technology, which was implemented in 2003, as a five years bachelor and master education.

Since the education started in 2003 more than 200 students have applied for one of the 60 available slots. You can read more about the education on: www.medicin-ing.dk. The first bachelors graduated in 2006 and they have all chosen to continue as master students and will graduate finally in 2008.



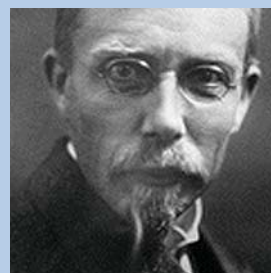
Grants and Foundations

Anne-Birgitte Mehlsen, Senior Registrar received DKK 115.000 from “Carl and Katy Kajsings Grant” for investigations of the parasympatic nervous system.

Andreas Kjær, Professor, DMSc received the August Krogh Prize and DKK 100.000 from the Danish Medical Society and the Novo Nordisk Foundation. The prize was given as “an acknowledgment for outstanding research within advanced use and implementation of molecular imaging in neuro-endocrinology, nuclear cardiology and cardial MR scan”.



Andreas Kjær



August Krogh

Education



The Department of Clinical Physiology and Nuclear Medicine & PET and Cyclotron Unit participates in the pre-graduate medical education at the Health Faculty of the University of Copenhagen within the following fields: human biology, clinical physiology and nuclear medicine, and in theoretical physiology by Professor Andreas Kjær, human biology and medical engineering by Professor Liselotte Højgaard and clinical physiology and nuclear medicine by Assistant Professor Jann Mortensen. The department participates in the OSVAL I and II programmes for medical students and the education of nuclear medicine technologists. As regards postgraduate education, the department participates in the specialist education of doctors in clinical physiology and nuclear medicine in Denmark.

The staff members attend numerous courses for both doctors and other academics in Denmark. Furthermore, the staff participates in international courses, symposiums, meetings, congresses and workshops.

The department's educational activities are very comprehensive and include all staff members. The Nuclear Medicine Technologists have participated in our special dedicated CT courses, which include 80 lectures and tutorials and is completed with an examination. This allows our staff to be in charge of the PET/CT and SPECT/CT scanners also for the CT part. Their CT competence is officially acknowledged by the Danish National Agency for Radiation Protection.

The Department of Clinical Physiology and Nuclear Medicine & PET and Cyclotron Unit performs extensive training to staff from other Nuclear Medicine and Radiological Departments in Denmark and the Nordic countries via study visits to our facilities of physicians and nuclear medicine technologists for periods of weeks up to 6 months. In addition, our staff travel to foreign hospitals e.g. Chief Physician Jann Mortensen and Chief Physician Esbern Friis from the Department of Surgery, Rigshospitalet implemented and supervised sentinel node scintigraphy and biopsy in the Faroe Islands.

Jann Mortensen is responsible for the education in the department.

Jann Mortensen



Nuclear Medicine Technologists



At the Department we employ 30 Nuclear Medicine Technologists, a staff nurse and a radiographer. The Nuclear Medicine Technologists produce the routine radiopharmaceuticals and they perform the daily patient investigations in nuclear medicine and PET. They also participate in the research and development projects. They have co-responsibility for the projects and are involved in both data management, quality assurance and patient- and animal studies. The research participants results in oral presentations and posters at both Danish and international meetings and symposia for technologists.

In 2006 two posters from the Nuclear Medicine Technologist group at the department were visible at the European Association of Nuclear Medicine Congress in Athens, and one of the posters acquired an award. Our technologist Marianne Federspiel and our radiographer Elisabeth Abrahamsson held the educational programme called "Children in a PET-center" in Athens.

The technologists take part in "continuous technology education" and four took the CTE examination.

The Nuclear Medicine Technologists are frequently asked to give courses and lectures both in Denmark, Scandinavia and at the

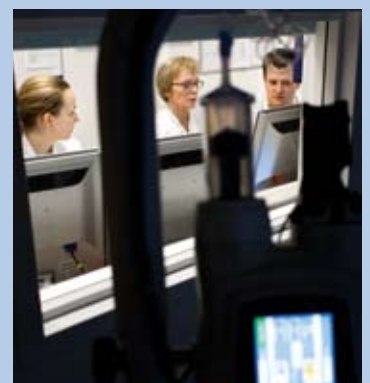
PET/CT courses in Vienna. Our Nuclear Medicine Technologists are dynamic, competent and responsible with a very important role for the development of the clinic. In 2006 four Nuclear Medicine Technologists participated in our own dedicated CT course, officially acknowledged by the "Danish National Agency for Radiation Protection".

During 2006 two Staff Nuclear Medicine Technologists participated in the Management Course for leaders at Righospitalet and graduated in October-November. Kate Pedersen from the PET section with a project titled "Implementation of PET/CT to radiotherapy" and Lis Larsen from the Nuclear Medicine section with a project titled "From management to leadership".

A large number of Nuclear Medicine Technologists from both Denmark and the Nordic countries are frequently educated in our department. They come to obtain education in management of PET/CT-scanners, gammacameras, SPECT/CT-camera and PET-radiochemistry.

Our Nuclear Medicine Technologist students have together with our Chief Technologist performed their bachelor project with the title "Optimized Stemcell Labeling".

Linda M. Kragh



Equipment

Department of Clinical Physiology and Nuclear Medicine, i.e. the divisions 4011, 4012 and 4112, is placed in the south wing of Rigshospitalet on the first floor. The Department is in possession of eight gamma cameras and two lung function equipments. One a Philips SPECT/CT with dedicated CT. The PET and Cyclotron Unit, division 3982, which is placed in the Finsen Building, is in possession of two PET/CT scanners, two PET scanners, two cyclotrons and a NMR spectrometer. Furthermore, three new radiochemistry laboratories are at our disposal and we have office and laboratory facilities in PET, division 3992. The Department has a Whole Body Counter with two chambers in the basement under the south wing, division 4191, which was renovated in 2002.

The John and Birthe Meyer Foundation has donated all the equipment in the PET and Cyclotron Unit.



Accreditation

The Joint Commission International, an international American accreditation board, performed a successful accreditation in the spring of 2002 of all the H:S hospitals including Rigshospitalet. In January 2005 the 2nd accreditation took place, also with success. The next review will be in January 2008.

We have worked on standards and politics, standard operation procedures, our quality handbook, patient informations and documentation. It has been an extensive task, and it has contributed to a positive improvement of the quality for the department.



Other Activities

Liselotte Højgaard, Professor, Head of Department, is member of the “Danish Council for Research Policy”, and member of “Arbejdsgruppen for Forskningsinfrastruktur” (AFI), a working group for research infrastructure in Denmark. Member of the Steering Group for Biological and Medical Sciences, the “European Strategy Forum on Research Infrastructures” (ESFRI Medical) and chair of the ESFRI Expert Group on Clinical and Translational Medical Research. Chair of the Council for “Medical Museion” (Museum of the History of Medicine in Copenhagen). She represents The University of Copenhagen and Rigshospitalet in the programme, MSc in Medicine and Technology in cooperation with The Technical University of Denmark (DTU). Member of ATV “The Danish Academy of Technical Sciences”. From September 2006 she was appointed Chair of the Standing Committee of the European Medical Research Councils (EMRC), at the European Science Foundation, Strasbourg.

Linda M. Kragh, Chief Nuclear Medicine Technologist, is a member of “Sundhedsfagligt Råd i Klinisk fysiologi og nuklearmedicin” in H:S, the Specialty Advisory Committee (SFR) in Clinical Physiology and Nuclear Medicine”, member of “Uddannelsesrådet for Bioanalytikeruddannelsen i Storkøbenhavn” in H:S (the speciality council for the education of laboratory technologists) and a member of the “Danish Society for Clinical Physiology and Nuclear Medicine”.

Andreas Kjær, Professor, Chief Physician is the Danish delegate in the “Scandinavian Society of Clinical Physiology & Nuclear Medicine” (SSCPNM). Chairman of the board of “Selskabet for Teoretisk og Anvendt Terapi” (the Society for Theoretical & Applied Therapy). Member of “Forskningsrådets formandskab” (The Research Council) at Rigshospitalet, member of “Sundhedsfagligt Råd i Klinisk fysiologi og nuklearmedicin” in the Region of Copenhagen, the Specialty Advisory Committee (SFR) in Clinical Physiology & Nuclear Medicine and member of the scientific committee of the Danish Cancer Society. Responsible for the course in heart pa-top physiology for nuclear medicine physicians. And Head of Cluster for Mole-

cular Imaging at the Faculty of Health Sciences, University of Copenhagen.

Jann Mortensen, Assistant Professor, Chief Physician is a member of “Sundhedsfagligt Råd i Onkologi” in H:S, the Specialty Advisory Committee (SFR) for Oncology. Member of the steering committee of “Dansk Lunge Cancer Gruppe” (Danish Lung Cancer Group) and member of the subcommittees “Dansk Diagnostik Lunge Cancer Gruppe” (Danish Diagnostic Lung Cancer Group) and the Danish Steering Committee for Screening of Lung Cancer. Member of the supplementary training committee of the “Danish Society for Clinical Physiology and Nuclear Medicine” and a substitute for the board of the “Danish Society for Clinical Physiology & Nuclear Medicine” and responsible for the specialist course in “Clinical respiratory physiology” for nuclear medicine physicians and internal medicine.

Annika Loft Jakobsen, Chief Physician is a member of the “European Organisation for Research and Treatment of Cancer” (EORTC), the Functional Imaging Group and “The British Institute of Radiology”. Member of the EANM, AML and BIR and Oncoradiological Society and chair of the Danish Lymphoma Group (DLG) and member of the guideline group for Pharynx/Larynx Cancer.

Birger Hesse, Chief Physician is a member of the “European Council of Nuclear Cardiology” (ECNC) and chair for “Medicinsk bibliotek” at Rigshospitalet (the Medical Library) and “Biblioteksgruppen” in H:S (Library group). Member of the “Cardiovascular Committee, EANM” and chair of “Sektorudvalg for diagnostiske specialer, DANAK”. Head of “Corelab for myocardial scintigraphy”. Editorial board in Eur J Nucl Med, Curr Med Imag Rev, Eur Ass Nucl Med Cardiovascular Com and Eur Council Nucl Cardiol Board.

Anne Kiil Berthelsen, Chief Physician is a member of “British Institute of Radiology”.

Søren Holm, Chief Physicist is a member of “Sundhedsfagligt Råd i Klinisk fysiologi

og nuklearmedicin” in H:S, the Specialty Advisory Committee (SFR) in Clinical physiology & nuclear medicine and a member of the board of the “Danish Society for Clinical Physiology & Nuclear Medicine”. Member of the educational board of the “Danish Society of Medical Physics” and a delegate for this society at the “European Federation of Organizations in Medical Physics” (EFOMP).

Jesper Graff, Chief Physician is chair for kursusudvalget in the “Danish Society of Clinical Physiology & Nuclear Medicine” and representative in “Vurderings- og Ansættelsesudvalget” in Clinical Physiology & Nuclear Medicine under the Danish Society of Clinical Physiology and Nuclear Medicine. Member of the Steering Committee of “DMCG Livertumors”.

Anne-Birgitte Mehlsen, is member of the Committee for “Yngre Nuklearmedicineres Klub”.

Ian Law, Staff Physician is a member of the board in the “Medical Society of Copenhagen” and member of the “Research Council” at Rigshospitalet.

Nic Gillings, Chief Radio Chemist is a member of the management committee of the EU COST Action B12 programme: “Radiotracers for in vivo assessment of biological function”.

Lis Larsen, Department Nuclear Medicine Technologist is a member of the supplementary training committee of the “Danish Society for Clinical physiology & nuclear medicine”, and member of “Udviklingsgruppen for Klinisk fysiologi og nuklearmedicin under Danske Bioanalytikere” (Developing Group for Clinical Physiology & Nuclear Medicine under “The Danish Association of Biomedical Laboratory Technologists”). She attended the Management Course at Rigshospitalet and graduated in November 2006.

Kate Pedersen, Nuclear Medicine Technologist is a member of the Technologist Committee under EANM and a member of “Udvalget for Ledende og Afdelingsbioanalytikere i Region Hovedstaden under Dbio”. She attended the Management Course at Rigshospitalet and graduated in October 2006.

European Medical Research Councils

The European Medical Research Councils (EMRC) is the membership organization of all the European medical research councils – for the EU member states, and for all the other European countries also.

Set up in 1971, the EMRC evolved into Standing Committee of the ESF in 1975. It covers broad range of disciplines and the Committee's objectives range from promoting interactions between the biological, biomedical and clinical research communities to developing European scientific strategies and stimulating collaboration in emerging and interdisciplinary research areas.

In pursuing these objectives, the EMRC seeks to ensure that its strategy takes into account the variety of sources of funding available across Europe.

The chair of the Committee for the European Medical Research Councils is Professor Liselotte Højgaard from the Rigshospitalet, University of Copenhagen, Denmark.





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