Rigshospitalet

Department of Clinical Physiology, Nuclear Medicine & PET

Annual Report 2015

Rigshospitalet · University of Copenhagen

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

Glostrup Hospital
Glostrup Hospital were established in 1958, and 1st of January 2015 Rigshospitalet, Blegdamsvej and Glostrup Hospital were unified as Rigshospitalet.

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

REGION Rigshospitalet

DTU

UNIVERSITY OF COPENHAGEN

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Preface

2015 was a year with New Beginnings: Rigshospitalet, Blegdamsvej and Glostrup Hospital were unified to one big hospital, and the Departments of Clinicial Physiology and Nuclear Medicine were unified to one big department with sections both in Glostrup and Rigshospitalet, Blegdamsvej. The leadership of the department is Heads of Department, Professor Liselotte Højgaard and Chief Technologist Linda M. Kragh.

The unification has been a positive process with a lot of work for everyone in terms of organisation, administration and economy, but it has had a positive synergistic effect for research, clinical patient investigations and education. We established a teleconference facility at both addresses and staff meetings, clinical conferences and presentations can be held with participants at the same time in Glostrup and Blegdamsvej. We are now a department with more than 240 employees, a big and busy clinical everyday practise at Blegdamsvej with over 100.000 investigations per year and in Glostrup more than 20.000 per year.

Researchwise Blegdamsvej published about 130 peer review publications and theses in 2015 and Glostrup about 35. Compared to the size of the sections it is for both very successful results, and we are well on track for our goal: To be one of the five leading departments in our area in 2020 on an international scale.

The Section in Glostrup was part of Diagnostic Department with radiology, clinical physiology, nuclear medicine and clinical biochemistry in one unit. Now Clinical Physiology from Glostrup is together with Clinical Physiology Rigshospitalet Blegdamsvej, and the little unit Biolab with assays for special biochemistry analyses has been placed in the big new Department of Clinical Biochemistry, as the professional and scientific competences belong there.

FIU, the Unit for Functional Imaging, with high profile MRI investigations and research of brain and heart is now part of the Department of Clinical Physiology, Nuclear Medicine and PET, and we are proud to welcome the fine research group lead by Professor Henrik Larsson.

The section in Glostrup is, as can be seen from our organisational diagram, 1 of 5 sections in the department, and it is led by Consultant Peter Hovind and Staff Technologist Lis Larsen. We look forward to the benefits of the full implementation here in 2016 and onward, and we anticipate a growing and strengthened program in clinical patient studies, research and education and PET/CT for 2016.

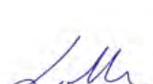
The research has been a tremendous success in 2015 with Professor Andreas Kjær at the helmet as responsible for research at the unified department. Andreas Kjær has had success himself personally with big grants from Danish and international foundations with the ERC Advanced Grant as the most exquisite. We are privileged to house his comprehensive program of molecular imaging and look very much forward to follow the development of the uPAR tracer for grading of invasiveness and malignancy in non-invasive PET/CT scanning.

To all the other researchers in the department we would like to say the same thank you and honors for a fine effort. Professor Ian Law has established his one-stop-shop PET/MR for diagnosis of patients with dementia and brain tumors, Consultant Lise Borgwardt has established the paediatric program with now 3.000 paediatric patient investigations 2015, Consultant Jann Mortensen has extended his comprehensive program in lung physiology and nuclear medicine, Consultant Annika Loft Jakobsen has extended the comprehensive program on PET/CT for clinical oncology, Consultant Philip Hasbak has established the cardiology research program with Rubidum-PET, Consultant Peter Oturai has, together with Jann Mortensen, developed the neuroendocrine tumor clinical program with now 100 patient treatments per year and Consultant Johan Löfgren has struggled very hard and made a big effort to secure the ICT in spite of a lousy performance of the PACS system in the hospital. To Consultant Malene Fischer honors for a research program in collaboration with your associate professorship.

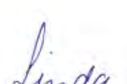
Thank you to Chief Production Manager, Chemist Jacob Madsen and Chief Radiochemist Nic Gillings for an exquisite radiochemistry unit, to Chief Cyclotron Physicist Holger Jensen and Cyclotron Physicist Jesper Jørgensen for the cyclotron productions from the two in house cyclotrons. To the team of physicists and computerscientist: Søren Holm, Thomas Levin Klausen, Bryan Haddock, Flemming Andersen and their team, thank you for making it all work - together with your own fine research production.

Thank you to our directors at the Center of Diagnostics, Rigshospitalet, Center Director Bettina Lundgren, MD DMSc and Vice Director Lene Ørnstrup and their team for important positive and helpful collaboration. Thank you to Department of Radiology, Head of Department Ilse Vejborg and Chief Radiographer Johnny Madelung for positive collaboration in the unification process.

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



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 of Rigshospitalet 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 investigations and patient treatment with radiopharmaceuticals
- 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 nationally and internationally
- to provide a good patient experience and ensure the wellbeing of patients, relatives and staff

We aim high – we strive to be one of the five best departments of this kind world wide before 2020.

The staff participates in 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.

Organisation and Staff 2015

Abrahamsson, Elisabeth, Radiographer.
Agner, Elissaveta Castella, Radiographer.
Albers, Mia C. Hjorth, Teaching NMT.
Albrecht-Beste, Elisabeth, MD, Consultant.
Alslev, Louise, MD, Staff Specialist.
Al-Tai, Reya Tarik Hamid, NMT.
Amtoft, Annemarie Gjelstrup, MD, Consultant.
Anderberg, Lasse, Student.
Andersen, Anne Sofie Bech, Student.
Andersen, Flemming, MSc, PhD, Chief Computer Scientist.
Andersen, Julie Bjerglund, MD, PhD Student.
Andersen, Kim Francis, MD, Staff Specialist.
Andersen, Ulrik Bjørn, MD, Consultant.
Anthony, Erwin Jørry, Cyclotron Technician.
Azizi, Nadia, Radiographer.
Barløse, Mads Christian Johannes, MD, Registrar.
Belmouhand, Mohamed, Scholarship.
Benjaminsen, Claus, MSc Engineer.
Benoit, Didier, Physicist, Postdoc.
Benzon, Eric von, MD, Consultant.
Berg, Ronan Martin Griffin, MD, Registrar.
Berthelsen, Anne Kiil, MD, Consultant.
Binderup, Tina, MSc Human Biology, PhD, Postdoc.
Birch, Kirsten Junker, NMT.
Bisgaard, Sissel, Student.
Borgwardt, Henrik Gutte, MD, PhD, Postdoc.
Borgwardt, Lise, MD, PhD, Consultant.
Børresen, Betina, DVM, PhD Student.
Brandt-Larsen, Malene, MSc, PhD, Chemist.
Brittain, Jane Maestri, MD, Senior Registrar.
Brogaard, Rikke Yding, MSc Engineer, PhD Student.
Buhelt, Sophie, Student.
Cappelen, Anna, Student
Cappelen, Katrine Louise, Engineer.
Choudry, Aisha Bilal, Student.
Christensen, Anders, MD, PhD Student.
Christensen, Camilla, Chemist.
Christensen, Camilla, NMT.
Christensen, Charlotte Birk, MD, Staff Specialist.
Christensen, Helle, NMT and Nurse.
Christensen, Jan Damgaard, Cyclotron Technician.
Christensen, Kirstine Kjær, Student.
Christensen, Thomas Emil, MD, PhD Student.
Christensen, Tine Nøhr, MD, PhD Student.
Clausen, Malene Martini, MD, PhD, Postdoc.
Clemmensen, Andreas Ettrup, MSc Med.Tech, PhD Student.
Cortsen, Annette, NMT.
Costa, Junia, MD, Staff Specialist.
Cramer, Stig Præstekjær, MD, PhD, Postdoc.
Dahan, Daniel, Cyclotron Technician.
Dähnhardt, Andreas, Computer Assistant.
Dall, Bente, NMT.
Damgaard, Jeannette, Radiographer.
de Nijs, Robin, Med. Physicist, MSc, PDEng, PhD.
Dejanovic, Danijela, Staff Specialist.
Denholt, Charlotte Lund, MSc, PhD, Chemist.
Do, Manh Tan, Student.
Døssing, Kristina Benedikte Vangsted, MSc Biology, PhD Student.
Drachmann, Anders Paaske, Student.
Dunbar, Douglas, NMT.
El-Ali, Henrik Hussein, Physicist, PhD, Ass. Prof.
Elkington, Sakeena, NMT.
Ellebæk, Sofie, MSc Biotech, PhD Student.
Ellegaard, Andreas Høyby, Student.
Enevoldsen, Lotte Hahn, MD, Consultant.
Engberg, Astrid, Student.
Federspiel, Marianne, NMT.
Fischer, Barbara Malene, MD, DMSc, PhD, Consultant.
Fishekxhiu, Elida Sinik, NMT.
Fliedner, Frederikke Petrine, Research Assistant.
Foldager, Annette, Teaching NMT.
Folkmann, Nanna Freja, Secretary.
Fosbøl, Marie Øbro, MD, Senior Registrar.
Frederiksen, Mette, NMT.
Frost, Nadia, Student.
Frydendahl, Christina Schjøth, MSc Chem, PhD, Postdoc.
Fuchs, Annette, Scholarship.
Gelle, Liibaan Mohamed, NMT.
Ghotbi, Adam Ali, MD, PhD Student.
Gillings, Nicholas, MSc, PhD, Chief Radiochemist.
Girkov, Mia Seremet, Scholarship.
Grave, Tine, Medical Secretary.
Gutt, Lars Emil, Student.
Haddock, Bryan Thomas, Chief Physicist.
Hag, Anne Mette Fisker, MSc Human Biology, PhD, Postdoc, Research Coordinator.
Hansen, Adam Espe, Physicist.
Hansen, Anders Elias, DVM, PhD, Postdoc.
Hansen, Anja Vallin, NMT, Clinical Instructor.
Hansen, Camilla Josephine Teglgaard, NMT.
Hansen, Casper, Student.
Hansen, Christian, Student.
Hansen, Lasse, NMT, Clinical Instructor.
Hansen, Matilde Bro, Student.
Hansen, Michele Zaugg, Student.
Hansen, Ole Michael Raun, NMT.
Hansen, Rie Beck, Student.
Harder, Fie Barbara, NMT.
Hasbak, Philip, MD, Consultant.
Hasler, Signe Winther, Student.
Hassan, Mariam, NMT.
Hassing, Christina, Student.
Henriksen, Frederik Hurup, Student.
Henriksen, Otto Mølby, MD, PhD, Consultant.
Hercman, Alexandra Regina Nowacka, NMT.
Hildebrand, Sanne, Secretary.
Hirsi, Abdi Hafied, Registrar.
Højgaard, Liselotte, MD, DMSc, Professor, Head of Department.
Holm, Søren, MSc, PhD, Chief Physicist.
Holm, Stine, NMT.
Holten, Victoria, Student.
Holtz, Simon Herken, MSc, QA Academic.
Hovind, Peter, MD, DMSc, Consultant.
Hurry, Preetee Kapisha, Senior Registrar.
Iljazovska, Cejlan Zulfovska, NMT.
Ismaili Abd, Schorlarship.
Jakobsen, Annika Loft, MD, PhD, Consultant.
Jensen, Berit, NMT.
Jensen, Holger, MSc, PhD, Chief Cyclotron Physicist.
Jensen, Irene Cecilie, Student.
Jensen, Julie Milbak, Student.
Jensen, Line Due, Radiographer.
Jensen, Martin Juul Ravn, NMT.

Jensen, Mathilde Daniele Ørbæk, Scholarship.
Jensen, Mathilde Dyrholm, Student.
Jensen, Mette Munk, MSc Human Biology, PhD, Postdoc.
Jensen, Rasmus Ramsbøl, MSc Engineer, PhD.
Jensen, Tina Gade, QA Assistant.
Jeppesen, Troels Elmer, Chemist, PhD Student.
Johannesen, Helle Hjorth, MD, Consultant.
Johnbeck, Camilla Bardram, MD, PhD Student.
Jørgensen, Annegrethe, NMT.
Jørgensen, Jennifer Solgaard, MSc Engineer Biotech, PhD Student.
Jørgensen, Jesper Tranekjær, MSc Human Biology, PhD, Postdoc.
Jørgensen, Jesper, MSc, Cyclotron Physicist.
Jørgensen, Louise, MD, Research Assistant.
Jørgensen, Mette Møller, NMT.
Juhl, Karina, MSc Human Biology, PhD Student.
Juul, Christian Ammitzbøll, MSc Biology, PhD Student.
Kaijer, Michelle Nymann, Technologist, PA Professor Andreas Kjær.
Karnov, Kirstine, MD, PhD Student.
Keller, Sune Høgild, MSc, PhD, Computer Scientist.
Kielsgaard, Kathrine, Student.
Kjær, Andreas, MD, DMSc, PhD, MBA, Consultant, Professor.
Kjær, Kristian Skov, Student.
Klausen, Thomas Levin, MSc, Chief Physicist.
Kleczewski, Karina, Medical Secretary.
Klyver, Cecilia, Student.
Knigge, Pauline Natalie Seindal, Student.
Knudsen, Camilla Sloth, NMT.
Knudsen, Jesper Andreas, MD, PhD, Post doc.
Korsholm, Kirsten, MD, Senior Registrar.
Kragh, Linda M., Chief NMT.
Kristensen, Lotte Kellemann, MSc Human Biology, Research Assistant.
Kristiansen, Jonas Frimer, Student.
Krogager, Louise, Student.
Kronvall, Johanna, NMT.
la Cour, Jeppe Lerche, MD, PhD Student.
Ladefoged, Claes Nøhr, Computer Scientist, PhD Student.
Lærke, Sonja Pedersen, Technician.
Langer, Jonathan Andreas Wang, Student.
Langer, Natasha Hemicke, Scholarship.
Larsen, Anne Fensløv, Student.
Larsen, Christina Vang, NMT.
Larsen, Lis, Staff Technologist.
Larsen, Trine Bjørnbo, MSc Pharm Tech, Phd Student.
Larsson, Henrik Bo Wiberg, MD, DMSc, Consultant, Professor.
Lass, Jakob, Student.
Laugesen, Monika, Student.
Law, Ian, MD, PhD, Consultant, Professor.
Lehel, Szabolcs, MSc, PhD, Chemist.
Li, Fan, MSc Med Tech, PhD, Postdoc.
Lindberg, Ulrich, MSc. Engineer, PhD.
Lindell, Elin, NMT.
Linnet, Solveig, NMT.
Ljunggren, Anna, NMT.
Löfgren, Johan, MD, Consultant.
Ludvig, Helle, NMT.
Lundberg, Helena Inez Sofia, MD, Registrar.
Lundby, Tim Mølgaard, Staff Technologist.
Lundsgaard, Christoffer Cramer, Student.
Madsen, Casper Lillegård, Student.
Madsen, Jacob, MSc, PhD, Chemist, Chief Production Manager.
Madsen, Lasse Ahlbech, Student.
Magnusson, Linda Helena Margaretha, Technologist.
Malmberg, Catarina Anna Evelina, Scholarship.
Mark, Peter Dall, Student.
Marner, Lisbeth, MD, DMSc, PhD, Staff Specialist.
Martín, Marina Simón, Student.
Mehlsen, Anne-Birgitte, Consultant.
Mikkelsen, Mathias, Student.
Mistry, Jacqueline Møller, Student.
Mohebi, Ali, Student.
Mølvig, Bjørn Hübschmann, Student.
Mortensen, Jann, MD, DMSc, Consultant, Ass. Professor.
Mose, Camilla, NMT.
Mottelson, Mathis Nygaard, Student.
Munkholm-Larsen, Mathias, Student.
Myltoft, Mette Gylling, Medical Secretary.
Myschetzky, Rebecca Sue Main, NMT.
Nedergaard, Mette Kjølhede, MD, PhD, Postdoc.
Nehme, Ghina, NMT.
Nielsen, Anders Bo, Student.
Nielsen, Carsten Haagen, MSc Med.Tech, PhD Student.
Nielsen, Cora Schaumann, NMT.
Nielsen, Dorthe Baunbjerg, NMT.
Nielsen, Kirstine, Student.
Nielsen, Mariane, Service Assistant.
Nielsen, Tina Vikmann, Medical Secretary.
Nørgaard, Martin, Engineer.
Nørregaard, Kamilla, MSc Physicist, PhD, Postdoc.
Nørst, Tim Niclas, NMT.
Nyrnberg, David Enslev, Student.
Olesen, Oline Vinter, MSc Engineer, PhD.
Olin, Anders. Student.
Olsen, Ingrid Marie Holst, MD, PhD, Postdoc.
Olsen, Paw Winther, Engineer.
Omanovic, Dzenita, Student.
Ørting, Silas, Student.
Østergaard, Daniella Elisabet, Scholarship.
Østrem, Ragnhild Garborg, MSc Nanosci, PhD Student.
Oturai, Peter, MD, Consultant.
Oxbøl, Jytte, Chief Technologist.
Pedersen, Kate, Staff Technologist.
Pedersen, Kirsten Foldberg, Radiographer.
Pedersen, Maria Badir, Student.
Pedersen, Sune Folke, MSc Human Biology, PhD, Postdoc.
Pejtersen, Maria, NMT.
Petersen, Lars Ringgaard, MSc Bio.Med, PhD Student.
Petersen, Lotte Pia, Service Assistant.
Philipsen, Frederik Ersø, Student.
Porojan, Monica, Technician.
Poulsen, Constance Eline Grandjean, Student.
Poulsen, Jákup Martin, Radiographer.
Pourhassan, Houman, MSc Bio.Chem, PhD Student.
Raghava, Jayachandra Mitta, MSc, Postdoc.
Rahbek, Rikke Sofie, Student.
Rasmussen, Sine Hvid, Scholarship.

Rasmussen, Thomas, MD, PhD, Postdoc.
Rexhepi, Lume, NMT.
Ripa, Rasmus Sejersten, MD, DMSc, Staff Specialist.
Risør, Louise Madeleine, Registrar.
Rømer, Maria Unni Koefoed, MD, PhD, Registrar.
Rønbirk, Lilian, Medical Secretary.
Rønn, Vibeke, Head Medical Secretary, PA Professor Liselotte Højgaard.
Rønne, Frederik Malmborg, MD, Senior Registrar.
Rosiek, Christian Anker, Student.
Rostrup, Egill, MD, DMSc, Consultant.
Salihu, Armend, NMT.
Saxtoft, Eunice, NMT, Clinical Instructor.
Schou, Mikkel, Student.
Schou, Peter, Cyclotron Technician.
Schulze, Christina, NMT.
Semitoje, Gudrun, Medical Secretary.
Setterberg, Victoria, NMT.
Simonsen, Helle Juhl, NMT.
Skou, Katrine Bugge, MSc Med.Tech, Research Assistant.
Skovgaard, Dorthe Charlotte, MD, PhD, Postdoc.
Sommer, Niyan, NMT.
Sørensen, Anne, Staff Technologist.
Sørensen, Jette Bitten, Service Assistant
Sørensen, Louise Lendorf Sørup, NMT.
Stahlfest, Marianne, Medical Secretary.
Stahr, Karin, NMT.
Suetta, Charlotte Arneboe, MD, PhD, Consultant, Ass. Professor.
Svalling, Susanne, NMT.
Svendsen, Nini Hvidtfeldt, NMT.
Teksen, Alime Sema, Student.
Therkildsen, Pia, Secretary.
Tolstrup, Britt Maria Jæger, Radiographer.
Tønnesen, Rune, MD, PhD Student.
Vensby, Philip Hvalsøe, Registrar.
Vestergaard, Mark Bitch, PhD Student.
Vignisdottir, Lilja Dögg, Radiographer.
Vinther, Johanne Constance Ilve, Management Secretary.
Weihrauch, Per, Cyclotron Technician.
Weihrauch, Simone, Student.
Wikke, Tina, NMT.
Wittekind, Anne-Mette Nielsen, QA Pharmacist.
Wrang, Helene, NMT.
Yerst, Joo Lærke, NMT.
Zarnani, Kiyana, PhD Student.
Zornhagen, Kamilla Westarp, DVM, PhD Student.
Aagaard, Christina Byrne Faurholt, MD, PhD Student.

Medical secretaries

In PET, in KF and in Glostrup we have our highly competent secretaries extremely important for referral of patients, organisation of the flow of patients through the department, writing the reports and sending them to the departments. They do a very dedicated effort so that we have no waiting lists for the patients or for the reports. In all three sections we have been challenged by staff members who have been ill for longer periods, but in spite of that the teams have performed brilliantly. They master the complicated booking and secure that the waiting lists, the patient control examinations and research scans can be done in spite of the very high work load. A dedicated thank you to Medical Secretary Tina Vikmann Nielsen, Medical Secretary Gudrun Semitoje, Medical Secretary Mette Gylling Myltoft, Medical Secretary Lilian Rønbirk, Medical Secretary Marianne Stahlfest, Secretary Sanne Hildebrand, Medical Secretary Karina Kleczewski, Medical Secretary Tine Grave, Management Secretary Johanne Vinther, Secretary Nanna Folkmann and Secretary Pia Therkildsen.

Our Chief Medical Secretary Vibeke Rønn is assistant to the Heads of Department and is also a great help in the daily work, when it is needed.

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

Highlights

The Department of Clinical Physiology, Nuclear Medicine and PET, Rigshospitalet was unified with the Clinical Physiology and Nuclear Medicine part of Diagnostic Department, Glostrup, and we are now one big Department of Clinical Physiology, Nuclear Medicine and PET at both Glostrup and Rigshospitalet, Blegdamsvej.

Patient no 200 for Radium-223 treatment was celebrated to expres gratitude to our dedicated staff

A figure from Claes N Ladefoged et al. Phys. Med. Biol. 608047 (2015) was chosen as the first ever cover image of Physics in Medicine and Biology. The paper describes a clinically viable solution for PET/MR brain attenuation correction.

Our Head of Department, Professor Liselotte Højgaard received "Chevalier d'lordre de la legion d'honnour" from the French ambassador in Denmark, Francois Zimeray

The department was the main organizer of 'PET/MR brain MRAC workshop II' at Kings College London, September 2-3, 2015. The workshop was part of a multi-center effort to develop a clinically viable solution for PET/MR brain attenuation correction.

Professor Andreas Kjær received an ERC Advanced Grant summer 2015. The department is very proud of this.

The prestigious BMJ Christmas edition published our article "Julestemning i hjernen"

The department had 3 teams participating in the DHL-race

Nuclear Medicine Technologist Joo Lærker Yerst volunteered in Sierra Leone for the Ebola battle. We are all very impressed by Joo's contribution to world health

The annual Summer Symposium for the new unified department was celebrated with a relevant tutorial movie and a nice dinner afterwards in Tivoli for all of us.

Postdoc Tina Binderup and Professor Andreas Kjaer participated in a joint project between Icahn School of Medicine at Mount Sinai (NY), Mass. General Hospital & Harvard Medical School (MA), Amsterdam Medical Center and Rigshospitalet that as the first showed that FLT-PET can be used as an imaging biomarker for cell proliferation in plaques and hematopoietic activity in atherosclerosis. The results were published in Circulatory Research. The frontcover illustration was made by Postdoc Tina Binderup.

Nuclear Medicine

Diagnostics and treatment
Blegdamsvej

Jann Mortensen and Peter Oturai

The KF Section at Blegdamsvej offers a broad variety of nuclear medicine and clinical physiological examinations. Among these are PET/CT for cardiac, neuroendocrine and paediatric diseases. Other frequent investigations are SPECT/CT and scintigraphy for various pulmological, oncological, endocrine and nephrourologial diseases. Furthermore DXA-scan for bone mineral density and whole body composition, lung function test and EDTA-clearance for GFR measurement.

To provide these state-of-the-art nuclear medicine investigations to most clinical departments in the hospital the department makes use of: one PET/CT scanner, three hybrid SPECT/CT cameras, one dual-head gamma camera, four single-head cameras, two Jaeger body plethysmographs, and a DXA-scanner. All the equipment is extensively used for both routine patients and for research investigations.

Diagnostic ultrasound is used as an adjunct to thyroid scintigraphy in patients having thyroid diseases or hyperparathyroidism.

Treatment with ^{177}Lu-DOTATATE to patients with neuroendocrine tumors (NET) has been performed in the department since May 2009. Until the end of 2015, 162 patients have been given a total of 561 treatments. We are an active part of the NET-Center at Rigshospitalet working in close collaboration with the departments of Gastro Surgery, Oncology, Radiology, Pathology and Endocrinology at Rigshospitalet. Our performance of more than 550 ^{68}Ga-DOTATOC-PET/CT scans specific for NET diagnostics is a central function for the care of the patients at the NET-Center. Patients from Odense University Hospital, Aarhus University Hospital and abroad are referred to us for ^{177}Lu-DOTATATE treatment. The NET-Center at Rigshospitalet has been accredited as *Center of Excellence* by the European Neuroendocrine Tumour Society (eNETS).

^{177}Lu-DOTATATE - synthesised and labelled at the Hevesy Laboratory at Risø, DTU, and administered in our facilities - binds to neuroendocrine tumors expressing somatostatin receptors. Beta-particles from the ^{177}Lu-isotope destroy the tumor cells and the gamma photons are used for scintigraphic imaging and dosimetry.

Since May 2014 the department has given 381 Radium-223 treatments to 113 patients with castration resistant prostate cancer and symptomatic bone metastases. The treatment is given to outpatients from all over the country as an intravenous injection typically every four weeks for a total of six planned series. Since ^{223}Ra is an alpha-emitter, extra safety hand-ling procedures are needed to protect the staff involved in the direct handling and administration. These procedures include whole body counter measurements to ensure no internal contamination to the staff.

For many years the department has successfully treated patients with benign thyroid diseases – goitre and hyperthyroidism – with ^{131}I-Iodine.

In 2015 we have had weekly and monthly conferences dealing with neuroendocrine tumors, thyroid diseases, paediatric oncology, cardiology, and lung, adrenal and orthodontic diseases.

Clinical physiology and nuclear medicine

The Glostrup section

Peter Hovind

In 2015 Glostrup Hospital was merged with Rigshopitalet, and Clinical Physiology and Nuclear Medicine at the former Glostrup Hospital became a part of the Department of Clinical Physiology, Nuclear Medicine and PET at Rigshospitalet.

The Section of Clinical Physiology and Nuclear Medicine residing in Glostrup examines patients hospitalized at the Glostrup part of Rigshospitalet, patients from the outpatient clinic the same place as well as patients from general practice in the surrounding area.
In the Glostrup section we have a long tradition of combining classical clinical physiology with modern nuclear medicine methods.

For routine nuclear medicine imaging, the section has three dedicated gamma SPECT/CT cameras and two single head gamma cameras. On this equipment we perform many different types of planar and SPECT/CT examinations. Examples are DAT-scanning, visualising dopamine transport receptor binding in the brain for diagnosing Parkinson's disease and other neurological diseases involving dopamine transport receptors, bone scintigraphy for rheumatologic diseases, and evaluation of surgery performed in the spine with various prosthesis, as well as renography for kidney diseases and follow-up on kidney function in patients with spinal cord injury.

We perform classical physiological examination with tilt test examination under standardized situations with our two Task Force tilt test monitors, where patients are examined for syncope, episodes of falling and dizziness. We have equipment for measuring blood pressure on the extremities, where blood pressure in the lower limbs can be evaluated in patients with claudication or ulcers, as well as equipment for measurement of systemic blood pressure over 24 hours for detection and evaluation of hypertension in adults and children. We assist in diagnosing secondary hypertension with Captopril renography, Doppler ultrasound of renal arteries, adrenal vein catherization and analysis of urinary steroid metabolism and receive patients from the Capital Region and Region of Sealand.

In patients with stroke, we examine the arteries to the brain for plaques and eventually stenoses of the vessels. Diagnostic ultrasound is also used together with thyroid scintigraphy in patients with disease in the thyroid.

For testing of lung function, we have a Jaeger body pletysmograph, where patients with COPD, asthma and preoperative lung testing are performed. We participate as a part of a large multicenter study, where a Danish reference material is collected.

We have three DXA-scanners, two Lunar Prodigy scanners and one Lunar iDXA scanner. The two Prodigy scanners are mainly used for the measurement of bone mineral density in patients with or suspected for osteoporosis. Our iDXA scanner is at present exclusively used for research purposes where bone mineral density and whole body composition is determined. At present we are establishing a Danish reference material consisting of 1,500 healthy controls for muscle mass in collaboration with the Copenhagen City Heart study.

A part of our section in Glostrup is a Magnetic Resonance Imaging (MRI) research group, where functional imaging using MRI is performed in collaboration with the section of Radiology. The research areas are within functional imaging and brain physiology, measurement of perfusion using MRI, cardiac functional imaging, normal ageing of the brain as well as other applications of advanced MRI methods in clinical practice and research

We have frequent multidisciplinary conferences dealing with thyroid diseases, cerebral disorders, secondary hypertension, geriatric patients and general medical disorders with collaborating units and departments at the section.

Radionuclide monitoring of leakage during hyperthermic isolated limb perfusion

Jann Mortensen and Peter Oturai

Since 1993, 5-20 hyperthermic isolated limb perfusions (HILP) have been performed annually at Rigshospitalet as the only center in Denmark. It demands a highly specialized team effort from specially trained plastic surgeons, anaesthesiologists, perfusionists and nuclear medicine specialists.

The indication for the treatment is inoperable disseminated melanoma or soft tissue sarcoma in a limb.

The procedure includes isolation of the circulation of an extremity by a tourniquet, cannulation of the artery and vein supplying the extremity, and connection to a heart-lung machine. This enables regional administration of cytotoxic drugs at doses up to 20 times higher than the systemically tolerable concentration.

Because of the risk of leakage of the cytotoxic drugs (melphalan and TNF-alfa) from the isolated limb into the systemic circulation, possibly causing systemic toxicity, leakage is monitored by a radionuclide technique and should not exceed a generally recommended limit of 10 %.

Radionuclide monitoring is performed with continuous, precordial count rate determination of in vitro ^{99m}Tc-labelled autologous erythrocytes infused into the isolated limb circulation.

Recently we published our results from the procedures performed in melanoma patients between 1993 and 2011 in 131 consecutive HILP procedures (1,2). 89 % HILP procedures were completed with a median leakage of 2 % (0-9 %).

In 85 % of the patients ≥ 50 % tumor regression was observed. While no patients had systemic toxicity requiring treatment, considerable or serious local toxicity was observed in 14 %.

Paulsen IF, Chakera AH, Schmidt G, Drejøe J, Klyver H, Oturai PS, Hesse B, Drzewiecki K, Mortensen J. Radionuclide leakage monitoring during hyperthermic isolated limb perfusion for treatment of local melanoma metastasis in an extremity. Clin Physiol Funct Imaging. 2014 Jun 5. doi: 10.1111/cpf.12164.

Paulsen IF, Chakera AH, Drejøe JB, Klyver H, Dahlstrøm K, Mortensen J, Oturai PS, Hesse B, Schmidt G, Drzewiecki K. Tumour response after hyperthermic isolated limb perfusion for locally advanced melanoma. Dan Med J. 2014. Jan; 61(1): A4741.

Paediatric Nuclear Medicine

Lise Borgwardt

In 2015 we performed almost 3,000 paediatric nuclear medicine investigations, thereof 300 paediatric PET scans, mainly for the large paediatric clinics 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 Paediatric Committee and the Paediatric Imaging Harmonization SNM/EANM.

In our children section we have a children-friendly PET/128 Slice CT, SPECT/CT, an EDTA Clearance room and a renography room. PET/MR-scans are performed in the PET Section. In each scanner room in the children's section, high quality projectors are showing films at the ceiling to secure and entertain the child during the scan. In the waiting area the children have the opportunity to watch the animated decorations, use apps or watch films at the tablets giving when entering the section or play in the toy corner.

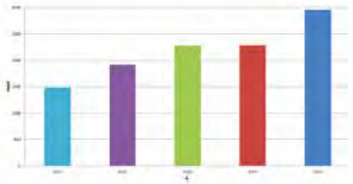
In February we launched the 20 specially produced films and audio essays: "20 stories for the children of Rigshospitalet" sponsored by the The A.P. Møller and Chastine Mc-Kinney Møller Foundation for General Purposes, both films for projection on the ceiling and audios essays to listen to while walking around looking at the wall decoration during tracer uptake period. We are very happy about this generous donation and this fantastic work by the artist that make our children have less sedation and feel entertained and secure while visiting our department.

Our multidisciplinary paediatric haematology and oncology conferences are presented as a web-based nuclear medical platform combined with videoconference including districts outside the capital. Our collaborators are very pleased with the possibilities and the advantages in the diagnostic evaluation of the children.

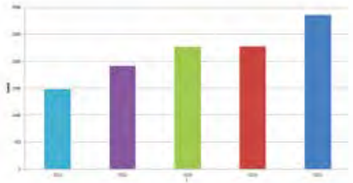
Our Glostrup Section is specialized in detection and evaluation of hypertension in children with equipment for measurement of systemic blood pressure over 24 hours. And assists in the assessment for secondary hypertension in children with Doppler ultrasound of renal arteries, receiving patients from the Capital Region and the Region of Zealand.

Research in Paediatric Nuclear Medicine and PET is necessary, as we have an increasing amount of medical doctors, PhD 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 Paediatric Committee, EANM this year has been very interesting and inspiring, and we are looking forward to next year's work in the committee.

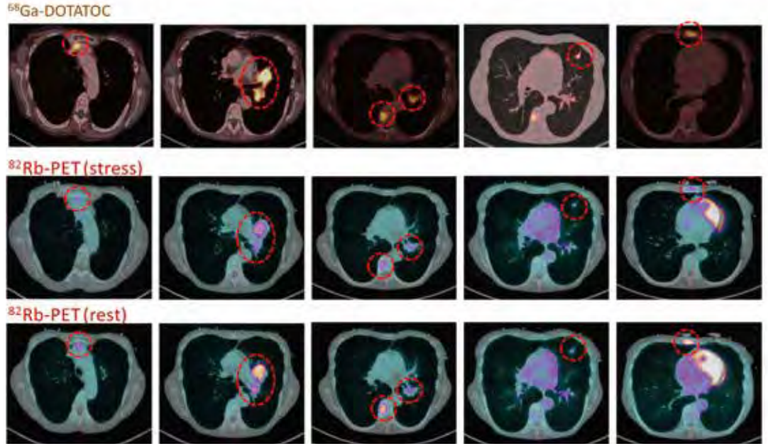


Number of children investigations, <18 years, 2011-2015, incl. cancelled investigations



Number of children investigations, <18 years, 2011-2015, excl. cancelled investigations

Cardiac ^{82}Rb-PET/CT



^{82}Rubidium uptake in metastases from neuroendocrine tumors
62-year-old woman with a neuroendocrine tumor in the small bowel and metastases to Th6, the sternum, the left lung, and mediastinal lymph nodes. Top panel ^{68}Ga DOTATOC PET/ CT imaging with uptake in the above-mentioned foci. Middle and bottom panel ^{82}Rb PET/CT imaging with uptake in the heart and extra cardiac foci during adenosine-induced hyperemic stress and during rest. These foci correspond to the foci on the ^{68}Ga-DOTATOC scan. The images of ^{68}Ga and ^{82}Rb rest do not have the same intensity and color scale and cannot be used for a direct absolute comparison.

Philip Hasbak

Rigshospitalet was the first hospital in Scandinavia and one of the first in Europe to diagnose ischemic heart disease using cardiac ^{82}Rb-PET/CT as a new type of advanced imaging system.

At Rigshospitalet there is a special need to provide cardiac PET every day, since a large proportion of our patients with ischemic heart disease need an acute or sub-acute work-up that requires quick decision making as to coronary revascularisation strategy. Patients with unstable angina or non-STEMI should be revascularised with percutaneous coronary intervention (PCI) within 3 days after admission or with coronary artery bypass graft surgery (CABG) within 5-7 days according to The Danish National Board of Health. Non-invasive assessment of myocardial function is an important domain of cardiac ^{82}Rb-PET. Traditionally, cardiac PET images have been visually interpreted, using uptake as a measure of function. This approach, however, takes only a fraction of the full PET information into account. The application of tracer kinetic modelling to dynamically measured data is able to extract objective measures of perfusion and/or metabolism, depending on the tracer. While such true cardiac quantification has been troublesome and time-consuming in the past, our new cardiac tools now make this state-of-the-art technology readily available. Further, we offer CT coronary angiography (CTCA), which is useful for planning many invasive cardiac procedures, particularly complex PCI procedures including chronic total occlusions (CTOs) and bifurcation stenting.

Cardiac and renal ^{123}I-MIBG scintigraphy
In 2010 we introduced cardiac ^{123}I-metaiodobenzylguanidine (^{123}I-MIBG). Radiotracer analogs of the sympathetic mediator norepinephrine have been investigated extensively, and are at the brink of potential widespread clinical use, especially after the presentation of the ADVANCE-HF trial. The most widely studied SPECT tracer, ^{123}I-MIBG has consistently shown a strong, independent ability to risk stratify patients with advanced congestive heart failure. Recently we have evaluated ^{123}I-MIBG as an estimate of renal sympathetic nervous activity.

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

Education 2015

Jann Mortensen, Peter Hovind and Peter Oturai

The educational activities have expanded following the hospital fusion in early 2015. All together the Glostrup Section and the facilities at Blegdamsvej comprize seven educational positions for young physicians training to become specialists in clinical physiology and nuclear medicine. Other roles in the specialist education of physicians are related to the dedi cated courses in oncology, cardiology, pulmonology and endocrinology and pathophysiology as well as more basic courses in methodology (Magnetic Ressonance and Kinetics), all held at our department and arranged by our professors and consultants. Furthermore, we contribute to the specialist education of physicians from other specialities such as urology, nephrology, radiology, oncology, haematology, pulmonology and thoracic surgery. A high number of PhD students are associated with the research activities in the department.

Regarding *undergraduate education*, nuclear medicine technologist students and radiographer students receive part of their education from the department. The department contributes to the activities of the Faculty of Health Sciences at the University of Copenhagen for medical students, human biology students and medicine & technology students in collaboration with DTU in various subjects, e.g. physiology, nuclear medicine and medical technology.

Colleagues and students from Denmark and abroad have visited the department for educational and research purposes for periods ranging from weeks to months.

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

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

Consultant Peter Oturai and Consultant Peter Hovind are responsible for the postgraduate education of physicians in the department. Associate Professor Jann Mortensen and Professor Henrik Larsson are responsible for the undergraduate education of medical students in the department.

Nuclear medicine technologists, radiographers and lab technicians

Tim Mølgaard Lundby, Kate Pedersen, Lis Larsen and Anne Sørensen

Our group of nuclear medicine technologists, radiographers and lab technicians are competent, professional and characterized by high spirit and dedication in spite of the demanding work with high efficiency. Their dedicated effort ensures that our patients are investigated without waiting lists and within the demands from the political and health care system.

We secure this by a voluntary scheme with extended opening hours for patient investigations, treatment with radioisotopes and production. In 2015 the group has been extended with the new section Clinical Physiology and Nuclear Medicine at Glostrup Hospital due to the fusion of Rigshospitalet and Glostrup Hospital.

The nuclear medicine technologists, radiographers and lab technicians participate actively in national and international meetings, courses and congresses. This secures training and lifelong learning for all through new knowledge and exchange of practical experiences with colleagues from Denmark and abroad. We participate in the biannual meetings of the Danish Society of Clinical Physiology and the Nuclear Medicine and Danish Society of Radiology with oral presentations and posters, in the annual meeting of Danish Society of Clinical Physiology and Nuclear Medicine with posters and presentations a Friday and a Saturday in September, in radiochemistry meetings for nuclear medicine technologists/lab technicians and in European Association of Nuclear Medicine and Society of Nuclear Medicine international congresses. We also participate in specific courses for upgrade of competences in nuclear medicine, dedicated CT courses, courses on knowledge of radioactivity and isotopes and dedicated courses on organ system diseases held by national societies and associations and the local University College Metropol.

In February 2015 our employee responsible for the quality assurance system, Tina Gade Jensen, who had been with us for the last 5 years, changed to a new position near her home, and due to the fusion between Rigshospitalet and Glostrup Hospital we postponed the hiering a new person for the job. This autumn Nuclear Medicine Technologist Mette Frederiksen was employed as quality coordinator after a job advertisement with very many qualified applicants. Mette Frederiksen came from a position as nuclear medicine technologist in the Nuclear Medicine section KF, Blegdamsvej and has a thorough knowledge of the tasks in the whole department. In the period where we had no dedicated quality coordinator our Pharmacist for Quality Assurance Anne-Mette Wittekind from Radiochemistry has helped with the function also for nuclear medicine and secured that the document system was updated. Thank you to Anne-Mette Wittekind for the dedicated work and effort. It is highly acknowledged this flexibility from our staff when the sections help each other.

Over the year we have put resources into configuration of the new Agfa RIS/PACS System, and it is a challenge. One nuclear medicine technologist from KF and one from the PET section and together with the staff nuclear medicine technologists they have worked dedicated with the configuration. From the Glostrup Section the ICT nuclear medicine technologist is also involved. We look very much forward to a new RIS/PACS system in 2016

Radiochemistry Section

Our five nuclear medicine technologists/lab technicians start every morning at 6 AM to initiate the production of PET tracers with ^{18}F-FDG for PET. We produce to our own department and to other hospitals in the greater

Copenhagen region. This year we have initiated the use of GE Fastlab Synthesis equipment for the FDG production which means higher yields from each production. On Saturdays we produce ^{18}F-FDG for in house use for research studies on the PET/MRI scanner.

Tina Wikke has participated in the development of ^{18}F-SFB, which is a key intermediate in the labelling of ^{18}F-ASIS. ^{18}F-ASIS binds to tissue factor. Tissue factor is overexpressed in several cancer types and therefore interesting. Sonja Pedersen Lærke participated in the first experiments for production of ^{68}Ga-PSMA for the diagnosis of prostate cancer.

PET scanner section

In spring 2015 we had a follow up on our LEAN project and the improvements made in 2013 and introduced new improvements. Instead of making sodiumchloride syringes ourselves, we tested a prefabricated product from an external provider, and as it was a cost effective solution, it has been introduced. We went through the scheme for patient injections of PET tracers and adjusted the scheme to obtain a more efficient program. Booking of PET studies is a complex task, as the scanners are more than fully booked, and as the patient investigations have to be performed without waiting lists, and at the same time we need the secure space for research projects. In the department we publish about 150 peer review publications per year. We have initiated a new interdisciplinary booking group with nuclear medicine physicians, medical secretaries and nuclear medicine technologists. An optimal booking is essential and demanding, and we have now prolonged the task force, and they work together every afternoon. This LEAN follow up effort resulted in a session at the annual meeting in European Association of Nuclear Medicine, Hamburg, 2015.

The 15 nuclear medicine technologists and 4 radiographers in the PET scanner section volunteer for extended hours once or twice a week to keep the waiting list down. Thank you very much to the staff for this flexibility and helpful attitude. Apart from the daily production all the nuclear medicine technologists and radiographers participate voluntary in research outside opening hours. Some research scans run until 10 PM, and sometimes the PET/MRI is demanding that we start at 6.30 AM. On Saturday for the special PET/MRI scanner study on atherosclerosis in a special animal model together with Novo Nordisk we are in from 6.30 AM to 11 PM. Thank you very much to all for this great voluntary and interdisciplinary research effort.

Nuclear Medicine Section KF

In 2015 we have renovated our room for patient injections and it is "a walk in lab", where the nuclear medicine technologist can walk in directly and prepare injections of tracers instead of having to change to go into the clean room. This is another of our LEAN actions, and the laborious procedure with clean room admittances has been reduced with 25 %. The section has had a rather high exchange of staff in the nuclear medicine technologist/radiographer group, (21 nuclear medicine technologists and 4 radiographers). This has been a challenge and the organisation and education has been demanding for everyone, to assure that all investigations and all rooms were staffed. We have initiated "a work planner group" with the staff nuclear medicine technologist and the nuclear medicine tutors, the clinical teachers and the nuclear medicine chief technologist. It has been a challenge - but now it works well with a dialogue based planning of the daily schedules 3-4 weeks ahead. Meetings at the blackboard were introduced in 2015 and works well with staff meetings every morning at 8.05.

We are working on a scheme to optimize the patient throughput and this year we have initiated "one day protocol" for parathyroid scintigraphies instead of the old protocol on two separate days. To secure information and communication Staff Technologist Tim Lundby has implemented an internal messenger system that also works on the Glostrup Section, where Nuclear Medicine Technologist Annegrethe Jørgensen has introduced it.

To asure the daily production staff members start at 7 AM to secure that the scanners are ready for the patients at 8 AM. Apart from the daily production all nuclear medicine technologists and radiograpers participate in research on a volunteer basis outside opening hours. In spring 2015 Nuclear Medicine Technologist Joo Lærke Yerst had leave to participate in the team in Sierra Leone to fight ebola. After Joo Lærke Yerst came home she gave a talk to the department and to the Danish Society of Clinical Physiology and Nuclear Medicine about her experiences in Sierra Leone. We all pay due respect to Joo Lærke Yerst for the great humanitarian action she participated in.

Mia Hjorth Albers and Joo Lærke Yerst gave a course for DSKFNM on the 10th of June on nuclear medicine and bone pathophysiology and investigations.

Glostrup Section

The Glostrup Section has both clinical physiology examinations and a program of nuclear medicine. The clinical physiology examinations new to the department are:

- 24 hour blood pressure measurements, including in small children, where the section has special experience
- Blood pressure in arms, legs and toes
- Tilt-examinations
- Ultrasound of carotid arteries
- Ultrasound of renal arteries

The Glostrup Section has implemented a new electronic booking system, Carestream RIS, and a dedicated effort from everyone, including ICT responsible Nuclear Medicine Technologist Annegrethe Jørgensen, is highly appreciated. Through the RIS the clinical departments and GPs refer patients electronically and receive patient reports electronically.

In 2015 the nuclear medicine technologists have initiated daily meetings at the blackboard. Every day at 8.05 AM the 12 nuclear medicine technologists meet at the office of the staff nuclear medicine technologist and go through the program of the day. The staff participates in a big research project on public health with participation of 1,500 patients investigated with DXA whole body measurements of body composition and bone density measurements including investigating for muscular strength in hands, legs and exercise test.

The Glostrup Section held a course about the brain through DBIO with Staff Nuclear Medicine Technologist Lis Larsen in charge. In the FIU, Functional Imaging Unit, Nuclear Medicine Technologist Helle Simonsen performs research and MRI scans. She also teaches internal and external staff members on MRI security, and PhD working at the scanner have to pass a small written examination held by Helle Simonsen. She was also in charge and chair of a two day international course on Glostrup, DSMMR and ISMRM Nordic Chapter Joint Meeting.

Education

In all the clinical sections, PET, KF and Glostrup we have nuclear medicine technologist students, and we are rated positively from the students and the staff looks upon this task as a positive asset. They even volunteer for the young ones to learn how to make blood samples.

On Blegdamsvej, Mia Hjorth Albers and in Glostrup, Annette Foldager are our nuclear medicine technologist tutors, and they are both responsible for the student education for nuclear medicine technolgists and radiographers. Nuclear medicine technologists Camilla Mose, KF and Elin Lindell, PET are new clinical teachers. Elin Lindell has passed the Metropol University College examination as clinical teacher.

PET and PET hybrid systems

Søren Holm

In 2015, the only new, large piece of equipment in the department was not a PET, but a small animal SPECT/CT (nanoScan) installed in the Cluster for Molecular Imaging at Panum, the Faculty of Health Sciences, University of Copenhagen. Here we also operate 3 research scanners for PET and CT of small animals. The "older" systems (from 2006) are a separate PET (Focus 120) and CT (microCAT II). More recently, an integrated PET/CT system, the Inveon, was acquired and a Bruker 7T MR scanner for small animals was installed.

In the hospital itself, the department has one dedicated, stand-alone brain PET system, five combined whole-body PET/CT systems and one integrated PET/MR system.

In the hospital brain research continues on the PET-only HRRT (High Resolution Research Tomograph) in close collaboration with the Neurobiology Research Unit (NRU), but the system also works as a clinical instrument.

The four PET/CT's in the PET Section are all Siemens systems. Two are Biograph TrueV, one with 40 and one with 64 slice CT, acquired in 2007 and 2009. The other two (from 2010 and 2011) are mCTs with 64 slice CT and time-of-flight but overall with rather similar specifications, which provides an important flexibility in patient scheduling. The majority of the studies in the PET Section continues to be FDG whole-body scans for cancer diagnosis, staging, planning and follow-up, but in the recent years a significant number of FET, FLT, ^{11}C-PiB, and ^{68}Ga-Dotatoc examinations have been added. All these scans are routinely performed with the use of combined PET and CT, and most CT scans are performed as full diagnostic quality CT including contrast enhancement. One of the mCTs is run 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 most recent (fifth) PET/CT is similar to the two previous mCTs, but with 128 CT-slices. It is installed in the KF Section. This scanner mainly performs paediatric PET scans and scans with ^{82}-Rb (heart perfusion), ^{68}Ga-Dotatoc (neuroendocrine tumors), and ^{18}F- NaF, replacing some bone scintigraphy or SPECT/CT.

The fully integrated PET/MR scanner (Siemens mMR) 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 gantries). 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 improves 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. The physics group has been working on the issues of attenuation correction and artefact suppression in order to support the clinical research protocols. In particular for quantitative results in brain scanning, the lack of direct attenuation measurements is a challenge, and we have been addressing these issues with a post-doc and a PhD project in collaboration with Siemens (Erlangen and Knoxville), University of Leuven, and the institute of Computer Science at Copenhagen University.

Recently the PET/MR installation was complemented with an MR hyperpolarizer (GE SPINlab), allowing the production of ^{13}C-labelled pyruvate, although not yet for human use.

Cyclotron unit

Holger J. Jensen

During the last years we have experienced a stable number of productions at our two cyclotrons of approximately 1,200±100 per year, see figure 1. In 2015 we had in total 1,129 successful productions (512 and 617 for our Scanditronix MC32 and Siemens RDS Eclipse cyclotrons respectively). Last year we had to cancel 6 productions in total – 4 due to technical difficulties and 2 due to our RF electronics upgrade project – resulting in a success rate of 98.9 %. As in the previous years we also managed to keep the average radiation dose to the employees in the cyclotron- and radiochemistry unit at a low level, see figure 2.

Several upgrade projects are going on for our Scanditronix MC32 cyclotron:

→ A new 18F target loading- and unloading system has been designed and build together with our colleagues in Uppsala. The target system can serve two ^{18}F targets at the same time. The control system was integrated in our new S7 PLC cyclotron SCADA system in 2014 and 2015, and makes the old IBA system obsolete. The new system gives us full control and flexibility on all details of the system. Hardware, coding and operation details can easily be copied to other targets that are planned to be renovated/upgraded in near future (^{13}N, ^{15}O and Rb/Kr).

→ A new target for our Rb/Kr production was designed and built last year. The target is going to be a replacement for the 23 years old target. Installation and validation will be done primo 2016.

→ A replacement of the original Siemens Simatic S5 and CP521 based control system from 1992 with a new S7 and IGSS based SCADA system was started in 2012. Most of the project was finished in 2015 except for the replacement of the I/O boards (for the more than 1,000 digital and analog signals) that is planned to be done early 2016. This part has been postponed until the RF upgrade was completely finished. The update 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 future plans for the MC32 cyclotron.

→ The last project to be mentioned here is the project on replacing major parts of the electronics in the RF system (RLC, RPM, RDRC and RDRA). The original system is more than 22 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. In the new design 46 electronic boards are replaced with only 8 boards and all parts are replaced with modern and up to date technology. The project was funded in 2013, build in 2014 and the new modules were installed January 2015. Except for a few minor problems the new modules have been running satisfactory ever since.

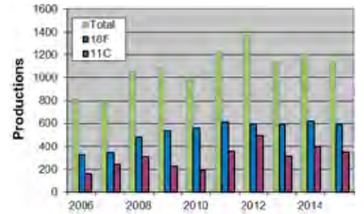


Figure 1 Development in total number of productions, ^{18}F and ^{11}C productions since 2006.

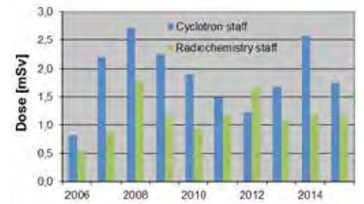


Figure 2 Average received doses for employees in the Cyclotron- and Radiochemistry Unit since 2006.

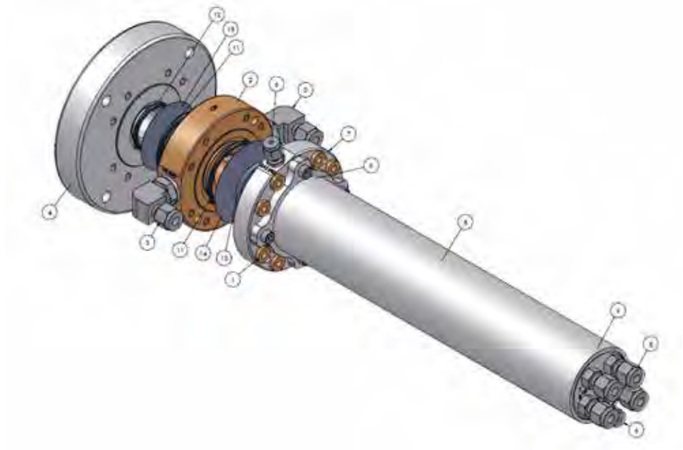
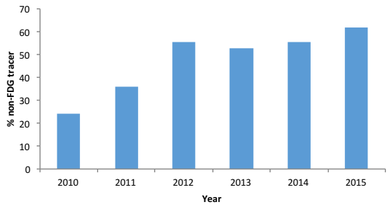


Figure 3 The new Rb/Kr target.

The building of the new "Nordfløj" at Rigshospitalet has initiated another big project for our department. Already in 2010 it was realized that our existing chimney for release of radioactive gases produced in our growing radiopharmacy production, would not be sufficient to fulfill the requirement from the authorities (SIS) during and after the building of the new building. The requirements are that, we by a risk analysis can guarantee that no one in the general publication will receive more than 100 μSv/y from our activities (or approximately 30 times lower than the average background dose in Denmark). In 2011 we made a new risk analysis together with the Wind Energy Section at Risø for a new chimney 2 meter higher than the highest building at Rigshospitalet (as it is demanded in the legislation) and placed at the south-east corner of Centralkomplekset. In 2012 the plans were accepted by SIS. The funding was finally approved in early 2014 and the building project was transferred to Byg og Teknik medio 2014.

The project has been extended, so we as a part of this project also extend the target bunker room for cyclotron 1 and build a new underground bunker for the active charcoal filters. The filter room will be placed at the south-east corner of UK556 and UK566. The filters will be used for a filtration/trapping of radioactive ventilation air from the cyclotrons and the chemistry laboratories. All projects are planned to start May 2016.

Radiochemistry



The dominance of [18F]FDG is gradually decreasing due to the implementation of new PET radiopharmaceuticals in the department. The percentage of non-[18F]FDG productions over the last six years is shown.

Jacob Madsen and Nic Gillings

Highlights

- → In 2015 we produced the in-house developed uPAR imaging tracer, [68Ga]NOTA-AE105, which was evaluated in a clinical trial of 10 cancer patients.
- → In 2015 Valdemar Lykke Andersen and Christina Schjøth-Eskesen successfully defended their PhD theses in radiopharmaceutical chemistry.
- → In 2015 we took part in a successful application for an EU grant (Horizon 2020) concerning the development of in vivo click PET imaging agents. Six million Euros was granted to 5 European research groups and 1 industrial partner for a 5 year period.
- → In 2015 a new radiopharmaceutical education program was planned. The first master students will attend lectures in spring 2016.

Production for clinical and research PET investigations in humans

Production of [18F]FDG and krypton-81m generators along with [18F]FET, [18F]FLT, [68Ga]DOTATOC and [11C]PIB was at a similar level compared to 2014. After considerable validation efforts and approval by The Danish Medicines Agency, [18F]FDG production on our new GE FASTlab modules commenced in August. The new system gives higher radiochemical yields thus providing adequate amounts of [18F]FDG to meet demand from one daily synthesis, freeing up personnel for other tasks. The new system should also be more reliable and use of the old modules will be phased out within 6 months. Following evaluation of the promising uPAR imaging agent, [64Cu]DOTA-AE105 in 2014, a gallium-68 labelled version, [68Ga]NOTA-AE105, was evaluated in 10 patients in 2015. Production of neuroreceptor tracers for various research projects conducted by the Neurobiology Research Unit continued on a par with previous years.

The number of productions of radiopharmaceuticals for human use continues to increase, with a total of 1,038 in 2015. In the past, [18F]FDG accounted for the majority of productions but gradually new more specific tracers are being introduced for clinical use. In 2015, more than sixty percent of PET radiopharmaceutical productions for humans were non-[18F]FDG (see figure above).

Radiopharmaceutical development

Oncology

We have started to investigate preparation of the prostate imaging agent, [68Ga]PSMA. Validation and application for human use of this tracer will take place in 2016. For angiogenesis imaging, [68Ga]NODAGA-cRGDyK$_2$ has shown promise in animal studies and process optimization and validation for human use was started in 2015. The first studies in humans are planned for 2016. The production of [18F]ASIS (active site-inhibited factor VIIa) for human use is currently being validated and a clinical trial application will be submitted in mid 2016. Several other tracers targeting biological processes related to cancer are available for preclinical investigations, for example [18F]Apo-Pep-1 for imaging of apoptosis or [18F]HX-4 for hypoxia imaging.

Neurobiology

Our collaboration with the Neurobiology Research Unit, Rigshospitalet and the Department of Drug Design and Pharmacology, Faculty of Health and Medical Sciences, University of Copenhagen continued in as in previous years. Development and evaluation of new PET tracers for a number of targets was undertaken in 2015. Among these are [11C]Martinostat for HDAC and [18F]ASEM for the alpha-7 receptor. There were 68 radiopharmaceutical productions for animal studies in 2015. Further evaluation of our in-house developed 5-HT2A agonist tracer, [11C]Cimbi-36 continued in 2015. A study investigating the impact of the radiolabelling position revealed deeper insight to the metabolic fate of this compound. Furthermore, a [11C]Cimbi-36 dosimetry study will commence in 2016.

Radiopharmaceutical	Batches Produced	Usage/Target
[^{18}F]FDG	333	Oncology/Glucose metabolism
[^{68}Ga]DOTATOC	266	Neuroendocrine tumors/Somatostatin receptors
Krypton-81m generator	146	Lung ventilation
[^{11}C]PIB	89	Alzheimer's Disease/β-amyloid plaques
[^{18}F]FET	71	Oncology/amino acid transport
[^{18}F]FLT	28	Oncology/cell proliferation tracer
[^{68}Ga]NOTA-AE105	10	Oncology/uPAR imaging
[^{15}O]Water	7	Cerebral blood flow
[^{11}C]AZ10419369	38	Brain Research/5-HT$_{1B}$ receptors
[^{11}C]SB207145	34	Brain Research/5-HT$_{4}$ receptors
[^{11}C]Cimbi-36	16	Brain Research/5-HT$_{2A}$ receptors

Radiopharmaceuticals produced for human use in 2015.

Radiopharmaceutical research and PhD projects

Technetium-99m labelled aprotinin is used routinely for diagnostic scanning of amyloidosis patients. In 2014 we developed fluorine-18 and gallium-68 labelled analogues and evaluation of these in an animal model of amyloidosis commenced in 2015 and will continue in 2016.

The successful, but rather lengthy, fluorine-18 labelling of ASIS prompted us to search for faster and more selective labelling strategies. In his PhD project Troels Elmer Jeppesen has modified the protein (ASIS) and developed fluorine-18 labelled aldehydes for selective oxime couplings as well as copper-64 labelled NOTA chelators for copper-free click reactions.

The promising results obtained with [^{11}C]Cimbi-36 encouraged us to look for a fluorine-18 labelled analogue. In her PhD project, Ida Nymann Petersen has labelled a number of analogues using various labelling strategies. Animal testing of these compounds has given mixed results and as yet a successful fluorine-18 substitute for [^{11}C]Cimbi-36 eludes us.

In vivo click radiochemistry is a promising emerging field in radiopharmaceutical science. Possibly, it will allow imaging of long-circulating nanostructures with short-lived isotopes. In 2016, Johanna Steen started her PhD project in this field. She is evaluating in-house developed carbon-11 in vivo click agents and will develop fluorine-18 labelled derivatives.

In January 2015, radiochemist Valdemar Lykke Andersen successfully defended his Ph.D. thesis entitled *Development of PET-tracers for the 5-HT$_7$ receptor* and in March, Radiochemist Christina Schjøth-Eskesen successfully defended her PhD thesis entitled *Aziridine Ring-Opening Reactions with [^{18}F]fluoride, Strategies in the Synthesis of [^{18}F]-Labelled Peptides and [^{64}Cu]-labelled Trastuzumab for Targeting Cancer.*

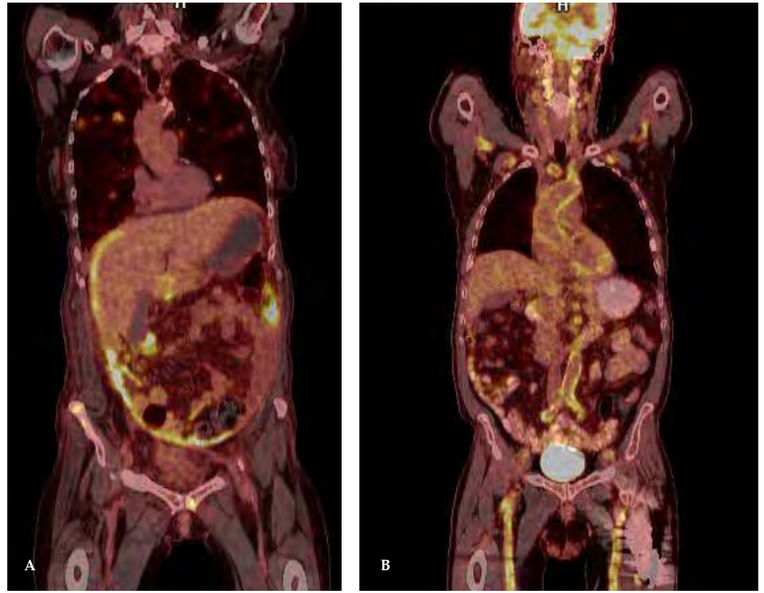
PET/CT in oncology, infection and inflammation

Annika Loft Jakobsen and Anne Kiil Berthelsen

In oncology indications for PET/CT are diagnosis, staging, therapy planning and monitoring, besides detection of recurrent disease in patients with a variety of malignant diagnoses. PET/CT is a well-integrated tool due to the high sensitivity and specificity and has in many workflows replaced other imaging modalities.

At Rigshospitalet the CT scans of our PET/CT's are performed as high quality diagnostic scans with the use of oral and intravenous contrast media. The PET- and the CT scans are interpreted by an expert in nuclear medicine and an expert in radiology side-by-side reporting a final, combined conclusion taking both the PET and the CT examinations into account besides the fused images. This provides the clinician with a more precise PET result, a better CT result, and also a more useful conclusion. To improve the diagnostic quality we have included a supplementary CT of the lungs with breath hold technique.

We participate in 17 weekly multidisciplinary team conferences (MDT's), where our PET/CT scan results are discussed with the clinical experts. This teamwork is inspiring and crucial for improving the diagnostic quality of our PET/CT scan interpretation. The number of PET/CT scans is still increasing. We also review an increasing number of PET/CT scans performed at other hospitals, when patients are referred for an MDT.



A) Cervix cancer with peritoneal carcinosis and bone metastases easily depicted on PET/CT. These metastases can be difficult to detect on CT alone.

B) High FDG uptake in all the large vessels indicating vasculitis in a 77 year old man with fever and weight loss.

Approximately, 50 % of our patients participate in various clinical research protocols. Our main topics are gynaecological cancers, malignant lymphoma, neuroendocrine tumors, head & neck cancer and lung cancer.

FDG is still the main tracer in oncology, but we also use ^{18}F-NaF, ^{18}F-FET, ^{18}F-FLT, ^{68}Ga-DOTATOC and ^{64}Cu-DOTATATE in clinical studies as well as in research protocols.
The use of PET/CT in infectious and inflammatory diseases is increasing for diagnostic purposes as well as treatment monitoring. The idea of exchanging leucocyte scintigraphy with PET is quite obvious for the patient due to the time-saving procedure of the PET/CT, and the clinical results are promising but not yet confirmed in large randomized protocols.

Working with PET/CT is fascinating due to the great clinical impact of the method as well as the inspiring collaboration with the clinical departments and there is no doubt that PET/CT has found its place in the everyday clinical work. However, research and clinical trials are still necessary to verify the usefulness of the method, to refine the scanning protocols as well as to exploit new indications.

PET/CT- scanning in radiation therapy

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: Breathhold 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.

Annika Loft Jakobsen and Anne Kiil Berthelsen

We now perform 600 PET/CT scans every year for radiotherapy planning of cancer patients and it has become a daily routine procedure in our department for patients with brain, head & neck-, lung-, oesophageal-, cardia-, cervix- and vulva cancer as well as malignant lymphoma and sarcoma.

We are fortunate to have an excellent collaboration with the Department of Oncology, The Radiotherapy Section between all involved professional groups. The workflow is facilitated due to our location in the same building as well as the fact that some of our radiologists are employed in both departments.

The advantages of implementing PET/CT in the workflow 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. 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 hereby optimizing the quality of the method by including all relevant experts in the process. We rely on visual analysis more than fixed threshold levels due to heterogeneity of most of the tumors.

In order to utilize the high sensitivity of PET/CT, our therapy scans are always performed as whole-body examinations which in almost one fifth of the cases reveal unknown distant metastases or new primary tumors. These are findings that can change the treatment plan for the patient.

Research in this field is crucial. We have increased our focus on breath hold PET/CT not only on mediastinal lymphoma which now is implemented as a routine procedure hereby reducing the radiation dose to the heart and lungs. Due to this important impact it was obvious to focus on the possibility of implementing breath hold PET/CT on children. Other new indications for this method are being validated in research protocols with lung cancer. We are involved in numerous research protocols, local as well as multicentre including the clinical impact of using PET/MR for radiotherapy planning.

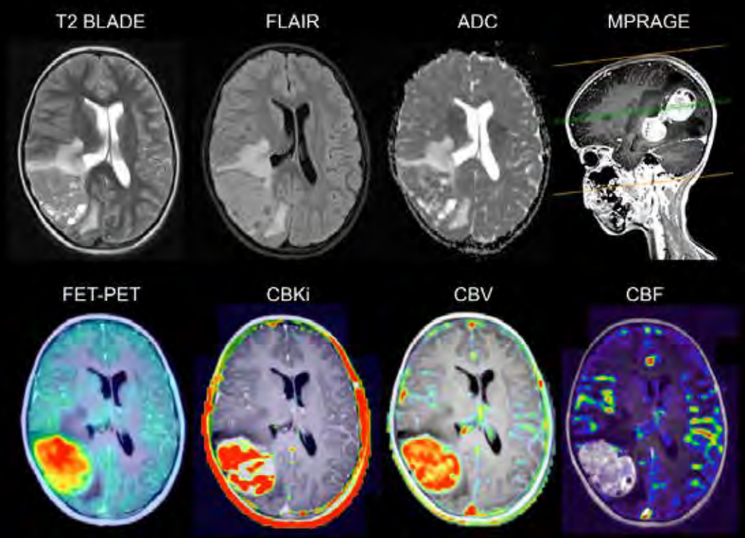
Clinical PET scanning of the brain

Ian Law and Otto M Henriksen

The Siemens hybrid PET/MR scanner has been implemented into clinical routine investigations for dementia. A diagnostic package consisting of 4-5 standard MR sequences focused at localizing cerebral ischemia, infarcts, haemorrhages, tumors and normal pressure hydrocephalus have been combined with primarily FDG in a short and very comprehensive one-stop imaging shop for dementia.

Our experience is that PET/MR can solve real life clinical diagnostic dilemmas and PET/MR is indeed a technique that can be used robustly in clinical practice. In a single 15 min. session a patient may receive a thorough and comprehensive structural and function neuroimaging examination of outstanding image quality with little risk.

Multiparametric PET/MR scans of 8 year old girl with a primary brain tumor (Ependymoma III) showing standard structural MRI (Top) and function tumor characteristics (Bottom) of aminoacid uptake (FET), permeability (CBKi), blood volume (CBV), and tissue perfusion (CBF). Data collected by Dr L. Marner.



Our non-FDG radiotracers have had a relative increase in the overall production. They consist of the amino acid analogue [F18] Flouro-Ethyl-Tyrosine (FET), the somatostatin II receptor ligand [Ga68]-DOTATOC, and [C11]-PiB.

FET has an established role in the management of brain tumor, and is increasingly been evaluated using PET/MR. We are in the process of developing FET PET/MR as a multiparametric tool in paediatric neurooncology to reduce the stress of anaesthesia and improve patient management in this sensitive population.

For radiotherapy planning and the evaluation of recurrent meningioma we are employing [Ga68]-DOTATOC using our high resolution research tomograph (HRRT) PET scanner, as the growth pattern of meningioma, and the small margins of the stereotactic radiation therapy used make a 2 mm resolution desirable.

[C11]-PiB amyloid binds to amyloid plaques, a pathological hallmark for Alzheimers disease, and is used to support the diagnosis.

In 2015 we participated in 1 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.

PET/MR

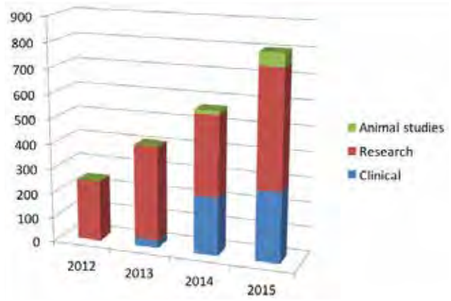


Figure 1. Illustrates the number of PET/MR examinations per year.

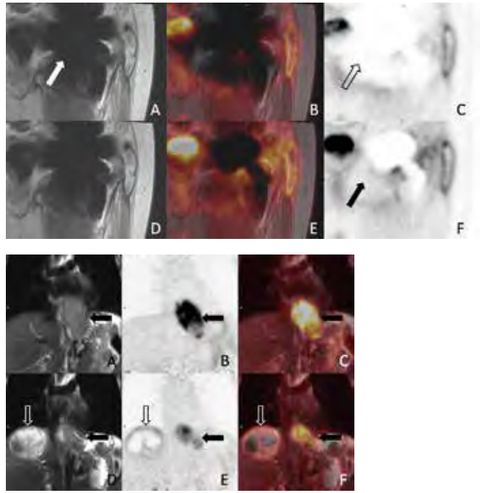


Figure 2. PET/MR examination of a left sided hip prosthesis with complications in a 66 year old male. Images illustrate an improved PET image quality after post processing attenuation correction reconstruction using semiautomatic µmap correction. Coronal PET/MR images, top row from left (A-C), anatomic MRI (T1 TSE), PET/MR fused and PET with huge attenuation correction artifact (white and hollow arrow) due to hip prosthesis. Bottom row (D-F) show markedly improved PET/MR images after semiautomatic µmap correction (black arrow).

Figure 3. Two PET/MR examinations of a 56 year old male acquired 6 weeks apart, in a gastro oesophageal junction cancer response evaluation project. Coronal PET/MR images, top row from left (A-C), anatomic MRI (T2 HASTE), PET and PET/MR show a gastro oesophageal junction cancer (black arrows). Bottom row (D-F) show markedly shrinkage and reduced metabolic activity of the gastro oesophageal junction cancer 6 weeks later (black arrows) but also reveals a complication - creation of an 8 cm large subphrenic abscess (hollow arrows).

Johan Löfgren and Adam Espe Hansen

The PET/MR scanner has, since it was installed, mainly been used in clinical, translational and basic research. The last two years it has grown to be a valuable tool especially in clinical neurology and neurooncology. In addition to being a convenient one stop shop for the patients it has also facilitated our cooperation with neuroradiology. The number of exams performed has increased steadily over the years, (figure 1), with the number of clinical scans in particular dementia (see Section on PET scanning of the brain).

I addition to neurology and neurooncology we have over the years gained sufficient experience and confidence in examining paediatric oncology patients to implement this new and promising technique in clinical routine. For children the obvious advantage is reduction of radiation exposure compared to traditional PET/CT where CT normally accounts for 2/3 of the total radiation dose. We are examining the role of clinical PET/MR for a number of oncologic indications, including treatment evaluation of lung cancer and cardia cancer, as well as radiation therapy planning of cancers of the head/neck and spine metastases, but also for indications as infection. Infection is illustrated in Figure 2 showing a PET/MR examination of a left sided hip prosthesis with complications in a 66 year old male a patient and Figure 3 showing an example of an oncology protocol, where PET/MR in this case is used in a gastro oesophageal junction cancer response evaluation project.

Current research topics including oncology, inflammation/infection, dementia, atherosclerosis, neurobiology and the new multi-modality functional molecular imaging based on the combination of PET and hyperpolarized MRI (see sections about Research and HyperPET). We have at the end of 2015, 25 active research protocols.

Magnetic Resonance Imaging provides clinical physiological information

Henrik Larsson

Functional Imaging Unit (FIU) at Glostrup has become part of Department of Clinical Physiology, Nuclear Medicine and PET, Rigshospitalet, after Glostrup Hospital and Rigshospitalet have been united in one large hospital in 2015. FIU is heavily involved in basic physiological research, but there is an increasing request for clinical investigations of patients where functional information is required, and FIU has the knowledge and want to comply with these requests. Especially children with various kinds of brain diseases, such as encephalitis, congenital malformation and tumors, often suffering from epilepsy resistant to medical treatment, are referred before neurosurgical intervention. The aim is to localize important functional brain centres for language, motor centres for hands and feet. We use advanced ultrafast Magnetic Resonance Imaging (MRI), sensitive for local neural activity dependent perfusion changes with a concomitant change in the level of deoxyhemoglobin, so-called BOLD imaging. The level of deoxyhemoglobin has a profound influence on the MRI signal, allowing us to localize the eloquent cortex structure. An example is seen in figure 1, where both the frontal (Brocca) and the parieto-temporal (Wernicke) language centre are seen in a patient. This kind of information provide the clinicians with a fundament for further decision making and the surgeon with a picture of important brain structures to be spared during operation.

There is a growing clinical interest of quantifying brain perfusion (CBF), brain blood volume (CBV) and subtle increase of the blood brain barrier (BBB) permeability (PS product), in patients with brain tumor and patients with various neurodegenerative and inflammatory diseases. In patients with small and large vessel disease in the brain, interest is on mean transit time and variation of the capillary transit times. During the last two decades we have developed the so-called Dynamic Contrast Enhanced T1 weighted perfusion MRI (DCE-MRI) allowing us estimate all relevant parameters in a one-go set-up using a bolus injection of a MR contrast agent. Although computationally demanding, the measurement is straightforward and cheap to perform using a 3 Tesla MR scanner. We are now in the process of implementing this method in various clinical MR scanning protocols, especially in

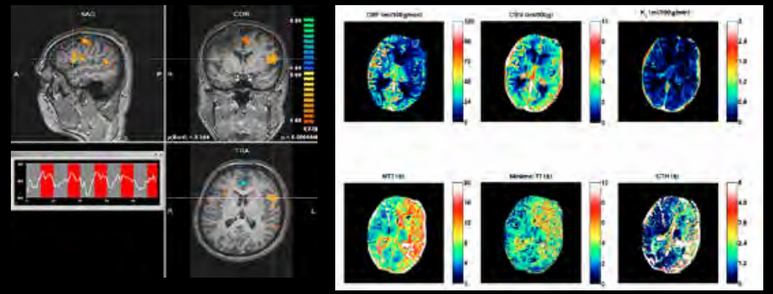


Figure 1. The Language centre are clearly detected, with the cross pointing to Brocca, from which the BOLD signal has been obtained during a verb generation test paradigm. The patient has a tumor in the opposite hemisphere.

Figure 2. The figures show results from a patient with left sided internal carotid stenosis, with multiple thrombo-embolic episodes. Perfusion (CBF) is decreased while the cerebral blood volume (CBV) is increased in the fronto-parietal region, but the permeability (K_i) seems relatively normal. The mean transit time (MTT), the minimal transit time (minimal TT) and capillary transit tine heterogeneity (CTH) is prolonged in the entire region showing altered perfusion.

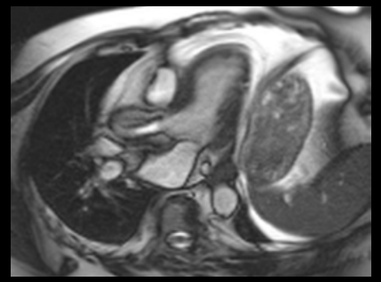


Figure 3. Delineation of the inner and outer border of the left ventricle in the diastolic phase. Precise delineation of all cardiac phases give raise to the dynamic red curve showing the dynamic volume change of the heart.

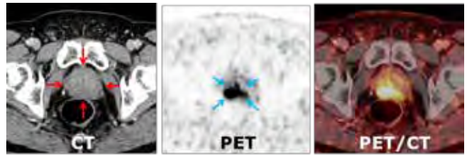
Figure 4. A three-chamber view through the heart, also called left ventricular outflow tract image, showing left atrium, left ventricle and the initial part of aorta during the systole. Here the signal is both very bright and dark due to the turbulent flow through narrow aortic valves. After visualization of the stenosis, absolute quantification of the stenosis is performed using phase mapping of the flow through the valves.

brain tumor patients. The method may provide important information with regards to tumor differentiation, recurrence of tumor versus radiation necrosis and treatment response. Figure 2 shows the result of a DCE-MRI of a patient with a left sided internal carotid stenosis.

MRI is extremely versatile in cardiac diagnostic imaging, and can provide quantitative information about right and left ventricular volumes, left ventricular myocardial mass, ejection fraction, regional wall motion, myocardial perfusion, vascular reserve capacity (the ability to increase perfusion during a stressful stimulation), delineate non-viable myocardial tissue based on the so-called late enhancement, quantify the level of stenosis or regurgitation through heart valves, depict areas of myocarditis and systemic diseases involving the heart as sacoidosis and hemachromatosis. Heart patients are being referred increasingly, and once a week we have a dedicated time slot at a 1.5 Tesla MRI scanner for MR heart examinations. Reading the information is done jointly by a cardiologist and us. Figure 3 shows how we can delineate the inner and outer border of the left heart ventricle in short axis orientation. Figure 4 shows an example of a patient with a severe stenosis of the aorta valves.

^{64}Cu-DOTA-AE105 PET

First-in-humans study of a new PET tracer that can visualize invasive cancer



First-in-humans uPAR-PET of prostate cancer. Red arrows on CT show the prostate gland and blue arrows on PET the uPAR positive tumor (images provided by Morten Persson & Dorthe Skovgaard).

First-in-humans uPAR-PET of breast cancer. Blue arrows on CT show the breast tumor. On PET the tumor is clearly uPAR positive (images provided by Dorthe Skovgaard & Morten Persson).

Andreas Kjær

Prediction of cancer aggressiveness and metastatic potential is urgently needed for better selection of best therapeutic strategy in the individual patient, i.e. for tailoring therapy (personalized medicine). As an example, the treatment strategy for prostate cancer ideally depends on aggressiveness of the tumor. However, currently there is no efficient way to stratify these tumors. Accordingly, in prostate cancer, where the majority of tumors are non-aggressive, the lack of effective tools leads to substantial overtreatment and in those patients to unnecessary side effects such as erectile dysfunction.

To serve this unmet medical need for identification of aggressive cancers, a translational research program headed by Professor Andreas Kjær was initiated several years ago in order to develop PET based imaging for non-invasive visualization of the aggressive cancer phenotype. As target was chosen the urokinase-type plasminogen activator receptor (uPAR), a proteolytic system that has been shown to be responsible for invasion of surrounding tissues by solid tumors such as prostate and breast cancer, and thereby predicts metastatic spread. Basic research in uPAR has been pioneered by the Finsen laboratory in Copenhagen.

In collaboration with both national and international partners, a total of 10 PET tracer candidates have been synthesized, radiolabeled and tested in human xenograft tumor mouse models over the last years. Based on these preclinical results, a most promising candidate, ^{64}Cu-DOTA-AE105, was selected for clinical translation. Following rigorous toxicological testing and after approval by the Danish Medicines Agency, a clinical phase I trial in 10 patients with prostate, breast or bladder cancer, all cancer types where FDG-PET is of limited value, was undertaken at our department in close collaboration with the clinical departments of Breast Surgery, Urology and Oncology at Rigshospitalet.

Results obtained from this first-ever study of uPAR-PET in humans, which were recently published in the journal *Theranostics*, were most encouraging: high uptake in tumors and metastases and a low radiation burden to the patient. Accordingly, further studies using uPAR-PET are currently planned. Examples of images obtained by the first-in-humans uPAR-PET study are shown below.

Academic and other activities

Andreas Kjær, Professor, Consultant, ERC advanced grantee, is President of the Scandinavian Society of Clinical Physiology and Nuclear Medicine (SSCPNM), member of the Oncology Committee of the European Association of Nuclear Medicine (EANM), national representative of the European Society for Molecular Imaging (ESMI), board member of the Cancer Research Foundation at University of Copenhagen, previous member of the Scientific Committee of the Danish Cancer Society, Editor-in-Chief of Diagnostics. Leader of project for development of theranostics for aggressive cancer and for project of hyperPET, funded by the Innovation Fund Denmark, Coordinator of an H2020 project on click-chemistry for PET, 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 Director of EATRIS (the European Advanced Translational Research Infrastructure in Medicine), Head of the Cluster for Molecular Imaging and Director of the PhD Program for Medical & Molecular Imaging at the Faculty of Health and Medical Sciences, University of Copenhagen. Co-chair of the Lundbeck Foundation Clinical Research Fellowship Program (US-DK). Member of the Academy of Technical Sciences (ATV).

Anne Kiil Berthelsen, Consultant, is member of the International Lymphoma Radiation Oncology Group, Steering Committee (ILROG), "European Organisation for Research and Treatment of Cancer Lymphoma Group " (EORTC), the Danish Society of Radiology, the Danish and the Nordic Society of Gynaecological Oncology, British institute of Radiology (BIR), Billeddiagnostisk udvalg Ukendt Primærtumor (DAHANCA), National PET/CT Group, the Danish Society of Clinical Oncology, the Danish Society of Magnetic Imaging and Diagnostic Imaging Group under Danish Lymphoma Group, ERS European Society of Radiology.

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

Annika Loft Jakobsen, Consultant, is involved in a various number of clinical research protocols, teaching at national and international courses pre- and postgraduate for medical doctors, technologists, radiographers and nurses and is invited speaker at national and international meetings and congresses. She is supervisor for several PhD students and 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). Member of the Oncology Committee of EANM, and member of BIR, Danish Society of Oncologial 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, and suspicion of severe disease. 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 and board member of DGCG (Danish Gynecological Cancer Group) and DCCG (Danish Colorectal Cancer Group).

Egill Rostrup, MSc, MD, DMSc, Consultant, Member of the editorial board of the Journal of Cerebral Blood Flow and Metabolism, Management board of EU COST Action (BM1103): "Arterial Spin Labelling in Dementia", Steering committee of the Healthy Aging Clinical Neuroproject at Glostrup.

Helle Hjorth Johannesen, Consultant, is member of Danish Society of Radiology, President of Danish Society of Oncoradiology, member of Danish Society of Medical Magnetic Resonans Imaging and Danish Society for Good Clinical Practice.

Helle Juhl Simonsen, Research MRT, Biomedical Laboratory Scientist, is board member and treasurer in the International Society for Magnetic Resonance in Medicine (ISMRM)/Nordic Chapter, Chair of the local organizing committee for DSMMR & ISMRM Nordic Chapter joint meeting, MRI from head to toe, April 2015. Member of the Membership Committee, the Nominations Committee, the External Relations Sub-Committee Global Relations and the Publications Committee in International Society for Magnetic Resonance in Medicine (ISMRM)/Section for MR Technologist (SMRT), Member of the Members and Services Committee, the Structure and Governance Committee in European Society for Magnetic Resonance in Medicine and Biology (ESMEMB).

Henrik B. W Larsson, MD, DMSc , Consultant, Head of Functional Imaging Unit, Professor in Clinical and Comparative Physiology, Institute of Clinical Medicine, The Faculty of Health and Medical Science, Copenhagen University, Denmark, Representing professor (Ordførende professor) in Clinical Physiology and Nuclear

Medicine, Institute of Clinical Medicine, The Faculty of Health and Medical Science, Copenhagen University, Denmark, Professor in Medical Magnetic Resonance Imaging, Norwegian University of Science and Technology, Norway, Responsible for specialist course in tracer kinetic theory, math and statistic for nuclear medicine physicians. Responsible for specialist course in functional imaging (MRI, PET-MRI, UL) for nuclear medicine physicians, Management board of EU COST Action (BM1103): "Arterial Spin Labelling in Dementia", Steering committee of the 7 Tesla project, Copenhagen, Denmark.

Ian Law, Professor, Consultant, is Member of the Neuroimaging Comittee, European Association of Nuclear Medicine (EANM), Member of the "PET Response Assessment in Neurooncology (RANO) working group" under the European Association of Nuclear Medicine (EANM), European Association of Neurooncology (EANO), and Society of Neurooncology (SNO). Member of the Danish Neurooncology group (DNOG). Member of the working group for "Clinical Guidelines for the Treatment of Brain Metastases", Danish Neurosurgical Society (DNKS), responsible for the specialist training course in the central nervous system for nuclear medicine physicians.

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, Consultant, is member of "Den Regionale Videnskabsetiske Komité F for Hovedstaden (Regional Ethics Committee). He is responsible for the specialist course in "Clinical Respiratory Physiology" for Nuclear Medicine physicians and Respiratory Physicians, he is the responsible physician for Nuclear Medicine in the Faroe Islands, member of the steering committee of "Dansk Lungecancer Gruppe" (Danish Lung Cancer Group), the subcommittees for "Dansk Diagnostisk Lungecancer Gruppe" (Danish Diagnostic Lung Cancer Group) and "Lungecancer Screeningsgruppen" (Screening of Lung Cancer Group), member of the steering committee and the quality subcommittee for creating Danish reference values for lung function and member of an editorial board.

Kim Francis Andersen, Staff Specialist, is member of the Board of Danish Sarcoma Group (DSG). He teaches at specialist courses for nuclear medicine physicians and orthopedic surgeons.

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 Clinicial Physiology and Nuclear Medicine in the Capital Region), Head of the DRG Committee of DSKFNM, member of Uddannelsesforum for bioanalytikeruddannelsen i Region H, (the Speciality Council for the Education of Technologists in the Capital Region) and member of Uddannelsesudvalget på Radiografuddannelsen at Metropol (the Speciality Council for the Education of Radiographers at Metropol).

Lise Borgwardt, Consultant, is Scientific Committee member of the EANM, member at the Pediatric Committee under EANM, member of the Pediatric Imaging Harmonization Group, member of the Tumorboard for Pediatric Solid Tumors at Rigshospitalet, Chair of the Pediatric Focus Group at the Department of Clinical Physiology, Nuclear Medicine and PET and member of the Process Group for the development of the Children's Hospital at Rigshospitalet. She is involved in clinical research protocols, supervisor for PhD students, teaching at national and international courses pre- and post- graduate for medical doctors and is invited speaker at national and international meetings and congresses.

Liselotte Højgaard, Professor, Head of Department. Chairman of the Board of the Danish National Research Foundation. She is Member of Conseil d'Administration, INSERM, L'Institut National de la Santé et de la Recherches Médicales, Frankrig. Advisor to the French Government in the strategic "Médecine du Future". Chair of EU Science Advisory Board in Health Research. She represents the University of Copenhagen, Rigshospitalet in the Medicine and Technology Bioengineer program, the Technical University of Denmark (DTU), where she is also adj. professor. Elected Member of the Royal Danish Academy of Sciences and Letters, member of ATV "The Danish Academy of Technical Sciences", member of the Olav Thon Foundation, Science Advisory Board, member of the Board of the Crown Prince Frederik and Crown Princess Mary's Foundation and member of the Board of Arvid Nilssons Foundation and Tagea Brandt's prize.

Malene Fischer, Clinical Professor of Research, Consultant, is supervisor for several PhD students and involved in both pre- and postgraduate teaching. Course Director of "Introduction to Clinical Medical Imaging" at the Medicine and Technology Bioengineer programme, member of the European Association of Nuclear Medicine (EANM) and the Danish Society of Clinical Physiology and Nuclear Medicine (DSKFNM). Affiliated to the Centre of Excellence for Personalised Medicine of Infectious Complications in Immune Deficiency (PERSIMUNE) and the steering committee of MATCH (Managing of Post-Transplant Infections in Collaborating Hospitals). Elected member of the board of representatives, the Association of Consultants in Denmark.

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

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

Marie Øbro Fosbøl, Senior Registrar, President of Society of Young Nuclear Medicine Physicians (YNK), member of the board of Danish Society of Clinical Physiology and Nuclear Medicine (DSKFNM) and member of the course committee in clinical physiology and nuclear medicine.

Otto Mølby Henriksen, Consultant, PhD, is member of the DRG Committee in Danish Society for Clinical Physiology and Nuclear Medicine (DSKFNM).

Peter Hovind, Consultant, participates in several clinical research protocols and is co-supervisor for a PhD Student. As the Head of the specialist courses in Clinical Physiology and Nuclear Medicine under the Danish Health and Medicines Authority he is responsible for the theoretical part of the specialist training in Clinical Physiology and Nuclear Medicine in Denmark. He is the Head of the Doctors Clinical Physiology and Nuclear Medicine Training Committee of the Danish Society for Clinical Physiology and Nuclear Medicine and member of the board of the Danish Endocrine Society (DES) and the Niels A. Lassen Foundation. He is co-editor for the Danish Medical Journal in the medical imaging section. He is responsible for the postgraduate education in the Glostrup section of the department.

Peter Oturai, Consultant, is responsible for the postgraduate education of physicians 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) and deputy delegate in the European Association of Nuclear Medicine (EANM). He has been representing DSKFNM in the Danish Health and Medicines Authority's committee for speciality planning of Clinical Physiology and Nuclear Medicine (CPNM). He is member of the Danish Thyroid Cancer Guideline Group (DATHYRCA), member of the Doctors CPNM Training Committee and member of the CME and Educational Committee – both affiliated to DSKFNM. He is responsible for the specialist course in Endocrine Pathophysiology for CPNM physicians in Denmark.

Robin de Nijs, MSc, PDEng, PhD, Specialist Medical Physicist, is member of EANM's Network of Excellence for Brain Imaging, member of the Danish Society for Medical Physics and lecturer at EFOMP's school for Medical Physics Experts.

Søren Holm, Chief Physicist, is member of the EANM Physics Committee with special tasks in Radiation Protection, a delegate for DSMF to the European and International organisations for Medical Physics (EFOMP and IOMP), board member of the Nordic Society for Radiation Protection (NSFS), member of one IAEA advisory group concerned with QA/QC and image artefacts affecting SPECT/CT and another IAEA advisory group regarding staffing in Medical Physics, member of Sundhedsfagligt Råd i Klinisk Fysiologi og Nuklearmedicin in the Capital Region, the Specialty Advisory Committee (SFR) in Clinical Physiology and Nuclear Medicine and external lecturer at Copenhagen University.

Tim Lundby, Staff Technologist, is member of Lederrådet i Danske Bioanalytikere.

Ulrik B. Andersen, Consultant, Co-supervisor for PhD students in the department. Former member of the board of Danish Society of Hypertension. Member of European Society of Hypertension and acknowledged hypertension specialist by this society. Responsible for the specialist course in cardiovascular circulation for nuclear medicine physicians in Denmark. Member of the Danish Society of Clinical Physiology and Nuclear medicine, Danish Society of Cardiology and Danish Society of Diagnostic Ultrasound.

Studies 2015

Blegdamsvej

CNS and peripheral nervous system	
Regional cerebral blood flow, DIAMOX, ^{15}O-H_2O	3
Regional cerebral blood flow, ^{15}O-H2O	4
Regional cerebral metabolism, ^{18}F-FDG	834
Regional cerebral receptor, ^{11}C-PIB	139
Regional cerebral receptor, ^{18}F-FET	393
Regional cerebral receptor, ^{11}C different tracers human (NRU)	89
Regional cerebral receptor, ^{11}C differenct tracers animal (NRU)	25
Regional cerebral receptor, ^{18}F-Florbetapir	11
Regional cerebral receptor, ^{18}F-FLT	42
Regional cerebral receptor, ^{68}Ga-Dotatoc	34
CT-scanning of cerebrum	323
MR-scanning of cerebrum	413
Total	**2,310**

Respiratory organs	
Lung function test, whole body plethysmography	1,832
Lung function test, whole body plethysmography w/reversibility	143
Lung function test, spirometry,	1,980
Lung function test, spirometry w/reversibility	100
Lung function test, diffusion capacity (CO)	4,002
Lung function test, peak flow w/ reversibility	3
Max. insp. abd exspir. muscle pressure	117
Lung perfusion scintigraphy, ^{99m}Tc-MAA	9
Lung perfusion scintigraphy, regional, ^{99m}Tc-MAA	18
Lung perfusion scintigraphy, SPECT, ^{99m}Tc-MAA	290
Lung ventilation scintigraphy, ^{81m}Kr-gas	14
Lung ventilation scintigraphy, regional, ^{81m}Kr-gas	156
Lung ventilation scintigraphy, SPECT, ^{81m}Kr-gas	292
Lung ventilation scintigraphy, SPECT ^{99m}Tc-Technegas	2
Mucociliary clearance, ^{99m}Tc-Venticolloid	32
PET thorax ^{18}F-FDG PET/CT breathhold	2
CT thorax PET/CT breathhold	8
Total	**9,000**

Heart and cardiovascular system	
Isotope cardiography, RVEF pass, ^{99m}Tc-HSA	2
Isotope cardiography, LVEF, ^{99m}Tc-HSA	1,524
Myocardial perf. scintigr. gated, ^{99m}Tc-MIBI, pharmacol. stress, adeno.	1
Myocardial perf. scintigr. gated, ^{99m}Tc-MIBI, NTG	1
Myocardial ^{123}I- MIBG, sympaticus activity	27
Myocardial calcium score	558
PET myocardial metabolism, ^{18}F-FDG	50
PET myocardial perfusion, ^{82}Rb	564
PET myocardial perfusion, ^{82}Rb, pharmacological stress, adeno	555
CT cardiac angiography	24
Total	**3,306**

Peripheral vessels	
Isolated limb perfusion leakage monitoring, ^{99m}Tc-erythrocyt	8
Total	**8**

Gastrin intestinal tract, liver, biliary tract and pancreas	
Salivary gland scintigraphy ^{99m}Tc-Pertechnetat	19
Biliary tract scintigraphy, ^{99m}Tc-Mebrofenin	32
Meckels diverticulum scintigraphy, ^{99m}Tc-Pertechnetat	4
Bleeding scintigraphy (abdomen) ^{99m}Tc-erytrocytter	1
Total	**56**

Kidneys and urinary tract	
Glomerular filtration, ^{51}Cr-EDTA, several samples	93
Glomerular filtration, ^{51}Cr-EDTA, one sample	4,046
Renal scintigraphy, ^{99m}Tc-DMSA	20
Renography, ^{99m}Tc-MAG, diuresis	45
Renography, ^{99m}Tc-MAG 3, graft	3
Renography, ^{99m}Tc-MAG 3, ACE-inhibitor	47
Renography, ^{99m}Tc-MAG 3	1,898
Renography, ^{99m}Tc-MAG 3, dual head	9
Sympaticus activity, kidneys, ^{123}I-MIBG	48
Total	**6,209**

Bone and joint	
Bone scintigraphy, ^{99m}Tc-HDP, regional, static	39
Bone scintigraphy, ^{99m}Tc-HDP, whole body, static	598
Bone scintigraphy, ^{99m}Tc-HDP, SPECT	617
Bone scintigraphy, ^{18}F-fluorid, whole body, static	6
Osteodens. dual X-ray absorptiometri (DXA), columna lumb.	2,041
Osteodens. dual X-ray absorptiometri (DXA), lat.spine	3
Osteodens. dual X-ray absorptiometri (DXA), radius	139
Osteodensitometri, dual X-ray absorptiometri collum fem.	4,022
DXA, body composition	827
Total	**8,292**

Endocrine organs	
Thyroid scintigraphy, ^{99m}Tc-Pertechnetat	513
Thyroid scintigraphy, ^{123}I-Iodide	1
Thyroid, ultrasound	513
Thyroid scintigraphy, ^{99m}Tc-Pertechnetat, SPECT	1
Parathyroid scintigraphy, ^{99m}Tc-Stamisis	10
Parathyroid scintigraphy, ^{99m}Tc-Stamisis, SPECT	43
Tumorscintigraphy, ^{123}I-Iodide	1
Tumorscintigraphy, ^{123}I-Iodide, rh-TSH	30
Adrenal marrow scintigraphy, ^{123}I-MIBG	38
Scintigraphy after ^{177}Lu- Dotatate therapy	145
Total	**1,295**

Blood and lymph system	
Erythrocyt volume, ^{99m}Tc-erythrocytter	16
Plasma volume, ^{125}I-HSA	16
Lymph scintigraphy, extremities, ^{99m}Tc- Nanocolloid , stasis	1
Lymph scintigraphy, extremities, ^{99m}Tc-HSA, leakage	1
Sentinel node scintigr. tumor drainage, c. mammae, ^{99m}Tc-Nanocolloid	33
Sentinel node scintigr. tumor drainage, mel. malign., ^{99m}Tc-Nanocolloid	160
Sentinel node scintigr. tumor drainage, c. penis, ^{99m}Tc-Nanocolloid	27
Sentinel node scintigr. tumor drainage, c. vulvae, ^{99m}Tc-Nanocolloid	34
Sentinel node scintigr. tumor drainage, head/neck, ^{99m}Tc-Nanocolloid	100
Sentinel node, peroperative with gamma probe, ^{99m}Tc-Nanocolloid	2
Peritumoral injection of ^{99m}Tc-Nanocolloid for sentinel node	688
Spleen scintigraphy, ^{99m}Tc-erythrocyte, heated	4
Total	**1,082**

Other diagnostic procedures	
Aprotinin scintigraphy, ^{99m}Tc-Aprotinin	4
PET tumor scanning, ^{18}F-FDG	5,109
PET scanning, ^{18}F-FDG	310
PET infection scanning, ^{18}F-FDG	101
PET tumor scanning, ^{68}Ga-Dotatoc	613
White blood cell scintigraphy, ^{99m}Tc-white blood cell	18
White blood cell scintigraphy, ^{99m}Tc-white blood cell, SPECT	26
White blood cell scintigraphy, ^{111}In-white blood cell	11
White blood cell scintigraphy, ^{111}In-white blood cell, SPECT	7
Whole body, contamination measurement	148
Image fusion (PET, SPECT, MRI, CT or planar)	9,351
CT head/neck SPECT/CT	224
CT wb SPECT/CT	606
CT thorax SPECT/CT	492
CT pelvis SPECT/CT	77
CT abdomen SPECT/CT	294
CT lower extremities SPECT/CT	22
CT upper extremities SPECT/CT	2
CT wb PET/CT (KF)	1,212
CT wb PET/CT (PET)	5,129
MR wb PET/MR	356
CT lover extremities PET/CT	50
Second opinions external PET, PET/CT, SPECT/CT, CT and MR	1,178
Extra tumor delineation	105
Other investigations	218
Supplementary/repeated imaging	2,526
Total	**28,189**

Radiotherapy	
Treatment with ^{131}I, benign thyroid	42
Isotope treatment with ^{177}Lu-Dotatate	124
Isotope treatment with ^{223}Ra-Dichlorid	273
Total	**439**

In vitro analysis	
Plasma and protein analysis	3.792
Gene expression analysis	10.994
Immunohistiochemistry	1.465
Flow cytometry	7.396
Total	**23.647**

Glostrup

CNS and peripheral nervous system	
Regional cerebral blood flow, ^{99m}Tc- HMPAO, pharm.prov.	22
Regional cerebral blood flow, ^{99m}Tc- HMPAO	81
Regional Dopamine Transporter (DAT) receptor imaging, ^{123}I-FP-CIT	321
MR-scanning of cerebrum	1,606
Total	**2,030**

Respiratory organs	
Lung function test, whole body plethysmography	471
Lung function test, spirometry	474
Lung function test, spirometry w/reversibility	133
Lung function test, diffusion capacity (CO)	472
Max. insp. abd exspir. muscle pressure	4
Lung perfusion scintigraphy, SPECT, ^{99m}Tc-MAA	68
Lung ventilation scintigraphy, SPECT ^{99m}Tc-Technegas	65
Total	**1,687**

Heart and cardiovascular system	
Myocardial perf. scintigr. gated, ^{99m}Tc-MIBI, pharmacol. stress, adeno.	247
Myocardial perf. scintigr.^{99m}Tc-MIBI	178
Tilt table test	297
Analysis of heart rate variability	199
MR scanning of the heart	104
Total	**1,025**

Peripheral vasculature	
Systolic blood pressure, fingers	6
Systolic blood pressure, ancle and toes	467
Systolic blood pressure, ancle-brachial index after treadmill	112
24 hours blood pressure measurement	344
Doppler ultrasound of carotid arteries	4,334
Total	**5,263**

Gastrin intestinal tract, liver, biliary tract and pancreas	
Salivary gland scintigraphy ^{99m}Tc-Pertechnetat	2
Doppler ultrasound of splanchnic blood flow	409
Glucose tolerance test	16
Lactose tolerance test	20
Helicobacter pylori testing	52
Iron uptake test	1
Total	**500**

Kidneys and urinary tract	
Glomerular filtration, ^{51}Cr-EDTA, several samples	3
Glomerular filtration, ^{51}Cr-EDTA, one sample	589
Renal scintigraphy, ^{99m}Tc-DMSA	2
Renography, ^{99m}Tc-MAG 3 , diuresis	2
Renography, ^{99m}Tc-MAG 3	524
Renography, ^{99m}Tc-DTPA, ACE-inhibitor	167
Renography, ^{99m}Tc-DTPA	80
Doppler ultrasound of renal blood flow	370
Ultrasound kidneys	363
CT kidneys	463
CT bladder	463
Total	**3,026**

Bone and joint	
Bone scintigraphy, ^{99m}Tc-HDP, regional, static	10
Bone scintigraphy, ^{99m}Tc-HDP, whole body, static	335
Bone scintigraphy, ^{99m}Tc-HDP, SPECT	186
Osteodens. dual X-ray absorptiometri (DXA), columna lumb.	3,066
Osteodens. dual X-ray absorptiometri (DXA), lat.spine	742
Osteodensitometri, dual X-ray absorptiometri af collum fem.	6,045
DXA, body composition	9
MR scanning hands and fingers	46
MR scanning wrist	68
MR scanning sternum	1
MR scanning thorax	4
MR scanning columna thoracalis	59
MR scanning columna cervicalis	59
MR scanning columna lumbalis	59
MR scanning os sacrum	59
MR scanning pelvis and hips	59
MR scanning femur	108
Total	**10,915**

Endocrine organs	
Thyroid scintigraphy, ^{99m}Tc-Pertechnetat	440
Thyroid, ultrasound	454
Thyroid, fine needle aspiration biopsy	33
Iodine uptake test, ^{131}I-Iodide	14
Catheterization, adrenal vein sampling	10
Synacthen test	86
Total	**1,037**

Other diagnostic procedures	
White blood cell scintigraphy, ^{99m}Tc-white blood cell	16
White blood cell scintigraphy, ^{99m}Tc-white blood cell, SPECT	12
White blood cell scintigraphy, ^{99}Tc-leucoscan	3
Assessment of blood samples	3
MR scanning upper abdomen	54
MR scanning lower abdomen and pelvis	54
Total	**142**

Radiotherapy	
Treatment with ^{131}I, benign thyroid	14
Total	**14**

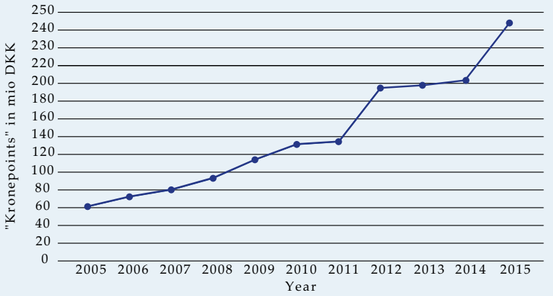
Animal studies

Dogs	
^{18}F-FDG	4
^{18}F-FDG/^{13}C-Pyruvate	12
^{18}F-Asis/^{13}C-Pyruvate	1
^{64}Cu-liposomes	22
CT–scans for image fusion	23
MR-scans	4
Pigs	
^{18}F-FDG	3
^{64}Cu-DOTATATE	29
^{68}Ga-RGD	22
^{82}Rubidium	22
MR-scans	32
CT-scans for image fusion	22
Rats	
^{18}F-FDG	59
^{82}Rubidium	112
MR-scans	4
MR-scans, Late Gadolinium Enhancement	108
MR-scans DWI	4
CT-scans for image fusion	137
Optical imaging	7
Radiotherapy	42
Mices	
^{13}C-PIB	23
^{18}F-ASIS	28
^{18}F-FDG	618
^{18}F-FET	293
^{18}F-FLT	69
^{18}F-Aprotinin	27
^{124}Iodine	16
^{18}F-HX4 – hypoxi-tracer	16
^{64}Cu-Albumin	17
^{64}Cu-DOTA-AE105	4
^{64}Cu-TRIS	2
^{64}Cu-liposomes	251
^{64}Cu-liposomes, targeted	42
^{64}Cu-Na	2
^{64}Cu-ASIS	53
^{64}Cu-Aprotinin	27
^{64}Cu-X	16
^{68}Ga-DOTATOC	25
^{68}Ga-RGD	36
^{18}F-FDG/^{13}C-Pyruvate	40
^{13}C-Pyruvate s	10
MR-scans	777
MR-scans DWI	55
MR-spectroscopy	55
Optical imaging	954
Radiotherapy	240
CT-scans	44
CT-scans for image fusion	1,252
Total	**5,661**

Total number of studies 115,133

Finance

Turnover



The increase in activities measured in "krone point" rose from 61,6 mio DKK in 2005 to 243,5 mio DKK in 2015.

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

Balance 2015

Expenditure (DKK mio.)	
Running costs	24.4
Staff	70.9
In total	**94.3**
Receipts	19.7

Equipment 2015

Blegdamsvej

Equipment	Product	Purchase year
Gamma cameras	Mie-Scintron	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
	Siemens mCT-S (128)	2013
PET/MR scanner	Siemens mMR	2011
	GE SPINlab MR Hyperpolarizer	2014
Lung function	Jaeger Masterscreen w/bodybox	2005
	Jaeger PFT pro w/bodybox	2007/13
DXA scanner	GE Lunar Prodigy	2011
Whole body counter	WBC w/NaI counting chamber	1977
	WBC w/plast counting chamber	1978
Cyclotrons	Scanditronix 32 MeV	1991
	RDS Eclipse cyclotron, CTI	2005
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
	Bruker preclinical MRI PharmaScan 7T	2013
	Siemens preclinical PET/CT Inveon	2013
	PX Inc. preclinical RT X-RAD 320	2013

Glostrup

Equipment	Product	Purchase year
Gamma cameras	Mediso Nucline TH45	2007
	Mediso Nucline X-Ring	2003
	DDD SoloMobile	2012
SPECT/CT cameras	GE Infinia Hawkeye	2004
	Siemens SymbiaT2	2006
	GE Discovery 670	2010
DXA scanner	GE Lunar iDXA	2014
	GE Lunar Prodigy	2005
	GE Lunar Prodigy	2004
Lung function	Jæger Masterscreen w/bodybox	2007

Publications 2015

Theses

Andersen VL. PhD thesis. Development of probes for in vivo molecular brain imaging of serotonin markers. Defended on the 16th of January 2015, University of Copenhagen.

Brinth LS. PhD thesis. Carotid sinus hypersensitivity - an age related baroreflex dysfunction. Defended on the 12th of November 2015, University of Copenhagen.

Cramer SP. PhD thesis. Permeability of the blood-brain barrier as measured by dynamic contrast-enhanced perfusion MRI. Defended on the 30th of June 2015, University of Copenhagen.

Knudsen A. PhD thesis. Mechanisms behind the increased risk of cardiovascular disease in HIV-infected patients. Defended on the 24th of April 2015, University of Copenhagen.

Lindberg U. PhD thesis. Measurement of the neurovascular coupling in the healthy and diseased brain using fMRI. Defended on 11th of June 2015, University of Copenhagen.

Li F. PhD thesis. ^{64}Cu-ATSM PET for hypoxia imaging - kinetic modelling and evaluation using pO_2 measurements. Defended on the 30th of June 2015, University of Copenhagen.

Nedergaard MK. PhD thesis. ^{18}F-FET PET to monitor tumour response development and assess treatment response in Glioblastoma Multiforme: Multimodal imaging in orthotopic xenograft models. Defended on the 30th of March 2015, University of Copenhagen.

Olsen IH. PhD thesis. Studies of neuroendocrine carcinomas and goblet cell carcinoids. Defended on the 15th of December 2015, University of Copenhagen.

Pfeifer AK. PhD thesis. Theranostics in neuroendocrine tumors: evaluation of a new PET tracer & peptide receptor radionuclide, therapy response. Defended on the 15th of September 2015, University of Copenhagen.

Schjoeth-Eskesen C. PhD thesis. Aziridine ring-opening reactions with [18F]fluoride, strategies in the synthesis of [18F]-labelled peptides and [64Cu]-labelled trastuzumab for targeting cancer. Defended on the 17th of March 2015, University of Copenhagen.

Wulff S. PhD thesis. The connection between dopamine D2 activity, reward disturbances and psychopathology. Defended on the 26th of February 2015, University of Copenhagen.

Patents

Kjær A (with co-inventors). ^{177}Lu labeled peptide for site-specific uPAR-targeting. EP-2846826 and US-20150132219. March 18 and May 14, 2015.

Kjær A (with co-inventors). Positron emitting radionuclide labeled peptides for human uPAR PET imaging. EP-2928505. October 14, 2015.

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Olesen OV. Method for Surface Scanning in Medical Imaging and Related Apparatus. WO2015071369 . May 21, 2015.

Publications

Andersen KF, Fuglo HM, Rasmussen SH, Petersen MM, Loft A. Volume-Based ^{18}F-FDG PET/CT Imaging Markers Provide Supplemental Prognostic Information to Histologic Grading in Patients With High-Grade Bone or Soft Tissue Sarcoma. Medicine (Baltimore). 2015 Dec;94(51):e2319.

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Andersen KF, Albrecht-Beste E. Brown Tumors Due to Primary Hyperparathyroidism in a Patient with Parathyroid Carcinoma Mimicking Skeletal Metastases on ^{18}F-FDG PET/CT. Diagnostics. 2015;5(3):290-3.

Andersen KF, Albrecht-Beste E, Berthelsen AK, Loft A. Angiosarcoma of the Scalp: Metastatic Pulmonary Cystic Lesions Initially Misinterpreted as Benign Findings on ^{18}F-FDG PET/CT. Diagnostics. 2015;6(1):1-4.

Andersen JB, Henning WS, Lindberg U, Ladefoged CN, Højgaard L, Greisen G, Law I. Positron emission tomography/magnetic resonance hybrid scanner imaging of cerebral blood flow using ^{15}O-water positron emission tomography and arterial spin labeling magnetic resonance imaging in newborn piglets. Journal of cerebral blood flow and metabolism. 2015 Nov;35(11):1703-10.

Andrésdóttir G, Jensen ML, Carstensen B, Parving HH, Hovind P, Hansen TW, Rossing P. Improved prognosis of diabetic nephropathy in type 1 diabetes. Kidney Int. 2015 Feb;87(2):417-26.

Aneheim E, Albertsson P, Bäck T, Jensen H, Palm S, Lindegren S. Automated astatination of biomolecules - a stepping stone towards multicenter clinical trials. Scientific Reports. 2015;5:12025.

Aneheim E, Foreman MRS, Jensen H, Lindegren S. N-[2-(maleimido)ethyl]-3-(trimethylstannyl) benzamide, a molecule for radiohalogenation of proteins and peptides. Applied radiation and isotopes : including data, instrumentation and methods for use in agriculture, industry and medicine. 2015 Feb;96:1-5.

Aneheim E, Halleröd J, Albertsson P, Jensen H, Holgersson S, Lindegren S. Shelf-life of ^{t}-lysyl-3-(trimethylstannyl)benzamide immunoconjugates, precursors for ^{211}At labeling of antibodies. Cancer Biotherapy & Radiopharmaceuticals. 2015 Feb;30(1):41-5.

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Asghar MS, Pereira MP, Werner MU, Mårtensson J, Larsson HBW, Dahl JB. Secondary Hyperalgesia Phenotypes Exhibit Differences in Brain Activation during Noxious Stimulation. P L o S One. 2015;10(1):e0114840.

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Bandel I, Bungum M, Richtoff J, Malm J, Axelsson J, Pedersen HS, Ludwicki JK, Czaja K, Hernik A, Toft G, Bonde JP, Spanò M, Malm G, Haugen TB, Giwercman A. No association between body mass index and sperm DNA integrity. Human reproduction (Oxford, England). 2015 Jul;30(7):1704-13.

Barloese MCJ, Mehlsen J, Brinth L, Lundberg HIS, Jennum PJ, Jensen RH. Reduced Baroreflex Sensitivity in Cluster Headache Patients. Headache. 2015 Jun;55(6):815-24.

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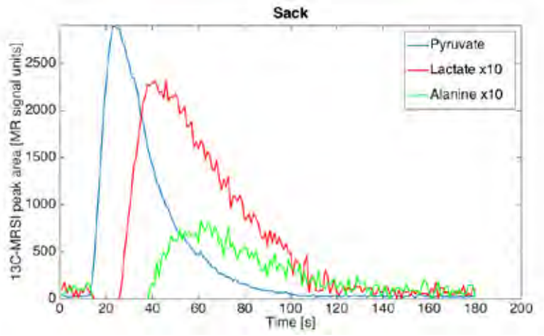
As in previous reports we have listed scientific papers only and not the many abstracs and proceedings from the department.

SpinLab MR Hyperpolarizer

The hyperpolarized Pyruvate is drawn into a vial. The PET/MR scanner is right behind the hatch.



Example of hyperpolarized MRS in a dog with thyroid cancer. Lactate and Alanine is produced from the injected hyperpolarized Pyruvate, as a result of the shift to aerobic glycolysis in the cancer (Warburg effect).

Andreas Kjær and Adam Espe Hansen

In 2014 the department was the first worldwide to have a combined PET/MR system with a MR hyperpolarizer installed.

Through hyperpolarization the signal from ^{13}C-compounds, e.g. ^{13}C-pyruvated to study metabolism, is made 10,000 to 100,000 fold higher. The hyperpolarization is obtained by a combination of low temperature (1 K), a magnetic field og 4 Tesla and irradiation by micro waves.

When a hyperpolarized compound like ^{13}C-Pyruvate is then injected, its conversion to ^{13}C-Lactate can be followed in real time.

The system is integrated with quality control and can hyperpolarize 4 samples at the same time. The system is operated by specially trained PET technologists. The technologists have been able to obtain a success rate for sample production of 87 % during the first 1½ years of operation. With procedures still improving, we have a strong basis for future human studies.

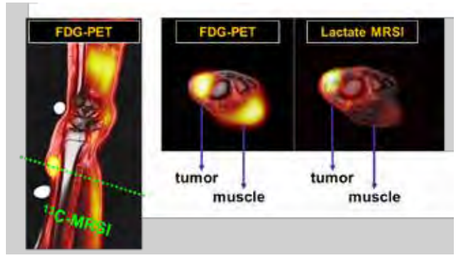
As of the end of 2015 more than 70 animal studies have been performed in canines, pigs and rodents by us. The biological compound, which has been used so far is Carbon-13 enriched Pyruvate. In all studies an MR signal from the injected Pyruvate has been detected, along with one or more metabolites generated in real time.

HyperPET

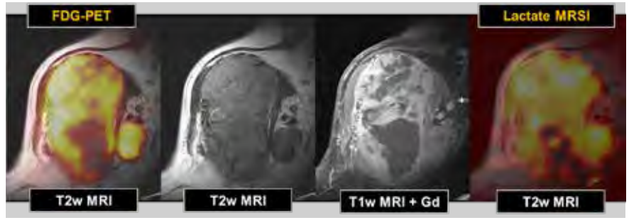
Andreas Kjær and Adam Espe Hansen

Since installation of the SpinLab MR hyperpolarizer system in proximity to the PET/MR scanner on March 25, 2014, more than 70 animal studies have been performed in canines, pigs and rodents.

In 2014 we performed the first scan using simultaneous combined hyperpolarized MR and PET. Since then, continued studies have shown in a series of canine cancer patients that hyperPET, a name given by us to the combined technique, is feasible and can easily be performed within 2 hours. We showed a rough correspondence between ^{13}C-lactate production and ^{18}F-FDG uptake and expect the combined modalities to reveal additional metabolic information to improve prognostic value and improve response monitoring.



HyperPET with combined ^{18}F-FDG-PET and ^{13}C-Lactate-MRSI performed in the dog Fiola (32 kg) with a sarcoma on the right forepaw. Coronal image (left) shows location of tumor and slice section for MRSI. Axial images (right) show ^{18}F-FDG-PET and ^{13}C-Lactate-MRSI.



Example of HyperPET with combined ^{18}F-FDG-PET and ^{13}C-Lactate-MRSI performed in a dog (39 kg) with a sarcoma in the axilla. FDG uptake and lactate generation is observed both in the tumor and a proximal lymph node.

Research

Andreas Kjær

A continuous focus on research and development is a keystone of the department. Over the years, we have developed a comprehensive research program with strong national and international collaborations. We constantly adjust our research program to develop solutions to health challenges in patients. Particularly, our research program focuses on development of new tracers for PET, PET/MRI hybrid imaging, *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 molecular imaging is given special attention in order to accelerate translation of new tracers into clinical use in patients. Current major research areas, many of which are seeking to fulfill unmet patient needs, are mentioned below

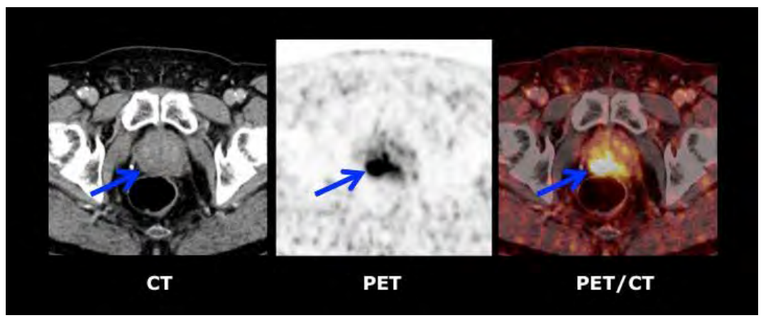


Figure showing first-in-humans uPAR-PET/CT imaging in a patient with prostate cancer using the PET tracer ^{64}Cu-DOTA-AE105.

New tracers

Numerous ongoing projects are aimed at development of new, specific tracers for non-invasive tissue characterization. These tracers are to be used for the diagnosis of different cancer types as well as for planning and monitoring of thera-py. The projects, which are translational in nature, are carried out in collaboration with other departments and laboratories both nationally and internionally. A recent example of such new tracer developed at the department is the first PET tracer to visualize the invasive cancer phenotype based on uPAR targeting. This tracer, ^{64}Cu-DOTA-AE105, was recently taken into first-in-humans and showed promising results in several cancer forms. 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. We currently have several promising new PET tracers in our developmental pipeline and expect several of these to be translated into clinical use within the next years.

PET/MRI

Being one of the first centers to have an integrated PET/MRI scanner installed, we have over the years continuously developed and expanded our research program on this topic with focus on the added value of combining PET and MRI. With the aim of unfolding the full potential of PET/MRI through combining PET molecular imaging and MRI multiparametric imaging a large number of clinical trials as well as projects on method development are currently undertaken. The focus is on the combined use of the modalities for improved tissue characterization and response monitoring in cancer treatment, paediatric 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). Most recently, the use of PET/MRI for radiation therapy is being evaluated. With access also to preclinical PET and MRI, we are capable of working translational when developing and evaluating new methods.

Hyperpolarized ^{13}C-MRSI

With the installation of equipment for dynamic nuclear polarization of ^{13}C-labeled compound, e.g. ^{13}C-pyruvate we have developed a research program with focus on the use of this technique for tissue characterization in cancer and cardiovascular disease, but not limited to these areas. Since the system is the first in the World that is installed next to a PET/MRI scanner, special attention is given to how the combination of hyperpolarized ^{13}C-MRS and PET can be combined in what we have named *hyperPET*. We have demonstrated not only that hyperPET is feasible but when performed with FDG and ^{13}C-Pyruvate it can discriminate the Warburg effect from other causes of increased glucose uptake. This is a most powerful, non-invasive tool for the study of metabolism in cancer and other pathological conditions. Currently other PET tracers are combined with hyperpolarized ^{13}C-MRSI to evaluate which combinations may hold valuable clinical information. Our goal is to develop methods that through use of the combined modalities, are superior in cancer phenotyping and therapy monitoring with the intention of providing better tools for tailoring therapy. Like in other of our research fields, our approach is translational.

Clinical PET/CT in oncology

A large number of prospective protocols are undertaken to evaluate the diagnostic and prognostic value of PET/CT with different tracers, including our in-house developed ones, in various forms of cancer both in children and in 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 also now include PET/MRI to study the added value compared to PET/CT.

Paediatric nuclear medicine investigations

The department conducts many paediatric investigations. Several research protocols with the use of PET and SPECT are carried out in cooperation with clinical departments, particularly within oncology and function of the hepato-biliary system. 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 fully 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.

Functional MR

With focus on the brain and in collaboration with clinical departments including neurology and psychiatry, development of new methods for functional MRI and clinical application of new functional and molecular MR methods are pursued. Methods are targeted at obtaining information on tissue physiology, organ perfusion and molecular biology.

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. Since we as the first published data showing advantages of PET/MRI over PET/CT for carotid artery imaging we have continued to develop vascular imaging using PET/MRI with special focus on new PET tracers.

Nuclear cardiology

With the ability to measure absolute coronary flow and myocardial perfusion by ^{82}Rb PET, several studies on the regulation of these pa-

rameters are undertaken. Studies include the effect of various 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, e.g. HIV and hepatitis 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 to obtain 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. Finally, the department is participating in a large study colleting data for a lung function test reference database.

Studies of muscle function

Using methods from clinical physiology and nuclear medicine as well as molecular analyses, muscle function, bone density and body composition are studied with focus on the effect of exercise, immobilization and ageing. Also, data are collected on these parameters from a population-based study. These data will serve as a reference database and elucidate markers to predict aging-related disease.

Inflammation, infection and rejection

Research with non-invasive imaging of inflammation and infection is currently being undertaken at the department. Also studies on how rejection reactions can be visualized and evaluated are now performed. In some studies, the added value of MR-derived parameters of PET/MR is studied. The department is partner in the PERSIMUNE program, personalized medicine of infection complications in immune deficiency. Finally, on a translational basis development of new PET ligands for immune response monitoring is currently being pursued.

Radionuclide treatment and theranostics

Localized radiation therapy using beta- or alpha-emitting specific ligands binding to certain cancer forms has been undertaken for several years at the department. The department takes part in research within this area by testing new ligands and producing relevant isotopes. We also develop several 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. The concept of a tracer that visualizes the target prior to starting therapy is also known as companion diagnostics.

Image guided surgery

Intraoperative guidance using either radioactive or optical imaging ligands is increasingly used for surgery. In collaboration with clinical departments we have recently developed one of our most promising PET ligands targeting uPAR into an optical probe. This probe will be used for intraoperative delineation of cancer to ensure free margins while leaving normal tissue intact. The technology, which will be used in pair with preoperative PET imaging of the same target, is particularly promising in concert with robotic surgery.

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.

BIIC

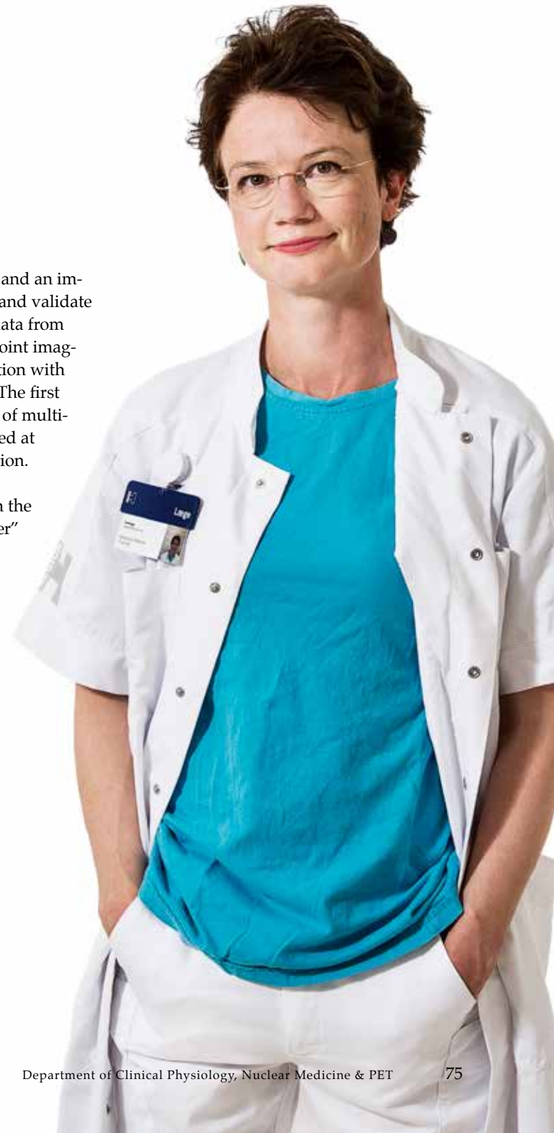
Malene Fischer

BIIC is an acronym for Better Imaging in Inflammation and Cancer. BIIC might sound big, but denotes a small albeit growing research group centred on a portfolio of clinical research projects. These projects aim to increase our understanding of the intersection between inflammation and cancer in an imaging perspective. All projects are based on a close collaboration with our clinical colleagues, especially the departments of Oncology and Infectious Diseases, as well as the MATCH (Managing of Post-Transplant Infections in Collaborating Hospitals) and the PERSIMUNE collaboration.

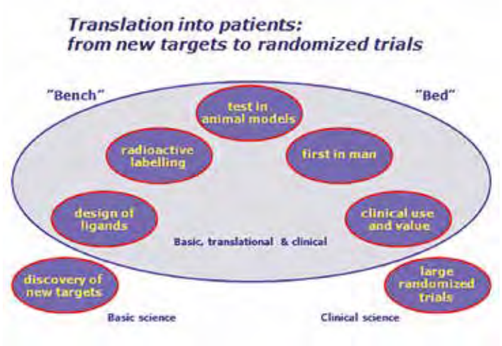
In short, BIIC examines the inflammation-cancer intersection in two main areas: First, inflammation as a predisposing factor, increasing the risk of cancer. To this end we examine the use of PET/CT and PET/MR for detection of focal inflammation/infection and early detection of cancer. Second, inflammation induced during or after therapy, e.g. flare during chemotherapy and inflammation after radiotherapy, hampering our ability to perform early therapy evaluation and detection of relapse. The latter is explored in an on-going clinical trial comparing FDG and FLT-PET.

In the WHEN study we explore whether PET/MR with FDG and DWI performed before, during (up to 3 times) and after the first cycle of chemotherapy can discriminate between therapy induced inflammation, tumor response and lack of response. This study generates highly complex datasets and an important part of this study is to test and validate different methods for integrating data from multi-parametric and multi-time point imaging. This is done in close collaboration with PET/MR physicist and engineers. The first preliminary results on the analysis of multi-parametric imaging where presented at EANM in 2015 as an oral presentation.

In 2015 BIIC received funding from the Danish Cancer Society “Knæk Cancer” and the Michaelsen Foundation. Both contributions are highly appreciated and a prerequisite for our continuing research.



Cluster for Molecular Imaging



The "translational bridge" with our key competencies highlighted in grey

Andreas Kjær

The paradigm of precision medicine, i.e. tailoring therapy to the individual characteristics of each patient, 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 whole-body non-invasive studies at the molecular level in intact organisms circumventing sampling error. It is possible to label almost any molecule with radioactive isotopes suitable for PET imaging. Such molecular imaging ligands can be used for 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 as they can be directly transferred from animal models to use 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 in animal models
- → Use for diagnosing, therapy planning and monitoring in patients
- → Use for testing of new drugs
- → Use as starting point for new targeted therapies, in particular radionuclide based therapies

Through establishment in 2003 of Cluster for Molecular Imaging at the Faculty of Health and Medical Sciences, University of Copenhagen (headed by Professor Andreas Kjær) a specialized facility at the Panum Institute for molecular imaging in animals with PET, SPECT, CT, MRI and optical imaging 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 more clinically relevant animal cancer models, which include orthotopic human xenograft tumors as well as metastatic cancer models using human cancer cell lines. Most recently, we also implemented the use of patient-derived tumors (PDX) for orthotopic implantation to even better mimic the conditions in cancer patients. Furthermore, we have also introduced and developed animal models of cardiovascular diseases including atherosclerosis, myocardial infarction and takotsubo. For studies of atherosclerosis also mini pigs and rabbits are used.

Over the last years 10 years we have build a translational platform for development of new PET tracers in cancer. The platform includes, after testing in orthotopic human xenograft tumors in mice, early use of promising PET tracers in companion dogs with spontaneous tumors scheduled for cancer therapy. The latter allows for testing in "full-size" as well as evaluation of tumor-stroma interaction due to the syngeneic tumor environment. In this way we bridge between xenograft models and first-in-human studies.

At Cluster for Molecular Imaging we always seek to match our clinical methods to be able to develop new techniques for use in patients. Accordingly, we have most recently added SPECT/CT capabilities to our existing PET/MRI/MRS capabilities. SPECT/CT will in particular be used to visualize ^{177}Lu-labeled radionuclide therapy ligands to investigate biodistribution and binding to tumors. Also, we currently perform pre-clinical studies in the field of hyperpolarized ^{13}C-MRS in collaboration with Hvidovre Hospital and DTU. Recently, also optical imaging has gained translational potential as it can be used intraoperatively for delineation of tumors.

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, we also perform studies within molecular imaging of inflammation and metabolism, e.g. activation of brown adipose tissue.

Some tissue characteristics currently targeted for imaging:

- → Cancer specific receptors (numerous projects, e.g. SST and HER2)
- → Glycolytic activity (PET and hyperpolarized MRSI)
- → Cell proliferation
- → Amino acid transport
- → Hypoxia
- → Apoptosis
- → Angiogenesis
- → Invasive cancer phenotype
- → Atherosclerotic plaque vulnerability
- → Immune-response

Collaboration with Landssygehuset, Faroe Islands

Jann Mortensen and Thomas Levin Klausen

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 160 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 Clinical Physiology and Nuclear Medicine, Rigshospitalet.

The Department of Clinical Physiology and Nuclear Medicine in Tórshavn performed 452 (511 in 2014) scintigraphies of lungs, bones, thyroid, kidneys, sentinel nodes and renography in 2015 on the department´s 2-headed Skylight camera. A total of 425 (627 in 2014) lung functions test were performed with the Jaeger whole body plethysmograph. The Norland DXA 840 scanner has been used for a total of 470 (410 in 2014) routine and reseach studies. Second opinion on scintigraphy and lung function measurements is provided via a direct telemedicine connection. The responsible physician and phycisist for Nuclear Medicine in Tórshavn is Consultant, DMSc Jann Mortensen and Physicist Thomas Levin Klausen.

Danish-Chinese and Danish-Indian Research Collaborations

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

In 2015 the Department continued its collaboration with leading research institutions in China through the Danish-Chinese Centre for Proteases and Cancer where Professor Andreas Kjær is senior partner. The Centre is funded by the Danish National Research Foundation (Danmarks Grundforskningsfond) and the National Natural Science Foundation of China.

The main focus of the Centre is to perform research that amongst other applications should lead to new molecular imaging ligands and tailored therapies. Our focus has throughout been development of new PET imaging ligands to identify the invasive cancer phenotype and their translation into clinical use. It is with proud that we have in 2015, the last year the Centre is funded, reached our goal of clinical testing of uPAR-PET.

In addition to Rigshospitalet, the partners are Aarhus University, Chinese Academy of Sciences, Fuzhou and Soochow University, Suzhou.

Also with India, we continued our collaboration in 2015 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, the largest cancer hospital in Asia. The collaboration continues to work on development of new and cost-effective methods for targeted radionuclide therapy in patients with breast cancer. Currently, also the potential of using alpha-emitters is pursued. Experimental work is undertaken both in India and Denmark.

PhD degree in medical and molecular imaging

The research at our department involves numerous PhD students. These PhD students are enrolled in the PhD program for Medical and Molecular Imaging at the Faculty of Health and Medical Sciences, University of Copenhagen. The program was established in 2010 in acknowledgment of the ever-increasing research field of medical and molecular imaging. Professor Andreas Kjaer heads the program. The program offers PhD courses covering both technical aspects of PET, CT, MRI and optical imaging as well as disease oriented courses in imaging, e.g. imaging in oncology.

In 2015 a two-day workshop for enrolled PhD students of the program was held in Helsingør. During the workshop the PhD students presented their projects with the aim of generating new ideas and invite to collaborations across disciplines and departments. In addition, affiliated professors and senior researchers gave lectures on subjects of general interest, e.g. why scientific articles get rejected (editors view), how to attend conferences, web-based imaging tools and regulatory issues.

In 2015 a total of 11 PhD students from our department were granted the PhD degree. The majority of these were enrolled in the PhD program for Medical and Molecular Imaging.

Global Academic Program

MD Anderson's Sister Institution Network

Consultant Annika Loft Jakobsen and Professor Andreas Kjær presented clinical data on two new PET tracers developed at our department at the 2015 GAP Conference.

In 2014 Rigshospitalet was selected as the first Danish institution to become a sister institution of MD Anderson Cancer Center and be part of the Global Academic Programs (GAP). GAP facilitates and administers MD Anderson's Sister Institution Network, which is the largest global network of cancer centers working collaboratively on research and education aimed at lessening the world's cancer burden.

Each year, a GAP Conference is held to provide a forum for faculty from MD Anderson and Sister Institutions to develop collaborations and exchange research results and ideas. Sessions are formed around topics of interest to the members of the Sister Institution Network. The event is held at MD Anderson in odd years and is hosted by a Sister Institution in even years.

Accordingly, in 2015 the GAP Conference was held at MD Anderson Cancer Center in Houston, TX. From Rigshospitalet a delegation of 10 persons, headed by Medical Director Jannik Hilsted, participated in the conference. Our department was represented by Consultant Annika Loft Jakobsen and Professor Andreas Kjær. They presented clinical data on two new PET tracers, which were developed at our department. During the conference fruitful discussions on future collaborative projects were discussed and organized.

Young Investigator Prizes

Awardee Karina Juhl together with Dr. Anders Christensen and Professor Andreas Kjaer at the WMIC conference.

The 2015 Lundbeck Foundation Clinical Research Fellowship awardees. Mathias Dyrberg Loft is number 2 from right.

PhD student Ingrid Holst Olsen (joint with Dept. of Endocrinology, Abdominal Surgery, Oncology and Pathology): Nordic Neuroendocrine Tumour Group Scholarship for Young Researchers in Neuroendocrine Tumors, Stockholm, Sweden, October 2015. Project title: *Nordic study on the impact of surgery on patients with gastroenteropancreatic neuroendocrine carcinomas (GEP-NECs). Characterization of GEP-NECs by imaging, immunohistochemistry and qPCR.*

Research assistant Karina Juhl: Student Travel Stipend Award based on abstract score. World Molecular Imaging Congress, Honolulu, USA, September 2015. Abstract: Juhl K, Christensen A et al. *Delineation of tumor margins in vivo with a uPAR-targeted NIR optical imaging probe, using the fluorophor indocyanine green.*

Postdoc Morten Persson: International Best Abstract Award at the annual meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI), Baltimore, USA, June 2015: Abstract: Persson M, Skovgaard D et al. *Safety and dosimetry of first-in-humans uPAR PET imaging.*

Lundbeck Foundation Clinical Research Fellowship Program

Medical student Mathias Dyrberg Loft from our department was awarded a one-year Lundbeck Foundation Clinical Research Fellowship Program stipend to perform a joint project at Stanford University. Project title: *Plasma PSA and uPAR PET imaging for early Identification of Invasive Prostate Cancer Phenotypes* (co-supervisors: Assoc. Professor Zhen Cheng and Professor Andreas Kjær).

^{64}Cu-DOTATATE PET

Prospective study of 112 neuroendocrine tumor patients published in the Journal of Nuclear Medicine

Andreas Kjær

Results from the prospective study using ^{64}Cu-DOTATATE PET/CT in 112 neuroendocrine tumor patients were presented by Professor Andreas Kjær as a plenary lecture at the 2015 Annual Meeting of ENETS in Barcelona, Spain.

As part of our program for development of new PET tracers, we published in 2012 first-in-humans data from 14 patients using ^{64}Cu-DOTATATE, a new PET tracer for neuroendocrine tumors targeting somatostatin receptors.

The advantages of ^{64}Cu-DOTATATE include low-energy positrons and a physical half-life of 13 hours. These properties translate into a high spatial resolution and a wide time-frame for image acquisition. Results from these first patients were encouraging with substantially more foci detected by ^{64}Cu-DOTATATE compared to ^{111}In-DTPA-octreotide.

This led us to initiate a larger prospective study enrolling 112 patients over more than one year. All patients underwent both a ^{64}Cu-DOTATATE PET/CT and an ^{111}In-DTPA-octreotide SPECT/CT scan to allow for head-to-head comparison. Follow-up was undertaken for 42-60 months to determine if discrepant findings could be categorized as true or false.

In brief we found that patient-based, ^{64}Cu-DOTATATE PET/CT had a higher diagnostic sensitivity and accuracy than ^{111}In-DTPA-octreotide SPECT/CT. Lesion-based, more than twice as many foci were identified by ^{64}Cu-DOTATATE compared to ^{111}In-DTPA-octreotide. Follow-up in general proved most of the additional lesions detected only by ^{64}Cu-DOTATATE to be true positive and none were false positive.

The study was published in the Journal of Nuclear Medicine in 2015 and presented as a plenary lecture at the European Neuroendocrine Tumor Society (ENETS) annual meeting in Barcelona, Spain.

The development and testing of the new tracer was headed by Professor Andreas Kjær and undertaken as a multidisciplinary collaboration within the European Center of Excellence for Neuroendocrine Tumors at Rigshospitalet and with DTU.

CIMBI

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

We appreciate the excellent collaboration 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.

The focus of the research program is neurobiology, physiology and pathophsiology, molecular imaging and neuroreceptor ligands with focus on the serotonergic system.

https://cimbi.dk/

Professor Liselotte Højgaard received: "Chevalier d'lordre de la legion d'honnour" from the French ambassador to Denmark, Francois Zimeray

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 degreee at bachelor and master level. The first masters graduated in 2008. You can read more about the program at www. medicin-ing.dk.

At present several 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.

A warm thank you to Professor Jørgen Arendt Jensen, Associate Professor Kaj-Åge Henneberg, Professor Jens E. Wilhjelm, DTU and Associate Professor Bente Stallknecht and Associate Professor Tine Alkjær Eriksen, University of Copenhagen, for their great effort and our fine collaboration both on education and research.

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Research Foundation

Professor Liselotte Højgaard is Chair of the Board of the Danish National Research Foundation. The board members are end 2015: Professor Liselotte Højgaard, Professor Eivind Hiis Hauge, Professor Eero Vuorio, Professor Dr. Bart De Moor, Professor Chistina Moberg, Professor Morten Overgaard Ravn, Professor Minik Rosing, Professor Jesper Ryberg and Professor Anne Scott Sørensen.

The Danish National Research Foundation (DNRF) is an independent organisation established by the Danish Parliament in 1991 with the objective to promote and stimulate basic research at the highest international level at the frontiers of all scientific fields. The Center of Excellence (DoE) program is the main funding mechanism together with the Niels Bohr professorships. Since 1991 the Foundation has commited itself to support Danish Research with more than 6 billion DKK (≈ 800 mio €).

The Center of Excellence is the primary funding mechanism and the Foundations' flagship. A center grant is large and flexible, and a center may have a lifetime up to 10 years. Only top researchers with the most ambitious ideas will be awarded a CoE through fierce competition involving af two-stage application process. The objective of the CoE program is to strengthen Danish research by providing the best possible working conditions and organisational setup for selected top researchers. Centers may be established within or across all fields of research. A total of 100 Centers of Excellence have been established so far, and a new generation of 12 centers are up and running by the 1st of January 2015 as a result of the 8th application round. The DNRF also has the Niels Bohr professorships.

In 2013 DNRF was evaluated by an international panel leader by Dr. Wilhelm Krull, Secretary General of Die Volkswagen Stiftung. The outcome was very positive and showed that the DNRF CoE's are on level with the very best researches in the world. The outcome was very positive, and a continuation of DNRF was recommended to the Danish Parliament and Government. The Danish Parliament gave the Foundation 3 bio DKK on the State Budget for 2015 to secure the Foundation to 2036.

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
» 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

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