Department of Nuclear Medicine

Chair of Clinical Nuclear Medicine

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Research focus
- Imaging and physics research group
- Molecular imaging and radiochemistry

Structure of the Department

Professorships: 2
Personnel: 45
- Doctors (of Medicine): 9
- Scientists: 10 (thereof funded externally: 4)
- Graduate students: 9

Clinical focus areas
All currently available diagnostic and therapeutic procedures of this specialty

Research

The research of the Chair of Clinical Nuclear Medicine is methodologically oriented. This involves the development of innovative hard- and software of imaging systems together with industrial partners as well as that of new radiopharmaceuticals in cooperation with the Department of Chemistry and Pharmacy at FAU.

Imaging and physics research group
PI: Dr.-Ing. P. Ritt
Advances in medical imaging have led to numerous modalities for observing the functions and structures of the human body. In the field of nuclear medicine, imaging aims to depict specific metabolic processes as well as expression and biological activity of proteins. To accomplish this goal, the distribution of radioactive tracers in the human body is measured. Images are formed by detecting the emissions of these substances as they decay (e.g. gamma photons or positrons), using SPECT (Single-Photon Emission Computed Tomography) and PET (Positron Emission Tomography) systems. The diagnostic confidence of PET and SPECT for certain radiotracers may be increased if they are combined with modalities which image anatomical features, such as CT and MRI. These so-called multimodal devices (SPECT/CT, PET/CT, PET/MRI) represent the cutting edge in medical imaging.
In addition to imaging, the field of nuclear medicine is also responsible for therapies using liquid radioactive substances. These treatments are often applied in oncological cases and involve radiopharmaceuticals which lead to local irradiation of specific tissues in the body. The type and quantity of the radioactive substance employed are individually chosen for each patient. For the assessment of risk and benefits of a treatment, it is of great importance to determine the dose of ionizing radiation to tumor and organs as accurately as possible (dosimetry).
The focus of the imaging and physics group is the development of imaging in nuclear medicine and the improvement of image-based dosimetry.
The group has worked on the following topics during the period covered in this report:
- Absolute quantification in Tc-99mand Lu177-SPECT/CT

In SPECT, image quality is dependent on several factors, including photon attenuation, photon scatter, the partial volume effect, and motion artefacts. These variables confound the capacity of SPECT to quantify the concentration of radioactivity within given volumes of interest in absolute units, e.g. as kilobecquerels per cubic centimeter. In the last decade, considerable technical progress has been achieved in SPECT/CT imaging, which has led to a broader availability of absolute quantification capabilities. For this, absolute quantification is one of the hot topics in nuclear medicine and there is hope that it will lead to more inter-reader standardization and more accurate diagnoses. The group aims at evaluating the possibilities and limitations of this new technique, especially for application in dosimetry.
- Data-driven tracking of respiratory motion in SPECT/CT

SPECT imaging is vulnerable to blur and artifacts caused by respiratory motion occurring during respiratory cycles shorter than typical projection dwell times. In order to overcome artifacts due to respiratory motion, a number of methods have been proposed that seek to subdivide the acquisition into time bins, or gates, during which motion is small. Individual gates may then be reconstructed and evaluated separately or used to produce a single motion-corrected reconstruction. Critical to each approach is a surrogate signal describing the respiratory state over time that can be used to drive the gating process. The imaging and physics group developed a data-driven method for extracting a respiratory surrogate signal from SPECT list-mode data without the need for costly external sensors. The approach is based on dimensionality reduction with Laplacian Eigenmaps. Using this technique, the bias resulting from respiratory motion and methods for correcting the motion are evaluated.
- Multi-modal reconstruction of SPECT data

Multimodal devices, such as SPECT/CT, PET/ CT, and PET/MRI, routinely use data from an anatomical imaging modality (CT, MRI) for correction of scattered and attenuated photons in the reconstruction of the emission data. Lately, approaches that feature deeper integration of anatomical information into reconstruction have been developed. For example, anatomical images can be used to constrain the reconstruction of the spatial position of radioactive sources to the tissue types that are common for the specific radio-tracer. The research group helps in refining this method further and expanding its use to a wider range of radiopharmaceuticals.
- Voxel-wise dosimetry for therapies in nuclear medicine

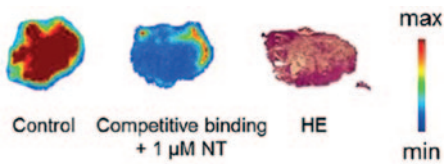
Conventionally, image-based dosimetry for nuclear medicine therapies is carried out for individual volumes of interest (VOI), such as organs or target structures like tumors. This results in a value of ionizing radiation dose (measured in units of Gray), which effectively is averaged over the entire VOI. Consequently, more refined information about the spatial distribution of the dose is not available, and techniques offering more detailed information, such as dose-volume-histograms known from external beam radiation, are not available. The research group develops methods for calculating dose values on a voxel level, e.g. by application of dose-voxel-kernels or by patient-individual Monte-Carlo simulations of radiation transport.
The imaging and physics group has cooperations with multiple companies and institutes, including the Pattern Recognition Lab (Faculty of Engineering), Siemens Healthineers (Molecular Imaging), and Progenics Radiopharmaceuticals. During the period covered in this report, selected research projects were supported by Siemens Healthineers and Progenics Radiopharmaceuticals.

Molecular imaging and radiochemistry
PI: Prof. Dr. O. Prante
Diagnostic nuclear medicine images the distribution of radioactively labeled substances within the body of patients. This distribution is a consequence of the interaction of the radiopharmaceuticals with functionally relevant proteins. By visualizing this interaction and thus expressing

and activating the proteins, nuclear medicine can bridge the gap between molecular biology and clinical imaging and can correlate imaging results to the specific reason of disease or metabolic disorder. Following this idea and the use of molecular tracers in functional imaging, the term molecular imaging has recently been implemented in this field of research.

The main research foci of the Professorship of Molecular Imaging and Radiochemistry are the development of new radiochemical labeling methods for the production of radiopharmaceuticals, the preclinical evaluation of novel radiopharmaceuticals *in vitro* and *in vivo*, and the translation of new radiotracers into the clinic for patient application. Important recent examples for these projects are the development of new and mild labeling techniques via F-18-fluorophenylazacarboxylate, the development of new F-18-labeled glycoconjugates and Ga-68- and Lu-177-labeled ligands for the neurotensin receptor (NTS1) and for the neuropeptide-Y receptor (Y1R). We were successful to evaluate the first F-18-labeled antagonist radioligand for the *in vivo* detection of mammary carcinoma and to study new D3-subtype selective radioligand for the detection of D3 receptor in the brain using preclinical animal models. These projects were supported by the DFG and were performed in close cooperation with the Chair of Pharmaceutical Chemistry (Faculty of Sciences). The development of all new radiotracers has been intensively supported by small animal PET imaging studies. Moreover, the radiopharmaceutical research projects are supported by the Emerging Field Initiative of the FAU.

The GMP radiopharmacy of the clinic has the approval for the production of radiopharmaceuticals according to §13, AMG (Medicinal Products Act). Based on the translational research efforts, new radiopharmaceuticals, such as Tc-99m-MIP-1404 or Ga-68-PSMA-11 for the diagnosis of prostate cancer, have been introduced into the clinic. In the future, various new radiopharmaceuticals will be available for clinical use within the Department of Nuclear Medicine.



Evaluation of specific binding of new radiopharmaceuticals for the neurotensin receptor (NTS1): The binding of a Ga-68-labeled NTS1 ligand on tumor tissue slices (left: Control) is diminished in the presence of neurotensin (NT; middle: Competitive binding). Right: histological HE-staining of the same tumor tissue

Teaching

The head of the Department teaches nuclear medicine to students of Medicine. Furthermore, the head of the Department organizes the course on radiation safety for students of the degree program Molecular Medicine. He also participates in teaching physiology, pharmacology, and Medical Process Management. In a broad fashion, the head of the Department performs postgraduate teaching for physicians in Middle and Upper Franconia. The Professor for Molecular Imaging and Radiochemistry offers practical trainings for students of Molecular Medicine and provides lectures for students of degree program Molecular Sciences of the Faculty of Sciences.

The Department supervises Bachelor's and Master's theses as well as MD and PhD theses.

Selected publications

Reinfelder J, Kuwert T, Beck M, Sanders JC, Ritt P, Schmidkonz C, Hennig P, Prante O, Uder M, Wullich B, Goebell P. First Experience With SPECT/CT Using a 99mTc-Labeled Inhibitor for Prostate-Specific Membrane Antigen in Patients With Biochemical Recurrence of Prostate Cancer. Clin Nucl Med. 2017, 42(1):26-33

Maschauer S, Einsiedel J, Reich D, Hübner H, Gmeiner P, Wester HJ, Prante O, Notni J. Theranostic Value of Multimers: Lessons Learned from Trimerization of Neurotensin Receptor Ligands and Other Targeting Vectors. Pharmaceuticals 2017, 10(1):E29

Keller M, Maschauer S, Brennauer A, Tripal P, Koglin N, Dittrich R, Bernhardt G, Kuwert T, Wester HJ, Buschauer A, Prante O. Prototypic 18F-Labeled Argininamide-Type Neuropeptide Y Y1R Antagonists as Tracers for PET Imaging of Mammary Carcinoma. ACS Med Chem Lett. 2017, 8(3):304-309

Wetzl M, Sanders JC, Kuwert T, Ritt P. Effect of reduced photon count levels and choice of normal data on semi-automated image assessment in cardiac SPECT. J Nucl Cardiol. 2018, Apr 13

Schmidkonz C, Cordes M, Schmidt D, Bäuerle T, Goetz TI, Beck M, Prante O, Cavallaro A, Uder M, Wullich B, Goebell P, Kuwert T, Ritt P. 68Ga-PSMA-11 PET/CT-derived metabolic parameters for determination of whole-body tumor burden and treatment response in prostate cancer. Eur J Nucl Med Mol Imaging. 2018, 45(11):1862-1872

Schmidkonz C, Cordes M, Beck M, Goetz TI, Schmidt D, Prante O, Bäuerle T, Cavallaro A, Uder M, Wullich B, Goebell P, Kuwert T, Ritt P. Assessment of Treatment Response by 99mTc-MIP-1404 SPECT/CT: A Pilot Study in Patients With Metastatic Prostate Cancer. Clin Nucl Med. 2018, 43(8):e250-e258

International cooperations

A.H. Vija, PhD, Siemens Molecular Imaging, Hofmann Estates: USA

A. Opanowski, Progenics Pharmaceuticals, New York: USA

Dr. R. Haubner, Department of Nuclear Medicine, Medizinische Universität Innsbruck, Innsbruck: Austria

Prof. Dr. M. Pomper, Johns Hopkins University, Baltimore: USA

Prof. Dr. P. Cumming, Queensland University of Technology, Brisbane: Australia