INTRODUCING FELLOWSHIP PROGRAMS

Introducing Fellowship Programs: Cardiovascular Nuclear Imaging at Hannover Medical School, Germany

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Abstract

The Department of Nuclear Medicine at Hannover Medical School (MHH), Germany, accepts international research fellows in Cardiovascular Nuclear Imaging at any time, depending on pre-existing experience, scientific track record and availability of external funding. The program, which is introduced in this article, covers both preclinical as well as clinical projects, with a focus on translational molecular imaging. Work may be conducted in the areas of radiotracer development (radiochemistry), imaging technology development, imaging of basic systems biology and/or mechanistic clinical studies. Research projects typically relate to the major cross-sectional research areas of MHH in the fields of immunology/inflammation, biomedical device technology, regeneration and transplantation.

Keywords: Molecular imaging, Translational imaging, Positron emission tomography, Preclinical imaging, Radiotracer development, Postdoctoral fellowship
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Hannover Medical School (MHH) was founded in 1965 and is one of the leading university medical centers in Germany. It integrates clinical care in a 1500 bed supra-maximal care hospital and multiple high-end specialty outpatient services with a multi-disciplinary biomedical research campus, and with extensive teaching and training facilities for more than 3000 students enrolled in its medical school program.

The major cross-sectional research areas at MHH are in transplantation and regeneration, immunology and infection, and biomedical technology/implants. The multidisciplinary research community at MHH is extensively funded through its large clusters of excellence－"REBIRTH"（"from REgenerative BIology to Reconstructive THerapy"）and "H4A"（"Hearing for all"）－its coordinating role in both the German Center for Lung Research（DZL）and the German Center for Research in Infectious Diseases（DZI）, its "Integrated Research Area Transplantation"（"IFB-Tx"）, and multiple program project grants from the German Research Foundation（DFG）, the European Union（EU）and other funding institutions. External funding per professor at MHH is the highest among all German medical institutions, underscoring its leadership role in biomedical research.

Nuclear Medicine at MHH

Nuclear Medicine traditionally has been a key discipline at MHH, whereby it supports the clinical and research efforts of all areas of the academic institution while developing novel radiopharmaceuticals and imaging techniques that are translated from research into clinical practice. MHH is one of the birthplaces of Nuclear Medicine in Europe. It was among the first

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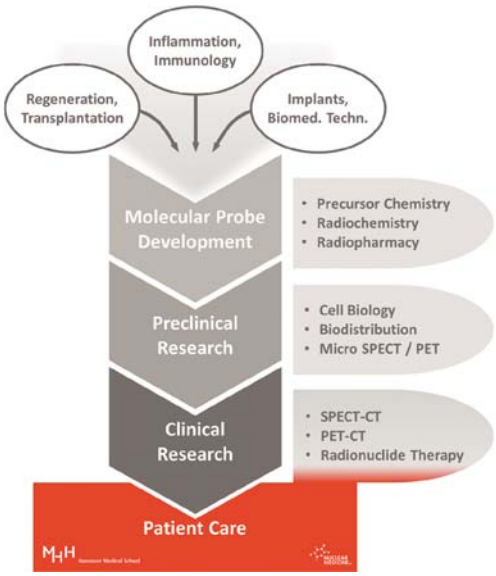

Fig. 1 Schematic display of research infrastructure in molecular imaging at MHH.

clinical centers to operate a medical cyclotron and a PET unit（established in 1976）, and among the earliest users of magnetic resonance imaging（established in 1983）. It has taken a leading role in establishing specialty training and founding national and European specialty associations. Based on strong partnerships with cardiology and cardiothoracic surgery, including one of the largest transplant programs in Europe, cardiovascular applications of Nuclear medicine have constituted a key area of both research and clinical services（1-7）.

The Department of Nuclear Medicine at MHH is currently building a translational framework for molecular imaging research（Fig. 1）. Interactive networking across multiple disciplines identifies biomechanisms that are relevant for major MHH cross-sectional research areas. Development of molecular probes for the respective biomechanism leads to initial preclinical application. When successful, the approach is further explored in the clinical setting before entering routine patient care. The infrastructure for this research is in place, and it is continuously updated with state-of-the-art technology.

Equipment

The department operates multiple sections which contribute to its clinical and scientific output:

Radiotracer development and production is conducted in the division of radiopharmaceutical chemistry. The division operates a 35 MeV cyclotron and extensive hot and cold lab space for handling of SPECT, PET and therapeutic radiopharmaceuticals.

The division of preclinical molecular imaging operates a high-resolution small animal PET/CT（Siemens Inveon®）and a SPECT/CT（GE SPECZT explore 120®）, equipped with cadmium-zinc-telluride（CZT）ring detector SPECT and a powerful CT capable of ECG- and respiratory-gating. It also includes an animal housing facility and lab space for small animal surgical and ex vivo techniques（biodistribution, autoradiography, microtome sectioning, histology）. The section contributes to early tracer development, but also provides services for institutional partners and conducts its own research in multiple mechanistic and drug development studies.

Clinical imaging is conducted in the PET center, which operates a Siemens Biograph mCT 128 Flow PET/CT scanner, equipped with an extended field-of-view time-of-flight PET, capable of continuous table motion, and a 128-slice CT. Routine clinical PET services employ the following tracers: ^{13}N ammonia, ^{11}C acetate, ^{11}C methionine, ^{11}C hydroxyephedrine, ^{11}C PK11195, ^{18}F deoxyglucose, ^{18}F fluoride, ^{18}F ethylthyrosine, ^{18}F DOPA, ^{68}Ga DOTA-TATE, ^{68}Ga PSMA I&T and ^{68}Ga pentixafor（CXCR4）. In parallel, the department operates conventional nuclear medicine services with 2 SPECT/CT systems（16-slice and 2-slice CTs）, 2 conventional gamma cameras and a CZT-detector-equipped dedicated cardiac camera（GE Discovery NM 530c）. Routine tracers for cardiac SPECT imaging include ^{99m}Tc based perfusion agents, In-111 labelled white blood cells and other cells, and ^{123}I MIBG. Radionuclide therapy is performed in a 12-bed inpatient ward, equipped with dedicated waste management.

The department is an international reference center and holds technology partnerships with Siemens in the area of PET, and with GE in the area of SPECT. Through these partnerships, it is continuously equipped with latest state-of-the-art technology.

Finally, MHH has recently started operation of the Clinical Research Center（CRC）Hannover, a dedicated research facility where clinical phase 1 and 2 trials, as well as mechanistic studies are performed. Within this environment, installation of a dedicated hybrid PET/MR scanner is planned for 2016. This will coincide with expansion of radiochemistry facilities through installation of a new cyclotron and a GMP-conform PET hot lab with 9 hot cells.

Cardiovascular nuclear medicine research－Basic philosophy

The cardiovascular nuclear imaging program pursues research along several lines. One focus is on the development and implementation of new imaging technology. This includes both solid-state-detector-ba-

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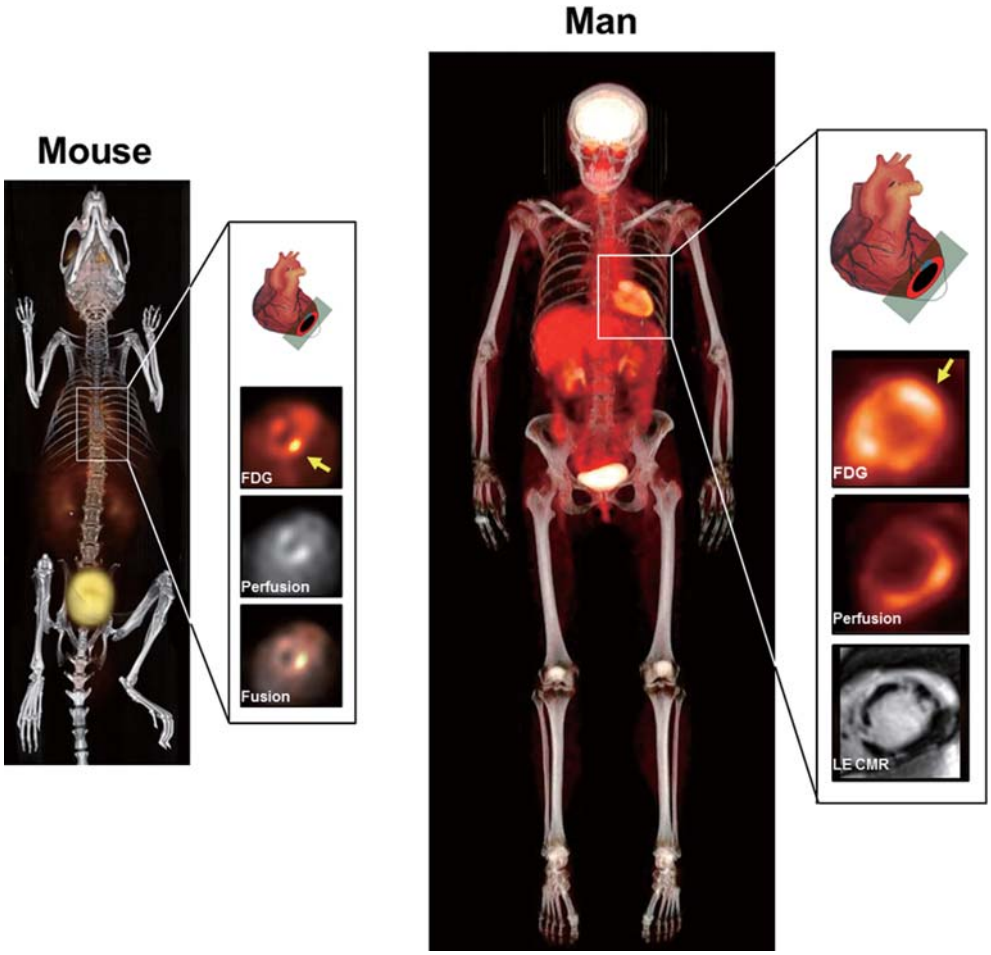

Fig. 2 Translational environment for cardiovascular nuclear imaging at MHH. Shown is the example of preclinical and clinical imaging of myocardial inflammation after acute myocardial infarction using ^{18}F deoxyglucose.

sed SPECT imaging and high-end listmode PET imaging, as well as the integration of SPECT/PET with CT in hybrid imaging systems. All technologies are available at the preclinical and clinical level, such that the full translational spectrum is covered. Recent projects in this area include the exploration of dynamic and multi-tracer imaging capabilities of CZT detector-based systems, dual cardiac- and respiratory-gated PET imaging, as well as motion-frozen fusion imaging of the myocardium, valves and coronary arteries（8）.

A second focus is on the exploration of novel molecular imaging probes to characterize the biology of the cardiovascular system. Novel targets and compounds are developed in close collaboration with basic scientists and radiochemists, and explored in the preclinical environment, with a strong focus on subsequent translation. Recent projects include the labeling of micro RNAs to monitor their therapeutic application（9）, the development of bacteria-targeted probes for imaging of infection（10）, and the development of folate receptor-based imaging agents to elucidate mechanisms of inflammation and for receptor-targeted shuttling of therapeutic agents（11）.

The third and major focus is on the implementation of biologic imaging techniques for specific monitoring of the effect of molecular- and cellular-targeted therapeutic interventions. For this purpose, close collaboration with various cardiobiology and cardiology groups has been established. Along the line of major MHH research areas, the primary goal of interventions is cardiovascular regeneration and inflammation（12）. Another major goal of this research is to establish a translational environment which enables the application of imaging both in a clinical scenario, as well as in a preclinical model of the same disease. Such an approach is thought to expedite progress in the joint development of image-guided cardiovascular therapy（Fig. 2）. A recent example is the development of cell tracking techniques（13）, and imaging of post-infarct inflammation, a potential target of novel therapies, which has been conducted in preclinical animals（14, 15）as well as in humans（16）.

Finally, once a novel tracer or technique is identified, the focus shifts toward clinical application in a pathway-based, cross-sectional manner. In essence, this focus means that the pathway targeted by the new approach is examined across organ barriers in multiple disorders, that the axis between multiple organs is studied, and/or that the effects of disease or therapy in one system is interrogated in other physiologic systems. A recent example is the determination of the effects of anti-tumor radionuclide therapy on the biology of atherosclerotic plaques（17）.

In summary, the focus on a translational environment, the joint development of imaging alongside novel therapies, and the pathway-based cross-sectional application of molecular imaging techniques are the key principles that are pursued in cardiovascular nuclear medicine research at MHH.

Program director

The fellowship program director, Frank M. Bengel, MD, FAHA, is also the director of the Department of Nuclear Medicine at MHH. He has longstanding expertise in preclinical and clinical cardiovascular molecular imaging and multimodality imaging. He also has a longstanding track record of mentoring international postdoctoral fellows. Under his guidance, his fellows have published numerous papers（15, 18-26）, won grants from German and international institutions, and won awards such as the Cardiovascular Council Young Investigator Award of the Society of Nuclear Medicine and Molecular Imaging（SNMMI）, the Young Investigator Award at the International Conference of Nuclear Cardiology（ICNC）, or the Melvin Judkins Award of the American Heart Association（AHA）.

Fellowship details

Acceptance for a postdoctoral fellowship is typically dependent on availability of funding, which may be secured through the applicant's home country or, alternatively, through German institutions（e.g. DAAD, Alexander-von-Humboldt-Foundation）or the EU（Marie Curie fellowships）. The fellow should have experience and a track record of successfully completed and published research in the field of cardiovascular imaging. Assistance is provided with regards to the research topic and supporting information. Length of stay is preferably a 2-year period to obtain maximum benefit. MHH may arrange on-campus housing for international fellows. An international office assists with acquisition of visas and work permits. Fluency in English is required; sufficient German skills are not necessary. There will be extensive networking opportunities on site－within nuclear medicine, across disciplines between departments, and translational between clinical and preclinical research－which should contribute to a stimulating and successful research tenure.

Conflicts of Interest

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