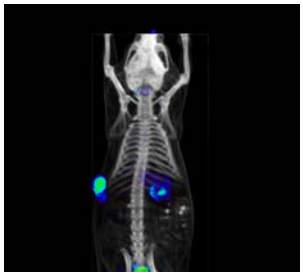
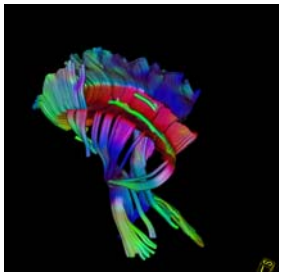
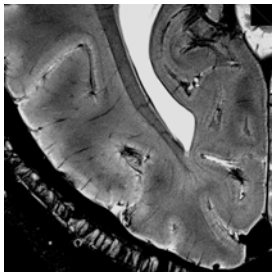
Lund University Bioimaging Center (LBIC)
Progress Report June 2010



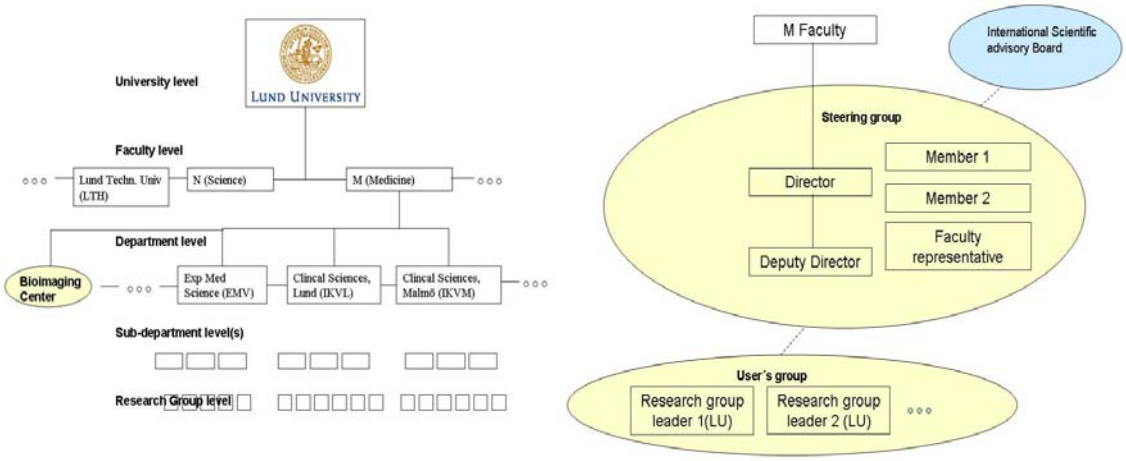
Lund University Bioimaging Center (LBIC)

http://www.med.lu.se/bioimaging_center

LBIC is a major trans-faculty bio-imaging center at Lund University (LU), combining knowledge in the fields of medical physics, preclinical and clinical medicine, chemistry, technology and applied mathematics in order to develop imaging methods for the advanced study of human morphology, cellular metabolism and physiological function in health and disease. The role of LBIC is to give researchers within as well as outside LU access to state-of-the art bio-imaging equipment and imaging procedures for translational (physical/technical, preclinical and clinical) research. Present core techniques supported by LBIC is Magnetic Resonance (MR) and Positron Emission Computed Tomography (PET) and present key applications lie within oncology and neuroscience. LBIC will be equipped for front-end bioimaging research in the fields of MRI and PET, as well as with selected supplementary imaging techniques, for experimental and human use.

Organization

LBIC was established as a center within the medical faculty at Lund University in autumn 2008, directly under the faculty leadership and in parallel with the faculty departments as shown in the figure below:



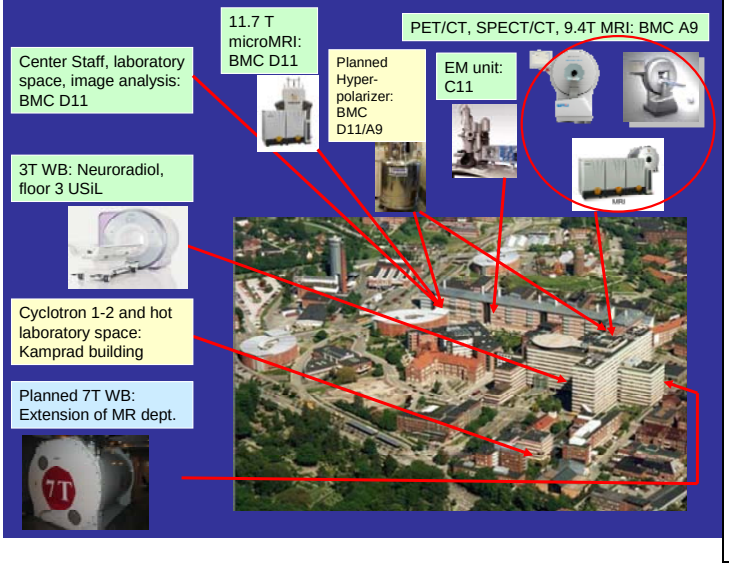
LBIC is led and coordinated by a steering group, where the competence reflects the different core imaging modalities within LBIC. The director and the deputy director represents competence in experimental (preclinical) and human imaging and shares the responsibility of center leadership. During 2011, we plan to establish a formal board.

Steering group 2010:
Prof. Freddy Ståhlberg (director); Prof. Deniz Kirik, EMV (deputy director); Prof. Sven-Erik Strand, IKVL; Assoc. prof. Isabella Björkman- Burtscher, IKVL; Prof. Ingemar Carlstedt (vice-dean, deputy director).

Equipment and Purchase Procedure

Subsequent to a major donation from the Knut and Alice Wallenberg foundation (40 MSEK, KAW 2007.0126), a purchase procedure led by the Lund university purchase and procurement department was initialized in late 2008 and finalized in mid-2009 (For step 1B spring 2010). With support also from other external funding sources up to a present total of approximately 65 MSEK, the two first major steps (1A-B, 2A-B) in LBIC is now being accomplished as described in the figures below.

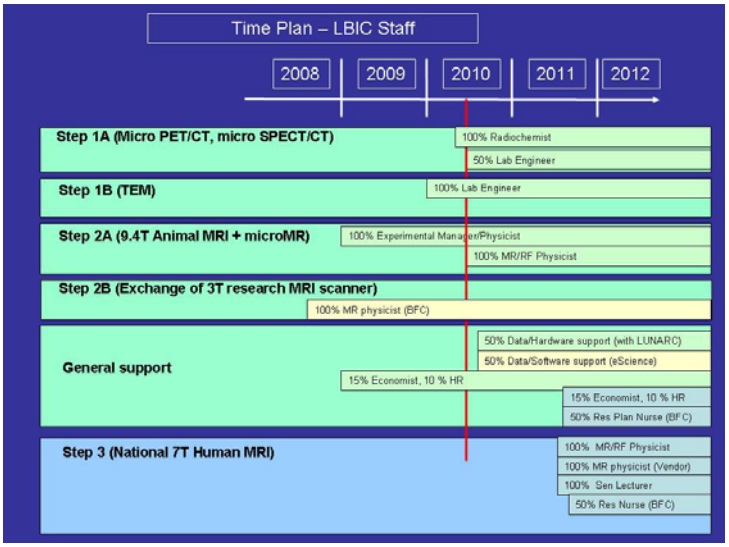
Step	PI	Equipment	Delivery	Funding
1A	Prof. Sven-Erik Strand	BioScan: Micro-PET/CT and Micro-SPECT/CT	October-November 2010	KAW, Kamprad, Lundberg and the Swedish Cancer foundations; Science faculty, LU; ALF, LU
1B	Prof. Ingemar Carlstedt	FEI: TEM (transmission electron microscope)	September-October 2010	The Crafoord foundation
2A	Prof. Deniz Kirik	Varian: 9.4 T Animal MR 11.7 T micro-MR	March-June 2010	The Knut and Alice Wallenberg foundation
2B	Assoc. Prof. Isabella Björkman-Burtscher	Siemens: Skyra 3T WB MRI	June 2010	The Knut and Alice Wallenberg foundation (50%), Region Skåne (50%)
3	Prof. Freddy Ståhlberg	7T MR	In planning phase	Planning grant VR/RFI



LBIC core steps (green):
As seen from the illustration to the left the two first major core steps in LBIC have passed the purchase procedure and are entering the delivery phase during 2010. Laboratory spaces include dry and wet labs and labs for image anlysis, the latter supported by a dedicated server system which is presently under installation.
Major rebuilding for steps 2A and 2B were finalized during spring 2010, while rebuilding for step 1A will take place during early autumn 2010. Initial rebuilding costs are part of the LU/M faculty cofunding, except for step 2B where funding is obtained from Region Skåne.
Related projects (yellow):
A combined clinical and research cyclotron was installed already 2005, and a second is planned for 2012 (Region Skåne) including a hot lab space for research (M faculty/LBIC).
A hyperpolarizer equipment for ^{13}C metabolic MRI/MRS is planned for 2011 (D Kirik, equipment grant VR/KFI).
Planned projects (blue):
As the third core step in LBIC, a national facility for human 7T MRI is presently in its planning phase (F Ståhlberg, planning grant VR/RFI).

Staff and human resources (HR)

As part of the co-funding from Lund University and the Medical faculty, we are building up the technical and administrative staff at LBIC according to the figure below:



During 2010, the core LBIC staff will increase to 5 full-time positions. In addition, one MR physicist is supported via ALF grants (F Stahlberg) and 50% software support is obtained in cooperation with the strategic research area eScience. Provided that step 3 is funded, we plan a staff expansion of 4 full-time positions.

At present, three PhD students are taking active part in the LBIC buildup phase, in particular with respect to step 1A. Furthermore, several researchers at the Medical faculty are associated with the stepwise buildup of LBIC, e.g. senior lecturers Matthias Mörgelin (1B), Prof. Pia Maly-Sundgren (2B) and senior lecturers Bo-Anders Jönsson and Catharina Sjögreen-Gleisner (1A).

Budget

The budget for LBIC covers costs for equipment, rebuilding, rent of laboratory space, staff costs and running expenses. While equipment costs are covered by external grants, initial rebuilding costs have been covered by a combination of co-funding from LU centrally and from the Medical faculty. Staff costs are similarly covered by co-funding from central LU- and from Medical faculty funding, while rental costs are presently (2010) and subsequent to application covered by the ALF system. Finally, a limited expense budget is applied yearly from the Medical faculty. While initial costs hence have been covered by a combination of external and internal grants, user fees will be used to successively cover an increasing part of the yearly LBIC running costs once the operational phases are entered.

Summary

LBIC is during 2010 entering its second full year of activity. During late 2008, LBIC was formally established, and during 2009 we focused on the purchase and rebuilding procedures. The major undertakings during the first part of 2010 have been equipment installation and staff recruitment. During the second half of 2010, the LBIC steering committee will develop routines for scientific evaluation of proposed projects, calculate reasonable user fees and establish an on-line booking system for LBIC equipment.
In parallel, during late 2010 we expect to enter the exciting operation phase for steps 1 and 2, and on the following pages a short overview of each step is given.

Step	PI	Equipment	Delivery	Funding
1A	Prof. Sven-Erik Strand	BioScan: Micro-PET/CT and Micro-SPECT/CT 	October-November 2010	KAW, Kamprad, Lundberg and the Swedish Cancer foundations; Science faculty, LU; ALF, LU

Step 1A: Micro-PET/SPECT/CT, related radiochemistry and in vitro analyses.

The overall objective is to provide a core facility/service platform for research groups and industries that need to develop novel molecular imaging probes and techniques for non-invasive detection of different diseases using microPET/SPECT/CT systems. The radiolabeling service at the radiochemistry lab and the techniques developed at this LBIC unit will allow investigations of the molecular, cellular, metabolic and physiological features of certain diseases.

Instrumentation

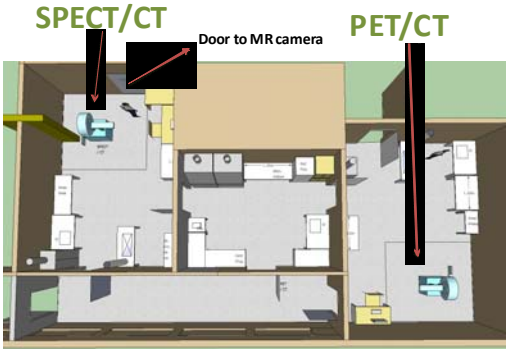
The LBIC laboratory Step 1A is to be equipped with a PET/CT (BIOSCAN NanoPET/CT) and a SPECT/CT (BIOSCAN NanoSPECT/CT) for in vivo imaging, with animal handling systems compatible with imaging in the MR unit. The SPECT/CT will have four detectors (two from the beginning) for highest spatial resolution and sensitivity. The PET instrument will have a spatial resolution of 2 mm, the SPECT of 300 µm and the CT of 10-150 µm.

Staff and associated researchers

PI for Step 1A is Prof Sven-Erik Strand. Present LBIC staff comprises one 100% employed Radiochemist/Researcher (Thuy Tran, MSc Pharm, PhD) and one 50% employed Medical Radiation Physicist for operating instruments and data analysis (Gustav Grafström, Ph.D). Associated researchers are senior lecturers Bo-Anders Jönsson, Lena Jönsson and Katarina Sjögreen Gleisner, all at Dept of Medical Radiation Physics.

Laboratory buildings

In the BMC building at floor A9 adjacent to the animal MR camera (Step 2A), rooms are rebuilt to accommodate the two cameras. In addition a room for handling radiopharmaceuticals and tissue samples is built. The work flow of animals to be imaged has been optimized in constructing the laboratory. A laboratory space at BMC D11 will include radiochemistry laboratory, radioactive cell laboratory, conjugation laboratory, auto-radiography laboratory, histology laboratory and a data evaluation/group meeting room.



Radiochemistry

Radioactive labeling of biomarkers, proteins, peptides and small ligands using a number of different radioisotopes (for example ^{125}I, ^{111}In, ^{18}F, ^{68}Ga); Optimization and quality control of the labeled substances regarding their labeling yields, stability and radiochemical purity; *In vitro* studies to follow the cellular processing (binding specificity, binding affinity, cellular characteristics of a certain labeled substance) and to follow the molecular features of the substance of interest.

Foreseen projects 2010/2011

The equipment has already been of great interest to many research groups in Lund/Malmö and even before we have the facility in operation several groups are in queue to start imaging. Proposed research projects include prostate cancer, breast cancer, arteriosclerotic plaque formation, neurodegenerative diseases such as Parkinson's and Huntington's decease.

Step	PI	Equipment	Delivery	Funding
1B	Prof. Ingemar Carlstedt	FEI: TEM (transmission electron microscope) 	September-October 2010	The Crafoord foundation

Step 1B: Electron microscopy (EM)

The overall research aim is to provide both the latest-state-of-the-art, as well as more routine facilities for electron microscopy users.

Instrumentation

The FEI Tecnai™ G2 Spirit BioTWIN transmission electron microscope at LBIC is a general-purpose, user-friendly instrument to be used in a multi-user core facility environment. It is designed for high resolution and contrast imaging and analysis of low contrast soft matter. It enables to explore the native state of low-contrast, beam-sensitive biological specimens, or other soft materials like polymers. Samples can be unstained or stained. It enables the 2D and 3D ultra-structure exploration of cells and cell constituents, as well as the morphology, chemical composition and function of natural or artificial materials. Low Dose observation of beam sensitive and cryo samples is a key performance aspect. The technique of Cryo-TEM enables visualization of frozen-hydrated thin film preparations of particles where dehydration and negative staining is undesired. The feature of electron tomography is of paramount importance to obtain high magnification and high resolution 3D information of cells and organelles or even smaller cell constituents.

Staff and associated researchers

PI for Step 1B is Prof. Ingemar Carlstedt. Present LBIC staff comprise one 100% employed research engineer (Lina Gefors). Associated researchers are senior lecturers Matthias Mörgelin, division of infection medicine and senior lecturer emeritus Eric Carlemalm.

Laboratory buildings

In the BMC building at floor C11 rooms are rebuilt to accommodate the instrument. As auxiliary equipment the facility will house a comprehensive preparation laboratory which includes a range of specialized sample preparation equipment, digital imaging facilities and computer workstations for image processing. Additionally, a somewhat older scanning electron microscope (Philips) is available at the present EM facility and will be moved to BMC, C11. Pending additional funding, it will be replaced by a modern state-of-art instrument.

Foreseen projects 2010/2011

The new EM equipment constitutes an essential research support to all other steps in LBIC, in particular step 1A. Furthermore, the present EM facility, which will be moved to BMC C11 when the new TEM microscope arrives, is actively involved in a wide range of research topics across the Medical Faculty and contributes to about 20 scientific publications per year in high profile biological journals. Major research areas that can be foreseen during the next year are: Bacterial infection and proteomics; host-pathogen interactions – primary adhesion, inflammation, innate immunity, biofilm; chronic obstructive lung disease (COPD), pulmonary fibrosis and extracellular matrix remodeling; intracellular signaling in diabetes and cancer.

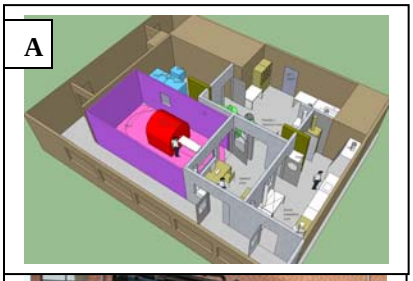
Step	PI	Equipment	Delivery	Funding
2A	Prof. Deniz Kirik	Varian: 9.4 T Animal MR 11.7 T micro-MR 	March-June 2010	The Knut and Alice Wallenberg foundation

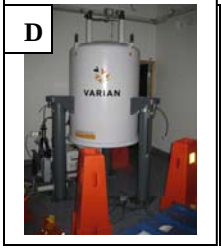
Step 2A: In vivo animal MRI and in vitro micro-MRI/MRS

The goal in this step is to establish the animal MR imaging and spectroscopic analysis facilities at the Biomedical Center in Lund University. The platform is envisioned as an open core facility and a competence center for advanced imaging techniques.

Instrumentation

We have a 30 cm bore size horizontal MRI system operating at 9.4 T, with gradient strengths between 300 mT/m and 1000 mT/m, allowing top quality imaging from small mice to rats and even rabbits or cats. The system has not only ^{1}H but also 2 additional channel X-nuclei imaging capabilities making it perfectly suited in a variety of experimental applications from neuroscience to oncology and stem cell biology. In addition, we have obtained an in vitro high-resolution micro-imaging system, which operates at 11.7 T and uses exactly the same software platform and thus will allow seamless transfer of experience and know-how between the two units.





Staff and associated researchers

PI for Step 2A is Prof. Deniz Kirik. Present LBIC staff comprise two 100% MR Physicists (Vladimir Denisov, PhD, experimental manager and Carina Dahlberg, PhD). Prof. Freddy Ståhlberg acts as associated researcher.

Laboratory buildings

Several rooms have been rebuilt to accommodate the systems in the BMC building on A9 (9.4T), adjacent to the PET/SPECT unit (Step 1A), and on D11. During this work, special attention has been paid to optimizing animal handling routines within the unit and between the MR and PET/SPECT units. The laboratory space at D11 will also include RF coil lab and post-processing unit for modeling and image analysis.

Foreseen projects 2010/2011

We have entered into initial planning discussions with major preclinical research groups at LU (neurodegenerative disease), as well as with international collaborators, e.g. Arnaud Comment (EPFL, Lausanne), Philippe Hantraye (CEA, Paris) and Marcus Zweckstetter (MPI, Göttingen). We have also identified flagship projects driven from within core LBIC affiliated groups that will push the boundaries for new innovative ideas in MR imaging, including hyperpolarization-enhanced MR spectroscopy.

A) Lab overview, 9.4T facility in A9. Door on upper side enters to PET/SPECT facility (Step 1A). Experimental MRI as well as PET/SPECT equipment are integrated in the animal house at BMC A9;
B) Installation of 9.4T on March 31, 2010;
C) Interior view with animal lab and 9.4T;
D) Interior view of 11.7 T installation at D11.

Step	PI	Equipment	Delivery	Funding
2B	Assoc. Prof. Isabella Björkman-Burtscher	Siemens: Skyra 3T WB MRI 	June 2010	The Knut and Alice Wallenberg foundation (50%), Region Skåne (50%)

Step 2B: 3T MRI for neuro research

In 2001, Sweden's first 3T scanner was installed in Lund for 50% neuro research (funded by KAW), combined with 50% clinical operation (funded by Region Skåne). The goal of LBIC step 2B is to continue this successful research path by replacing this equipment and installing a new state-of-the art 3T scanner at the Dept. of Neuroradiology, Skåne University Hospital, Lund.

Instrumentation

The Siemens Magnetom Skyra 3.0T was, as the first equipment of its kind in Europe, delivered to Lund on June 2, 2010. The Skyra is a whole-body scanner with 70 cm bore size and a gradient system operating at 45mT/m@200µs. It has a digital RF system fully integrated in the magnet housing, 48 receive channels and it is prepared for parallel transmit technology (8ch Tx). The system utilize the TIM 4G coil technology and it will be equipped with 32-channel head-, 20-channel head&neck- and 32-channel spine-receiver coils. The tender includes a comprehensive research agreement supporting ongoing and future research activities within the field of neuroimaging and technical development.

Staff and associated researchers

PI for Step 2B is Assoc. Prof. Isabella Björkman-Burtscher. In cooperation with the Center for Imaging and Physiology (BFC) at Skåne University Hospital, Lund, MR physics support is provided by one 100% MR physicist. Associated researchers/groups are Prof. Pia Maly-Sundgren and Dr. Danielle van Westen, dept. of Neuoradiology and the MR Physics group at Lund University.

Laboratory Buildings

At the Dept. of neuroradiology, the old 3T scanner has been removed and the new system is recently installed into a comprehensive clinical surrounding including 11 trained neuroradiologists, one 64-slice CT and 2 angiography labs for interventional neuroradiology in close proximity and an additional 4 MRs and 4 CTs within the BFC organization.

Foreseen projects 2010/2011

The clinical MR research in Lund has, since 2001, been governed by a local MR council, selecting research projects based on scientific quality. Ongoing research which will be transferred to the new system in its operative phase comprises development of perfusion quantification techniques (DSC and time-resolved ASL), development of new biomarkers based on high b-value diffusion imaging and optimization of fMRI methods to extend their clinical use at 3T. Among clinical projects in our pipe-line are translational clinical research projects on Parkinson's disease, dementia and neuropsychology as well as psychiatry related projects in cooperation with basic and clinical neurosciences. Furthermore, research will focus on stroke and neurovascular disease as well as neuro MRI in the newborn.