Consortium meeting for the FMT-XCT project
“Hybrid Fluorescence Molecular Tomography and X-ray Computer Tomography system and method”

EU-FP7 grant agreement no. 201792

Munich, Klinikum rechts der Isar, Pavillon, April 24, 2009, 11 a.m – 18 p.m.

Participants for

1. HMGU (project co-ordinator)
   - Vasilis Ntziachristos
   - Ralf Schulz
   - Veronika Erben
   - Eric Söhngen
   - Marta Zientkowska
   - Angelique Ale
   - Saskia Björn
   - Thomas Jetzelfiener
   - Marcus Freyer
   - Tatjana Wunderlich
   - Irina Uhlig

2. CEA
   - Leti: Marco Bramilla
   - Lime: Anikitos Garofalakis

3. FORTH
   - Giannis Zacharakis

4. UCL
   - Simon Arridge
   - Vadim Soloviev
   - Tim Rudge
   - Josias Elisee

5. FIBGHM
   - Juan José Vaquero
   - Juan Aguirre

6. UZH
   - Florian Stuker
   - Katerina Dikaiou

7. VAMP
   - Holger Brünner

Chair of the meeting: Vasilis Ntziachristos

Minutes: Veronika Erben
Initially, Vasilis Ntziachristos welcomes all participants and introduces Veronika Erben, who talks about financial and administrative issues related to the project.

Veronika Erben, as the project manager, gives a short overview of the project, followed by notes related to the reporting and finishes with the list of deliverables and milestones for reporting period one and two. The most important points are:

- Since all documents (scientific and financial) required for the year one report arrived in time, the second rate of prefinancing will be transferred to all partners, presumably in May 2009 (exception VAMP: second rate prefinancing was already transferred). As soon as the European Commission (EC) transfers the first interim payment (=sum of costs claimed in Form Cs) to the Helmholtz Zentrum München (HMGU) the money will be transferred to all partners.
- The next consortium meeting (month 24=Feb. 2010) is planned in Herakleon, Crete. This meeting will be co-localized together with a workshop on free space FMT (mo24).
- A training session on XCT is planned as described in Annex1 (WP2 and WP9) and will be an opportunity of training in dual energy XCT. It should be housed by CEA-LETI at Grenoble in second part of June 2009.
- If there is a delay in deliverables, milestones or similar (compared to Annex 1) this is not problematic as long as it is stated in the report (clarified with Dr. Ingemansson, the responsible project officer at the European Commission).
- Time sheets are obligatory.
- A platform for data exchange between all partners will be established (already initialized).
- After submission of the first report to the European Commission and approval by the project officer Dr. Ingemansson, all partners/beneficiaries will receive the report.

Marco Brambilla (CEA-LETI) and Holger Bruenner (VAMP) together present the results of the first year within WP2, the XCT development.

- X-ray CT design (task 2.1): The XCT design (deliverable 2.1) was finalized in November 2008 and distributed to the consortium. This report fulfils most of the objectives of the task 2.7 « optimal XCT design », this was decided because of the (long) delivery time of the system key components.
- X-ray CT dual energy development (task 2.2): In order to help dual energy development and validation a on-bench CT at LETI has been built.
- The XCT prototype is now under development at VAMP. First parts have been constructed and others ordered. Transfer to HMGU is planned for the end of the year (mo 22= Dec. 2009).

Juan José Vaquero (FIBHGM) introduces the contribution of FIBHGM to WP2 (XCT Development), in particular the use of X-ray contrast agents, double exposure techniques and a dual energy X-ray source. Juan Aguirre (FIBHGM) presents the studies performed required for manufacturing physical phantoms that will be used for FMT-XCT system validation (WP8).

**Consortium decision on phantom design:**

- Cylinder (bulk material resin) with different size insertions (open capillaries).
- There will be some initial phantoms circulated among the partner. According to the feedback of the partners, phantoms will be modified.
- With regard to standardization, imaging results obtained in different labs will be compared.
Giannis Zacharakis (FORTH) presents the progress of WP3 (Theory for 360 degree FMT) during year one:

- An inversion method for FMT based on boundary removal and back-propagating the data has been developed and is available to all partners (Objective 3.1).
- A direct inversion method based on reconstruction in Fourier space has been developed and is also available to all partners (Objective 3.2).
- The direct inversion has been tested and compared with the standard methods and proved to be significantly faster when a large number of sources has been used. However, for small number of sources as in the case of FMT acquisitions, it does not give satisfactory results (Objective 3.3).
- A multispectral algorithm has been developed and tested for simultaneous detection of multiple fluorophores and absorbers. It will be incorporated in the FMT software in the next reporting period according to the time schedule (Objective 3.4).
- A user-friendly software has been developed under Matlab and Labview environments, enabling users to analyze experimental data and visualize results in a fast and efficient way (Objective 3.5).
- A large number of experimental measurements have been acquired that are available to all partners for optimization and finalization of algorithms. These measurements involve phantoms as well as in vivo experiments (Objective 3.6).
- A decision has been made to start a new Deliverable “Ultra – fast Inversion for FMT” that will be delivered on the next reporting period.

Simon Arridge (UCL) introduces the department of Computer Science at the University College London and describes the progress towards objectives within WP4 (FMT inversion with image priors).

- Structured priors orientating the reconstructed FMT images to have level sets parallel to those of XCT image and theoretic priors orientating the reconstructed FMT images to have maximum joint entropy with the XCT image were developed. Initial tests on simulated 3D images of mouse from a realistic atlas were performed (Objective 4.1).
- Segmentation of XCT based on anisotropic diffusion (Peronal-Malik algorithm) and hexahedral adaptive mesh generation from XCT images were developed. Mesh reduction methods using public-domain software ISO2MESH were incorporated and Boundary Element (BEM) and hybrid Boundary-Finite Element (BEM-FEM) methods were developed (Objective 4.2).
- A Non-linear reconstruction method for attenuation making use of Louiville transformation from diffusion to Schrodinger equation was developed (Objective 4.3).
- A combined reconstruction/segmentation method combining Gauss-Newton image reconstruction with fuzzy-kmeans image classification and a fully hierarchical Bayesian framework was developed (Objective 4.4).
- A workshop “Image reconstruction algorithms and the use of priors” is planned for September 2009 in London.

Ralf Schultz (HMGU) describes the progress within WP5 (FMT-XCT integration), which focuses on the development of a 360 degree hybrid FMT-XCT imaging system.

- According to schedule a 360-degree functional FMT prototype was developed.
- The XCT module, developed within WP2, will be integrated into a hybrid imaging system at the end of the year (mo 22= Dec. 2009).
- A FMT-XCT prototype, based on a commercial XCT (General Electric (GE) Locus Preclinical µCT Scanner) system in which imaging at two wavelengths is supported was developed.
- First in vivo studies are already on-going ahead of schedule.
Anikitos Garofalakis (CEA-LIME) describes the animal models and fluorescent probes, which have been established at CEA-LIME within WP6 (Cancer imaging with focus on breast cancer):

- **mammary tumor xenografts:**
  - MDAMB-231 human breast adenocarcinoma cells over-expressing MT4-MMP, a metalloproteinase which does not affect in vitro cell proliferation or invasion but strongly promotes primary tumor growth and associated lung metastases in RAG-1 immunodeficient mice 8 weeks post-injection.
  - primary cell cultures from human tumors that either express or do not express erb-B2, the target of trastuzumab (Herceptin®), a monoclonal antibody used in breast cancer chemotherapy.

- **mammary tumor transgenic mice models:**
  - CEA-LIME has bred a transgenic strain of mice expressing the polyoma middle T oncprotein (PyMT), under the control of the mouse mammary tumor virus long terminal repeat (MMTV LTR). These mice develop breast cancer with four distinct stages of tumor progression, from premalignant to malignant stages.

- **Probes :**
  - commercial probes (Angiosense 680, Superhance 680)
  - home-made probes (Trastuzumab, Aptamers)

One breeding accident with the PyMT mice has delayed partly the programme with these animals.

Florian Stuker (UZH) presents the work of Steffi Lehmann, illustrating the feasibility of hypoxia-inducible factor (HIF) stabilization and activity in tumor cells, performed within WP7 (Imaging cancer therapy for enabling intervention), and subsequently describes the development of a new MRI-FMT system.

- Multiple reporter assays for measurement of HIF pathway activity were developed.
- HIF1α activity by expressing firefly luciferase under the control of the HIF-responsive element HRE identified as most promising readout for fluorescence imaging.
- Tumor cells (C51 colon carcinoma) have been transfected using the HRE constructs and injected subcutaneously in nude mice. In vivo imaging has been performed.
- Initial FMT experiments with protease imaging in tumor models were performed.
- The development of the MRI-FMT system is based on:
  - Setup design without fibers,
  - Free beam illumination and point grid scan,
  - Detector operation inside the magnet,
  - Investigation of the interaction between the modalities.

Munich, 05 May 2009

Vasilis Ntziachristos