Euro-BioImaging

European Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences

WP9
Access to Innovative Technologies – Medical Imaging

Deliverable 9.3
Summarizing report on emerging technologies in medical imaging with potential and demand for access

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1 Executive Summary

Work package 9 “Access to Innovative Technologies – Medical Imaging” is aiming to provide access to novel medical imaging methods in Europe for biological and medical researchers. Important steps towards the achievement of this goal are the identification of emerging imaging technologies, the evaluation of their maturation level, the determination of needs and requirements to provide user access to these technologies, the organization of the respective scientific communities, and the evaluation of the user demand.

Important and quickly developing modalities, such as ultra-high field MRI or combined MR-PET, had already been identified at the onset of Euro-BioImaging and are becoming commercially available at high investment costs. A small number of research institutions are currently operating these modalities, continue their technical development, and at the same time have demonstrated their high potential for application in clinical science and basic research in humans. Therefore, these modalities are in high demand that is not met by the currently available resources (see D9.5 Report on infrastructure survey). Due to the high scientific relevance and the high user demand, these modalities are proposed to be included in the Euro-BioImaging infrastructure.

Phase contrast X-ray imaging (PCI) had also been identified at the start of Euro-BioImaging. This technology is not yet commercially available but first research systems have demonstrated the high potential to provide added information that is not available with current CT systems. In addition, first clinical research studies have successfully been performed using PCI. At the current level of development, PCI is a high potential medical imaging modality that should be included in the Euro-BioImaging infrastructure with very few nodes during the construction phase that may be extended during later operation.

Further modalities that have been identified during the first half of the preparatory phase of Euro-BioImaging are combined MEG and ultra-low-field MRI (MEG-MRI), magnetic particle imaging (MPI) and electron paramagnetic resonance imaging (EPRI). The technology for these modalities is still under development and it has been demonstrated that they can provide novel and interesting insights into the human body. First installations have shown the general feasibility of the methods and applications for clinical imaging or clinical research have not been fully evaluated. Very few of these systems exist across Europe or funding for very few installations has been secured. These technologies are at an early stage and will require not only further technology development but also research into possible applications in order to be of general interest to the European researchers.

2 Introduction

This report is reviewing the current status of the various emerging medical imaging technologies that have been addressed by WP9 up to date. The respective communities are still small and thus European rather than national representatives have been asked to provide information about the organization of these communities, the development of the modalities, and the level of implementation. During the Euro-BioImaging Stakeholder Meetings and during meetings within the respective communities, information about Euro-BioImaging has been disseminated and feedback in the form of reports has been sent to the WP9 coordinators. In addition, the results of the Euro-BioImaging infrastructure survey have been taken into consideration as well as the provider and user interest in the proof-of-concept studies. Finally, the level of maturation of the modalities and their current application in clinical and basic science has been considered.

Despite our best effort, we are aware that this report cannot represent the view of all researchers involved and that the selection of modalities may not be complete. It may be in the nature of this process that those modalities that are represented by active communities are more likely to be noted. However, WP9 will continue to be open for emerging and future technologies that can serve as tools for biomedical research. Before inclusion of emerging imaging technologies in Euro-BioImaging, they will need to be tested for their robustness in technical feasibility studies under the service conditions of open user access, e.g. similar to the Proof-of-Concept studies conducted in 2012 by Euro-BioImaging.

The main objectives of this report are therefore:

- Present the state of development of the selected emerging imaging technologies.
- Estimate the current availability and demand.
- Review the demonstration of the feasibility of providing open pan-European access.

3 Presentation of the emerging medical imaging modalities

3.1 UHF-MR

Ultra-high field human MRI (7 tesla and higher) has been included into the emerging imaging modalities from the beginning of the Euro-BioImaging project. During approx. the last 5 years UHF-MR has developed from very few highly experimental systems to a research modality with clear benefits for a number of applications in human subjects. Basic science as well and clinical science is benefiting from the increased sensitivity of UHF-MRI leading to higher spatial resolution, reduced scan times, higher contrast and/or higher detection sensitivity of brain activation or metabolite concentrations. Despite the fact that these systems are now commercially available, their costs remain very high and a number of technical challenges are still to be solved, including image inhomogeneities due to short radiofrequency wave length, high specific absorption rate and magnetic field inhomogeneities that limit the applicability of the technology to targeted body regions and image contrasts.

The UHF-MR community in Europe is well informed about the Euro-BioImaging project and has held meetings on several occasions (see also D9.1). According to the Euro-BioImaging infrastructure survey, UHF-MR is in very high demand in particular in the best developed countries within Europe while in other parts of Europe, lower field MRI (3 tesla) is also highly requested. During the proof-of-concept studies, UHF-MR contributed the largest number (6 of the approx. 15 installations in all of Europe) of infrastructure providers in medical imaging (6 of in total 11 providers in WP9 and WP10) and has received the largest number of applications in medical imaging (14 of 25). In contrast to this demand, currently most UHF-MRI centers cannot provide regular open access to their infrastructure due to insufficient resources.

A number of countries are already preparing to include UHF-MRI in the Euro-BioImaging infrastructure and funding for access to these modalities has been allocated in a few countries. Depending on their successful evaluation during the Euro-BioImaging open call for nodes, the sufficient European user demand and the financial support for their implementation, it is possible that several complementary UHF-MRI nodes will be integrated in the Euro-BioImaging infrastructure. The UHF-MRI centers specialize in different aspects of imaging as well as providing access to different technical innovations and research applications. In addition, as the modality is still under rapid development and not fully mature, access to new technology developments by the Euro-BioImaging UHF-MRI nodes would profit from coordination, if multiple nodes exist. In addition to the central access coordination, this could be achieved by a technology coordinator who would be incorporated into the executive structure of the European hub.

3.2 MR-PET

With the recent introduction of PET/MRI as preclinical and clinical hybrid imaging modality, there is increasing interest throughout Europe to include this technique as scientific infrastructure in academic institutions. Germany invested considerably in PET/MRI technology by providing DFG-funds for the purchase of 4 integrated PET/MRI units in Munich, Tübingen, Leipzig and Essen. In addition, integrated systems have been or will be installed in the near future in London, Napoli and Lyon. 2 PET/MR scanners using separated PET and MR gantries have been installed at the Helmholtz Institute in Rossendorf/Germany and at the University of Geneva and will be available in Barcelona. A number of countries are planning to include PET/MRI in the Euro-BioImaging infrastructure to meet the expressed

interest of the European academic imaging community. Preclinical work using PET/MR has been pioneered by the University of Tübingen, where a large preclinical multimodal imaging laboratory has been established. The European PET/MRI activities have been successfully networked within the last year. The growing PET/MRI community is well aware of the Euro-BioImaging initiative and has organized several meetings (Tübingen, Barcelona, Elba) to initiate a European network concentrating on the successful application of PET/MRI in translational and clinical research. It was felt, that training of technologists and scientists is of upmost importance for the introduction of this new technique. Workshops are planned in Tübingen, Munich, Barcelona and Geneva to provide platforms for teaching, training and scientific exchange. In Germany, a registry of PET/MRI examinations in oncology has been started including also sites in Geneva and London. Part of the DFG PET/MRI initiative is also the availability of imaging time on the funded PET/MRI installations for external researchers from Germany and abroad. At the PET/MR sites in Munich and Tübingen fellowships have been organized to provide specific training for scientists, clinicians and technologists. It is expected that specific PET/MRI sites will focus on defined research projects in neuroscience, oncology and cardiovascular medicine. The PET component needs the availability of radiopharmaceutical production close to the PET/MRI facilities. Therefore the proposed nodes for PET/MRI imaging need to be closely interlinked with cyclotron and GMP facilities within the European network. It is expected, that such integrated MRI-PET facilities will be extremely attractive for cooperation with pharmaceutical industry. It is thus proposed to include MR-PET in the Euro-BioImaging infrastructure as integrated multi-modal nodes with specific expertise and focus after demonstration of the technical feasibility. Similar to UHF-MR, coordination of multiple MR-PET nodes as part of the pan-European research infrastructure could be achieved by a technology coordinator who would be incorporated into the executive structure of the European hub.

3.3 PCI

Phase Contrast Imaging is an X-ray imaging modality that exploits not only the absorption properties of material but also the diffraction that leads to phase changes of the transmitted X-ray beam. This allows a much larger contrast range in X-ray imaging with previously unseen soft tissue contrast and very high spatial resolution. Technical challenges include the need for a coherent high intensity X-ray source and phase sensitive detectors. PCI had been mentioned as an emerging medical imaging technology in the Euro-BioImaging proposal. At that time, it was a highly experimental technology that required access to a synchrotron radiation source. In the last few years, significant progress has been made in the field of PCI and besides a number of technological developments and proof of principle studies, even first clinical research studies have been performed demonstrating the high potential of this technology. In addition, the European PCI community has been very active in promoting the technology and organizing coordination and communication between the research centers. A first European Symposium of PCI has been held in 2012 with an overwhelming success of 100 participants that demonstrated the rapid development of this field. Despite this progress and success, PCI is still a technology under development and only 3 centers (in Germany, Italy and Switzerland) can offer this technology due to its high complexity and costs. Considering that the technology is not widely known to researchers, the results of the survey are positive and the only proof-of-concept site offering PCI had received 11 applications for research projects.

Due to its high potential and the relatively high demand, PCI is proposed to be included as a Euro-BioImaging modality. One or very few nodes should provide open access that may be expanded at a later stage.

3.4 MEG-MRI

The combination of magnetoencephalography and ultra-low-field MRI is a novel combined imaging method that is still in a very early stage of development. In contrast to high field MRI, the MR signal is not detected by RF-coils but with highly sensitive SQUID devices. Within an FP7 consortium, three different human MEG-MRI demonstrator systems have been developed and first images have been produced. This modality offers potential benefits over traditional MEG due to the simultaneous imaging capability. Although the signal to noise ratio of microtesla MRI is much lower than for conventional MRI, beneficial aspects arise, such as superior T1 contrast, no projectile forces, safe for implants, no acoustic noise, and superb registration of the MEG and MRI coordinate systems. This opens a number of potential scientific applications that have, however, not yet been explored. During the first half of the preparatory phase of Euro-BioImaging, MEG-MRI has been identified as an emerging medical imaging device that may provide methods for clinical diagnosis or basic research in the future. Due to the early stage of development and the lack of clinical research data, the focus will remain to be on technology development for some time to come. Due to the novelty of the modality it had not been included in the proof-of-concept study. Within Euro-BioImaging, MEG-MRI should be carefully followed. Given technological progress and stable operation of the systems, one or very few nodes could be established in the future.

3.5 MPI

Magnetic particle imaging is still under development, first commercial small animal instruments are expected to be installed in 2013, and the MPI-community is still under formation. First experimental systems have shown the technological potential of this new imaging modality in small animals. MPI therefore continues to be an emerging medical imaging modality that will be further followed within the scope of Euro-BioImaging. At the current time, nodes for medical imaging are not expected in the near future.

3.6 EPRI

Electron paramagnetic resonance imaging (EPR imaging) is a technique for in vitro or in vivo imaging of paramagnetic species. EPRI is an emerging technology that is able to provide molecular images of paramagnetic centers, from the microscopic level to large animals and human patients. The in-vivo and EPRI European community, distributed in 8 different centers of 8 different European countries, is currently limited to analysis in vitro, ex vivo and small animals. However, recently funds have been granted to two EPRI centers (in France and in Belgium) that will allow the development of system for the applications in humans. From the point of an emerging medical imaging technology, EPRI is therefore in a similarly early stage as MEG-MRI, or even a bit earlier. As no systems for human studies are currently available, EPRI has not been included as medical imaging device in the Euro-BioImaging survey and no proof-of-concept study could be performed. As a small imaging device, EPRI is likely to become a modality in future animal imaging facilities. Once established as such, studies in small animals will allow to estimate the potential for human or clinical application.

EPRI should therefore be continued to be included in the emerging medical imaging technologies. Once the feasibility and first potential research applications in humans have been demonstrated, one or very few nodes within Euro-BioImaging could be established.

Conclusions

The modalities that have thus for been considered in WP9 as innovative medical imaging technologies can be categorized as follows:

(i) Technologies that have already proven to be of major advantage for research studies, show high future potential and are technically advanced but still developing rapidly. They are low in supply due to high costs and high demand of the user community has been identified across Europe. Therefore WP9 recommends including open access nodes for these technologies, which are required to meet the need of the researchers. These modalities are currently UHF-MR and MR-PET.

(ii) Emerging technologies that have high potential to develop into a high impact modality and that have currently extremely low availability. WP9 recommends to include one or very few nodes for such technologies to provide open access for the early adopters that want to explore and extend the possibilities of the technology. These modalities include PCI and MEG-MRI. The results of the survey and proof-of-concept studies indicate that currently the unmet scientific need and existing structure among European researchers is higher for PCI than for MEG-MRI, which would therefore rather require more maturation.

(iii) Emerging technologies that have shown to have high potential in small animal imaging but are currently not available for imaging in humans. These modalities should be continued to be observed as emerging imaging modalities for potential future inclusion in the Euro-BioImaging infrastructure. This applies to EPRI and MPI.