Euro-BioImaging

European Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences

WP8 Molecular Imaging

Task 8.2
Organize European community

Deliverable 8.5
Report on emerging technologies in Molecular Imaging with the potential and demand to provide access

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November 2013

1 Introduction

The aim of Euro-BioImaging, a project on the roadmap of the European Strategy Forum on Research Infrastructures (ESFRI), is to provide scientists throughout Europe open access to state-of-the-art imaging technologies at all levels of biological and biomedical research, from bench to bedside. Within this project, WP8 deals with imaging technologies related to Molecular Imaging and will pave the way for implementing an integrated imaging infrastructure for both probe development and imaging technologies for molecular imaging, including multi-tracer and multi-modal molecular imaging applications in model animals as well as emerging tissue imaging technologies. In this way, this WP will bridge the gap between basic biological imaging and clinical medical imaging.

To develop such a pan-European infrastructure for Molecular Imaging in a harmonized, coordinated and well-balanced way, an overview of (i) emerging molecular imaging technologies with the potential and demand to provide access, of (ii) existing and potential European infrastructure centres capable of providing access to molecular imaging technologies, and of (iii) the expectations, needs and requirements of all interested parties are required.
One important and effective way to gain insights in available infrastructures, emerging technologies and in the necessities desired by the research community is to survey the imaging community. Furthermore, relevant information on emerging technologies can be collected at dedicated meetings of the imaging community, above all the Euro-BioImaging Stakeholder Meetings and the European Molecular Imaging Meetings (EMIM) or the World Molecular Imaging Congresses (WMIC) for the specific field of Molecular Imaging.
In such a way it can be ensured that Euro-BioImaging keeps pace with changing trends and remains able to adjust to emerging technologies and also to changes in user needs in the biological, medical and molecular imaging communities.

2 About the deliverable and the work package/task

2.1 Objective

Analysis of the emerging technologies in molecular imaging with the potential and demand to provide access.

2.2 Approach

This report is a follow-up report on D8.4 and complements the technologies described therein.

Consultations of the imaging community during dedicated conferences are particularly suited to gain insight into new and emerging developments within the field. Such consultations took place during the Euro-BioImaging Stakeholder Meetings and dedicated imaging conferences, such as EMIM and WMIC, as well in national/regional meetings of the molecular imaging communities.

2.3 Results

Additional ***emerging technologies*** identified during the WMIC2012 scientific and the EMIM2013 scientific and educational sessions are:

- Opto- or photoacoustic imaging
- Raman spectroscopy
- MALDI mass spectrometric imaging
- Cerenkov luminescence imaging
- Hybrid multimodality imaging technologies: PET-MRI, FMT-CT and MRI-US

Photoacoustic imaging: PAI is a hybrid imaging modality based on the photo-acoustic effect: by applying pulsed or modulated non-ionising electromagnetic waves, acoustic pressure waves are generated by rapid thermal expansion within the tissue. The acoustic waves are then detected by ultrasonic transducers at the tissue surface and are related to the optical absorption distribution within the tissue. Since image contrast is obtained from optical absorption properties, imaging can be performed using endogenous or exogenous contrast in tissue. PAI can effectively detect relevant functional features of tissues in real time with favourable penetration depth, spatial resolution and sensitivity. Two types of systems are emerging: photoacoustic microscopy (PAM) and photoacoustic computed tomography (PACT) with several fields of application (endoscopic PI, spectroscopic/multispectral PAI, molecular (in contrast to non-targeted) PAI, small animal PAI) for diagnostic and image-guided therapy purposes. References: congress books, doi:10.1517/17530059.2010.529127 and doi:10.1088/0031-9155/54/19/R01.

Raman spectroscopy: This spectroscopic technique relies on the inelastic scattering, or Raman scattering, of monochromatic light, usually from a laser in the near infrared range for biological and medical specimens. A number of advanced types of Raman spectroscopy are being developed with high potential for biomedical applications (e.g. brain tumour diagnostics, detection of pathogen or circulating tumour cells, cardiovascular diseases, targeted drug delivery and photothermal therapy, intraoperative image-guided tumour resection). These types include surface enhanced (SERS) or surface enhanced resonance raman spectroscopy (SERRS), coherent anti-Stokes raman spectroscopy (CARS), tip-enhanced raman spectroscopy (TERS), among others. References: congress books, doi:10.1016/j.tibtech.2013.01.013

MALDI mass spectrometric imaging: In MALDI imaging matrix-assisted laser desorption ionization is used as a mass spectrometry imaging technique to visualise the spatial distribution of proteins, peptides, drug candidate compounds and their metabolites, biomarkers or other chemicals within thin slices of sample such as animal or human tissue. The technique allows completely label free imaging of multiple analytes simultaneously. Measurements performed with MALDI IMS combine mass spectrometric analysis with conventional histology and can be used for instance for molecular classification, to complement histological diagnostics or to predict prognosis, response, or metastasis potential of cancers. References: congress books, doi:10.1016/j.clinbiochem.2013.01.018

Cerenkov luminescence imaging: This emerging imaging modality captures visible photons emitted by Cherenkov radiation and can be used to image radionuclides (beta and positron emitting radioisotopes) with OI instruments. First applications have been reported, also for the use of Cerenkov Resonance Energy Transfer (CRET) to increase sensitivity. References: congress books, doi: 10.1098/rsta.2011.0271.

Hybrid multimodality imaging techniques: Single devices combining more than one molecular imaging technique are highly valuable tools as they complement each other to reach the best output in terms of sensitivity, specificity, depth penetration, temporal and spatial resolution. Hybrid instruments integrate multiple imaging modalities and enable simultaneous acquisition of data to obtain synergistic information. Emerging combinations are PET-MRI, FMT-CT and MRI-US. References: congress books.

The importance of intraoperative imaging and imaging-guided surgery as well as imaging-guided drug delivery as new ***emerging applications*** for the molecular imaging community has been stressed by the recent establishment of the study groups 'Intra-operative imaging – IOI' and 'Image-guided drug delivery – IGDD' within the European Society for Molecular Imaging (esmi).

Intra-operative imaging: Surgical vision enhanced by molecular imaging has the potential to shape the future of surgical procedures by improving the sensitivity, accuracy and contrast of tumor delineation and lymph node interrogation. Fluorescent dyes such as fluorescein and indocyanine green (ICG) have been used for many year in clinical practice. They can outline the vascular system and help to identify areas of high perfusion or permeability. Recently, targeted fluorescent probes emerged as another class of promising contrast agents. Antibody, peptide, and minibody-based fluorescent probes can improve the detection ability of tumor margins or metastatic microfoci by attaching to upregulated cancer receptors. Similarly, engineered probes can capitalize on tumor-specific physiological or molecular parameters. The use of labelled molecules with tissue specificity is expected to become a crucial platform in the propagation of fluorescence surgical imaging into the clinic. A first successful translation of such targeted probes, together with their real-time intra-operative imaging, has already been reported for ovarian carcinomas. Furthermore, magneto-fluorescent particles offer the possibility for multi-modal imaging by combining fluorescence with the whole-body imaging capability of MRI. Such novel magnetic resonance-based molecular imaging techniques can help to detect the early responses of tumours to therapy, with a view to translating these into clinical application.

Image-guided drug delivery: Imaging can be used to support and improve various different aspects of drug delivery and drug therapy. It can e.g. be employed to visualize and quantify the biodistribution and target site accumulation of drugs and drug delivery systems, and to non-invasively assess their efficacy. In addition, molecular imaging techniques can be used to assess drug delivery across biological barriers (by monitoring its temporal and spatial parameters), and to evaluate strategies that aim to improve this process. Furthermore, image-guidance is highly useful for triggering and quantifying drug release from stimuli-responsive carrier materials, such temperature-sensitive liposomes and ultrasound- responsive microbubbles. Finally, by rationally combining drug targeting and imaging, patients can be pre-selected, and treatment protocols can be individualized and optimized, thereby paving the way for personalized (nano-)medicine.

3 Conclusion

Several emerging technologies and applications within Molecular Imaging with the potential and demand to provide access have been identified during consultations within the field. These field consultations will be carried on, also beyond the preparatory phase of EuBI, in order to keep the planned pan-European imaging infrastructure not only state-of-the-art but also adjusted to emerging technologies and changing user needs, innovative and competitive with the extra-European international imaging research landscape. These emerging technologies might be considered in upcoming open calls for Nodes when further field-

consultations endorse actual user need (e.g. by means of a survey) and feasibility is demonstrated by Proof-of-Concept or equivalent mechanisms.

4 Abbreviations

PET Positiron-emission tomography
MRI Magnetic resonance imaging
FMT Fluorescence molecular tomography
CT Computed tomography
US Ultrasound
MALDI Matrix-assisted laser desorption/ionization