Mediterranean Thematic Workshops in Advanced Molecular Imaging

28 May, 2016

Multiparametric molecular imaging technologies for personalised medicine

Vision paper - Conclusions of the MEDAMI 2016 workshop[1]

Preamble

In Europe there are almost ten thousand medical physicists, engineers, and other scientists working in a clinical environment, mostly in radiotherapy, radiology, and nuclear medicine. This diverse community is, in part, represented by European scientific-professional associations such as EFOMP (Medical Physics), EANM (Nuclear Medicine), ESR (Radiology), and ESTRO (Radiation Oncology). In addition, hundreds of scientists are working on the development, innovation, and translation of new approaches to the clinic - in academia, research institutions, and industry

Among these, the molecular - and more recently hybrid - imaging community is a very large and dynamic multidisciplinary group, albeit recurrently suffering from too high a fragmentation at the decisional and funding levels. This results in too much subdivision and disconnection across projects at local, national, and international levels, which then lack the necessary critical mass and support for their crucial translation and optimal deployment to the clinic.

The recent series of MEDAMI and workshops has led the European molecular imaging community to realise the innovation value of its scientific and technical potential - further reinforced through strong ties with colleagues in America and Asia, as well as with the medical imaging industry and institutes and professional societies, such as EIBIR (European Institute for Biomedical Imaging Research), ESMI (European Society of Molecular Imaging), EANM (European Association of Nuclear Medicine) and ESR (European Society of Radiology). Indeed, this multidisciplinary community can be the cornerstone of a strategy that will bring Europe in a leadership position in the development, deployment, and exploitation of molecular imaging technologies as a keystone of personalised medicine.

Our vision

To enable access to personalised/precision diagnosis and treatment for every citizen by establishing a European public-private collaborative research roadmap towards the development and widespread clinical use of cost-effective multiparametric and quantitative molecular imaging technologies.

Our ambition

1. To develop In-vivo molecular imaging into a standard tool for personalised medicine.

2. To enable the development and validation of at least 100 new biomarkers in the next 10 years.

Our foci

Keeping in mind that innovative molecular imaging research themes should always strongly focus on the clinical needs, we propose to concentrate our intellectual, technical, and financial resources on the following ambitious targets:

- to realise a 10-fold improvement in molecular imaging sensitivity, amongst others through the implementation of transformative Time-of-Flight (TOF) image acquisition technologies developed in part for other applications;
- to reduce the doses of molecular imaging procedures involving ionizing radiation to negligibly low levels (i.e., less than 1mSv, the equivalent of a flight from Paris to San Francisco),
- to reduce by a factor of 2 the cost of in-vivo molecular imaging procedures;
- to further extend the benefit of molecular imaging procedures beyond oncology – towards cardiovascular, neurological, metabolic, inflammatory, and other diseases, including paediatric, neonatal, and prenatal applications;
- to make molecular imaging widely available to patients worldwide through miniaturization, transportability, ubiquity, remote operation, and significant cost reduction.
- to contribute to a better overall healthcare cost management through more accurate early diagnosis and therapies, increasingly guided by molecular imaging;

[1] https://indico.cern.ch/event/446975/

Technical Objectives

Based on the key themes stemming from recent workshops, the White Paper from the European Society of Radiology (ESR)[2], and central to recent EU submitted proposals (e.g., ERAMMIT[3]), we will initially focus on the development of new instrumentation and software, new drug/radiotracer design, synthesis, and validation, and the production and exploitation pipeline of the corresponding data for advanced biomarkers and theranostic approaches.

These are all inherently multidisciplinary tasks with a strong innovative impetus from research to industry – from medical devices to pharma – for optimal validation, deployment, and clinical exploitation.

Our technical objectives can be summarised as follows:

- to introduce technologies (e.g., 10ps TOF) for enhancing image quality and achieving a 10-fold improvement to PET sensitivity;
- to enable multiparametric, quantitative, and dynamic molecular imaging through the development of highly-integrated multimodal devices with advanced signal processing and image analysis;
- to better target disease phenotypes through the development of organ-specific devices and new radiolabelled theranostic agents;
- in all these domains, to develop and introduce transformative technologies to improve performance while reducing costs.

Methodology

Realising our vision requires strong collaboration between the different stakeholders (physics community and industry involved in medical applications, EIBIR, EIBALL (European Imaging Biomarkers Alliance), ESMI, EANM, ESR), and a common purpose and vision throughout the EU research community. This will be achieved through four main actions:

- launching an ambitious flagship project at the European level;
- establishing fruitful public-private partnerships to federate a maximum of European stakeholders and actors from academia and industry along the aforementioned technical objectives;
- implementing a translational and transnational infrastructure network under an open-access model for the benefit of the whole community;
- establishing a European public-private research roadmap on in-vivo molecular imaging.

Flagship programme

There is a consensus for gathering Europe's multidisciplinary academic and industrial excellence around the ambitious goal to develop a 10ps TOF PET scanner (TOFPET). This will cause a paradigm shift in in-vivo molecular imaging, by enabling on-the-fly image formation and observation of bio-distribution and biochemistry in animals and patients, as well as an order-of-magnitude leap in molecular sensitivity and speed.

Research to reach the 10ps limit is already supported by EU funded projects[4]. In the USA, the Explorer project[5] has a similar goal through the world's first total-body PET/CT scanner with a length of 2 m. This scanner will demonstrate the clinical value of a ~40-fold increase in system sensitivity, which can in particular be used to reduce radiotracer dose and scan times. However, the retained system concept is intrinsically expensive as it is primarily based on a multiplication of existing scintillation detector technology.

EU researchers are in an excellent position to develop an alternative technology that can be translated into clinical solutions, provided that they are united and cohesively supported towards this goal. A European flagship project for a 10ps TOFPET will not only have a strong federative power for the different EU stakeholders (academy, industry, funding agencies, patient associations), but will also further stimulate EU-US collaboration.

Public-Private Partnership

[2] Medical imaging in personalised medicine: a white paper of the research committee of the European Society of Radiology (ESR), Insights Imaging (2015) 6:141–155, DOI 10.1007/s13244-015-0394-0

[3] ERAMMIT: "Enabling Research Access to Multiparametric Molecular Imaging Technologies", Horizon2020 INFRA-IA2 proposal submitted in March2016

[4] ERC Advanced grant #338953, COST action FAST #TD1401

[5] UC Davis, Berkeley Lab, and U Penn, funded by a $15.5 million, 5-year NIH Transformative Research Award

Connecting public and private funding sources is a prerequisite for shortening the translational path from technology development to healthcare outcomes and economy. We aim at preventing excessive fragmentation of funding streams and strategies at the regional, national, and European levels, and at establishing the best conditions for public-private partnerships.

The Innovative Medicines Initiative (IMI)[6] emerges as an excellent model of such a public-private partnership between the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA).

We propose to implement a similar approach between the different academic institutions active in the development of molecular imaging technologies and the medical imaging industry. Alternatively the instrumental aspects of personalised medicine could be introduced as bona-fide components of the IMI programme.

Organization

A first step towards overcoming the fragmentation of the molecular imaging community is represented by the proposed ERAMMIT EU infrastructure project. ERAMMIT will mobilise a consortium of partners encompassing the whole value chain – clinical and industrial stakeholders as well as research institutions – necessary to support the advanced development, deployment and exploitation of multiparametric molecular imaging technologies.

Challenging flagship projects, such as a 10-fold improvement in molecular imaging sensitivity, will require highly collaborative working models at the scale of "big science". In this respect, and as an example, particle physics has been outstandingly successful: thousands of physicists, engineers, and PhD students from over 40 countries have been working together for more then three decades on CERN's Large Hadron Collider and its experiments, in a collective effort that was recently rewarded by the discovery of the Higgs Boson.

We intend to capitalise upon a long-established multidisciplinary collaborative culture such as CERN's in order to foster a similarly federating approach in tackling the challenges of molecular imaging. In addition to detector technologies, expertise in data storage and handling (including big data filtering and analytics, alongside machine learning) will also be extremely valuable to our community due to the growing volume of structured and unstructured data generated by the medical imaging and decision-making processes. In the wider domain of internet technologies, CERN openlab is a successful public-private partnership that shares some similarities with the IMI programme and can thus also help shaping our efforts in this direction.

Under such model, collaboration agreements could allow the molecular imaging community to access European facilities (including CERN's) covering the whole translational chain from technologies to patients and economy. This is already foreseen by ERAMMIT. Indeed, transnational access to world-class facilities will be critical to our community for most effectively addressing the technical challenges outlined herein.

Our roadmap (5 years)

- ***Set up a concrete collaboration based on a consortium agreement among the leading actors in molecular imaging.***
- ***Be an integral part of a public-private funding scheme such as IMI.***
- ***Provide a 5-year timescale for selected relevant projects, e.g, 10ps PET, organ-specific PET scanners, hybrid systems, theranostic drugs.***
- ***Implement appropriate academia-industry partnerships for related developments, in close collaboration with the end-users, i.e. medical diagnostic and therapeutic associations, pharma, scientists and clinicians.***
- ***Design, implement, and evaluate on patients the corresponding cost-effective approaches and devices.***

Luc Bidaut, ***UK***

Manuela Cirilli, ***CERN***

Alberto Del Guerra, ***University of Pisa and INFN***

York Haemisch, ***LDTEC Consulting***

Paul Lecoq, ***CERN***

Dennis R. Schaart, ***Delft University of Technology***

[6] https://www.imi.europa.eu