EMRP Call 2011 - Health, SI Broader Scope & New Technologies

Selected Research Topic number: **SRT-h08**
Version: 1.0

Title: Metrology for chemical and functional imaging of skin and tissue

Abstract

The biochemical imaging and characterisation of skin and tissue is one of the most important measurement advances in health care, as it has direct impact on clinical diagnosis through the identification and localisation of biomarkers as well as the design and targeting of therapeutics. A wide range of techniques are available for the biochemical imaging and characterisation of skin and tissue, such as imaging mass spectrometry and non-invasive optical techniques. However, there is an urgent need to develop the metrology and standards required to underpin these techniques.

Conformity with the Work Programme

This Call for JRPs conforms to the EMRP Outline 2008, section on “Grand Challenges” related to Health on pages 7 and 8.

Keywords

Biomedical imaging, *in vivo*, quantitative imaging, molecular imaging, non-invasive, skin, tissue

Background to the Metrological Challenges

The European Strategy Forum on Research Initiatives; Biological and Medical Sciences Working Group has stated that ‘Innovative imaging techniques are the key tools for all scientists from the Life Sciences’ and that ‘Imaging is essential for studying living systems at the molecular, the cellular and the physiological level from single cells through model organisms to humans’.

As part of this strategy the Euro-BioImaging project has been funded. The project covers techniques such as Matrix Assisted Laser Desorption Ionisation (MALDI), Desorption Electrospray Ionisation (DESI), Secondary Ion Mass Spectrometry (SIMS), Near Infrared (NIR) imaging, and Coherent anti-Stokes Raman spectroscopy (CARS), and other non-linear optical techniques for the analysis of skin and tissue. However, the focus of Euro-BioImaging is not on the metrology required for these imaging techniques. Metrologically, what these techniques need is an increased confidence in, and greater comparability of results, which can only be achieved through improved repeatability, better quantification and a clearer understanding of the measurand.

Further to this, whilst there is a strong international standards infrastructure for techniques such as SIMS in ISO TC 201, this does not cover biological materials or extend to the techniques in the Euro-BioImaging project. ISO TC 201 is developing a strategic plan for these standards however, again, this requires the development of the metrology for these techniques.

Chemical and functional imaging of skin and tissue is key in four healthcare areas; 1) diagnosis, 2) treatment monitoring and efficiency (e.g. stratifying patient groups using biomarkers or physiological measurements), 3) designing treatments (e.g. targeted drug delivery) and 4) screening of new treatments (e.g. tissue arrays). Indeed, imaging mass spectrometry techniques such as MALDI, SIMS and DESI have already demonstrated significant impact in these areas for pancreatic, lung, breast, prostate and ovarian cancers. The capability to detect and localise unlabeled compounds using imaging mass spectrometry techniques could also be vital for medical research, drug industry and medical diagnostics.

Non-invasive, *in vivo*, methods are also extremely important for skin and tissue characterisation. Quantitative NIR spectroscopy characterises tissue oxygenation and perfusion, *in vivo* fluorescence imaging of skin and tissue gives access to intrinsic as well as extrinsic biomarkers and contrast agents and nonlinear optical

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techniques such as CARS and stimulated Raman scattering have been demonstrated to image biomolecules such as lipids and antioxidants in skin. *In vivo* optical imaging also has the potential to improve the treatment of patients. For example, in breast cancer treatment, the patient's response to chemotherapy could be quickly measured from the haemoglobin concentration in the carcinoma during therapy. Other possible applications include the measurement of tissue oxygenation in the brain during open-heart surgery or functional imaging of the brain to study motor rehabilitation after stroke. However, in all these possible applications the diagnostic or therapeutic output strongly depends on the reliable quantification of the optical measurands.

Scientific and Technological Objectives

Proposers should address the objectives stated below, which are based on the PRT submissions. Proposers may identify amendments to the objectives or choose to address a subset of them in order to maximise the overall impact, or address budgetary or scientific / technical constraints, but the reasons for this should be clearly stated in the JRP-Protocol.

The JRP shall focus on the traceable biochemical imaging and characterisation of skin and tissue with the help of imaging mass spectrometry and non-invasive optical techniques.

The specific objectives are:

1. To develop methodologies for the quantitative and traceable analysis of biomolecules and pharmaceuticals in skin and tissue using imaging mass spectrometry techniques (e.g. SIMS, DESI and MALDI). Methods should address sample preparation, quantification of matrix effects and unwanted artefacts and aim to achieve repeatable spectral intensities of better than 10 %. Methods should also include highly multiplexed biomolecule analysis at high spatial resolution (< 1 micrometre) in skin and tissue.
2. To develop methodologies for imaging mass spectral identification using modern informatics methods (e.g. graph theory and LipidMaps).
3. To develop methodologies in *in vivo* optical imaging of skin (e.g. laminar optical tomography, multiphoton fluorescence imaging, CARS and SRS) and tissue (e.g. diffuse optical imaging, spectroscopy and fluorescence imaging). Methods should quantitatively determine:
   - tissue optical properties,
   - physiological properties (e.g. tissue oxygenation) and
   - concentrations of biomarkers and contrast agents

   with the aim of detecting and characterising diseases with an uncertainty of less than 10 %.
4. To quantify the spatial resolution and related sensitivity of *in vivo* optical methods for different types of skin and tissue and including tissue phantoms and under *in vivo* conditions. This should also include the evaluation of CARS and SRS imaging techniques (e.g. using lipids in tissue sections and molecules in skin) with the aim of providing a sensitivity equivalent to solution state detection limits of better than 100 mmol/mol.
5. To develop methodologies for combining data from imaging mass spectrometry and non-invasive optical imaging in order to quantify and understand any differences between the techniques.

These objectives will require large-scale approaches that are beyond the capabilities of single National Metrology Institutes and Designated Institutes, and it is expected that multidisciplinary teams will be required. To enhance the impact of the research, the involvement of the appropriate user community such as medical practitioners and industry is strongly recommended, both prior to and during methodology development.

Proposers should establish the current state of the art, and explain how their proposed project goes beyond this. Proposers should also consult with the Euro-BioImaging project, with the aim of increasing the application and impact of their proposed project.

The total eligible cost of any proposal received for this SRT is expected to be around the 2.7 M€ guideline for proposals in this call.

Potential Impact

Proposals must demonstrate adequate and appropriate participation/links to the "end user" community. This may be through the inclusion of unfunded JRP partners or collaborators, or by including links to

industrial/policy advisory committees, standards committees or other bodies. Evidence of support from the "end user" community (eg letters of support) is encouraged.

You should detail other impacts of your proposed JRP as detailed in the document "Guide 4: Writing a Joint Research Project"

You should detail how your JRP results are going to:

- feed into the development of urgent documentary standards through appropriate standards bodies
- transfer knowledge to the medical community.

You should also detail how your approach to realising the objectives will further the aim of the EMRP to develop a coherent approach at the European level in the field of metrology. Specifically the opportunities for:

- improvement of the efficiency of use of available resources to better meet metrological needs and to assure the traceability of national standards
- the metrology capacity of Member States and countries associated with the Seventh Framework Programme whose metrology programmes are at an early stage of development to be increased
- outside researchers & research organisations other than NMIs and DIs to be involved in the work

Time-scale

The project should be of up to 3 years duration.