EMPIR Call 2018 – Health, SI Broader Scope, Normative and Research Potential

Selected Research Topic number: **SRT-h03**
Version: 1.0

Title: Metrological challenges in multimodal bio-imaging for diagnosis and therapies of cancer

Abstract

Based on current data, approximately one third of European citizens will be diagnosed with cancer and a quarter will die as a result of it. But in order to improve measurements involved in the bio-imaging of cancer, traceable, quantitative, analytical methodology is needed. Such methods are needed for establishing the presence (or absence) of single and multiple key cancer biomarkers and hence for the successful development of improved diagnostics and targeted therapies for cancer. They can also be used to establish traceable quantitative imaging of selected analytes at resolution levels, from tissues down to the subcellular level. Further to this, algorithms and computer models are needed for the analysis of high volumes of data for bio-processes relevant to the diagnosis and treatment of the most common cancers.

Keywords

Bio-imaging, quantitative imaging, diagnostic, targeted therapies, biomarkers, metal tagged antibodies, cancer

Background to the Metrological Challenges

Modern cancer diagnostics and therapies require an ever-increasing number of questions to be answered before the right treatment for a patient can be selected. However, the number of questions that can often be answered is limited by the sample available for testing and the accessibility to reliable analytical techniques used for the early detection of a tumour specific biomarkers.

Over the past few decades the ‘gold standard’ for the diagnosis of almost all types of cancer has been histopathological image analysis of tissue or cells samples taken directly from a tumour. But quantitative analysis of pathology images is now needed for cancer diagnosis and therapies, for example to understand the biological mechanisms of the disease process or for evaluating the efficacy of anticancer drugs. Such imaging includes a range of spectroscopy, microscopy and mass spectrometry techniques which can be used for analyte quantification and distribution. However, currently there are no suitable techniques for quantifying bio-species at low ppm concentrations in biological samples, such as tumour tissues and subcellular compartments.

The study of metal-tagged drugs, contrast agents and nanoparticle drug carriers in pre-clinical cancer research is currently hindered by a lack of sufficiently representative in vitro models. The multifactorial nature of cancer means that it cannot be fully represented by the use of traditional 2D in vitro models. Therefore, 3D cultures, also known as spheroids, are becoming increasingly used, due to their ability to preserve specific molecular, biochemical and physiological features of the corresponding tissue in vivo. Specifically for tumour (3D) spheroids, the development of hypoxia in the centre of spheroid along with the lack of nutrients due to impaired diffusion better represents the in vivo situation. But despite their use, there are currently no standardised protocols for the use of spheroids.

In order to ensure comparability of the data generated by multimodal imaging techniques for their fusion, and handling, validated, traceable and quantitative measurements are needed. This includes multimodal data fusion and big data handling, which also require reproducible algorithms. Together with computer models, the use of multimodal classifiers for cancer therapy recommendations will be indispensable in computer-based, personalised targeted treatment.

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

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overall impact, or address budgetary or scientific / technical constraints, but the reasons for this should be clearly stated in the protocol.

The JRP shall focus on improved, traceable measurements for multimodal bio-imaging for the diagnosis and treatment of cancer.

The specific objectives are

1. To develop traceable methods for quantifying the distribution of biomarkers relevant for cancer diagnosis and treatment in (i) tumour (3D) spheroid models, (ii) biological tissue, and (iii) single cells. The target level for analytes should be low ng/g concentrations and resolution from 100 nm (subcellular level) to 1 µm (tissue level).
2. To develop accurate and validated methods for the concentration, size distribution and imaging of nanoparticles used for cancer diagnosis, in biological tissue and single cells.
3. To develop accurate and validated methods for multiple biomarker identification, quantification and imaging in biological tissue and single cells (e.g. using metal tagged antibody detection coupled with spectrometry and confocal imaging).
4. To develop reproducible algorithms and computer models for the comparison and analysis of high volumes of data for bio-processes relevant to the diagnosis and treatment of the most common cancers.
5. To facilitate the take up of the technology and measurement infrastructure developed in the project by the measurement supply chain, standards developing organisations (e.g. ISO/TC 229 and those associated with the EC Regulation 2017/746) and end users (e.g. clinical laboratories, hospitals).

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, hospitals 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.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 1.8 M€, and has defined an upper limit of 2.1 M€ for this project.

EURAMET also expects the EU Contribution to the external funded partners to not exceed 35 % of the total EU Contribution across all selected projects in this TP.

Potential Impact

Proposals must demonstrate adequate and appropriate participation/links to the “end user” community, describing how the project partners will engage with relevant communities during the project to facilitate knowledge transfer and accelerate the uptake of project outputs. Evidence of support from the “end user” community (e.g. letters of support) is also encouraged.

You should detail how your JRP results are going to:

- Address the SRT objectives and deliver solutions to the documented needs,
- Feed into the development of urgent documentary standards through appropriate standards bodies,
- Transfer knowledge to the medical and health sector.

You should detail other impacts of your proposed JRP as specified in the document “Guide 4: Writing Joint Research Projects (JRPs)”

You should also detail how your approach to realising the objectives will further the aim of EMPIR to develop a coherent approach at the European level in the field of metrology and include the best available contributions from across the metrology community. 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 EURAMET Member States whose metrology programmes are at an early stage of development to be increased
- organisations other than NMIs and DIs to be involved in the work

Time-scale

The project should be of up to 3 years duration.