EMPIR Call 2017 – Industry, Fundamental, Normative and Research Potential

Selected Research Topic number: **SRT-f10**
Version: 1.0

Title: Metrological quantification of physical, chemical and biological radio-sensitising effects of high-Z nanomaterials

Abstract

High-Z nanomaterials such as gold nanoparticles are a promising new irradiation treatment for cancer or disease diagnosis. These materials are able to efficiently transform incident radiation into strongly localised tumour damage. However, a lack of understanding of the mechanisms underpinning the radio-sensitisation caused by high-Z nanomaterials is preventing the necessary regulatory approvals and, consequently, the development of clinical products, procedures and cancer treatment plans. Suitable reference standards would significantly improve the predictability of treatment outcome and risks, drive forward the development of new radio-sensitising agents and provide the framework for regulatory approvals. This requires an interdisciplinary, coordinated and fundamental research approach combining physical, chemical and biological expertise. The goal is to identify reliable and traceable quantities to describe radio-biophysically relevant effects and to establish a metrological framework by means of coherent results.

Keywords

Radiobiological, radiation quality, radiation treatment, nanomaterials, nanoparticles, biomarkers, radio-sensitising

Background to the Metrological Challenges

Research on the application of high-Z nanomaterials is quite challenging as there is evidence pointing to three main mechanisms for their radiobiological effect: physical (dose enhancement and changes in the radiation quality on the nanoscale), chemical (change in the spectrum and yield of reactive radical species) and biological (alteration of cellular metabolic processes such as DNA repair pathways or cell cycles). Metrological research on these effects are urgently needed for more effective cancer treatments as well as for new diagnostic and theranostic (novel combined therapeutic and diagnostic) approaches.

Currently biological cell based experiments are often supported by Monte Carlo simulations performed using a variety of codes, but these do not necessarily use track structure calculations which are essential for assessing the radiation damage caused by low-energy electrons on the nanoscale. In addition, the focus is on predicting dose enhancement which can differ by several orders of magnitude between research groups due to a lack of measurement standardisation. These differences are increased when calculated doses are used as input for models to estimate radiobiological effects in clinical applications. A number of such models are in use but validation is not currently possible, as appropriate traceable measurements of the underlying physical, chemical and biological processes are not available.

An interdisciplinary collaborative approach is needed to develop devices suitable for direct and traceable radiation quality measurements, as well as the development of a traceable characterisations of the proposed nanomaterials. To assess the biological effects of irradiating nanoparticles, a coordinated and sustainable approach is needed based on the production and quantity of chemical radicals formed in the vicinity of nanoparticles. This will form the basis for quantification of the initial chemical and biological effects in any proposed treatment in which nanoparticles are used to enhance radiation therapy delivery. This should take into account the control and measurement of physical and chemical conditions (such as parameters characterising the cellular state) and an improved physico-chemical characterisation of the incorporated nanomaterial. The quantification of cellular metabolic processes (such as the changes in cell cycle and DNA repair kinetics) and an investigation of suitable and robust biomarkers for an early response to radio-sensitising agents would further enhance the validity of results.

EURAMET MSU, Hampton Road, Teddington, Middlesex, TW11 0LW, UK
Phone: +44 20 8943 6666 Email: msu@npl.co.uk
msu.euramet.org

The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

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 protocol.

The overall objective is to identify traceable quantities and direct measurements for physical, chemical and biological changes induced by exposure to radiation in the presence of high atomic number (high-Z) nanomaterials.

The specific objectives are

1. To develop nanoscale dosimetric methods to relate physical, chemical and biological changes to cells from ionising radiation exposure in the presence of high-Z nanomaterials.
2. To quantify relative effects of physical, chemical and biological changes at the cellular level caused by ionising radiation exposure in the presence of high-Z nanomaterials. This should include experiments for both early and late biological effects and the development of radiobiological models for evaluating relationships between cell survival, genomic instability, biomarkers and individually measured physico-chemical changes.
3. To investigate the predictability and robustness of cell biomarkers responding to radiation effects in the presence of high-Z nanomaterials and to assess the accuracy of measurement techniques used to detect these biomarkers.
4. To explore the definition and development of suitable reference standards to allow radiobiological effects to be determined using physically measurable quantities and biological endpoints.
5. To develop a strategy for establishing the proposed reference standards within appropriate traceability chains by engaging with the relevant medical research communities.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 1.5 M€, and has defined an upper limit of 1.8M€ for this project.

EURAMET also expects the EU Contribution to the external funded partners to not exceed 40 % of the total EU Contribution to the project.

Proposers shall give priority to work that aims at excellent science exploring new techniques or methods for metrology and novel primary measurement standards, and brings together the best scientists in Europe and beyond, whilst exploiting the unique capabilities of the National Metrology Institutes and Designated Institutes.

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,

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.