Title: Biologically weighted quantities in radiotherapy

Abstract

There is a need to define a new dosimetric quantity for radiotherapy, which conventionally is prescribed in terms of absorbed dose. For proton and ion beams an additional biological effectiveness factor has to be accounted for which has raised the need for a new physical quantity more closely related to the biological response of radiation. This quantity will depend on the distribution of energy deposition and ionisation at the nano-, micro- and macro-scale. Methodologies to quantify physical parameters linked with the biological effects are being developed such as micro-calorimetry, nanodosimetry the use of chemical probes and track structure measurements.

Conformity with the Work Programme

This Call for JRPs conforms to the EMRP Outline 2008, section on “Grand Challenges” related to Health, New Technologies & Fundamental Metrology on pages 29 and 30.

Keywords

Ionising radiation metrology, Radiotherapy, Proton Beam, Carbon Ion Beam, Microcalorimetry, Reactive oxygen, Monte Carlo, Particle Track Structure, Biological Multiscale Model

Background to the Metrological Challenges

The quantity used at present for clinical prescription in radiotherapy deliveries is defined as the energy (absorbed dose to water) imparted by ionising radiation per unit of mass of the medium. The Consultative Committee for Standards of Ionising Radiations has expressed strong support for defining a new quantity for use when treatments involve the use of one or more multiplying factors to describe the corresponding biological effects of the absorbed dose [1]. The proposed new quantity is for radiotherapy applications and must not be confused with the established quantity, dose equivalent, and its unit, the sievert, used in radiological protection.

The main requirement for this quantity is that it is more representative of the biological effect(s) of radiotherapy level doses of ionising radiation than the currently employed quantity, absorbed dose. The need of the new quantity is the result of the increased diversity of treatment modalities available; while the quantity absorbed dose has proven to be well representative for treatment outcome of high-energy photon and electron beams, for proton and carbon ion beams as well as for brachytherapy using low-energy gamma-emitters and x-ray sources multiplying factors are required that are a complex function of beam or source emission spectra, dose, dose rate, fractionation and tumour and tissue type.

The new quantity will depend on energy deposition distributions on the nano-, micro- and macro scale. A large effort is required combining the metrological techniques for macroscopic dosimetry with micro-dosimetry, nano-dosimetry and measurements of track structure to determine physical variables at multiple geometrical scale levels. The link between the physical characteristics of the radiation and the biological response to it needs to be clearly identified and studied by bringing together multi-scale modelling and radiobiology research.

The use of protons and ion beams for radiotherapy is about to become a mainstream treatment option mainly because of the recent establishment of proton and carbon ion therapy facilities as a commercial product by a limited number of companies. Furthermore, in proton and ion beam therapy [2] as well as in brachytherapy using low-energy gamma emitters or low-energy x-ray sources [3], an additional factor which depends on the beam energy and tissue type is needed to characterise the biological response of tissues to radiation. This factor is currently determined in extensive radiobiological experiments.

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 overall aim of this SRT is to define a new physical quantity closely related to the biological response to emerging radiotherapy modalities using proton and ion beams.

The specific objectives are:

1. Comparison of directly measured energy deposition spectra recorded using micro-calorimeters with spectra obtained indirectly through the measurement of ionisation using tissue-equivalent proportional counters or silicon based microdosimeters;
2. Methods for measuring the production rate of reactive oxygen radical species in tissue exposed to proton and ion beams as a function of particle type and energy and the 3D distributions of these radical formations;
3. Improved techniques for measuring ionising-particle track structure ant its characteristics with nanometre resolution;
4. Development of a multi-scale model for the biological effects of ionising radiation. This may be based on an integrated numerical tool for Monte Carlo modelling of macroscopic radiation transport and nanodosimetric and microdosimetric distributions derived from particle track structure;
5. Development of quantitative models to link the physical quantities with the biological outcome.

These objectives will require large-scale approaches that are beyond the capabilities of single National Metrology Institutes and Designated Institutes. To enhance the impact of the research work, the involvement of the larger community of metrology R&D resources outside Europe is recommended.

Proposers should establish the current state of the art, and explain how their proposed project goes beyond this. They should also describe how the stakeholders, such as radiologists and international committees responsible for the units in this field, are included.

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 radiology sector.

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.

Additional information

The references were provided by PRT submitters; proposers should therefore establish the relevance of any references.

[1] BIPM-CCRI. Report of the 19th Meeting, Bureau International des Poids et Mesures. Consultative Committee for Ionizing Radiation Report, BIPM. Published online at http://www.bipm.org/utils/common/pdf/CCRI19.pdf (2005).

[2] A. Wambersie, J. H. Hendry, P. Andreo, P. M. DeLuca, R. Gahbauer, H. Menzel and G. Whitmore, "The RBE issues in ion-beam therapy: conclusions of a joint IAEA/ICRU working group regarding quantities and units," Radiat. Prot. Dosim. 122:463-470 (2006).

[3] M. A. Hill, "The variation in biological effectiveness of x-rays and gamma rays with energy," Radiat. Prot. Dosim. 112:471-481 (2004).