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MRTDosimetry - Metrology for clinical implementation of dosimetry in molecular radiotherapy

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In the last few years there has been an increase in Europe in the development and use of radiopharmaceuticals for treating cancer as well as an increase in the number of molecular radiotherapy (MRT) clinical trials that are expected to start in the near future. Currently, MRT provides a valuable treatment modality to around 50 000 to 100 000 cancer patients per year in Europe, including patients whose cancer responds poorly to all other types of treatment (e.g. neuroendocrine tumours). A similar number of treatments are estimated to be given for non-cancer diseases such as hyperthyroidism and joint effusions. However, in spite of the growing acceptance that an accurate knowledge of the radiation absorbed dose to critical tissues would provide a more effective targeted use of MRT, most patient treatments still follow the historical practice of administering a nominal activity of the radiopharmaceutical with a standard activity determined on the basis of Phase I or I/II clinical trials in order to find the activity level that causes serious normal tissue damage to less than an acceptable fraction of the clinical trial population (typically 5 %). The EC Directive 2013/59/EURATOM, Article 56 states that "For all medical exposure of patients for radiotherapeutic purposes, exposures of target volumes shall be individually planned and their delivery appropriately verified taking into account that doses to non-target volumes and tissues shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose of the exposure."

The main objective of the European Metrology Programme for Innovation and Research (EMPIR) project MRTDosimetry is to provide metrology for clinical implementation of absorbed dose calculations in Molecular Radiotherapy (MRT). The focus of this project is on clinical implementation and is strongly directed by the involvement of leading scientists at MRT clinics across Europe while building on metrology expertise and involving stakeholders.

This will be achieved by

• determining branching ratios and emission probabilities for 90Y and 166Ho in order to enable improved quantitative imaging (QI) accuracy and dose estimation for these radionuclides, and to exploit new technologies in order to develop a suitable transfer instrument optimised for accuracy of measurements of the activity of MRT agents in clinics and radiopharmaceutical companies

• developing 3D printing methods in order to generate a range of quasi-realistic anthropomorphic phantoms containing compartments fillable with known activities of radioactive liquid or standardised sealed radioactive test sources, having a range of geometrical complexity for validation of multimodal QI or absorbed dose measurement, and estimation of the uncertainties of measurement

• generating multimodal images either from SPECT or PET-CT phantom measurements or Monte Carlo (MC) simulations to provide material for an open-access database of reference images to be used as reference data for commissioning and Quality Control (QC) of QI using SPECT or PET-CT

• improving the accuracy and metrological traceability in the calculation of dose from time-sequences of QI measurements

• determining uncertainties in relation to the full MRT dose measurement chain from a primary standard to a range of commercial and non-commercial dosimetry calculation platforms

• facilitating the take up by healthcare professionals (clinical centres) and industry (scanner manufacturers and software developers) of the technology and measurement infrastructure developed by the project.

MRT dosimetry, as currently performed, has no traceability to primary standards of absorbed dose. Therefore there is an urgent need to achieve traceability and to validate the calculation methods used for dose. Further to this, and central to any recommendations for dosimetry methods, is knowledge of the overall uncertainty associated with any particular method. Hence, the uncertainties in relation to the full MRT dose measurement chain (i.e. from a primary standard to a dosimetry calculation platform) also need to be determined. The MRT community has an urgent need for dosimetry calibration standards, validation methods, and clear guidance on how to implement MRT dosimetry in every European clinic offering MRT. Without this, it will not be possible to comply with EC Directive 2013/59/EURATOM, Article 56, which states that individual dose planning for radiotherapy patients (including MRT) must be enforced in legislation by EU member states by 6 February 2018.

The current, main source of uncertainty in MRT dosimetry is in taking the step from dose measurements on simple reference geometries to QI measurements of the complex and varying geometries of the activity localised in real patients, as well as activity measurements over the time of treatment. All these issues will be addressed by this project using SPECT and PET methods, through the development of 3D printed quasi-realistic anthropomorphic phantoms and by creating a database of reference images of geometries covering typical clinical situations.

The presentation will visualize the objectives and results of MRTDosimetry and invite the community to participate and share their knowledge.

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