Publishable Summary for 19SIP01 PINICAL-MRT
Protocols for clinical impact in molecular radiotherapy

Overview

An estimated 4.3 million new cases of cancer are being diagnosed annually and treatments based on molecular radiotherapy (MRT) are being increasingly used to treat them, creating a $7.27 billion market in radiopharmaceuticals. Ensuring patients receive the prescribed therapeutic doses whilst mapping drug delivery to tumour sites is routinely performed using Single Photon Emission Computed Tomography (SPECT) or Positron Emission Tomography (PET). For clinicians to comply with EC Directive 2013/59/EURATOM, Article 56, which requires confirmation that the administered patient dose matches the prescription, whilst delivering optimised healthcare outcomes, requires the adoption of improved practices in the commissioning, calibration and quality control of these mapping instruments. This project will provide the nuclear medicine community with calibration protocols, and commissioning and quality control guidance, for quantitative SPECT imaging and absorbed dose calculations that were developed in EMPIR JRP 15HLT06 MRTDosimetry. Supported by the European Association of Nuclear Medicine (EANM), the largest organisation facilitating nuclear medicine communication worldwide, the project aims to increase the adoption of best practice in clinics using MRT. This will foster greater harmonisation in MRT delivery, and it will enable improved assessments of radiopharmaceuticals during clinical trials thus speeding the introduction of more effective cancer therapies.

Need

One in two people will develop cancer during their life and there were an estimated 4.3 million new cases diagnosed in 2018, which lead to 1.9 million deaths. This makes cancer the second most common cause of death in Europe. Molecular radiotherapy using radiopharmaceuticals is becoming a first line cancer treatment, and it represents a global radiopharmaceuticals market that is expected to reach $7.27 billion by 2021. However, despite 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.

Delivering optimised, patient specific therapies through the clinical application of MRT dosimetry, supported by training (objective 3) and published good practice guidelines for calibrating, commissioning and QC (quality control) of quantitative imaging (objective 1) based on the outcomes from EMPIR JRP 15HLT06 MRTDosimetry will improve healthcare delivery and reduce clinical costs.

Clinical trials play a major role in the development of standardised dosimetry (including MRT). Absorbed dose is a critical parameter in both assessing treatment effectiveness and harmful side-effects, therefore a reduction in the uncertainty of the absorbed dose calculation (currently estimated to be of the order of 8 % - 40 %) will give a corresponding greater statistical power to clinical trials. In turn, this should support the incorporation of standardised dosimetry into clinical trials and hence this will lead to the greater adoption of MRT as a routine treatment.

EC Directive 2013/59/EURATOM, Article 56 introduces requirements for individual dose planning for radiotherapy patients (including MRT) which is being introduced in legislation by EU member states. Quantitative imaging using SPECT or PET enables the precise location of administered activity in the tissue to be assessed. The EMRP JRP HLT11 MetroMRT and EMPIR JRP 15HLT06 MRTDosimetry put in place the foundations for a traceable MRT calibration infrastructure. EMPIR JRP 15HLT06 MRTDosimetry developed a traceable SPECT/CT calibration protocol and demonstrated the capability for harmonising imaging across multiple centres, systems and countries. It performed the first cross comparison “ground truth” exercise between clinical centres and the project’s commercial partners using “known dose” to establish uncertainties and accuracy for a given clinical dosimetry system. This project’s novel range of quasi-realistic 3D printed anthropomorphic phantoms, the dataset of SPECT/CT images and the associated Monte Carlo dosimetry calculations will provide a unique tool for the validation of the dosimetry chain.

The long-term results of EMPIR JRP 15HLT06 MRTDosimetry need to be extended and promoted in this project as training materials and good practice guidance in order to provide a significant contribution to delivering more effective, better targeted cancer treatments, improved patient outcomes, a more harmonised approach to determining the dosimetry underpinning clinical trials, and significant cost savings to national and European cancer treatment centres. This project will prepare calibration, commissioning and QC best practice guidance for quantified SPECT imaging for MRT dosimetry for use in clinical centres. It will also prepare a practical protocol (objective 2) for the commissioning and validation of a clinical MRT dosimetry calculation platform (with accompanying freely available validation datasets). This will allow the nuclear medicine community to set standards for dosimetry imaging with clinical equipment that commercial companies can incorporate into these systems. It will also extend the e-learning training material produced in EMPIR JRP 15HLT06 MRTDosimetry to support the use of the project developed guidance and protocols in clinical centres delivering cancer treatments (objective 3).

Just as the success of EMPIR JRP 15HLT06 MRTDosimetry was primarily due to strong engagement with the clinical MRT community as demonstrated by the 250 attendees at project workshops; ***the defining impact from the project, in improving outcomes for patients, will only be delivered through clinical uptake of project outputs***. The support from the EANM in promoting the outputs from this project to European MRT dosimetry clinics will provide the strongest possible pathway to deliver this impact.

Objectives

The overall aim of this project is to deliver practical impact from the outputs of JRP 15HLT06 MRTDosimetry by incorporating them into protocols and guidelines which will be promoted and made available by the project's primary supporter, EANM to MRT dosimetry clinics. The protocols will be supported by training materials and by the provision of freely available datasets and 3D printed phantoms.

The objectives of this project are:

1. To prepare good practice guidance and guidelines based on the protocols developed in EMPIR JRP 15HLT06 MRTDosimetry for the calibration, commissioning and QC of SPECTdosimetry for use in clinical centres. In addition, to enable the protocol to be used, validated 3D printed phantoms will be loaned to clinical sites that do not have the capability to make their own. The project's primary supporter, EANM, will promote and make the guidance documents available to European MRT dosimetry clinics and will also assess the suitability of the guidance documents for use in a new EARL accreditation service for SPECT/CT systems analogous to those for Fludeoxyglucose-PET/CT.

2. To publish a practical protocol for the commissioning and validation of a clinical MRT dosimetry calculation platform (with accompanying freely available validation datasets). The protocol will be based on the commissioning procedure developed in the EMPIR JRP 15HLT06 MRTDosimetry and it will incorporate input from external funded partners that are experts in MRT dosimetry calculations.

3. To further develop the e-learning training material produced in EMPIR JRP 15HLT06 MRTDosimetry to support the use of the protocol. These materials will be incorporated into the ESMPE (European School for Medical Physics Experts) lectures that are dedicated to nuclear medicine dosimetry and into other national training schemes. The Christie leads the MRT component of the UK National Health Service Higher Specialist Training Programme (HSST) through which these training materials will be disseminated.

Results

The first half of the project has made good progress on all objectives. A series of peer-reviewed papers, guidelines and protocols, with accompanying validation datasets has been planned as outputs from this project. These publications will complement existing and upcoming guidance documents, with a focus on ensuring traceability of measurements.

Objective 1. To prepare good practice guidance and guidelines based on the protocols developed in EMPIR JRP 15HLT06 MRTDosimetry. A paper presenting the results of a multicentre and multi-national evaluation of the accuracy of quantitative ^{177}Lu SPECT/CT imaging has been published [1]. This work demonstrates that reliable quantitative SPECT/CT is feasible following the dedicated calibration protocol developed within the MRTDosimetry project. The 3D printable phantom designs used in this work (consisting of a kidney and spleen model) have been made publicly available on the project's open-access data repository [2] allowing them to be used by clinical centres.

Objective 2. To publish a practical protocol for the commissioning and validation of a clinical MRT dosimetry calculation platform (with accompanying freely available validation datasets). 3D printable designs for the phantom used to produce the validation dataset for clinical MRT dosimetry calculation platforms, have also been made available on the project's open-access data repository [2]. This consists of a larger four organ phantom (left kidney, right kidney, spleen and liver) and dedicated elliptical phantom.

Objective 3. To further develop the e-learning training material produced in EMPIR JRP 15HLT06 MRTDosimetry to support the use of the protocol. The consortium has to date delivered 11 lectures as part of training courses endorsed by EFOMP, SGNM, SSRMP, BAG, DGMAP and NHS HSST. Work from the project has also been presented at 4 international and national workshops.

The expected results from the remainder of the project are:

The production of guidance documents for the calibration, commissioning and QC of quantitative imaging for dosimetry. The publication of the world's first practical protocol for the commissioning and validation of a clinical MRT dosimetry calculation platform. The complete validation dataset will be made available on project's open-access data repository. Widespread adoption of these protocols promoted through dissemination at major international and national nuclear medicine conferences and through professional societies.

Impact

Impact achieved to date: During the past 12 months the project has delivered training to ~1000 participants across a number of international and national courses. The project's open-access data repository (https://doi.org/10.17605/OSF.IO/69NGE) has been established. This resource has seen a significant increase in unique visits following the training courses and citation in [1].

Good practice guidance is being developed for the project's primary supporter, EANM, on the commissioning, calibration and quality control of SPECT imaging for MRT dosimetry. In addition guidance is also being developed for the clinical MRT dosimetry calculation platforms associated with these imaging techniques. This is in line with EANM's mission to facilitate communication worldwide among individuals pursuing clinical and research excellence in nuclear medicine. Currently, the EANM represents more than 9,000 specialists from 41 different countries within Europe and it serves the interests of a community that goes far beyond these numbers and geographical boundaries.

This project will provide the EANM and nuclear medicine standardisation bodies with easily available practical guidelines to support the robust application of MRT dosimetry in clinics. Combing the disciplines of clinical science and metrology will deliver a series of unique outputs which couple traceability and a metrological treatment of the clinical measurement chain with medical expertise for the delivery of MRT across a range of European healthcare systems.

The incorporation of training material specifically designed to support the uptake and use of these protocols into national and European ESMPE lectures dedicated to nuclear medicine dosimetry and national training schemes will ensure that EMPIR JRP 15HLT06 MRTDosimetry delivers a significant impact on nuclear medicine across Europe.

The good practice guidelines for SPECT activity calibration and for the commissioning and QC of SPECT for MRT dosimetry developed in this project will support the establishment of clinical trials protocols for MRT. An early example of this impact is engagement with UK NCRI (National Cancer Research Institute) Radiotherapy Trials Quality Assurance Team (RTTQA) who are responsible for the design and implementation of quality

assurance programmes for all NIHR CRN (National Institute for Health Research Clinical Research Network) Clinical Research Portfolio trials.

The uptake of the developed guidelines will provide a foundation for the harmonisation of quantitative imaging and for the validation of dosimetry calculation systems across Europe. This will form an important metrology contribution to delivering more effective, better targeted treatments, improved outcomes for the patients receiving them, and savings to the national and European health systems that are providing this care.

Project start date and duration:	1 September 2020, 24 months	
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Primary Supporter: Michael Lassmann, European Association of Nuclear Medicine		
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