

Publishable Summary for 19NRM01 MRgRT-DOS

Traceable dosimetry for small fields in MR-guided radiotherapy

Overview

There are 1.4M radiotherapy treatments in Europe annually, extensively using small radiation beams (x-rays or proton beams) to deliver optimized dose distributions to the cancer patient. MR guided RadioTherapy (MRgRT), the combined use of radiation beams to target the tumours and Magnetic Resonance Imaging (MRI) to provide image of soft tissue contrast, was recently introduced into clinics. This combined treatment has demonstrated the potential for delivering fewer adverse side-effects and more effective treatments, however full clinical utilisation of the treatment is hampered by the lack of standards for small field dosimetry. This project has delivered a methodology to extend the TRS-483 protocol for small field dosimetry towards application in MRgRT using x-rays (MRgXT). In addition, it has demonstrated traceable methods for MRgRT based on proton beams (MRgPT)

Need

MRgRT allows the patient anatomy to be imaged during the treatment and is therefore the next step in the ongoing development of radiotherapy to improve treatment efficacy. The number of clinical MR-guided X-ray Therapy (MRgXT) facilities (combining X-ray beams and MRI) has increased rapidly in the last few years which is expected to continue. Although not as clinically advanced, significant developments have also been made with MR-guided Proton Therapy (MRgPT) which combines proton beams and MRI.

For modern dose delivery techniques, the recent Code of Practice (CoP) TRS-483, enables medical physicists to perform traceable small field dosimetry. For MRgRT, small radiation fields are equally important and even though developments in MRgPT are lagging behind MRgXT, universities and industry, prior to the start of this projects, needed traceable methods for dosimetry to show the feasibility of dose delivery with MRgPT and to prepare for (pre)-clinical investigations.

In MRgRT, dosimetry needs to be performed in the presence of the magnetic field of the MRI scanner, which is known to affect both the (small) radiation field characteristics and the calibration of detectors. CoPs for small field dosimetry use an output correction factor to convert the detector calibration coefficient in a reference radiation field to small field based on the (small) radiation field characteristics. Consequently, existing CoPs for small field dosimetry are inadequate for application in MRgRT. Therefore, prior to the start of this project, medical physicists needed CoPs for traceable dosimetry for small fields in MRgRT.

Manufacturers have developed detectors for small field dosimetry in conventional radiotherapy. To assure the quality and the suitability of their products for application in small field dosimetry in MRgRT, they needed methods to assess detector characteristics in the presence of magnetic fields. The need for the work delivered in this project to elaborate standards for MRgXT and MRgPT harmonized with TRS-483 is also underlined by Standards Developing Organisations (SDOs) in their strategic documents; IAEA, IEC TC 62 and ISO/TC85/SC2.

Objectives

The project enabled traceable measurement of absorbed dose-to-water in small x-ray (photon) and proton beams (field size < 3 cm) in the presence of strong magnetic fields in support of future standards for small field dosimetry in MRgRT.

The specific objectives of the project were:

1. To determine a data set of correction factors and develop a measurement methodology for small fields in MRgXT extending the concept of IAEA/AAPM TRS-483 with a target uncertainty of 2.0 % ($k = 1$).
2. To investigate whether established traceable dose measurement methods for MRgXT and the concept of IAEA/AAPM TRS-483 can be adapted for scanned pencil-beam based MRgPT modalities.

3. To design and carry out Monte Carlo simulations of x-ray and proton beams in the presence of magnetic field to investigate radiation field characteristics, detector responses for on- and off-axis conditions and to determine detector properties and their suitability for small field dosimetry in MRgXT.
4. To design and carry out experiments (in laboratories and commercial MR-linacs) to provide dosimetrical measurement data on x-ray and proton beams in the presence of magnetic fields traceable to primary standards, to investigate radiation field characteristics and detector responses for on- and off-axis conditions and to determine detector properties and their suitability for small field dosimetry in MRgXT and MRgPT.
5. To facilitate the take up of methods, technology, guidelines, Codes of Practice and measurement infrastructure developed in the project by the standards developing organizations (such as IAEA) and end-users, such as clinical stakeholders, and manufacturers of facilities and measurement equipment.

Progress beyond the state of the art

Prior to the start of this project the state of the art was the TRS-483 CoP which provides a formalism for traceable small field dosimetry in conventional radiotherapy facilities. This formalism uses an output correction factor to convert the detector calibration coefficient in a reference field to one for a small field. For a large set of detector types, detector type specific output correction factors and other detector characteristics are tabulated as function of equivalent square field side (0.4–8.0 cm).

Correction factors and methodology for small field dosimetry in MRgXT (Obj. 1)

TRS-483 does not account for the presence of a magnetic field. The use of small off-axis fields, i.e. radiation fields for which the beam axis does not coincide with the machine isocentre, increases for MRgXT considerably. This project has progressed beyond the state of the art by determining a data set of output correction factors (target uncertainty=2.0 %) in the presence of magnetic fields, and by investigating the influence of *off-axis* conditions on these correction factors.

The magnetic field influences the symmetry of radiation fields in MRgXT facilities. Consequently, the position of the maximum dose drifts away from the central axis position compared to no magnetic field present. This effect increases with decreasing field size. Therefore, MRgXT field characteristics are incompatible with the TRS-483 methodology for both the determination of equivalent square field size and the positioning of the detector. This project has progressed beyond this by development of a methodology for traceable small field dosimetry in MRgXT facilities in line with TRS-483 accounting for these incompatibilities.

Small field dosimetry for MRgPT (Obj. 2)

The fringe part and homogeneous part of the MRI magnetic field strongly affects field characteristics in MRgPT. However, their impact on the definition of the reference field in MRgPT needs further investigations. Prior to the start of this project, no traceable method for dosimetry in MRgPT was available. This project has progressed beyond this, by developing a methodology for effectively and efficient mapping of the magnetic field of and in-beam MRI scanner and by developing a method, based on measurements and Monte Carlo simulations for traceable dosimetry in MRgPT and by investigating the impact of the magnetic field on the proton beam characteristics.

Detector properties in MRgXT and MRgPT (Obj. 3 and 4)

Small x-ray and proton radiation fields require the use of other detectors than those deployed for reference dosimetry. An overview with the relevant characteristics of these detectors for small x-ray fields is provided by TRS-483.

The impact of the magnetic field on these characteristics, e.g. volume averaging and the effective point of measurement, has been investigated and assessed in MRgRT-DOS. In addition, dead volume effects, which are important for Monte Carlo modelling of detector response in presence of magnetic fields have been investigated. It has been demonstrated that, for small field dosimetry detectors, the impact of the dead volume is larger than for reference dosimetry and that by accurate modelling of this dead volume the detectors response simulated is in agreement with measured data.

This project has gone beyond the state of the art by in-depth investigations on these characteristics for a set of detectors used for small field dosimetry in MRgRT.

Results

The project produced ten publications [1-10] where detailed analysis and discussion is provided. Below is a summary of the most important results by each objective.

Correction factors and methodology for small field dosimetry in MRgXT (Obj. 1)

Based on simulations, the first detector type specific correction factors for small square radiation fields in presence of magnetic fields have been published ([2], <https://iopscience.iop.org/article/10.1088/1361-6560/ac3344>). This allows for traceable measurements on the beam axis of small square radiation fields in MRgXT facilities. In addition, a method has been developed to extend TRS-483 for small field dosimetry in presence of magnetic fields using an existing dataset of output correction factors for conventional radiotherapy beams combined with calculated correction factors from MRgRT-DOS. This method has been validated against measurements in a clinical MR-linac facility. This demonstrated that the target uncertainty of 2.0 % could be achieved. These results have been presented and discussed at the ESTRO congress in Vienna ([http://dx.doi.org/10.1016/S0167-8140\(23\)08527-4](http://dx.doi.org/10.1016/S0167-8140(23)08527-4)) and a paper on this subject is close to submission.

Furthermore, all measured and calculated output correction factors for both MR-linacs and experimental facilities has been collected. During the review of this data set some discrepancies were identified for the output correction factors. The consortium partners are still analysing the cause for these discrepancies. Subsets of data from the data set will be made publicly available once published in peer-reviewed papers. One subset has been published in <https://doi.org/10.5281/zenodo.8413987>. The project partially achieved the objective.

Small field dosimetry for MRgPT (Obj. 2)

A key aspect in the concept of IAEA/AAPM TRS-483 are the definition of reference fields. To extend this concept to MRgPT, it is essential to determine the impact of the 3D magnetic field on the deflection of the scanned proton beam. Based on a custom-built semi-automatic method for 3D magnetic field mapping of large volumes, highly accurate magnetic field homogeneity measurements were performed with the 0.32 T in-beam MRI scanner of a proto-type MRgPT facility. Work has started to optimize simple 3D dose distributions in the presence of the 0.32 T in-beam MRIs magnetic field by incorporating the measured 3D magnetic fringe field map.

The impact of the MR gradient fields on the proton beam deflection, on spot position and pencil beam shape was determined by radiochromic film measurements. Apart from the expected energy dependent lateral horizontal beam deflection caused by the vertical magnetic field, an asymmetric vertical spot pattern distortion with maximum vertical displacement of the outer spots was also observed. These results have been published in a peer-reviewed paper ([9], <https://dx.doi.org/10.1002/mp.16448>). And can be used in future definitions of reference fields for MRgPT. Furthermore, an initial method based on alanine dosimetry has been applied to realize traceability for dosimetry in a proto-type MRgPT facility. The project partially achieved the objective.

Monte Carlo simulations of detector properties and radiation field characteristics in MRgXT and MRgPT (Obj. 3)

Finite Element Model (FEM) simulations have been used to estimate the dead volume effects for a set of detectors for small field dosimetry. These results show that small ionisation chambers used for small field dosimetry have a much larger dead volume compared to their total cavity volume than reference ionisation chambers. This emphasizes the importance of accurate determination of dead volume in ionization chambers in the context of chamber response simulations for MRgRT.

Monte Carlo investigations on the effective point of measurements demonstrate that the shift decreases in presence of magnetic fields with 40 % compared to the magnetic field-free case. This result allows for more accurate positioning of the detectors for measurements of relative dose profiles.

Charged particle equilibrium (CPE) is an essential radiation field characteristic for small field dosimetry. The impact of the magnetic field on CPE has been extensively studied by pencil beam simulations and calculation of the ratio K_w and D_w . These investigations have provided more fundamental insight in:

- the characteristics of small radiation fields in presence of magnetic fields;
- the shift of the point of maximum dose under influence of the magnetic field;
- the impact of the magnetic field on the lateral range of the secondary electrons.

In addition, these results allowed for a first assessment of the validity of the small field conditions given in TRS-483, which is under investigation. A paper, named as [The impact of ion chamber components on \$k_{B,Q}\$ for reference dosimetry in MRgRT \[6\]](#), has been published which demonstrates a novel method to assess the impact of chamber components on $k_{B,Q}$ factors. The project successfully achieved the objective.

Experiments of detector properties and radiation field characteristics in MRgXT and MRgPT (Obj. 4)

The project has realised several experimental facilities consisting of a linac and an electromagnet which have been optimized for small field dosimetry in presence of magnetic fields. Many data sets of output factors, cross- and depth-profiles have been measured for the various facilities: experimental facilities (with an electromagnet and linac) and clinical MR-linacs. To harmonize the methods and conditions between the various experimental facilities and MR-linacs used in the project, an overview of the experimental conditions have been drafted and the beam characteristics of all facilities have been summarized in a report. These data sets can be used to compare the machine and radiation field characteristics between experimental facilities and commercial MR-linacs to assess their suitability as a test facility for small field dosimetry in MRgXT.

Furthermore, time-resolved measurements using scintillators in clinical MR-linac facilities highlighted a dose transient at the start of every beam delivery. This potentially affects homogeneity of dose delivery. These results have been published ([7], <https://doi.org/10.1016/j.radmeas.2022.106759>).

Monte Carlo simulations of detector responses for proton beams in the presence of magnetic fields have been carried out. Additionally, measurements with plane parallel ionisation chambers and cylindrical ionisation chambers have been carried under the same conditions. From these results the impact of the magnetic field on chamber response could be determined for plane-parallel and cylindrical ionisation chambers. Part of the results have been published ([8], <https://aapm.onlinelibrary.wiley.com/doi/10.1002/mp.16368>) another paper has been submitted for publication. This gives the first insights on the impact of the magnetic on detector response for MRgPT.

Investigations on the application of passive detectors in a proto-type MRgPT facility demonstrates that important characteristics for alanine dosimetry (linearity, fading, and the impact of air gaps around the alanine pellet) remain unaffected by the magnetic field for measurements in MRgPT facilities.

Using the developed method for magnetic field mapping (under Objective 2), a high-resolution 3D magnetic field map has been successfully acquired of the in-beam MRI scanner. The results of these measurements are available and allow researchers to build an accurate Monte Carlo model to simulate the proton pencil beam transport through the magnetic field of the in-line MRI scanner, and to investigate the field characteristics of the deflected proton beam. Both are essential requirements for the development of MRgPT.

As part of a Research Mobility Grant (RMG), characteristics of radiochromic films for applications in solid phantoms with varying densities have been investigated. The results of these investigations have been presented by the RMG researcher at the SROC II International Conference in November 2022. The project successfully achieved the objective.

Impact

The project had impact on SDOs, the growing number of hospitals beginning to introduce MRgRT and the medical device industry; more specifically manufacturers of dosimetry equipment and MRgRT facilities. This will be of great benefit to a large population of patients in Europe and worldwide. The existing website of the previous project 15HLT08 MRgRT has been updated with results from the MRgRT-DOS project <https://mrgrtmetrology.com/>. The consortium has published ten peer-reviewed publications (3 more have been submitted, of which one has been accepted) and 27 conference contributions on dosimetry for MRgRT.

An online satellite symposium was organised in connection to the MRinRT 2021 congress in April 2021 with more than 200 participants. Participants from SDOs, hospitals and industry attended the symposium with many presentations from the MRgRT-DOS consortium. The symposium was used to inform the participants in general and stakeholders specially on the progress of MRgRT-DOS and developments since the previous symposium organised in the previous project 15HLT08 MRgRT.

Two online stakeholder meeting have been organised with the project's stakeholder committee including key representatives from SDO's, hospitals and industry. The work of the project was presented to the stakeholders and the current knowledge gaps in dosimetry for MRgRT were identified in a moderated discussion session. The information from this discussion session allows to consortium to get a more balanced view on the needs

for the difference stakeholder groups. For example, hospitals expressed their need for methods and data for small field dosimetry in MRgXT, while SDOs do not have established working groups on this specific topic.

Information on the project has been shared in four standards committees (AAPM TG 351, ESTRO ACROP Physics, NCS MR-linac QA, DIN). The results of the project have been presented at the annual meeting of EURAMET TC-IR in February 2022. The consortium is preparing an on-line webinar which will be organized in collaboration with the BIPM and CCRI on September 12 2023. The webinar has been published online as part of the CCRI webinar series and is available via <https://youtu.be/BkWrPrTo-6Y?si=H0FxmKVObxsKs32t>.

Part of the work being carried out in the project demonstrates the negative impact of small air volumes in ionisation chamber for small field dosimetry in presence of magnetic fields. Based on these results, a manufacturer of dosimetry equipment has started to optimise their design of ionisation chambers for measurements in presence of magnetic fields and has already completed this for two types of chambers.

The review paper [1], named as Reference dosimetry in MRI-linacs: evaluation of available protocols and data to establish a Code of Practice, is considered as the basis of future Codes of Practice for reference dosimetry in MRgXT.

Impact on industrial and other user communities

The project has developed traceable methods to determine detector type specific output correction factors for small field dosimetry in MRgXT and it has determined a dataset of detector type specific output correction factors. Furthermore, it has developed a methodology consistent with TRS-483 for small field dosimetry in MRgXT facilities with an uncertainty similar to the uncertainty reported in TRS-483 for small field dosimetry in conventional radiotherapy (2.0 %).

These results will accelerate the development of CoPs for small field dosimetry in MRgXT by SDOs. The methodology developed in MRgRT-DOS for small field dosimetry in square fields was shown to yield an uncertainty of 2.0 % for field sizes down to 0.5 x 0.5 cm². This methodology was presented to the stakeholder committee in the last stakeholder meeting (Oct. 2022). Final results of this method were presented at the 4th ECMP congress in Dublin and the ESTRO congress in Vienna. A publication is in preparation.

The experimental setups for small field dosimetry in the presence of magnetic fields characterised in the project enable the assessment of detector performance and suitability in well-defined test conditions. This allows manufacturers of measurement equipment to assure the quality of their products for application in small-field dosimetry in MRgRT. In addition, it will enable and support manufacturers of radiotherapy equipment, by demonstrating that MRgXT and future MRgPT facilities are compliant with regulatory criteria. A short overview of preliminary results from the various experimental and clinical facilities was presented to the stakeholder committee in the 1st stakeholder meeting.

The project has developed traceable dose measurement for proton beam dosimetry in the presence of magnetic fields. This will enable industry and research groups to show the feasibility of dose delivery of prototype MRgPT devices. The involvement of industry in the stakeholder committee and a collaborator from a research centre active in MRgPT enhances the dissemination of these methods. Therefore, this methodology will impact the future development of documentary standards in MRgPT. At the last PTCOG meeting a presentation on ionization chamber response to protons in presence of magnetic field was given. Overall, the results of this project have been disseminated to the medical physics community, via publications, the webinar, and an organized symposium.

Impact on the metrology and scientific communities

European National Metrology Institutes (NMIs) are global leaders in the field of dosimetry for MRgRT. This project has improved their existing measurement infrastructure for dosimetry in MRgRT, by extending the range of application in MRgXT dosimetry to small field dosimetry and to dosimetry for MRgPT facilities. Results, capabilities and improved knowledge has been disseminated to the European and international metrological community via their annual meetings. At the meeting of Euramet TC-IR in 2021, 2022 and 2023 and the CCRI meeting of 2021 an overview of the achievements of MRgRT-DOS has been presented. In the framework of an RMG, a guest researcher from a European DI outside the consortium has worked on the MRgRT-DOS project.

Several university groups are exploring new MRgPT facilities by the integration of proton beams with MRI scanners. The consortium has intensively collaborated with one of these groups (Medical University of Vienna) and therefore this project contributed to and support the scientific activities in this field. Furthermore, CoPs for

dosimetry in radiotherapy are based on a vast amount of scientific publication. Given the lack of scientific publications on small field dosimetry for MRgXT and dosimetry for MRgPT, the publications of this project will impact the development of CoPs for small field dosimetry in MRgRT considerably.

Impact on relevant standards

The project has developed a methodology for and has determined detector type specific correction factors for small field dosimetry in MRgRT. Via active participation in standard committees of AAPM, NCS ESTRO and DIN and by active engagement of SDOs in the stakeholder committee (IPEM, IEC, IAEA) the consortium has ensured that the results will be used in future standards for small field dosimetry in MRgXT and for the future MRgPT, in line with IAEA TRS-483. Consortium partners actively participate in the working groups ESTRO-ACROP physics, NCS subcommittee on MR linac QA, AAPM TG-351 and DIN NA 080-00-01 AA. The SDOs related to these working groups participate in the stakeholder committee.

Longer-term economic, social and environmental impacts

The rough estimate of the 1.4 million patients undergoing radiotherapy in Europe annually, that will benefit from MRgRT in the long-term, is >50 %. In addition, MRgRT will enable non-invasive treatments on a range of cancers, for which conventional radiotherapy, to date is inadequate, e.g., lung and pancreatic cancers.

MRgXT is a technique clinically introduced only recently by pioneering European hospitals and early adopters. Currently, the broader hospital community starts with the clinical implementation of MRgRT and the adoption rate will increase. The dissemination of the metrological research from this project via peer-reviewed publications, documentary standards and potential commercialisation of methodologies, will enhance the safe introduction of MRgXT and accelerates clinical acceptance by the broader community of European hospitals.

Proton therapy is considered as the treatment of choice in the field of paediatric oncology, and for a selected group of adult patients. MRgPT which combines superior soft tissue contrast from MR images with superior dose distributions from proton beams is considered the next major advancement in radiotherapy in the mid and long-term. The metrological research carried out in the project will be a key enabler for future translation of current prototyping efforts of manufacturers to a clinical setting. As such, this project enhances improved patient care in radiotherapy and future innovations in radiotherapy. Therefore, it will improve the quality of life of a large group of patients.

Market sales of MRgXT facilities have continuously increased since CE mark approvals mid-2016 and mid-2018 and represents a total revenue of more than 800 million Euro. Therefore, the economic value of MRgRT facilities is high. The outcome of this project and the dissemination of the results via peer-reviewed publications and documentary standards will enhance the speed of the commissioning process, increase the safety of the clinical implementation and accelerate propagation of MRgRT into the market.

List of publications

- [1] de Pooter, J.A., Billas, I., de Prez, L.A., Duane, S., Kapsch, R-P., Karger, C.P., van Asselen, B. and Wolthaus, J.W.H. *Physics in Medicine & Biology* 1 (2020) , 1, Reference dosimetry in MRI-linacs: evaluation of available protocols and data to establish a code of practice. <https://doi.org/10.1088/1361-6560/ab9efe>
- [2] Cervantes, Y., Duchaine, J., Billas, I., Duane, S. and Bouchard, H., *Physics in Medicine & Biology* 66 (2021), Monte Carlo calculation of detector perturbation and quality correction factors in a 1.5 T magnetic resonance guided radiation therapy small photon beams. <https://doi.org/10.1088/1361-6560/ac3344>
- [3] Billas, I., Bouchard, H., Oelfke, U. and Duane, S., *Physics in Medicine & Biology* 66 (2021), Traceable reference dosimetry in MRI guided radiotherapy using alanine: calibration and magnetic field correction factors of ionisation chambers. <https://doi.org/10.1088/1361-6560/ac0680>
- [4] Pojtinger, S., Nachbar, M., Ghandour, S., Pisaturo, O., Pachoud, M., Kapsch, R-P. and Thorwarth, D., *Physics in Medicine & Biology* 65 (2020), Experimental determination of magnetic field correction factors for ionization chambers in parallel and perpendicular orientations. <https://doi.org/10.1088/1361-6560/abca06>
- [5] Pojtinger, S., Nachbar, M., Kapsch, R-P. and Thorwarth, D., *Physics and Imaging in Radiation Oncology* 16 (2020), p 95-98, Influence of beam quality on reference dosimetry correction factors in magnetic resonance guided radiation therapy. <https://doi.org/10.1016/j.phro.2020.10.005>

[6] Navarro Campos, J., de Pooter, J.A., de Prez, L.A., Jansen, B. *Physics in Medicine & Biology* 67 (2022), The impact of ion chamber components on $k_{B,Q}$ for reference dosimetry in MRgRT. <https://doi.org/10.1088/1361-6560/ac77d0>

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[8] Mathieu Marot, Sonja Surla, Elisa Burke, Stephan Brons, Armin Runz, Steffen Greilich, Christian P. Karger, Oliver Jäkel, Lucas N. Burigo, *Medical Physics* (2023) Proton beam dosimetry in the presence of magnetic fields using Farmer-type ionization chambers of different radii. <https://doi.org/10.1002/mp.16368>

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[10] M F Klavsen, C Ankjærgaard, K Boye, C P Behrens, I R Vogelius, S Ehrbar, M Baumgartl, C Rippke, C Buchele, C K Renkamp, G V Santurio and C E Andersen, *Biomedical Physics & Engineering Express* (2023) Accumulated dose implications from systematic dose-rate transients in gated treatments with View ray MRIdian accelerators. <https://doi.org/10.1088/2057-1976/acf138>.

This list is also available here: <https://www.euramet.org/repository/research-publications-repository-link/>

Project start date and duration:		1 May 2020 (36 months)
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RMG1: VINS, Serbia (Employing organisation); VSL, Netherlands (Guestworking organisation).		