Publishable Summary for 16NRM03 RTNORM
k_Q factors in modern external beam radiotherapy applications to update IAEA TRS-398

Overview

The purpose of the present project was to contribute, by measuring and calculating k_{QQ_0} factors, towards the update of the ‘Absorbed Dose Determination in External Beam Radiotherapy: An International Code of Practice for Dosimetry based on Standards of Absorbed Dose to Water’, by the International Atomic Energy Agency (IAEA). The fundamental contribution made by the project towards this update was on a self-assessment of all generated dataset, via internal comparisons, before their submission to the IAEA.

Data generated such as p_Q and k_{QQ_0} factors for a range of ionization chamber types, and multiple radiation beam modalities (e.g. latest beam technologies), were submitted to contribute towards this update on medium energy x-rays, conventional (filtered) and flattening filter free (FFF) MV photons, and scanned proton beam modalities.

Need

Prior to the start of this project, 3.4 million Europeans were diagnosed with cancer every year and about half of the resulting treatments involve radiation therapy with ionising radiation. Accurate beam delivery and dosimetry are critical for successful and safe treatments. Hospital physicists are therefore required to perform measurements in accordance with validated measurement codes of practice or protocols, ensuring that doses delivered to patients at European hospitals are traceable to the quantity ‘absorbed dose to water’ measured in the SI unit gray (Gy). It is important that such a protocol is to be able to correct the dosimeter response for differences between the beam quality, which relates to the energy distribution of the radiation field, at the calibration laboratory (Q_0) and the beam qualities at the hospitals (Q). These corrections are called ‘beam quality correction factors’ and are known as $k_{Q,Q0}$.

The IAEA issued such a Code of Practice (the ‘TRS-398’) in 2000, which is the *de facto* norm for external beam radiotherapy dosimetry and is used on a worldwide basis. The data in TRS-398 include values of $k_{Q,Q0}$ factors that were calculated for clinical radiotherapy beams over the entire range of beam modalities that were available in the mid-1990s. Since the IAEA TRS-398 Code of Practice was first published, there have been significant advances in at least four areas: (i) treatment technology, including new beam modalities such as scanned proton beams, and flattening filter free photon beams, (ii) detector technology, *i.e.* new ionisation chamber types, (iii) improved metrology including the availability of new primary standards, and (iv) improved Monte Carlo simulation techniques. Prior to the start of the project, a major revision of 6 chapters of the IAEA TRS-398 was initiated in 2016 with a planned completion in 2019. New measured and calculated $k_{Q,Q0}$ factors based on modern treatment modalities, equipment, and computational codes were therefore required for this update. Therefore, the present project followed the IAEA call for organisations, and established consortia, to determine and provide up-to-date data for the TRS-398 update. The main goal of the present project included $k_{Q,Q0}$ factors traceable to absorbed dose to water primary standards needed to be measured and calculated for a selection of beam modalities and ionising radiation dosimeters (ionisation chambers).

Objectives

The overall objective of this project was to provide validated measured and calculated values of k_{QQ_0} factors for a series of ionisation chambers and a range of radiation beam modalities, which will contribute to the on-going revision of the Code of Practice IAEA TRS-398.

The specific objectives of the project were:

1. ***kV x-ray beams between 100 kV and 250 kV:*** (i) to measure k_{QQ_0} factors for 3 types of ionisation chambers and at least 8 beam qualities, ensuring direct traceability of the k_{QQ_0} factors to primary

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standards of absorbed dose to water; (ii) to calculate k_{QQ_0} factors for these beams using several validated Monte Carlo codes; (iii) to compare the new absorbed dose-to-water based formalism using k_{QQ_0} with a traditional air-kerma based formalism; iv) to compare the measured and calculated k_{QQ_0} factors for kV x-ray beams, and to provide IAEA with a validated consistent new dataset of k_{QQ_0} factors with target standard uncertainties better than 1.0 %.

2. ***High-energy- (MV) photon beams between 4 MV and 20 MV, including flattening filter free beams (FFF):*** (i) to measure k_{QQ_0} factors for at least 6 types of ionisation chambers and a range of beam qualities, ensuring direct traceability of the k_{QQ_0} factors to primary standards of absorbed dose to water; (ii) to calculate k_{QQ_0} factors for these beams using several validated Monte Carlo codes; (iii) to compare the measured and calculated k_{QQ_0} factors for high-energy (MV) photon beams, and to provide IAEA with a validated consistent new dataset of k_{QQ_0} factors with target standard uncertainties better than 0.7 %.
3. ***Scanned proton beams between 60 MeV and 250 MeV:*** (i) to measure k_{QQ_0} factors for at least 4 types of ionisation chambers and a range of beam qualities, ensuring direct traceability of the k_{QQ_0} factors to primary standards of absorbed dose to water; (ii) to calculate k_{QQ_0} factors for these beams using several validated Monte Carlo codes; (iii) to compare the measured and calculated k_{QQ_0} factors for scanned proton beams, and to provide IAEA with a validated consistent new dataset of k_{QQ_0} factors with target standard uncertainties better than 2.0 %.
4. To work closely with the IAEA task group 'Update of TRS-398', to ensure that the outputs of the project are aligned with their needs toward the revision of the Code of Practice, therefore providing experimental and calculated data that can be incorporated in the upcoming revision of the Code of Practice. To facilitate the take up of the project’s outputs by the end-users e.g. clinics, hospitals and manufacturers of ionisation chambers.

Progress beyond the state of the art

Updated $k_{Q,Q0}$ factors for kV x-rays

Prior to the start of this project, dosimetry in radiotherapy treatments using kV x-ray beams was largely based on primary standards for air kerma. To express dosimetry in terms of absorbed dose to water, current codes of practice include a conversion procedure based on several correction factors, which introduces additional uncertainties and leads to potential errors. While this approach remains valid, the present project supported a framework based on the direct use of the quantity of interest in all radiotherapy modalities, absorbed dose to water (D_w). In this framework, the use of ionisation chambers relies on the application of measured and calculated k_{QQ_0} values for a selection of beam qualities at the required reference conditions. Throughout the project, the $k_{Q,Q0}$ values were estimated with measurements traceable to recently developed absorbed dose to water primary standards for kV x-rays, a set of *unique calorimeters*, and calculated using some of the most advanced Monte Carlo codes for radiation dosimetry computations. Adding to the original plans to concentrate only on D_w-based dosimetry, the more traditional traceability chain based on the quantity *air kerma* (K_a) was also assessed, and the two traceability routes compared.

Updated k_{QQ_0} factors for high-energy (MV) photons

Dosimetry in radiotherapy treatment using high-energy photons was already underpinned by the availability of primary standards for absorbed dose to water. However, since the publication of the current version of the TRS-398 code of practice in 2000, new commercial ionisation chambers models and new radiation beam modalities (*e.g.* flattening filter-free beams) had emerged.

Updated k_{QQ_0} factors for scanned proton beams

Although some existing dosimetry codes of practice mention scanned proton beams, no specific guidance was yet provided at the onset of this project. Recent modelling had shown that the measured ion recombination correction factor in a scanned proton beam is significantly different from both continuous and pulsed beams. The requirements for absorbed dose reference conditions and beam quality parameters appropriate to scanned proton beams were only just becoming clear, and new absolute dosimetry measurements were required to determine k_{QQ_0} values.

Contribution to the revision of the TRS-398 Code of Practice

Measured and calculated datasets for kV x-rays, MV photons and scanned proton beams were each compared to provide a consistent, validated set for submission to the IAEA task group 'Update TRS-398'. To this end, the project partners worked on shared inputs: by sharing digital information such as the phase-space files that describe the radiation sources for the Monte Carlo computations, by sharing physical information, such as the computed tomographies of the ionisation chambers used in this project, and by circulating ionization chambers for cross-calibrations and to validate degrees of equivalence in the context of all measurements. This information-sharing strategy went beyond both the measuring and the computational capacity of any individual partners, and provided insights in the variations that may arise between the measured and the computed values, prior to their submission to the IAEA task group 'Update TRS-398'.

Results

Updated k_{QQ_0} factors for kV x-rays

Extensive data sets of both k_{QQ_0} (D_w-based dosimetry formalism) and p_Q factors (K_a-based dosimetry formalism) were generated, based both on measurements and Monte Carlo computations using the codes EGSnrc and PENELOPE. For measurements linked to the D_w-based dosimetry formalism, ionization chambers calibration coefficients were obtained in terms of the dosimetric quantity *absorbed dose to water* (D_w), where traceability was provided by three independent calorimeters previous to the project. During the present project, these calorimeters were used and improved further to expand the calibration capacities of their institutes (ENEA, LNHB and VSL) in a domain that has been explored to a relatively limited extent, that of kV x-rays dosimetry in terms of the quantity absorbed dose to water. Given the size of the datasets generated, methods were adopted during the project that were inspired by big-data analysis, using script-based procedures in combination with databases. Expanding on the initial project's goals in the domain of kV x-rays dosimetry, calibration of the same ionization chambers was additionally obtained in terms of the quantity *air kerma*, where traceability is provided by existing free-air chambers at the site of the participating institutes. As a result of both calibrations in terms of absorbed dose to water and kerma in air, two traceability routes were investigated which were of great importance to the validity of contemporary dosimetry protocols: the air-kerma route and the direct absorbed dose to water route.

Monte Carlo computations also played an essential role towards this objective as they provided fundamental ICRU-90 compliant data for conversion and correction factors that were needed for the D_w measurements, and by calculating, independently of all measurements, k_{QQ_0} factors under the same experimental conditions. Monte Carlo computations made it clear how critical is the geometric modelling (based on design blueprints) of the ionization chambers in the domain of kV x-rays dosimetry, with most critical aspects being the correct dimensions of the measurement volume and the definition of the materials in its immediate proximity, a condition that is relatively less critical in the domain of MV photon dosimetry. The datasets generated using Monte Carlo computation were both D_w-based and K_a-based.

Using measurements and Monte Carlo computations, it emerged that a k_{QQ_0} based approach to estimate a calibration coefficient at the user's radiation beam quality Q, when a calibration coefficient is available at the beam quality Q_0, is *not providing any clear advantage* in kV x-rays dosimetry, compared to a calibration of the same ionization chamber obtained in terms of the quantity *air kerma* at the user's radiation beam quality Q and later converted to a calibration coefficient expressed in terms of D_w via the application of air-kerma-based dosimetric protocols. These results were obtained considering that a D_w measurement is needed at the final user's beam quality Q and when the ionization chamber was calibrated again in terms of D_w, at the reference quality Q_0. However, given the accuracy of the measurements of D_w that can be obtained with the advancements of the calorimetric standards, and the simplicity of the formalism, it remains highly recommended that a user obtains, wherever possible, a calibration certificate in terms of D_w directly at their quality of interest Q.

This objective was fully achieved with datasets of k_{QQ_0} factors and p_Q factors compiled for five models of ionization chambers and for eight types of kV x-rays beam with combined standard uncertainties within the original target of 1.0 % (k=1) in most cases and, in the worst cases, up to about 1.6 %.

Updated k_Q factors for high-energy (MV) photons

An extended dataset of k_Q values was determined for clinical use and comparison purposes within the project. As for k_Q factors in kV x-rays, the dataset for MV photon dosimetry was based both on experimental measurements and Monte Carlo computations using the same computer codes EGSnrc and PENELOPE. For measurements, ionization chambers calibration coefficients were obtained in terms of the dosimetric quantity absorbed dose to water with traceability to graphite or water calorimeters, whose measurement capacity is internationally validated through their participation in the key comparison BIPM.RI(I)-K6 [6, 8]. As for kV x-rays, the size of the generated dataset analysis used techniques based on big data, scripts, and databases, to minimize the risk of errors and to ensure a coherent analysis procedure.

k_Q values for MV photons were calculated for 10 different types of ionization chamber (Exradin A1SL, Exradin A12S, IBA CC13, IBA FC65-G, IBA FC65-P, NE 2571, PTW 30013, PTW 31010, PTW 31013 and PTW 31021) in beams with and without flattening filters and applying recommendations from the recently published ICRU n°90 report although the effect was small. For ionization chambers whose calculations were performed by several partners, results showed a good agreement with a maximum deviation of 0.3 %. It became clear that volume-averaging corrections should be applied on the volume of water used to calculate the absorbed dose to water at the reference point and on the volume of the ionization chamber cavity used to calculate the absorbed dose to air inside the ionization chamber. As these terms appear in a ratio, corrections must and have been included in case of strong beam anisotropies, or large difference between the ionization chamber cavity volume and the water volume. The Monte Carlo results were published [7]. The statistical standard uncertainties (k=1) on calculated k_Q were lower than 0.3 % and most of the time around 0.1 %.

New k_Q values based on graphite calorimetry were measured for 3 types of ionization chamber (NE 2571, Exradin A1SL and PTW 30013) in beams with flattening filters (GE Saturne 43 or Varian TrueBeam). New k_Q values based on water calorimetry were measured for 4 types of ionization chamber (IBAFC65-G, NE 2571, PTW 30013 and PTW 31021) in beams with (wFF) and without (FFF) flattening filters (Varian TrueBeam). The k_Q values were corrected for the volume averaging effect (as if the beam was homogeneous on the dosimeter volume). This correction is small in the ^{60}Co and new linac wFF beams, but not in the FFF beams. The combined standard uncertainties (k=1) on measured k_Q factors were around 0.5 %. For ionization chambers where measurements were performed by several partners, and except for the lowest energies (6 MV and below), all the k_Q values measured in the present project and those previously published were in good agreement at one standard deviation and were lower than the TRS-398 values. The measured k_Q in FFF and wFF beams were in good agreement in an Elekta linac but not in a TrueBeam linac (with much more differences in the corresponding $TPR_{20,10}$) for which different k_Q = f ($TPR_{20,10}$) curves should be used for wFF and FFF beams.

k_Q factors were experimentally determined for five out of six ionization chamber models, and for ten models using Monte Carlo calculations, which overall exceeds the original number of detectors investigated and for which datasets were compiled. Datasets were also compared across the two methods, and this strengthened confidence in the data generated before they were submitted for inclusion in the TRS-398 update, with uncertainties that were within the target 0.7% (k=1). Taken together, the objective was fulfilled.

Updated $k_{Q,Q0}$ factors for scanned proton beams

For the first time, different Monte Carlo codes capable of transporting protons (PENELOPE /PENH, TOPAS/Geant4 and FLUKA) were compared with each other in terms of k_Q-factor calculation in scanned proton beams. For simplified geometries, it was found that these three Monte Carlo codes agreed with each other within 0.7 % or better, leading to the conclusion that these codes are suitable for k_Q-factor calculations in proton beams. As a result, k_Q-factors were calculated for 8 different proton beams qualities ranging from 60 MeV to 250 MeV and using two different Monte Carlo codes: PENELOPE /PENH and TOPAS/Geant4. The k_Q-factors of 15 ionization chambers were calculated using PENELOPE /PENH and those of 10 ionization chambers were calculated using TOPAS/Geant4—with an overlap of 9 ionization chambers with k_Q-factors calculated using two independent Monte Carlo codes, which constitutes a unique dataset of calculated k_Q-factors in proton beams [1, 2, 4]. The combined standard uncertainty of the calculated k_Q-factors was smaller than 1 % (*k=1*) and the agreement with the scarce experimental data available in the literature was always better than 1.2 %. The maximum difference between PENELOPE /PENH - and TOPAS/Geant4-calculated k_Q-factors was 2.2 %, which was consistent with a combined standard uncertainty of the order of 1 % (*k=1*), well within the original target of 2 % (*k=1*).

Although experimental datasets of k_Q factors did not achieve the targeted uncertainty of 2 % (k=1), the dataset of calculated k_Q factors listed 15 types of chambers which largely exceeded the target of 4 chambers. Monte Carlo generated datasets could not be benchmarked against experimental determinations, but a validation was achieved through a cross-comparison of the results that were obtained using two independent codes. Taken together, the objective was not fulfilled for the experimental data part but was compensated by a large data set produced via the calculations.

Impact

The project key route to a high impact was the publication of its unique measured and calculated data on k_Q factors towards the revision of IAEA TRS-398 Code of Practice. During the TRS-398 revision process, the IAEA received data from all over the world, to be selected and compiled after a thoughtful revision. Using a coordinated approach to validate data by means of internal comparisons, i.e. comparisons of results within this consortium, the present project ensured that the IAEA TRS-398 Update Core Group received high-quality data for the key European detectors and for new treatment modalities directly applicable to the medical physics communities at the cancer centres in Europe.

Project researchers offered fifteen presentations at European and Asian conferences (e.g. MCMA2017, ESTRO 37 and ESTRO 38). The project had major presence at various national meetings with end users such as hospital physicists in Italy, Germany, Spain, and Japan. The project successfully planned three training courses with ~400 attendees from European countries. One PhD thesis was part of the present project. The consortium published nine manuscripts and two more papers are pending. Finally, the project presented their progress regarding the datasets at EURAMET TC-IR, BIPM CCRI(I), ESTRO, NCS meetings, and IPEM committees.

Impact on clinical communities

The IAEA TRS-398 is the world's leading protocol for radiotherapy dosimetry and has been endorsed by organisations such as the World Health Organization (WHO) and the European Society for Radiotherapy and Oncology (ESTRO). The IAEA TRS-398 is used worldwide, in Europe and beyond. The data obtained in this project are critical for dosimetry underpinning accurate cancer treatments in Europe. The $k_{Q,Q0}$ factors are essential for current and future dosimetry with ionisation chambers in modern clinical beams. With the eventual inclusion of its production in the TRS-398 update (projected late in 2020 or early in 2021), this project had a direct and substantial impact since European radiotherapy clinics use this code of practice on a daily basis for critical tasks, such as the calibration of linear accelerators used in external-beam radiotherapy. This project will ultimately benefit 1.7 million citizens undergoing radiotherapy cancer treatment annually as radiotherapy clinics will use and rely on the correction factors and measurement procedures described in the revision of the TRS-398 Code of Practice.

For reference dosimetry, hospitals generally do not use correction factors directly from the scientific literature, and hence in order to comply with TRS-398 the correction factors for their type of reference dosimetry ionisation chamber need to be included in that norm. In the case where new treatments are available for which the reference dosimetry is not covered in TRS-398 (such as flattening filter-free photon beams), hospitals may have to resort to alternative procedures, or they may decide not to offer the treatments to patients. The outputs of this project will therefore lead to further harmonisation of clinical reference dosimetry for both conventional radiotherapy modalities and recently developed beam modalities and enable hospitals and clinics to improve their existing radiotherapy and to adopt new treatment modalities.

Impact on industrial and other user communities

This project ensured data for the leading producers of ionisation chambers (including European industry) and manufacturers of treatment equipment through the IAEA TRS-398. This will enhance their economic position, since the new ionisation chamber models potentially available in TRS-398 will be used as reference dosimetry at hospitals. European manufacturers of radiotherapy facilities have recently developed innovative new radiotherapy modalities such as scanned proton beams and flattening filter-free photon beams. They will benefit from the updated data sets determined in this project, as this new information will provide data which were lacking in previous version of the IAEA TRS-398 ensuring that these new modalities can be safely adopted in radiotherapy clinics.

Impact on the metrology and scientific communities

One of the absorbed doses to water standards was used on two of the major commercially available clinical accelerators. This strengthens confidence in the use of the beam quality specifier for these radiation therapy modalities. Additionally, this project has shown what impact the adoption of the ICRU report n°90 recommendations has had on calculated correction factors for reference dosimetry [3, 5, 7].

Impact on relevant standards

This project focused on the update of data that were central for the revision of the IAEA TRS-398, the world's leading dosimetry Code of Practice. In so doing, this project embraced the fundamental ideas underpinning the Code of Practice, which is to organise radiation dosimetry in a coherent manner and provide traceability to primary standards of the physical quantity *absorbed dose to water*. The chapters that received contributions from the project were IAEA update TRS-398 TG 'kV X-rays', IAEA update TRS-398 TG 'high energy photons', and IAEA update TRS-398 'protons and heavy ion beams'. A contribution was also made to the CCRI(I) and the EURAMET Technical Committee on Ionizing Radiation meetings.

Longer-term economic, social and environmental impacts

In line with the original drivers for the first edition of the TRS-398 Code of Practice, the coherence that is ensured by the concerted traceability to primary standards of absorbed dose to water, in all radiation therapy modalities, will result in the simplification of clinical dosimetry procedures, will reduce the risk of errors in the clinical setting, and will overall strengthen the confidence in cancer radiotherapy. An improved radiotherapy will offer both social and economic benefits in the form of better treatments, better therapeutic outcomes, and higher patient survival rates.

List of publications

[1] Baumann K S, Kaupa S, Bach C, Engenhart-Cabillic R and Zink K 2020 Monte Carlo calculation of beam quality correction factors in proton beams using TOPAS/GEANT4 *Phys Med Biol* **65** 055015 https://iopscience.iop.org/article/10.1088/1361-6560/ab6e53

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[3] Czarnecki D, Poppe B and Zink K 2018 Impact of new ICRU Report 90 recommendations on calculated correction factors for reference dosimetry *Phys Med Biol* **63** 155015. https://iopscience.iop.org/article/10.1088/1361-6560/aad148

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[5] Pimpinella M, Silvi L and Pinto M 2019 Calculation of kQ factors for Farmer-type ionization chambers following the recent recommendations on new key dosimetry data *Physica Medica* **57** 221–30. https://www.physicamedica.com/article/S1120-1797(18)31343-7/fulltext

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[9] Andreo P, Burns D T, Kapsch R P, McEwen M, Vatnitsky S, Andersen C E, Ballester F, Borbinha J, Delaunay F, Francescon P, Hanlon M D, Mirzakhanian L, Muir B, Ojala J, Oliver C P, Pimpinella M, Pinto M, de Prez L A, Seuntjens J, Sommier L, Teles P, Tikkanen J, Vijande J and Zink K 2020 Determination of consensus k_Q values for megavoltage photon beams for the update of IAEA TRS-398 https://doi.org/10.5281/zenodo.3903294

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