Publishable Summary for 18NRM02 PRISM-eBT
Primary standards and traceable measurement methods for X-ray emitting electronic brachytherapy devices

Overview

Electronic brachytherapy (eBT) is a cost-effective radiotherapeutic modality for the treatment of skin lesions, intraoperative partial breast irradiation, intracavitary and interstitial sites, brain tumours and kypho-Intraoperative Radiotherapy (IORT). While it offers potential for an extensive utilisation, this is unlikely to be achieved whilst eBT systems rely on individual calibration procedures. In most cases these systems are not directly traceable to NMIs and rely on indirect calibration methods with uncertainties larger than clinically acceptable. This project delivered a harmonised, simplified and traceable dosimetry for eBT, detectors and measurement devices for the determination of 3D dose distributions in water, to ensure that these systems can achieve their full clinical potential. During the project several primary realizations were established for both intercavitary and superficial treatment. (obj 1 &2). Standardized traceable calibration process for 3D detectors were established (obj 3) to provide traceable dosimetry for 3D dose distribution measurements (obj.4). Contribution to standard developing organizations were performed.

Need

Currently, most commercial eBT systems rely on specific calibration tools and procedures. It is therefore difficult to adopt clinically established treatment plans from one system to another, which impedes progress in this modality of radiotherapy. Direct traceability to an NMI is non-existent in terms of absorbed dose to water, the standard quantity in radiation therapy. Traceability has only been achieved for one commercially available device – outside Europe - in terms of air kerma strength, a quantity for which dosimetry for this type of sources is less robust than in terms of absorbed dose to water. Thus, the core requirement of clinical medical physics that dosimetry should be subject to independent and traceable verification is not yet met. Additionally, typical uncertainties of ± 10-15 % (k = 1) for IORT procedures using eBT are reported, which are larger than clinically acceptable.

Therefore, primary standards and suitable transfer instruments must be established for internal radiotherapy as well as for superficial (skin) external radiotherapy. Additionally, it is necessary to provide traceability for 3D dose distribution measurements. In contrast to external beam therapy, this is hardly existent in brachytherapy in general, due to the high demands on the experimental work in positioning and dosimetry.

Harmonized methodologies need to be developed to simplify calibration procedures for a generic set of radiation conditions for each device. Measurement procedures need to be established to facilitate quality assurance measurements and ensure traceability of commercial eBT treatment planning systems.

Objectives

The overall goal of this project was to carry out pre-normative research on eBT to simplify and harmonise eBT dosimetric procedures and provide metrological input to standardisation bodies.

The specific objectives were:

1. To establish primary standards for the absorbed dose rate to water for eBT devices at 1 cm depth of water for internal radiotherapy. To evaluate currently used transfer instruments and corresponding measurement procedures and to establish simple and robust tools for dissemination of the absorbed dose rate to water to clinical practice.
2. To establish a dosimetric methodology for superficial eBT aligned with or similar to the recommendations for superficial (skin) external radiotherapy given in International Atomic Energy Agency - Technical Reports Series (IAEA-TRS) 398, Deutsches Institut für Normung (DIN) 6809-4, Nederlandse Commissie voor Stralingsdosimetrie (NCS)-10 and Institute of Physics and Engineering

in Medicine (IPEM). The target uncertainty for the conversion of dose at the surface (i.e. 70 µm) to dose at 1 cm depth is 5 %.

3. To characterise detectors and measurement instruments suitable for the determination of 3D dose distributions in water by eBT devices. To develop a standardised traceable calibration process for these detectors, allowing a reduction in the uncertainties in dose, dose distribution and dose-effect-relation to a level recommended in IAEA Human Health Report No 31. The aim was to achieve uncertainties (k = 1) for the calibration coefficients of not more than: 1 % - 2 % (NMIs) and 2 % - 3 % (clinic) for the scintillation detectors and for the small volume ionisation chambers, 3.5 % for the gel dosimeter and 2.5 % for the alanine pellets.
4. To provide traceable dosimetry for 3D dose distribution measurements for at least three eBT commercial systems for which no dosimetry system currently exists and to make them available for the end user community.
5. To contribute to the development of technical work of IAEA and others where appropriate to ensure that the outputs of the project are aligned with their needs, communicated quickly to those developing the standards and to those who will use them, and in a form that can be incorporated into the standards at the earliest opportunity.

Progress beyond the state of the art

Objective 1: Primary standards and traceability route for internal radiotherapy

Four primary standards were developed for the realisation of the absorbed dose to water for internal radiotherapy with eBT devices at 1 cm depth within a water phantom. These were developed to provide a more direct traceability to absorbed dose to water and hence achieve better uncertainties than attainable with currently available primary standards. Selected ionisation transfer instruments (PTW 34013 and PTW 23342) currently used in radiotherapy were investigated to establish simple and robust measurement procedures and tools for dissemination of the absorbed dose rate to water to clinical practice. This will improve patient safety.

Objective 2: Superficial eBT

This project established a dosimetric methodology for superficial (skin) treatment with eBT, in terms of absorbed dose to water at the surface of a water phantom. The basis of this traceability route was formed by existing formalisms for low energy X-rays and implemented for eBT systems. The recommendations developed within the project were aligned with the recommendations for superficial (skin) external radiotherapy given in TRS 398, DIN 6809-4, NCS-10 and IPEM.

Objective 3: Characterisation and calibration of detectors for 3D dose distribution measurements

Different radiation detectors, scintillator, diamond detector, micro ionization chambers, Fricke gel, alanine were characterised for the measurement of 3D dose distributions close to various commercially available low energy eBT X-ray devices with or without fitted applicators. A standardised traceable calibration process for these detectors was established. The aim was to achieve relative standard uncertainties (k = 1) for the calibration coefficients of not more than: 2.5 % for the scintillation detectors, 2.5 % for the small volume ionisation chambers, 3.5 % for the gel dosimeter and 2.5 % for the alanine pellets. This will enable more accurate 3D dose distribution measurements close to eBT sources compared to currently used methods.

Objective 4: 3D dose distribution measurements and comparison with vendor-supplied dose maps

Based on the detector characterisations, traceable dosimetry for 3D dose distribution measurements was provided for eBT systems, for which no dosimetry system existed. The methodology was validated by comparing the measured 3D dose distributions with vendor-supplied dose maps. The methodology was described in Good Practice Guides (GPGs) which will be provided to Standards Developing Organisations (SDOs).

Results

Objective 1: Primary standards and traceability route for internal radiotherapy

For the realisation of the quantity absorbed dose to water, the different institutes had different approaches. The approaches of ENEA, CEA and CMI were based on modifications of conventional x-ray calibration set-ups, whilst with PTB's primary standard measurements were performed with dedicated miniature x-ray tubes. For this work, in order to obtain the emitted x-ray spectra, a catalogue of photon fluence spectra emitted by different eBT devices was prepared. The spectra were measured and analysed and were published as a

separate catalogue of spectra, publicly available online. The primary standards were established and a comparison of the determined dose values has been performed by a comparison with ion chambers.

However, significant differences in the calibration factors were observed, which could partly be explained by the fact, that it was not possible to calibrate in the same condition for the miniature x-ray tubes and the conventional x-ray tubes due to geometrical restrictions and lower output of the miniature x-ray tubes. Additionally, differences among the conventional x-ray tube set-ups were observed. Finding a solution for this problem must be addressed by further research. However, the project successfully achieved the objective.

Objective 2: Superficial eBT

The absorbed dose to water at 10 mm and on the phantom surface (depth of 70 µm) as well as the air kerma free in air were calculated with the penEasy Monte Carlo code using a published and validated phase space file for the Esteya eBT system with a 30 mm applicator. A separate Monte Carlo model was created using Topas for the Axxent eBT system with a 35 mm diameter skin applicator. This model was validated.

The spectrum of the Esteya eBT system with a 30 mm diameter collimator was measured at VSL with a high-purity germanium detector. Spectra from the Axxent source with and without applicator have been measured with a CdTe spectrometer. Using the obtained x-ray spectra from measurements, Monte Carlo and existing literature, the respective beam qualities were matched by the VSL x-ray facility using the software programs SpekCalc v1.1 and SpekPy v2.0.3.

The selected ion chambers used as transfer instruments between the participants, were calibrated in the matched beam qualities at the reference distance. As eBT surface clinic applications are performed on the skin the calibration coefficient was corrected for differences between the scatter and primary photon contributions at the reference and the surface distance.

Measurement with the selected ion chambers and the VSL Free-Air-Chamber (FAC) were done to determine output ratios at various distances from the applicators for the Esteya and the Axxent eBT systems and to validate the ion chamber calibrations at various distances. Together with the Monte Carlo calculations these was used to determine k_Q and conversion factors from air-kerma to absorbed dose to water.

The relevant correction and conversion factors for measurement with the chambers in terms of air-kerma to absorbed dose, based on the obtained spectra, were established using methods described in existing Codes of Practice.

A water phantom and a solid phantom were constructed and conversion from dose-at-surface to dose-at-1cm depth was measured and calculated, together with the beam profiles at both depths. Calculations were validated with measurements using GafChromic films for the Esteya eBT system. The project successfully achieved the objective.

Objective 3: Characterisation and calibration of detectors for 3D dose distribution measurements

A BCF-12 organic plastic scintillation detector (PSD) was calibrated and characterised in terms of energy response for photon energies up to 50 keV. The response of the PSD was found to be decreasing linearly with increasing dose rates.

The air kerma response of two ionisation chambers (Exradin A26 and IBA RAZOR Nano) and a solid state detector (PTW 60019 microDiamond) was measured using low energy kV photon beams. Monte Carlo simulations were used to determine correction factors to convert the detector responses measured in terms of air kerma to absorbed dose to water. Simulations in water using eBT spectra to determine detector specific correction factors are ongoing.

A Fricke gel dosimeter doped with Xylenol Orange was calibrated and characterised for electronic brachytherapy applications. Measurements covered the dose range from 0 – 20 Gy. The gel samples were read out using an MRI scanner. Alanine dosimeters were calibrated and characterised in terms of energy response using 8 - 20 keV monoenergetic X-rays at the Diamond Light Source (DLS) synchrotron facility. For higher energies up to around 70 keV, alanine response data from the Anton and Büermann (2015) study was used. The uncertainties in the alanine responses ranged from 1.8 to 3.9%. The project successfully achieved the objective.

Objective 4: 3D dose distribution measurements and comparison with vendor-supplied dose maps

Discussion was held with project partners and external stakeholders to decide where absorbed dose measurements should be performed. Some of the regions of interest were close to specific electronic brachytherapy sources inside the water phantom. Dedicated phantoms were designed for the measurements using alanine pellets and Fricke gels. The Fricke gel composition was studied in detail and the appropriate correction factors determined in order to achieve the best possible uncertainty for the measurements.

Appropriate adaptations were done to allow accurate measurements in commercially available water phantoms with scintillator, ionization chamber and diamond-based detectors.

Measurements of the depth dose and beam profile were performed in the water phantom (PTW MP3) using scintillator detectors for the Papillon50 device and with ionization chambers and diamond detectors for the INTRABEAM device with and without spherical applicators in the PTB water phantom.

NPL used alanine pellets in custom-made water equivalent plastic phantoms to measure the absorbed dose to water close to the INTRABEAM eBT and Papillon 50 eBT X-ray sources with and without applicators fitted. Measurements were done by CEA using custom-made Fricke gel-based dosimeters with dedicated phantom for the INTRABEAM eBT system with 4 cm applicator fitted. Good agreement was found between the relative dose distributions. The project successfully achieved the objective.

Impact

Dissemination activities included a presentation of the consortium outline to the EURAMET Technical Committee for Ionising Radiation (TC-IR) annually. Contributions to the IAEA Brachytherapy COP, German DIN 6803 “Photonen-Brachytherapie” and German Standards Committee Radiology (NAR): NAR AA1 AK 6803. Furthermore, for the Nederlandse Commissie voor Stralingsdosimetrie, the Bureau National des étudiants en École de Management (BNEM) and ISO TC 85 Nuclear energy, nuclear technologies, and radiological protection. Poster and oral presentations of the project outline and individual results were given in a range of conferences, e.g. the World conference of Brachytherapy, ESTRO 21 and ESTRO22, the Joint Meeting of ÖGMP, SGSMP and DGMP, the BiGART 2021, the Meeting of the Dutch society of medical physics engineers (NVKFM), and the Days of radiation protection. Six successful technical training visits of Consortium members among themselves and to stakeholders (e.g. PTB and AU) were organized. An invited talk of the outline of the project was given at CIRMS 2022.

Impact on industrial and other user communities

A calibration method for eBT in terms of absorbed dose rate to water directly traceable to NMIs will be available for the first time for all commercially available eBT devices. New calibration services for EU end users will be offered. Robust and efficient procedures will be established based on metrological standards and corresponding transfer instruments resulting in improved acceptance and marketability of eBT devices. Standardisation and harmonisation in calibration methods will improve health care, due to a more precise and less error-prone dose delivery, and harmonised and improved reporting within Europe. It will also reduce effort and costs of manufacturers of eBT systems, when developing quality assurance procedures and calibrations for their eBT devices.

Impact on the metrology and scientific communities

Primary standards for absorbed dose to water are being realised. Moreover, new “eBT equivalent” X-ray qualities are being established which can be adopted, without high costs, by NMIs in other countries enabling them to open a calibration service in their country. This will enable the dissemination of absorbed dose to water at 1 cm depth in Europe and worldwide, which will improve the comparability of clinical studies with these devices.

As radiation fields in BT have steep gradients in lateral and longitudinal extension, their dosimetric complexity is similar to external small field dosimetry. Therefore, this project will have impact on the metrology related to both detectors and measurement procedures. This project will also lay the dosimetric foundation for future topics, such as dose enhancement effects of gold nanoparticles in combination with eBT-devices.

Impact on relevant standards

Relevant standards comprising all eBT devices were non-existent and are being prepared now. This project has provided substantial contribution to a manuscript of an updated version of IAEA-TECDOC-1274, covering the major topics of brachytherapy and now eBT as well. The manuscript was finalized and submitted to the IAEA publication committee in May 2022, and will be published shortly. The German standard DIN 6803-4 electronic BT is based on PRISM-eBT. All members of this working group are either collaborators, advisors, or core members of PRISM-eBT and have access to all the data on the SharePoint. This project will also provide valuable fundamental insight and missing information for the development of dosimetric methods for high energy photon emitting sources to the German DIN Standards Committee for Radiology (NAR) respectively (DIN 6803-3). Additionally, the consortium will inform other standardisation bodies (e.g EURAMET-TC-IR, CCRI(I) and ISO TC85 SC2) on the progress of the project.

Longer-term economic, social and environmental impacts

According to the European Cancer Observatory the estimated cancer incidence in the European Union is set to reach 3.0 million people in 2018, and approximately half of these patients receive radiotherapy as part of their treatment course. Because the treatment costs for eBT are lower compared to conventional radiotherapy, a higher acceptance and wide use of eBT will contribute to a reduction in costs to the health systems of European countries. Standardisation and harmonisation in calibration methods, as promoted by this project, will improve health care due to a more precise and less error-prone dose delivery as well as harmonised and improved reporting within Europe.

List of publications

- F. Garcia Yip et al. Characterization of small active detectors for electronic brachytherapy dosimetry, Journal of Instrumentation, February 2022. DOI: https://doi.org/10.1088/1748-0221/17/03/P03001
- P. Georgi et al. Towards 3D dose verification of an electronic brachytherapy source with a plastic scintillation detector, Medical Physics, February 2022. DOI: https://doi.org/10.1002/mp.15568
- P. van den Elzenet al. Alanine response to low energy synchrotron X-ray radiation, Physics in Medicine & Biology, March 2023. DOI: https://doi.org/10.1088/1361-6560/acb886

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

Project start date and duration:	1 July 2019, 42 months	
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Internal Funded Partners: 1. PTB, Germany 2. CEA, France 3. CMI, Czech Republic 4. ENEA, Italy 5. NPL, United Kingdom 6. VSL, Netherlands	External Funded Partners: 7. AU, Denmark 8. MAASTRO clinic, Netherlands	Unfunded Partners: 9. Hasselt University Belgium (joined from 22 February 2021)
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