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PRISM-eBT

Primary standards and traceable measurement methods for X-ray emitting electronic brachytherapy devices

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1 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.

2 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 \pm 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.

3 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.

4 Results

Objective 1: Primary standards and traceability route for internal radiotherapy

The primary standards were developed for the dose-to-water rate in water at 1 cm distance from the surface of the applicator with 40 mm diameter generated by INTRABEAM eBT device on the device axis for the high bias voltage of 50 kV.

PTB: The former primary standard for I-125 seeds was upgraded. The phantom material was replaced, new apertures and aperture holders, new measurement electronics and software were designed and implemented. This major overhaul was used as an opportunity to rename the chamber ipFAC (in phantom Free Air Chamber), as the name extrapolation chamber does not contribute to the understanding of the measurement method. Spectra were measured with a HPGe-Detector (Canberra GL0110P) in 30 cm distance from the source. The detector's efficiency was calibrated by means of activity standards. Based on this measurement and available information a Detector model was set-up to calculate a response matrix. Spectra were unfolded by a software based on Bayesian procedure. The spectra are given in the catalogue of spectra of this project. MC-calculations were performed with the software toolkits EGSnrc and MCNP. Results: In figure 1 below a measurement of the water-kerma with the ipFAC is presented for the INTRABEAM with 4 cm diameter spherical applicator. Given are the water-kerma values determined for a combinations of plate separations x_{i+1} and x_i, X being the mean value of both. The mean water kerma was determined to 5.885E-05 Gy/s. This value is related to 30 cm distance between source and measuring point. From this value the absorbed dose to water at 1 cm distance in a water phantom results in: 1.16E-02 Gy/s.



Figure 1. measurement of the water-kerma with the ipFAC is presented for the INTRABEAM with 4 cm diameter spherical applicator. Given are the water-kerma values determined for a combinations of plate separations xi+1 and xi, X being the mean value of both.



CEA: A new primary standard for absorbed dose to water at 1 cm depth has been established for the INTRABEAM device in the configuration using 4 cm diameter applicator. The method is based on air kerma standard established using a free air ionization chamber and further conversion to absorbed dose to water using a combination of on-site measurements in the beam delivered by an INTRABEAM device and Monte-Carlo calculations with PENELOPE code accurately modeling the geometry of the INTRABEAM and the measurement configuration. The new reference beam has been set using conventional X-Ray generators by reproducing with appropriate additional filtration and using accurate X-Ray spectrometry the beam quality corresponding to the INTRABEAM device with 4 cm applicator. A procedure on beam reproduction using this method has been provided allowing a broader use of the methodology by other NMIs/DIs and for the reproduction of other beam qualities. The reference air kerma value for the reproduced beam was measured at 3.353E-03 Gy/s (uncertainty 1.48 % at k=1) and the corresponding absorbed dose to water at 1 cm depth 4.951E-03 Gy/s (uncertainty 2.45 % at k=1). Two ionization chambers, selected as candidates for the transfer of the primary standard to the final users, have been calibrated in terms of absorbed dose to water at 1 cm depth in the frame of an inter-comparison organized within the project involving four participants (figure 2).



Figure 2. New reference beam quality obtained by reproducing the photon spectrum of the INTRABEAM device with 4 cm diameter applicator configuration using a conventional X-Ray generator (left) and the methodology developed by CEA for the establishment of the primary standard in absorbed dose to water at 1 cm depth for the electronic brachytherapy devices (right).

CMI primary standard

CMI established an ionometric primary standard of absorbed dose to water at 1 cm water depth from the INTRABEAM applicator on the INTRABEAM axis, $D_{w,1cm}$, based on the existing free air chamber primary standard **Error! Reference source not found.** The conversion of the reference air kerma rate in air to the absorbed dose in water at the depth of 1 cm from INTRABEAM applicator is largely based on the method published in **Error! Reference source not found.** that was updated in the PRISM-eBT project and adopted by CMI. The $D_{w,1cm}$ was expressed as follows:

$$\dot{D}_{w,1cm} = F_{KD}(r) \cdot \dot{K}_{eBT,air}(r) = F_{KD}(r) \cdot N_{K,ref} \cdot I_{TC,eBT}(r) \cdot k_{field}(r) \cdot k_{OrefOeBT}$$

where F_{KD} is $K_{air,eBT}$ to $D_{w,1cm}$ conversion factor, $N_{K,ref}$ is the transfer chamber calibration coefficient for air kerma in the eBT-equivalent beam, $I_{TC,eBT}(r)$ is the ionization current measured by the transfer chamber at the distance r, k_{field} is the field inhomogeneity correction for the transfer chamber, and $k_{QrefQeBT}$ is the beam quality correction which corrects for the difference of the chamber response to the eBT-equivalent and to the eBT photon fluence spectra. For r = 30 cm distance of the chamber reference point to the applicator centre, the chamber calibration coefficient in the absorbed dose-to-water at 1 cm water depth is $N_{Dw,1cm}(30 \text{ cm}) =$ $(8.79 \pm 0.18) \cdot 10^8 \text{ Gy/C } (2,1\%; \text{ k=1})$. The uncertainty budget for the $N_{Dw,1cm}(r)$ determined for the CMI RC6M ionization chamber in air at a distance of r = 30 cm from the applicator centre is presented in **Error! Reference source not found.**.



Table 1: Uncertainty budget for $N_{Dw,1cm}$ of RC6M chamber in air at the distance r = 30 cm from the applicator centre.

Uncer	tainty component	Value	u _A (%) u _B (%)	
Nĸ,ref		4.799.10 ⁶ Gy/0	0.36	0.63
FKD	applicator density uncertainty (1)_	-	1.73
	chamber positioning ⁽²⁾	-	-	0.67
	others	185.4	0.25	0.61
k field		0.990	-	0.22
	ЗТ	0.998	-	0.26
Combi	ined uncertainty (k=1)		0.44	2.05
NDw,1cm	n(r) (<i>k</i> =1; r = 30.0 cm)	8.79·10 ⁸ Gy/C	2.10	

1. Difference in F_{KD} for applicator material density of 1.27 g/cm³ and 1.40 g/cm³;

2. ±1 mm, at end-user site.

The main uncertainty component is the density of the applicator material which was determined as the difference in F_{KD} for low (1.27 g/cm³) and high (1.40 g/cm³) values mentioned in literature. If the density is known, this component can be significantly reduced.

ENEA primary standard

As for both CMI and LNHB, ENEA's primary realisation of the quantity D_w hinges on the realisation of the air kerma via the Italian National Standard of air kerma for medium energy x-rays, an Attix-type chamber which ENEA uses for the Italian participation in the BIPM.RI(I)-K3 key comparison. This is an unusual scenario in that ENEA had earlier committed to the use of the parallel-plates free air chamber that constitutes the basis for the participation of Italy in the BIPM.RI(I)-K2 and -K7 key comparisons and, notably, the low-energy x-ray tube with it associated. This tube however experienced a failure in spring 2022 and an emergency solution had to be found in the use of the alternate, medium-energy x-ray tube, where the eBT beam qualities were established.

The primary standard of air kerma in medium-energy X-rays has been used at ENEA to determine the air kerma in two beam qualities at the distance of 100 cm: eBT-bare (supplementary to the intercomparison) and eBT+4 cm applicator (quality of choice for the Dw,1cm intercomparison). The determination of the air kerma at this distance was used to calibrate a transfer instrument, a RadCal RC6M ser. no. 10206, so that the air kerma could be established also at a shorter distance from the x-ray source, and therefore increase the air kerma rate and the associated signal-to-noise ratio, particularly for the chambers of smaller volume. The final distance chosen for the calibration of transfer chambers was 81 cm.

The eBT simulated beam qualities were realized at ENEA on the medium-energy x-ray tube based on the eBT catalogue created as part of the project. As part of the realization of these qualities, an x-ray spectrometry comparison was run together with CMI at ENEA (see below). These beam qualities were realized on a bipolar x-ray tube whose fixed filtration is 3 mm Be (see Table 2) (figure 3).

Quality	eBT "bare"	eBT with 4 cm applicator
kV	50	50
Additional filtration	0.90 mm Al	1.69 mm Al
Half-value layer (HVL, mm of aluminium)	1.04	Not determined experimentally
μ/ ho , mass attenuation coefficient, cm^2g^{-1}	0.56	0.45

Table 2: Realisation of two eBT-equivalent qualities on the medium-energy x-ray tube of ENEA-INMRI





Figure 3. X-ray spectrometry at ENEA. In the picture, the CdTe spectrometer of CMI positioned in the medium-energy Xray beam of ENEA-INMRI.

The eBT equivalent qualities summarised in Table 2 were used to determine the air kerma at 100 cm distance, which is the distance where the Attix chamber operates. The determination of air kerma at this distance was then used to calibrate a transfer chamber, a low-energy thin-windowed RadCal RC6M serial number 10206, so that the air kerma could be later established at 81 cm distance where all calibrations with the transfer chambers were carried out. Conversion to the quantity Dw, 1cm in eBT sources is based on F_{KD} is $K_{air,eBT}$ to $D_{w,1cm}$ conversion factor has described above for CMI.

Evaluation of transfer instruments:

The energy and angular dependence of ionization chambers PTW 23344 and Radcal RC6M was measured by the partners. The RC6M is much weaker energy dependent at low energies (< 20 keV) compared to PTW23344 (**Error! Reference source not found.**4). Photons with energies in the range 8-25 keV are largely represented in the eBT spectra therefore the energy dependence in this energy range is a drawback. Angular dependence of both chambers is very weak (around ± 1 % for PTW23344 and around ± 0.5 % for RC6M) and corresponds to the measurement uncertainty. As a result, it was decided that the chamber RC6M is a better candidate for a secondary transfer standard.





Figure 4: Relative difference of energy dependence of studied ionization chambers with respect to spectrum N40.

Catalogue of eBT spectra

The main goal of the catalogue was to develop a set of reference X-ray qualities denoted as "eBT equivalent" that would be established for in-laboratory activities by the X-ray tubes with tungsten anode usually available in calibration laboratories, but the tube voltage and the filter are specifically selected to simulate the energy spectrum of the requested eBT radiation. The catalogue was compiled from suitable data available in literature and from the data measured or created by the project. The catalogues were compiled for Axxent (by Xoft), Esteya (by Elekta), INTRABEAM (by ZEISS), ioRT-50 (by WOmed), and Papillon 50 (by Ariane Medical Systems) eBT devices. They are available at the project website and Zenodo data storage. The project successfully achieved the objective.

Objective 2: Superficial eBT

For dosimetry in electronic brachytherapy (eBT) for superficial treatments, there has been no harmonized methodology traceable to national metrology institutes. Discrepancies between absorbed doses predicted by manufacturers and those estimated by metrology laboratories have been reported. The objective of this work package was to propose a simple method and formalism for dosimetry for superficial eBT. **(VSL, Maastro clinic, UHasselt**) The basis of this formalism formed the existing air-kerma based protocols of the AAMP, NCS and IPEMB. However, the method to arrive to the relevant correction factors was different: less complicated to obtain the correction factors and more straightforward to apply them. The method does not involve a detailed simulation of the ionization chamber. The feasibility of this formalism was studied with measurements and calculations performed in eBT systems from Xoft Axxent, Zeiss INTRAEAM and Elekta Esteya. Eventually, the methods were validated for an Elekta Esteya with 30 mm applicator. These results have been submitted for publication in a peer reviewed journal.

Measured and calculated eBT photon spectra were matched to that produced at the calibration laboratory with conventional x-ray systems. Two different ionisation chambers, calibrated against a primary standard, were used to measure signal ratios at different distances from the source in-air along the beam axis. Monte Carlo (MC) calculated average mass energy absorption ratios were obtained in water and air. Backscatter factors in water were calculated and validated with publications. Additionally, air-kerma ratios were calculated in different positions along the beam axis. Finally, measurements with radiochromic films were performed in a water phantom to determine the ratio of dose to the surface to dose at 1 cm depth in water. These were compared with Monte Carlo calculations.

Calculations and measurements were combined to estimate the dose at the surface of a water phantom (~70 μ m) and the dose at 1 cm depth in water. Discrepancies between different ion chambers were observed



at the surface between 1 % and 9 % for the different systems of. They were not considered significant for the Esteya and Axxent systems but significant for the INTRABEAM.

For the Elekta Esteya system with 30 mm surface applicator more data was obtained than for the other two systems. These data were used to validate the proposed method for one system. For this system, the obtained calculations and measurements were combined to estimate the dose at the surface (~70 μ m) and at 1 cm depth in water. The uncertainty for absorbed dose at the surface was established to be 5.8 % (k = 2). Agreement between the two different ion chambers was 1.7 %, i.e. well within the uncertainty. The agreement with the manufacturer dosimetry was within 2 %, with an uncertainty of 4 % (k = 2). The feasibility of the proposed formalism and methodology for an Esteya was demonstrated. In the future the method could be investigated for different superficial eBT systems with different surface applicators.

As another route a primary standard for the absorbed dose to water for surface applications with 70 kV electronic brachytherapy sources was established (PTB). For this, the method of evaluation was modified to account for the different geometries in interstitial and surface brachytherapy and for the different energy distributions of the radiation fields, respectively. The correction factors required to determine the absorbed dose to water were evaluated using Monte Carlo (MC) simulations. MC-calculations were also used to estimate the uncertainties of this method. It could be shown that determining the absorbed dose to water in 1 cm depth below the surface of a water phantom Dw (1°cm) is feasible with the ipFAC. Thereby the method to determine Dw (1°cm) when the source is placed at 50 cm distance and the beam is collimated turns out to be more robust than placing the source applicator assembly directly on the phantom. The latter method features significantly larger uncertainties, 3.7 % compared to 1.4 % (both for k = 2), but it is more practical and easier to implement in clinical routine. The project successfully achieved the objective.

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

Six different dosimeters for possible use in eBT dosimetry were characterised and/or calibrated within the framework of the PRISM-eBT project: two commercially available ionisation chambers and one diamond detector, one custom-built plastic scintillation detector and two chemical dosimeters, i.e., Fricke gel and alanine pellets. The response of all dosimeters showed a strong energy dependence in the low energy kilovoltage eBT X-ray range. All of the detectors were characterised and found to be suitable for measurements in the steep dose gradients close to eBT X-ray sources.

PTB: Three active detectors, Exradin A26 chamber (A26), IBA RAZOR Nano chamber (RN), and PTW 60019 microDiamond (mD), were characterized for their use in electronic BrachyTherapy (eBT) dosimetry. The detectors were calibrated in terms of air kerma using the ISO "N" (narrow) and "TW" (therapy) X-rays series from 7.5 kV to 100 kV. The responses to mono-energetic photons and their uncertainties were determined with Bayesian parameter estimation, assuming a model that incorporated smoothness via a spline function. The response functions obtained this way are consistent with 18 calibration qualities simultaneously. This approach improves on the traditional procedure of associating the response to the mean energy of the corresponding spectra. The energy responses were obtained in 0.25 keV energy steps from 6 keV to 70 keV, see figure 5. An uncertainty of about 2 % standard deviation was achieved – meeting the upper limit of the foreseen uncertainty range of 1 % to 2 % for NMIs according to the corresponding objective. With differences in magnitude due to their sizes and the nature of their active volumes, the energy responses of the three detectors follow a similar relative behaviour. Even when the response is far from flat at low energies, i.e., below about 20 keV, the determination of reliable energy dependence curves enables the use of these detectors for dosimetry in the vicinity of eBT units.

The angular dependence of the three detectors with respect to beam incidence was also measured in air in a 180° range in steps of 10° using the Zeiss INTRABEAM system (50 kV), see figure 6. For both energy and angular response characterization, the axes of the detectors were aligned in parallel with the beam axis (end-on) since this is the expected orientation in further measurements of absorbed dose distribution in water around eBT sources at PTB.





Figure 5: Air kerma response (fitted splines as lines) of the Exradin A26 ion chamber (A26), IBA razor nano chamber (RN) and PTW microDiamond detector (mD) in the interval from 6 keV to 70 keV. The symbols (labeled "msrd") represent the measured response at the indicated series. The right axes accounts for the response normalized to N-30 (30 kV narrow beam). The 95 % coverage intervals of the fitted splines are also shown.





Figure 6: Angular dependance (from -90° to 90°) of the A26, RAZOR Nano and microDiamond measured in air. Response to the INTRABEAM at 50 kV normalized to the value at 0° (parallel incidence) with, collimated beam (Ø 1 cm) at source detector distance 145 mm.

CEA: A new dosimeter based on EasyDosit Fricke gels have been developed for the measurement of the 3D distributions of absorbed dose to water for the INTRABEAM device with 4 cm diameter applicator. The new dosimeter has been fully characterized in terms of energy response and linearity of the response with the irradiating dose. The later has been achieved by improving the methodology of gel preparation with a new approach using oxygen bubbling. The gel sensitivity has also been increased by about 20 % by this technique. A dedicated phantom has been designed and manufactured allowing the measurements with the INTRABEAM device at the user's site. The readings of the MRI signal from gels after irradiation has been automatized using a Python program specially developed in the frame of the project. The measured absorbed dose to gel has been finally converted to absorbed dose to water using conversion coefficients calculated by Monte-Carlo simulations with PENELOPE code by accurately modeling the measurement conditions (figure 7).





Figure 7. New preparation of Fricke gels using oxygen bubbling allowing the linearity of the dosimeter response with the dose delivered and the increase of its sensitivity.

NPL: Alanine pellets with a nominal thickness of 0.5 mm and 5 mm diameter were characterised and calibrated for use in eBT applications. The pellets consisted of (by weight) 90.9 % L- α -alanine amino acid and 9.1 % paraffin wax. They were measured in kV X-rays down to energies of 8 keV using two different methods.

To quantify the alanine response in the 8 to 20 keV range relative to ⁶⁰Co radiation, the alanine pellets were irradiated in monoenergetic X-rays at the Diamond Light Source synchrotron (van den Elzen *et al.*2023). The absorbed dose to graphite was measured with NPL's small portable graphite calorimeter (SPGC). The alanine pellets were set up in a graphite phantom which had the same dimensions as the graphite components of the SPGC. At NPL, alanine is traceably calibrated against the ⁶⁰Co absorbed dose primary standard. The alanine response to low energy X-rays was measured by comparing the dose to alanine to the dose measured with the SPGC after the application of Monte Carlo calculated conversion factors between the measured dose to graphite and the absorbed dose to water delivered to the alanine pellets. Figure 8 shows the alanine response as a function of X-ray energy. The uncertainty in the response factors measured by NPL was found to be ranging from 3.4 to 3.5 % (*k* = 2). For higher energies, data from the Anton and Büermann (2015) study are shown in figure 8.





Response of alanine to low energy X-rays relative to ⁶⁰Co

Figure 8. Alanine response to low energy X-rays relative to 60 Co. Black dots: response measured at the DLS synchrotron. White triangles: data from the Anton and Büermann (2015) study. All error bars represent the expanded uncertainty (k=2).

Other beamlines with higher X-ray energies were not available during the PRISM-eBT project due to Covid restrictions, so the alanine response in 8.5 to 47.9 keV ISO 4037 narrow series X-rays relative to the response to ⁶⁰Co radiation was measured at NPL using conventional X-ray sources. For this second method, the absorbed dose was derived from measurements with ionisation chambers calibrated in terms of air kerma and a subsequent conversion to absorbed dose to water by using the AAPM TG-41 protocol.

The uncertainties in the alanine response measured with the ionometric method based on ISO 4037 X-rays and the conversion to absorbed dose (7.4 %, k = 2) were found to be much greater than for the calorimetric method based on monoenergetic synchrotron X-rays. The alanine responses shown in figure 8 are therefore considered to be the final results within the framework of the PRISM-eBT project.

AU: A new small-point scintillator-based detector developed at PTB has been characterized for 3D dose distribution measurements of a Papillon50 eBT device. The detector consisted of a 1mm3 plastic scintillator (BCF12) probe coupled to an electrometer through an optical fiber. The dose-rate and energy dependency of the plastic scintillator was determined. The dose-rate dependency was determined by measuring the dose rate from a Papillo50 device with the plastic scintillator and a well-type ionization chamber (HDR1000+, Standard Imaging), figure 9a. The difference dose rates were obtained by varying the current of the Papillon50 X-ray tube from 0.3 mA to 3.0 mA. A slight linear decrease in the measured dose rate with the plastic scintillator was observed, figure 9b. This leads to a relative change of 3 % in the dose rate span investigated, which can be accounted for by using the linear function.





Figure 9. a) A schematic drawing of the setup for the dose rate dependency of the plastic scintillator (PSD). The PSD was placed ~2/3 down the well-type ionization chamber and then the Papillon50 tube was placed in the top of the ionization chamber. The two detectors were therefore irradiated simultaneous. B) The relative signal of the two detectors as function of the measured dose in the PSD.

The energy dependency was determined through Monte Carlo simulations. The Papillon50 X-ray tube was modelled in Geant4 and a set of phase-space files was determined. These phase-space files were then used to score the dose at various depths in water from 0 mm to 50 mm. The dose was scored both in water and polystyrene. A 4 % change in the relative absorbed dose between water and polystyrene was observed over the range, figure 10. This also was corrected for when using the plastic scintillator for depth dose measurements. The project successfully achieved the objective.



Figure 10. The relative absorbed dose in water and in polystyrene as function of depth based on the E-spectrum from a Papillon50 source.

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

The 3D distributions of absorbed dose to water have been measured and compared with the data provided by the manufacturers for two electronic brachytherapy devices. For the INTRABEAM device (Zeiss) two configurations have been considered (bare needle and with 4 cm diameter applicator) and measurements



were done with four different detector types. For the Papillon 50 (Ariane Medical Systems) the configuration used an open-ended applicator with a 25 mm inner diameter and the dose distributions were measured with three different detector types.

CEA: The Fricke gel based EasyDosit dosimeter developed in the frame of the project was used to determine the absorbed dose distributions in a gel phantom encapsulating the 4 cm diameter spherical applicator with the INTRABEAM probe tip inserted. At first, the gel phantom associated to the spherical applicator was irradiated by the INTRABEAM source and the signal read by MRI. The homogeneity of the magnetic field over the whole volume of the gel phantom is considered. Then, the relative absorbed dose distribution is deduced. The relative absorbed dose in water was determined by adopting a gel to water conversion factor calculated by a Monte-Carlo based method. Finally, the measured absolute absorbed dose rate distributions in water (uncertainty of 6.62 % k=2) were compared to the data provided by the manufacturer Zeiss. The absolute dose values were determined from the relative ones using the established primary standard in terms of D_{w,1cm} which was a result of Objective 1 (figure 11).



Figure 11. Photo taken during the measurements with the EasyDosit gel dosimeter and its phantom for the INTRABEAM device with 4 cm diameter applicator at St. Louis hospital in Paris and example of the obtained measured distributions compared to data from the vendor.

PTB: A methodology to determine the absorbed dose rate to water distribution from electronic brachytherapy (eBT) units was suggested. It consists in measuring directly in a full scatter water phantom with small active detectors which energy response at low X-ray photon energy had been previously characterized, see above, objective 3. Dose distributions of INTRABEAM 500 system in two configurations – bare needle and with the spherical 40 mm applicator – were measured in water using the Exradin A26 ionization chamber and the PTW 60019 microDiamond detector. The continuous energy response of these two detectors in terms of air kerma from 5 keV to 70 keV (eBT energy range) was available from objective 3. These responses were converted to the corresponding responses–in absorbed dose to water using correction factors obtained with Monte Carlo (MC) particle transport simulations. The detectors were modelled using the MCNP code and their calibrations in air were simulated to refine and validate the model.

Furthermore, a series of simulations of the experimental arrangement of the INTRABEAM and the detector were carried out for determining the system specific detector correction factors. These values are distance-dependent due to the steep dose gradient and the remarkable spectral changes around the eBT source in water.

Finally, the resulting radial and the polar dose rate distributions depending on the distance from the INTRABEAM device are reported and compared with the manufacturer supplied data, see figures 12 and 13. The dose rate profiles for the bare needle configuration of the two detectors and the manufacturer's data quite well agree, see figure 12, while for the 40 mm applicator (figure 14), significant differences between the different measurement methods and the manufacturer's data are present. The uncertainties are in the order of a few percent and, accordingly, smaller than the symbols. Possible reasons for the inconsistencies for the 40 mm applicator are the uncertainties in the positioning as well as the calibration methods used for the different detectors.





Figure 12. Comparison of the dose rate distributions in the axis of the bare needle configuration. Detector measurements and data distributed by the manufacturer (Carl Zeiss).



Figure 13. Comparison of the dose rate distributions in the axis of the 40 mm spherical applicator configuration (top direction) measured with the A26 chamber and with the microDiamond detector as well as the manufacturer's data.





Figure 14. Dose rate distributions of the 40 mm spherical applicator configuration measured in four different directions at the horizontal plane of the isocenter, see right part of figure 13.

NPL: 3D dose distributions close to two selected eBT sources, an INTRABEAM and a Papillon 50 X-ray source, were measured with alanine dosimeters. Watertight plastic phantoms which could be loaded with the alanine pellets characterised as part of objective 3 were designed and built at NPL. One measurement campaign was performed at the PTB (Braunschweig, Germany) to measure the dose rate to water close to an INTRABEAM eBT source for both the bare needle configuration and the 40 mm diameter spherical applicator configuration. For the bare needle measurements, the alanine pellets were fixed inside the plastic phantom at 5, 10, 15, 20 and 25 mm depth from the tip of the needle along its longitudinal axis. For the 40 mm spherical applicator, the alanine pellets were fixed at 5, 10 and 15 mm depth from the surface of the sphere. All measurements were performed in water in a large water tank under full scatter conditions.

The second measurement campaign was performed at Aarhus University Hospital (Aarhus, Denmark), where a Papillon 50 eBT source was used. The Papillon 50 device was fitted with a 25 mm straight applicator tube. The third plastic phantom for alanine pellets which was designed and built at NPL was fitted to the applicator tube and set up at the top of a full scatter water tank. For the absorbed dose measurements, the alanine pellets were fixed at 0, 5, 10, 15, 20 and 25 mm depth from the exit plane of the 25 mm applicator and along the central beam axis of the collimated X-ray beam. The '0 mm' depth coincided with the exit plane of the 25 mm applicator at the waterline of the filled water tank.

The alanine pellets in each of the three plastic phantoms were irradiated simultaneously. The absorbed dose to the alanine was then read out with an electron paramagnetic resonance unit at NPL. Monte Carlo simulations were performed to calculate photon fluence spectra and mean X-ray energies at the centre of the alanine pellets to derive k_Q factors for each of the measurement points for the three setups. This was necessary because of the considerable decrease of the alanine response for the low energy eBT X-rays.

Finally, the measured dose rates were compared against published dose rates. Good agreement was found between the dose rates measured with alanine close to the INTRABEAM source and the dose map provided by the manufacturer (Zeiss) (see figures 15 and 16). For the Papillon 50 source, however, no dose maps were available from the manufacturer (Ariane Medical Systems), so the measurements were compared against a generic data set from the literature, which resulted in large discrepancies (see figure 17).





Figure 15. Dose rate to water as a function of the distance from the tip of the INTRABEAM bare needle parallel to the longitudinal axis. Black dots: mean dose rates measured at the centre of the alanine pellets. The measured dose rates were compared against the Calibration V4.0 dose rate data from the manufacturer (Zeiss).



Figure 16. Dose rate to water as a function of the distance from the centre of the INTRABEAM 40 mm diameter spherical applicator. Black dots: mean dose rates measured at the centre of the alanine pellets in the transverse plane; black triangles: mean dose rates measured at the centre of the alanine pellets at the top of the applicator parallel to the needle. The measured dose rates were compared against the Calibration V4.0 dose rate data from the manufacturer (Zeiss).





Figure 17. Dose rate to water close to the Papillon 50 X-ray source as a function of the distance from the exit plane of the 25 mm applicator along the central beam axis. Black dots: mean dose rates measured at the centre of the alanine pellets. The measured dose rates were compared against the MC calculated dose rate data published by Croce et al. in 2012. The difference between the two datasets was found to be ranging from 43 % at 0 mm to 54 % at 25 mm depth in water.

AU: A method to measure the percentage depth dose and profiles of eBT devices with a focused beam line was developed and tested on a Papillon50 eBT device at Aarhus University Hospital. The method consisted of a small point scintillator-based detector (1 mm³ active area) placed on a moveable stage in a large water phantom (600x500x408 mm³) (MP3 water phantom, PTW) to ensure full scatter. The Papillon50 tube was placed above the water surface with the tube pointing downward and just breaching the water surface.

The positional accuracy of the motorized stage was determined by moving the stage in 1 mm steps and recording the step length with an external camera. The measurement uncertainty was 0.1 mm (k=1), figure 18.



Figure 18. Histogram of the measured phantom stage step-size when expecting 1 mm steps along the three axes of movement. The SD along each axis is denoted with dotted lines, and the mean step size is denoted with dashed lines.

The percentage depth dose of the Papillon50 was determined by measuring the dose rate for 2 s in a range from 0 mm to 50 mm depth with steps of 1-3 mm. The measurements were compared to Monte Carlo simulations, figure 19. The profiles were similarly measured with the plastic scintillator. Profiles were measured in five depths and compared to Monte Carlo simulations, figure 20. The project successfully achieved the objective.





Figure 19: a) PDD curve as measured with the PSD (diamonds) and scored with Monte Carlo simulation (squares). The dashed line is a linear interpolation of the MC results. Error bars indicate ±1 SD. (b) The ratio between the measured and scored doses (dots). Error bars indicate ±1 SD. Lines denote 0 % (dashed) and 1 % (dotted) deviations.





P50 dose profiles

Figure 20. Dose profiles as measured along the x-axis (crosses) and y-axis (circles) and scored with MC simulation (solid line). Graph (f) shows the FWHM of the profiles (dots) as a function of depth along with linear fits (dashed line along x-axis measurements, dotted line along y-axis measurements, and dotted-dashed line for MC results).

5 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.

6 List of publications

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

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