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TRACEABILITY TO ABSORBED-DOSE-TO-WATER PRIMARY STANDARDS IN DOSIMETRY OF BRACHYTHERAPY SOURCES USED FOR RADIOTHERAPY

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Abstract – In the current brachytherapy practice, the procedures to determine the absorbed dose imparted to the patient are affected by an uncertainty higher than in radiotherapy with external beams. That could reduce the success of brachytherapy treatments. Most of the uncertainty is due to a lacking metrology: no absorbed-dose primary standards are so far available to assure direct traceability in dosimetry of brachytherapy sources. This paper outlines the project “Increasing cancer treatment efficacy using 3D brachytherapy”, co-funded in the framework of the project iMERA-Plus according to the Grant Agreement No. 217257 between the European Commission and the European Association of National Metrology Institutes. The aim of the project is to develop methods for the direct measurement of the absorbed dose to water and to extend the use of this reference quantity to brachytherapy dosimetry with an uncertainty on the dose delivered to the target volume less than 5% ($k=1$) at clinical level. The present project will potentially increase the accuracy and safety of brachytherapy to a level comparable to that typical of radiotherapy with external accelerator beams.

Keywords: brachytherapy, dosimetry, dose distribution.

1. INTRODUCTION

Brachytherapy (BT) is a particular radiotherapy technique in which small encapsulated radioactive sources are placed inside or in close proximity to the treatment volume delivering a high dose to the tumour at small distances while sparing the surrounding tissue. In recent years, the use of BT has increased in Europe and in the rest of the world but in order to optimize these treatments there is still a need for more accurate dosimetry with high spatial resolution. The absorbed dose to water, D_w , is the quantity of interest for dosimetry in BT treatments. No D_w primary standards are so far available to assure traceability in dosimetry of BT sources. Currently D_w in brachytherapy is determined indirectly by a conversion procedure –applied at clinical level– starting from measurements that are traceable to air kerma standards [1, 2]. This conversion procedure is a considerable source of uncertainty and potential error on the absorbed dose imparted to the patient. On the other hand a large uncertainty on the delivered absorbed dose can have a negative influence on the clinical success of radiotherapy [3]. This paper outlines the European joint research project

T2.J06 “Brachytherapy”, co-funded in the framework of the project iMERA-Plus according to the Grant Agreement No. 217257 between the European Commission and the European Association of National Metrology Institutes (EURAMET). The project is focussed on the programme “Health” and responds to the necessity that dose measurements of radiation sources for BT treatments carried out in the clinic be traceable to D_w primary standards. The aim of the project is to develop methods for the direct measurement of D_w and to extend the use of this reference quantity to BT dosimetry with an uncertainty on the dose delivered to the target volume to a level comparable to that typical of radiotherapy with external accelerator beams.

2. DESCRIPTION OF THE PROJECT

2.1. Participants and objectives

To achieve the objectives of the project, the research and measurement capabilities of the following European National Metrology Institutes (NMIs) –in the field of ionizing radiation measurements– are brought together: BEV, Austria; CMI, Czech Republic; ENEA-INMRI, Italy; ITN, Portugal; LNE-LNHB, France; VSL, The Netherlands; NPL, United Kingdom; PTB, Germany; SSM, Sweden; STUK, Finland. Project coordination has been entrusted to the ENEA-INMRI. Most of these NMIs have a long experience in the design and construction of air kerma and absorbed dose standards in a wide range of radiation qualities. All of these NMIs have a broad experience in dosimetric procedures and related Monte Carlo (MC) calculations so that the whole group of the institutes achieves a critical mass to accomplish the objectives of the project. The project “Brachytherapy” aims at establishing across Europe a more accurate metrological basis in an important medical application of ionizing radiation –brachytherapy– by a significant improvement of the accuracy on the absorbed dose imparted to cancer patients receiving BT treatments. The project responds to the necessity for traceability –to D_w primary standards– of dose measurements carried out in the clinic with BT radiation sources. The first objective of the project is to construct primary standards to measure D_w due to radioactive sources for BT. Once these new standards are developed, the project aims to implement a metrological chain based on direct D_w measurements, in order to assure traceability of BT dosimetry at secondary standards laboratories and at radiotherapy centres. Finally, the project aims at optimising BT by accounting for the strong spatial variation of absorbed dose around BT sources. To this end, the project will develop high-resolution methods to allow an accurate determination of 3D dose distributions. The final target uncertainty on the dose delivered to the target volume is less than 5% ($k=1$) at clinical level.

2.2. Planned activities

The project started on 1 July 2008 for a period of 36 months. It is structured with four technical work packages (WP2, WP3, WP4 and WP5). Work packages WP2 and

WP3 constitute the core of the project, aiming at using D_w as the reference quantity to be directly measured for BT sources. To this end, a robust system of D_w standards will be delivered in WP2 for Low Dose Rate, LDR, BT sources and in WP3 for High Dose Rate, HDR, BT sources. Various standards have been developing within each of these two work packages. These standards differ from each another in design in order to highlight possible systematic errors and give together a more robust D_w determination. In particular, three LDR standards –based on ionometry– have been developed by ENEA-INMRI (§ 3.1), LNE-LNHB (§ 3.3) and PTB (§ 3.5), respectively. Two HDR standards –based on water calorimetry– have been developed by PTB (§ 3.6) and VSL (§ 3.7); two HDR standards –based on graphite calorimetry– have been developed by ENEA-INMRI (§ 3.2) and NPL (§ 3.4). With these new standards, reference values of D_w at the reference distance of 1 cm from LDR and HDR BT sources will be determined with a target value for the best measurement relative uncertainty $u(D_w, 1\text{ cm}) \leq 2\%$ ($k=1$). Once the above results have been obtained, work packages WP4 and WP5 are addressed to the stakeholders (e.g. radiotherapy medical centres and secondary standards laboratories). The objective of work package WP4 is to develop a calibration chain and an associated measurement procedure to transfer the new reference quantity to the end users minimizing the uncertainty. To allow the linkage between the current (air kerma strength or reference air kerma rate) and the new (absorbed dose to water) reference quantities, work package WP4 aims at experimentally re-determining the dose rate constant, Λ , with a lower uncertainty (about 3% ($k=1$)) for some of the most widely used BT sources. The aim of work package WP5 is to identify and optimize a dosimetry procedure for checking D_w spatial distribution, effective for the standardization of measurements at radiotherapy centres in irregularly shaped fields by BT sources in water or water equivalent phantoms. The expected output is the availability of suitable portable methods with assessed reliability and accuracy –leading to the target of a delivered dose with an uncertainty less than 5% ($k=1$)– at clinical level. At first, accurate determination of energy and dose response curves is carried out for various detection methods: gel dosimeters, radiochromic films, scintillation detectors, TLD dosimeters, alanine dosimeters, liquid ionization chambers, semiconductor detectors, and 2D multidetector systems. Then, the spatial dose distributions around BT sources used in clinical applications will be determined, in water or water-equivalent phantoms, and supported by MC simulations using EGSnrc, PENELOPE, and MCNP codes [4, 5 and 6]. A final comparison among the different detection methods will show possible advantages and disadvantages of each method and allow selecting the methods more suitable to attain the JRP major task of a lower uncertainty in BT dosimetry.

3. RESULTS SO FAR OBTAINED

3.1 The ENEA-INMRI standard for LDR BT sources

The ENEA-INMRI standard for low-intensity and low-

energy ($E < 40$ keV) BT sources is based on water kerma determination in phantom by ionometric measurement and a conversion procedure based on MC calculations. A large angle and variable volume ionization chamber (LA-GRF chamber) has been designed in order to carry out air kerma determination in a graphite phantom at a point positioned at a distance 30 cm from the radioactive source and at a water equivalent depth of 1 cm (Fig. 1). The chamber design is similar to that of the existing ENEA-INMRI standard chamber for absorbed dose measurement due to beta radiation (an extrapolation chamber based on Böhm design), but it is designed to work with low energy photons [7] and has a thick front window equivalent to a depth of 1 cm of water. In particular, the chamber minimum measuring volume has a depth larger than the maximum range of the secondary electrons produced in the chamber front window by 40 keV photons. A MC calculated correction factor accounts for the non-linearity of the measured charge as a function of the chamber volume. The mechanical construction of the LA-GRF chamber is at an advanced stage and the correction and/or conversion factors assessment is underway.

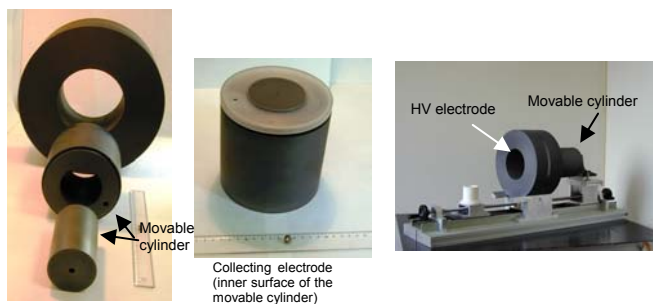


Fig. 1. Mechanical components of the ENEA-INMRI in-graphite-phantom LA-GRF chamber.

3.2 The ENEA-INMRI standard for HDR BT sources

The design of a graphite calorimeter for ^{192}Ir BT sources has been conceived and optimised on the basis of MC and heat transfer simulations. The calorimeter is disc-shaped and has a nested construction. The core is ring-shaped, 2 mm thick and 5 mm high, with a radius of 25 mm. The core is surrounded by a 0.5 mm thick graphite jacket. Both these bodies are surrounded by the graphite medium. The core, the jacket and the medium are thermally insulated by 0.5 mm gaps, in which high vacuum is obtained by a pumping unit. The graphite parts are coupled to a PMMA housing to which the vacuum flange is fixed (Fig. 2). The internal surfaces of the calorimeter are coated by thin aluminized Mylar to minimize radiative heat transfer.

The calorimeter is intended to be electrically calibrated. For this purpose heaters having different sizes are distributed in the three calorimeter bodies. In the core and in the jacket very small thermistors (0.3 mm diameter) are used as sensors and as heaters, in order to minimize the amount of non-graphite materials in these two components. A 3D-model of the calorimeter has been developed for heat transfer calculation by the finite element method, to

optimize the number and the position of the sensing and heating thermistors (Fig. 3).

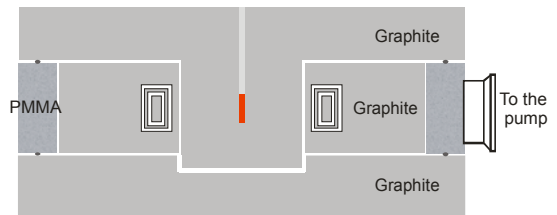


Fig. 2. Schematic drawing of the graphite calorimeter. The calorimeter is disc-shaped, with a nested construction around the ring-shaped graphite core.

MC calculations have been performed by the EGSnrc/DOSRZnrc code [4]. The depth dose distribution in graphite resulting from a typical ^{192}Ir source used in BT was calculated and used for modelling the heat source in the heat transfer calculations. The heat transfer calculation showed that at 25 mm distance the core senses less thermal gradients than at smaller distances. Therefore a source-core distance of 25 mm was considered suitable for measurements –at a dose rate still sufficient to obtain reproducible results– of the temperature rise in graphite. The minimum size of the cylindrical graphite phantom needed to ensure about 99.5% of backscatter at the measurement point was determined by MC calculations. The minimum phantom radius is 10 cm for a source-core distance of 25 mm. The calorimeter will be included in a larger cylindrical graphite phantom, at least 20 cm diameter and 20 cm height, that will ensure the full-backscatter conditions at the measurement point. To test the proper coupling between the graphite and the PMMA housing a scale model of the calorimeter top part and housing was constructed. A satisfactory vacuum value was obtained, showing the feasibility of the proposed arrangement of the different calorimeter parts. The assembly of the calorimeter is well underway.

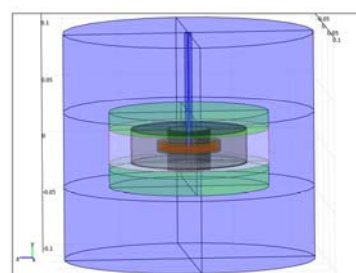


Fig. 3. 3D calorimeter model built for the heat transfer calculations, aimed at optimizing the number and the position of the thermistors and of the heaters in the calorimeter.

3.3 The LNE-LNHB standard for LDR BT sources

LNE-LNHB is establishing a two-step procedure that overcomes practical difficulties encountered when measuring directly D_w for LDR BT sources [8].

The first step of LNE-LNHB's methodology is based on the determination of the water kerma rate, at the surface S of a 1 cm radius water-equivalent spherical phantom placed in air and containing the LDR seed in its centre. As shown in Fig. 4 that quantity is measured in the plane passing through the seed centre and perpendicular to its longitudinal axis. A free-in-air ring-shaped ionization chamber (see Fig. 5) and a

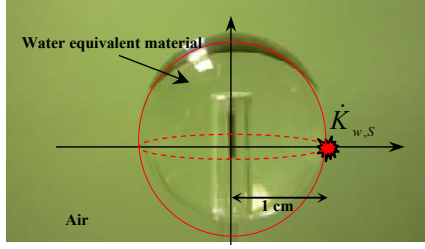


Fig. 4. Photograph of the source-phantom assembly with the representation of the point of interest to determine the absorbed dose (at 90 ° and 1 cm distance from the source seed).

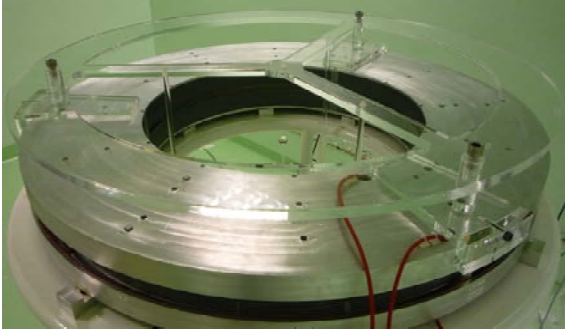


Fig. 5. Photograph of the LNE-LNHB free-in-air ring-shaped chamber.

photon spectrometer are used for the measurements.

The second step of LNE-LNHB's methodology consists in applying a correction factor to account for the contribution of additional scattered photons when replacing air by water as surrounding medium. A preliminary study was performed by MC simulations to estimate this backscattering correction factor, here referred to as F_{bscatt} . This study considered the ^{125}I seed modeled as a point source using three codes: the PENELOPE 2006 code [5], and two versions of the MC N-particle code, MCNP5 1.4 and MCNPX 2.5 [6]. All results were in good agreement and led to an estimate of F_{bscatt} of about 1.1703 ± 0.0013 . The adopted standard uncertainty is the standard deviation of the distribution of the three values, the statistical uncertainty components being negligible (see table 1) compared to observed discrepancies.

Table 1: Calculations of the scattering factor, F_{bscatt} , and of its statistical standard uncertainty when modeling the ^{125}I seed source as a point source.

	MCNP5	MCNPX2.5	PENELOPE 2006
	(MCPLIB4, EL03)	(MCPLIB4, EL03)	(EPDL, EPDL97, EADL)
History number	10 ⁸	10 ⁸	10 ⁷
F_{bscatt}	1.1695	1.1696	1.1717
$u_{\text{rel}}(F_{\text{bscatt}})$	0.001 %	0.001 %	0.01 %

3.4 The NPL standard for HDR brachytherapy sources

NPL's new absorbed dose graphite calorimeter for the measurement of HDR ^{192}Ir BT sources is currently being assembled. The new calorimeter will realise absorbed dose to graphite at a reference distance of 2.5 cm away from the centre of the ^{192}Ir source on its perpendicular bisector. This

quantity will be converted to the quantity of interest, D_w at 1 cm. The dimensions and materials for the new calorimeter were chosen based on MC simulations (EGSnrc [4]) and heat transfer simulations using COMSOL MultiphysicsTM [9]. The annular core of the calorimeter is 2 mm thick, 5 mm high and has a mean radius of 25 mm. For the operation in isothermal mode, eight small thermistors (four sensors and four heaters) are embedded in the graphite core (Fig. 6) and further thermistors were glued to the other graphite pieces. The graphite ring will be separated from the surrounding cylindrical graphite phantom (20 cm diameter, 14 cm height) by a 1 mm vacuum gap. The vacuum gap is needed for minimising the heat transfer from the core (point of measurement) to the environment and to control the self-heating of a typical HDR ^{192}Ir source (approximately 18 mW). A vacuum can surrounds the graphite calorimeter and the BT source will be inserted into the graphite phantom through an aluminium tube. Both the gamma spectrum and the beta spectrum of the ^{192}Ir source were considered in the MC simulations. The average dose rate to the core due to a 370 GBq Nucletron microSelectron-v1 classic ^{192}Ir source was found to be $1.61 \times 10^{-2} \text{ Gy s}^{-1}$.

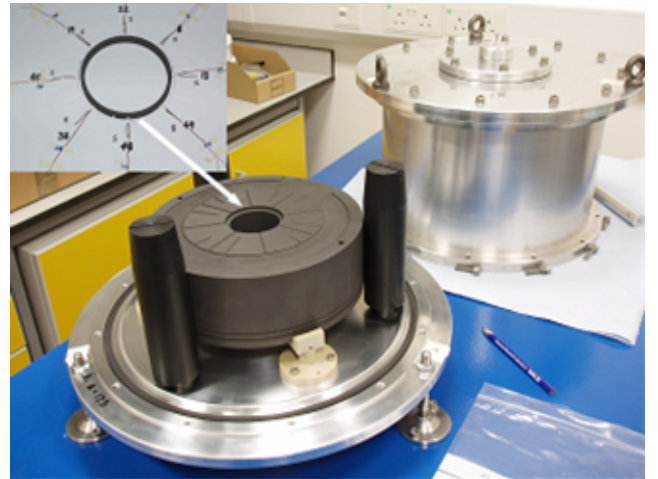


Fig. 6. Test assembly of the lower half of the graphite phantom inside the vacuum housing. Top left: Ring-shaped graphite core with heating and sensing thermistors. The white arrow indicates the position of the graphite core in the calorimeter.

Correction factors for the new standard were calculated with DOSRZnrc [4]. The refined simulations were based on the final design of the calorimeter and the following correction factors with a statistical uncertainty of less than 0.1% were determined: volume averaging correction (1.0036), vacuum gap correction (0.9992), inhomogeneity correction (1.0008) and full scatter correction (1.0060). Further refined simulations will be made to estimate the conversion from graphite to water.

3.5 The PTB standard for LDR brachytherapy sources

The PTB has developed a new primary standard for the realization of D_w close to low energy and low dose rate (LDR) BT sources (^{125}I and ^{103}Pd seeds). The new standard for LDR sources (GROVEX II) is based on a similar design as developed for the PTB standard for reference air kerma

rate for LDR sources [10]. The GROVEX II consists of a large air-filled parallel plate extrapolation chamber with water equivalent walls, as shown in Fig. 7. The entrance and the back plate of the extrapolation chamber are made of a water-equivalent material (RW1) with a measured density of 0.976 g/cm^3 .

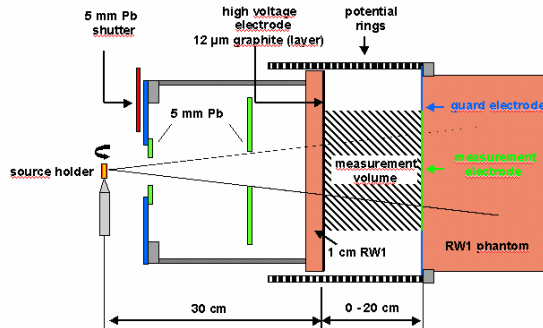


Fig. 7. Schematics of the GROVEX II measurement system.

The thickness of the entrance plate defines the measurement depth within the water phantom. Graphite was diffused onto the inner side of the entrance plate. Biased at the potential U , this layer acts as the polarizing electrode and serves as the reference plane for the measurement. 100 mm in front of the reference plane an exchangeable aperture is positioned defining the cross-sectional area for the measuring volume at the reference plane. On the back plate thin graphite layers were diffused, building the central collecting electrode and an outer guard ring both at ground potential. 40 potential rings on the outer PMMA-cylinder are providing a parallel electrical field between the high voltage and collecting electrode. For the determination of D_w a new algorithm was developed, allowing the calculation of D_w in 1 cm depth of water from air kerma measurements by MC simulations without the need of considering the electron transport. A prerequisite for the use of this algorithm is that the limits of the measurement volume are at least one CSDA range greater than the irradiated volume.

First test measurements with the GROVEX II in the PTB's reference fields for X-radiation have already been performed.

3.6 The PTB standard for HDR brachytherapy sources

For the realization of D_w in the vicinity of ^{192}Ir and ^{60}Co HDR BT sources PTB has modified one of the existing water calorimeters. The design of this calorimeter is essentially the same as of PTB's primary standard water calorimeter operated in a ^{60}Co [11] external radiation field. It is also operated at a water temperature of 4°C and uses the same type of calorimetric detector. Some modifications, however, have been made to ensure that the HDR source can be positioned close to the detector. Using an afterloading system, the source is moved through a plastic catheter into the water phantom of the calorimeter, where the catheter is connected to a stainless steel needle with an inner diameter of 1.35 mm. The needle is fixed at a short distance from the detector, a parallel-plate glass cylinder, by help of a

mechanical frame made of PMMA (Fig. 8). The frame was adapted such that a nominal distance of 24.5 mm between the ^{192}Ir -source and the two thermistors of the calorimetric detector could be realized both in front and behind the glass cylinder. A further fixation allowed an additional distance of 48 mm in front of the cylinder. Between single measurements with the calorimeter, the HDR source stays within a temperature stabilized lead block in the outer container of the water calorimeter. This keeps the source near the water temperature of 4°C and additionally, the radiation of the source is shielded from the calorimetric detector between the measurements. Heat conduction calculations with regard to the self-heating power of the source (22 mW for a 370 GBq source) have been performed by Finite-Element-Method (FEM) calculations and heat transfer correction factors, including the influence of the self-heating of the source, were evaluated.

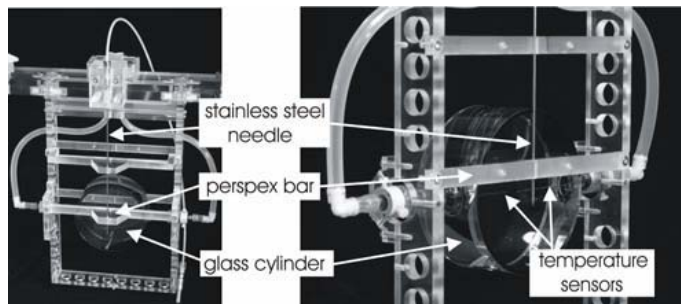


Fig. 8. Calorimetric detector with additional bars to fix the stainless steel needle at both sides of the detector.

First absorbed dose measurements with a 370 GBq ^{192}Ir source at distances of 24.5 mm and 48 mm have been performed. The combined standard uncertainty of the D_w values at these two distances was determined to 0.9% ($k=1$). Relative dose rate measurements with a plastic scintillation measurement system are currently being performed with the aim to extrapolate the results of the calorimetric measurements from 46 mm and 24.5 mm to the desired 10 mm distance from the source. The additional uncertainty of these relative measurements is estimated to be 1.0% ($k=1$).

3.7 The VSL standard for HDR brachytherapy sources

At VSL a primary standard for D_w due to HDR ^{192}Ir BT sources by means of water calorimetry is being developed by extending the existing external beam water calorimeter. The design of the new high purity cell (HPC) has been completed and the HPC is currently being build. The goal of obtaining a standard uncertainty of 2% at 2 cm from the source is compromised by the following two major contributions [12]: the added temperature rise due to the radiation induced source self-heating; the variation in the measurement signal due to variation in source positioning. These effects are reduced in the design of the calorimeter (Fig. 9) by a heat sink to reduce the self-heating and by opposing thermistors to reduce the sensitivity to positioning variations. Simulations (COMSOL MultiphysicsTM [9]) have been made to estimate the influence of the self-heating and the effectiveness of the heat sink. The reduction of the source self-heating effect due to the heat sink is considerable

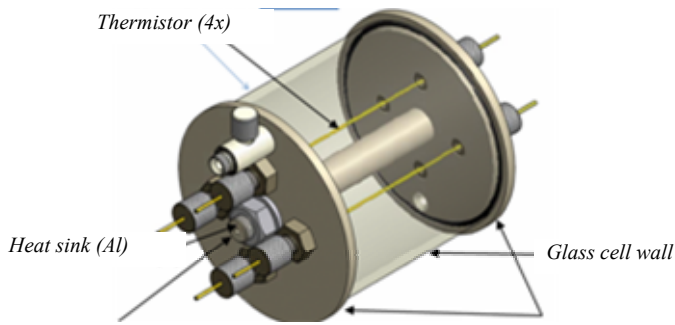


Fig. 9. Design of the VSL HPC with an aluminium cylinder as heat sink, and four radially distributed thermistors to reduce the variations in dose related to variation in positioning.

as can be seen from Fig. 10.

Calculations have been made to estimate the sensitivity of the standard to variation in source positioning. Because of the opposing thermistors, the variation in dose was 0.01% in case the source position varied with 0.1 mm, compared to 1% in case only one thermistor was used. Therefore, fewer measurements are needed to obtain an acceptable statistical error.

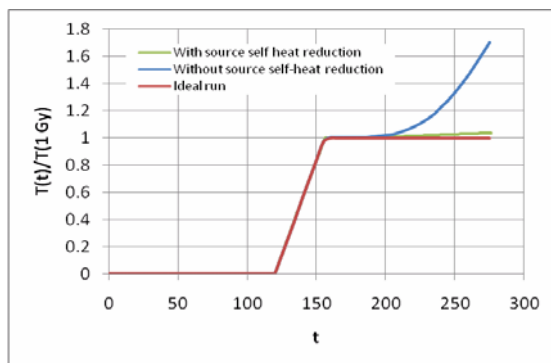


Fig. 10. Heat transfer simulations of a full calorimeter run, to estimate the influence of the source self-heat with and without heat sink, compared to the case without self heat (ideal run).

4. CONCLUSION

The metrological research of the iMERA-Plus Brachytherapy project will contribute to the “improvement of procedures and better knowledge of multidimensional dose distributions delivered to patients for radiotherapy”, and to the “realization of new devices for the traceable characterization of radiation sources”. By this collaborative project a strengthened impact –compared to the dispersed individual initiatives– will be achieved. The dissemination of the JRP results is of direct interest to the international community of radiotherapy centres performing BT clinical treatments. In this respect, all the National Metrology Institutes partners in this project have direct links with the radiotherapy centres in their respective countries, thus the

dissemination of the joint research project results will be effective and will impact directly on the improvement of the EU citizens’ lives. The relevant project result is the construction of two groups of primary standards –seven standard devices in total– for the realization of D_w close to LDR and HDR BT sources. A preliminary trial comparison is scheduled by the end of 2010 for both LDR and HDT BT standards.

After a successful conclusion of the project, a new international protocol for dosimetry in BT could be promoted, based on D_w standards.

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