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Dose verification of eye plaque brachytherapy using spectroscopic dosimetry

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Abstract

Eye plaque brachytherapy has been developed and refined for the last 80 years, demonstrating effective results in the treatment of ocular malignancies. Current dosimetry techniques for eye plaque brachytherapy (such as TLD- and film-based techniques) are time consuming and cannot be used prior to treatment in a sterile environment. The measurement of the expected dose distribution within the eye, prior to insertion within the clinical setting, would be advantageous, as any errors in source loading will lead to an erroneous dose distribution and inferior treatment outcomes. This study investigated the use of spectroscopic dosimetry techniques for real-time quality assurance of I-125 based eye plaques, immediately prior to insertion. A silicon detector based probe, operating in spectroscopy mode was constructed, containing a small (1 mm3) silicon detector, mounted within a ceramic holder, all encapsulated within a rubber sheath to prevent water infiltration of the electronics. Preliminary tests of the prototype demonstrated that the depth dose distribution through the central axis of an I-125 based eye plaque may be determined from AAPM Task Group 43 recommendations to a deviation of 6 % at 3 mm depth, 7 % at 5 mm depth, 1 % at 10 mm depth and 13 % at 20 mm depth, with the deviations attributed to the construction of the probe. A new probe design aims to reduce these discrepancies, however the concept of spectroscopic dosimetry shows great promise for use in eye plaque quality assurance in the clinical setting.

Keywords

verification, eye, dose, plaque, dosimetry, brachytherapy, spectroscopic

Disciplines

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DOSE VERIFICATION OF EYE PLAQUE BRACHYTHERAPY USING SPECTROSCOPIC DOSIMETRY

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ABSTRACT

Eye plaque brachytherapy has been developed and refined for the last 80 years, demonstrating effective results in the treatment of ocular malignancies. Current dosimetry techniques for eye plaque brachytherapy (such as TLD- and film- based techniques) are time consuming and cannot be used prior to treatment in a sterile environment. The measurement of the expected dose distribution within the eye, prior to insertion within the clinical setting, would be advantageous, as any errors in source loading will lead to an erroneous dose distribution and inferior treatment outcomes. This study investigated the use of spectroscopic dosimetry techniques for real-time quality assurance of I-125 based eye plaques, immediately prior to insertion. A silicon detector based probe, operating in spectroscopy mode was constructed, containing a small ($1mm^3$) silicon detector, mounted within a ceramic holder, all encapsulated within a rubber sheath to prevent water infiltration of the electronics. Preliminary tests of the prototype demonstrated that the depth dose distribution through the central axis of an I-125 based eye plaque may be determined from AAPM Task Group 43 recommendations to a deviation of 6% at 3mm depth, 7% at 5mm depth, 1% at 10mm depth and 13% at 20mm depth, with the deviations attributed to the construction of the probe. A new probe design aims to reduce these discrepancies, however the concept of spectroscopic dosimetry shows great promise for use in eye plaque quality assurance in the clinical setting.

KEYWORDS

Eye Plaque Brachytherapy, Spectroscopic Dosimetry, Dose Verification

1. Purpose

Ocular malignancies make up only a small fraction of incidences of malignancies and in 2011, there were predicted to be only 326 new cases of ocular malignancies in Australia [1, 2]. The use of eye plaque brachytherapy for the treatment of ocular malignancies has been researched and developed since the treatment's first success using radon seeds in 1933 [3, 4]. Without eye plaque brachytherapy techniques, conditions such as uveal melanoma and squamous cell carcinoma would most likely be treated using enucleation. As other effective treatments such as proton therapy are not available in Australia, eye plaque brachytherapy has become the primary treatment method for many ocular malignancies as vision preservation is often a priority in treatment considerations [3].

In modern brachytherapy treatment centres, one of the most widely used isotopes for low dose-rate brachytherapy is Iodine 125 (I-125) [5]. The relatively low cost, short half-life (59.4 days), low emission energy and availability [6] have all led to frequent use of this radionuclide. In Australia, ROPES (Radiation and Oncology Physics and Engineering Services, Australia) eye plaques (Figure 1) are commonly used for eye plaque brachytherapy, and are designed to hold I-125 based seeds on an acrylic insert [5]. A stainless steel housing is used to contain the acrylic insert and radioactive seeds, reducing exposure to the brain.

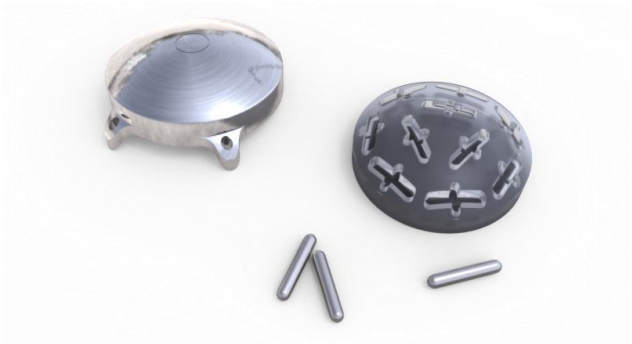


Figure 1. A rendering of the ROPES^{TM} eye plaque, with stainless steel housing (left), acrylic insert (right) and I-125 based seeds (lower)

All treatments incorporating the use of radiation should be patient specific [7]. However, dosimetry for each individual treatment comprising physical measurements is challenging. Dose-rate measurements for eye plaque brachytherapy treatments have commonly been completed using thermoluminescent detectors (TLDs), film and Monte Carlo simulations [5]. The well-established protocol used for low dose-rate brachytherapy dose calculations is the AAPM Task Group 43 recommendations (TG-43) [6, 8], which uses analytical calculations constructed from measured and Monte Carlo generated point dose data.

The procedure for using TLDs for pre-insertion verification in a clinical setting is designed to determine gross errors in plaque loading, including incorrect seed (activity) placement and potential rotational errors during loading [9]. However, as a dosimetric tool, TLDs do not have the spatial resolution required to gain important information about the effect of the treatment on small structures such as the optic disc and nerve, nor the intricate dose distribution within the eye [10].

Radio-sensitive films may also be used for dosimetric verification. However the time needed for film processing renders it impractical for clinical pre-insertion dose verification. It is recommended that GafChromic EBT3 films be left at least 2 hours to achieve a stable reading [11, 12], hence resulting in the modality being incapable of providing accurate results instantaneously.

Fast, pre-insertion dose verification of eye plaques would be beneficial to the treatment of ocular malignancies. One solution for the challenges presented by these common dosimetric techniques is the utilisation of spectroscopic dosimeters [13], which are able to produce results within a clinically appropriate timeframe, allowing gross dosimetric errors to be detected prior to plaque insertion. This is essential for verifying that the planned dose distribution will be delivered to the tumour. The Centre for Medical Radiation Physics (CMRP), University of Wollongong, has developed such a device [14], allowing fast point dose measurements for I-125 based brachytherapy treatments. This study was completed to determine the initial validity of spectroscopic dosimetry use in eye plaque brachytherapy.

2. Theory

I-125 based brachytherapy seeds such as the Oncura model 6711 and IsoAid Advantage IAI-125A have the unique advantage of emitting a pseudo mono-energetic spectrum. I-125 has dominant energy peaks at 27 keV, 31 keV, 32 keV and 35.5 keV [13, 15]. Fluorescent peaks are observed at 22 keV and 25 keV caused by the silver rod within the brachytherapy seed [15]. Additionally, the dominant 27 keV peak is located centrally to the smaller surrounding peaks. At these low energies, the photoelectric effect is the major contributor to energy loss of photons in water. Although the Compton cross-section is significant, the energy loss due to Compton interactions is minimal. As a result, when traversing a water medium, the average energy of the spectrum does not significantly vary, with little formation of low energy tails on the photopeaks. Thus, with a consistent spectral shape, the number of events within the photopeaks of a measured spectrum per unit time will be proportional to the dose-rate at the point of measurement [16]. This is the basis of using spectroscopic dosimetry as an effective dosimetry tool for I-125 based treatments.

While employing a detector and amplification system in spectroscopy mode, by setting a lower level threshold corresponding to events of energies lower than approximately 20 keV (below the photopeaks), the integral of counts within the spectrum above the threshold per unit time is used as the dose-rate measure. Spectroscopic dosimetry systems require an integral to dose conversion, which is obtained through calibration using sources of known activity at a fixed distance to the detector in a large water phantom. This may be achieved by placing the detector in a large water phantom along the transverse axis of an I-125 seed of known activity at a distance of 10 mm along and obtaining integral counts within the measured spectrum. In this case TG-43 recommendations will be used as the accepted protocol.

3. Materials and Methods

A spectroscopic dosimeter probe was developed as a prototype [14] featuring a $1mm^3$ silicon diode within a ceramic housing, mounted on a circuit board with preamplifier, covered in a polyethylene shield to provide a hermetic seal, as shown in Figure 2. The probe was connected to a data acquisition unit, containing a shaping amplifier, pulse height threshold gate, MCA/oscilloscope BNC output and onboard microprocessor for dosimetric calculations.

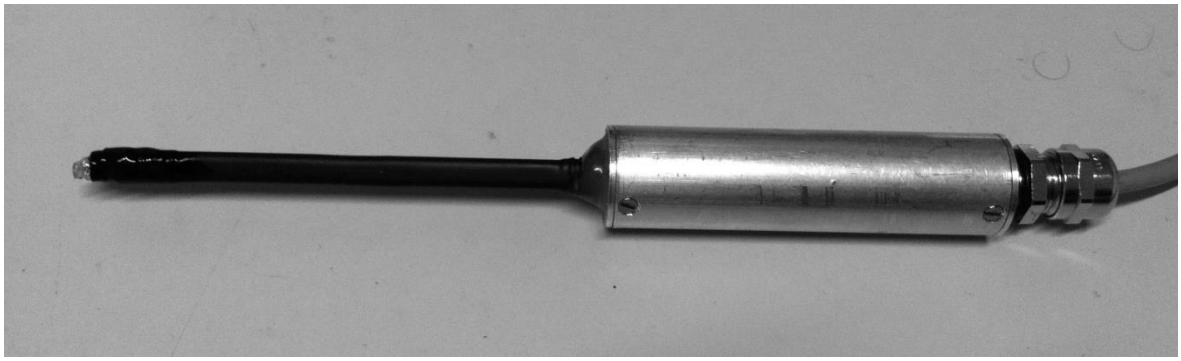


Figure 2- Spectroscopic dosimeter developed at the CMRP, University of Wollongong. The tip is to the left, with the preamplifier on the right.

In this prototype detector, the sensitive volume of the spectroscopic dosimeter was found to be approximately 3 mm from the tip of the probe, as determined using a fluoroscopic x-ray, seen in Figure 3, limiting the minimum distance of measurement to a source to detector distance of 3mm.

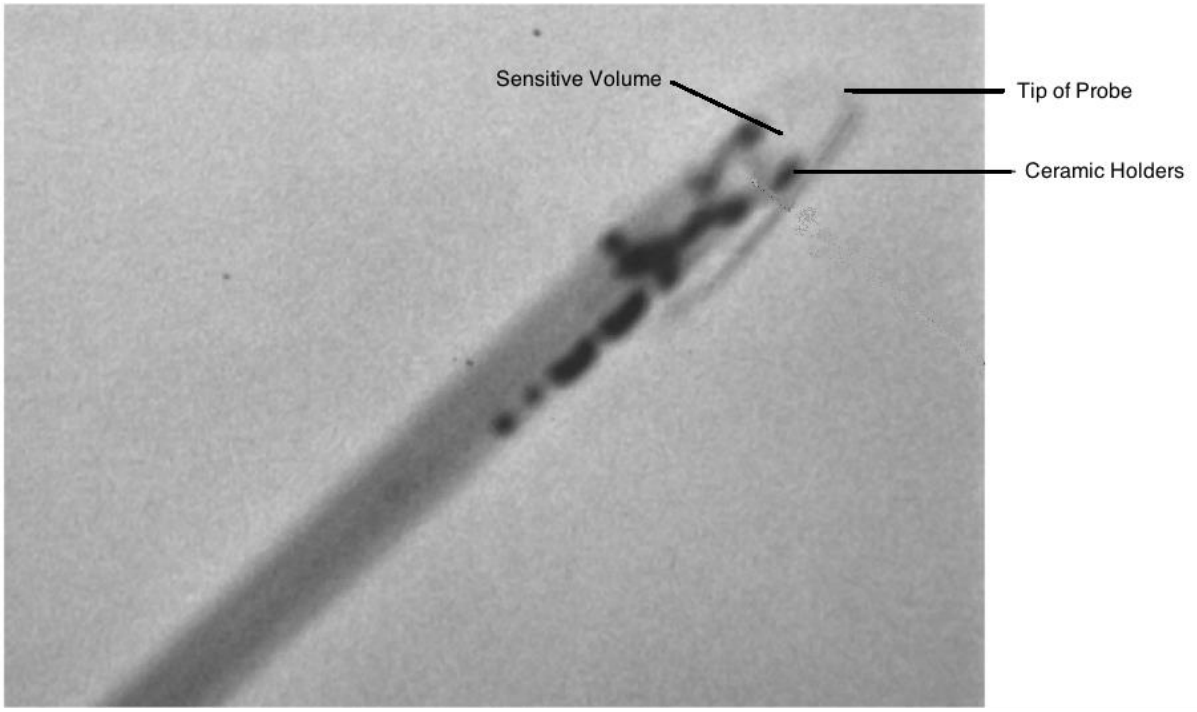


Figure 3- X-ray of the spectroscopic dosimeter showing the location of the sensitive volume relative to the tip

Schematics of a clinical device for the quality assurance of an eye plaque prior to insertion, have been produced, as shown in Figure 4, with the prototype under development. This will allow for fast measurement and verification of the depth-dose profile along the central axis of treatment. The design features a water chamber with an internal holder for the eye plaque to separate the water from the plaque to retain a sterile condition. With the plaque facing upward in the water chamber, a probe of length approximately 50 mm, containing a silicon diode in the tip is lowered into the chamber, to the center of the plaque, against the inner surface. A computerised translational motion device is used to move the probe vertically away from the plaque in small increments, with the probe using spectroscopic dosimetry to provide a dose rate measure at each point. Measured point dose-rates are then correlated to planned dose-rates, with the entire measurement process estimated to take approximately one minute.

Figure 4. A rendering of the spectroscopic eye plaque verification system

3.1. Calibration and verification

As all of the measurements were performed over a large time period, the results from all calibrations and measurements were normalised to the use of seeds of activity 0.4 mCi for consistency. Calibration of the system was verified using a single seed (IsoAid Advantage IAI-125), with an activity of 0.144 mCi, positioned 10 mm from the sensitive volume (detector) in liquid water. The system was programmed to count the number of pulses from the shaping amplifier which were above a threshold, representing the lowest energy to consider when tallying events in the detector (approximately 20 keV), with the threshold accurate to $6x10^{-4}$ keV. Once the lower level threshold was set, the dose calculation algorithm of the microprocessor was manually adjusted to give 0.20 cGy/hr dose-rate output on the data acquisition unit display.

To ensure that the concept of spectroscopic dosimetry was valid across all depth measurements, an analysis of the spectrum was completed at each depth. The Full Width Half Maximum (FWHM) of the two dominant spectral peaks (22 and 27 keV), as seen in Figure 6 , were calculated with distances between the tip of the probe and the surface of the ROPES plaque ranging from 3 mm to 25 mm, as this range extends from close to the plaque surface to beyond the treatment range. For the concept of spectroscopic dosimetry to be valid, only the intensity of the peaks was expected to vary, with the FWHM and peak locations to have minimal change.

3.2. Depth Dose Measurements

Depth dose measurements through the central axis of the plaque were obtained using the prototype probe and were compared to analytically calculated doses (TG-43). The TG-43 calculations were performed over the range from 0.1 mm to 23 mm from the plaque inner surface, along the central axis, and were based on the location, orientation and activity of each seed within the plaque.

To determine the depth dose curve of the ROPES eye plaque, water was used as the phantom material in a Perspex holder, designed specifically to ensure maximum setup reproducibility, as illustrated in Figure 5. Spectra were acquired at various depths, defined with a micrometer, and the dose-rate observed. This was completed in small increments. With the limitations of the current version of the probe, these started at 3 mm from the surface of the eye plaque and extended to 23 mm (approximately the diameter of the human eye) from the surface of the plaque. The depth was defined as the distance between the sensitive volume of the detector and the seed. The eye plaque was placed in a Perspex holder facing upwards, submerged in water. The

spectroscopic dosimeter was then attached to a micrometer to ensure accurate depth readings, as shown in Figure 5.

All experimental setups and measurements were taken a minimum of 4 times to ensure accurate reproducibility of setup and movement of the detector, and were taken in both directions to rule out the introduction of hysteresis from the micrometer. This was limited by the orthogonality of the probe in relation to the Perspex holder.

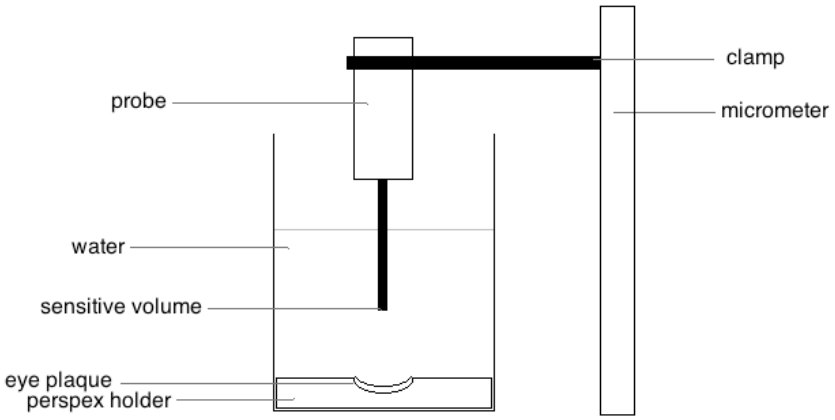
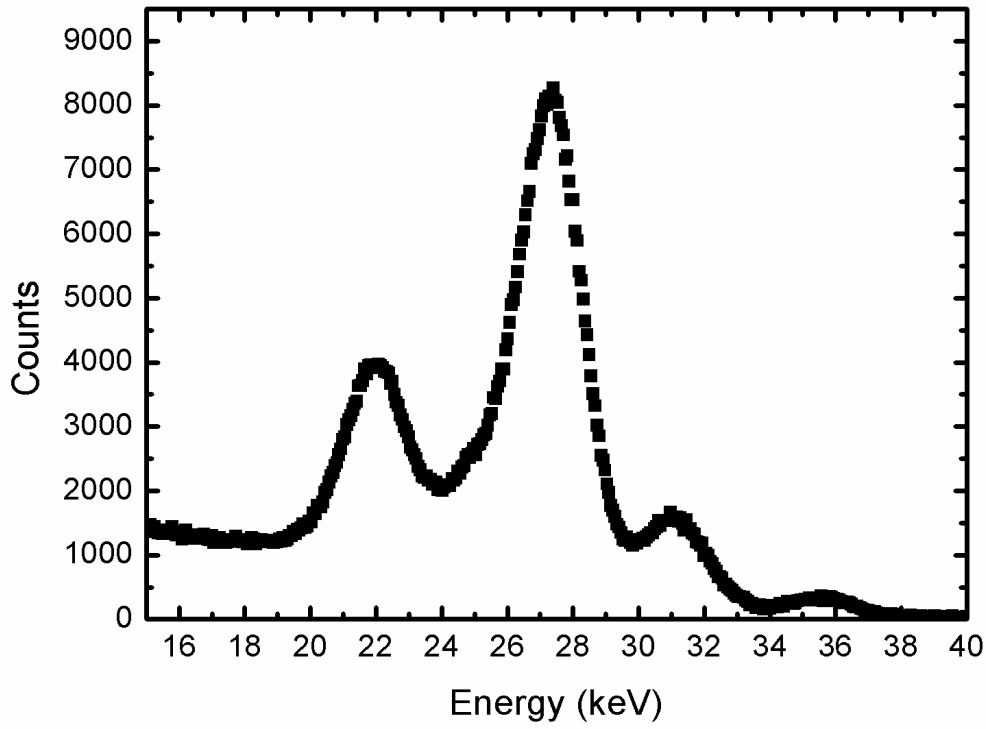


Figure 5 Schematic of spectroscopic dosimeter apparatus.

4. Results

4.1. Calibration and verification

The obtained spectrum at a depth of 1cm from the plaque surface on the central axis is shown in Figure 6. Four separate peaks are visible, located at approximately 22, 27, 31 and 36 keV, with the largest peaks being 22 and 27 keV. The FWHM obtained for the 22 keV and 27 keV peaks as well as the relative location of the centroid (for a fixed calibration) are presented in Table 1 for varying depths in water. From the calibration depth of 10 mm, the peak centroid energy was within ±0.4 keV for both peaks, with the FWHM within ±0.3keV. The lack of spectral peak energy shift or change in FWHM demonstrates that the spectroscopic dosimeter should provide accurate dosimetric measurements within the required range of depths. The concept of spectroscopic dosimetry should thus be applicable to applications in I-125 based eye plaque dosimetry.



206
207 **Figure 6 I-125 based ROPES plaque spectrum, 10 mm in water from the plaque surface on the central**
208 **axis**

209
210 **Table 1 Analysis of the spectral peaks of I-125 at varying depths in water, distance measured from the sensitive**
211 **volume of the probe**

	22 keV Centroid (keV)	22 keV FWHM (keV)	27 keV Centroid (keV)	27 keV FWHM (keV)
5 mm	21.9	2.2	27.2	2.2
10 mm	22	2.2	27.2	2.2
15 mm	22.5	2.4	27.6	2.2
20 mm	22.6	2.7	27.6	2.3
25 mm	22.6	2.7	27.6	2.2

4.2. Depth Dose Measurements

As shown in Figure 7, the experimental results gained from the spectroscopic dosimeter are accurate to within 6% standard uncertainty at 3 mm depth, 7% at 5 mm depth, 1% at 10 mm depth and 13% at 20 mm depth, when compared to TG-43 calculations.

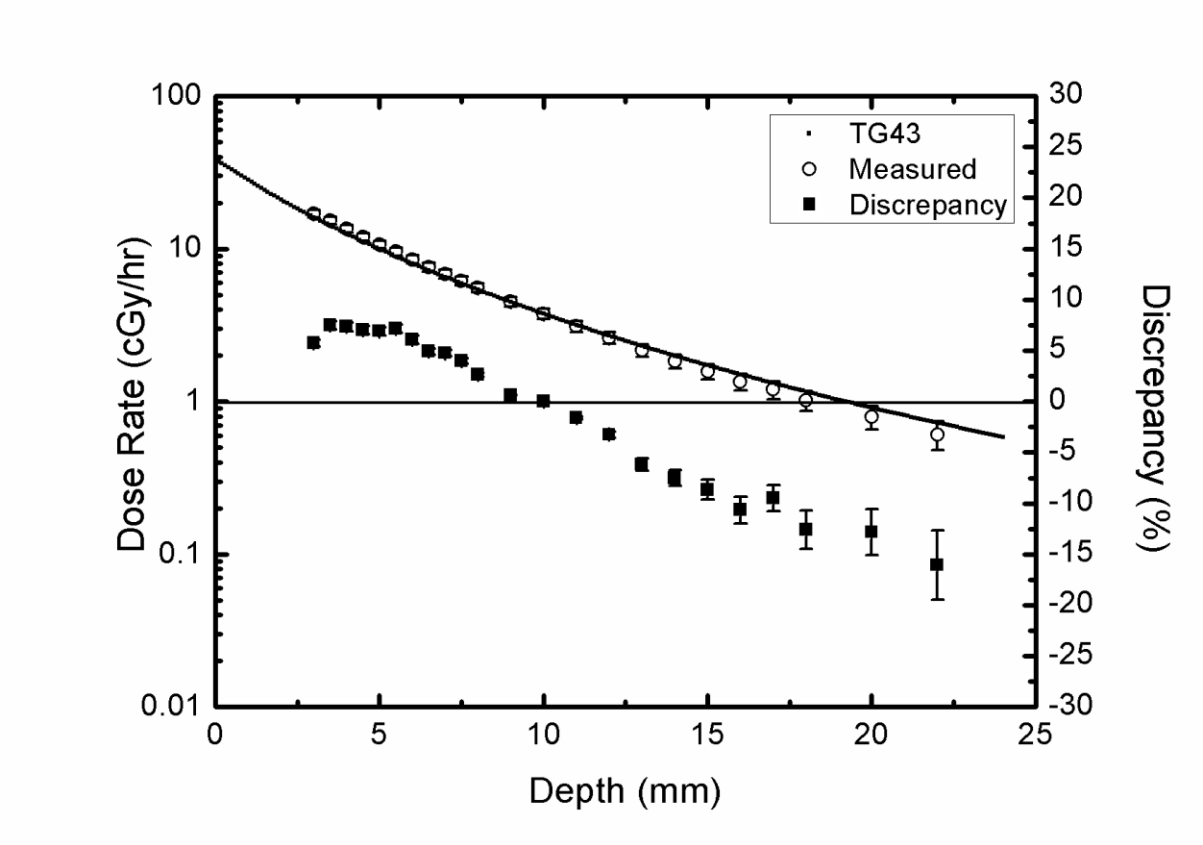


Figure 7 Depth dose data from 10, 0.4 mCi Oncura 6711 I-125 seeds loaded into a ROPES 15 mm eye plaque using the spectroscopic dosimeter. Uncertainties shown are standard uncertainties from multiple measurements.

5. Discussion

The depth-dose plot shows an over-response at close distances to the plaque and under-response at large distances. The main contributor to this discrepancy is the localisation of the sensitive volume within the probe tip. A mismatch of the sensitive volume location with respect to the probe tip will lead to an incorrect dose point location (at both calibration and measurement). The negative gradient in the discrepancy plot, whilst maintaining a high accuracy near the calibration depth (1cm) indicates that such a mismatch is present, with the detector being at a slightly smaller depth that 3mm from the probe tip. This emphasises the necessity that in the future detector design, the sensitive volume must be placed as close to the tip of the probe as possible, ensuring improved accuracy in the calibration and resultant measurements, as well as providing measurements closer to the plaque surface.

Poder et al, 2013 [17], showed a decrease in dose at shallow depths from the plaque surface relative to TG-43 dose calculations due to the presence of the stainless steel plaque encapsulation. In its current form, the eye plaque spectroscopic dosimeter does not have the accuracy to measure the dose rate at shallow depths from the plaque surface to verify this, however, the concept shows great promise to provide fast verification of dosimetry prior to plaque insertion. Future designs of the spectroscopic probe will have the detector housed within a 3D printed shell, with no presence of ceramic holders and with the detector location known to a more accurate level, which will greatly improve the accuracy of measurement over the required depth range.

5.1. Error Analysis

Calibration was completed using a commercially available I-125 seed. This may have introduced additional errors into the measurements that were unaccounted for, as the seed strength was not traceable to a primary standards laboratory. However, as the purpose of this work was to determine if the detector had potential to be further developed as a real time dosimeter in eye plaque brachytherapy, the seed calibration was not of the utmost importance. Any variation in activity across the batch of seeds would have contributed to discrepancies in the plaque depth dose measurements. In future works, this will be of a higher priority.

5.2. Limitations and further work

One limitation encountered in this work is that presented by the TG-43 formalism. The formalism does not account for the backscatter introduced by the steel backing plate of the ROPES eye plaque. In future studies, modelling the eye plaque and seeds using Monte Carlo may give a better standard to which the results may be compared. However, this particular work was limited to exploring the results against the current "gold standard" of brachytherapy, TG-43, regardless of the flaws it presents.

Future work will address the limitation of alignment that would have been easily introduced into this work through the production of an automated measurement system. Great care was taken to ensure that the probe was moving perpendicularly to the center of the plaque at all times. However, there was no way to verify that the central axis of movement aligned orthogonally with the centre of the plaque. Small angulations and geometric uncertainties, such as central axis alignment, do have the potential to produce an incorrect assessment of dose-rate, despite the reproducibility of the setup. Results presented in this study were a combination of data points collected over multiple studies, minimising the influence of many geometric errors.

Looking beyond the scope of this project, it will be possible to apply this approach to develop an estimation of the radiation dose to the organs at risk in the immediate vicinity of the orbit. This would be of particular advantage in terms of the dose received by the region of the brain closest to the orbit and could be achieved through a slight modification of the experimental setup. Most importantly, it would require expanding the phantom dimensions and utilising a 3D motion controlling system.

6. Conclusion

Eye plaque brachytherapy treatments require rigorous planning and dosimetry considerations due to the delicate nature of the procedure. A fast quality assurance system for the verification of treatment dosimetry immediately prior to insertion is desired, however, prohibited by limitations on current dosimetry techniques. For use in the dosimetry of eye plaque brachytherapy, spectroscopic dosimetry has the potential to provide results that are accurate, informative and instantaneous. The results from the spectroscopic dosimeter, being easily reproduced and giving real time data are evidence toward the implementation of such detectors in centres using eye plaque brachytherapy, as a common treatment modality. As the spectroscopic dosimetry system displays the measured dose-rates in real time, the dosimetric technique has the potential to be used clinically for eye plaque brachytherapy. Based on the presented prototype, version II of the eye plaque spectroscopic dosimeter as well as the computer controlled eye plaque verification system, is in production, with clinical implementation to proceed in the near future.

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