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SCIENTIFIC PAPER

Dosimetric validation of the Theragenics AgX-100® I-125 seed for ROPES eye plaque brachytherapy

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Abstract

With the discontinued distribution of the I-125 Oncura Onco seed (model 6711), the Theragenics AgX100® I-125 seeds were considered as a suitable alternative for eye plaque brachytherapy as their physical properties matched the requirements for use with the ROPES eye plaques. The purpose of this study aims at validating the dosimetry of the AgX-100 loaded ROPES plaques (11 mm diameter, 15 mm diameter with flange, 15 mm diameter with notch, 18 mm diameter) and assess the differences with the discontinued I-125 6711 model. To independently verify the plaque dosimetry, the brachytherapy module of RADCALC® version 6.2.3.6 was commissioned for the new AgX-100 I-125 seed using the published AAPM TG43 data from the literature. Experimental dosimetry verification was performed using EBT3 Gafchromic™ film and TLD-100 micro-cubes in a specially designed Solid Water® phantom. Both RADCALC® and film confirmed the dosimetry calculated by Plaque Simulator (PS) version 6.4.6 The dose calculated by PS agrees with RADCALC® to within 2% for depths of 1–15 mm for the 4 available ROPES plaques. The dosimetric measurements agreed with the calculations of PS for clinically relevant depths (4 mm to 6 mm) within the evaluated uncertainties of 4.7% and 7.2% for EBT3 film and TLDs respectively. The AgX-100 I-125 seed was a suitable replacement for the 6711 I-125 seed. Due to the introduction of the stainless-steel backscatter factor in PS v6.4.6, the department has decided to report both the homogenous dose and heterogeneity corrected dose for each eye plaque patient.

Keywords ROPES · Eye plaques · I-125 seeds · Brachytherapy · Ocular melanoma

Introduction

Radioactive eye plaque therapy is primarily used in the treatment of ocular melanomas. Historically, there have been a number of different radionuclides used in treating ocular melanomas such as, I-125, Pd-103, Cs-131, Ir-192, Co-60, Sr-90, Au-198, and Ru-106 [1]. The most common plaques used currently are the Ru-106 eye plaque, which is a pre-coated radioactive plaque and requires no assembly, and the seed-loaded I-125 plaques, which require assembly before treatment. The 27–35 keV photons of I-125 exhibit desirable penetration in tissue, making I-125 an appropriate source to use for the treatment of small to medium sized tumours in the eye. According to the Collaborative Ocular Melanoma Study (COMS), brachytherapy with I-125 eye plaques is confirmed to be as effective as enucleation for medium-sized choroidal melanomas, with the added advantages of eye and vision preservation. The American Brachytherapy Society has reported specific clinical recommendations for choroidal melanoma with a typical dose of 80–100 Gy prescribed to the apex of the tumour at a dose rate of 0.60 Gy/h – 1.05 Gy/h. Typically this would deliver the total dose in 3–7 consecutive days and minimise the radiation induced effects to the optic nerve and lens [1].

There are several designs of seed-loaded eye plaques used for the treatment of ocular tumours. Some are composed of a plastic (Perspex) insert with recesses to affix I-125 or Pd-103 [2] radioactive seeds and a metallic shell to protect from radiation as well as to suture the plaque to the sclera close to the tumour. The ROPES (Radiation and Oncology Physics and Engineering Services, Australia) eye plaques are commonly used for eye plaque brachytherapy and are available in

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multiple sizes (i.e. 11 mm, 15 mm and 18 mm). Depending on the size of the plaque, the seed arrangement in the Perspex insert differs with 4, 9 (or 10) or 14 seeds respectively. The 15 mm plaque offers two different seed arrangements, one fully circular plaque and one with a 'notched' shape to account for treatments performed close to the optic nerve.

In early 2017, it was reported that the Oncura Oncoseed I-125 model 6711 seed (Amersham Health Princeton, NJ) was no longer available for distribution. In order to continue the service of eye plaque brachytherapy, the department decided to investigate the possibility of using the Theragenics Corporation® AgX100® I-125 seed (Buford, GA), as a replacement.

The AgX100® seed is a relatively new model that was introduced in 2010 for interstitial brachytherapy. At the time of this study, there were limited publications reporting on the dosimetry parameters required for dose calculations based on the AAPM TG-43 dose calculation formalism.

The treatment planning system (TPS) used in this study, Plaque Simulator (PS) v.6.4.6 (BEBIG© GmbH, Berlin, Germany) uses a dose calculation algorithm based on the AAPM TG-43 dose calculation formalism. This planning system uses the superposition of the contributions of the total dose of individual seeds and was validated for the ROPES eye plaques using the I-125 source model 6711 in a study by Poder et al. Dose calculations and prescriptions within this study were based on the COMS protocol recommendations for episcleral plaque therapy [1].

The Brachytherapy Module in the independent MU checking software, RADCALC® v6.2 (Lifeline Software, Inc. USA) was used as an independent checking program for eye plaque brachytherapy implant times as calculated by PS. It also utilises the AAPM TG-43 dose calculation formalism for its dose calculations.

The purpose of this work is to validate the AgX100® I-125 seeds for ROPES eye plaque brachytherapy and assess AgX100® I-125 seeds before they are accepted for clinical use using independent calculation systems (PS, RADCALC®) and dosimetric measurements with Gafchromic™ EBT3 film and TLD dosimetry. To our knowledge, this is the first report describing the use of AgX100 seeds for ROPES eye plaques brachytherapy.

Materials and Methods

Three main steps were involved in effectively verifying the AgX100® seed for use in the ROPES eye plaques: i) Implementation in Plaque Simulator v.6.4.6 and seed modelling, ii) Independent dose calculation using RADCALC® software and comparison to the treatment planning systems dose calculations and iii) dosimetric measurements using Gafchromic™ EBT3 film and TLD-100 micro-cubes.

I-125 seed selection and ROPES eye plaque

The Theragenics Corporation® AgX100® seed is similar in exterior dimensions to the Oncura Oncoseed 6711. This is an important consideration to ensure that the AgX100® seed safely fits into the recesses of the ROPES plaque's Perspex insert. The 6711 seed consists of a ratio of radioactive AgI and AgBr (density of 6.2 g/cm $^{3)}$ coated on a 2.80 mm long cylindrical silver rod of radius 0.25 mm. The silver rod is encapsulated in a 3.75 mm long titanium tube of 0.07 mm thickness and an 0.80 mm outer diameter. The overall source length is 4.55 mm and the active length is 2.80 mm [3]. The AgX100® seed consists of a radio-opaque silver marker coated with a 2 μm thick layer of radioactive AgI (density of 5.675 g/cm^3). The silver marker is a 3.50 mm long cylindrical silver (density of 10.5 g/cm^3) rod with a 0.293 mm (0.295 mm with coating) radius. The silver marker is encapsulated in a 4.00 mm long titanium (density of 4.54 g/cm^3) tube with 0.05 mm thick walls, a 0.4 mm outer radius and 0.4 mm thick hemispherical end welds. The overall source length is 4.50 mm and the active length is 3.50 mm [4].

ROPES plaques consist of three pieces; a Perspex insert to affix the radioactive seeds, a stainless-steel concave backing and an ejector plug. The ROPES plaques are available in a variety of sizes, including; 11 mm, 15 mm, 15 mm (notched) and 18 mm diameter plaques. These four plaque arrangements have been investigated in this study.

Treatment planning system

Plaque simulator upgrade to v.6.4.6

The Bebig Plaque Simulator treatment planning system required upgrading from version 6.0.4 to version 6.4.6 to activate the Theragenics AgX100® seed. The plaque inventory was transferred from v6.0.4 to v6.4.6 allowing the ROPES plaque parameters to be compared between versions, for each plaque. In v6.4.6 of PS is introduced a new default global scalar dose calibration factor for the ROPES plaque of 0.96, to account for the effect of the stainless-steel backing of the plaque upon scattering conditions. To match the previous dose calculations, new ROPES plaque models were created for each size plaque. To verify the upgrade and the implementation of the dose calibration factor, the factor was set to 1.0 and dose comparisons between the default value and 1.0 were made for different prescription depths and plaque sizes using the I-125 6711 model. The parameters for the calculated plans were as follows; prescription dose of 85 Gy to tumour depth (excluding sclera thickness), treatment time of 22 h

Table 1 Published data for dose rate constant (∧) for AgX100® I-125 seed

Mourtada et al. [4]	
$_{\text{MC, point}}$	0.943 ± 0.015 cGy/(U h)
$\wedge_{\text{MC, WAFAC}}$	0.918 ± 0.015 cGy/(U h)
Chen et al. [5]	
$\wedge_{\text{PST}}$	0.957 ± 0.037 cGy/(U h)
$\wedge_{\text{TLD}}$	0.995 ± 0.066 cGy/(U h)

and seed activity of 10 U. Once it was confirmed that the upgrade had been successful, the AgX100® TG-43 source was activated for use in the treatment planning system.

AgX100® seed modelling

The anisotropy data used in PS v6.4.6 was taken from Mourtada et al. for 0.25 cm ≤ r ≤ 5 cm [4]. The data in PS was linearly interpolated in increments of 1° from 0° to 90°. The radial function data used in PS was also taken from Mourtada et al. for r ≤ 4 cm. The data was linearly interpolated into steps of 0.02 mm [4]. According to the published literature at the time of implementation of the AgX100® seed model, two papers published the dose rate constant, ∧ for the AgX100® seed, shown in Table 1.

PS v6.4.6 uses the average value of these published results, ∧ = 0.953 cGy/(U h). This value is comparable to the consensus value that was published in the TG-43 Supplement 2, $\wedge_{CON}$ = 0.952 ± 0.043 cGy (U h) [6]. To alter this value in PS v6.4.6 runs the risk of file corruption and if the default value is reloaded then care must be taken to ensure that the correct value is re-entered into the system. Since the difference is significantly small (0.1%), it was decided to leave the dose rate constant as the default value of 0.953 cGy/(U h). A comparison was made for the away and along tables for PS v6.4.6 with the Monte-Carlo derived values from Mourtada et al. and once Supplement 2 for TG43 was made available, recalculations were made to compare to consensus data [6].

Independent check software

The brachytherapy module in RADCALC® (Lifeline Software Inc.) was used as an independent dose calculation for comparison with the treatment planning system, PS. A previous publication by Poder et al. has validated the implementation of the seed coordinates of the ROPES eye plaques in both PS and RADCALC® [7].

The AgX100® TG-43 seed parameters were entered into RADCALC® and the seed model was commissioned by checking the away and along tables with published values [4]. An absorbed dose calculation comparison with PS was performed for all available ROPES plaque sizes. Treatment plans for each size ROPES plaque were created and the homogenous absorbed dose to an identical point calculated in both PS v6.4.6 and RADCALC® with the following parameters; seed type: AgX100® I-125, seed activity: 100 U, treatment time: 1 h, treatment depth: from 0 mm (sclera) to 14 mm. The results of the absorbed dose point calculations in PS and RADCALC® were compared to verify the accuracy of both independent calculation systems and the implementation of the AgX100® seed model.

A further dose calculation comparison was performed in RADCALC® between AgX100® seeds and 6711 seeds. ROPES plaques (11 mm, 15 mm, 15 mm notched and 18 mm) in RADCALC® were loaded with the respective series of seeds and the absorbed dose was calculated to various depths. The dose calculated for the different seeds was compared to investigate the suitability of the AgX100® seed for eye plaque brachytherapy (Fig. 1).

EBT3 film dosimetry

With the introduction of the AGX100® seeds into the department, physical measurements were performed using an in-house Gammex RMI 457 Solid Water® (Gammex Inc. Wisconsin, USA) eyeball phantom, with diameter of 24 mm, able to be dissected into 2 mm slice thicknesses for depth measurements. The step size for depths was limited by the 2 mm layers from which the eyeball phantom is constructed. Measurements were performed with EBT3 Gafchromic™ Film (Ashland Inc., Wayne, NJ, USA). Two sets of EBT3 Film measurements were conducted to verify the accuracy of the TPS: (i) A single AgX100® seed and (ii) A 15 mm ROPES eye plaque loaded with ten AgX100® seeds.

The EBT3 films were scanned three times each and the scan result averaged prior to and 24 h after exposure in an Epson 10000XL flatbed scanner (SEIKO Epson Co, Japan), in the same position to account for any sub-pixel variation in the homogeneity of the scanning area, with a scanning

Fig. 1 Gammex RMI 457 Solid Water® eyeball phantom composed of 2 mm slices forming 24 mm diameter sphere

resolution of 75 dpi and saved as 48-bit RGB TIFF file. The films were analysed using the net optical density method to calculate dose planes using the red colour channel. Proper film handling in accordance with AAPM TG-55 was exercised to reduce the influence of possible uncertainties [8].

Film Calibration

Calibration films were cut to 5 × 5 cm^2 and irradiated on a 30 cm × 30 cm × 5 cm block of Solid Water®. The EBT3 films were irradiated using a Pantak Therapax DXT 300 Orthovoltage unit on central axis (CAX) with a 10 × 10 cm^2, 50 cm SSD applicator and a 75 kVp, 30 mA beam with HVL 2.63 mm Al. This energy was chosen for the calibration of the EBT3 films as the spectrum was comparable to the 27–35 keV photons of the AGX-100 I-125 seed. The calibration films were exposed to doses ranging from 0 to 2 Gy in 0.2 Gy increments.

Single AgX100® seed measurement

A single calibrated AgX100® seed absorbed dose measurement was conducted to verify the calibration of the EBT3 films, by placing a single I-125 AgX100® seed in a Solid Water® phantom. This phantom consists of a recess which was machined to fit a single I-125 seed. A 5 cm block of Solid Water® was placed under the phantom for full backscatter and measurements were taken for two depths; 3 mm and 6 mm. Solid Water® of this thickness was placed over the phantom and the EBT3 film was sandwiched between the build-up and a further 5 cm block of Solid Water® placed on top for full scatter conditions. An additional 0.14 mm and 0.49 mm was included in the measured depth when analysing the measured dose to account for the depth to the centre of the EBT3 film and a minor air gap between the seed and the film, respectively.

ROPES eye plaque measurements

Ten AgX-100® I-125 seeds of activity 11.9 U were loaded in a 15 mm ROPES eye plaque. 5 × 5 cm^2 pieces of EBT3 film at depths 4 mm, 6 mm, 8 mm and 10 mm were irradiated by the loaded ROPES plaque. Each measurement had 5 cm Solid Water® backscatter and was enclosed within a water phantom placed on top of the plaque for full water scatter conditions. Irradiation times were calculated in PS v6.4.6 and ranged between 49 and 106 min, depending on the absorbed dose prescription to the depth of the EBT3 film (1–1.5 Gy) (Fig. 2).

Using in-house developed film analysis software, the mean dose was measured in a small region of interest (ROI) surrounding CAX for each measurement depth and was compared to the expected dose calculated by PS. A relative correction factor for the conversion of Solid Water® (measurement conditions) to liquid water (TG-43 dose calculation conditions) of 1.038 was applied to each measurement. This value is an average based on previous publications by Luxton et al., Williamson, Meigooni et al. and Tailor et al. who determined a correction factor from Solid Water® to liquid water of 1.038, 1.043, 1.032 and 1.040 respectively [7, 9–11].

Thermoluminescent dosimeters (TLD-100) micro-cubes

LiF:Mg, Ti TLD-100 micro-cubes with dimensions 1 × 1 × 1 mm^3, were chosen for point dose verification measurements due to their small physical size. LiF:Mg, Ti TLDs have been shown to over-respond to low energy

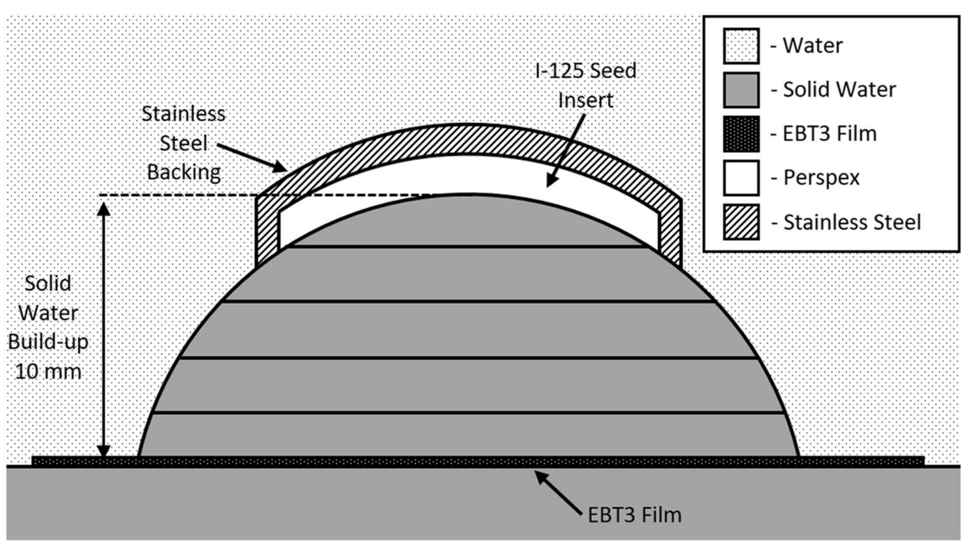


Fig. 2 Schematic diagram demonstrating measurement with loaded ROPES eye plaque and EBT3 film

photons when calibrated using high energy photon beam qualities, such as Co-60 [12–14]. This intrinsic energy dependence of the TLD-100 has been minimised by calibrating the dosimeter in a kilovoltage photon beam with similar effective energy as the I-125 seed used for irradiation.

The micro-cubes were calibrated by irradiating eight micro-cubes on central axis using a Pantak Therapax DXT 300 Orthovoltage with a 75 kVp, 30 mA beam and HVL 2.63 mm Al. Point dose measurements of a 15 mm ROPES plaque loaded with AgX100® seeds was acquired in a micro-cube Solid Water® phantom under the Solid Water® eyeball phantom at specified depths. The irradiation times for each micro-cube varied between 45–100 min, depending on the prescription dose, which ranged between 1 and 1.5 Gy. Readings were taken with the effective point of measurement (EPOM) at the centre of the micro-cube. Thus, the effective measurement depths investigated were 4.5, 6.5, 8.5 and 10.5 mm. An additional 0.25 mm was included in the total depth to account for an air gap present between the top of the micro-cube and the surface of the phantom, thus the final depths for comparison were determined to be 4.75 mm, 6.75 mm, 8.75 mm and 10.75 mm. Since only one micro-cube could be used at any one measurement depth, readings were repeated three times for each depth, each using a different micro-cube to eliminate any systematic errors with individual TLDs. The TLD reader used to process the TLDs was a Thermo Fisher Scientific™ Harshaw TLD Model 5500 Automatic Reader connected to a desktop PC using the Thermo Fisher WinREMS software v.8.2.3.0. The correction factor for the conversion of Solid Water® (measurement conditions) to liquid water (TG-43 dose calculation conditions) of 1.038 was applied to each measurement (Fig. 3).

Uncertainty analysis

An uncertainty analysis was performed for the dosimetric measurements to quantify the random and systematic errors that may arise during the measurement process. The uncertainty in EBT3 film measurements was influenced by several factors. The measurement, calculation and use of the EBT3 film calibration curve for transforming net optical density to dose has been described previously [8] with the upper estimate of uncertainty of 3.2% [15] used in the uncertainty budget for this study. The uncertainty for the energy response between the film across the 75 kVp spectral beam compared to the mono-energetic source of the I-125 seed has been estimated to be 1% [16]. The selection of the region of interest (ROI) for measurement of the mean dose from the EBT3 film was determined by statistical processes to influence uncertainty by 1.0%. The scanner reproducibility and homogeneity uncertainty was determined to be 0.7% from the literature [17].

The uncertainties associated with the micro-cube TLD measurements arise from; accuracy in the calibration set of TLDs, uncertainty from the TLD reader, individual TLD measurement uncertainties and accuracy of the calibration kV source delivering a known dose quantity. For each TLD measurement, only one TLD can be used at a time, due to their size, therefore multiple repetitions were performed at each depth. To eliminate any systematic uncertainties with individual TLD chips, a different chip was used for each dose measurement. The uncertainty related to the sensitivity

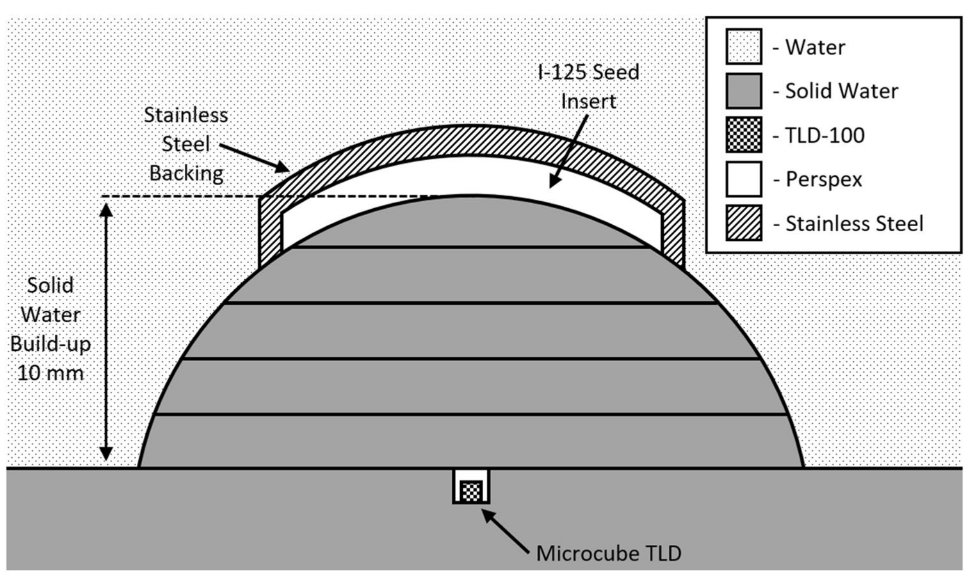


Fig. 3 Schematic diagram of experimental setup for micro-cube TLD-100 measurements in Solid Water® phantom with ROPES eye plaque

of the TLDs was found to be 2.0% from statistical assessment. Uncertainty in the delivery of dose to the TLDs was found to be 2.0% based on the output fluctuations of the kV source and uncertainty related to the reproducibility of the TLD reader was determined to be 0.2% [12]. An estimate has been included for the energy dependence of the TLDs of 1% [13].

The most significant uncertainty associated with both the EBT3 film and the micro-cube TLD measurements was determined to be the influence of uncertainty in the depth of measurement. The magnitude of this quantities influence was determined to be 2.3% and 5.9% based on 0.1 mm and 0.5 mm uncertainty in the measurement points location relative to the plaque, for EBT3 film and TLD's respectively. Furthermore, the positioning of the eye plaque on the Solid Water® phantom, the plaques orthogonality in relation to the measurement plane, was estimated to result in an additional uncertainty of 1.0%. The Solid Water® correction factor used had an established uncertainty of 0.6% [7]. Uncertainty related to the accurate measurement of the required irradiation time was greater for shallower depths, where less time is required to achieve a higher dose delivery to the dosimeter. The influence of this uncertainty in time upon the dose measurement was evaluated to be 1.1%. Uncertainty in the I-125 sources air kerma strength was found to be 1.3% [18].

The total plaque CAX measurement uncertainty (k = 1) for the EBT3 film and TLD micro-cubes was estimated to be 4.7% and 7.2% respectively. This is an estimation based on Type A uncertainties; classified into random uncertainties evaluated by statistical methods and Type B uncertainties which are systematic errors. The final measured dose from either dosimeter is influenced by several factors which are outlined in Table 4.

Results

Verification of PS upgrade to v6.4.6

Treatment plans were calculated in PS v6.4.6 using the 6711 seeds with the default dose calibration factor applied (POWH_ROPES##) and compared to plans calculated with the dose calibration factor set to 1.0 (ROPES##). From these results, summarised in Tables 2, 3, and 4, the dose calibration factor, a scalar parameter introduced in v6.4.6, was verified to be 0.96 for each ROPES plaque size and found to not vary with depth. This scalar correction factor in PS corrects for the dose homogeneity effect of the stainless-steel plaque backing and has been verified in previous work by Poder et al. to agree with measured EBT3 film measurements [7] (Fig. 4).

Table 2 Comparison of PS expected dose with the EBT3 film measured dose performed with a single AgX100® seed

Depth (mm)	EBT3 film measured dose (cGy)	PS expected dose (cGy)
6.63	25 ± 1	25.0
3.63	79 ± 4	83.0

Table 3 Central ROI results of EBT3 film dose planes for the 15 mm ROPES plaque and the relative difference between measured and expected doses calculated with PS

Depth (mm)	EBT3 film measured dose (cGy)	PS expected dose (cGy)	Relative difference (%)
4.14	146.9 ± 6.9	145.0	1.6
6.14	94.6 ± 4.4	97.4	0.8
8.14	96.8 ± 4.5	98.1	2.4
10.14	98.2 ± 4.5	98.1	3.7

Comparison of PS and RADCALC®

The AgX100® I-125 source was enabled in both PS and RADCALC® and a series of dose calculations were performed for different depths with a one hour treatment time and seed activity of 100 U for each ROPES plaque size. The results showed agreement between the treatment planning system, PS, and the independent checking software, RADCALC®, to within 2% for all clinically relevant tumour depths. As shown in Fig. 5, the largest discrepancy was observed in the 18 mm plaque at 0 mm depth. This was still considered acceptable as treatments are not prescribed to the surface of the eye.

Comparison of AgX100® and 6711 seeds

The relative difference in agreement of ≤ 1.6% when comparing the AgX100® seeds to the 6711 model loaded in a ROPES plaque arrangement within RADCALC®, showed that the AgX100® seeds were a suitable replacement in the ROPES eye plaques for the 6711 seed. The agreement in RADCALC® between both models is shown to be within 1% beyond 2 mm depth, and clinically relevant depths (4 mm to 6 mm) were within 0.6%. Figure 6 illustrates the relative difference between the AgX100® seed with respect to the 6711 seeds for each ROPES plaque size.

Table 4 Uncertainty budget for EBT3 film and TLD measurements

Parameter	EBT3 film (%)		Micro-cube TLD (%)	
	Type A	Type B	Type A	Type B
Calibration of dosimeter:				
i. Calibration measurement		3.2	2.0	
ii. kV unit output, dose accuracy				2.0
Scanner/Reader reproducibility and homogeneity		0.7		0.2
Individual TLD sensitivity factor	–	–	2.0	
Energy dependence of detector	–	1.0		1.0
EBT3 film ROI selection	1.0		–	–
Phantom construction, i.e. depth of measurement		2.3		5.9
CAX positioning uncertainty of eye plaque on Solid Water® phantom		1.0		1.0
Solid Water® correction factor		0.6		0.6
Total Irradiation time		1.1		1.1
Air kerma strength measurement of I-125 seed, S_K		1.3		1.3
Total uncertainty (k = 1)	4.7		7.2	
Total expanded uncertainty (k = 2)	9.4		14.4	

EBT3 film dosimetry

Single AgX100® seed measurement

The single AgX100® seed was measured at depths of 3.63 mm and 6.63 mm. The dose comparison between PS and the EBT3 films showed that the values agreed within the associated measurement uncertainty. The results are summarised below in Table 2.

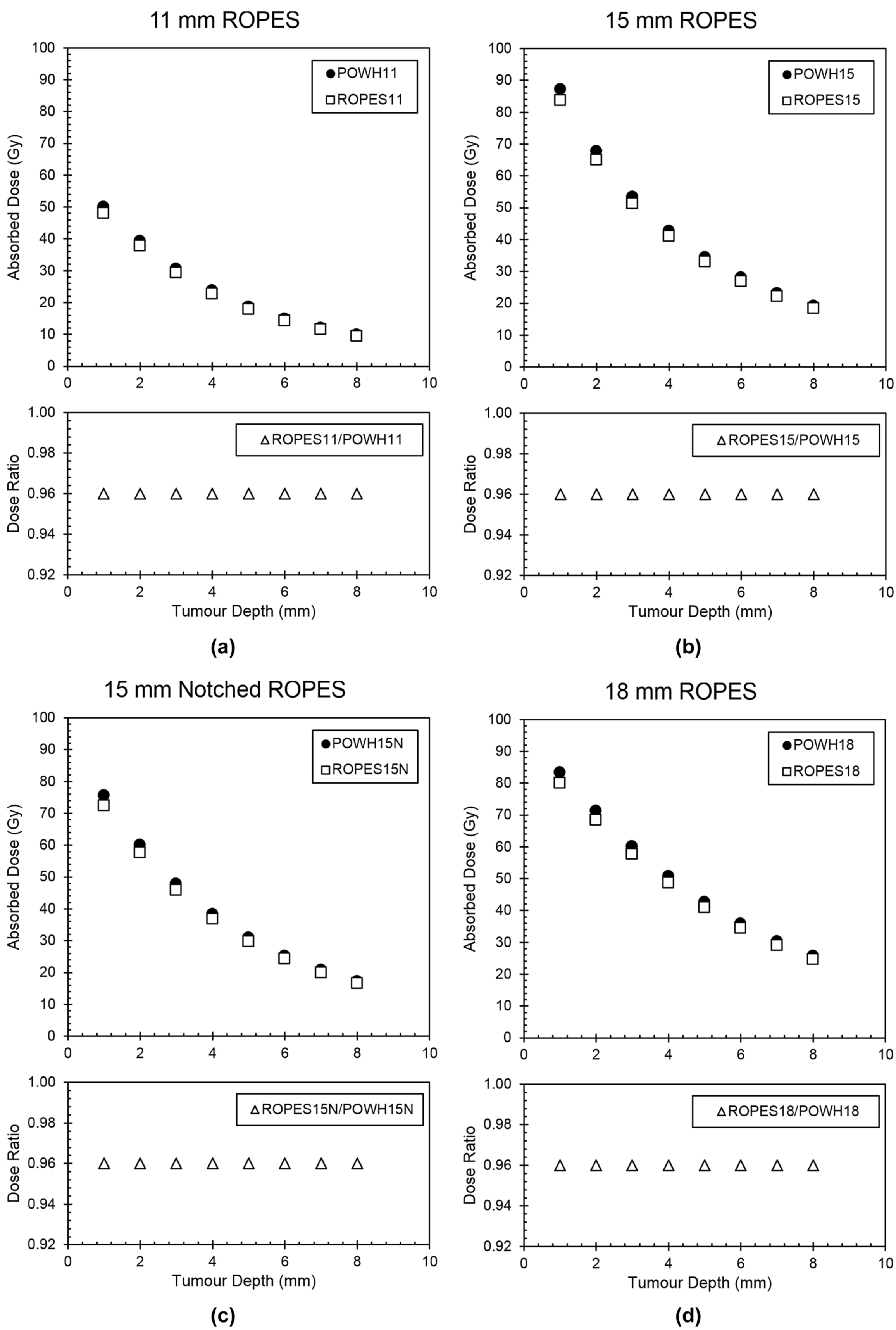
ROPES eye plaque measurements

The EBT3 film dose planes measured at CAX of the ROPES plaque were analysed using an in-house software, taking a small ROI in the centre of the exposed area of the film for each depth investigated. The measurement depth was determined to include 0.14 mm to account for the thickness to the centre of the EBT3 film. The CAX dose for the EBT3 films agreed with PS to within 2% for the most clinically relevant depths, 4.14 mm and 6.14 mm, receiving (146.9 ± 6.9) cGy and (94.7 ± 4.4) cGy respectively. The results are summarised in Table 3. It is evident that the uncertainty is larger at depths 8.14 mm and 10.14 mm as minor positional uncertainties in the setup of the ROPES plaque become increasingly influential, contributing to the discrepancies in the results at these depths.

TLD-100™ micro-cubes

Measurements were conducted with TLD-100 micro-cubes and the results readout using the HARSHAW TLD Model 5500 Manual Reader, to confirm agreement of the CAX percentage depth dose (PDD) in the Solid Water® eyeball phantom with the expected absorbed dose calculated by PS, for each irradiation time. The results were analysed by determining the integral dose for 4.25 mm, 4.75 mm and 5.25 mm, where 4.75 mm is the distance to the centre of the micro-cube TLD. The expected absorbed dose calculation was decay corrected for the time required to irradiate each repetition of the measurement and each measurement was conducted with a new micro-cube TLD for an increasing irradiation time to achieve similar dose delivery. The uncertainty in the physical position of the ROPES plaque, upon the phantom, with respect to the micro-cube TLD is larger for deeper depths, resulting in a greater percentage difference in dose when comparing the measured dose to the expected dose, from PS. At clinically relevant depths, the TLD measurement results agree with PS to within the evaluated measurement uncertainty of 7.2%, the results are shown in Fig. 7.

Uncertainties inherently associated with measurements conducted using TLDs can also be attributed to the orientation of the face of the micro-cubes during irradiation and


11 mm ROPES
POWH11
ROPES11
Absorbed Dose (Gy)
ROPES11/POWH11
Dose Ratio
Tumour Depth (mm)
(a)
15 mm ROPES
POWH15
ROPES15
Absorbed Dose (Gy)
ROPES15/POWH15
Dose Ratio
Tumour Depth (mm)
(b)
15 mm Notched ROPES
POWH15N
ROPES15N
Absorbed Dose (Gy)
ROPES15N/POWH15N
Dose Ratio
Tumour Depth (mm)
(c)
18 mm ROPES
POWH18
ROPES18
Absorbed Dose (Gy)
ROPES18/POWH18
Dose Ratio
Tumour Depth (mm)
(d)

◂**Fig. 4** Absorbed doses calculated using PS v6.4.6 for instances with and without the default dose calibration factor applied were compared for different plaque sizes and depths. The ratio of dose calculated with and without the dose calibration factor applied is displayed below each plot. **a** 11 mm ROPES plaque, **b** 15 mm ROPES plaque, **c** 15 mm notched ROPES plaque, **d** 18 mm ROPES plaque

readout. The precision in irradiation time, from the application of the plaque to the plaque removal has a significant impact upon the depths which require shorter irradiation times. The impact of this factor is less significant for deeper depths such as 8.75 mm and 10.75 mm, as the irradiation time is greater to achieve similar dose prescription, thus the contribution to uncertainty from this factor is reduced, but positioning uncertainties become more influential. The TLD results confirm the validity of the measurements performed with EBT3 film as the prescribed dose to the investigated depth is achieved.

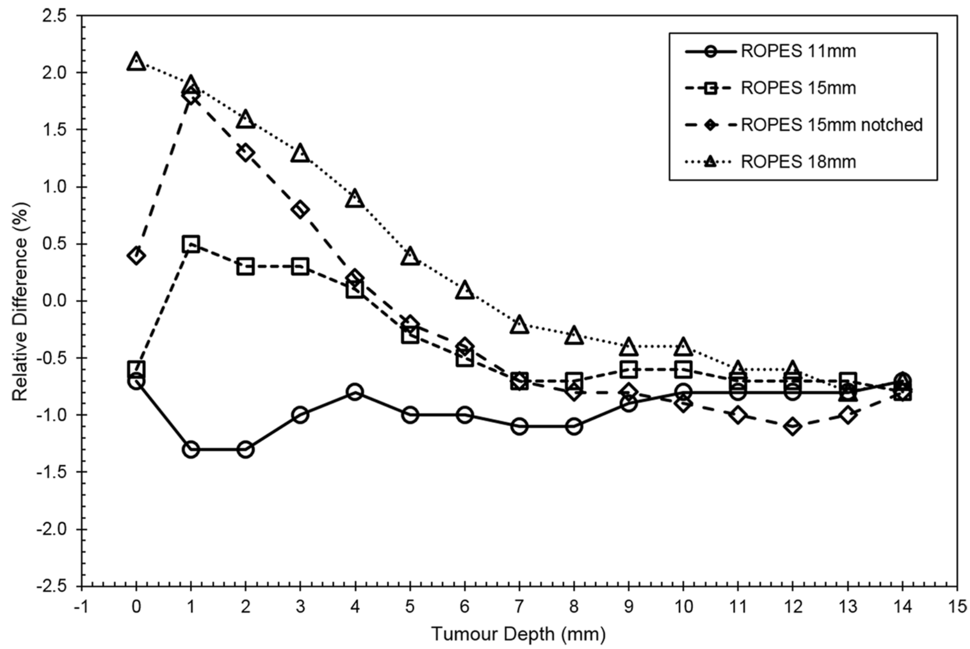


Fig. 5 Relative difference determined between calculation of dose with PS and RADCALC® for ROPES plaques loaded with AgX100® seeds

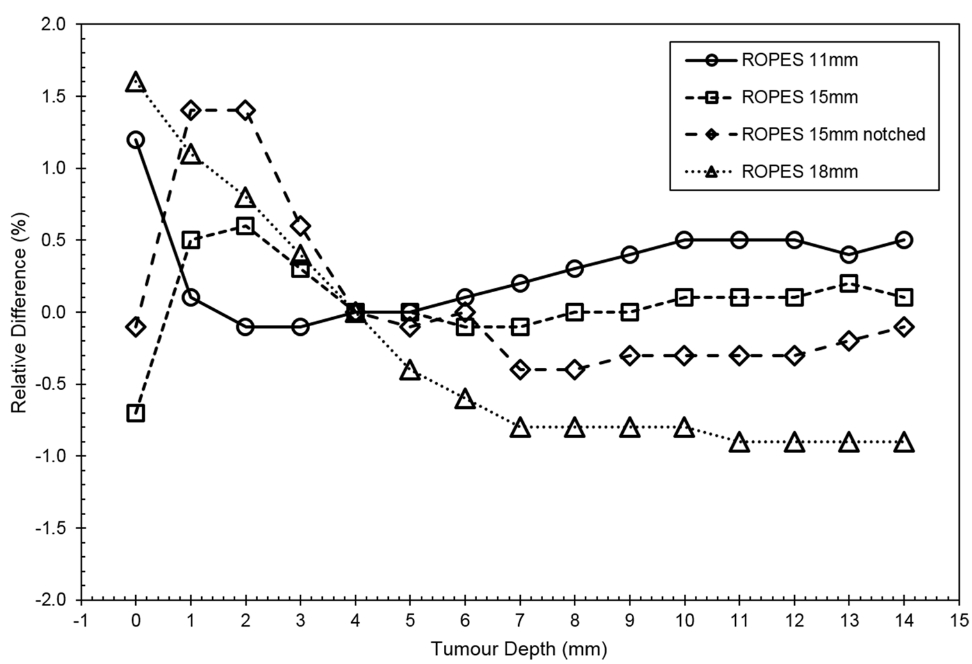


Fig. 6 Relative difference in dose calculated in RADCALC® for ROPES plaques loaded with 6711 seeds to loading with AgX100® seeds, as a function of depth

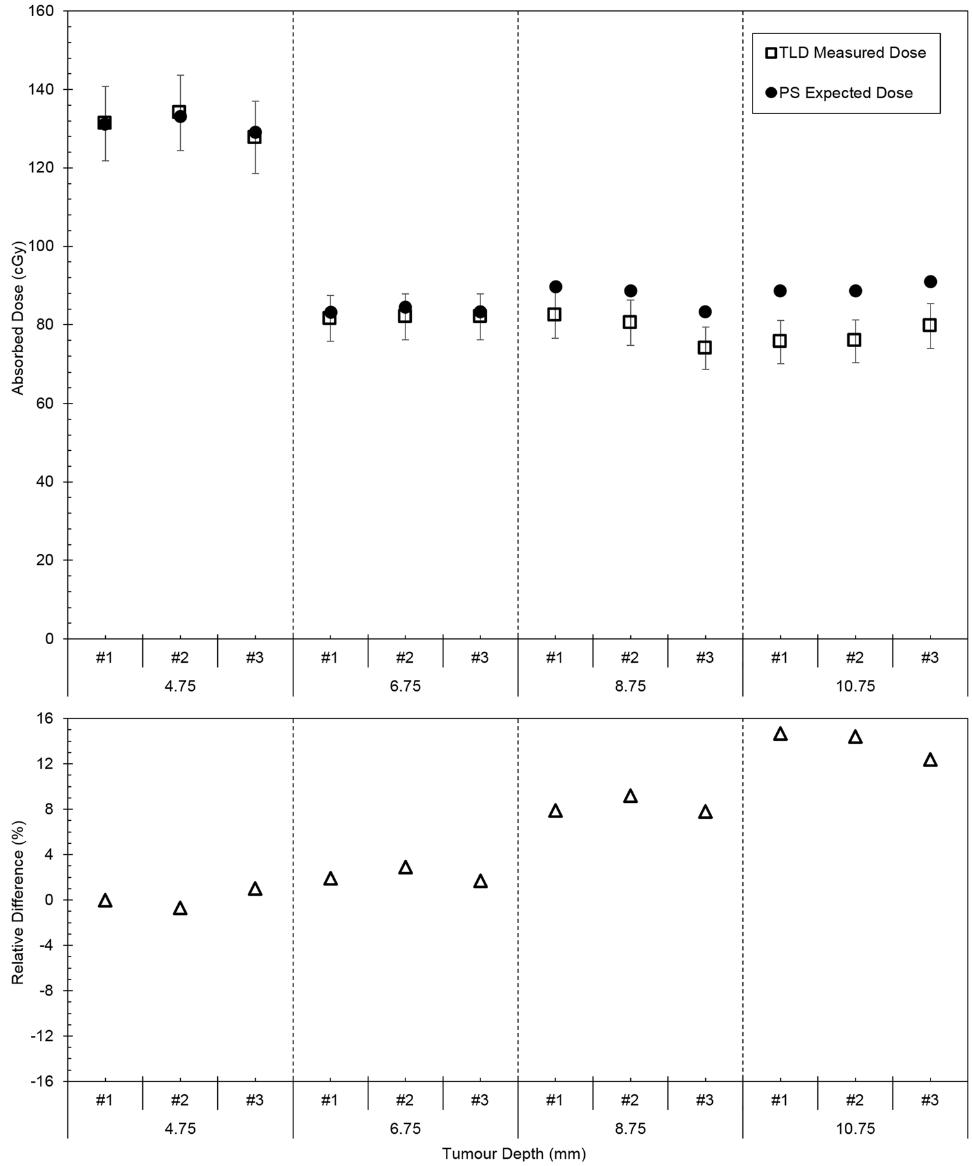


Fig. 7 Comparison of the doses measured with micro-cube TLDs and the doses expected from the PS planning system, for each investigated depth. The relative percentage difference between expected and measured dose is displayed below

Discussion

The implementation of the AgX100® seeds was acceptable for clinical use through the validation of dosimetry data in the software, independent checking software RADCALC®, standard plans and dosimetric verification using EBT3 film and TLDs. It was observed through the comparison of each version of PS that v6.4.6 included a default global scalar dose calibration factor for the ROPES plaque of 0.96 to account for the effect of the stainless-steel backing of the plaque. This meant that the workflow practices in our department had to be revised and homogenous and heterogeneous dose was reported in the prescription [1]. In the case of standard plans, excellent agreement (less than 2%) between PS and RADCALC® is obtained. Although the differences were observed at the surface for 18 mm, this was considered not clinically significant.

In contrast, there was good agreement between the dosimetric measurements and the treatment planning software to further confirm the agreement with the independent checking software. The single seed measurement confirmed the accuracy of the EBT3 film calibration process. The CAX dose for the films agreed with PS to within 2% for clinically relevant depths 4.14 mm and 6.14 mm receiving (146.9 ± 6.9) cGy and (94.7 ± 4.4) cGy on the film respectively. The film measurements performed with the loaded eye plaque confirmed the dose calculation in PS within experimental uncertainty. The greatest significance was observed in the larger depths, 8 mm and 10 mm, however in terms of the calculated uncertainty for the overall measurements and the clinical relevance at these depths, these results can be considered acceptable. Measurements performed with the micro-cubes generally showed good agreement with PS within the estimated uncertainty of 7.2%. The obvious trend being that the positional uncertainties have a substantial effect at greater depths and this could be minimised by improving the construction of the Solid Water® phantom. For this study and in terms of clinical relevance, it is still acceptable. Further work in the Solid Water® phantom is currently undergoing to develop a faster and more accurate method of ROPES eye plaque quality assurance for subsequent batches of AgX100® I-125 seeds.

Conclusion

The Plaque Simulator v6.4.6 was found to be acceptable for clinical use for the AgX100® I-125 seed in the ROPES plaques. Independent dose checks were performed using RADCALC® v6.2.3.6 for the ROPES plaques and the agreement between PS and RADCALC® is less than 2% for clinically relevant tumour depths. Dose measurements were performed with EBT3 film and TLD micro-cubes to further confirm the validity of PS for eye plaque treatments. The dosimetric measurements agreed with the calculations of PS for clinically relevant depths (less than 6 mm) within the evaluated uncertainties of 4.7% for EBT3 film and 7.2% for TLDs. The AgX100® I-125 seed was released for clinical use with the ROPES eye plaque.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This research did not involve any human participants or animal experiments.

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