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To cite this article before publication: Moradi et al, 2017, Phys. Med. Biol., at press:
https://doi.org/10.1088/1361-6560/aa7fe6

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Monte Carlo skin dose simulation in intraoperative radiotherapy of breast cancer using spherical applicators

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Abstract: The relatively new treatment modality electronic intraoperative radiotherapy (IORT) is gaining popularity, irradiation being obtained within a surgically produced cavity being delivered via a low-energy X-ray source and spherical applicators, primarily for early stage breast cancer. Due to the spatially dramatic dose-rate fall off with radial distance from the source and effects related to changes in the beam quality of the low keV photon spectra, dosimetric account of the Intrabeam system is rather complex. Skin dose monitoring in IORT is of importance due to the high dose prescription per treatment fraction. In this study, modeling of the X-ray source and related applicators were performed using the Monte Carlo N-Particle (MCNP) transport code. The dosimetric characteristics of the model were validated against measured data obtained using an ionization chamber and EBT3 film as dosimeters. By using a simulated breast phantom, absorbed doses to the skin for different combinations of applicator size (1.5 to 5 cm) and treatment depth (0.5 to 3 cm) were calculated. Simulation results showed overdosing of the skin (> 30% of prescribed dose) at a treatment depth of 0.5 cm using applicator sizes larger than 1.5 cm. Skin doses were significantly increased with applicator size, insofar as delivering 12 Gy (60% of the prescribed dose) to skin for the largest sized applicator (5 cm diameter) and treatment depth of 0.5 cm. It is concluded that the recommended 0.5 to 1 cm distance between the skin and applicator surface does not guarantee skin safety and skin dose is generally more significant in case of the larger applicators.

Key words: breast IORT, Intrabeam, Monte Carlo simulation, skin dose, photon spectrum

Highlights:

- Intrabeam X-ray source and spherical applicators were simulated and skin dose was calculated
- Skin dose for constant skin to applicator distance strongly depends on applicator size
- Use of larger applicators generally results in higher skin dose
- The recommended 0.5 to 1 cm skin to applicator distance does not guarantee skin safety

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1. Introduction

The (IORT) Intrabeam system (Carl Zeiss Surgical, Oberkochen, Germany) is one of a number of soft x-ray systems that have become commercially available over the last decade or so, providing what is now referred to as electronic brachytherapy, distinguishing the modality from radioactive source brachytherapy. Offering the ability to generate isotropic dose distribution in a tumour cavity subsequent to lumpectomy as a particular example, this situation could similarly be obtained using small radioactive brachytherapy sources. Thus said, IORT X-ray source (XRS) systems offer potential advantages, providing constant dose-rate delivery at given distances from the source to allow an associated fixed treatment duration, additionally avoiding potential risks from the handling of radioactive sources. It should also be mentioned that changes in dose-rate at given distances from the source will have radiobiological consequences, a complex issue explored most predominantly using cultured cell lines (Zaider and Minerbo 2000). Gaining popularity, most notably in treatment of the postlumpectomy primary breast tumour bed, advantages in such therapy include greater sparing of normal tissue compared to whole breast radiotherapy treatment, also radically mitigating against radiation-induced injury complications to adjacent organs, the heart and lungs specifically, pneumonitis and lung fibrosis being two such examples (Njeh et al, 2010).

Relative to other partial breast radiotherapy methods, IORT uses low energy photons, this treatment typically applying elevated radiation dose in one session, therefore decreasing the postoperative radiotherapy burden (Vaidya et al., 2005). In addition, this technique allows improved tumour ablation because of the increased biological effect of low energy photons (Brenner et al., 1999). The Intrabeam system is designed to operate at nominal accelerating potential of 50 kVp and produces a photon field at an elevated dose-rate of approximately several tens Gy/min at a few mm distance from the XRS, falling off to several cGy/min at a distance of 45 mm. The associated steep dose gradient provides the possibility of delivering high doses to the target in a single fraction as mentioned, while keeping the dose to healthy tissues within an acceptable range (Keshtgar et al., 2014). Thus said, due to the pronounced change in dose-rate over very short distances from the source, the dosimetry of an IORT system can be rather complex.

In breast IORT, as is the situation for all radiotherapy, doses to the different organs at risk are an important consideration, including the lungs, heart, ribs and skin. The heart and lung are protected to a degree by the chest wall, lying at relatively large distances from the source. Conversely, skin doses can be rathermore critical, most particularly when the tumour is very close to the skin. In the Keshtgar et al. (2014) booklet on targeted IORT, guidance is offered that, to avoid severe fibrosis (with a threshold dose of 13-14 Gy), a minimum distance of 5 to 10 mm between the skin and applicator surface should be considered. Observance of the minimum distance of 5 mm has been emphasized, as for example in using folded soaked gauze around the applicator to keep the skin dose below the aforementioned threshold. Although recently Radiance (GMV Innovating Solutions Corporation, Tres Cantos, Spain), a commercial computerized treatment planning system (TPS), has been developed to include provision for dose calculations of the Intrabeam system for the various applicators and clinical situations, the system has yet to be implemented in many of the centres using the Intrabeam system as a standard treatment modality. The Radiance TPS uses hybrid Monte Carlo, enabling users to perform fast dose calculations (taking of the order of several minutes, a clinically practical time), working from patient computed tomography (CT) images (Valdivieso-Casique et al., 2015).

In order to prevent late detrimental cosmetic effects due to chronic dermal exposure, the ICRP (1992) recommends limiting life-time dose to the skin of no more than 30 Gy, the occupational annual dose limit of 0.5 Sv implying a life-time dose limit of about 20 Sv. While the threshold dose for radiation
induced skin effects is 2 Gy, transient skin injury in the average population is not expected to occur for doses to the epidermis of less than 6 Gy (Geleijns and Wondergem, 2005). Hence, the skin dose limit in IORT is also usually set at 6 Gy (Avanzo et al., 2012; Fogg et al., 2010; Price et al., 2013).

In regard to physics knowledge and associated uncertainties in high dose rate (HDR) radionuclide brachytherapy dosimetry, a detailed review is provided by Palmer et al. (2012), focusing on the use of a range of dosimeters as well as the Monte Carlo simulation of dose. Conversely, Issa et al. (2012) have investigated the specific use of optical fibre thermoluminescence (TL), regardless of dose rate. In regard to breast IORT, several studies have reported skin dose measurements using different types of dosimeter, including films (Avanzo et al., 2012; Price et al., 2013), TL dosimeters (TLDs) (Bouzid et al., 2015; Eaton et al., 2012; Fogg, 2010) and optically stimulated luminescent dosimeters (OSLDS) (Price et al., 2013). The accuracy of the measurement in such a radiation field, of low keV photon energy and severe dose-rate change, in addition to usual calibration uncertainties, is affected by many other factors such as positioning uncertainty, dosimeter energy response, thickness of the dosimeter (Fogg et al., 2010; Soares et al., 2006) and even dose-rate dependence of the dosimeter. The combined uncertainty from all of these influencing factors have been reported to be up to 77 % (Eaton, 2012). Conversely, the Monte Carlo method provides precision point dose assessments (Spezi and Lewis, 2008), the deposited energy at sites of interest under any condition can be directly simulated by creating particles of the radiation field and tracking their interactions in the attenuating medium.

In spite of recommendations for skin protection during IORT of breast cancer, the overdosing of skin has been reported through in-vivo measurements (Eaton et al., 2012; Fogg et al., 2010). Thus said, in general less attention has been devoted to breast skin dose and its variations as a function of distance from the applicator surface, also potentially being influenced by applicator size. Present work has sought to use a Monte Carlo simulation method to simulate the IORT XRS and its spherical applicators to create a realistic model of the Intrabeam radiation field and to calculate the dose received to breast skin in various clinical conditions. The x-ray spectrum was also investigated to trace changes in beam quality due to the presence of applicators and also energy transport in the interposing attenuating media. The simulation results have been validated against measured dose values comprising of the depth doses and surface doses. In addition, for the purpose of skin dose calculation, a breast phantom including realistic tissue compositions and skin layers was modeled and skin dose was calculated for all applicator sizes considering different treatment depths.

2. Materials and methods:

2.1. X-ray source specification

The Intrabeam IORT x-ray source (XRS) includes a 10 cm long, 3.2 mm outer diameter tube, made from mu-metal for magnetic shielding, the exception being the 1.6 cm end part, made from beryllium to provide a quasi x-ray transparent window, terminating in the form of a hemispherical cap (Yanch and Harte, 1996). This needle shaped tube is attached to an electron gun that generates the electrons which are then accelerated through the evacuated tube, bremsstrahlung and characteristic lines production yielding a mean energy of 20 to 30 keV markedly less than that of the maximum energy of 50 keV. Electrons strike the very thin gold target (presumably chosen to be of a thickness optimal in stopping the majority of electrons, generating maximal bremsstrahlung and characteristic lines from this high atomic number target) deposited on the inner layer at the end of the tube. Based on manufacturer data, electrons reaching the gold target have a Gaussian energy distribution of full width at half maximum (FWHM) of 5 keV (Clausen et al., 2012). The outer surface of the tube is coated along its whole length with a thin layer of chromium nitride (CrN) (Bouzid et al., 2014), providing both for durability and biocompatibility (Keshtgar et al., 2014). The resulting bremsstrahlung x-ray spectrum
with a maximum energy of approximate 50 keV eventuates an almost isotropic dose distribution showing maximum angular variation of 15 % (Yanch and Harte, 1996).

The Intrabeam system was initially introduced with cylindrical, spherical and needle applicators (Keshtgar et al., 2014) and then was later equipped with superficial (flat) applicators that are capable of converting spherical dose distributions to flat circular shapes (Schneider et al., 2014). The system of interest in treatment of the post-lumpectomy primary breast tumour bed includes eight different diameter spherical applicators made of polyetherimide, ranging in diameter from 1.5 cm to 5 cm in 0.5 cm increments. For the smaller size applicators (diameters from 1.5 to 3 cm), an aluminum attenuator has been designed which is placed between the applicator body and the XRS probe (Eaton, 2012). This intentional beam hardening (removing the very low energy photons from the treatment spectrum by the aluminum) is sufficiently performed by the applicator body itself when larger applicator sizes are being utilized (Keshtgar et al., 2014).

2.2. MCNP simulations

The MCNP code is known to be a multipurpose, widespread and powerful Monte Carlo tool for simulation of radiation transportation. Version MCNPX of the code was used in this study, due to the accessibility and different possibilities that the code allows users in calculating energy spectrum, particle fluence and deposited energy in any 3D cell of interest (Pelowitz, 2007). The MCNP input file includes the definition of cells, surfaces and complementary information which contains elemental compositions and densities, source description, tallies (for desired output definition) and variance reduction functions. The IORT x-ray source was simulated based on the accurate geometrical and compositional data provided by the manufacturer (Carl Zeiss, Germany). Accurate description of the electron source is usually the most basic issue, of high importance in simulation that needs high accuracy but then often a number of approximations and further detailed verifications are needed. Clausen et al. (2012) have investigated the impact of radius of the electron beam hitting the gold target of the IORT system. It was reported that effective points of incidence of the diverged electron beam to the target, which agreed with the available experimental dose distribution, were obtained with a value of the radius that ranged from 0.6 to 0.7 mm and from 0.7 to 0.8 mm, with weighting factors of 1.05 and 1.55 respectively. The same electron beam lines were used in the current study with the Gaussian energy spectrum as described previously.

The first series of models were simulated to obtain the energy spectra at different surfaces, including different depths in water and the various applicator surfaces. Photon counts in 0.2 keV energy bins, from 0 to 63 keV (the maximum electron energy of the Gaussian distribution), were performed using tally F4. Energy cut off for both electron and photon transportations in all simulations was set at 1 keV to ensure maximum accuracy. Other than the XRS tip, the photon spectra were calculated at different depths in water to investigate the changes in beam quality. As can be seen in Figure 1-A, 1×1 cm² area scoring planes were positioned at 5 mm intervals from the tip of the XRS.
The contribution of each primary electron to generate a photon passing through the XRS exit plane was 0.0129 which indicated that only 129 photons will be emanated from XRS for every 10^4 initially emitted electrons. Subsequently, calculation of dose distribution by tracing initial electrons becomes impractical, since the calculation time increases. This is because an extremely large number of photon interactions, of the order of a few hundred millions, is necessary to obtain dose calculation uncertainty within the acceptable range. Thus, for the purpose of acquiring absorbed dose in the second series of simulations, a photon source with the calculated spectrum from the first series and with an isotropic emission was positioned on the outer surface of the XRS tip instead of the electron source definition. Tally *F8 which is equivalent to the detector pulse height was used to calculate dose at this stage. This tally calculates the energy deposition in cells of interest, by all photons and electrons, in terms of MeV per initial emitted particle from the source. Depth doses in water were calculated using deposited energies in cylindrical cells of 1 mm length and 1 mm radius positioned on the symmetry axis of the beam, with their flat-surfaces faced to the source. A low energy cut off of 1 keV for both electrons and photons was set. This is the minimum possible tracking level in MCNPX code that allows obtaining minimum relative error for dose, eventuating in maximum accuracy. Simulations were continued with increasing the number of primary particles (electrons for the spectrum simulations and photons for the dose simulations) until acceptable calculation uncertainties were obtained. Depth dose calculation in water were performed for the bare probe and also for spherical applicators. Figure 1-B shows 4.5 cm applicator and scoring cells for dose calculation in water, while Figure 1-C demonstrates the internal structure of smallest applicator (1.5 cm diameter) with respective materials.

### 2.3. Validation of dose calculations

Depth dose data produced by the Intrabeam XRS and spherical applicators as measured by a PTW TN34013A ionization chamber (IC) (PTW, Freiburg, Germany) in water was taken as the benchmark to be compared to our simulation results. In addition, an additional measurement using Gafchromic EBT3 film (Radiation Products Design Inc., USA) was performed to verify the surface dose predicted through simulation. In the measurement, EBT3 film was cut and positioned on the surface of the water phantom and in the vicinity of the applicator stem using very thin transparent PVC sheet (Figure 2-A).

Prior to this experiment, a calibration curve for EBT3 films was obtained by considering a fixed distance of 10 mm between the Intrabeam bare probe tip and films. Films (cut into 20 mm × 20 mm) were irradiated with doses of 1, 2, 3, 5, 10, 15, 20 and 25 Gy and each experiment was repeated three times. The films were scanned 24 hours after irradiation to allow for post-irradiation colour changes, using an Epson 10000 XL flat-bed scanner (Epson America Inc., Long Beach, CA) in transmission mode, at a resolution of 75 dots per inch (dpi). The raw images of the EBT3 films were analyzed using the ImageJ
1.47 software (National Institution of Health, USA) and calibration curve relating the pixel value and the doses was established.

A 5 cm diameter spherical applicator was placed in the water phantom where a distance of 1 cm was set between the neck of the applicator and water surface where the film was positioned. This identical setup was simulated within the MNCP software with circular shaped water cells (1 mm width) arranged on the surface 0 to 40 mm distance from the applicator stem (Figure 2-B and C). Since the goal of simulations in the last part of this work is evaluation of received dose to skin, and skin dose should be calculated relative to the prescription dose at applicator surface, the identical thickness of water layer needed to be considered for both cells, i.e. the cell around the applicator surface and every cells of interest (those in which dose is calculated). The cell thickness for the current model was set to 80 µm, to be made comparable with the thickness of skin layers in the subsequent section. A greater thickness was also examined, of the order of 1 mm, the outcome of which showed the smaller thickness to better reproduce the experimental results.

![Fig. 2. A) Experimental setup for EBT3 film positioning on water surface B) MCNP modeled geometry of Intrabeam 5 cm applicator in water phantom C) Ring shape water voxels for surface dose determination](image)

2.4. Skin dose simulations

Skin thickness and composition vary among different body sites (Ham and Cormack, 1987) and real skin dose is affected by individual patient geometry and attenuating media. Therefore for the purpose of simulating breast skin and acquiring a general estimation of the skin dose at different clinical conditions including various combinations of applicator sizes and treatment depths (distance between skin and applicator surface), an average breast skin thickness of 1.45 mm was used (Huang et al., 2008). Depending on the biological effect of interest, measurement of absorbed dose was performed at different depths. The dose to the basal layer (the innermost layer of the epidermis) is responsible for deterministic effects and skin erythema while higher doses will cause damage to deeper layers in the skin (ICRP 28, 1978). Among the deeper structures of the skin, the upper dermal layer is the most sensitive to radiation and is responsible for stochastic effects and cancer risk (ICRP 59, 1992). In the present work the epidermal and dermal layers were simulated at the depths 20- to 100 µm and 300- to 500 µm respectively (ICRP 59, 1992). A breast phantom with the size of 24 cm separation was simulated to provide the possibility of placing in it the largest applicator (the 5 cm diameter sphere). In addition, complementary tissues including the soft tissue, lung tissue and ribs were also introduced within the breast phantom model. A schematic view of the simulation geometry of the breast phantom is shown in Figure 3-A. Ring shaped skin cells were designed for dose deposition measurements (Figure 3-B), every
layer being composed of different skin substrates (Figure 3-C). Materials compositions and mass densities of the different tissues were derived from published reports and are presented in Table 1.

![Diagram showing different skin substrates](image1)

**Fig. 3.** A) MCNP simulated breast phantom (treatment depth and vertical distance of voxels from applicator stem are shown by D and R). B) ring voxels of skin and C) different simulated skin layers

**Table 1.** Material composition and densities used for breast phantom simulation

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Composition (%)</th>
<th>Density (g/cm³)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>10 20.4 4.2 64.5 0.2</td>
<td>1.09</td>
<td>Woodward and White 1986</td>
</tr>
<tr>
<td>Breast tissue</td>
<td>10.6 33.2 3 52.7 0.1</td>
<td>1.02</td>
<td>ICRU 44</td>
</tr>
<tr>
<td>Soft tissue</td>
<td>10.2 14.3 3.4 70.8 0.2</td>
<td>1.06</td>
<td>ICRU 44</td>
</tr>
<tr>
<td>Ribs</td>
<td>3.4 15.5 4.2 43.5 0.1 0.2</td>
<td>22.5</td>
<td>ICRU 44</td>
</tr>
<tr>
<td>Lung</td>
<td>10.3 10.5 3.1 75.9 0.2</td>
<td>0.24</td>
<td>ICRR 44 and Van Dyk et al. 1982</td>
</tr>
</tbody>
</table>

3. Results and Discussion:

3.1. X-ray energy spectrum and beam quality

Measured spectra for different electron accelerating potentials, for IORT sources similar to that of the Intrabeam system, have been reported by Beaty et al. (1996) and Ebert and Carruthers (2003). However, different measurement conditions including detector efficiency, measurement medium as well as different coating materials of the initial version of XRS (Yanch and Harte, 1996) did not allow direct comparison of these spectrums with our results. The x-ray spectra obtained in this work were calculated in water at the tip of the XRS probe, which is displayed in Figure 4. These spectra cover a range of up to 50 keV with two distinct characteristic X-ray lines originating from the gold and chromium present at the probe tip. The shape of the spectra are in good agreement with previous simulated spectra (Bouzid et al., 2015; Nwankwo et al., 2013; White et al., 2016) calculated using the Geant4 Monte Carlo code.
Fig. 4. X-ray spectrum produced in simulation of the XRS operating at nominal energy of 50 kVp. The lower energy characteristic X-ray lines (5.4 and 6 keV) and the greater energy peaks (10.4, 11.8 and 13.6 keV) are relevant to chromium (the biocompatible coating) and gold (target) respectively (in agreement with characteristic X-rays of mentioned elements (Thompson and Vaughan, 2001)).

Figure 5 (plotted on a logarithmic scale) demonstrates the photon spectra obtained at the tip of the XRS bare probe compared to those attenuated by different thicknesses of water between the tip and scoring plane (Figure 1-A). Larger fluctuations were observed in photon spectra scored at deeper depths due to the increase in photon calculation uncertainties, less particles reaching the scoring planes at larger distances from the source. It should be noted that these spectra were acquired by tracing primary electrons incident on the target, not by definition of the photon source at the XRS tip.

Fig. 5. X-ray spectra at XRS tip and at different depths in water obtained by MC simulation

3.2. Beam hardening effect of applicators
Photon spectra on the surface of the different sized applicators were obtained using the same procedure as described in Section 2.2, with the difference that the photon spectrum calculated at the XRS tip was considered to be the initial source. Comparison of these spectra to the one acquired at the probe tip are shown in Figure 6. Photons with energy below 20 keV are strongly attenuated by the applicators, the intensity of photons of energy less than 8 keV dropping to close to zero.

![Figure 6. X-ray spectrum at XRS tip compared to that of various size applicator surfaces obtained by Monte Carlo simulation](image)

To make a quantitative evaluation of beam hardening effect of the applicators, beam quality can be presented by the mean energy of each spectrum that characterizes the spectral distribution of the radiation field by distribution of the fluence with respect to energy (Khan, 2003). These mean energies were calculated using Equation 1, where $E_m$ represents the mean energy of the spectrum, and $N(E_i)$ is the number of photons acquired in the $E_i$ energy bin, and $i$ varies from the minimum ($m = 1$) to the maximum value ($n = kVp$, here this fixes the maximum electron energy of the initial Gaussian distribution) of the energy spectrum.

$$E_m = \frac{\sum_{m}^n N(E_i) E_i}{\sum_{m}^n N(E_i)}$$

Table 2. Mean photon energies of the XRS spectra (bare probe) obtained at different depths in water

<table>
<thead>
<tr>
<th>Scoring plane</th>
<th>Mean photon energy (keV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tip of the x-ray source</td>
<td>19.45</td>
</tr>
<tr>
<td>5 mm</td>
<td>27.04</td>
</tr>
<tr>
<td>10 mm</td>
<td>28.47</td>
</tr>
<tr>
<td>15 mm</td>
<td>29.42</td>
</tr>
<tr>
<td>20 mm</td>
<td>30.3</td>
</tr>
</tbody>
</table>
Table 3. Mean photon energies of the XRS spectra obtained on the surface of the various applicator sizes

<table>
<thead>
<tr>
<th>Scoring plane</th>
<th>Mean photon energy (keV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>On the surface of</td>
<td></td>
</tr>
<tr>
<td>1.5 cm applicator</td>
<td>27.8</td>
</tr>
<tr>
<td>2 cm applicator</td>
<td>28.3</td>
</tr>
<tr>
<td>2.5 cm applicator</td>
<td>28.6</td>
</tr>
<tr>
<td>3 cm applicator</td>
<td>28.9</td>
</tr>
<tr>
<td>3.5 cm applicator</td>
<td>28.1</td>
</tr>
<tr>
<td>4 cm applicator</td>
<td>28.5</td>
</tr>
<tr>
<td>4.5 cm applicator</td>
<td>28.8</td>
</tr>
<tr>
<td>5 cm applicator</td>
<td>29</td>
</tr>
</tbody>
</table>

Table 2 shows the calculated mean energies of the bare probe spectrum at different depth in water and Table 3 at the surface of the various size applicators. These mean energies are in agreement with the effective energy of the Intrabeam source of between 20-30 keV as reported by Keshtgar et al. (2014). As expected, beam hardening happens for the bare probe spectrum in water and mean energy increases from 19.45 keV at the tip of the XRS needle to 30.3 keV at 20 mm depth in water. The mean energy of the photon field at the surface of applicators does not change significantly for different applicator sizes, ranging from 27.8 to 29 keV. The mean energy shows small incremental increase, from 27.8 keV for the 1.5 cm applicator to 28.9 keV for the 3 cm applicator and from 28.1 keV for the 3.5 cm applicator to 29 keV for the 5 cm applicator. This is caused by the presence of aluminum attenuator for the four smaller size applicators which is not present for the four larger ones.

3.3. Simulation results versus measurements

Figure 7-A shows the depth-dose data for the bare probe measured by the ionization chamber (IC) in water for the two XRS units available in our center (denoted as XRS 1 and XRS 2). Comparison was made against the MCNP calculated depth-dose data which have been normalized to the maximum value at 3 mm depth. It was observed that simulation results conformed well to the dose fall off in water for unit XRS 2. However, a systematic difference was noted between the simulated and the XRS 1 depth-dose data. This difference in the output dose rate of different sources has been reported elsewhere (Armoogum et al., 2007), suggestive of difference in the various structures involved in the generation of x-rays, including the electron source, the beam deflector as well as the gold target. Since the target has a micrometer scale thickness (Clausen et al., 2012), the difference between manufactured and ideal target thickness would be one plausible reason for this observation. This means that in detail the calculated photon spectra may also be different for any individual XRS. Difference between MC calculated depth doses and those measured by IC for two XRSs, shown in Figure 7-B, demonstrate maximum deviation of 7.45% at 25 mm depth for XRS 2, while deviation is much higher in case of XRS 1. Figure 7-B also shows the MC calculation uncertainty (1SD) which is increasing with depth in water due to the increasing distance between scoring cells and source. Eventually it reaches to 3.68% at 45 mm depth. Comparison between MC calculated dose rates for the biggest applicators, 4.5 and 5 cm diameters, and measured values with respective deviations are also presented in Figure 7-C and D. MC simulation uncertainty shown in Figure 7-D is related to depth dose calculation for the 5 cm applicator.
Fig. 7. A) Depth-dose fall off calculated by MCNP versus the ionization chamber measured values for the two different XRS units, XRS1 and XRS2, B) Deviation of MC calculated dose rates from those of two XRSs and one standard deviation of MC calculated values, C) Depth-dose fall off in water for the largest size applicators and D) Deviations of MC calculated dose rates from those of measured by IC for applicators (MC uncertainty for 5 cm applicator is shown).

Dose to the water surface was measured in order to verify the results of surface dose simulations. Surface dose from simulation was calculated using Equation 2, where $E_n$ and $M_n$ are the deposited energy (in MeV) and mass (in g) in cell n, whereas $E_0$ and $M_0$ are related to the same quantities in the reference cell around the applicator which receives the prescribed dose (20 Gy in this experiment). The ring shaped water cells have 1 mm width and 80 µm thickness. Results of surface dose calculation as a function of distance for a 5 cm applicator, compared to measured values by the EBT3 film are shown in Figure 8-A, while Figure 8-B shows deviation of MC results from measurement. A notable deviation of the measured dose with the simulated dose was observed at both ends of the curve which may be due to the uncertainty in positioning of the film at a fixed position on the water surface and/or response of the film at the edges. The film was attached to the stem of the applicator and it is thought that the most distal part of the film may have entered into the water to a small extent and thus received a greater dose than predicted from the simulation.

Equation 2. \[ \frac{E_n/M_n}{E_0/M_0} \times 20 \text{ Gy} \]
3.4. Skin dose for various applicator sizes and treatment depths

Skin dose simulations were performed as described in Section 2.4. Skin doses were calculated with treatment depths of 0.5 cm to 3 cm in 0.5 cm intervals for all applicator sizes from 1.5 cm to 5 cm diameter. Calculation times of between 10 to 24 hours were noted, using a standard computing system (CPU Intel Core i7/RAM 8 GB) to obtain calculation uncertainties of less than 5% in all scoring cells. Figures 9 and 10 show the results of these simulations for different applicator sizes. The vertical axis shows the skin dose in percentage terms relative to the prescription dose. The skin doses for the various treatment depths are shown using different colours while epidermal and dermal doses are indicated by solid and dashed lines respectively. The dose to the dermal layer is observed to be greater, by a few percentage points (maximum of 4% difference), than that of the epidermal layer as it is closer to the source and also receive backscattered radiation from the epidermal layer. Doses to the skin generally decreased with increasing treatment depths, the source being located further from the skin. Dose to the dermis is more marked for the smaller treatment depths because of the drastic dose-rate fall off at positions closer to the applicator surface.
Fig. 9. Dose to skin layers at different treatment depths for different applicator sizes (1.5 to 3 cm diameter applicators)

Fig. 10. Dose to skin layers at different treatment depths for different applicator sizes (3.5 to 5 cm diameter applicators)

Considering 20 Gy as the usual prescribed dose at the applicator surface (Vaidya et al., 2005) and 6 Gy as the dose limit for the epidermis layer in order to avoid transient skin injury (Geleijns and Wondergem, 2005), in Figures 9 and 10 the overdosing zone is taken to be the area receiving doses 30% greater than the prescribed dose. Table 4 provides a summary. It is observed that if a distance of 1 cm between the
skin and applicator stem is implemented (e.g., using the soaked gauze mentioned earlier) then, for all applicators less than 4 cm diameter, doses above 6 Gy will not be delivered to the skin. However, it does appear that the 1 cm distance would be insufficient for the cases of the 4, 4.5 and 5 cm diameter applicators. Having a 0.5 cm distance between the skin and applicator surface as mentioned in the IORT booklet (Keshtgar et al., 2014) resulted in 6 Gy delivered to the skin for all simulated applicator sizes other than the smallest applicator of 1.5 cm diameter. Our results concur with a clinical study wherein skin dose measurements of 72 patients resulted in doses greater than 6 Gy for separations between the skin and applicator surface of less than 1 cm (Eaton et al., 2012). This is due to dose-rate fall-off from the applicator surface proceeding to depth, being more marked at close-up distances in the case of small applicators (Eaton and Duck, 2010). Therefore, at certain distances from the applicator surface, the ratio of dose at depth to dose at the applicator surface is greater in the case of the larger applicators.

Table 4. Overdosing area around applicators (designated as those areas receiving >30% of the prescription dose)

<table>
<thead>
<tr>
<th>Applicator size (cm)</th>
<th>Distance between skin and applicator surface (treatment depth) (cm)</th>
<th>Distance from applicator stem to skin receiving &gt;30% of the 6 Gy prescribed dose (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>0.5</td>
<td>----</td>
</tr>
<tr>
<td>2</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>2.5</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>3.5</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>4.5</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>0.5</td>
<td>1</td>
</tr>
</tbody>
</table>

As Table 4 indicates, in the case of the smaller applicators (those less than 4 cm diameter), skin dose does not exceed the 6 Gy limit when located at 1 cm distance to the applicator surface. In the case of the 1.5 cm applicator, a small distance between the applicator surface and the skin of 0.5 cm enables sparing of the skin from receiving doses greater than 6 Gy. Increase in applicator size results in increase in the ratio of “skin to prescription dose”, the skin dose eventually exceeding the dose limit, the overdosing area becoming wider, reaching to 1.9 cm around the 5 cm applicator stem in the case of a treatment depth of 0.5 cm. It should be noted that the results obtained from this part of study was based on simulations on a generic breast phantom. Skin dose may vary for any individual patient based on the IORT setup as well as the geometry and compositions of the treated breast. However, the results presented in Table 4 provide an insight into the trend in skin dose variation as a function of applicator size as well as the distance between applicator surface and the skin.

4. Conclusion
In this work, simulation using the MCNP code was made of an Intrabeam IORT x-ray source and related spherical applicators, the latter ranging in diameter from 1.5 to 5 cm, detailed specification data being provided by the manufacturer. Photon energy spectra calculated on the surface of all of the applicator sizes showed the mean energy of the output X-ray spectrum from the XRS tip to be obtained at 19.45 keV. Beam hardening due to the applicators increased the mean energy value minimally as a function of applicator size, from 27.8 keV to 29 keV. As such, the output beam quality varies is similar for all applicators in terms of distance from applicators surface. Spectra related to all spherical applicators have been presented here for the first time. Calculated spectra were also found to be in good agreement with previous published data. Dose-distance data obtained from simulation was then compared with the reference depth dose obtained with IC measurements and the accuracy of the model for dose calculations was verified. EBT3 film was used to measure exit dose from the water surface and results were compared with calculated dose, being found to be in good agreement. A breast phantom comprising of different tissues was simulated and different size spherical applicators were located in the phantom. Calculations show that, in addition to an increase in skin dose with decrease in distance between skin and applicator surface, the size of the applicator also has a marked effect. Generally speaking, the ratio of skin dose to prescription dose increases with applicator size, due to the pronounced dose-rate gradient fall off with distance from the applicator surface. In the case of the largest applicator of 5 cm diameter, and considering a distance of 0.5 cm between skin and applicator surface, the area around the applicator stem that receives doses beyond the threshold limit of 6 Gy has a radius of 1.9 cm, although doses of even greater than 10 Gy can be delivered to areas closer than 0.5 cm to applicator (Figure 10). Therefore consideration of skin/applicator distance is more critical for larger applicators and 1 cm recommended distance does not guarantee sufficiently low doses, if no shielding is used for skin.

Acknowledgment

This study was funded in part by a University of Malaya IPPP grant (PG210-2015A) and grant UMRG (RP046C-15HTM). The kind cooperation of the Carl Zeiss Surgical Malaysian representative is acknowledged, providing detailed specifications of the X-ray source and applicators. The authors also wish to thank medical physicists at the University of Malaya hospital for their collaboration, notably Mrs. Azleen binti Mohd Zain and Mrs. Faizah binti Ahmad.

References


