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Original Research Article

Assessment of leakage dose *in vivo* in patients undergoing radiotherapy for breast cancer

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ABSTRACT

Background and purpose: Accurate quantification of the relatively small radiation doses delivered to untargeted regions during breast irradiation in patients with breast cancer is of increasing clinical interest for the purpose of estimating long-term radiation-related risks. Out-of-field dose calculations from commercial planning systems however may be inaccurate which can impact estimates for long-term risks associated with treatment. This work compares calculated and measured dose out-of-field and explores the application of a correction for leakage radiation.
Materials and methods: Dose calculations of a Boltzmann transport equation solver, pencil beam-type, and superposition-type algorithms from a commercial treatment planning system (TPS) were compared with *in vivo* thermoluminescent dosimetry (TLD) measurements conducted out-of-field on the contralateral chest at points corresponding to the thyroid, axilla and contralateral breast of eleven patients undergoing tangential beam radiotherapy for breast cancer.
Results: Overall, the TPS was found to under-estimate doses at points distal to the radiation field edge with a modern linear Boltzmann transport equation solver providing the best estimates. Application of an additive correction for leakage (0.04% of central axis dose) improved correlation between the measured and calculated doses at points greater than 15 cm from the field edge.
Conclusions: Application of a correction for leakage doses within peripheral regions is feasible and could improve accuracy of TPS in estimating out-of-field doses in breast radiotherapy.

1. Introduction

With a significant reduction in recurrence rates and breast cancer mortality compared with surgery alone [1,2] whole breast irradiation following breast conserving surgery is standard practice for patients with early stage breast cancer. However, there is concern that incidental out-of-field radiation doses to the untargeted normal tissues during breast radiotherapy may be associated with an increased risk of secondary malignancy [3–7]. The improving survival of patients with early breast cancer underpins this concern, and adds emphasis to the need to accurately quantify radiation doses to untargeted healthy tissues during treatment for a more accurate estimation of the risk of radiation-related second malignancy. In addition, the out-of-field radiation received by surrounding healthy tissues during breast irradiation is associated with toxicities of the heart, lung and thyroid [8–10].

Risk of ischemic heart disease in patients following radiotherapy for left sided breast cancer has been shown to be dose dependent [8]. The geometry of tangential beam radiotherapy in particular raises questions regarding the dose delivered to the contralateral breast. This is particularly important as the breast tissue is assigned a relatively high weighting factor for radiation protection purposes, reflecting its sensitivity to radiation [11]. The risk of radiation-related contralateral breast cancer following ipsilateral breast radiotherapy is thought to be dose-dependent [12,13]. Any reduction in out-of-field dose to healthy tissue is therefore important for long term risk reduction, and accurate calculation of out-of-field dose to the contralateral breast is crucial for informing risk estimates.

The out-of-field dose results from leakage radiation from the linear accelerator scatter from the collimators and beam modifiers, and in-patient scatter. The latter contribution is accounted for by the treatment

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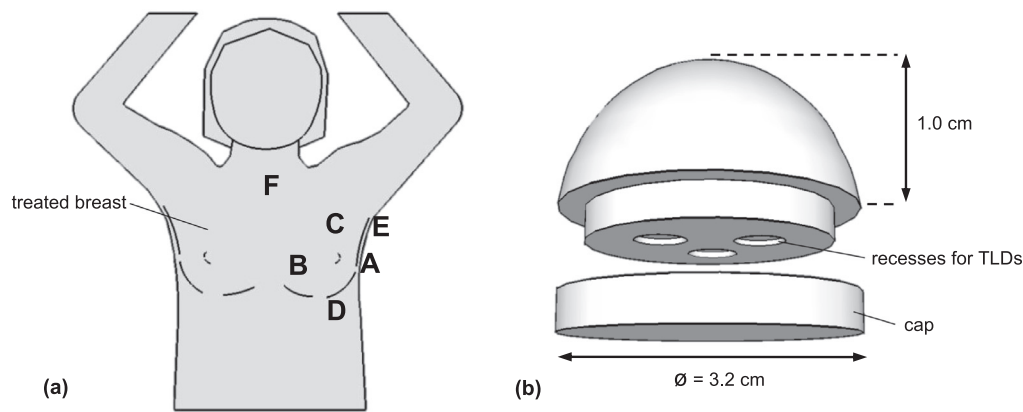*E-mail address:* peta.lonski@petermac.org (P. Lonski).

Fig. 1. (a) Diagram depicting measurement Points A, B, C and D on the contralateral breast (3 cm from the nipple in four cardinal directions); Point E at the contralateral mid axilla; and Point F at the suprasternal notch, and (b) diagram depicting build-up domes used for *in vivo* measurements, adapted from Lonski et al. 2014 [30].

planning system (TPS) at regions relatively close to the beam. However, linear accelerator-specific contribution to out-of-field dose is largely unaccounted for by dose calculation algorithms since head leakage contributions are usually not explicitly considered during beam data acquisition at commissioning of a new TPS. Thus, radiation dose from machine leakage and head scatter is not accounted for at peripheral regions during treatment planning. These are also the dominant contributors to out-of-field dose at distances greater than approximately 30 cm from the beam edge depending on treatment parameters [14] corresponding to regions of untargeted healthy tissue. Others have shown that neutron contamination also begins to contribute to out-of-field dose in higher energy treatments above approximately 10 MV [15,16], which is also not explicitly modelled.

Previous work has provided systematic analysis of out-of-field dose profiles under various treatment parameters in a phantom. Howell et al. reported a commercial system to have underestimated out-of-field dose by an average of 40% between 3.75 and 11.25 cm from the field edge [17], with the magnitude of this discrepancy increasing at larger distances. Huang et al. analysed the out-of-field dose for IMRT treatments and similarly concluded the TPS underestimated out-of-field dose, in this case by an average of 50% [18]. The recent AAPM TG 158 publication [19] discussed the challenges associated with quantifying out-of-field dose in modern radiotherapy, highlighting the importance of extra target doses as a consideration for long term patient outcomes and providing physicists and clinicians with guidance for assessing such doses. A comprehensive review of out-of-field dose and risk estimates in radiotherapy is also provided by Xu et al. [20].

Previous groups have analysed the out-of-field dose from different TPS algorithms in water phantoms [21,22], with others using anthropomorphic phantoms to better represent patient treatment [17,23]. Such phantom studies allow treatment parameters to be systematically altered to study their individual effects on the out-of-field dose, and in turn the ability of the TPS to model these effects. Johansen et al. [24] measured higher contralateral breast dose with inclusion of a supraclavicular fossa field in regional nodal irradiation following TLD measurements, concluding that a collapsed cone algorithm was better able to estimate the out-of-field dose compared to a pencil beam algorithm. Saur et al. used GafChromic ECT film in a phantom to assess contralateral breast dose from different planning techniques, demonstrating higher contralateral breast dose from hard wedges compared to virtual wedges and concluding the TPS algorithms were inadequate for modelling these doses [25]. Joosten et al. [26] performed Monte Carlo simulations on patient CT scans to compare out-of-field dose from IMRT and conventional tangent breast irradiation techniques. They found that out-of-field head scatter, which is not adequately modelled by the TPS, contributed a large portion of the out-of-field dose. Similarly to phantom studies, the TPS was found to under-estimate dose to healthy

tissues beyond the treatment beams. Monte Carlo is the 'gold standard' for calculating dose deposition in various media and provides the opportunity to compare out-of-field dose from different planning techniques on a patient CT scan – which cannot be done via *in vivo* dosimetry – however, with the peripheral dose shown to vary among different accelerator designs [27], direct measurement is still required to accurately assess patient doses from a given radiotherapy treatment.

In vivo dosimetry at peripheral locations during radiotherapy is not common practice. As a result, dose calculations by the TPS are usually the only indication of the dose to peripheral tissues such as the contralateral breast. Thus, the aim of the current study was to assess the accuracy of dose calculations at peripheral locations using different algorithms from a commercial treatment planning system by comparing the calculated doses with *in vivo* thermoluminescent dosimeter (TLD) measurements conducted out-of-field on the contralateral chest of eleven patients undergoing breast radiotherapy. In addition, the current study aimed to improve the TPS calculation accuracy with the application of a correction for leakage dose.

2. Materials and methods

2.1. Patient cohort

In vivo thermoluminescent dosimetry (TLD) measurements were performed in eleven patients who underwent ipsilateral whole breast irradiation following breast conserving surgery for early breast cancer (Table 1, Supplementary material). All patients provided informed consent for this study which was approved by the Human Research Ethics Committee of the Peter MacCallum Cancer Centre in Melbourne, Australia.

2.2. Treatment planning system calculations

A tangential photon beam treatment plan was created on the planning CT scan for each patient as per institutional practice. The laterality of the treated site, use of a field-in-field technique, gantry angle, dynamic wedge angle, field size, and number of monitor units used for each patient are summarised in Table 1 (Supplementary material). Each patient underwent treatment as planned. The dose at each pre-specified measurement point (Fig. 1a) was re-calculated in the TPS software (Eclipse version 13.6, Varian Medical Systems, Palo Alto, CA) using the convolution-based Analytical Anisotropic Algorithm (AAA, referred to as "convolution" herein), Pencil Beam Convolution (PBC, referred to as "pencil beam" herein), and a more modern linear Boltzmann transport equation solver Acuros XB (referred to as "Boltzmann solver" herein). A 1.0 cm thick layer of bolus was added to each patient CT dataset to simulate buildup conditions provided by the TLD perspex holders,
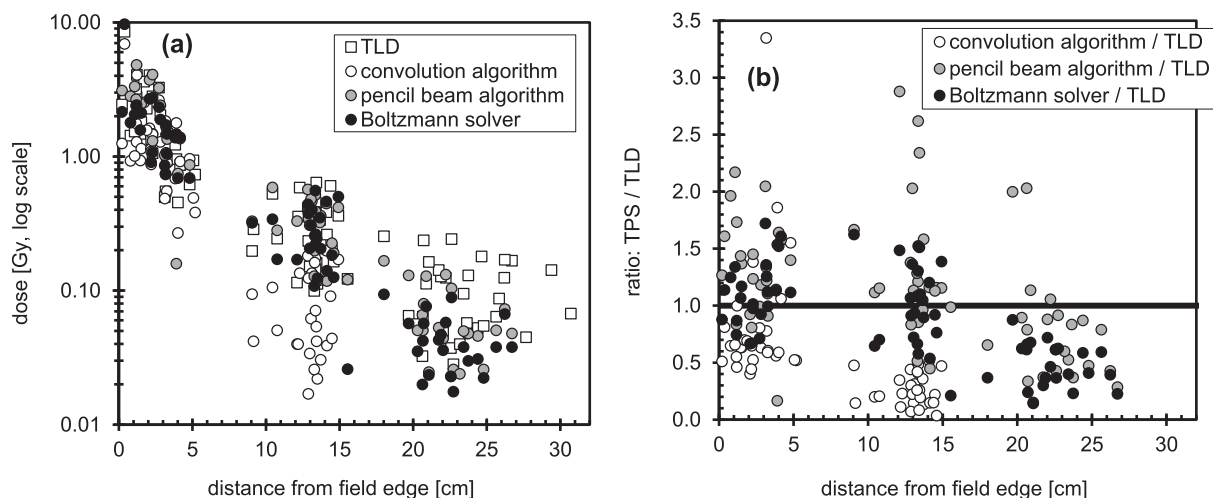
Fig. 2. (a) Doses from TPS calculations and TLD measurements as a function of distance from the field edge at out-of-field regions for eleven breast cancer patients treated with ipsilateral whole breast radiotherapy; and (b) ratios of TPS calculated dose: TLD measured dose as a function of distance from the field edge.

which were not applied during the planning CT scan. The dose to each measurement point was recorded for each algorithm and compared to the measured dose acquired *in vivo*.

2.3. In vivo measurements

Measurements were performed using high sensitivity TLD chips which were placed inside custom-made perspex 'build-up domes'. The domes (Fig. 1b) were designed to provide 1 cm build-up material with minimal directional dependence. LiF:Mg,Cu,P, or "TLD-100H", chips (Harshaw, Kansas, USA) were selected for their high sensitivity and near-tissue radiological equivalence, making them a suitable dosimeter for *in vivo* measurements at peripheral locations [28]. Three TLD chips were used at each measurement location. The chips were calibrated prior to use in a 6 MV photon beam using solid water slabs and each chip was assigned an individual sensitivity factor according to its individual response to the batch average following irradiation. TLD chips were read out using a Harshaw 5500 automatic TLD reader. For TLD-100H, the combined use of multiple chips for each measurement and a careful calibration process with tightly controlled handling and readout process yields an overall measurement uncertainty of ± 2% at the 95% confidence level for each measurement [29]. For *in vivo* dosimetry, positioning of the buildup domes and dose gradients across the dome area increases the measurement uncertainties, estimated here to be 10% (Type B).

All patients were treated on a Varian 21-X medical linear accelerator. *In vivo* measurements were conducted at six pre-defined points peripheral to the treated region which were nominally identical on all patients: four on the contralateral breast, one at the contralateral mid axilla and one at the suprasternal notch, indicating dose to the thyroid gland (Fig. 1a). Three TLD chips were placed inside each buildup dome and a single dome was taped to the patients' skin at each point. Measurements were taken for a single fraction and results extrapolated for a complete 25-fraction treatment. All patients were treated on a Varian 21-iX medical linear accelerator using 6 MV (TPR$_{20,10}$ = 0.668) photon beams.

Based on the TLD measurement locations (Fig. 1a), there were three distinct regions defined as a function of distance from the most proximal edge of the largest field (0–5 cm, denoted region 1; 10–15 cm, denoted region 2; and > 15 cm, denoted region 3 herein). Points B and F were located in region 1, Points C and D were located in region 2, and Points A and E were located in region 3 (with a maximum distance of 24 cm from the field edge).

2.4. Analysis

TLD data was compared to TPS point dose calculations at Points A to F (Fig. 1a). Discrepancies between the planned and measured doses were evaluated as a function of distance from the most proximal radiation field edge.

2.5. Leakage dose correction

Discrepancies at locations distal to the primary radiation field were assumed to be due to machine leakage radiation. The use of a single-value correction factor for leakage radiation was assessed to determine if it improved accuracy of TPS in estimating doses at peripheral sites where TPS calculations did not explicitly account for leakage contributions. Measured doses which were less than 1 Gy total over the 25 fraction treatment were considered for this leakage correction. The leakage component was assumed to be additive. The corrected dose, D$_{corr}$, in Gy, may be expressed as:

$$D_{corr}(Gy) = D_{calc}(Gy) + (C_{leak} \times 50 \text{ Gy prescribed dose}) \qquad (1)$$

where D$_{calc}$ is the uncorrected calculated TPS dose; and C$_{leak}$ is the correction for leakage dose expressed as a percentage of a 50 Gy prescription. The optimal C$_{leak}$ value was determined mathematically by considering the discrepancies at each point between measured dose and calculated dose for the cohort of eleven patients.

For *in vivo* data, the sensitivity-corrected thermoluminescence signal was expressed as measured dose (Gy) calibrated against standard TLDs irradiated to a known dose delivered under standard conditions using a 6 MV 10 × 10 cm^2 field at the depth of maximum build-up with the provision of sufficient backscatter material. The measured dose for a single fraction was extrapolated to a measured dose for the entire treatment course and was accordingly expressed in the following sections.

3. Results

3.1. TPS accuracy

Measured and calculated doses decreased approximately exponentially as a function of distance from the field edge at peripheral regions as is shown in Fig. 2a. However, TLD doses decreased less rapidly with distance than the TPS calculated doses in regions beyond 20 cm from the field edge. The correlation between calculated and measured data is shown in Fig. 2b. The ratios of TPS calculated dose: TLD measured dose are shown as a function of distance from the field

edge. The Boltzmann solver was shown to be the most accurate algorithm in general across all regions but it under-estimated the measured dose in region 3.

The average ratios of calculated dose: measured dose in region 1 were 0.84, 1.31 and 1.12 for the convolution-based algorithm, pencil beam type algorithm and Boltzmann solver, respectively. In region 2, these ratios were 0.27, 1.32 and 1.01, respectively. In region 3, the convolution algorithm did not provide an estimate of the dose. The ratios were 0.74 for the pencil beam and 0.48 for the Boltzmann solver. The spread of the data can be seen in Fig. 2b.

3.2. Consideration of leakage radiation

The value at which TPS-calculated and TLD-measured dose differences was at a minimum for all dose points less than 1 Gy was taken as the leakage correction. Discrepancies between the TPS-calculated and TLD-measured doses reduced to a minimum for all patients when an additive leakage correction of 0.04% was applied to the Boltzmann solver out-of-field calculation dose as per Equation 1. A single value leakage correction was not able to improve the out-of-field dose calculations for the convolution based or pencil beam type algorithms. Without a leakage correction, the Boltzmann solver was found to be the most accurate algorithm (Fig. 2b). The correlation between the Boltzmann solver calculated doses and TLD measured doses before and after application of leakage correction is shown in Fig. 3.

The addition of a 0.04% leakage correction to the Boltzmann solver data improved the average ratio of TPS-calculated dose: TLD-measured dose for this patient cohort in region 3. The correction did not improve dose calculations in regions closer to the radiation fields. The average ratios of TPS-calculated dose: TLD-measured dose for the Boltzmann solver were 1.12 in region 1, 1.01 in region 2 and 0.48 in region 3 without a leakage correction, and 1.13, 1.10 and 0.66 in the corresponding regions after correction.

4. Discussion

In the present study, accuracy of the out-of-field doses calculated by three TPS algorithms commonly used in clinical practice were compared to measured data acquired *in vivo* on patients undergoing breast radiotherapy. The measurement points represented locations of dosimetric interest for the purpose of radiation-related risk assessment.

The results showed that accuracy of calculated doses at each measurement point varied amongst the three TPS algorithms. The

Fig. 3. Comparison of the Boltzmann solver calculations with TLD measured data with and without application of a leakage dose correction factor of 0.04% of the delivered dose.

discrepancy in calculated doses in comparison to measured doses could be attributed to varying levels of sophistication of the TPS algorithms. Overall, the Boltzmann solver data correlated better with *in vivo* measurements than the convolution-based and pencil beam type algorithms. At measurement points beyond 15 cm from the field edge, the convolution algorithm did not calculate dose. A thorough discussion on this algorithm is provided by Van Esch et al. [31], who demonstrated improved accuracy compared to single pencil beam algorithms for in-field locations. The more advanced Boltzmann transport equation solver was tested by Fogliata et al. [32] in various field sizes in the presence of heterogeneities. It was found to be in close agreement with Monte Carlo simulations and a marked improvement over convolution-based methods. Despite varying degrees of sophistication and accuracy in-field, each algorithm in the present work was found to suffer inaccuracies out-of-field, and each to varying degrees. This study was not designed to ascertain the cause of differences in performance between algorithms. The Boltzmann solver uses a variable dose calculation grid size and therefore out-of-field dose calculations are averaged over a larger volume compared with the convolution-based and pencil beam algorithms. The Boltzmann transport equation solver also models radiation dose distributions in the presence of heterogeneous media with greater accuracy. A combination of these factors may have contributed to the improved accuracy at out-of-field locations demonstrated in this study.

Application of a leakage correction improved accuracy of dose calculations by the Boltzmann solver beyond 19 cm from the field edge. The measured leakage correction of 0.04% is consistent with International Electrotechnical Commission (IEC) recommendations that the leakage dose from a medical linear accelerator does not exceed 0.1% of the primary beam at 1 m from the source [33]. The leakage component was likely to be more prominent in distal regions and was not explicitly modelled by the TPS. However, the correction did not improve accuracy of calculated doses by the three TPS algorithms at more proximal measurement points in regions 1 and 2 where the leakage component was likely to be dominated by head scatter. Out-of-field doses from medical linear accelerators have been shown to vary with machine design [26,27]. Therefore, leakage corrections would require experimental verification as they are likely to vary depending on design of the linear accelerators. The single value correction for leakage dose in the present study did not provide a complete solution for all measurement regions, as it over-corrected for the discrepancy in calculated doses by the Boltzmann solver in regions close to the treatment field. Nevertheless, an improvement in calculation accuracy was demonstrated with the added correction for this cohort of patients. Further work is required to assess the application of this correction to a wider patient cohort including different planning techniques, treatment sites and linac models. A limitation of this study is that *in vivo* data is included from one particular linear accelerator design and calculated data is a from one TPS vendor. Application of results to a wider patient population would therefore require further investigation.

The radiation leakage doses, albeit low, are of clinical relevance and potential significance for long term risk-assessment, for example, in a patient undergoing radiotherapy who is found to be pregnant. The International Commission on Radiological Protection (ICRP) report 84 [34] states that termination of pregnancy for foetal doses below 100 mGy are not recommended, as the risk of foetal complications is low. For a patient who received a total dose of 50 Gy, the present study demonstrated that the leakage dose was approximately 20 mGy. Although this leakage dose on its own is below the threshold stipulated in the ICRP guidelines for consideration of termination of pregnancy, in conjunction with diagnostic imaging and radiation treatment planning CT scans, the cumulative doses may reach the threshold.

TPS algorithms are not designed nor commissioned to model out-of-field dose. Moreover, the commissioning process can influence overall accuracy. The over-estimation of TPS-calculated doses in regions proximal to the field edge may be reduced by modifying the beam
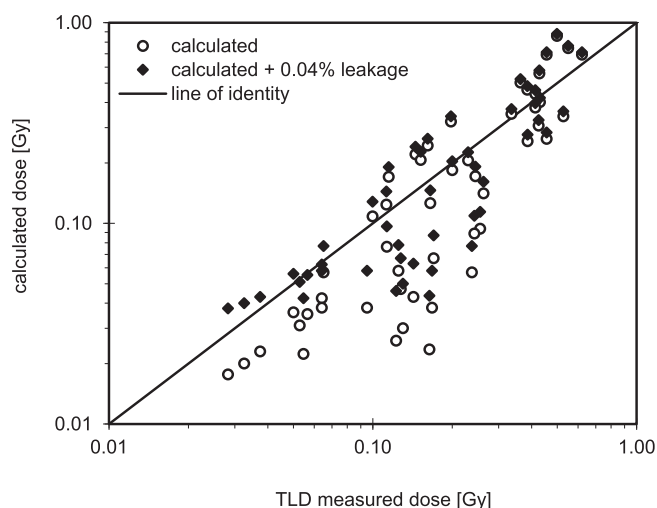
model in the TPS. However, the present study primarily aimed to improve accuracy of out-of-field dose estimates in regions distal from the field edge, which typically corresponded to untargeted healthy tissue. Thus, accurate quantification of radiation doses in these regions is necessary to improve assessment of the long-term risks associated with radiotherapy, particularly in patients who are likely to be long-term survivors including patients with early-stage breast cancer.

The present study showed that the accuracy of radiation dose calculations diminished at peripheral locations where linear accelerator-specific leakage and head scatter components were dominant. The application of a leakage correction in radiation treatment planning improved TPS dose calculations out-of-field. Further investigation into the application of a leakage dose correction is warranted to improve accuracy of out-of-field dose calculations involving critical healthy tissue.

Conflict of interest

Authors and authors' institutions have no conflict of interest.

Acknowledgements

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.phro.2018.03.004.

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