

Evaluation of surface dose outside the treatment area for five breast cancer irradiation modalities using thermo-luminescent dosimeters

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Original Article

Abstract

Purpose: To measure and compare the surface dose outside the treatment area at six different points of interest (POIs) for five different breast cancer radiation treatment modalities by using thermo-luminescent dosimeters (TLDs). This experiment will evaluate the magnitude of the dose due to scatter and leakage radiation at different areas outside the target on a patient that could potentially lead, in the long term, to radiation induced secondary malignancies. **Methods:** TLD-100 were calibrated according to the University of Wisconsin Radiation Calibration Laboratory protocol and then used for dose measurements at selected POIs namely sternum, lower abdomen, contralateral breast, thyroid, shoulder, and eye. Twenty five breast cancer patients and the following modalities were included in this study: Strut-adjusted volume implant (SAVI), mammosite multi-lumen (ML), Accuboot, electron boost and photon boost. The surface doses in all patients were measured in a single fraction. The delivered target doses were normalized to 200 cGy. Finally, breast quadrant analysis was performed. **Results:** The maximum average dose for each POI was as follows: Sternum 6.51 cGy (SD 2.93), lower abdomen 4.50 cGy (SD 2.63), contralateral breast 8.52 cGy (SD 3.86), thyroid 5.50 cGy (SD 2.75), shoulder 5.58 cGy (SD 2.77), and eye 2.65 cGy (SD 0.68). The highest POI dose of 15.84 cGy was found in contralateral breast. **Conclusion:** The measured surface dose at each POI varies with the modality of treatment. The surface doses show a strong correlation to the tumor bed location in the breast quadrant. The SAVI, electron boost, and photon boost modalities had delivered smaller surface dose at POIs than the Accuboot and Mammosite ML modalities. While the measured doses fall within the low range, its significance in producing second malignancies would require a large cohort of patients and a longer follow up.

Keywords: TLDs; Absorbed Dose; Deterministic Effect; Boost; Induced Cancer

Introduction

Breast conservation surgery combined with radiation has become an accepted alternative to total mastectomy for selected patients with early-stage breast cancer because of its comparable overall survival rate and positive impact on quality of life.¹ About 30% of U.S. women with breast cancer undergo breast conservation surgery with radiation therapy.² It is reported that, irradiation of surrounding tissues during breast radiotherapy can cause development of secondary cancers within these tissues.³ Consequently, there is increasing concern regarding radiation-related secondary cancer risks in long term radiotherapy survivors and a need to evaluate cancer risks at high radiation doses.⁴

The doses at the points outside the treatment area are small compared to the target dose. Nonetheless, these doses are of

clinical interest because they are given to large parts of the body and there is a potential for long term adverse effects.⁵ In addition, low doses of radiation also have potential to induce secondary cancers.^{6, 7} Concern for risk of radiation-induced malignancy is growing with the increasing number of cancer patients and several publications have widely discussed the probability of secondary malignancies after primary radiation treatment.^{8, 9-19} Out-of-field doses due to radiation are responsible for affecting cataract formation, fetus, cardiac toxicity, infertility and hypothyroidism.^{5, 20-25}

The estimated threshold doses for the most radiosensitive tissues in humans are: 15 cGy for temporary sterility of testes, 50-200 cGy for detectable opacity of lens and 50 cGy for depression of hematopoiesis.²⁶ It is reported that about 22% of

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secondary cancers are induced in regions more than 5 cm away from the irradiated volume.²⁷ The latency period for secondary cancer development varies with tissue type. Overall, the median secondary tumor latency period is reported as 7.4 years.²⁸

The surrounding normal tissues outside the treated area inevitably receive some radiation dose, regardless of the treatment modality. Contributing factors include leakage from housing source, scatter from beam modifiers, and internal scatter from the patient.²⁹ Accurate measurement of surface dose allows for estimation of the damage risk especially to those organs that are sensitive to relatively low doses of radiation. Several papers are published on the evaluation of peripheral and organ doses due to breast cancer radiotherapy; among those the *in vivo* and phantom measurements using thermo-luminescent dosimeters (TLDs), a computerized Monte Carlo (MC) technique using a mathematical phantom, and several commercial treatment planning software (TPS).³⁰⁻³³ Their results vary from method to method, i.e., the peripheral dose difference between TPS and MC was reported up to 70%,³⁴ while the mean difference between MC out-of-field doses and TLD measurements was found $11.4\% \pm 5.9\%$.³⁰ The percent difference between the TPS and TLD measurement skin doses was found in the range from -15% to 44%.³⁵

The peripheral doses at 20cm away from the target area was found 2.52 cGy and 2.07 cGy using TLDs in LINAC and tomotherapy delivery correspondingly, for a planning target volume (PTV) dose of 200 cGy.³⁶ However, the surface dose measurement outside the treatment area at several points of interest in a real patient using TLDs is limited.

There are several treatment modalities for breast cancer. This study includes SAVI, Mammosite ML, Accuboot, Electron boost, Photon boost. SAVI uses 6, 8 or 10 peripheral source channels with one center channel and inserted in collapse form into the tumor cavity through a small incision in the breast.^{37,38} The catheters are then expanded to conform to the shape of the cavity and allow for precise delivery of radiation. MammoSite ML consists of a balloon catheter that is inserted into the lumpectomy then expanded, and radiation is delivered through a tiny seed attached to the catheter, irradiating the area surrounding the cavity.^{39, 40} Accuboot applies breast brachytherapy without invasive catheters.

Two parallel-opposed beams are directed into the breast maximizing the target dose uniformity and minimizing the dose to the skin and other healthy breast tissues.⁴¹ The Boost dose is radiation targeted at the tissue near the lumpectomy site; this tissue needs the extra dose, because it is thought to contain "pre-cancerous" cells, therefore it is most likely to develop reoccurrences.^{42, 43} The modalities for supplementary doses after lumpectomy are electrons and photon boosts.

Electron boost is the favored method of boost delivery, because electrons permit penetration of superficial tissues with limited radiation deeper into the lung, heart and other internal organs. Photon boost is encouraged only for deep seated tumors for better coverage with sparing of organ at risk.⁴⁴

The aim of this study is to measure and compare the surface dose outside the irradiated volume in breast cancer patients at six different POIs in the proximity of critical structures for five different radiation treatment modalities: SAVI, Mammosite ML, Accuboot, Electron boost and Photon boost. Such study could be of interest to clinical investigation for the risk of late radiation effects in a breast cancer patient as a result of primary radiotherapy. The delivered doses for all modalities were normalized to 200 cGy in order to compare the doses in the POIs. The effective dose equivalent is estimated for all modalities.

Methods and Materials

Calibration of TLDs and Sorting

The TLD-100 (92.5% ⁷LiF + 7.5% ⁶LiF) of size $3 \times 3 \times 0.89$ mm³ detector was chosen because it is sensitive to electrons, photons and neutrons. The TLDs were calibrated according to the protocol of the University of Wisconsin. First, 500 TLD-100 chips were annealed at a 400°C oven for one hour in an aluminum tray in order to de-excite all the traps in the crystal and erase all residual doses. Then the TLDs were transferred in an acrylic holder with numbered positions and placed in an annealing oven at 80°C for 24 hours in order to redistribute traps to the desired single peak glow curve. Then they were cooled down to room temperature overnight. All the TLDs were irradiated by a Hopewell G10 ¹³⁷Cs irradiator in the UWRCL. The exposure of the ¹³⁷Cs was 500 mR. The TLDs were read by using a Harshaw-5500 automatic reader after 24 hours. The whole process was repeated three times, except for the 400°C annealing process to determine the individual sensitivities of the TLDs.

During the final sorting process, TLDs with a reading deviation greater than 3% were ignored. Average readings more than 51 nC and less than 36 nC were also ignored in order to control the large variation of readings among the TLDs. The average deviation (stand/mean) was 1.41%.

Energy and dose dependence of TLDs

The dose response of the TLD-100 material depends on the energy that it has been exposed to.⁴⁵ In the dose measurements, the relative dose response depends on the energy that has been used in calibrating the dosimeters. TLD-100 chips were calibrated with a relatively high energy source (¹³⁷Cs, average energy 662 keV) so that the response of a megavoltage photon beam will be very close to the calibrated energy. The used TLD intrinsic energy conversion factor for ¹⁹²Ir to

¹³⁷Cs was 1.041 ± 0.018 .³⁵ For the electron beam of 6 MeV to ⁶⁰Co the conversion factor was 0.965 ± 0.013 ⁴⁶ and for ⁶⁰Co to ¹³⁷Cs was 0.960.⁴⁷

The response of the TLDs is also dose dependent. For low doses, the response is linear for photons and electrons, but for higher doses (>10 Gy) the response is non-linear.⁴⁸ In this study, the maximum dose delivered at the central axis of target volume during treatment was 340 cGy. Therefore, a linear model has been applied to normalize the doses.

Patient selection

Twenty five cases of breast cancer patients had been selected to evaluate the skin surface dose outside the treatment area at six different points for five different treatment modalities. The number of patients in each modality, planning target volume (PTV), patient’s body mass index (BMI), prescribed dose and pertinent treatment planning software are given in the **Table 1**. The patients were selected according to the policies and guidelines of the institutional review board (IRB) of the Boca Raton Regional Hospital, Boca Raton, FL. Patients’ consent had been taken to participate in the study.

Points of interest (POIs)

The skin surface of sternum, lower abdomen, contralateral breast (CLB), thyroid, shoulder, and eye (superficial surface of eyelid) were chosen as POIs as shown in **Figure 2**. These POIs are considered clinically important because of their high radiation sensitivity.

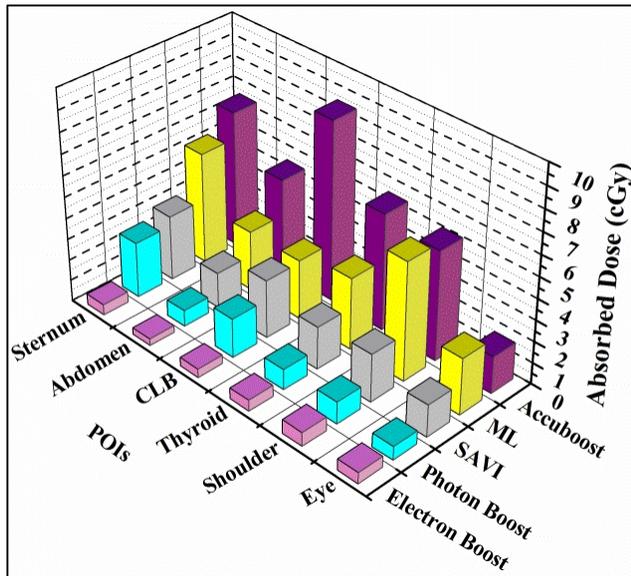


FIG. 1: The absorbed doses outside the treatment area at six POIs versus the treatment modalities. The delivered doses for all cases were normalized to 200 cGy.

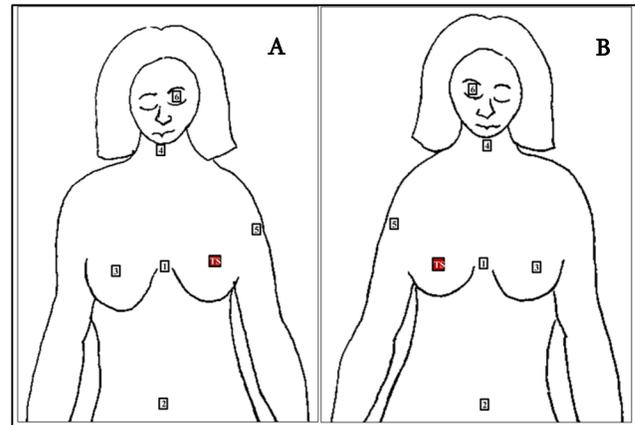


FIG. 2: A schematic diagram to show the points of interest (POIs). Six points were selected for TLDs placement. (1) Sternum; (2) Lower abdomen; (3) Contralateral breast (CLB); (4) Thyroid; (5) Shoulder; (6) Eye. Abbreviations: TS = Treatment site; A = Left breast treatment B = Right breast treatment.

Method of study

The calibrated TLDs were placed on the skin surface at six different POIs of the patients by the same person to minimize the placement errors of the chips. These points were selected such that the region of interest was most proximal to the tumor location. The TLDs were then exposed during patient treatment and read for evaluation. In each set of TLDs, two were held as control to account for shipping and transit dose. The absorbed dose was calculated by taking into account the background dose, an energy response factor, and a Cs-137 calibration factor using **Equation (1)**.

$$Absorbed\ dose\ (cGy) = \frac{reading(nC)}{Cs-137\ calibration\ factor(nC/cGy) \times energy\ response\ factor} \quad \text{----- (1)}$$

The patient’s data were grouped under each modality and on tumor location in breast quadrant for comparison.

Quadrant analysis

Quadrant analysis was performed to investigate the relationship between the absorbed dose at the different POIs and the area of breast where the tumor is located. For this purpose, the breasts are divided into quadrants and named: Right upper outer quadrant (RUOQ), Right lower outer quadrant (RLOQ), Right upper inner quadrant (RUIQ), Right lower inner quadrant (RLIQ), Left upper outer quadrant (LUOQ), Left lower outer quadrant (LLOQ), Left upper inner quadrant (LUIQ) and Left lower inner quadrant (LLIQ). From the patients’ records, it was found that the numbers of tumor location were: RUOQ (2), RLOQ (5), RUIQ (2), RLIQ (2), LUOQ (4), LLOQ (3), LUIQ (2) and LLIQ (1). The records of 4 out of 25 patients did not include the quadrant information.

TABLE 1: The studied modalities with patients and treatment planning information.

Modality	Number of patient	PTV volume (cc)	Skin to tumor distance (mm)	Patient's BMI	Prescribed dose/tx (cGy)	TPS
Mammosite ML	4	26-60	8-12	21-29	340	Oncentra
Accuboot	7	29-80	9-15	20-25	180-200	Nucletron-ART
SAVI	6	20-66	6-10	24-50	340	Oncentra
Electron Boost	4	54-150	9-14	20-32	200	Eclipse
Photon Boost	4	55-174	6-14	22-32	200	Eclipse

Abbreviations: PTV = Planning target volume; BMI = Body mass index; TPS = Treatment planning software

TABLE 2: The averaged absorbed dose in centigray (cGy) outside the treatment area at six different POIs for the five studied modalities. The standard deviations are given in parenthesis.

POI	Absorbed dose in cGy for the studied modalities				
	Accuboot	SAVI	ML	Electron Boost	Photon Boost
Sternum	6.51 (2.93)	3.06 (1.28)	5.27 (2.12)	0.52 (0.20)	2.62 (1.82)
Abdomen	4.50 (2.64)	1.67 (1.22)	2.81 (2.26)	0.32 (0.18)	0.76 (0.11)
CLB	8.52 (3.87)	2.74 (1.49)	2.80 (1.22)	0.41 (0.24)	1.84 (0.69)
Thyroid	5.50 (2.75)	2.00 (0.73)	3.38 (1.03)	0.52 (0.13)	0.96 (0.55)
Shoulder	5.18 (2.21)	2.26 (1.11)	5.58 (2.77)	0.66 (0.16)	1.02 (0.42)
Eye	1.74 (0.84)	1.51 (0.52)	2.64 (0.69)	0.52 (0.29)	0.64 (0.20)

Results

The results of the out-of-field surface dose measurements on these 25 breast cancer patients for five different treatment modalities are listed in **Table 2** and plotted in **Figure 1**. The absorbed doses in each POI were averaged for each modality group. As **Figure 1** shows, the highest average skin surface dose was measured at contralateral breast treated with Accuboot modality. The high standard deviations in **Table 2** are related to the number and specifics of patients in each modality.

From the quadrant analysis of the data in **Table 3**, it was found that 10 patients had cancer at the left breast and 11 patients had cancer at the right breast while about 67% of patients had a tumor in the outer quadrant. As **Table 3** shows, four out of six patients having a tumor in the inner quadrant were treated with Accuboot. The ones with tumor in the inner upper quadrant had received higher doses to the thyroid, contralateral breast and the sternum. In patients with tumor in the left outer upper quadrant, the shoulder had received the highest dose. Relatively higher skin surface doses have been measured at the lower abdomen, contralateral breast and the sternum compared to the other POIs for patients treated with a tumor in the lower inner quadrants.

From all the modalities and patients studied, the maximum surface doses vary at the POIs with values: 15.84 cGy (7.92%) in contralateral breast, 12.66 cGy (6.33%) in sternum, 11.50 cGy (5.75%) in thyroid, 11.13 cGy (5.56%) in shoulder, 3.86 cGy (1.93%) in eye and 8.6 cGy (4.30%) in lower abdomen.

The numbers in parentheses are the corresponding percentages of the normalized delivered dose.

TABLE 3: Quadrant analysis result from the twenty one patients treated with different modalities. Tumor bed locations in the breast and corresponding maximum absorbed dose to the POIs are also given.

Modalities	Number of patients treated (tumor bed location)	POIs with maximum dose
AB	1 (RLIQ)	CLB (6.41 cGy)
	1 (RUIQ)	Thyroid (11.50 cGy)
	1 (LUOQ)	Shoulder (8.25 cGy)
	1 (LUIQ)	CLB (15.84 cGy)
	1 (LLIQ)	Sternum (12.66 cGy)
ML	2 (RUOQ)	Shoulder (11.13)
	1 (LUIQ)	Sternum (3.72 cGy)
	1 (RLOQ)	Sternum (5.64 cGy)
SV	3 (RLOQ)	Sternum (3.10 cGy), Shoulder (4.19 cGy)
	2 (LUOQ)	Sternum (2.75 cGy)
	1 (LLOQ)	Sternum (5.26 cGy)
PB	1 (RUIQ)	Sternum (5.23 cGy)
	1 (RLOQ)	Sternum (1.12 cGy)
	1 (RLIQ)	Sternum (2.46 cGy)
	1 (LLOQ)	CLB (2.37 cGy)
EB	1 (LLOQ)	Shoulder (0.78 cGy)
	1 (LUOQ)	Eye (0.98 cGy)

Abbreviations: AB = Accuboot; ML = Mammosite multi lumen; SV = SAVI; PB = Photon boost; EB = Electron boost

TABLE 4: The two way analysis of variance (ANOVA) test to compare the treatment modalities in terms of measured surface doses at POIs.

Modalities	AB vs SV	AB vs ML	AB vs EB	AB vs PB	SV vs ML	SV vs EB	SV vs PB	ML vs EB	ML vs PB	EB vs PB
p-value	0.008	0.16	0.003	0.003	0.02	9E-04	4E-04	0.001	0.004	0.049

The two way analysis of variance (ANOVA) test was performed to compare the average doses at POIs for the five different treatment modalities. Results of the test are given in **Table 4**. It can be seen that Accuboot and Mammosite multi-lumen are not significantly different ($p = 0.16$, at 5% significant level). SAVI values are significantly different from these two modalities (AB and ML) with $p < 0.05$. The out-of-field skin surface doses measured with APBI (AB, SV and ML) modalities are significantly different compared to electron boosts or photon boosts ($p < 0.05$). In addition the p-value for EB and PB are close to the significant level of 5%.

The effective dose ($H_E = \Sigma W_T H_T$) provides a number that is proportional to the radiobiological adverse effect from an inhomogeneous type of radiation exposure. It has been defined and introduced by ICRP for risk management purposes. According to the ICRP (2007), the tissue specific weighting factors (W_T) for thyroid, breast, stomach, lungs, gonads and remainder tissues are 0.04, 0.12, 0.12, 0.08 and 0.12 respectively. Considering the closest tissues/organs from the skin surface, the calculated effective doses for the studied modalities are: Accuboot 3.45 rem, SAVI 1.45 rem, ML 2.46 rem, electron boost 0.32 rem and photon boost 0.87 rem. The beam quality factor for the photon and electrons are taken unity. The neutron generation term is ignored because of the low photon energy (less than 6 MV).

Discussion

This study shows that the measured absorbed doses at POIs treated with the same modality display large variations. The highest variation was found for the contralateral breast site treated with the Accuboot modality with a range from 2.67 cGy to 15.84 cGy. The tumors were located in the left upper outer quadrant (LUOQ) and the left upper inner quadrant (LUIQ) correspondingly. The second major variation was found in the shoulder treated with Mammosite ML with the dose range between 2.52 cGy and 11.13 cGy. The tumors were located in the left upper inner quadrant (LUIQ) and the right upper outer quadrant (RUOQ) respectively.

The location of the tumor in the breast quadrant and distance of POIs from the treatment site are the two major factors influencing the dose to the POI, as expected from the inverse square law. Patient's BMI, size of tumor, size of breast, duration of treatment, orientation of field, patients' set up, applicators and catheters used during treatment could be additional affecting factors in receiving different skin surface doses at different POIs.

In the case of electron boosts, the measured out-of-field surface doses were small in all POIs due to predominantly ionizing events with atomic electrons of the tissue, resulting to absorbance of the incident electrons' energy within a few millimeters. However, in order to accurately justify the absorbed dose results with electron boost, calibration of TLDs has to be done with an electron beam, whereas the TLDs of the present study were calibrated with a photon beam.

Conclusion

The measured surface dose at each POI varies with the modalities of treatment. The surface doses show a strong correlation to the tumor bed location in the breast quadrant. The SAVI, electron boost, and photon boost had delivered smaller surface doses at POIs than the Accuboot and Mammosite ML modalities. While these doses are found within the low range, a longer follow up and a large cohort of patients could provide valuable information regarding the radiation induced secondary malignancies. It should be reminded that special care should be given to delivery parameters such as patient set up, transfer tube orientation, applicator orientation, and field set up in order to minimize the surface dose.

Conflict of interest

The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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