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Estimation of oesophageal surface dose in breast cancer patients undergoing supraclavicular irradiation by thermoluminescent dosimeter (TLD) and treatment planning system (TPS)

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ABSTRACT

***Background*:** The purpose of this study was to measure the surface dose in breast cancer patients undergoing supraclavicular irradiation using a thermoluminescent dosimeter (TLD) and compare the measurements to calculated doses determined by the treatment planning system (TPS). The results of in vivo patients' measurements were verified using a phantom. ***Materials and Methods*:** The oesophageal surface dose of 30 breast cancer patients undergoing supraclavicular lymph node irradiation was measured by TLD and TPS. For each patient, two TLDs were positioned on the oesophageal surface. The TLD and TPS results were verified using a phantom that covered from the oesophagus to the supraclavicular area. The TLD was positioned within or outside the treatment field on the phantom depending on the patient. ***Results*:** The average oesophagus surface dose was 9.04 ± 5.07 Gy and 8.06 ± 6.17 Gy for TLD and TPS, respectively (p=0.09). Oesophagus surface doses were greater for the left than for the right side. The calculated and measured dose values at the surface for the phantom were 0.78 Gy and 0.96 Gy, respectively, with the TLD placed inside the radiation field (p=0.02). The calculated and measured dose values at the surface for the phantom were 0.024 Gy and 0.10 Gy, respectively, with the TLD placed outside the radiation field (p=0.01). ***Conclusion*:** The results showed a good agreement between TLD measurements and TPS calculations, except when the TLD was placed outside the radiation field. Therefore, dose calculations in peripheral regions should be used with caution.

INTRODUCTION

Breast cancer is the most prevalent cancer among women worldwide and a leading cause of cancer death [1]. The occurrence of breast cancer has increased worldwide over the past few decades, with the largest growth in Asia [2]. In Asia, the incidence of breast cancer in women peaks at age 40, and in the United States and Europe, it is after age 60 [3].

Treatment for breast cancer includes surgery, radiation therapy, chemotherapy and hormone therapy [4]. Factors influencing treatment choices include patient age, tumour size, menopause status, tumour markers, lymph node status, oestrogen or progesterone receptors [5], and adverse effects of the selected method [6].

Radiation therapy (RT) as a strategy for breast cancer treatment is an important topical therapy to reduce local recurrence and increase survival rates after radical mastectomy or breast-conserving surgery [7-9]. Clinical trials and meta-analyses have shown that regional nodular irradiation reduced breast cancer mortality and the rate of recurrence in women with positive lymph nodes [10-12].

Despite its positive effects, RT has several *negative* effects when irradiated to other structures and organs at the treatment site, which may affect patient quality of life [13]. In general, when performing radiation therapy involving regional lymph nodes for breast cancer, three-dimensional conformal radiation therapy (3DCRT) has been used with a tangential field for the chest area and a separate field for the supraclavicular node [14]. Since the oesophagus is proximal to the supraclavicular fossa nodule (SCF) lymph node, primarily on the left side of the cervical spine [15], radiotherapy of the supraclavicular lymph nodes may expose a significant part of the oesophagus to radiation. This may increase the occurrence of acute and late radiation effects [16-17]. A study reported that irradiation of the SCF in breast cancer resulted in patients developing grade 2–3 esophagitis during the first 2 weeks of treatment [16]. In addition, a randomized trial showed heart disease, lung cancer and oesophageal cancer as major diseases following breast cancer RT [17]. The radiation -related risks of these diseases depend respectively

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on the dose absorbed by the heart, lungs and oesophagus [17-19]. A systematic review showed an association between oesophageal cancer and oesophageal dose volume in breast cancer patients undergoing RT [19]. The importance of assessing the oesophageal dose increases in women at high risk of breast cancer with lymph node involvement when the tangential and supraclavicular fields are combined and the oesophagus is within the radiation field [21]. However, the oesophageal dose from out-of-field treatment is not negligible. The absorbed dose in the oesophagus is caused by photon scattering. The main source of photon scattering is scatter from the patient and collimators [22]. Therefore, measuring the dose received by the oesophagus, and ensuring it does not exceed the values established in the treatment planning system (TPS), is essential.

This study aimed to measure the oesophageal dose in breast cancer patients undergoing supraclavicular irradiation using TLD and compare the *in vivo* thermoluminescent dosimeter (TLD) measurements to calculated doses determined by the TPS. Furthermore, the results of the in vivo measurements were verified using a phantom.

METHODS AND MATERIALS

Patient selection

We assigned 30 patients with breast cancer and supraclavicular involvement who were undergoing chest wall irradiation in addition to supraclavicular region irradiation. Eligible patients were treated surgically by either mastectomy or breast-conservation surgery. Of the 30 patients, 16 patients had stage II cancer, 13 had stage III, and one had stage IV cancer. Mastectomy was performed in 24 patients, and breast-conserving surgery was performed in six. Twenty patients had right-sided breast cancer, and 10 patients had left-sided breast cancer. The age range of patients was from 35 to 66 years. The demographic data of patients are shown in table 1.

Table 1. Patient characteristics.

Variable	Content	N (%)
Age	Mean (min, max)	42(35,66)
Laterality of treatment area	Right	20(66.6)
	Left	10(33.3)
Surgery	Mastectomy	24(80.0)
	Breast-conserving surgery	6(20.0)
Marital status	Single	6(20.0)
	Married	24(80.0)
	Divorced / widowed	0(0.0)
Stage of disease	Stage II	16(53.3)
	Stage III	13(43.3)
	Stage IV	1(3.33)

Treatment planning system

All patients were simulated by computed tomography (CT) simulation (LIGHT SPEED 16, General Electric, USA; model GE) with 5-mm-thickness slices. A breast board (Aktina Medical, New York, NY, USA) was used to prevent patient movement. The TPS was DOSIsoft ISOgray version 4.1.

The planning target volume was defined according to the guidelines of the radiation therapy oncology group (RTOG). The concerned organs at risk (OARs) were the heart, lungs, spinal cord and oesophagus. No planning constraint was given to the oesophagus in this study. All the concerned OARs were delineated by an experienced radiation oncologist. All patients were irradiated by 6-MV X-rays using an Elekta Synergy® linac (Elekta Ltd, Crawley, United Kingdom). The prescription dose was 50 Gy in 25 fractions (in 2Gy daily fractions).

Dose measurements on patients

A TLD was used to measure the dose to the oesophagus. It was located 2 cm above the sternal notch. The TLD position for each patient was marked during CT scanning by an oncologist to avoid any discrepancy between the TPS and the patient's setup during treatment. Therefore, two TLDs were positioned on the marker during each treatment session. Oesophageal surface dose measurements were performed in one fraction, and the results were extrapolated to a complete treatment of 25 fractions. In addition, the dose to the oesophagus was calculated by TPS, and the results were compared to the oesophagus dose measured by TLD.

Dose measurement on phantom

A phantom was created using a CT scan of a patient with right-sided breast cancer and supraclavicular involvement. This phantom with a length of 16 cm was made with poly methyl methacrylate (PMMA), and it was dosimetrically water equivalent. The phantom consisted of 32 slices with a thickness of 0.5 cm, covering from the oesophagus to the supraclavicular area, as shown in figure 1; 16 slices had several holes with a diameter of around 5.0 mm for introducing a dosimeter such as a TLD to different depths. The holes were numbered to provide an accurate dose estimate for each measurement, as seen in figure 2.

To plan for the phantom, CT images were obtained from a phantom and then imported into the TPS. The TPS was generated, and the TLDs' positions were contoured. The TLDs were positioned within or outside the treatment field on the phantom depending on the patient. Hence, we classified the TLDs into two groups according to their positions. In group A, TLDs were positioned inside the treatment field, whereas in group B, the TLDs were kept 0.25 cm from the treatment field edge. The surface and depth dose of the phantom in the oesophagus region for groups A and B were measured, with one TLD positioned on the surfaces and four TLDs located at

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different depths (with 1-cm intervals).

The phantom was irradiated with a total of 200 MU of 6-MV photons on an Elekta Synergy® linac (Elekta Ltd, Crawley, United Kingdom) after it had been equipped with TLDs. The TPS-calculated doses at the selected points in the phantom were compared to the TLD-measured dose.

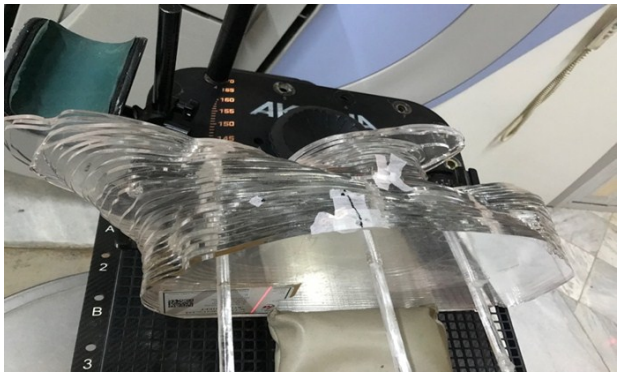


Figure 1. A phantom with a length of 16 cm is made of poly methyl methacrylate (PMMA), and it is dosimetrically equivalent to water. The phantom consists of 32 slices with a thickness of (0.5) cm that cover from the esophagus to supraclavicular.



Figure 2. Slice number of 16 has several holes with a diameter of about 5.0 mm for introducing a dosimeter such as a TLD in different depths. The holes were numbered to provide an accurate dose estimate for each measurement.

TLD measurement

A GR200 TLD was used to measure the absorbed doses to the oesophagus of breast cancer patients treated with 3D-CRT. The GR200 (LiF:Mg, Cu,P) is produced by Method Laboratory (Beijing, China) and has a high sensitivity to photon radiation. It is a detector with a size of 5 × 5 mm and a 1-mm thickness that can be inserted into the phantom. The TLD groups were positioned inside the phantoms according to the oesophagus distributions. TLD measurements of organ doses depend on the size and volume of the organs.

The difference between the TPS dose and the TLD dose is defined according to equation 1:

Diff% = $(D_{TPS}-D_{TLD})/D_{TLD}$ (equation 1), where D_{TPS} and D_{TLD} are the dose calculated by TPS and the dose measured by TLD, respectively.

TLD calibration

To prepare and apply the TLD chips, they were first incubated in a furnace at 240 ˚C for 10 minutes for annealing. All of the dosimeters were then irritated uniformly for a day and read to calculate the element correction coefficient (ECC). Next, all reading was averaged, and every reading was divided into the total, producing an ECC for each TLD. Finally, the TLD chips with errors of more than 15% were excluded from the experiment. The TLD chips were divided into two groups. Each group was irritated by doses of (a) 10, 100, 300, 500, 700, or 1000, 1500 and 2000 mGy by a caesium 137 (Cs 137) source. After reading by a Harshaw 5500 TLD reader, the results were obtained in nanocoulombs (nC). The calibration curve was drawn, and the line coefficient obtained was considered as a calibration factor or the conversion factor of nC to dose.

Statistical analysis

The data were statistically analysed using SPSS version 21. P-values of <0.05 were considered significant. To compare the dose measured by TLD to the dose calculated by TPS, a non-parametric test (Wilcoxon signed-rank test) was used. A non-parametric test (Mann–Whitney U test) was performed to compare doses from right to left breasts. To compare TLD and TPS doses in group A and group B from the phantom, a paired samples t-test was used.

RESULTS

Surface dose to oesophagus measured by TLD

The dose to the oesophagus was measured for 30 breast cancer patients treated with 3D-CRT. The average oesophageal surface dose measured by TLD was 9.04 ± 5.07 Gy, and the minimum and maximum were 3.87 and 21.07 Gy, respectively. The measured oesophageal surface dose in 50 % of patients was 7–21 Gy.

Surface dose to oesophagus calculated by TPS

The average oesophageal surface dose calculated by TPS was 8.06 ± 6.17 Gy, as shown in figure 3. The oesophageal surface dose obtained by TLD was greater than that determined by TPS, but this was not a significant difference (p= 0.09).

The average TPS-calculated dose and average TLD -measured dose, as well as their mean differences, are shown in table 2. The + sign in this table indicates that the TPS overestimated the dose, whereas the – sign indicates that the TPS underestimated the dose.

Table 3. Shows the results of average TPS- calculated dose and TLD-measured dose, along their mean differences in right-sided and left-sided breast cancer patients.

Effected sided-breast cancer	Esophagus Surface dose (calculated) Gy mean ± SD	Esophagus Surface dose (measured) Gy mean ± SD	Differences	TLD' position	P-value
Right-sided breast cancer	4.34±2.26	6.86±3.49	-40%	out-filed	0.075
Left-sided breast cancer	15.82±6.71	13.28±5.6	34%	inside-filed	0.08

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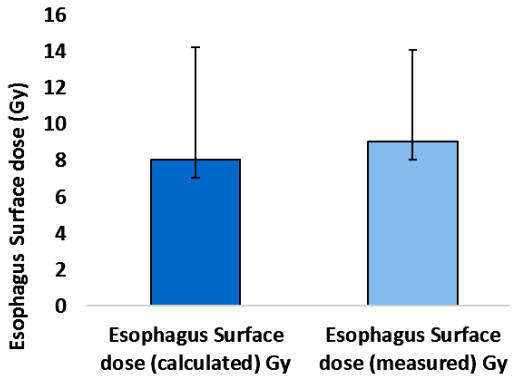


Figure 3. Shows the calculated and the measured dose in 30 Patients. The average dose of esophagus that measured by TLD was 9.04 ± 5.07Gy, while the average dose of esophagus calculated by TPS was 8.06 ± 6.17Gy.

Surface dose to oesophagus in right- and left-sided breast cancer patients

The oesophageal surface dose was higher in patients with left-sided breast cancer, with values of 13.28 ± 5.6 and 15.82 ± 6.71 Gy (p=0.08) for TLD and TPS, respectively, with the TLD located inside the field of treatment. In comparison, the average oesophageal surface dose for the right breast was 4.34 ± 2.26 Gy for TPS and 6.86 ± 3.49 Gy for TLD (p=0.075; table 3). A significant difference existed in oesophageal surface dose between right- and left-sided breast cancers, as shown in figure 4 (p=0.047).

Surface and depth dose of phantom

The average value of the TPS-calculated dose was greater than the TLD-measured dose in group A. The TPS-calculated and TLD-measured dose discrepancy was at a minimum for group A, with a variation of 24%. The calculated and measured dose at a depth of 1 cm were 1.92 Gy and 1.67 Gy, respectively, and at 2 cm, these values were 1.92 Gy and 1.57 Gy, respectively. The remaining data are shown in table 4. In contrast to group A, group B overestimated the TLD dose by as much as 35.4% when compared to the TPS dose. The calculated and measured dose at a depth of 1 cm were 0.12 Gy and 0.14 Gy, respectively, and at 2 cm, these values were 0.13Gy and 0.16 Gy, respectively. The remaining data are shown in table 4, along with their mean differences. A positive number in this table indicates that the TPS overestimated the dose, whereas a negative number indicates that the TPS underestimated the dose.

The TPS-calculated dose was significantly different from the TLD-measured dose (p=0.02) in group A. Similarly, the TPS-calculated dose was significantly different from the TLD-measured dose (p=0.01) in group B. The correlation between the calculated and measured dose is displayed in figure 5.

Table 4. shows the results of TPS- calculated dose and TLD-measured dose, along their mean differences in phantom in group A and group B. Group A, TLDs positioned inside treatment field while in a group B, TLDs were kept at 0.25cm from the treatment field edge.

Depth (cm)	Group (A) Calculated dose (Gy) mean ± SD	Group (A) Measured dose (Gy) mean ± SD	P-value 0.02	Group (B) Calculated dose (Gy) mean ± SD	Group (B) Measured dose (Gy) mean ± SD	p-value 0.01	Group A Differences	Group B Differences
0	0.96±0.030	0.78±0.132		0.024±0.001	0.10±0.054		23%	-76%
1	1.92±0.028	1.67±0.135		0.12±0.041	0.14±0.059		15%	-14%
2	1.92±0.021	1.57±0.124		0.13±0.045	0.16±0.061		22%	-19%
3	1.90±0.022	1.53±0.125		0.14±0.039	0.24±0.059		24%	-42%
4	1.84±0.022	1.35±0.124		0.22±0.041	0.27±0.064		36%	-26%

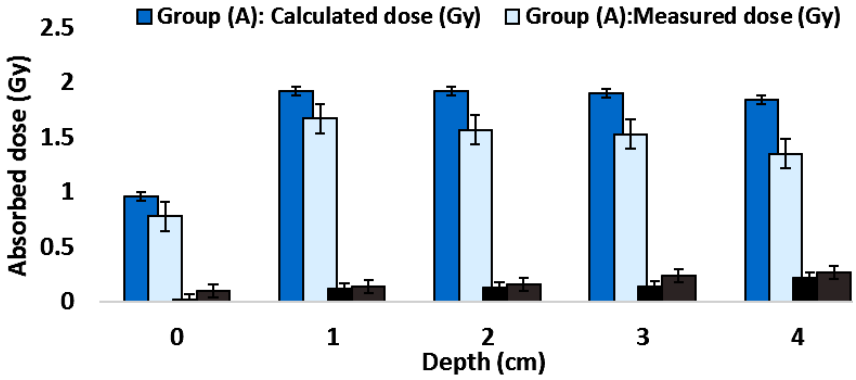


Figure 5. Shows the correlation between calculated and measured dose in in group A, when TLDs positioned inside treatment field, and in group B phantom, when TLDs were kept at 0.25cm from the treatment field edge.

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DISCUSSION

This is one of the few studies to date that have measured the surface dose of the oesophagus during RT, using TLD in breast cancer patients with regional lymph node involvement. The oesophageal dose the most important parameter in the development of esophagitis and oesophageal cancer [20-26]. Therefore, studying the dose that received by oesophagus is critical.

Our results showed that the oesophageal surface dose measured by TLD ranged from 3.87 to 21.07 Gy. This discrepancy can be attributed to differences in tumour volume, oesophagus distance from the radiation field, and TLD position. We revealed a 10% TLD dose overestimation compared to the TPS dose. The dose disparity might be due to limitations of the TPS dose calculation algorithm [28] and TLD limitations [29]. Underestimating the TPS-calculated dose was increased in patients with the TLD placed on the radiation field boundary or outside the radiation field. This could be explained by TPS only accounting for patient scatter at the field boundary [30] and underestimating scatter from the collimators and other beam line components. The intensity of underestimation increased as the distance increased from the field boundary. This result is consistent with Lonski *et al.* [31], who compared TLD dose measurement with TPS dose calculation at out-of-field locations using three different algorithms in healthy tissue during radiotherapy for breast cancer. They found that the calculated doses underestimated the dose compared to the measured dose. They concluded that the dose underestimation may be due to TPS dose calculation algorithms being not made to accurately estimate peripheral doses. Although the oesophageal surface dose determined by TPS was underestimated in the majority of patients, TPS overestimated the oesophageal surface dose in a few patients because the TLD's position in these patients was towards the inside of the treatment field. Hence, a small locational mistake in TLD measurements can induce error in the TPS-calculated dose.

The surface doses measured by TLD were lower in patients and the phantom when TLDs were placed inside the radiation field. However, the surface doses measured by TLD were greater in patients and the phantom when TLDs were placed outside the radiation field. Surface doses can be affected by electron contamination from the collimator system and secondary scattered photons in the gantry, all of which are unanticipated with TPS [32]. Additionally, doses obtained were by TPS overestimated in group A when TLDs were positioned inside the treatment field. This finding is comparable with the results of Abdemanafi *et al.* [33] The authors measured the absorbed dose in the lung of a phantom treated for breast cancer. Their results showed that TPS generally overestimated doses compared to TLD measurements. In addition, Davidson *et al.* [34] performed a study with an anthropomorphic phantom with polyvinylchloride plates and reported a 10% TPS dose overestimation compared to the TLD dose. However, in the present study, the dose determined by TPS was underestimated in group B when TLDs were kept 0.25 cm from the treatment field edge. A reasonable cause may be that TPS only accounted for phantom scatter at the field boundary. Previous papers have provided a comprehensive study of outside field patterns for phantoms under various treatment conditions. Howell *et al.* showed that the TPS underestimated by 40% outside field, on average between 3.75 and 11.25 cm at the field boundary [35]. Similar results were reported by Huang *et al.*, who found at a distance of 3–4 cm from the edge of the field a 30% TPS dose underestimate compared to the TLD dose [26].

The difference between the TPS-calculated dose and the TLD-measured dose inside the radiation field was 19%. The largest differences were outside the field, where the dose was 0.024 to 0.22 Gy. Dose disparities are generated by substantial density changes induced by a wider range of electrons [8]. A similar result was obtained by Kowalik *et al.*, who reported that the largest difference occurred at the boundaries of the radiation field, with doses ranging from 0.08 to 1 Gy [36].

Doses at a depth of 1 to 4 cm were found by TPS and TLD in the phantom. The TPS overestimated doses at depths of 1 and 2 cm in group A. However, the TPS underestimates doses at depths of 1 and 2 cm by approximately 20% in group B. This dose overestimation might be attributed to erroneous modelling of the dose contribution of contaminated electrons and secondary scattered photons received from the accelerator head in the build region. TPSs are known to be inaccurate in regions outside the electronic unbalance, such as the build-up region.

Based on the obtained results, TPS-calculated outfield doses exhibit little depth dependence. In addition, our study has demonstrated that outfield dose measurements collected at a fixed distance from the field edge have very little depth dependency [37].

CONCLUSION

The oesophageal surface doses measured by TLD were compared to TPS calculations. The results showed good agreement between TLD measurements and TPS calculations except in patients with right-sided breast cancer when the TLD was placed outside the radiation field. A phantom showed a similar result: in contrast to TLDs placed inside the treatment field, TLDs placed outside the treatment field overestimated the TLD dose compared to the TPS dose. Therefore, dose calculations in peripheral regions should be used with caution.

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***Author contribution*:** All authors contributed equally to the design of the study, data collection and analysis, and the writing of the manuscript. All authors read and approved the final manuscript.

***Ethical Approval*:** This study was approved by ethics committee College of Health and Medical Technology (code: MLD00075). Also the ethical committee of Kurdistan University of Medical Sciences approved the protocol of this study (code: IR.MUK.REC.1399.187).

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