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Author for correspondence:
Khaldoon Mahmoud Radaideh, PhD, Qassim University, Buraidah, Saudi Arabia,
E-mail: khaldoonmah1@yahoo.com

A dosimetric study of skin toxicity induced by 3-D conventional and intensity-modulated radiotherapy techniques using immobilization mask for treatment of head-and-neck (nasopharyngeal cancer) carcinoma: a prospective study

Khaldoon Mahmoud Radaideh

Radiological Technology Department, College of Applied Medical Sciences, Qassim University, Buraydah, Saudi Arabia

Abstract

Background: The purpose of this study was to investigate variations in surface dose, with and without the use of a Klarity® Mask (Orfit Industries America, Wijnegem, Belgium), using intensity-modulated radiotherapy (IMRT) and 3-D conventional radiotherapy (3D-CRT). *Materials and methods:* Thermoluminescent dosimeters (TLDs) together with a phantom were used to examine acute skin toxicity during nasopharyngeal cancer treatment. These plans were sequentially delivered to the perspex phantom. Dosimeters were placed in five fixed regions over the skin. A Klarity mask for immobilization was used for covering the head, neck, and shoulder. The phantom was irradiated with and without a Klarity Mask, using IMRT and 3D-CRT, respectively. *Results:* The Klarity mask increased the skin doses for IMRT and 3D-CRT approximately 18·6% and 8·6%, respectively, from the prescribed maximum skin dose using treatment planning system (TPS). Additionally, the average percentage dose between IMRT and 3D-CRT received on the surface region was 30·9%, 24·9% with and without Klarity mask respectively. The average percentage dose received on surfaces from the total therapeutic dose 70 Gy, without using the mask was 7·7% and 5·7%, for IMRT and 3D-CRT, respectively. The TPS overestimated the skin dose for IMRT planning by 20%, and for 3D-CRT by 16·6%, compared with TLD measurements. *Conclusions:* The results of this study revealed that IMRT significantly increases acute skin toxicity, compared with CRT. Although it is recommended to use Klarity mask as a sparing tool of normal tissue, it increases the risk of skin toxicity. In conclusion, skin dose is an important issue of focus during radiotherapy.

Introduction

The techniques of radiotherapy, chemotherapy and surgery, are methods to treat different kinds of tumors. Physicians, using treatment planning systems (TPS), try to prescribe doses as high as possible to the tumour, and low doses to the at-risk organs surrounding the tumour.[1] Intensity-modulated radiation therapy (IMRT), compared with other techniques like two-dimensional conformal and three-dimensional conventional radiotherapy (3D-CRT), allows higher radiation doses to be delivered to the tumor while keeping the surrounding organs at minimum doses.[2] Unfortunately, the unwanted and common side effect from using radiotherapy is the exact incidence of skin reaction, and the most of skin reactions are unknown.[3] External radiation therapy produces high incidence of skin toxicity from multi-beams, especially for head and neck, rectal or anal malignancies, skin reactions appeared in more than 90% out of 755 patients receiving treatment.[4]

Skin toxicity is a well-known complication during radiation therapy for head and neck cancer.[2,5–9] The most common acute effects of radiation are skin erythema and desquamation, followed by late toxicity in long-term damage such as xerostomia.[8,10] Skin is a deterministic factor for radiation, especially when the threshold dose has been exceeded.[11] The expression and severity of radiation injury depend on many factors, such as the radiation dose, the interval between irradiations, the size of the skin area irradiated and patient-related factors, for example, individual sensitivity and the presence of coexisting diseases.[11] Typically, skin erythema occurs at very high skin doses, exceeding 6–8 Gy, when treated with IMRT.[8,12,13] On the other hand, fractionation of the dose to several fractions can reduce the skin dose and the possibility of skin burn, as the effect of radiation tends to be cumulative.[2] Consequently, thermoplastic devices for the head and neck are used for fixation of the patient in order to achieve accurate radiation.[14] Typically, thermoplastic material such as Orfit masks (Orfit Industries, America, Wijnegem, Belgium) is used to cover the head and neck of the patient during radiation therapy.

Many researchers have described techniques to reduce the total radiation skin dose.[15] Recently, it was reported that head and neck cancer patients treated with IMRT had reduced skin toxicity compared with volumetric modulated arc therapy (VMAT).[16] This study was designed to compare the severity of skin toxicity induced by two different techniques: IMRT vs. 3D-CRT, using a fabricated anthropomorphic perspex head and neck phantom for dosimetric verification of treatment delivery and fixation using a Klarity mask (Orfit Industries America, Wijnegem, Belgium) for five patient plans treated for nasopharyngeal cancer (NPC). These results were then compared to the doses estimated by the TPS for each of the plans.[17,18]

It is important to study and compare the effect of these two techniques (IMRT and 3DCRT) on tumour coverage, minimisation of skin dose and to understand the effects of immobilisation on skin toxicity with different techniques, like IMRT and 3D-CRT, using a Klarity mask.

Material and methods

Patient selection

The five patients were scanned in the computed tomography (CT) simulator. Patients had histologically diagnosed NPC and all had pathology extending to the lymph nodes in the supraclavicular fossa region of the neck. Patients were aged between 40 and 50 years. Informed consent was obtained from each patient to use their data before commencing TPS.

For the CT scans, a 2-mm slice thickness was chosen for the head and neck imaging before the patient's scan was transferred to the TPS (Oncentra MasterPlan V3.3, Baltimore, MD, USA). Plans were then calculated for each technique: IMRT and 3D-CRT. Ten patient contour plans for nasopharyngeal tumors were transposed on to a Perspex phantom with simulated Thermoluminescent dosimeters (TLDs); five patients' plans used IMRT techniques and five patient plans used 3D-CRT. These plans were positioned with the help of immobilisation devices (Klarity mask) created for each patient and covering the head, neck, and shoulders, in the supine position. Three tattoo points were fixed using a laser on the Klarity mask during CT simulation.

Treatment planning and delivery

Two treatment plans with different techniques: 3D-CRT and IMRT, were created by TPS. After phantom's irradiation using the two techniques, the TLDs' surface doses were measured and compared with calculated doses using TPS. Once the overall target volume and dose has been decided, the TPS planner chooses beams' energy, shapes, intensity, and the directions, and then calculates the dose distributions.[5] Physicians chose the suitable IMRT plan and then calculate the dose and dose distribution using the TPS.[1] The skin surface is designated as unspecified tissue outside the targets; the dose absorbed by the skin should be less than 5% of the prescribed dose (70 Gy), and no more than 1% of the planning target volume (PTV) area can reach 77 Gy. All guidance advises to keep to these limits.[2]

The mechanical structure of the linear accelerator (Siemens Mevatron MX2 linear accelerator; Siemens Inc., USA) consisted of jaws and 66 pairs of the multi-leaf collimator (MLCs) to collimate the beam. The gantry rotates clockwise in two dimensions, and counterclockwise at 360°; this machine provides a one-monitor unit (MU) that is approximately equal to 1 cGy at D_{max} in water.

The plans for IMRT techniques were generated so that the primary PTV should receive at least 70 Gy overall in 33 fractions. During each fraction (2·12 Gy), 95% of it should be targeted to the secondary PTV to receive at least 2 Gy. Less than 1% of the primary and secondary PTVs should receive less than 93% of the prescribed dose. No organs at risk (OARs) such as eyes, salivary gland, brain stem and the spinal cords should receive a dose exceeding 1·5 Gy, and no more than 110% of the prescribed dose should be delivered to normal tissue, with dose constraints according to the Radiation Therapy Oncology Group (RTOG 0615).[2] For 3D-CRT, the primary PTV plans were to receive 70 Gy in 33 fractions, with 95% of the prescribed dose for each fraction to the primary PTV, and 60 Gy to the anterior neck.[2] It should be noted that the planning dose and number of fractions for IMRT and 3D-CRT were considered the same for this study.

TLD calibration

TLDs have commonly been used for measuring skin doses in previous studies that have focused on entry and exit doses.[19] The International Commission on Radiological Protection (ICRP), recommended using TLDs for skin dose measurement, as they have a very small thickness (about 0·009 mm), which is comparable to the skin reference depth of 0·007 cm.[20] Other researchers showed that the TPS does not give an accurate estimation of skin dose, overestimating it by 10–18·5%.[21–23] In addition, TLDs have an accuracy of ± 5% compared with Monte Carlo calculations and measurements in water.[24]

Chip-shaped LiF:Mg,Ti TLDs with the dimensions 0·03 cm × 0·03 cm, length and width, 0·009 cm height, as obtained from the manufacturer (Bicron NE, USA), were used in this study. Annealing treatment was performed prior to each irradiation using a Nabertherm oven (Nabertherm, Germany).[25] A Harshaw TLD reader model 3500 performed the readout of the TLD (Harshaw, Bicron NE, USA).

The calibration factor (F_{cal}) was calculated for each TLD from the ratio of ionisation chamber doses (D_{ic}) to TLD reading (TLD_r) at reference conditions,[26] and the fading effect within one day was negligible. For calibration of TLDs, a solid water phantom was used to determine the percentage depth dose (PDD), by which a correction factor was determined.[19] All ion chamber readings were corrected for water temperature and atmospheric pressure. TLDs were selected after a careful initialisation procedure.

Skin dose measurement

A total of 30 TLDs were taped on the skin inside the thermoplastic mask; six TLDs on each lateral side of Buccal, and 18 TLDs placed in fixed regions over the right, left and mid-neck. Five patients were planned, according to the PTV, to receive at least 70 Gy in 33 fractions, for both techniques. Surface doses were measured after each given fraction. The discrepancies between the three readings (right, left and mid neck) and the averages were

Table 1. The average of three delivered doses at different skin regions using patients' plan transferred on phantom covered with Klarity mask in comparison with two techniques

			The average of three shoots						
Patient number	# TLDs	Dose constraints (Gy)	IMRT-M_{av} ± SD (cGy)	3D-CRT-M_{av} ± SD (cGy)	IMRT-cumulative dose (GY)	%dose from (7 Gy)	3D-CRT-cumulative dose (Gy)	%dose from (7 Gy)	% Dose difference
Patient1	30	>7	21·8 ± 3·1	14·8 ± 2·3	7·2	102%	4·9	70%	30%
Patient2	30	>7	21·5 ± 2·6	14·5 ± 3·3	7·1	101%	4·8	68%	25%
Patient3	30	>7	19·4 ± 2·7	12·7 ± 3·7	6·4	91%	4·2	60%	26%
Patient4	30	>7	22·4 ± 3·5	15·7 ± 2·9	7·4	105%	5·2	74%	30%
Patient5	30	>7	16·4 ± 3·8	12·1 ± 2·6	5·4	77%	4·0	57%	25%
M					**6·7**	**95%**	**4·6**	**66%**	**30·9%**
SD%									**3·2%**

Abbreviations: Mav (Gy), average measurement cumulative doses in Gy using TLD; Mav (cGy), average measurement fraction dose in cGy; IMRT, intensity-modulated radiation therapy; 3D-CRT, three-dimensional radiation therapy.

Table 2. The average of three delivered doses at different skin regions using patients' plan transferred on phantom covered without Klarity mask in comparison with two techniques

			The average of three shoots						
Patient number	# TLDs	Dose constraints (Gy)	IMRT-M_{av} ± SD (cGy)	3D-CRT-M_{av} ± SD (cGy)	IMRT-cumulative dose (GY)	% dose from (7Gy)	3D-CRT-cumulative dose (Gy)	% dose from (7Gy)	% Dose difference
Patient 1	30	> 7	17·1 ± 3·5	12·7 ± 2·8	5·6	80%	4·2	60%	25%
Patient2	30	> 7	18·5 ± 3·6	12·7 ± 3·1	6·1	87%	4·2	60%	31%
Patient3	30	> 7	16·4 ± 2·9	13·6 ± 2·7	5·4	77%	4·5	64%	17%
Patient4	30	> 7	16·1 ± 3·2	11·2 ± 3·0	5·3	75%	3·7	52%	30%
Patient5	30	>7	14·2 ± 2·8	11·2 ± 2·6	4·7	67%	3·7	52%	21%
M					**5·4**	**77%**	**4**	**57%**	**24·9%**
SD%									**6%**

Abbreviations: Mav (Gy), average measurement cumulative doses in Gy using TLD; Mav (cGy), average measurement fraction dose in cGy; IMRT, intensity-modulated radiation therapy; 3D-CRT, three-dimensional radiation therapy.

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calculated, and then compared with the calculated dose from the TPS.

Results

The average percent standard deviation of the three surface TLD measurements was less than 5%. Furthermore, the Klarity mask increased the skin doses for IMRT and 3D-CRT approximately 18·6% and 8·6%, respectively. The average measured dose discrepancies between the mean IMRT measured dose and the 3D-CRT dose were 30·9% and 24·9%, with standard deviation 3·2% and 6·0% with and without the immobilization mask, respectively (Tables 1 and 2).

Clinical verification of IMRT and 3D-CRT patient treatment plans was implemented using a phantom, and all delivered doses at all surface regions were measured and compared with both the TPS doses and with a previous study that found skin doses constrained between 6 and 8 Gy.[1,8,12]

The current study revealed that surface doses for IMRT and 3D-CRT were 95% and 66%, respectively, when using a Klarity mask, and 77% and 57%, respectively, without using a Karity mask.

TPS was found to overestimate the skin dose by 20% for IMRT (Figure 1) and 16·6% for 3D-CRT (Figure 2). Using a head and neck phantom, the standard deviation of TLD/TPS was 2·4%.

Discussion

The reproducibility of the TLDs was examined, and the average of TLD measurements for three inter fraction techniques exhibited standard deviations ranging from 4% to 5%, for IMRT and 3D-CRT, respectively.[8,18,26] These findings are in agreement with studies that have found the reproducibility of TLD to be within the range of 3–5%.[2,27]

The correction value of the phantom material was evaluated in previous studies and found to be 1·05.[8,26] This correction replaces all corrections for measurement of TLD doses which resulted from the air gaps. The air gap within the TLDs holes and the slabs, is developed because of the difference in size between the TLD and the hole itself, to avoid scratching the TLD when constructing the slices of the phantom. This air gap could increase exposure to the TLDs, thus leading to such dose discrepancies.[17]

IMRT and 3D-CRT are commonly used for the treatment of NPC.[8] In terms of clinical outcomes, both offer comparable survival rates, locoregional control, and metastasis-free survival.[28] However, IMRT is still the preferred treatment for NPC[29] as it better spares the adjacent OAR, particularly the parotid glands, and reduces the risk of xerostomia, compared with 3D-CRT.[30–32] However, this study found that the average skin doses, for all patient plans transferred to the phantom, were higher with IMRT when compared to 3D-CRT. This could be explained by the use of multiple beams that tangentially enter the skin.

This study revealed that skin doses using IMRT were increased by 24·9% without a Klarity mask, when compared to 3D-CRT. This finding was in agreement with previous studies which found that IMRT increased the skin doses by about 27%, without using a mask.[32,33] Consequently, reducing the skin dose and applying measurements using IMRT sparing techniques for the head and neck are highly recommended.[8]

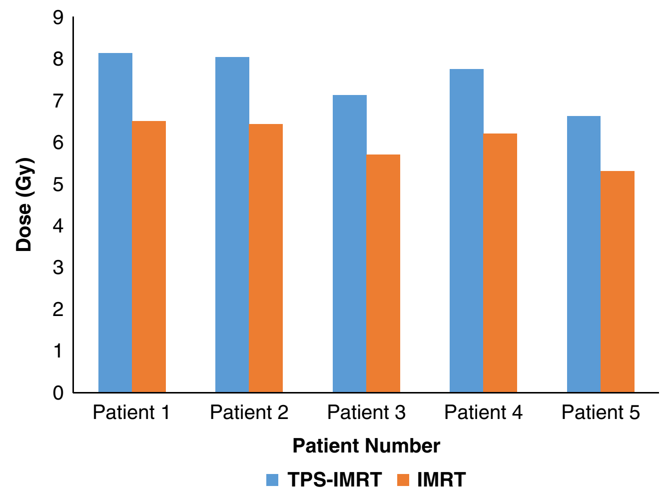

Figure 1. Comparison between measured average skin dose using IMRT and skin dose obtained from TPS.
Abbreviations: IMRT, intensity-modulated radiotherapy; TPS, treatment planning system.

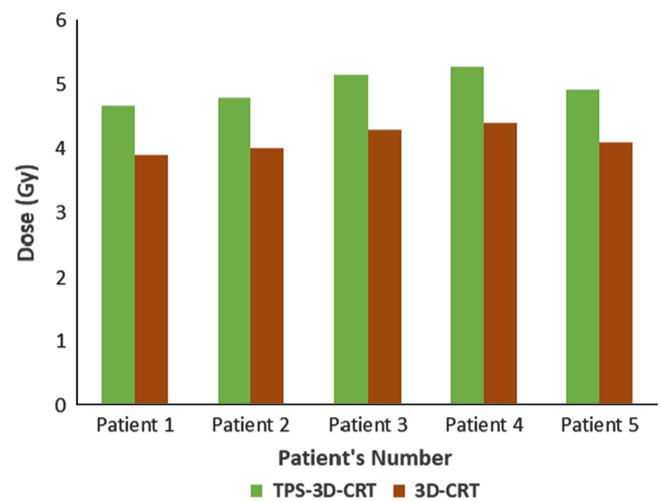

Figure 2. Comparison between measured average skin dose using 3D-CRT and skin dose obtained from TPS. (Abbreviations, TPS-3D-CRT (Gy): Calculated doses using treatment planning system for three-dimensional conformal radiation therapy).
Abbreviations: 3D-CRT, 3-D conventional radiotherapy; TPS, treatment planning system.

However, previous researchers have reported that IMRT using immobilization masks can lead to skin toxicity and increase the surface dose by 19%,[8,9,34] whereas in this study it increased significantly by 30·9%. The increased skin doses while using a Klarity mask may be caused by two main factors; the contaminant of electrons from the collimator air, and the scattering material in the beam path.[35]

The results of this study are consistent with a previous study that showed that skin doses for the first patient were 90% and 92% of the prescribed dose, as measured by metal–oxide–semiconductor field effect transistor MOSFET (TN-502RD, Springfield, VA, USA) and TLDs, respectively, while skin doses for the second patient were 88% and 86% of the prescribed dose.[23] Our study found that skin doses with the IMRT technique were 95% and 77% of the prescribed dose, with and without a Klarity mask, respectively, and 66% and 57%, with and without Klarity mask, respectively, with the use of 3D-CRT techniques. The average percentage dose on the neck surface when using a Klarity mask was increased, and when using IMRT, the skin dose was higher as compared with 3D-CRT.

Our study found that the average surface doses for IMRT were approximately 6·7 Gy and 5·4 Gy, with and without a Klarity mask, respectively. For 3D-CRT, the average surface doses were approximately 4·6 Gy and 4 Gy, with and without a Klarity mask, respectively. This is comparable with a previous study that estimated skin injuries among 86 patients undergoing intracoronary brachytherapy procedures; beta sources in this study reached 3·5 Gy and 4·6 Gy.[36] Other researchers have found that cumulative doses on the neck region exceeded 7 Gy, causing burns on the neck area during 3D-CRT and IMRT.[8] However, other studies have revealed that erythema occurs at skin doses of 6–8 Gy.[8,12] On the other hand, previous researchers have shown that cancer treatment using radiation therapy is well tolerated in older patients as the elderly have smaller mitosis indices, and given that radiation destroys cells mainly in the mitosis phase, this results in elderly people having less skin reactions.[37]

Dosimetric measurement is highly recommended for estimation of skin doses as TPS overestimates the skin dose. This is consistent with other researchers who have found that TPS overestimates the dose by 18·5%,[38] and others found that TPS overestimates the skin dose by 10–12% when compared with measurement using MOSFET and TLD.[23] Furthermore, using cobalt irradiation of a paediatric phantom, the average magnitude of local difference between the TPS doses and measured skin doses was 22%.[39]

Limitations

It was difficult to ensure the TLDs remained in the same position for all patient plans. The researchers tried to use the same TLD number at the same position during the experiment, for all patients plans transferred to the phantom; however, there may have been some change in TLD numbers.

Conclusion

Skin dose is an important issue of focus during treatment of malignant diseases using radiation. It is concluded that IMRT increases acute skin toxicity significantly when compared with conventional radiotherapy (CRT). Even though the Klarity mask provides superior target coverage and normal tissue sparing, it increases the skin toxicity risk using both techniques.

It is possible to reduce the skin dose, when considering the skin as a sensitive structure, without affecting tumour coverage. Furthermore, dosimetry measurements for individual planning before radiotherapy treatment are highly recommended as TPS is not accurately estimated the skin doses. The severity of skin burns is related to the total cumulative dose received, and burns can become serious after radiotherapy treatment; therefore, surface dose measurements should be taken be into account.

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Conflicts of Interest. Author has no conflict interest to declare.

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