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Assessment of skin dose in breast cancer radiotherapy: on-phantom measurement and Monte Carlo simulation☆

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ABSTRACT

Aim: The main purpose of the present study is assessment of skin dose in breast cancer radiotherapy.
Background: Accurate assessment of skin dose in radiotherapy can provide useful information for clinical considerations.
Materials and methods: A RANDO phantom was irradiated using a 6 MV Siemens Primus linac with medial and tangential radiotherapy fields for simulating breast cancer treatment. Dosimetry was also performed on various positions across the fields using an EBT3 radiochromic film. Similar conditions of measurement on the RANDO phantom including field size, irradiation angle, number of fields, etc. were subsequently simulated via the Monte Carlo N-Particle Transport code (MCNP). Ultimately, dose values for corresponding points from both methods were compared.
Results: Considering dosimetry using radiochromic films on the RANDO phantom, there were points having underdose and overdose based on the prescribed dose and skin tolerance levels. In this respect, 81.25% and 18.75% of the points had underdose and overdose, respectively. In some cases, several differences were observed between the measurement and the MCNP simulation results associated with skin dose.
Conclusion: Based on the results of the points which had underdose, it was suggested that a bolus should be used for the given points. With regard to overdose points, it was advocated to consider skin tolerance dose in treatment planning. Differences between the measurement and the MCNP simulation results might be due to voxel size of tally cells in simulations, effect of beam's angle of incidence, validation time of linac's head, lack of electronic equilibrium in the build-up region, as well as MCNP tally type.

1. Introduction

Breast cancer is one of the most prevalent types of cancer among women across the world.[1] In order to reduce the risk of local recurrence for lymph nodes and to conserve the breast and chest wall, radiotherapy is normally administered to breast cancer patients after surgery. However, skin reactions following radiotherapy are regarded as a limiting factor for breast cancer treatment.[2]

Skin is known as a complex organ, characterized by a layered structure with different types of cells. The basal cell layer of the skin is at the depth of about 70 μ,[3] and radiation damage to these cells can result in acute reactions and induce erythema or desquamation.[4] As well, the dermal vascularization is located at the depth of 0.5–3 mm and radiation damage to it may cause late reaction effects such as telangiectasia.[3] Therefore, adequate skin dose should be delivered by a radiotherapy regimen to minimize the chance of recurrence to superficial tissues.[5] For that reason, accurate assessment of surface dose in radiotherapy can provide useful information for clinical considerations in order to prevent near-surface recurrence as well as severe skin toxicity. This is especially of utmost importance for the treatment of breast and head-and-

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neck cancers due to the curvature of the external contour in such treatment sites.[6]

According to recommendations released by the International Commission on Radiological Protection, the depth of 70 μm should be considered for skin dose measurement, which corresponds to the interface between the layers of dermis and epidermis in the skin.[7] In this region, the percentage depth dose (PDD) curve of MV photons has a steep dose gradient. For example; within the first millimetre of a 6 MV photon beam, PDD increases from 14% to 43% in a $10 \times 10\,cm^2$ field size.[8,9] Therefore, measurement and estimation of skin dose can have practical difficulties.

Modern radiotherapy treatment planning systems (TPS) predict doses to different organs of a patient; however, they are characterized by high uncertainty in terms of calculation of skin dose. Furthermore, TPSs need computed tomography (CT) images along with calculation of a treatment plan.8 In this regard, some studies[2,9] have indicated that TPS estimations for surface and near-surface doses might be inaccurate. American Association of Physicists in Medicine in its report about commissioning of TPSs suggests a tolerance of up to 20% between measurements and TPS calculations for the build-up region in X-ray depth dose curves.[10] Devic et al.[9] demonstrated as well that TPSs could often apply the beam data measured for the maximum dose depth and then the dose distributions in other sections, including the surface dose and the build-up region could be estimated with fitting functions through extrapolating measured data into the surface.

Dose measurement can become even more intricate for curved structures, such as the skin contour of the breast. In this regard, Court et al.[11] reported acceptability criteria of up to 27% between Eclipse TPS (Varian Medical Systems, Palo Alto, CA) estimations and skin dose measurements via metal-oxide-semiconductor field-effect transistor (MOSFET) dosimeters on a semi-cylindrical water equivalent phantom with photon beams of 6 MV and 10 MV.

Generally, measurement of surface dose with a radiochromic film is also common due to its several advantageous features for dosimetry. High spatial resolution, low spectral sensitivity, setup feasibility, tissue equivalence, and self-development are among practical features of radiochromic films. Furthermore, several studies have evaluated energy response for various types of film dosimeters within different photon energies even though energy dependence of an EBT radiochromic film has remained minimal.[12,13] Accordingly, Devic et al.[9] measured surface dose using radiochromic films (HS, XR-type T, and EBT). For this purpose, the authors measured the PDD within the first millimetre on a water phantom in a 6 MV photon beam using a radiochromic film along with other dosimeters. Correction factors were also determined for radiochromic films with relevant measurements of effective points for skin dosimetry at the depth of 70 μm. While the study by Devic et al. determined the effective points for skin dosimetry, they have not compared skin dose from measurements and simulations and skin damage effects have not been predicted.

The International Specialty Products also introduced a new generation of films, i.e. EBT3 radiochromic film.[14] To the best of authors' knowledge, there are few studies evaluating this type of film in real conditions encountered in radiotherapy.[15] For example, measurements have been carried out on a geometric or slab phantom.

Using the Monte Carlo N-Particle Transport code (MCNP), the particles (namely, primary and scattered photons and electrons) can be tracked according to the related cross-sections and their interactions.[16,17] Therefore, the dose distribution predicted by MCNP as a potential means to measure skin dose is assumed valid and reliable.

The main purpose of the present study was to assess skin dose using an EBT3 radiochromic film and Monte Carlo simulation in three-dimensional (3D) conformal radiotherapy of breast cancer on a RANDO phantom.

2. Materials and methods

In this study, skin dose measurements were carried out on a RANDO phantom using an EBT3 radiochromic film, and then simulations were performed via the MCNP. To simulate a breast cancer treatment, the RANDO phantom was also irradiated by 6 MV photon beam of a Siemens Primus linac with medial and tangential fields.

2.1. Treatment planning of breast cancer

Treatment planning was performed by an oncologist and physicist to simulate a post-mastectomy case on a male RANDO phantom (Radiology Support Devices Inc., Long Beach, California, USA). Initially, contouring was fulfilled and the boundaries of the fields were determined on the RANDO phantom. As one step of treatment planning, scan images were taken of the RANDO phantom using a computed tomography (CT) scanner (Siemens Somatom Emotion Duo) at the Reza Radiation Oncology Center, Iran, in a horizontal situation in such a position that the body of the phantom was perpendicular to the incident beam with 0.5 cm slice thickness. The phantom was then scanned from its head, down to the pelvis. Using the images, treatment of the breast cancer (i.e. mastectomy) case was planned using Prowess Panther (version 5.1, Siemens, Germany) TPS. The characteristics of this treatment planning are presented in Table 1. It should be noted that the patients admitted to the Reza Radiation Oncology Center were treated by the SSD technique, so measurement and simulation setup was at SSD = 100 cm.

2.2. Calibration of EBT3 radiochromic film

In order to calibrate an EBT3 film, one part of one sheet from a batch (lot number: A04011301) was cut into 48 pieces of 2×1.5 cm films. These pieces were then classified into 12 groups, each one including 4 pieces. After that, these films were scanned 24 h before irradiation using a Microtek ScanMaker 1000XL Pro scanner (Microtek International Inc., Hsinchu, Taiwan) to obtain their background optical densities (ODs). To minimize the errors due to the effects of the warm-up, the scanner was turned on at least 30 min before scanning. The reading of the films was also accomplished with 1-minute intervals. The films were then positioned at the centre of the scanner's bed in a landscape mode in all of the scans. The readings were also carried out at room temperature. In order to record accurate optical densities, appropriate care was taken to prevent scratches and dust on the films. Therefore, the films were cleaned with a small piece of soft cloth before each scan.

The films were then scanned without any corrections as a positive transmission mode, 48 bit red, green, blue (RGB) colour images and with 100 dots per inch (dpi) resolution. All of the images were subsequently saved in tagged image file format (TIFF) files. To minimize noise effects, each film was scanned three times. Since the response was higher in the red colour channel for the EBT3 film, the red channel data was extracted after the scanning, using MATLAB script (version 7.11.0.584, MathWorks, Inc., Natwick, MA). Each group of the films was then irradiated in a PTW solid water phantom with a 10×10 cm 6 MV photon field of a Siemens Primus linac at the source-to-surface distance (SSD) of 100 cm at the depth of 10 cm with a wide range of doses (0.2, 0.5, 0.75, 1, 1.25, 1.5, 1.75, 2, 2.5, 3, and 4 Gy) at the Reza Radiation Oncology Centre.

The output of the linac was calibrated earlier by an ionization chamber for clinical applications. For this purpose, the IAEA TRS-398[18] dosimetry code of practice was utilized. The films were also scanned in the same conditions as those set for the background reading, 36 h after irradiation; and the net optical density (NOD)

Table 1
Characteristics of the tangential fields in breast cancer radiotherapy with 6 MV photon.

Tangential field	Medial field	
240.00	55.00	Gantry angle (degrees)
0.00	0.00	Couch angle (degrees)
14.17, −16.26, 53.85	6.17, −22.46, 53.85	Couch position (Lateral, Vertical, Longitudinal) (cm)
−14.17, −31.60, −6.22	−6.17, −31.60, −0.01	Isocenter (*X*, *Y*, *Z*) (cm)
100.00	100.00	SSD (cm)
0.00	0.00	Collimator angle (degrees)
8.00 × 18.00	8.00 × 18.00	Field size (cm)
1.19	1.19	Dose at d_{max} (Gy)

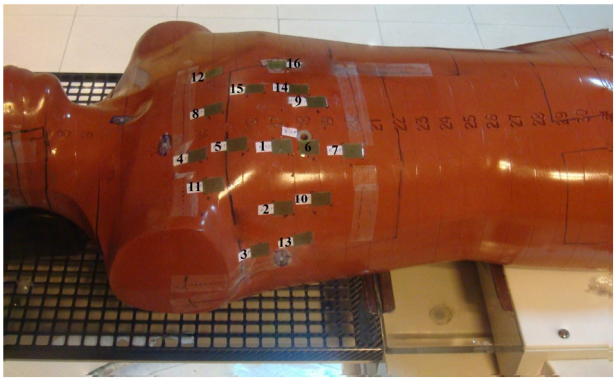

Fig. 1. Positions of radiochromic films in the tangential fields of breast cancer radiotherapy. Each number is corresponded to the number of film position in the field.

was calculated from the following formula by programs written in MATLAB software:

$$NOD = OD_{Cal}\text{-}OD_{Back} = -(\log_{10}(P_{Cal})\text{-}\log_{10}(P_{Back})) \quad (1)$$

wherein; OD_{Cal} is calibration optical density, OD_{Back} shows background optical density, P_{Cal} represents calibration pixel value, and P_{Back} refers to background pixel value. Then, NOD was plotted versus the given dose and an exponential function was fitted to the corresponding data. In order to calibrate the films, mean pixel values of the region of interest (ROI) on the film was used. This ROI was a square characterized by 1 cm dimensions.

2.3. Skin dose measurement on RANDO phantom

In order to assess skin dose in various parts of tangential radiation fields in breast cancer radiotherapy, one part of an EBT3 film sheet was cut into 16 pieces of 2 × 1.5 cm. This film sheet was from the same batch as that used in the calibration setup. Similar to the calibration step, the film pieces were scanned and read before irradiation. The position of each film was then determined by an oncologist and a physicist based on a treatment planning procedure on the phantom. Afterwards, the coordinates of each film were specified on the RANDO phantom by knowing the coordinates of the treatment couch. The pieces of the films were also attached on these points by adhesive tape, so that they could cover different parts of the medial and tangential fields as observed in Fig.1. Then, according to the TPS, the fields were set up and the RANDO phantom was irradiated using linac. The directions of the films were the same as those on the phantom. To reduce the related errors, this process was repeated three times. After irradiation of the films, scanning and reading were also performed, similar to those in the calibration step. It should be noted that the measured dose in one session was multiplied by 25 and the total dose delivered to the skin was obtained at 25 fraction.

2.4. Skin dose calculation by Monte Carlo simulation

MCNPX Monte Carlo code (version 2.6.0)[19] was used to simulate the setup conditions of the skin dose measurement on the RANDO phantom. The CT images of the RANDO phantom were also introduced into Scan2MCNP[20] software, developed by Van Riper to convert the CT and MRI image sets to the MCNP useable format. This program transforms pixel information to MCNP geometry depending on pixel intensities. So, pixel intensities are converted into grey colour tones and a variety of scanning intensities represents an individual material (e.g. soft tissue, lung, rib, etc.).

The output of this program was obtained according to the CT images of the RANDO phantom. In this simulation, 33 materials were defined for the RANDO Phantom. The input program of the linac's head was already validated in a previous study by Pakravan et a. [21] In the present study, a combination of the programs of linac's head and RANDO phantom was used for skin dose calculations. All of the experimental measurement conditions were also considered in the simulation program accordingly. Moreover, the radiochromic film was defined by a sphere with a radius of 1.5 mm. In order to reduce variance in the simulation program, energy cut-off points for photon and electron particles were set to 10 and 100 keV; respectively. The importance was also considered by 100 in the tally cells. Dose was also calculated by the F4 tally and flux-dose conversion factor. It should be noted that it was better to score the dose using *F8 tally although this would result in difficulties due to the large running time of the MCNP, which is normally required by this tally. To convert the MCNP output, which is per source particle to Gy, a cell was defined in the prescription point in the phantom and the dose was scored in the cell by the *F8 tally. Then, the conversion factor from per source particle to Gy was calculated by knowing about the prescription dose per fraction. In MCNP it is feasible to transport a maximum of 2×10^9 particles in one program. One such program was run, but the uncertainty in dose calculations was high. Therefore, to decrease the uncertainty in the calculations, nine programs were run and the dose was calculated as the average of the dose values from these programs. It should be noted that the calculated dose in one session was multiplied by 25 and the total dose delivered to the skin was obtained for 25 fractions.

2.5. Measurement and calculation uncertainty

As previously stated, three films were assigned to each spot on the RANDO phantom, and each piece of the film was read three times. To determine measurement uncertainty, the standard deviation for three readings was initially obtained; and, then, the standard deviation for three films was calculated. To determine the calculation uncertainty of the Monte Carlo simulation for each cell corresponding to a point, the following equation is used:

$$Total\ uncertainty = \sqrt{\left(\frac{n_1}{N}\right)^2 \sigma_1^2 + \left(\frac{n_2}{N}\right)^2 \sigma_2^2 + \dots} \quad (2)$$

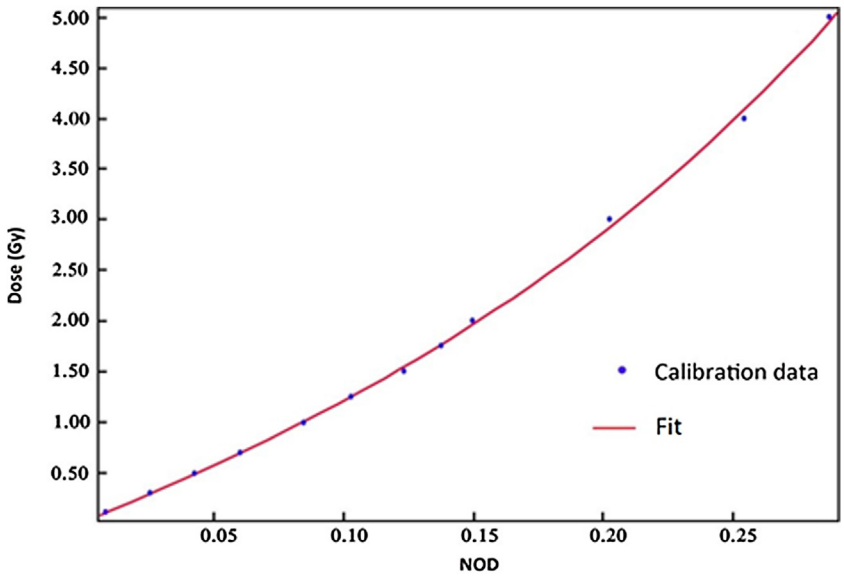

Fig. 2. Calibration curve (dose in Gy versus NOD) for Gafchromic EBT3 radiochromic film.

wherein; n_1, n_2, etc. are the number of particles in each program, N shows the total number of particles in all programs, and $\sigma 1$, $\sigma 2$, etc. represent uncertainties in the program number 1, number 2, etc.

2.6. Percentage difference between measurement and simulation

The percentage differences (%) between the measurement and the MCNP simulation were calculated by the following formula:

$$\text{Percentagedifference} = 100\times((D_{\text{Measurement}}\text{-}D_{\text{MC}})/D_{\text{MC}}) \quad (3)$$

3. Results

3.1. Calibration of EBT3 radiochromic film

Fig. 2 shows the calibration curve (dose in Gy versus NOD) for the Gafchromic EBT3 film. The data in this curve were processed through MATLAB software and the following equation was fitted to the data of the absorbed dose (in Gy) as a function of NOD:

$$D = -1.517e^{-2.121\text{NOD}} + 1.54e^{+4.608\text{NOD}},\ R2 = 0.99 \quad (4)$$

3.2. Skin dosimetry

Table 2 lists the skin doses (Gy) in the tangential fields planned for breast cancer treatment on the RANDO phantom using the EBT3 radiochromic film and the MCNPX code in 25 fractions. These data are related to the positions illustrated in Fig. 1. The percentage differences (%) between the measurement and the MCNP simulation data were calculated based on Eq. (2).

4. Discussion

In this study, skin dose assessments were carried out on a RANDO phantom via measurements by an EBT3 radiochromic film and simulation using MCNP. According to Table 2, the maximum skin dose at point 11 was equal to 59.00 Gy and the minimum skin dose at point 12 was equal to 17.00 Gy. Points 1, 5, 6, and 7 with 49.50, 49.00, 52.75 and 54.25 Gy were closer to the maximum dose. Points 1, 5, 6, 7 and 11 were also located in the overlap region between the medial and tangential fields in breast cancer radiotherapy. Skin dose in point 4 was lower since it was located in the upper portion of the breast and outside the edge of the tangential field.

Based on the prescribed dose by oncologists for breast cancer treatments, it is necessary to reach a dose of 50 Gy to the target volume in 25 fractions. Skin is also one part of the treatment volume for a mastectomy case in breast cancer radiotherapy. Considering this criterion, all points receiving total doses less than 50 Gy are introduced as underdose ones. These points are also those located at the edge of the field and receiving radiation only from one field. Tumour recurrence and failure in breast cancer treatment are thus considered as important adverse effects in this regard. In such cases, application of bolus material in the course of treatment is suggested for breast cancer radiotherapy. Once bolus is placed on the skin, the build-up region is moved towards the surface of the skin; therefore, the skin dose increases.

In this line, Soleymanifard et al.[22] put emphasis on the use of a bolus as one part of the treatment course in some fractions in breast cancer treatment. This effect becomes important as wedge filters are applied in treatment planning. Hsu et al.[6] also evaluated the effect of bolus material on the entrance dose. They observed that once 2 mm of an Aquaplast bolus was placed on the breast, the skin dose could increase up to 28%. Similarly, Kelly et al.[23] measured the effect of bolus material on the amount of skin dose using a radiochromic film and MOSFET, and observed that the skin dose in the presence of a bolus had increased by 45.7% and 62.30%; respectively.

Severity of early and late skin effects also depends on the skin dose. Additionally, there are time intervals after which skin effects might appear. For example, Archambeau et al.[24] reported that these effects could be predictable and such a prediction could be made from the measured dose according to Archambeau et al. criteria for all the measurement points on the RANDO phantom (Table 3). Based on this table, it was predicted that early and late effects would occur on the skin of patients treated by such a plan. A skin effect of higher probability is erythema which will occur in 43.75% of the points. Other skin effects (e.g. epilation, pigmentation, dry desquamation, and moist desquamation) can be also observed. Skin also exhibits a volume effect; in other words, skin receiving tolerance dose can be recovered by adjacent non-irradiated skin. However, high-dose areas should be considered in the TPS. In this respect, Archambeau, et al. advocated that suitable TPS and introduction of an adequate interval between treatment fractions were ben-

Table 2
Dosimetry results (Gy) using Monte Carlo simulation and EBT3 radiochromic film in the points presented in Fig. 1 at 25 fraction with 2 Gy dose per fraction.

Diff. (%)	Simulation dose (Gy) ± %uncertainty	Measurement dose (Gy) ± %uncertainty	Number of film position
10.00	55.00 ± 2.71	49.50 ± 0.30	1
33.63	56.50 ± 2.67	37.50 ± 0.17	2
52.09	65.75 ± 2.46	31.50 ± 0.10	3
22.32	56.00 ± 2.66	43.50 ± 0.10	4
10.09	54.50 ± 2.70	49.00 ± 0.10	5
7.86	57.25 ± 2.64	52.75 ± 0.50	6
14.90	63.75 ± 2.48	54.25 ± 0.40	7
34.89	58.75 ± 2.59	38.25 ± 0.30	8
20.09	53.50 ± 2.71	42.75 ± 0.20	9
25.00	55.00 ± 2.69	41.25 ± 0.10	10
10.61	66.00 ± 2.44	59.00 ± 0.70	11
74.81	67.50 ± 2.46	17.00 ± 1.00	12
38.67	56.25 ± 2.65	34.50 ± 0.00	13
26.29	53.25 ± 2.74	39.25 ± 0.20	14
28.44	52.75 ± 2.73	37.75 ± 0.10	15
39.59	49.25 ± 2.82	29.75 ± 0.10	16

Table 3
Skin reactions predicted based on the skin dosimetry results. The reactions were predicted based on the criteria by Archambeau et al.[18]

Gross change	Percentage (%)	Number of film position	Dose (Gy)
Epilation	6.25	12	~20
Erythema	43.75	2-3-8-13-14-15-16	20–40
Pigmentation, dry desquamation	18.75	4-9-10	~45
Moist desquamation that heals, telangiectasia	12.50	1-5	45–50
Moist desquamation that does not heal, non-healing necrosis	18.75	6-7-11	>50

eficial in minimizing skin reactions. Additionally, Soleymanifard et al.[22] suggested that the use of a wedge could be an option for diminishing skin dose.

According to the results associated with skin dose from Monte Carlo simulation in 25 treatment fractions in Table 2, the maximum skin dose in point 12 was equal to 67.50 Gy and the minimum skin dose in point 16 was equal to 49.25 Gy. Furthermore, there were differences between both methods (i.e. radiochromic film and Monte Carlo simulation). The discrepancies between these two methods originate from:

- Differences in defined volumes for the measurement of desired quantity (i.e. skin dose): In other words, the skin dose on the RANDO phantom was measured by a radiochromic film with a thickness of 267 μm, but the tally volumes in the Monte Carlo simulation were spheres with a diameter of 3 mm. One of the most important limitations of simulation is computation time. To reduce the computational time, the volume of the tally was slightly higher than that of the real film.
- Input beam angle: According to Soleymanifard et al.,[22] the angle of beam entrance could affect the skin dose. The scoring volumes in MCNP were also a bit different from the volume of films due to practical difficulty. Such small volumes for dose scoring could not be defined in the simulation because if the scoring volume of the simulation was defined as small as the thickness of the radiochromic film, the uncertainty in the tally calculation would be high. In other words, the smaller the volume of the scoring cell in Monte Carlo simulation, the higher is the scoring uncertainty. This was a limitation in the simulation. The effect of beam entrance angle could be different on non-equal volumes and this is another cause of the discrepancies.
- Type of tally used in simulation: It would be better to calculate the absorbed dose using the *F8 tally. But the uncertainties in calculations by the *F8 tally are normally high. Therefore, the F4 tally was used in the simulation. In this method, fluence values were obtained by the F4 tally through simulation and the absorbed dose (Gy) was then extracted by multiplication of fluence by fluence to dose conversion factors. Undeniably, inaccuracies could be created due to such approximations.
- Lack of electron equilibrium in the build-up region: There was no electron equilibrium in the build-up region and skin was located in this area; therefore, measurement of skin dose was a challenging topic, normally associated with errors.
- Time of linac simulation validation: The output of a linac is dependent on several factors including changes in linac's head geometry and variations of magnetron output. Validation of the Siemens Primus lianc's head was fulfilled in the study by Pakravan et al.[21] about 5 years ago. Within this time interval, the geometry of the components of the linac's head had not changed; however, some repairs have been done on the machine that might have changed the output spectrum of the photons. These effects were minor since the output of this linac is routinely in the centre and such changes were negligible.

It should be noted that the calibration of the radiochromic films was performed inside the phantom; however, the skin dosimetry was on the surface of the RANDO phantom. While this difference between the calibration and the measurement method should be avoided, it is not easy to do so; since calibration on the surface of a phantom may have inaccuracies due to the lack of electron equilibrium in the build-up region. Performing a radiochromic film measurement on the surface and at the depth of a slab phantom and comparing the results with corresponding data from Monte Carlo simulation can illuminate the cause of the discrepancies in this study which are due to the build-up effect. Performing such an experiment is suggested as further investigation in this field. Based on the results in Table 2, some points having relatively large differences between the skin doses from radiochromic film dosimetry and Monte Carlo simulation (e.g. points 3, 12, and 16) were located on the borders of the fields (i.e. penumbra region). Therefore, one part of the discrepancies would be justified due to differences which naturally exist in the dose results in the penumbra region.

5. Conclusion

Based on the obtained results; 81.25% of the measurement points corresponded to underdose in the skin dosimetry of breast cancer radiotherapy with 6 MV photon beam of a medical linac using a radiochromic film, so the bolus material could be used for treatments. Moreover, 18.75% of the points had overdose that might result in early and late skin reactions. Therefore, adopting strategies and taking precautions in TPS as well as noticing intervals between fractions could prevent these reactions.

There were differences between the skin dose results obtained by radiochromic film measurement and Monte Carlo simulation. Such discrepancies might be due to the defined volume, input beam angle, tally used in simulation, electron equilibrium in the build-up region, as well as time interval between linac validation and results of film dosimetry; which were more reliable than those of the Monte Carlo simulation because the measurement results were closer to the real clinical treatment conditions. Additionally, the measurement was characterized by fewer sources of error.

Conflict of interest

None declared.

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