Original Article

In vivo dosimetry of skin surface for breast cancer radiotherapy using intensity-modulated radiation therapy technique and helical tomotherapy

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Background: Planning skills such as skin flash in intensity-modulated radiation therapy (IMRT), virtual bolus in helical tomotherapy (HT) and tissue equivalent materials are widely used in breast cancer radiotherapy (RT) to ensure coverage of superficial target under respiration. This study was conducted to evaluate the exact skin dose under above treatment technique and planning skills.

Methods: Women who received whole breast RT (WBRT) or post-mastectomy RT (PMRT) were included. Treatment machines included Synergy® (Elekta, Stockholm, Sweden) and TomoTherapy Hi-ART® (Accuray, Sunnyvale, CA, USA). For WBRT, 20 mm "skin flash" was used in IMRT, and 10 mm "virtual bolus" was used in HT. For PMRT, 5 mm bolus plus skin flash was used in IMRT and 10 mm bolus was used in HT. GafChromic EBT3 (International Specialty Products, Wayne, NJ, USA) films were placed on patient's skin for measurement.

Results: Between July 2012 and December 2013, 17 patients in WBRT group and 13 patients in PMRT group were included. In WBRT group, patients received higher skin dose with IMRT than with HT (86.57% and 79.69% of prescribed dose, respectively, P<0.0001). IMRT delivered 4–5% higher dose to central skin region than bilateral regions, while skin dose distribution of HT was relatively homogeneous. In PMRT group, IMRT delivered higher surface dose than HT did (107.34% and 100.28% of prescribed dose, respectively, P<0.0001).

Conclusions: For WBRT, HT plus virtual bolus leads to homogeneous skin dose distribution and 7% lower skin dose than IMRT does. For PMRT, HT plus 10 mm bolus provides adequate surface dose which is close to 100% of prescribed dose; while IMRT plus 5 mm bolus and skin flash results in overdose with 7% more than prescribed dose. HT should be considered to be an option of breast RT.

Keywords: Breast cancer, radiotherapy (RT), skin dose, surface dose, virtual bolus, bolus materials, tomotherapy

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Introduction

Adjuvant radiotherapy (RT) has played an important role in multimodality treatment of breast cancer. For patients with early stage disease who receive breast conservative surgery (BCS), adjuvant RT to the residual breast tissue improved local control and survival (1). On the other hand, for patients with local advanced stage breast cancer who received mastectomy, adjuvant RT to chest wall and lymph node region reduced recurrent rate and breast cancer specific mortality (2,3).The target volume of RT after mastectomy typically includes ipsilateral chest wall, supraclavicular fossa (SCF), internal mammary lymph nodes (IMLN) and/or axillary lymph nodes (4,5).

Both linear accelerator-based intensity-modulated radiation therapy (IMRT) and helical tomotherapy (HT) are widely used for RT of breast cancer. Typical target volume of breast cancer is close to skin surface. However, most of treatment planning systems (TPS) in clinical practice do not provide accurate dose of skin surface and superficial target because inverse planning algorithm cannot accurately calculate the dose of build-up region (6-8). Skin surface will be potentially exposed to overdose or underdose due to inaccurate calculation in TPS, resulting in unexpected skin toxicity or decreased tumor control. The usual solutions used in clinical practice include adding bolus on the skin surface, using virtual bolus while treatment planning, and modified planning target volume (PTV) to avoid build-up region (9,10). On the other hand, some useful skills such as "skin flash" in IMRT and virtual bolus in HT are used to compensate the intra-fraction movement (11,12). However, accurate evaluation of skin dose becomes a challenge with the above approaches.

The purpose of this study is to measure the skin dose distributions of IMRT and HT by EBT films for patients who received breast cancer RT.

Methods

Eligibility criteria

Women who had undergone surgery, BCS or modified radical mastectomy (MRM), for invasive carcinoma or carcinoma *in situ* of the breast and were candidates for RT were included in this trial. Women who had breast reconstruction (either flap or any implantation), bilateral disease, wound infection before RT, surgical seroma requiring aspiration during treatment, or previous thoracic RT were excluded.

In this study, treatment machines were Synergy® (Elekta, Stockholm, Sweden) with Pinnacle planning system for linear accelerator-based IMRT, and TomoTherapy Hi-ART® (Accuray, Sunnyvale, CA, USA) for HT. Patients were assigned to IMRT or HT, depending on their decision. Daily image guided technique was essential to HT group with the use of megavoltage computed tomography (MVCT), but it was optional for IMRT group with the use of cone beam computed tomography (CBCT).

Target volume and treatment planning

The target volume was delineated according to Radiation Therapy Oncology Group (RTOG) atlas. Patients who underwent BCS were assigned to receive whole breast RT (WBRT). The clinical target volume (CTV) was ipsilateral residual breast tissue. The PTV was defined as CTV plus 5 mm margin and was modified to avoid the build-up region which was defined as 3 mm beneath the external surface. Prescribed dose was 50 Gy to PTV and/or a boost dose of 10 Gy to tumor bed. The daily fraction size was 2 Gy.

For patients who received post-mastectomy RT (PMRT) after MRM, the CTV included ipsilateral chest wall, axillary lymph node region, IMLN and SCF. The PTV was defined as CTV plus 5 mm margin. The PTV in PMRT group was also modified to avoid build-up region. Prescribed dose was 50 Gy to PTV and/or a boost dose of 10 Gy to surrounding region of operative scar. The daily fraction size was 2 Gy. All plans met the criteria of delivering more than 95% prescribed dose to 95% of the PTV and maximal dose less than 115%.

In WBRT group, an IMRT plan consisted of 2 to 7 IMRT field directions, depending on individual patient's anatomy and PTV distribution shape (*Figure 1A*). In addition, "skin flash", a field extension of 20 mm outside the skin surface, was used to deliver additional radiation on the space above the skin to cover the intra-fractional movement caused by respiration (*Figure 1B*). In HT plans for WBRT, a directional block at contralateral posterior thorax was designed to reduce the radiation from posterior and contralateral direction and reduce dose of lung and heart. Virtual bolus, which was a pretended material on the breast surface in treatment planning but absent during irradiation, was used in all the HT plans for WBRT to cover the patient's movement. The density of virtual bolus in this study was defined as 1.0 g/cm^3, and thickness was 10 mm.

In PMRT group, an IMRT plan consisting of 7 IMRT

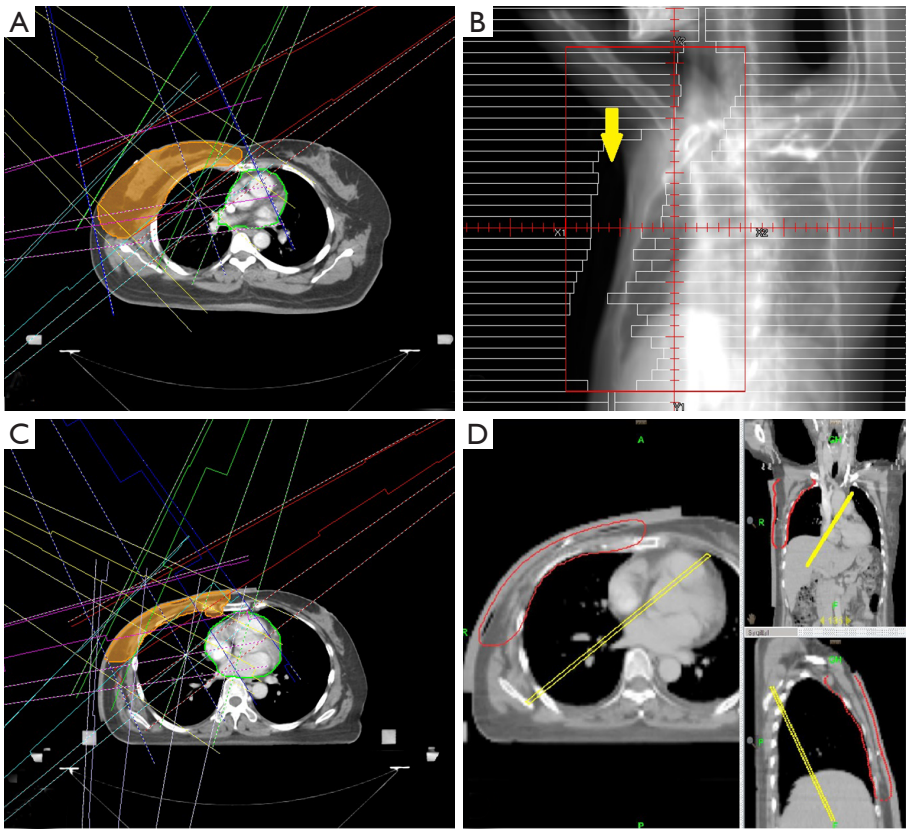

Figure 1 Illustrations of the treatment planning. (A) Beam arrangement of IMRT plans for WBRT. The PTV is displayed in orange; the heart in green. (B) Skin flash (yellow arrow) in beam eye view. (C) Beam arrangement of IMRT plans for PMRT. The PTV is displayed in orange; the heart in green. (D) Directional block (yellow bar) used in HT plans for WBRT and PMRT. The PTV is displayed in red. IMRT, intensity-modulated radiation therapy; WBRT, whole breast radiotherapy; PMRT, post-mastectomy radiotherapy; PTV, planning target volume; HT, helical tomotherapy.

field directions was designed with 20 mm skin flash (*Figure 1C*). A 5-mm tissue equivalent bolus was added on patient's ipsilateral chest wall to ensure the superficial coverage. On the other hand, 10 mm tissue equivalent bolus was added for patient in PMRT group treated with HT. A directional block was also used to restrict the beam angle (*Figure 1D*).

Measurement of surface dose

For each patient included, the skin surface of the breast or chest wall was divided into six areas including upper-lateral area, lower-lateral area, upper-central area, lower-central area, upper-medial area and lower-medial area, which were coded as No.1, 2, 3, 4, 5, 6, respectively (*Figure 2A,B*).

The "upper" and "lower" were defined as skin area above and below the horizontal level of the nipple; the "lateral", "central" and "medial" were defined as skin area outside, along and inside the longitudinal level of the nipple, respectively. For patients who received mastectomy without nipple sparing procedure, the above definition of division was referred to contralateral nipple and ipsilateral midclavicular line.

GafChromic EBT3 (International Specialty Products, Wayne, NJ, USA) has been proven to a viable tool for megavoltage radiation dosimetry (13,14). The product was suitable to surface measurement near build-up region due to thin configuration (thickness of ~0.278 mm) and near-tissue equivalence (13). Each EBT3 film piece was cut into 4 cm × 5 cm. Six EBT3 film pieces were taped on the six skin areas of the breast or chest wall. If bolus material was used, the film pieces would be placed between the patient's skin and bolus.

Each irradiated EBT3 film piece was scanned by Scanner

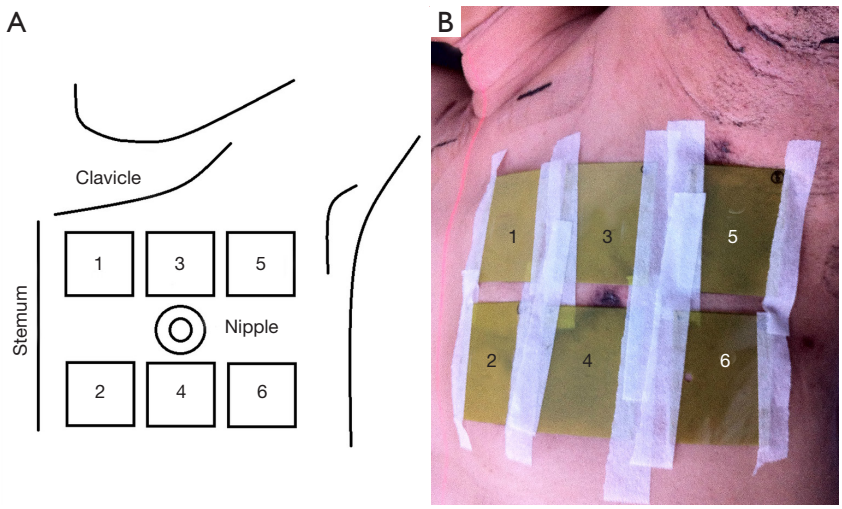

Figure 2 Each patient's skin surface of the breast or chest wall was divided into six areas and six EBT3 films pieces were taped on these areas. (A) diagram of distinct skin areas and EBT3 films placement. (B) Patient set up image.

Epson 10000XL at least 24 hours after irradiation. A region of interest (ROI) of 1 cm × 1 cm at the center was selected to collect the mean pixel value and standard deviation. Software FilmQA 2.20 was used for converting mean pixel value to absorbed dose of the skin areas. The calibration curve for pixel values of EBT3 film to absorbed dose was established on the same day when measurements were performed.

Absorbed dose of six EBT3 film pieces on six skin areas was defined as "film dose" of No.1, 2, 3, 4, 5 and 6, respectively. The average of six film dose in the same measurement was defined as "average surface dose". The dose of medial region, central region and lateral region represented film dose of No.1 and 2, No.3 and 4, No.5 and 6, respectively. The dose of upper region contained film dose of No.1, 3 and 5; the dose of lower region contained film dose of No.2, 4 and 6.

For patient whom six EBT3 film pieces were unable to be placed on following above protocol, five-film-piece protocol was performed. The films No.1, 2, 5, 6, were placed under the same rules as six-film-piece protocol. Only one EBT film was placed at "central" region of ipsilateral breast or chest wall. The absorbed dose of the "central film" was included in calculation of average surface dose and was excluded while analysis of surface dose difference among skin regions.

Each patient received three times of EBT3 measurement in three consecutive fractions during the first phase of RT; none of measurement was performed in the phase of tumor bed boost.

To figure the dose difference between calculation by TPS and EBT3 measurement, point dose at skin surface on CT image was used to represent the surface dose calculated by TPS. In each plan, six points at the external surface contour were chosen from upper-lateral area, lower-lateral area, upper-central area, lower-central area, upper-medial area and lower-medial area, respectively, as the protocol of EBT3 film placement. If bolus material or virtual bolus was used, the point dose would be obtained from the interface between bolus and patient's skin.

Statistic analysis

The average surface dose and film dose of No.1, 2, 3, 4, 5, and 6 from each skin area were compared between the different treatment techniques with the use of Mann-Whitney test. Furthermore, comparisons of medial surface dose (No.1 and 2), central surface dose (No.3 and 4) and lateral surface dose (No.5 and 6) were also performed using Friedman test. Comparisons of upper surface dose (No.1, 3 and 5) and central surface dose (No.2, 4 and 6) were also performed using Friedman test. This study was approved by the institutional review board as CGH P101029.

Results

Between July 2012 and December 2013, 30 patients were included; 17 patients were assigned to WBRT, 13 patients were assigned to PMRT. The characteristic of these patients was shown as *Table 1*.

Table 1 Characteristics of patients

Characteristics	Number (N=30)	Percent (%)
Median age at treatment (years)	47.5 (34–72)	–
Treatment technique		
IMRT	17	56.7
HT	13	43.3
Surgery		
BCS	17	56.7
MRM	13	43.3
Side		
Left	10	33.3
Right	20	66.7
Pathology stage		
0	2	6.7
I	13	43.3
II	3	10.0
III	10	33.3
IV	2	6.7
T stage		
0	2	6.7
T1	14	46.7
T2	11	36.7
T3	2	6.7
T4	1	3.3
N stage		
N0	16	53.3
N1	4	13.3
N2	4	13.3
N3	6	20.0
M stage		
M0	28	93.3
M1	2	6.7
Image-guided radiotherapy		
Daily CBCT (Synergy)	5	16.7
Weekly CBCT (Synergy)	12	40.0
Daily MVCT (Hi-ART)	13	43.3

IMRT, intensity-modulated radiation therapy; HT, helical tomotherapy; BCS, breast conserving surgery; MRM, modified radical mastectomy; CBCT, cone beam computed tomography; MVCT, megavoltage computed tomography.

In WBRT group, 7 patients received HT and 10 patients received linear accelerated-based IMRT; in PMRT group, 6 patients received HT and 7 patients received IMRT. The detail of treatment planning and dose distribution was shown in *Table 2* and *Figure 3*. Each patient was irradiated by a daily fraction of 2 Gy and three times of skin dose measurement was performed in three consecutive fractions. Totally, 51 times of measurement were performed in WBRT group and 39 times of measurement were performed in PMRT group.

Six-film-piece protocol was unable to be placed properly for 3 patients. Two of them were assigned to WBRT group. One patient's nipple located at relatively lower position so that No.4 EBT3 cannot be placed properly, and the other one has uneven surface of No.3 area. One patient in PMRT group presented with mildly erythematous change of operative scar at the No.3 area of the chest wall, and EBT film placement at that area was not recommended by physician. Five-film-piece protocol applied to these three patients.

WBRT group

Table 3 and *Figure 4A* showed the result of EBT3 measurement and calculated dose by TPS in WBRT group. Patients received WBRT with HT received significantly lower film dose of No.1, 2, 3, 4, 5 and 6 than those with IMRT (P=0.001, 0.001, <0.001, 0.002, <0.001, <0.001, <0.001, respectively). HT also delivered significantly lower average surface dose than IMRT did with a difference of 6.88% of prescribed dose (IMRT versus HT: 86.57% versus 79.69%, P<0.0001). The calculated dose of IMRT in different skin regions was lower than film dose; while calculated dose of HT was higher than film dose in different skin regions.

There was statistically significant dose difference among medial, central and lateral regions of patients received IMRT (84.42%, 89.00% and 87.34% of the prescribed dose, P<0.0001); IMRT delivered higher skin dose to the central regions than to the medial and lateral regions (*Table 4*). By contrast, HT resulted in relatively homogeneous dose distribution (mean dose of medial, central and lateral regions were 80.71%, 80.94% and 79.22%, P=0.199). As *Table 4* showed, there was no statistically significant dose difference between upper and lower regions, whether delivered by IMRT (P=0.088) or HT (P=0.503).

Table 2 Information about treatment planning

Treatment technique	WBRT (N=17)		PMRT (N=13)	
	IMRT (n=10)	HT (n=7)	IMRT (n=7)	HT (n=6)
Median number of IMRT fields	6	–	7	–
Median PTV (mL)[†]	770.39 (531.34–1389.71)	918.78 (626.27–1012.22)	756.58 (454.83–1677.25)	734.47 (531.42–869.48)
Median PTV coverage (%)				
V95%[‡]	99.19% (97.80–99.65%)	99.89% (99.78–99.98%)	98.72% (97.28–99.65%)	99.70% (99.20–99.92%)
V100%[‡]	94.24% (92.08–97.81%)	97.71% (96.88–98.19%)	96.33% (91.77–97.76%)	97.09% (96.64–98.28%)

[†], the PTV of nodal region was excluded; [‡], relative volume. WBRT, whole breast radiotherapy; PMRT, post-mastectomy radiotherapy; IMRT, intensity-modulated radiation therapy; HT, helical tomotherapy; PTV, planning target volume; V95%, PTV receiving ≥95% of the prescribed dose; V100%, PTV receiving ≥100% of the prescribed dose.

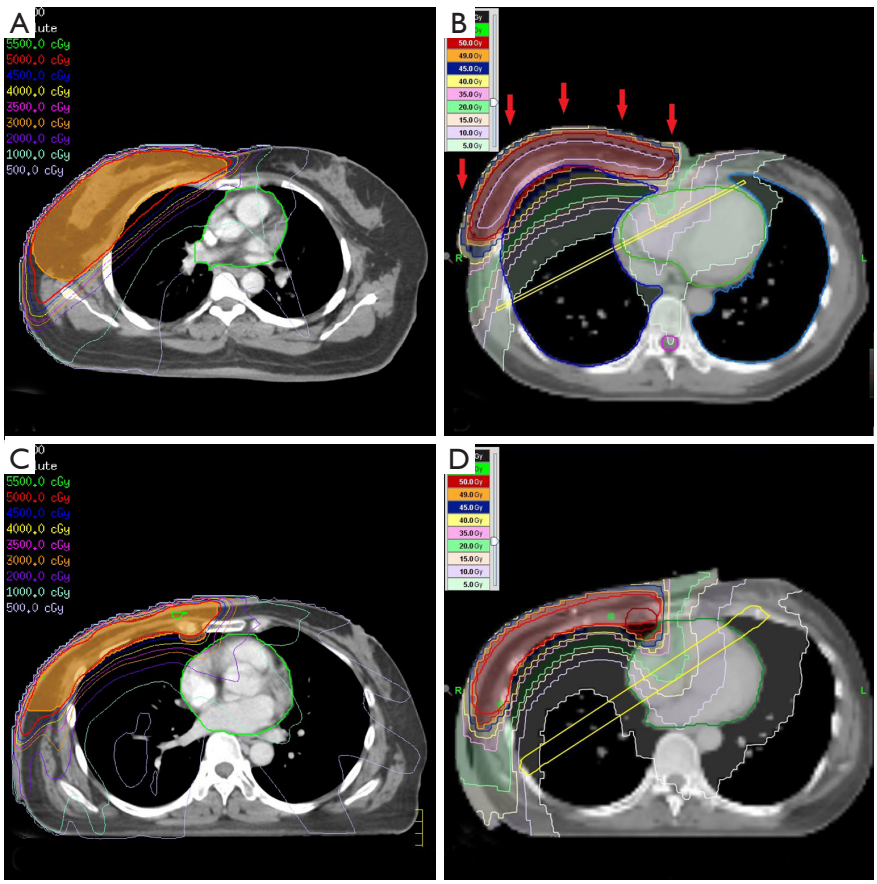

Figure 3 Dose distribution of the treatment technique in WBRT group and PMRT group. (A) IMRT plans for WBRT. (B) HT plans for WBRT (including virtual bolus, marked by red arrows). (C) IMRT plans for PMRT and (D) HT plans for PMRT. The PTV of IMRT plans is displayed in orange; the PTV of HT plans in red. The contour in light purple of the Figure 3B is CTV, which aligns true skin surface. IMRT, intensity-modulated radiation therapy; WBRT, whole breast radiotherapy; PMRT, post-mastectomy radiotherapy; PTV, planning target volume; HT, helical tomotherapy; CTV, clinical target volume.

Table 3 Result of measurement and calculated dose by treatment planning system in WBRT group

Skin area	IMRT group (N=30)		HT group (N=21)		P value
	Mean ± SD (cGy)	Percent (%)†	Mean ± SD (cGy)	Percent (%)†	
No.1					
Film dose	170.27±17.30	85.13	161.83±7.98	80.92	0.001
Calculated dose	124.22±29.93	–	174.86±8.76	–	
No.2					
Film dose	167.23±18.10	83.61	158.64±8.18	79.32	0.001
Calculated dose	110.02±32.16	–	165.43±15.41	–	
No.3					
Film dose	179.67±14.73	89.84	159.92±7.65	79.96	<0.001
Calculated dose	116.78±51.90	–	176.14±5.84	–	
No.4					
Film dose	176.32±18.35	88.16	163.84±9.53	81.92	0.002
Calculated dose	112.63±25.18	–	173.00±14.34	–	
No.5					
Film dose	173.81±14.55	86.90	158.18±10.69	79.09	<0.001
Calculated dose	117.78±24.80	–	182.86±9.99	–	
No.6					
Film dose	174.03±11.26	87.01	156.35±8.50	78.18	<0.001
Calculated dose	115.21±22.47	–	171.00±5.57	–	
Average surface dose					
Film dose	173.15±14.86	86.57	159.38±6.96	79.69	<0.001
Calculated dose	116.27±16.75	–	173.88±4.71	–	

†, the percentage of dose data normalized to prescribed dose of 200 cGy per fraction. WBRT, whole breast radiotherapy; IMRT, intensity-modulated radiation therapy; HT, helical tomotherapy.

PMRT group

The result of EBT3 measurement and calculated dose in PMRT group was shown in *Table 5* and *Figure 4B*. The mean film doses delivered by IMRT and by HT were within 105–110% and 99–101% of the prescribed dose, respectively. Compared to the IMRT, the HT resulted in reduction in average surface dose of 7.06% (IMRT versus HT: 107.34% versus 100.28%, P<0.0001), which was much close to 100% of prescribed dose. Patients received PMRT with HT received significantly lower film dose of No.2, 3, 4, 5 and 6 than those with IMRT (P<0.001, 0.002, <0.001, <0.001, <0.001, respectively). Most of the calculated dose of IMRT in different skin regions was lower than film dose by measurement. Compared to measurement result, HT provided slightly higher calculated dose in skin surface.

Table 6 showed that IMRT delivered 5% higher dose to the lateral regions than medial and central regions (110.49%, 105.92% and 105.52% of prescribed dose, respectively, P=0.014); while lower skin regions received higher skin dose by IMRT than upper regions did with dose difference less than 3% (108.48% versus 106.14%, P=0.002).

On the other hand, in PMRT group with HT, statistically inhomogeneous dose distribution was observed among medial, central, lateral regions, but the dose difference was less than 2% (101.18%, 100.39%, 99.27% of the prescribed dose, respectively; P=0.005).

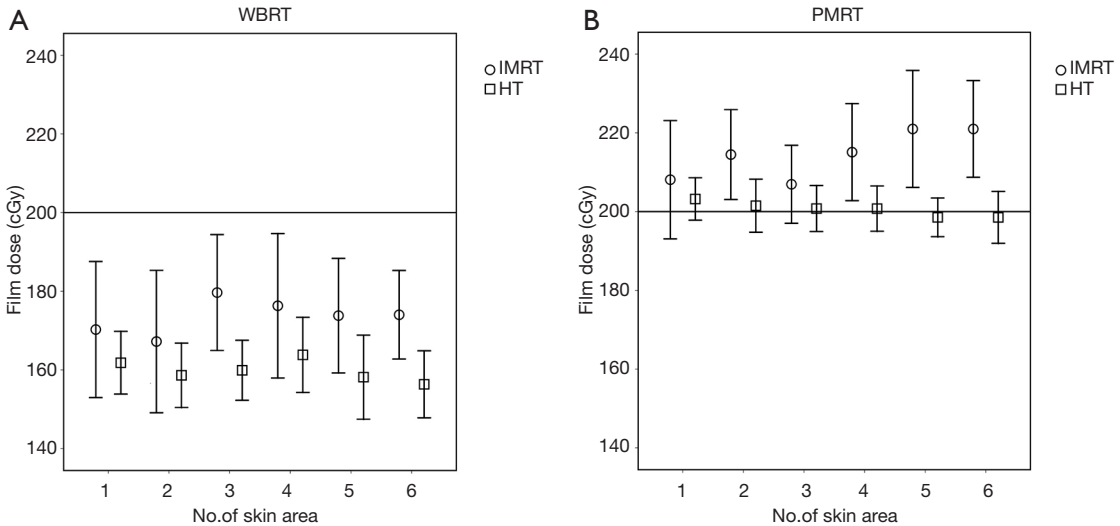

Figure 4 Surface doses for the different planning technique, measured by EBT3 film. (A) WBRT group. (B) PMRT group. The circles and squares reflect the mean surface dose on a distinct skin area with IMRT plans and HT plans, respectively. The horizontal lines represent the prescribed dose with 200 cGy. The bars correspond to ±1 standard deviation from the mean dose measured. IMRT, intensity-modulated radiation therapy; WBRT, whole breast radiotherapy; PMRT, post-mastectomy radiotherapy; HT, helical tomotherapy.

Table 4 Comparisons of skin dose among different skin regions of WBRT group

Region	IMRT			HT		
	Mean ± SD (cGy)	Percent (%)[†]	P value	Mean ± SD (cGy)	Percent (%)[†]	P value
Skin dose of medial region[‡]	168.84±18.44	84.42	<0.001	161.41±7.93	80.71	0.199
Skin dose of central region[‡]	177.99±16.57	89.00		161.88±8.75	80.94	
Skin dose of lateral region[‡]	174.68±13.18	87.34		158.44±9.77	79.22	
Skin dose of upper region[‡]	174.41±15.90	87.21	0.088	159.98±8.92	79.99	0.503
Skin dose of lower region[‡]	172.39±16.44	86.20		159.39±9.10	79.70	

[†], data normalized to prescribed dose of 200 cGy per fraction; [‡], skin dose of medial region: No.1 and 2 film dose; skin dose of central region: No.3 and 4 film dose; skin dose of lateral region: No.5 and 6 film dose; skin dose of upper region: No.1, 3, 5 film dose; skin dose of lower region: No.2, 4, 6 film dose. WBRT, whole breast radiotherapy; IMRT, intensity-modulated radiation therapy; HT, helical tomotherapy.

Discussion

Surface dose of WBRT group

Almberg *et al.* presented results of a phantom study against surface dose of whole breast irradiation using different treatment planning techniques including conventional tangential fields, tangential IMRT and 7-field IMRT plan (15). The surface dose, measured by EBT film on the phantom surface, of conventional tangential fields was 45% to 65% of the prescribed dose. By contrast, the tangential IMRT and 7-field IMRT plan reduced surface dose by approximately 4–5% and 15–50%, respectively. Akino *et al.* also reported that IMRT presented reduction of surface dose compared to standard tangential beams (6). In our study, a median of 6 fields (range from 2 to 7) was used in IMRT plans for WBRT. The surface dose, measured by EBT film on the patient skin, of IMRT was 85–90% of the prescribed dose. Noted that mean surface dose in our study was relatively higher than dose in previous study. The possible reason might be the technique of "skin flash", which delivered more fluence outside the PTV surface, to ensure the coverage of a moving target.

Zibold *et al.* reported the result of surface dose of WBRT using HT, measured by thermoluminescent

Table 5 Result of measurement and calculated dose by treatment planning system in PMRT group

Skin area	IMRT group (N=21)		HT group (N=18)		
	Mean ± SD (cGy)	Percent (%)[†]	Mean ± SD (cGy)	Percent (%)[†]	P value
No.1					
Film dose	208.11±15.02	104.05	203.21±5.38	101.60	0.335
Calculated dose	196.57±19.68	–	207.95±1.07	–	
No.2					
Film dose	214.49±11.42	107.24	201.51±6.76	100.75	<0.001
Calculated dose	208.37±5.83	–	207.31±2.00	–	
No.3					
Film dose	206.94±9.91	103.47	200.78±5.84	100.39	0.011
Calculated dose	210.39±6.80	–	207.09±1.82	–	
No.4					
Film dose	215.11±12.31	107.55	200.76±5.75	100.38	<0.001
Calculated dose	209.19±6.94	–	205.41±1.23	–	
No.5					
Film dose	221.00±14.87	110.50	198.54±4.91	99.27	<0.001
Calculated dose	208.80±4.85	–	206.69±2.17	–	
No.6					
Film dose	221.00±12.29	110.50	198.53±6.58	99.27	<0.001
Calculated dose	209.93±6.68	–	205.08±2.91	–	
Average surface dose					
Film dose	214.67±9.25	107.34	200.55±4.92	100.28	<0.001
Calculated dose	207.21±4.43	–	206.59±1.38	–	

[†], the percentage of dose data normalized to prescribed dose of 200 cGy per fraction. PMRT, post-mastectomy radiotherapy; IMRT, intensity-modulated radiation therapy; HT, helical tomotherapy.

Table 6 Comparisons of skin dose among different skin regions of PMRT group

Region	IMRT			HT		
	Mean ± SD (cGy)	Percent (%)[†]	P value	Mean ± SD (cGy)	Percent (%)[†]	P value
Skin dose of medial region[‡]	211.83±13.96	105.92	0.014	202.36±6.08	101.18	0.005
Skin dose of central region[‡]	211.03±11.77	105.52		200.77±5.71	100.39	
Skin dose of lateral region[‡]	220.97±14.27	110.49		198.54±5.72	99.27	
Skin dose of upper region[‡]	212.27±14.89	106.14	0.002	200.84±5.63	79.99	0.313
Skin dose of lower region[‡]	216.95±12.17	108.48		200.26±6.38	79.70	

[†], data normalized to prescribed dose of 200 cGy per fraction. [‡], skin dose of medial region: No.1 and 2 film dose; skin dose of central region: No.3 and 4 film dose; skin dose of lateral region: No.5 and 6 film dose; skin dose of upper region: No.1, 3, 5 film dose; skin dose of lower region: No.2, 4, 6 film dose. PMRT, post-mastectomy radiotherapy; IMRT, intensity-modulated radiation therapy; HT, helical tomotherapy.

dosimetry (TLD) on static phantom and patients (16). The mean dose on static phantom and patient was 80% of the prescribed dose. Although different dosimeter was used, in our study, similar result was presented that the surface dose of our patient received WBRT with HT was between 78% and 82% of the prescribed dose. The average surface dose delivered by tomotherapy was 7% lower than by IMRT in the WBRT group of prescribed dose, as shown in *Table 3* and *Figure 4A*. The finding of our study was consistent with those of previous studies which showed that more fields with different angle of incidence reduced surface dose (6,15).

Quach *et al.*, who used a hemicylindrical phantom to simulate chest skin and tangential photon beam, reported the maximal surface doses with 58% of prescribed dose was measured at the center with 90 degree of incidence angle, while the surface dose at beam entry position with zero degree of incidence angle was only 28% (17). From the other static phantom study for WBRT, the surface dose of central regions was approximately 20–40% higher than surface dose of medial and lateral regions; both tangential beam and 7-field IMRT provided in similar trend of surface dose distribution (15).

Our result of IMRT presented the same trend as the previous studies, but the difference of surface dose between central and other regions was only 4–5% (*Table 4*). It demonstrated that other factors, such as respiratory motion, set up error and skin flash technique, might eliminate the surface dose heterogeneity on real patient's skin. The relatively small difference might not be worthy to take into account in clinical practice. On the other hand, Tomotherapy delivered relatively homogeneous surface dose distribution in WBRT group with similar surface dose of central and bilateral skin regions (*Table 4*).

Panettieri *et al.* reported that the usual algorithms used for IMRT tend to underestimate the dose in the build-up region in comparison with Monte Carlo simulation (7). Ramsey *et al.* also revealed that the superficial calculated doses were overestimated by HT in comparison with measurement through a phantom study (8). Although the six positions where point dose was obtained in our study were not exactly equal to the positions of EBT3 films, a similar trend was observed in the result of WBRT group (*Table 3*).

Surface dose of PMRT group

Shiau *et al.* reported that four-field IMRT plans obtained more uniform surface dose distribution on static chest wall phantom than tangential wedged field plans did. The tangential wedged fields delivered higher surface dose to the central region than the bilateral border of PTV, with 75% and 51–56% of prescribed dose, respectively; while mean surface dose of four-field IMRT plan was 65% of prescribed dose, ranged from 54–70%, with a relatively uniform dose distribution (18). The dose heterogeneity caused by the oblique incidence, which was demonstrated by Quach et al, was reduced in the IMRT plans with multiple beam angles (17,18).

In our study, tissue-equivalent bolus was used for all patients in PMRT group. Our result indicated that adding bolus materials was effective to elevate skin dose up to 100% of prescription, as shown in *Table 5* and *Figure 4B*. Both of IMRT and HT showed relatively homogeneous skin dose distribution, compared to the result of previous studies of tangential planning (6,15,17,18). The possible reason was that impact of incidence angle and build-up region might be mostly eliminated by the use of bolus materials. Additionally, the use of bolus materials might be also the reason of that calculated dose by TPS in PMRT group was closer to measurement than calculated dose in WBRT group. With 5–10 mm tissue equivalent bolus, skin surface would be away from the build-up region where inverse planning algorithm was unable to provide accurate dosimetry (6-8).

Noted that the lateral skin region received 4–5% higher skin dose than the other skin regions did in the PMRT group with IMRT. HT plans also delivered statistically inhomogeneous skin dose distribution in PMRT group, but the dose difference was less than 2%. Although the quality of dosimetry was strictly controlled through establishing calibration curve of EBT3 films on the same day when measurement was performed, there were other factors which had an impact on dose measurement such as respiratory movement, set up error, daily output, and homogeneity of beam profile. The relatively small dose difference might not be clinically significant.

Skin flash, virtual bolus and bolus

Skin flash technique and virtual bolus were widely used in breast RT to overcome the dose uncertainty caused by respiratory motion (9-12). Sankar *et al.* reported that 20 mm “skin flash” and 20 mm virtual bolus had similar effect to elevate surface dose and reduce hot spot in IMRT (11). In our result, dose difference about 7% of prescription was

observed between 20 mm "skin flash" and 10 mm virtual bolus, despite different planning technique.

In our result of WBRT group, the surface dose did not reach the prescribed dose although skin flash or virtual bolus was used. If skin was defined as high risk area, a better solution to elevate superficial target coverage was covering skin by bolus materials. According to static phantom study, the build-up region for PMRT using 4 fields IMRT on chest wall is at least 2 mm beneath the surface (18). In our study for PMRT, tissue equivalent bolus with 5 mm in thickening and 20 mm skin flash were used in IMRT plans and mean surface dose was 7% higher than prescribed dose.

Kinoshita *et al.* showed that the average intra-fractional motion of the breast is 2.6±1.4 mm (mean ± standard deviation) for vertical direction (19). Considering lack of "skin flash" option in TPS of HT, 10 mm bolus was used for HT plans with more 5 mm in thickening than bolus used in IMRT to compensate the potential intra-fractional motion. In our result of PMRT group, the surface dose about 100% of prescription was obtained using this method.

Tournel *et al.* reported a static phantom study of Tomotherapy to simulate volume reduction with 10 mm bolus material added onto the phantom in the planning phase (20). Surface dose measurement was performed with bolus and repeated without bolus. A 19% drop in surface dose was observed in 10 mm reduction (20). Our result of PMRT group and WBRT group showed that skin surface dose of HT with 10 mm bolus and without bolus was about 100% and 80%, respectively. The efficacy of 10 mm bolus was similar to the result of Tournel *et al.*

Conclusions

Compared to the previous phantom studies, this study provided *in vivo* skin dose dosimetry in clinical situation with potential set up error and intra-fractional respiratory movement of real patients. The major limitation of this study was relatively small sample size and non-randomized design. Besides, the IMRT with Synergy was covered by national health insurance in Taiwan but the Tomotherapy was a self-paid treatment. It might contain bias of patient selection.

With the use of skin flash, virtual bolus or bolus materials, both IMRT and HT provided homogeneous surface dose distribution on the patient received breast RT, compared to result from static phantom studies.

In WBRT group, HT with virtual bolus led to more homogeneous dose distribution and nearing 7% lower surface dose than IMRT with skin flash did. For PMRT, despite lack of skin flash in TPS, HT plus 10 mm bolus still produced 100% of the prescribed dose to the skin surface. HT should be considered to be an option of breast RT and further investigation of correlation between adverse effect of the skin and surface dose distribution would be needed.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tro.2017.11.01). CJW serves as an unpaid editorial board member of *Therapeutic Radiology and Oncology* from Oct 2017 to Sep 2019. The other authors have no conflicts of interest to declare.

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