Evaluation of the Flash effect in breast irradiation using TomoDirect: an investigational study

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Flash is a specified function in TomoDirect that enables beam expansion by opening additional leaves to the target. This study assessed the theoretical dose distribution resulting from Flash in breast irradiation using TomoDirect. A cylindrical phantom that enabled dose distribution of the breast was used for verifying the effect of planning target volume (PTV) contouring and Flash. A total of 18 Gy in 10 fractions were prescribed to the PTV. Five PTVs were then created by Contracting this contour by 0, 1, 2, 3, 4 and 5 mm, giving PTV-\(x\). Flash \(\pm x\) is defined by opening \(x\) (number) of the leaves. The Flash effect in the air was compared with each set-up error of 5, 10 and 15 mm, respectively. The minimum PTV dose from PTV-1 to PTV-3 increased from 13.88 Gy to 15.86 Gy. In contrast, \(D_{\text{min}}\) in PTV-4 and PTV-5 was 17.80 Gy in 98.88% of the prescription dose. Without Flash, when 5-, 10- and 15-mm set-up errors applied in the PTV, relative doses of 87.88, 23.73 and 7.94% were observed, respectively. However, in Flash 3, which was equal to the usual air margin of 1.875 cm, a relative dose of 104.24% \(\pm 0.30\%\) was observed, irrespective of set-up errors (5 mm to 15 mm). Flash opening is useful for countervailing set-up errors in breast cancer patients who receive breast irradiation with TomoDirect.

Keywords: Flash effect; radiation therapy; set-up; TomoDirect

INTRODUCTION

TomoTherapy Hi-Art System (Accuray, Sunnyvale, CA) utilizes an intensity-modulated radiation of 6-MV in a gantry revolving around the patient. It uses megavoltage computed tomography of 3.5 MV to reflect the position of the patient and change in target position to perform image-guided radiation therapy [1–3]. In breast cancer patients, helical TomoTherapy is not a suitable option because the gantry continuously rotates around the patient, and this technique can deliver low-dose radiation to the lungs, which has been associated with an occurrence of radiation pneumonitis [4–6]. Moreover, when the range of the target approaches the air and moves due to respiration, achieving an accurate delivery of radiation to the planning target volume (PTV) is difficult in breast cancer radiation treatment. To avoid this inefficiency of beam usage, a TomoDirect option using static gantry positions combined with simultaneous couch translation and dynamic collimator modulation has been developed [7].

TomoDirect is a delivery mode option that enables non-rotational treatment with the addition of new hardware and software to the existing helical TomoTherapy. A fixed angle can be chosen using TomoDirect as the delivery mode in the planning procedure. The patient comes out of the gantry bore when one gantry angle finishes the investigation on the patient and enters the bore again to be applied at a different angle, repeating the procedure up to a maximum of 12 times [8].

Flash is a function used to enable beam expansion by opening additional leaves to targets. This adds a margin to the PTV by opening a maximum of five leaves in addition...
to the peripheral leaves in the \(-x\) and \(+x\) directions of each beam angle. This approach can be used to achieve more effective treatment results because it can reduce the inaccuracy caused by set-up error and respiration [2]. TomoDirect is also very attractive for radiotherapy departments without conventional Linacs and which are only equipped with helical TomoTherapy units [8]. While Flash is needed, this approach can also reduce treatment time by using a higher dose rate in the specific beam profile of TomoTherapy, which results from the absence of a flattening filter.

In this research, we investigated the effectiveness of Flash in breast irradiation using TomoDirect.

**MATERIALS AND METHODS**

Computed tomography (CT) scanning of 3-mm slices of the entire cylindrical solid water phantom was performed to evaluate the effectiveness of Flash used in breast irradiation. The PTV inside the phantom was divided into two volumes. A semicircular PTV (simulating breast shape) was designed to investigate the effectiveness of Flash at the body–air interface. A rectangular PTV was designed to investigate the effect of depth in the body. The superior–inferior length was set as 3 cm because this was the shortest length able to include the 2.5-cm jaw used in real treatment planning. We used a proper image value-to-density table (IVDT) in body contouring and TomoDirect treatment planning. This IVDT was made in accordance with the CT scanner by matching the CT number in the image with a corresponding real density value [3].

All measurements were performed with an Exradin A1SL ionization chamber (Standard Imaging, Madison, WI) according to the following TG-51 protocol:

\[
D^{Q/W} = M \cdot K_Q \cdot N_{D,W}
\]

[9], where \(D^{Q/W}\) is the absorbed dose to water at the point of measurement and \(M\) is the fully corrected electrometer reading (which has been corrected for ion recombination, polarity and electrometer calibration effects and corrected to standard environmental conditions of temperature (22°C) and pressure (760 mmHg)). The temperature and pressure in our TomoTherapy room was 754.3 mmHg and 21.5°C, respectively. \(K_Q\) is the beam quality conversion factor. The \(K_Q\) value was calculated as a function of the percentage depth dose specified at 10 cm and 100 cm source-to-surface dose for a 10 × 10-cm² reference field size. \(N_{D,W}\) is the absorbed-dose calibration constant, which is specific to the ion chamber.

TomoDirect plans were created and optimized with the TomoTherapy planning system (Hi-Art version 4.0, Accuray Inc., Sunnyvale, CA). For a treatment plan, the field width, pitch, and modulation factor need to be selected. Then, the dose distribution for each beamlet that passes through the target was calculated by a convolution/superposition algorithm. The intensity-modulated radiation therapy (IMRT) mode of TomoDirect for a jaw size of 2.5 cm, a pitch of 0.25 and a modulation factor of 2.0 was set. A normal calculation grid of 0.356 × 0.356 cm² was used in the optimization and calculation processes. A total of 18 Gy in 10 fractions were prescribed to the PTV to mimic the usual breast treatment fraction dose of 1.8 Gy [10]. Each plan involved 100 iterations, and all plans were averaged from at least three trials.

**Comparison of plans depending on the gap between the body surface and the PTV contour**

To investigate the effect of peripheral delineation in the skin direction of the PTV defined by the body contour, PTV\(\pm x\) was set on each PTV semicircle contour (Fig. 1). The PTV refers to the coincidence with body contour and PTV contour, and \(-1\), \(-2\), \(-3\), \(-4\), and \(-5\) refer to the decrease of depth in mm from the body contour to the phantom surface. Beam angles of 270° and 90° were applied using the TomoDirect mode. The settings were planned for all PTV\(\pm x\), and dose parameters were compared by creating dose–volume histograms (DVHs) for the PTV\(\pm x\).

**Comparison of plans according to the number of leaves with Flash in the tangential region**

Flash \(\pm x\) is defined by opening \(x\) number of the leaves. Flash 1 is defined as opening an extra outer leaf with a width of 0.625 cm in a distance from the source axis of 85 cm. Thus, opening five leaves indicates that an extra leaf opening is available to 3.125 cm. To investigate the characteristics of the plan according to the presence of Flash in the phantom, dose distribution parameters of plans were compared using beam angles of 90° and 270°. In order to allow for set-up error and respiration, a margin width of 1.5 to 2 cm was extended from the PTV of the glandular breast tissue when a breast was irradiated [10]. Thus, an investigational plan was designed using Flash 3 that equalled the usual air margin of 1.875 cm, and other plans without Flash were compared for point \(x\) of the tangential region (Fig. 2a).

**Flash effect in the phantom**

Plans for the normal rectangular PTV with Flash 0, 1, 2 and 3 applied in \(-x\) and \(+x\) directions of the cylindrical solid water phantom were designed to investigate the effect of Flash on increasing and decreasing depths inside the phantom. Plans for expanded rectangular PTVs including the entire Flash area were also designed to compare the Flash effects (Fig. 2b). The point doses were compared in the anterior (a, b, c), inner (a, b, c, d) and posterior (a, b, c) of the phantom. Two points of anterior (c) and posterior (a) were included in Flash 1 and two points of anterior (b) and posterior (b) were included in Flash 2 and 3. Anterior (a) and posterior (c) were out of the Flash region.
Flash effect in randomly created set-up error
To investigate the effect of Flash in air, the absolute dose was measured and compared in plans with PTV contouring. The approach compared several plans with either the Flash 3 plan or the non-Flash plan. For each plan, either correct set-up position or random errors of 5 mm, 10 mm and 15 mm in the anterior direction were used. Measurements were made using the A1SL ionization chamber (which was located 10 mm inside the skin for measuring the absolute dose). All measurements were repeated three times. The measured values in coulomb were converted to cGy units.

RESULTS
Relationship between the body contour and PTV delineation
The DVH showed notable gap-related differences between the body and the PTV contour (Fig. 3). The minimum, maximum and average doses for PTV-x are shown in Table 1. The dose parameter of the PTV in places where the body contour and the PTV contour concurred showed the worst dose distribution, with a maximum dose ($D_{\text{max}}$) of 21.29 Gy, a minimum dose ($D_{\text{min}}$) of 9.42 Gy, and an average dose ($D_{\text{avg}}$) of 19.05 Gy. For PTV-x, $D_{\text{max}}$ showed constant values of 20.85 ± 0.034 Gy from PTV-1 to PTV-5. $D_{\text{min}}$ from PTV-1 to PTV-3 increased from 13.88 Gy to 15.10 Gy and then to 15.86 Gy, but it was still smaller than the prescription dose of 18 Gy. In contrast, $D_{\text{min}}$ in PTV-4 and PTV-5 was 17.80 Gy in 98.88% of the prescription doses. Similar to $D_{\text{max}}, D_{\text{avg}}$ showed a constant dose distribution of 18.81 ± 0.03 Gy for all PTV-x. The PTV-4 contour, which has a constant dose distribution below PTV-4, is currently used in the evaluation of the Flash effect in the tangential region and is associated with breast irradiation using TomoDirect. When there was no Flash on PTV-4, the dose at point x was 18.92 Gy (Fig. 4a). When Flash was present, the dose at point x was 19.87 ± 0.035 Gy, a 5% increase regardless of the number of Flash x (Fig. 4b, c and d).

Flash effect inside the phantom
The Flash area dose in the exterior PTV differed from that in the interior PTV when the target was in the Flash area. On the other hand, it stayed constant in PTVs expanded to include the Flash area (Fig. 5). The Flash effect inside the phantom is documented in Table 2. When anterior c was compared with posterior a, anterior c was 2.9% higher in Flash 1, 2 and 3. However, when anterior b was compared with posterior b, the difference in depth was greater, and a 4.5% difference in Flash 1 and 2 and a 5.7% difference in Flash 3 were observed. Doses in anterior a and posterior c
located outside the Flash area did not show any difference with respect to non-Flash, Flash 1 and Flash 2. In contrast, the dose in anterior a was 10% higher than that in posterior c because anterior a and posterior c was close to Flash 3. However, a constant dose of $18.025 \pm 0.064 \text{ Gy}$ was observed in the entire expanded PTV area when Flash 3 was used.

**Verification of the Flash effect on set-up error occurring in the tangential direction of air**

The current TomoTherapy dose rate is 869 MU/min of 869 MU/min, and the actual dose rate in all experiments was $98.28\% \pm 0.04\%$. The relative dose for non-Flash was $97.88\%$ in the absence of set-up errors, and for Flash 3 with an air margin of 1.875 cm applied there was a relative dose of $103.03\%$ (an approximate increase of 5%). However, taking into consideration set-up errors, the non-Flash plan showed significant decreases in radiation doses. When 5-mm, 10-mm and 15-mm set-up errors were applied, relative doses of $87.88\%$, $23.73\%$ and $7.94\%$ were observed, respectively (Fig. 6). However, in Flash 3, which applied a field width of 1.875 cm, relative doses of $104.24\% \pm 0.303\%$ were observed for set-up errors of 5 mm to 15 mm.

**DISCUSSION**

Clinicians usually evaluate radiation dose distributions according to the CT dataset for each patient. In a clinical dosimetric study for human beings, investigators must apply
a radiation dosimeter to the body in order to measure the dose distribution in each patient. Patient consent is compulsory in an ethical approach to such a clinical trial, and it is not easy for us to execute a prospective clinical trial because there is no survival benefit in it for the patient. Thus, we used the entire cylindrical solid water phantom (which simulated the human breast) in order to evaluate the effectiveness of Flash when used in breast irradiation.

Modern radiation therapy has developed with improvements in the treatment equipment. TomoTherapy is a recent equipment innovation, and it can be used to treat multiple targets over the entire body. However, this approach can be difficult for certain therapy sites, such as lung or breast. Imaginary contours have been used in such cases in the past, but the treatment problems for these sites have now been solved with the recent development of TomoDirect delivery mode. Due to the use of a fixed angle, TomoDirect can cause a concentrated dose in sites other than the target. A dose distribution similar to that of fixed-gantry IMRT or conventional 3D conformal radiation therapy (3DCRT) using a linear accelerator can be achieved. Moreover, the beam-on time of TomoDirect during breast irradiation is less than for helical TomoTherapy [7, 8].

The present study investigated the effect of the PTV contour and the use of Flash on the dose distribution for breast radiation treatment planning through the use of a cylindrical phantom. With strength depending on the PTV contour of the target, the dose distribution produced a hot dose in the build-up area during dose optimization through IMRT. When a build-up region of 6-MV was included in the PTV contour of the breast cancer, then a hot spot occurred in the target region. However, the hot dose diminished in the tangential area when the PTV contour was set at 4 mm inside the body contour. In real patient planning, the DVHs showed variation according to the position and distribution of the tumour bed, even in the same prescription. The hot dose was lowest when the tumour bed was only present near the skin.

Fig. 3. The dose–volume histogram is shown according to PTV contouring. The PTV shows the phantom body and the PTV contour concurring. PTV-x shows the length in mm (-1, -2, -3, -4, -5) that was decreased from the body contour into the phantom.

Table 1. Minimum, maximum and average radiation dose in the planning target volume

| PTV delineation | D min (Gy) | D max (Gy) | D avg (Gy) |
|-----------------|-----------|-----------|-----------|
| PTV             | 9.42      | 21.29     | 19.05     |
| PTV-1           | 13.88     | 20.88     | 18.86     |
| PTV-2           | 15.10     | 20.88     | 18.84     |
| PTV-3           | 15.86     | 20.79     | 18.79     |
| PTV-4           | 17.80     | 20.84     | 18.78     |
| PTV-5           | 17.80     | 20.87     | 18.78     |

D min = minimum dose, D max = maximum dose, D avg = average dose, PTV = planning target volume.
Fig. 4. The plan image in tangential area according to the presence or existence of Flash. (A) Flash not applied, (B) Flash 1 applied, (C) Flash 2 applied and (D) Flash 3 applied.

Fig. 5. The Flash effect inside the phantom is shown. Decrease area refers to the area where the depth decreases over the target area. In increase area, the depth increases over the target area. Expanded target area is the area that includes target area, decrease area and increase area.
while the hot dose showed higher values when the tumour bed was distributed both near skin and more deeply into the breast [7].

In breast irradiation, attention must be given to the margin setting that includes the inter- and intrafraction motion of the breast tissue due to breathing. An air space margin of 2 cm is normally applied in breast tissue [11–13]. However, the PTV contour was defined only inside the breast tissue in TomoTherapy [14, 15]. TomoDirect can be used for breast radiation treatment not only because it uses fixed angles, but also because it can include a PTV margin using Flash. After applying the Flash function, the radiation field is expanded with the number of Flash in the beam’s eye view, and beam fluence is also reflected by the same fluence in the Flash region as for non-Flash.

The dose-delivery leaf (present in the peripheral tangential area) PTV-4 contour showed a 5% increase in radiation dose when Flash was used. This result was proven in experiments using a PTV rectangle inside the phantom. Due to the cylindrical shape of the phantom, changes in the beam-passway depth in Flash used in the PTV rectangle were observed. The radiation dose decreased in areas where the depth increased, and the radiation dose increased when the depth decreased. Constant dose distribution was observed when the area encompassing Flash was included in the PTV in the form of an expanded PTV. This effect of Flash could also be observed in randomly created set-up error. When Flash was not used, a dose decrease of 12.12% was observed, even with 5 mm of set-up error. In contrast, when Flash 3 with an air margin of 1.875 cm was used, accurate dose distribution (with changes within 1% for 15 mm of set-up error) was observed. The uncertainty of the tumour bed and set-up error in breast cancer patients is reported to be generally within 10 mm [16, 17]. A maximum of 15.6 mm of PTV margin in the anterior–posterior interfraction variation is required [18].

As a rule, the TomoDirect technique showed superior target coverage and normal tissue sparing as compared with conventional 3D radiation treatment [19–22]. However, some disadvantages exist for breast irradiation using TomoDirect [8]. One disadvantage of treating breast carcinoma with TomoDirect is the presence of hotspots at the beam entrance region due to the 6-MV beam generation of TomoDirect. Another disadvantage of treating breast carcinoma with TomoDirect could be the long beam-on time. In Reynders et al., the average beam-on time with TomoDirect is 2.2 times longer than the average beam-on time with conventional treatment [7]. Thus, physicians must assess the trade-offs of advantage and disadvantage for TomoDirect before choosing the breast irradiation technique.

## CONCLUSION

According to the investigational study of breast irradiation using TomoDirect, Flash, which can be applied to obtain the PTV with a relevant air margin, can reduce the effect of set-up errors in patient positioning.

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