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CLINICAL INVESTIGATION

Accuracy and efficiency of image-guided radiation therapy (IGRT) for preoperative partial breast radiosurgery

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ABSTRACT

Objective: To analyze and evaluate accuracy and efficiency of IGRT process for preoperative partial breast radiosurgery.

Methods: Patients were initially setup with skin marks and 5 steps were performed: (1) Initial orthogonal 2D kV images, (2) pre-treatment 3D CBCT images, (3) verification orthogonal 2D kV images, (4) treatment including mid-treatment 2D kV images (for the final 15 patients only), and (5) post-treatment orthogonal 2D kV or 3D CBCT images. Patient position was corrected at each step to align the biopsy clip and to verify surrounding soft tissue positioning.

Results: The mean combined vector magnitude shifts and standard deviations at the 5 imaging steps were (1) 0.96 ± 0.69, (2) 0.33 ± 0.40, (3) 0.05 ± 0.12, (4) 0.15 ± 0.17, and (5) 0.27 ± 0.24 in cm. The mean total IGRT time was 40.2 ± 13.2 minutes. Each step was shortened by 2 to 5 minutes with improvements implemented. Overall, improvements in the IGRT process reduced the mean total IGRT time by approximately 20 minutes. Clip visibility was improved by implementing oblique orthogonal images.

Conclusion: Multiple imaging steps confirmed accurate patient positioning. Appropriate planning and imaging strategies improved the effectiveness and efficiency of the IGRT process for preoperative partial breast radiosurgery.

Keywords: breast radiosurgery, IGRT, accuracy, efficiency

INTRODUCTION

Postoperative accelerated partial breast irradiation (APBI) using an external beam technique has been commonly used to treat low-risk early breast cancer patients with a smaller volume and larger fractional dose than standard whole breast irradiation (WBI).[1,2] However, outcome data raise concern that soft tissue fibrosis and cosmetic outcomes may be suboptimal with the external beam technique, possibly related to the large volume of tissue treated to high doses in the postoperative setting.[3-5] In contrast, a single large dose using intraoperative radiation therapy (IORT) technique has shown encouraging results in toxicity and cosmesis outcomes.[6,7] While IORT application is limited due to the costly equipment and specialized procedures, a radiosurgery technique using external beam is easily performed by most radiation facilities.

Feasibility of single-fraction partial breast radiation therapy using a radiosurgery technique has been investigated and shown promising early results.[8-14] Treatment of the intact tumor preoperatively allows a significant reduction in high-dose treatment volume with a more accurately defined high-risk target area than a postoperative seroma.[11,15] Definitive radiotherapy with stereotactic body radiotherapy technique has been also studied and showed positive results.[16] Based on these results, phase I and phase II clinical studies were proposed to evaluate preoperative partial breast radiosurgery for early-stage breast cancer patients and approved by the institutional review board (IRB) at our institution. We implemented Intensity modulated radiation therapy (IMRT)[17] and intensive image-guided radiation therapy (IGRT) techniques to treat the patients. This study aims to analyze and evaluate the accuracy and efficiency of the IGRT process used to treat preoperative partial breast radiosurgery patients.

MATERIALS AND METHODS

Treatment Planning

This study included 50 patients who were enrolled in the IRB approved institutional clinical trials (Phase I and Phase II) from August 2009 to February 2017. Patients' CT and MR images were imported into the Eclipse™ treatment planning system (TPS) (Varian Medial Systems, Inc., Palo Alto, CA) and registered to align the biopsy clip that was placed in the tumor or nearby during the biopsy and soft tissue around the tumor using manual rigid-body registration. Gross tumor volume (GTV) was identified by the radiation oncologist with input from a radiologist specializing in breast imaging. Clinical target volume (CTV) was defined with 1 to 1.5 cm margin from GTV, and an additional 0.3 to 0.5 cm margin to CTV was added to define the Planning target volume (PTV). Both CTV and PTV were modified to keep a minimum of 0.5 cm distance from the skin surface to ensure skin sparing. The prescriptions were 15 Gy to the first cohort of 8 patients, 18 Gy to the second cohort of 8 patients and 21 Gy to the remaining 34 patients, all delivered in a single fraction.

All plans used the Eclipse™ TPS with the anisotropic analytical algorithm (AAA version 10.0.28 or higher) with 2.5mm dose calculation grid and heterogeneity correction. Isocenter was set at GTV or as close to GTV as possible at the beginning. For later patients, the isocenter was placed at the level of the GTV in the superior/inferior direction, but at the center of the planning CT in the anterior/posterior and left/right directions (i.e. CT0). IMRT plans were made using 4 to 7 non-coplanar or coplanar beams with 6 MV photons. Early plans were delivered at a dose rate of 600 monitor unit per minute (6MV, 600 MU/min) with the Novalis Tx linear accelerator (Varian Medial Systems, Inc.); later plans were delivered using flattening filter free technology (6MV FFF) at 1400 MU/min with the Truebeam linear accelerator (Varian Medial Systems, Inc.). Gantry and/or couch angles were manually set to avoid collision between the gantry and the patient body or treatment couch, and also to avoid the contralateral breast and heart based on each beam's eye view (BEV). Optimization was performed to provide sufficient coverage for CTV and PTV while sparing the skin, heart, contralateral breast and lung.

Accuracy of Patient Positioning

In the treatment room, a patient was first aligned with the skin marks (from the planning CT scan) and room lasers. As the first IGRT step, initial orthogonal 2D kV images were taken with the on-board imaging (OBI) system (Varian Medial Systems, Inc.). The patient position was corrected by applying the translational couch shift to align the biopsy clip in acquired images with the one in planning images using the 2D/2D matching tool in the OBI system. This shift was recorded as (1) initial 2D/2D shift. Cone-beam CT (CBCT) images were taken to verify the biopsy clip and surrounding soft tissue alignment in 3D display. If the breast shape or overall patient positioning in CBCT did not match with the planning CT, therapists attempted to re-position the patient in the room and then repeated the CBCT images. After the radiation oncologist approved the patient positioning on CBCT matched to the planning CT, the treatment couch was remotely shifted. This shift was recorded as (2) pre-tx 3D shift. Another set of orthogonal 2D kV images were taken to verify the biopsy clip's position prior to treatment. Additional shifts were made if the clip was not aligned and recorded as (3) verification 2D/2D shift. Treatment beams were delivered. For the last 15 patients, mid-treatment 2D kV images were taken in-between treatment beams. If the clip was misaligned by more than 0.3 cm, a correction shift was made. This shift was recorded as (4) mid-tx 2D shift. After all treatment beams were delivered, post treatment orthogonal 2D kV images or CBCT were taken. Shifts were not made, but recorded as (5) post-tx shift. All imaging steps were implemented to achieve

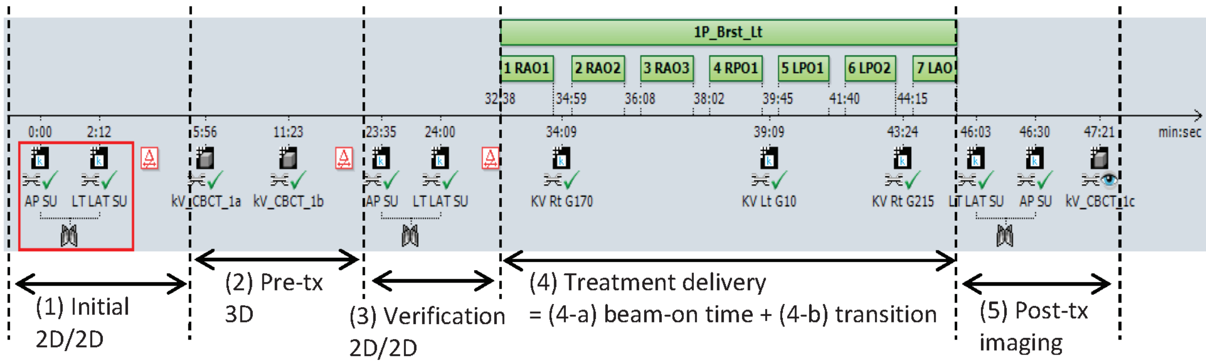

Figure 1. Illustration of the treatment timeline with an indication of time for each step in the IGRT process.

Table 1. Summary of IGRT analysis: mean couch shifts and standard deviations from each imaging step for the vertical, longitudinal and lateral directions and the combined vector magnitude.

	Vertical (cm)	Longitudinal (cm)	Lateral (cm)	Combined vector (cm)
Initial 2D/2D shift	–0.07 ± 0.54	0.23 ± 0.46	–0.16 ± 0.92	0.96 ± 0.69
Pre-tx 3D shift	–0.13 ± 0.35	–0.05 ± 0.19	–0.02 ± 0.30	0.33 ± 0.40
Verification 2D/2D shift	–0.04 ± 0.10	0.01 ± 0.05	0.01 ± 0.04	0.05 ± 0.12
Mid-tx 2D shift	–0.14 ± 0.10	0.00 ± 0.08	–0.01 ± 0.04	0.17 ± 0.19
Post-tx shift	–0.17 ± 0.23	–0.08 ± 0.14	–0.02 ± 0.16	0.27 ± 0.24

and confirm the positioning accuracy by aligning the biopsy clip and surrounding soft tissues.

Efficiency of IGRT Process

To evaluate the efficiency of the IGRT process, the total IGRT time was counted from the time of the first image to the time of the last image utilizing the session timeline in Offline Review (Varian Medical Systems, Inc.). The total IGRT time was divided into 5 steps for further evaluation: (1) time for initial 2D/2D – from the time of the first initial orthogonal image to the time of CBCT image, (2) time for pre-Tx 3D – from the time of CBCT image to the time of the first pre-tx orthogonal image, (3) time for verification 2D/2D – from the time of the first verification orthogonal image to the starting time of the first treatment beam, (4) time for treatment delivery – from the starting time of the first treatment beam to the time of the first post-tx image, and (5) time for post-tx imaging – from the first post-tx image to the last post-tx image. The time for treatment delivery was divided into two segments – (4-a) beam-on time and (4-b) time for transition from one beam to another beam. Beam-on time was calculated by dividing the total MU values from all beams by the dose rate. The transition time included time spent to load a next treatment beam, therapist's time-out, door opening/closing, in-room collision check, couch rotation, mid-tx imaging, etc. It was obtained by subtracting the beam-on time from the treatment delivery time. Figure 1 illustrates how time spent for each step in the IGRT process was obtained.

RESULTS

Accuracy of Patient Positioning

Table 1 summarizes the mean couch shift in three directions (vertical, longitudinal and lateral) and combined vector magnitude for each imaging step to correct the patient position in order to align the biopsy clip. The initial 2D/2D imaging had the largest combined shift among all imaging steps because it was the 1st imaging step to align the clip after patients were positioned based on the skin marks. For the clip had been aligned already in the initial 2D/2D imaging step, the following imaging steps were expected to show very small shifts and majority of patients indeed showed very small shifts.

Table 2. Summary of average IGRT time spent for each IGRT step in minutes.

IGRT step	Time [min]	IGRT step with different techniques	Time [min]
Initial 2D/2D	7.5 ± 4.1	Iso at or near GTV (32 patients)	9.1 ± 4.0
		Iso at CT0 (18 patients)	4.8 ± 2.5
Pre-tx 3D	14.6 ± 9.4		
Verification 2D/2D	4.8 ± 2.6	Non-coplanar beams (15 patients)	6.8 ± 2.5
		Coplanar beams (35 patients)	4.0 ± 2.2
Treatment delivery: Total	11.1 ± 4.7		
Treatment delivery: Beam-on time	4.8 ± 2.2	600MU/min (21 patients)	*8.1 ± 1.7
		1400MU/min (29 patients)	*3.3 ± 0.6
Treatment delivery: Transition**	6.3 ± 3.8	Non-coplanar without mid-tx imaging (15 patients)	8.2 ± 5.9
		Coplanar without mid-tx imaging (20 patients)	4.4 ± 1.3
		Coplanar with mid-tx imaging (15 patients)	6.8 ± 2.1
Post-tx imaging	2.5 ± 3.4		
Total IGRT time	40.2 ± 13.2	Iso at or near GTV, non-coplanar beams without mid-tx imaging, and 600 MU/min (12 patients)	52.8 ± 8.3
		Iso at CT0, coplanar beams with mid-tx imaging and 1400 MU/min (12 patients)	32.5 ± 13.8

* Beam-on time rescaled for the prescription 21Gy for comparison.

**Transition = Treatment delivery time – Beam-on time.

Efficiency of IGRT Process

Table 2 summarizes the time spent for each step in IGRT process. The initial 2D/2D step was 4.3 min faster on average with plans using the isocenter set at CT0 than with plans using the isocenter at or near GTV because therapists could set the gantry and imaging system from the treatment console without the collision concern. The 2nd imaging step took the longest time among all the IGRT steps because of two reasons. First, extra time and effort were spent for some patients due to repositioning and reimaging. Second, this step included a few minutes for the physician to arrive at the treatment console for image review and approval. This waiting time was highly variable and was not separately measured for analysis. The verification orthogonal 2D imaging step included the setting of the 1st treatment beam, and about 2.8 min on average was saved by using coplanar beams because therapists did not go into the room to set the couch rotation and check collision. The beam-on time for each plan was re-scaled for the 21 Gy-prescription for comparison. By using a Truebeam machine with 6X FFF 1400 MU/min, the beam-on time was reduced by 4.8 min on average compared to plans using 600 MU/min. For the transition time, coplanar plans saved about 3.8 min compared to non-coplanar plans without couch rotation and collision concern. The mid-tx imaging step added 2.4 minutes on average for the last 15 patients.

DISCUSSION

The IGRT process with multiple imaging steps was implemented to achieve and confirm positioning accuracy for preoperative partial breast radiosurgery. The goal to align the biopsy clip and surrounding soft tissue for the accurate treatment delivery was achieved with the kV imaging system.[18,19] This study analyzed and evaluated each imaging step for accuracy and efficiency. Through our experience, we implemented improvements in treatment planning and imaging. By setting the isocenter at CT0 and using co-planar beams, the imaging steps and treatment delivery became more efficient as well as safe without collision concern. With the Truebeam FFF technology, beam-on time was reduced. There were 12 cases with all 3 these improvements implemented and 12 cases without any of the improvements. The average total IGRT time for the former was 32.5 ± 13.8 minutes versus 52.8 ± 8.3 minutes for the latter as summarized in Table 2. Overall about 20 min was saved by implementing the improvements.

Not only efficiency but also efficacy was improved through our experience. Mid-tx imaging step was introduced for the last 15 patients as we noticed patient motion from the post-tx imaging. The mid-tx imaging step was critical only for a small subset of patients and took the extra time. However, this step was critical to correct unpredictable patient motion. The last improvement was to improve clip visibility. Due to the long imaging path length, the clip was often not visible even with higher x-ray output (e.g. mAs) and an adjusted irradiation area in the posterior-anterior image. In the lateral image, the clip was sometimes blocked by the breast board plate or sternum depending on the clip location and patient position. Among the first 43 patients, 15 patients had the clip invisible at least in one of orthogonal images. Oblique orthogonal setup beams were introduced to enhance the clip visibility for the last 7 patients, and all images had clear visibility of the clip. This idea was utilized in designing mid-tx imaging. Instead of taking an OBI kV image from the orthogonal direction of each treatment beam angle, 2 to 3 mid-tx images were taken from the lateral or lateral oblique direction to guarantee the clip visibility as well as to detect vertical patient motion.

All patients in this study were positioned prone to separate the tumor from the skin for skin toxicity except for two patients, who had a smaller body habitus and showed greater separation of the tumor from the skin in the supine position[11,20]. Breathing motion control was not implemented as studies found minimal breathing motion for prone breast irradiation[21,22], and two supine patients showed negligible breathing motion in the chest region. In this study, no external device was used to stabilize the breast except the prone breast board for patients' comfort and also to prevent unnatural and unreproducible force to the breast. However, a breast immobilization cup could be considered if a single-fraction treatment can be simulated and delivered within a short time period[23,24].

As the clip was aligned in the initial 2D/2D imaging step, the following imaging steps were expected to show very small shifts. However, large shifts greater than 0.3cm were found for some patients. For the initial 2D/2D imaging, the clip was not visible for 17 patients out of 50 patients in one or both of orthogonal images, and bony anatomy was aligned. Some of these patients in the pre-tx 3D imaging step had the large shifts. Shifts were also contributed by patient motion between two imaging steps. Six patients showed the breast shape noticeably different between CBCT and planning CT. Therapists attempted to re-position the patients in the room and CBCT was taken again. The shift values were obtained from the 2nd CBCT for those patients and contributed to the large shifts because the clip alignment from the initial 2D/2D imaging was not preserved. Such variables emphasize the significance of the pre-tx 3D imaging step.

We noticed that patients rolled down toward the opening area in the prone breast board causing a shift in the vertical direction as they were getting relaxed during the treatment. The verification 2D/2D imaging step was implemented mainly to correct such patient motion for the pre-tx 3D imaging step was lengthy. We found that 8 patients had shifts, which were all in the vertical direction ranged 0.1 – 0.4 cm. Only 4 patients out of the 8 patients had 0.1 to 0.3 cm shift in other directions. The mid-tx imaging was implemented for the last 15 patients to correct such patient motion during the treatment. Among the 15 patients, 3 patients had shifts applied based on the 1st mid-tx images as shifts were greater than 0.3 cm, and only one of the 3 patients had another 0.4 cm shift corrected based on the 2nd mid-tx imaging. The post-tx images confirmed that most shifts were less than 0.2 cm, and the vertical shift was the largest among the 3 directions as expected. The patient motion was very small overall and the treatment was delivered accurately, yet, it could be large enough to be corrected for a small subset of patients. Therefore, multiple imaging steps were necessary to verify the patient motion and correct if needed.

For the accurate positioning, the biopsy clip and surrounding soft tissue were to be aligned and monitored. Our procedure included intensive IGRT procedures. The verification 2D imaging step (i.e. the 3rd step) and the post-tx imaging step (i.e. the last step) were added mainly to verify and confirm; therefore, they could be omitted. We also learned that the 2D kV images did not display the clip clearly when imaged from anterior or posterior directions. Thus, the initial 2D/2D imaging step was not effective for all patients. The 3D CBCT images were more reliable because the breast shape and soft tissue around the tumor could be verified in addition to the clip visibility. The mid-tx 2D images taken from the lateral directions were critical to catch the anterior-posterior shift as patients rolled down even if it took a few minutes and no motion was found for majority patients. We believe that the pre-tx 3D imaging step and mid-tx 2D imaging step were critical for the effective and efficient IGRT procedure.

CONCLUSION

This study analyzed and evaluated the process of preoperative partial breast radiosurgery focusing on the IGRT process. Multiple imaging steps confirmed accurate patient positioning. Appropriate planning techniques and imaging strategies improved the effectiveness and efficiency of the IGRT process for preoperative partial breast radiosurgery.

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Authors' disclosure of potential conflicts of interest

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Author contributions

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Data collection: Sua Yoo and Jennifer O'Daninel
Data analysis and interpretation: Sua Yoo and Rachel Blitzblau
Manuscript writing: Sua Yoo, Jennifer O'Daneil, Rachel Blitzblau, and Janet Horton
Final approval of manuscript: Sua Yoo, Jennifer O'Daniel, Rachel Blitzblau, Fang-Fang Yin, and Janet Horton

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