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PHYSICS CONTRIBUTION

HELICAL TOMOTHERAPY PLANNING FOR LEFT-SIDED BREAST CANCER PATIENTS WITH POSITIVE LYMPH NODES: COMPARISON TO CONVENTIONAL MULTIPORT BREAST TECHNIQUE

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Purpose: To evaluate the feasibility of using helical tomotherapy for locally advanced left-sided breast cancer.

Methods and Materials: Treatment plans were generated for 10 left-sided breast cancer patients with positive lymph nodes comparing a multiport breast (three-dimensional) technique with the tomotherapy treatment planning system. The planning target volumes, including the chest wall/breast, supraclavicular, axillary, and internal mammary lymph nodes, were contoured. The treatment plans were generated on the tomotherapy treatment planning system to deliver 50.4 Gy to the planning target volume. To spare the contralateral tissues, directional blocking was applied to the right breast and right lung. The optimization goals were to protect the lungs, heart, and right breast.

Results: The tomotherapy plans increased the minimal dose to the planning target volume (minimal dose received by 99% of target volume = 46.2 ± 1.3 Gy vs. 27.9 ± 17.1 Gy) while improving the dose homogeneity (dose difference between the minimal dose received by 5% and 95% of the planning target volume = 7.5 ± 1.8 Gy vs. 37.5 ± 26.9 Gy). The mean percentage of the left lung volume receiving ≥20 Gy in the tomotherapy plans decreased from 32.6% ± 4.1% to 17.6% ± 3.5%, while restricting the right-lung mean dose to <5 Gy. However, the mean percentage of volume receiving ≥5 Gy for the total lung increased from 25.2% ± 4.2% for the three-dimensional technique to 46.9% ± 8.4% for the tomotherapy plan. The mean volume receiving ≥35 Gy for the heart decreased from 5.6% ± 4.8% to 2.2% ± 1.5% in the tomotherapy plans. However, the mean heart dose for tomotherapy delivery increased from 7.5 ± 3.4 Gy to 12.2 ± 1.8 Gy.

Conclusion: The tomotherapy plans provided better dose conformity and homogeneity than did the three-dimensional plans for treatment of left-sided breast tumors with regional lymph node involvement, while allowing greater sparing of the heart and left lung from doses associated with increased complications.

Helical tomotherapy, Treatment planning, Breast cancer, Intensity-modulated radiotherapy, IMRT, Radiotherapy, Conventional three-dimensional technique.

INTRODUCTION

Radiotherapy (RT) is a vital component in breast cancer management (1, 2). Conventionally, parallel-opposed tangential beams are used to treat the breast and chest wall tissue. Additional abutting megavoltage photon and electron fields are often added to treat the supraclavicular (SCV), axillary, and internal mammary (IM) lymph nodes (3, 4). Implementation of these complex treatments often results in heterogeneous dose distributions, particularly in the radiation field junctions, in which systematic increases in dose might result in fibrosis (5). Radiation-induced pneumonitis has been reported in approximately 30% of breast cancer patients treated with definitive radiotherapy (6–8). Also, several studies have shown that cardiac mortality due to acute myocardial ischemia can increase for left-sided breast cancer patients treated with three-dimensional (3D) planning because of the exposure of a portion of the left ventricle to high radiation doses (9–13).

Treatment of breast cancer patients with intensity-modulated RT (IMRT) has been studied and demonstrated dosimetric advantages compared with conventional delivery (14–17). Recently, a comparison of helical and static IMRT tomotherapy (18) treatment planning techniques was

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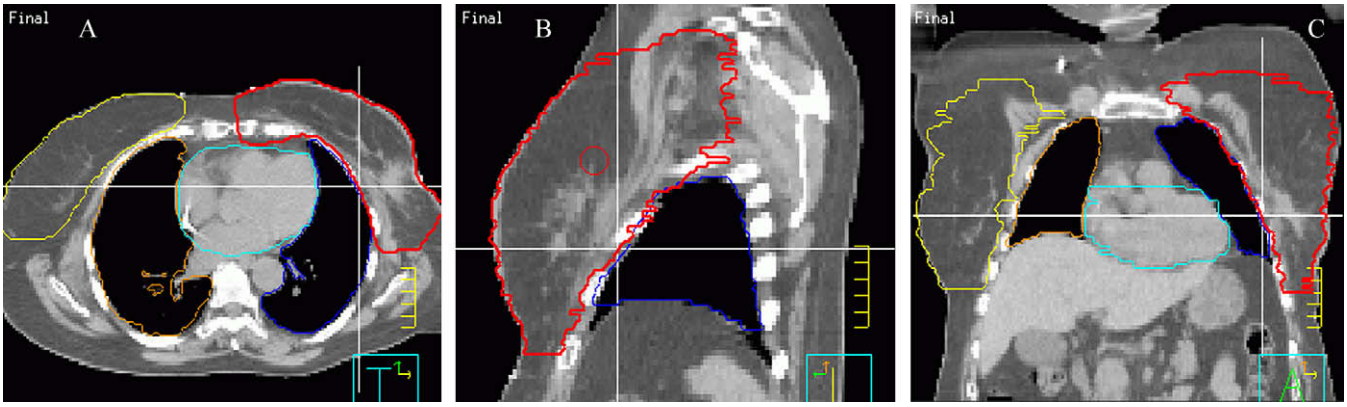

Fig. 1. (A) Transverse, (B) sagittal, and (C) coronal views of typical breast cancer patient showing planning target volume (red), right breast (yellow), left lung (blue), right lung (green), heart (cyan).

investigated for early-stage breast cancer without regional lymph node involvement; however, little has been written concerning helical tomotherapy for patients with nodal involvement. This study compared conventional abutted-beam treatment plans with tomotherapy treatment plans for left-sided breast cancer patients with regional lymph node involvement to evaluate the benefits and limitations of tomotherapy-based IMRT treatments.

METHODS AND MATERIALS

Plans were created on a Tomotherapy treatment planning system (TPS), version 2.0 (Tomotherapy, Madison, WI) for 10 left-sided breast cancer patients with nodal involvement, of whom 7 had undergone mastectomy (2 reconstructed) and 3 were intact. The patients were immobilized using custom-made body molds (19) with either their left arm or both arms raised above their heads. Computed tomography (CT) simulation data sets were acquired with a 16-slice large-bore CT simulator (Brilliance Big Bore, Philips Medical Systems, Cleveland, OH).

CT simulation

Radiopaque wires were placed on the patients at CT simulation to define the field edges for conventional treatment and provide a clinical margin around the palpable breast tissue. The SCV, IM, and axillary lymph node regions were defined using projected bony landmarks.

The lungs, heart, spinal cord, liver, right breast tissue, and a planning target volume (PTV) were delineated for IMRT planning and to evaluate the dose distributions. The medial PTV boundary was placed at the lung–chest wall interface, with a margin around the IM nodal region from the superior aspect of the 2nd rib to the inferior aspect of the 4th rib. More laterally, the posterior border was extended deep enough to cover the Level 1 axillary lymph nodes, generally to the anterior edge of the latissimus dorsi. Anteriorly, the PTV extended to the skin surface (Fig. 1). The CT images and accompanying contours were exported to the Tomotherapy TPS for planning.

Conventional 3D treatment planning

Conventional treatment plans were generated on the Pinnacle TPS (Philips Medical Systems, Cleveland, OH) using parallel-opposed tangential beams for the breast or chest wall tissue, with matching SCV and IM fields. Couch and collimator rotations were used to achieve nondiverging match lines with the SCV fields that used a split field to place the inferior SCV field through the central axis. The tangential fields included 2–3 cm of left lung tissue to cover the medial and lateral aspects of the breast tissue.

Table 1. Three-dimensional planning parameters

			Beam energy			
Pt. No.	Treatment site*	PTV (cm^3)	Medial and lateral tangents (MV)	SCV (MV)	Axilla (MV)	IM (MeV)
1	Chest wall	865	6	6	6	14e
2	Chest wall	898	10	6	—	†
3	Breast	2,167	10	10	6	†
4	Chest wall	1,004	10	6	6	14e
5	Breast implant	1,454	6	6	6	12e
6	Breast implant	667	6	6	—	†
7	Chest wall	701	10	10	—	†
8	Breast	1,780	10	6	6	14e
9	Chest wall	834	10	10	6	†
10	Breast	1,516	10	10	6	†

Abbreviations: Pt. No. = patient number; PTV = planning target volume; SCV = supraclavicular; IM = internal mammary; e = electron.

* Prescription for chest wall/breast: uniform dose of 50.4 Gy in 28 fractions to chest wall; for SCV: 50.4 Gy in 28 fractions at depth of 4–5 cm; for axilla field: to deliver 50 Gy in 28 fractions at mid-plane; and for IM: 50.4 Gy in 28 fractions.

† IM nodes included in tangential beam portals.

Table 2. Tomotherapy optimization parameters

	Importance	Maximal dose (Gy)	Maximal dose pen	DVH volume (%)	DVH dose (Gy)	Minimal dose (Gy)	Minimal dose pen
Tomotherapy PTV	2	50.4	1,215,050	95	50.4	50.4	131
Critical structures						DVH dose pen	
Left lung	2	50.4	1	29	16	59,094	
Right lung	2	10	13	8	5	334,849	
Heart	2	50.4	1	18	18	308,233	
Right breast	2	8	4	10	3	10,303	
Spinal cord	1	23	2	13	16	1	

Abbreviation: pen = penalty.

For each tangential field, three- to six-segment field-in-field modulation was used to homogenize the breast dose (20). The SCV lymph nodes were treated using a single, right-anterior oblique beam. Depending on the bridge separation, either 6- or 10-MV photon beams were used for the tangential fields (Table 1). A uniform dose of 50.4 Gy in 28 fractions was planned for the chest wall and breast; the same prescription was used for the SCV field at a depth of 4.0 cm. When necessary, the axillary lymph node region received a boost with a single posteroanterior beam to deliver a total of 50 Gy at the mid-plane. The IM lymph node chain was either included in the tangential fields or treated using a single, angled, en-face electron beam that was matched at the medial border of the breast tangential fields. The conventional photon beam dose calculations were performed using the convolution-superposition algorithm with tissue heterogeneity corrections. Electron beam doses were computed using a pencil beam algorithm.

Tomotherapy treatment planning

The parameters affecting dose conformity and treatment times for tomotherapy are the field width, pitch, and modulation factor (21). The longitudinal field width is defined by the fan beam width in the craniocaudal direction. The pitch is defined as the ratio of the couch travel per gantry rotation to the field width and is required to be <1.0. The modulation factor is defined as the intensity ratio between the most intense beamlet and the average of all the beamlets. The present study used a 2.5-cm field width, a pitch of 0.28 or 0.42, and a modulation factor of 4. Because of the tangential nature of tomotherapy delivery, no bolus was used in these plans. The target dose–volume prescription is a constraint for the Tomotherapy TPS; therefore, the treatment plan always meets the prescription. In the present study, 93–95% of the PTV was prescribed to receive 50.4 Gy in 28 fractions, with the ultimate goal to attain 99% of the PTV receiving ≥47.9 Gy. To limit the dose to the right lung and right breast tissue, directional blocking was applied to the right breast and lung, thus disabling the primary beam if the blocked structure was proximal to the target, but not if the beamlets entered the target first. The normal organ doses were limited to <5 Gy to the right lung and right breast. The heart volume receiving 25 Gy was limited to <10%, and the 35-Gy volume was minimized. The mean dose to the left lung was limited to 12 Gy, and an attempt was made to keep the 20-Gy volume to <22% (14). Finally, the 5-Gy volume of the total lung was restricted to <42% (Table 2).

Plan evaluation parameters

Dose–volume histograms were computed for the PTV and critical structures. The indicators of target dose homogeneity (20) were the dose difference between the minimal dose received by 5% and 95% of the PTVs (D_5-D_{95}); the percentage of the PTV receiving 95% (47.9 Gy) to 105% (52.9 Gy) of the prescription dose ($V_{95\%}-V_{105\%}$); and the difference between the PTVs receiving 109% dose and 95% of the dose ($V_{95\%}-V_{109\%}$). D_5-D_{95} is expressed as a percentage of the prescription dose.

The minimal and maximal doses were characterized by volumetric rather than single-voxel evaluations. The minimal dose was selected as the dose such that 99% of the PTV had a greater dose. The maximal dose was the dose to the hottest single 2-cm^3 region of the PTV.

Normal structure dosimetric indexes, such as the mean lung dose (MLD) (22), 20-Gy volume (23), 30-Gy volume (24), and, recently, 5–65-Gy volume (25), have been shown to be important in predicting radiation-induced pneumonitis and, therefore, were used in the treatment plan comparisons. For the right lung, the MLD and

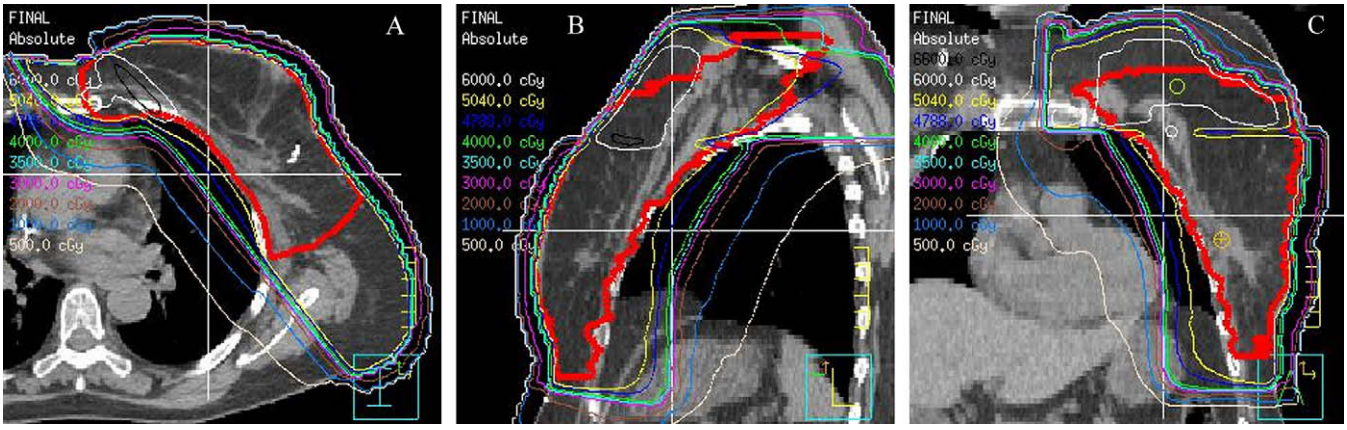

Fig. 2. (A) Transverse, (B) sagittal, and (C) coronal views showing isodose lines from conventional multiport breast treatment planning on Pinnacle treatment planning system.

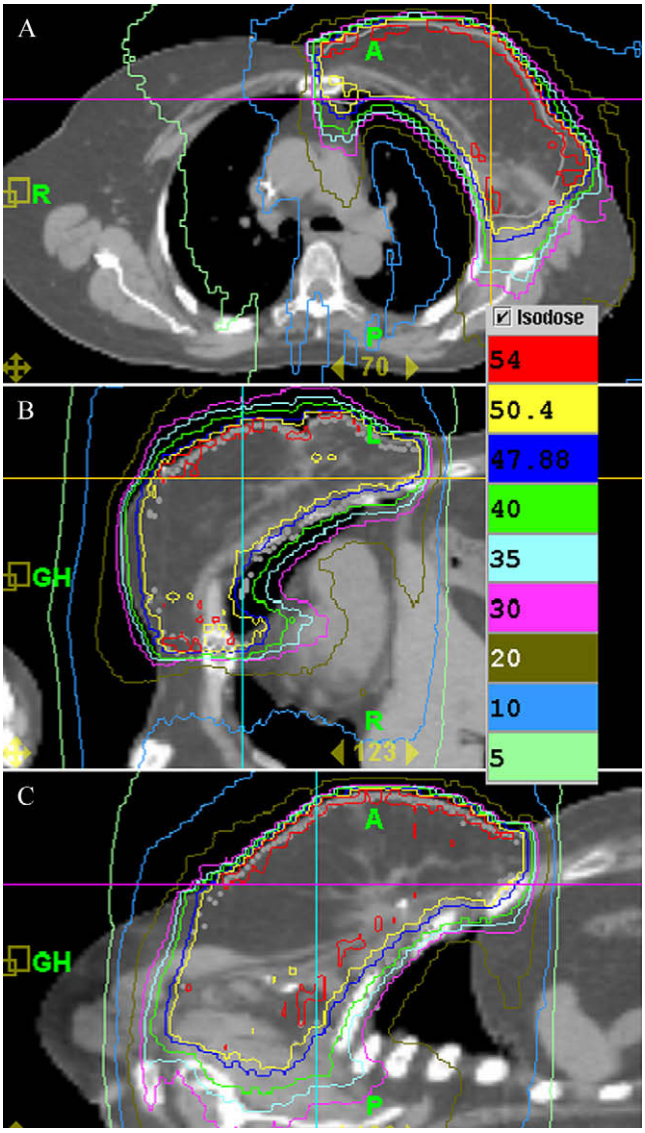

Fig. 3. (A) Transverse, (B) coronal, and (C) sagittal views showing isodose lines from typical tomotherapy treatment plan.

volumes of lung receiving doses of 5 Gy and 10 Gy were evaluated. Similarly, for the total lung volume, the MLD and percentage of volume receiving 5–45 Gy were compared. For right breast tissue, the mean dose, 5-Gy volume, and 10-Gy volume are reported. The dose–volume metrics for unspecified tissue, derived by subtracting the PTV, total lung, right breast, and heart volumes from the external body volume, were also evaluated.

RESULTS

A typical dose distribution from conventional multiport (3D) breast treatments is shown in Fig. 2. A 130% hot spot at the junction between the tangential photon and intramammary electron fields (Fig. 2A) is typical in 3D planning and resulted from the depth dependence of the electron beam penumbra. In some patients, a small portion of the PTV rested outside the 3D beam portals and did not receive the prescription dose. Isodose curves from a representative tomotherapy treatment plan (Fig. 3) were highly conformal to the PTV. The average modulation factor for these plans was 4.09 ± 0.14 (range, 4.01–4.39). The treatment delivery times varied from 12.2 to 16.8 min (average, 14.6). The average couch travel distance was 26.3 cm (range, 24.3–29.6). Finally, the gantry rotation period varied from 21 to 34.9 s (average, 25.8 ± 4.4). The treatment plan comparisons of the present study for the PTV and critical structures are summarized in Tables 3 and 4. Figure 4 shows the dose–volume histogram comparisons, along with their standard deviations. The dose homogeneity in the PTV was significantly improved in the tomotherapy plans compared with the 3D plans, as was the sparing of the critical structures.

Target volumes

The results showed that the average minimal dose (minimal dose to 99% of target volume) increased from 27.9 ± 17.1 Gy for 3D planning to 46.2 ± 1.3 Gy for tomotherapy. The average D_5-D_{95} value for tomotherapy (7.5% ± 1.8%) was about four times smaller than that for the 3D plans (37.5% ± 26.9%). The $V_{95\%}-V_{105\%}$ (ideally 100%) was also smaller for 3D planning (45.0% ± 25.6%) than for tomotherapy planning (80.8% ± 21.2%). The average value of $V_{95\%}-V_{109\%}$ for the tomotherapy plans was 96.6% ± 2.3% and was 66.0% ± 18.8% for the 3D plans. The PTV covered by the 95% isodose line in the tomotherapy plans was 98.0% ± 0.8%. The average hotspot for the 3D plans was 132.8% (66.9 ± 8.2 Gy), significantly greater than the 106.8% (53.8 ± 0.6 Gy) hotspot in the tomotherapy plans. The larger hotspots found in the 3D plans resulted from prescribing the IMC electron beam to the 90% isodose and the electron IMC field scatter into the abutting tangential photon fields.

Left lung

As shown in Table 4, the average MLD for the left lung was greater for the 3D breast treatments (16.6 ± 1.8 Gy) than for the tomotherapy ones (11.9 ± 1.4 Gy). Except for the 5-Gy volume, all other volume indexes revealed that the tomotherapy plans spared the left lung much better than did the 3D plans.

Right lung

The average MLD for the right lung was greater in the tomotherapy plans (4.2 ± 1.0 Gy) than in the conventional 3D plans (1.0 ± 0.4 Gy). The percentage of volume receiving 5 Gy and 10 Gy were smaller for 3D than for tomotherapy (Table 4) because with 3D planning, no primary or exit beams passed through the right lung and the tomotherapy treatment plans allowed beams to exit through this volume.

Total lung

The total lung MLD was greater for the 3D plans (8.0 ± 1.0 Gy) than for the tomotherapy plans (7.6 ± 1.0 Gy). The percentage of total lung receiving 20 Gy was smaller (7.9% ± 1.2%) for tomotherapy than for 3D (14.8% ± 2.0%). Except for the 5-Gy volume (46.9% ± 8.2% for tomotherapy and 25.2% ± 4.2% for 3D), all other volumes were

Table 3. Plan evaluation parameters for conventional multiport and tomotherapy plans

	Conventional multiport		Tomotherapy	
PTV	Range	Mean ± SD	Range	Mean ± SD
Mean dose	52.2–55.2	53.8 ± 1.3	50.8–53.1	51.6 ± 0.7
D_{99} (Gy)	6.3–46.7	27.9 ± 17.1	43.6–48.0	46.2 ± 1.3
D_5–D_{95} (%)	8.7–102.7	37.5 ± 26.9	5.6–11.3	7.5 ± 1.8
$V_{95\%}$–$V_{105\%}$ (%)	15.0–93.0	45.0 ± 25.6	26.1–95.5	80.9 ± 21.2
$V_{95\%}$–$V_{109\%}$ (%)	39.2–95.0	66.0 ± 18.8	91.0–98.4	96.5 ± 2.3
$V_{47.9}$	79.0–96.0	90.1 ± 5.2	96.7–99.1	98.0 ± 0.8
$V_{52.9}$	3.0–78.4	45.0 ± 24.9	3.1–71.9	17.3 ± 20.7
$V_{54.9}$	1.0 –54.4	24.1 ± 17.8	0.0–5.8	1.5 ± 1.8
$V_{60.5}$ (120%)	0.0–18.5	5.3 ± 5.8	0.0	0.0
$V_{65.5}$ (130%)	0.0–4.4	1.4 ± 1.8	0.0	0.0
$HS_{(R=7.5mm)}$	66.0–72.1	69.4 ± 2.6	53.9–56.4	54.8 ± 1.2

Abbreviations: PTV = planning target volume; SD = standard deviation; D99 = minimal dose received by 99% of target volume; D_5–D_{95} = percentage of planning target volume receiving 95% (47.9 Gy) to 105% (52.9 Gy) of prescription dose; $V_{95\%}$–$V_{105\%}$ = percentage of volume receiving doses of 47.9–52.9 Gy; $V_{95\%}$–$V_{109\%}$ = percentage of volume receiving doses of 47.9–54.9 Gy; $V_{47.9}$, $V_{52.9}$, $V_{54.9}$, $V_{60.5}$, $V_{65.5}$ = percentage of volume receiving ≥47.9, ≥52.9, ≥54.9, ≥60.5, ≥65.5 Gy, respectively; $HS_{(R=7.5mm)}$ = hot spot defined by the hottest single 2cc region.

smaller for tomotherapy than for 3D. Limiting the 5-Gy volume to <42% of the total lung was difficult in the tomotherapy plans without increasing the dose to the heart.

Heart

The mean heart dose was greater for the tomotherapy plans (12.2 ± 1.8 Gy) than for the 3D plans (7.5 ± 3.4 Gy). However, both the 25-Gy and 35-Gy volumes for the tomotherapy plans (25-Gy volume = 7.4% ± 3.0% and 35-Gy volume = 2.2% ± 1.5%) were smaller than with the 3D plans (25-Gy volume = 8.6% ± 5.9% and 35-Gy volume = 5.6% ± 4.8%). The mean dose to the heart could have been further reduced by allowing more of the left lung volume to receive >5 Gy.

Right breast

The average mean dose to the right breast was greater for the tomotherapy plans (4.3 ± 0.7 Gy) than for the 3D plans (2.3 ± 1.2 Gy). The volume receiving >5 Gy for tomotherapy (29.2% ± 8.7%) was also greater than for 3D (4.2% ± 3.0%). However, the average volume receiving >10 Gy was smaller for tomotherapy (2.7% ± 1.7%) than for the conventional treatment (3.5% ± 2.7%).

Unspecified tissue

The volume receiving >5 Gy for the tomotherapy plans (56.9% ± 13.0%) was two to three times greater than for the 3D plans (20.8% ± 4.5%). However, the average volume receiving >50 Gy was one-half for tomotherapy (2.2% ± 1.0%) relative to 3D (4.4% ± 1.5%).

DISCUSSION

Dosimetry of PTV

As expected, the dose conformity and homogeneity of the PTV were superior using tomotherapy. An independent examination of the dose–volume metrics for each of the 10 patients showed that, with exception of the heart, within each treatment planning category (3D or tomotherapy), the dose–volume parameters did not vary widely among patients; thus, their mean and standard deviation values are presented. A difference was seen in the heart irradiation between the electron and deep tangent treatments with the 3D treatment plans. When electrons were used, the mean dose to the heart was increased by 2.5 Gy; however, the left ventricle volumes receiving ≥40 Gy were approximately half.

To understand the relevance of the differences between the treatment planning approaches, we compared our results with those of Fogliata *et al*. (16), who created conventional IMRT plans for left-sided advanced-breast cancer patients, evaluating the results of 10 TPSs. They used similar criteria for PTV delineation as were used in the present study and found that the range of minimal PTV doses was 24.8–40.8 Gy. The average minimal dose from tomotherapy (46.2 ± 1.3 Gy) was greater than the entire range reported by Fogliata *et al*. (16). The average hotspots in that study were slightly greater (112–114%) than for the tomotherapy plans (107%) in our study and the 95-Gy volume was smaller (90.7% ± 1.6%) than for tomotherapy (98.0% ± 0.8). Krueger *et al*. (26) found similar results.

In most cases, the minimal PTV dose was near the skin surface, where dosimetric uncertainties in the calculation can be as greater as 14% (27, 28). The superficial dose overestimation is expected to be smaller with tomotherapy than with conventional TPSs using tangential or fixed IMRT fields.

Radiation-induced pneumonitis

The risk of radiation-induced pneumonitis (RP) is well documented in published studies (6, 29, 30). The Cancer and Leukemia Group B 9344 study (31–33) has been highly influential in increasing the use of taxanes (docetaxel or paclitaxel) as adjuvant therapy to RT. The addition of paclitaxel has been shown to elevate the RP risk to 14% (6, 33) in breast

Table 4. Plan evaluation parameters for conventional multiport and tomotherapy plans

	Conventional multiport		Tomotherapy	
Variable	Range	Mean ± SD	Range	Mean ± SD
Left Lung				
Mean dose (Gy)	13.8–19.5	16.6 ± 1.8	9.6–14.8	11.9 ± 1.4
V_5	42.2–72.0	53.7 ± 9.6	57.2–85.2	73.7 ± 8.5
V_{10}	34.3–51.1	41.2 ± 6.1	25.2–44.8	34.7 ± 5.5
V_{20}	28.2–41.4	32.6 ± 4.1	12.3–24.6	17.6 ± 3.5
V_{30}	24.6–35.2	30.0 ± 4.0	5.5–15.7	8.9 ± 3.2
V_{40}	15.9–25.4	20.7 ± 3.0	0.7–8.5	2.9 ± 2.2
V_{45}	9.0–17.9	14.2 ± 2.6	0.1–4.8	1.1 ± 1.4
Right lung				
Mean dose (Gy)	0.5–1.7	1.0 ± 0.4	2.1–5.7	4.2 ± 1.0
V_5	0.0–6.3	2.1 ± 2.2	4.8–46.0	25.7 ± 12.2
V_{10}	0.4–3.8	1.2 ± 1.4	0.4–8.2	3.0 ± 2.5
Total lung				
Mean dose (Gy)	6.1–9.4	8.0 ± 1.0	6.3–10.0	7.6 ± 1.0
V_5	18.1–31.1	25.2 ± 4.2	36.6–60.6	46.9 ± 8.4
V_{10}	13.9–24.0	19.0 ± 2.8	12.1–24.2	17.0 ± 3.1
V_{20}	12.2–19.0	14.8 ± 2.0	5.8–10.4	7.9 ± 1.2
V_{30}	9.1–16.4	12.3 ± 2.1	2.6–5.8	3.9 ± 1.0
V_{40}	6.0–11.4	9.2 ± 1.5	0.3–2.3	1.2 ± 0.6
V_{45}	3.0–8.2	6.3 ± 1.6	0.1–0.8	0.4 ± 0.2
Heart				
Mean dose (Gy)	2.5–12.1	7.5 ± 3.4	9.8–15.4	12.2 ± 1.8
V_{25}	0.0–16.3	8.6 ± 5.9	3.8–12.9	7.4 ± 3.0
V_{35}	0.0–13.3	5.6 ± 4.8	0.4–4.9	2.2 ± 1.5
V_{45}	0.0–10.7	2.4 ± 3.7	0.0–0.7	0.3 ± 0.3
Right breast				
Mean dose (Gy)	0.4–4.0	2.3 ± 1.2	3.1–5.1	4.3 ± 0.7
V_5	0.6–14.0	6.6 ± 4.2	12.7–41.2	29.5 ± 8.8
V_{10}	0.4–10.3	4.8 ± 2.9	0.2–5.2	2.8 ± 1.7
Unspecified tissue				
V_5	13.6–25.5	20.8 ± 4.5	32.9–73.6	56.9 ± 13.0
V_{10}	11.4–23.0	17.5 ± 3.7	22.4–52.0	38.5 ± 9.9
V_{20}	9.7–20.9	15.1 ± 3.5	13.7–30.4	21.8 ± 6.3
V_{30}	8.3–19.2	13.0 ± 3.3	5.7–17.2	11.9 ± 3.7
V_{40}	6.0–13.0	9.3 ± 2.4	2.8–10.1	6.7 ± 2.3
V_{50}	1.4–7.0	4.4 ± 1.5	0.9–3.8	2.2 ± 1.0

Abbreviations as in Table 3.

cancer patients. According to data from lung cancer RT patient populations, the probability of developing Grade 2 RP was low for patients who received 20 Gy to <22% of the normal lung volume (23). The RP risk correlated well with the MLD and 30-Gy volume (24). Little is known about the consequence of irradiating large volumes of lung tissue to a low dose (~5 Gy). The results of the present study revealed that the left lung volume receiving >20 Gy was reduced in the tomotherapy plans compared with the 3D plans. The mean left lung dose reported by Fogliata *et al.* (16) (12.8 ± 2.0 Gy for the best analyzed case) was greater than that with tomotherapy planning (11.9 ± 1.4 Gy). The average MLD for the right lung from that study (6.1 ± 0.3 Gy for the Hyperion TPS) and from the study by Krueger *et al.* (26) (5.8 ± 1.8 Gy) were also greater than that with tomotherapy (4.2 ± 1.0 Gy).

Cardiac toxicity

Doses of 25 Gy to the heart have been shown to induce temporary perfusion defects (12). Pericarditis is a rare toxicity that occurs in <1% of left-sided breast cancer patients (9–13) treated using conventional 3D techniques. Furthermore, studies (34) have shown no increase in ischemic heart deaths at 12 years after RT. Roychoudhuri *et al.* (10) reported that left-sided breast cancer patients had a 25% greater risk of both ischemic heart disease and cardiovascular disease compared with right-sided breast cancer patients. The results of the present study revealed that the tomotherapy plans effectively protected heart tissue from receiving toxic doses compared with conventional 3D plans. The mean heart dose for tomotherapy (12.2 ± 1.8 Gy) was comparable to that in the study by Fogliata *et al.* (16) (range, 8.7–21.1 Gy), primarily because of the increase in the low-dose volume, the clinical consequences of which are unknown.

Secondary breast cancers

The average mean dose to the right breast tissue was greater with the tomotherapy plans than with the conventional 3D plans. Boice *et al.* (35) retrospectively studied 41,109 breast cancer patients treated between 1935 and

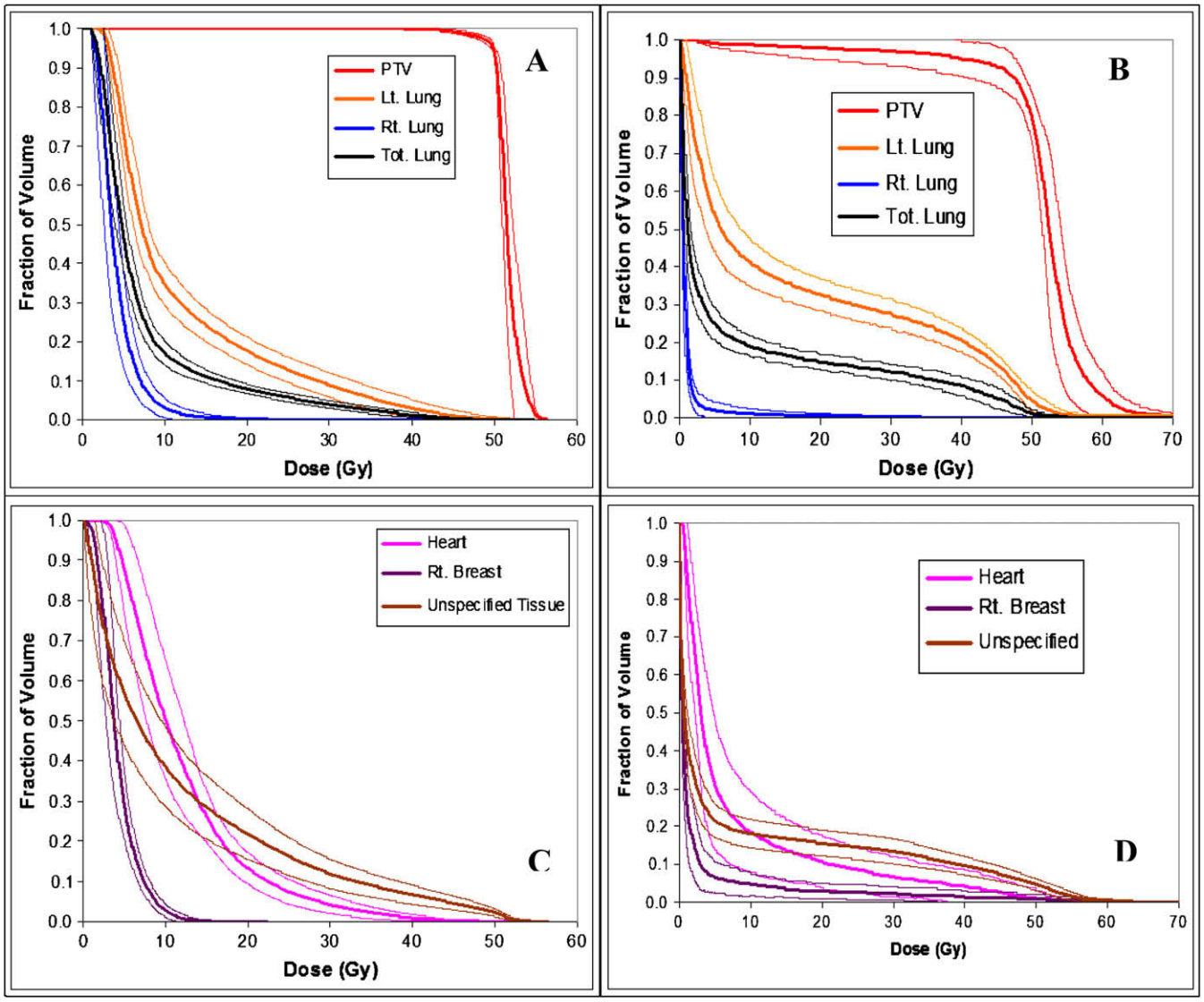

Fig. 4. Cumulative dose–volume histograms comparing three-dimensional breast plans against tomotherapy plans. Solid lines represent mean dose–volume histograms and dashed lines indicate standard deviations. (Top) Planning target volume (PTV) of left (Lt) lung, right (Rt) lung, and total (Tot) lung for (A) conventional three-dimensional multiport breast treatment plans and (B) tomotherapy plans. (Bottom) Skin-planning target volume of right breast and heart for (C) conventional three-dimensional multiport breast treatment plans and (D) tomotherapy plans.

1982 for secondary right-sided breast cancer. The study included 655 women who did, and 1189 women who did not, develop secondary breast cancer. These investigators reported a relative risk of only 1.19 for developing secondary breast cancer associated with RT. Their estimated average radiation dose to the right breast was 2.82 Gy, with a maximum of 7.1 Gy. Therefore, the risk of secondary breast cancers from a mean right breast dose of 4.3 $\pm$ 0.7 Gy (15 cGy/fraction) might not be significant.

Unspecified tissue

The increased unspecified tissue dose in tomotherapy treatments might come from two sources: (*1*) an increase of leakage radiation caused by the use of greater monitor units in the tomotherapy plan; and/or (*2*) irradiation of a greater normal tissue volume in the tomotherapy plans compared with the conventional 3D breast plans. The average number of monitor units used in the tomotherapy and 3D plans was 12,415 and 517, respectively. Ramsey *et al.* (27), however, reported that the peripheral dose from tomotherapy delivery was less than or equal to that of other IMRT deliveries that are typically greater than conventional 3D techniques. On average, the volume receiving <5 Gy with tomotherapy would be 2.7 times greater than with 3D, but the volume receiving a high dose (>30 Gy) would be halved. The clinical consequences of these differences are unknown.

CONCLUSION

Tomotherapy planning resulted in better dose homogeneity and conformity compared with 3D planning, while simultaneously decreasing the dose to the heart and left lung. The

low-dose volumes (percentage of volume receiving ≥5 Gy) and the average mean doses to the contralateral lung and breast tissues were slightly greater for tomotherapy, but they remained lower or comparable to those with conventional IMRT (16). The clinical consequences are unknown but should not be ignored. The average mean dose to the heart was greater with tomotherapy than with conventional multiport breast treatments but the 25-Gy and 35-Gy volumes were smaller for the tomotherapy plans than for the conventional multiport breast plans. Hence, tomotherapy might offer several dosimetric advantages in the treatment of locally advanced left-sided breast cancer.

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