TOMOTHERAPY FOR POST-MASTECTOMY RADIOTHERAPY (PMRT): COMPARISON WITH CONVENTIONAL ELECTRON BEAM TECHNIQUE

A THESIS

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by
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This work is dedicated to my late grandmother,
Adada
rest in peace

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Abstract

Purpose: TomoTherapy, capable of delivering intensity-modulated, image-guided radiotherapy with a helical fan-beam, multileaf-collimated beam and detector array mounted on a CT ring, is challenging the treatment techniques commonly used in today's radiotherapy clinic. The present works investigates the potential of using TomoTherapy in lieu of electron beams for treatment of the chest wall in post-mastectomy radiotherapy (PMRT). It is hypothesized that TomoTherapy can plan dose distributions for PMRT patients, that a pre-selected radiation oncologist judges to be equal to or better than that of a conventional plan treated with electron beams.

Methods: A patient database of retrospective conventional PMRT treatment plans was generated, including contoured target and critical structure region-of-interest volumes. A TomoTherapy plan was generated for five patients out of the database using the same treatment criteria as the conventional plan. The TomoTherapy plan and the conventional plan was evaluated and compared by a radiation oncologist using a simplified scoring system. Physical and radiobiological dose metrics were generated from the treatment plans to supplement the evaluation of the radiation oncologist.

Results: Four of the five TomoTherapy plans were rated superior to the rival conventional electron beam treatment plan, and the other Tomotherapy plan was rated marginally superior. The TomoTherapy plan was able to spare the ipsilateral lung and heart of excessive dose as well as the conventional plan, while delivering a more homogeneous dose distribution to the target volumes. However, the TomoTherapy plan showed the contralateral breast receiving an average dose of 2.9 Gy as opposed to 0.4 Gy for the conventional electron beam plan, and a greater volume of normal tissue outside

the target volumes receiving dose between 5 and 25 Gy (average percent volume was

33% for the TomoTherapy plan and 5 % for the electron beam plan). This could affect

the radiation oncologist's decision to use TomoTherapy for younger patients who are at

greater risk of developing radiation-induced secondary cancers.

Conclusion: The study showed TomoTherapy can deliver dose distributions the radiation

oncologist judges to be equal to or better than that of a conventional electron beam

PMRT plan for five treatment plans.

Chapter 1
Introduction

1.1. Overview

During the last decade, the radiotherapy clinic has seen numerous advances in technology designed to deliver practical and highly conformal dose distribution that better spare critical organs while dosing planning PTV volumes (PTVs) to tumorcidal levels. Intensity-modulated radiotherapy (IMRT), using multi-leaf collimators and advanced 3D treatment planning systems capable of inverse planning, is the most well known recent advance in radiotherapy technology (Galvin et al. 2001). IMRT with the help of a computerized optimization algorithms provides variable-intensity fields that replace uniform intensity ones. Typically, IMRT improves PTV coverage and conformality and reduces PTV dose inhomogeneity. The principle of IMRT is to treat a patient from a number of different directions (or continuous arcs) with beams of non-uniform fluences, which have been optimized to deliver a high dose to the PTV volume and acceptable low dose to the surrounding normal structures (Khan 2003).

Tomotherapy is a novel approach to the delivery of IMRT (Mackie et al. 1993). Figure 1 shows TomoTherapy Hi-Art System developed by the TomoTherapy Inc. (Madison, WI) was designed to provide tomotherapy in a helical motion much like current CT machines acquire images. TomoTherapy delivers photon IMRT dose distributions with a continuously rotating, helical fan beam using a binary multi-leaf collimator, and it utilizes an onboard mega-voltage computerized tomography system (MVCT) that allows for image-guided radiotherapy (IGRT). As in an ordinary helical computed tomography (CT) scanner, the patient is continuously translated through a ring gantry as the fan beam rotates.
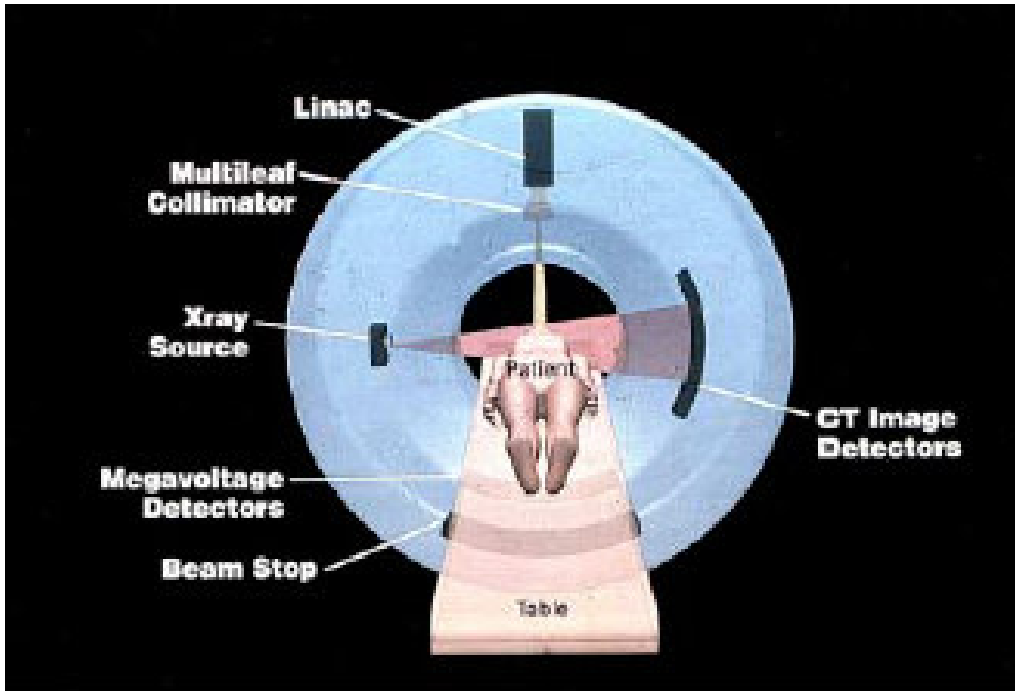
Figure 1. Schematic of helical TomoTherapy unit. The commercially available TomoTherapy system does not have an on-board kilo voltage imaging system, rather it uses a megavoltage CT (Courtesy TomoTherapy Inc. Madison, WI)

TomoTherapy differs from fixed-beam linear accelerator IMRT in several ways. First, in fixed-beam IMRT beam directions are selected by the planner before the beam intensity patterns are modulated with the optimizer. TomoTherapy uses all beamlet orientations within a 40-cm wide fan beam that intersect the PTVs and optimally weights them to achieve user-defined volumetric dose goals and limitations. A beamlet is a single leaf-pair opening in one projected angle. There are 64 binary leaf-pairs in any projected angle and 51 projected angles in each rotation, making a total of 3264 possible beamlets in each rotation. This greater degree of freedom on the part of the optimizer in selecting beam incidence may allow for improvements in the planning of more complex treatments. However, it also may irradiate significant regions of tissue outside the PTV to achieve volumetric dose goals unless dose constraints have been placed on those regions. Also, the TomoTherapy helical delivery allows the treatment of extended treatment

volumes without the need for junctioning fields (Bauman et al. 2005). However, TomoTherapy beams are limited to axial beams, i.e., beams directed perpendicular to the TomoTherapy gantry axis.

One obvious difference between a multi-modality linear accelerator and TomoTherapy is that the latter does not offer electron beams. Electron beams are advantageous in that dose falls rapidly off distal to the treatment volume which makes this modality ideal for treating superficial PTVs, often with a single beam. There are a multitude of treatment sites that use electrons exclusively or in combination with photon beams, especially sites within the breast and head and neck (Tapley 1976 and Hogstrom 2003a).

1.2. Significance of TomoTherapy vs. Electron Beams

Published comparisons between TomoTherapy and mixed beams are limited in number. Lock et al. (2002) compared a conventional photon/electron total scalp irradiation technique Tung et al. (1993) with a serial tomotherapy treatment delivered with the NOMOS MIMiC system. They concluded that the conventional technique was superior in sparing critical structures, such as the eyes, although the tomotherapy treatment delivered much greater dose homogeneity to the PTV and provided better sparing of the parotid glands. However, the study did not explore the possibility of relaxing PTV dose homogeneity to better spare critical structures and achieve a comparably similar plan to the conventional irradiation technique. Orton et al. (2005) showed that a TomoTherapy dose distribution was superior for treating total scalp due to PTV dose homogeneity and sparing of critical structures such as the eyes.

Superficial lesions (depth < 6cm) have traditionally been treated with the electron radiation techniques. Because electrons are directly ionizing particles and deliver high

dose on the surface while sparing critical structures due to limited particle range making electrons a good candidate to treat superficial PTVs. However for large treatment areas, abutting adjacent electron fields can in some circumstances result in either overdosing or under dosing the junctioned areas. In Mary Bird Perkins Cancer Center (MBPCC) where the project was conducted, shifting the abutment borders during the course of treatment is done to minimize dose heterogeneity at field junctions. This requires considerable effort in the planning of both field shapes and positions, and requires careful observation of the abutment regions during the course of radiotherapy.

Eliminating problems associated with a field junction is often necessary, especially for large, superficial chest wall PTVs in post-mastectomy radiation therapy (PMRT). An ideal technique should deliver a homogenous dose to the PTV including the matchline, if deemed to be a risk, while minimizing normal tissue radiation exposure without compromising the PTV treatment. Although this can be achieved in part with arc therapy (Hogstrom 2003a), that technology is complex and not often used.

Prior studies by Krueger et al. (2003) demonstrated the feasibility and possible utility of IMRT for post-mastectomy breast patients. Unlike traditional methods, the IMRT technique significantly reduced problems associated with field junctioning and improved the dose homogeneity in the chest wall. The natural extension of this technique for PMRT is the use of arcing modulated photon beams, and TomoTherapy may seem an ideal candidate for this technique. The ability to treat extended treatment volumes without the need for fixed-beam field junctioning, and the greater degree of freedom on part of the optimizer in selecting beam incidence, may give TomoTherapy an advantage over conventional fixed-beam linear accelerator techniques.

Although TomoTherapy is a relatively new technology, its presence is being felt throughout the radiotherapy community. When using a new technology, the question of improvement in dose delivery, cost, and outcome create a complex environment to answer the question: Does the technology significantly improve patient care (Lock et al. 2002)? This investigation focused on a more specific question: Are TomoTherapy treatment plans for PMRT patients comparable to conventional (electron field) technique treatment plans?

1.3. Postmastectomy Radiation Therapy (PMRT)

1.3.1. Overview

Although radiotherapy in the treatment of breast cancer is associated with an ncreased risk of complication, subsequent studies showed its advantage in improving cancer survival overrides the risks associated with the radiation treatment. Rutqvitst et al. (1990) showed that post-operative radiation therapy for early breast cancer produces a sustained improvement of recurrence free survival, mainly through prevention of locoregional recurrences. Other studies have subsequently shown a significant improvement in survival for patients who underwent radiation treatment after surgical mastectomy (Ragaz et al. 1997, Overgaard et al. 1997 and 1999). On the basis of these and other studies, a National Institutes of Health consensus panel recommended locoregional PMRT in patients with $\geq$ 4 positive axillary lymph nodes and/or T3 and T4 staged lesions (Eifel et al. 2000). As a result, many institutions offer comprehensive PMRT for high risk breast cancer patients who have undergone mastectomy.

PMRT PTVs the chest wall (CW) and regional lymph nodes such as the supraclavicular (SCl), the internal mammary chain (IMN), and the axillary (AX) nodes. Due to the complexity of the treatment, different techniques exist, with no single

technique being accepted as a gold standard. Pierce et al. (2002) investigated seven

commonly used conventional techniques for irradiation of post mastectomy CW patients,

namely: 1. Standard tangents; 2. Electron fields; 3. Cobalt fields; 4. Reverse hockey stick

(RHS); 5. 30%/70% Photon/Electron mix; 6. 20%/80% Photon/Electron mix; and 7.

Partially wide tangent fields (PWTF). The study concluded that none of the techniques

combined the best CW and IMN coverage with minimal lung and heart complication

probabilities, i.e., no single technique was found to be superior for all treatment goals.

However, among the seven discussed techniques, the use of PWTFs was found to

produce the most appropriate compromise of PTV coverage and normal tissue sparing.

The study did not take IMRT into consideration. In conclusion, the selection of PMRT

technique should be based on clinical discretion and technical expertise available to

implement complex treatment plans. Clinical discretion encompasses estimated risk

reduction in locoregional recurrence and its potential impact on survival, and the

predicted complication risk for each patient.

1.3.2. Conventional Electron PMRT Technique

In our study, we have chosen to compare TomoTherapy with a conventional electron

and photon beam technique commonly used to treat PMRT patients at Mary Bird Perkins

Cancer Center. In this technique, a total of five fields are typically used (Figure 2). The

medial CW is treated with an anterior electron field and the lateral CW is treated with an

oblique electron field. The IMN is treated with an anterior electron field, and parallel-

opposed photon fields (6 MV) are used to treat the region containing the

supraclavicular/axillary nodes (SCl/AX). As discussed in the previous section, matching

adjacent electron fields presents a considerable problem for this technique at the border

of medial and lateral chest-wall fields because converging central axes create a large

overlap (Hogstrom 2003a). This problem is addressed in the clinic by moving the junction between the lateral and medial fields every week over the typical 5-week course of treatment to reduce the magnitude of dose heterogeneity.
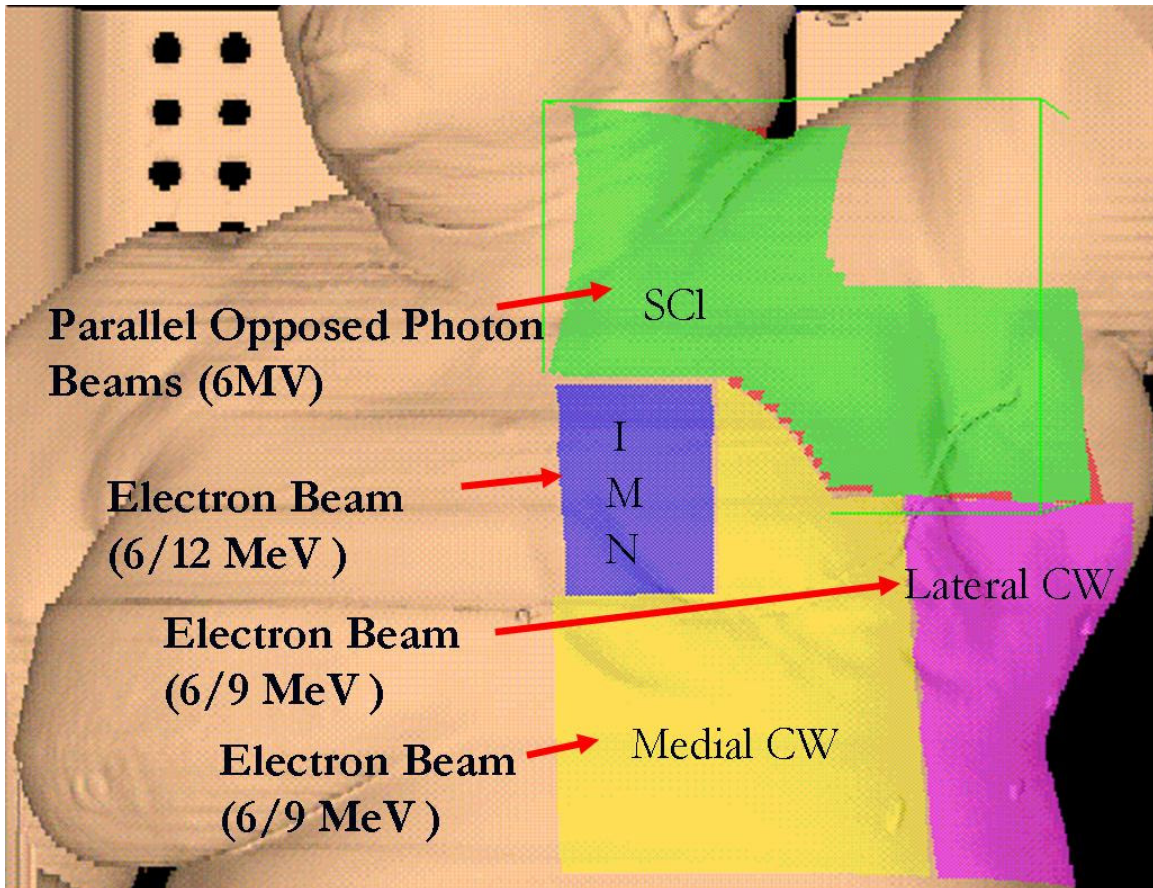
Figure 2. Conventional electron PMRT technique. The CW and IMN are treated with electron beams and the SCl/AX is treated with photon beams.

1.3.3. Complications Associated with PMRT

The close proximity of the lung and heart to the CW and IMN poses problems for PMRT. Radiation exposure risks to the heart and to the lung include pericarditis and pneumonitis respectively. According to Emami et al. (1991), 50 Gy causes a probability of 50 % complication (pericarditis) and 24.5 Gy causes a probability of 50 % complication (pneumonitis) within five years. The concern for complication is amplified

if patients are likely to receive systemic chemotherapy agents with known cardiac and pulmonary toxicity (Krueger et al. 2003). Hence, individual treatment planning warrants complex field arrangements that strive to spare critical structures but at the same time deliver the prescribed dose to designated treatment areas.

Biological dose-response models are useful for evaluating plans. Biological dose metrics associated with these models include the tumor control probability (TCP), the normal tissue complication probability (NTCP) for organs at risk, and the secondary cancer complication probability (SCCP). Researchers using available epidemiological data have used these models to describe complications associated with radiation therapy. However, the values generated by TCP, NTCP and SCCP models should not be used to predict absolute biological impact as there is still concern in the scientific community to their accuracy (Perez and Brady, 1998). On the other hand, TCP, NTCP and SCCP models are useful for comparing rival plans and techniques (Perez and Brady, 1998).

Gagliardi et al. (1996) demonstrated the relative seriality model (Kallman et al., 1992) can be used to quantitatively describe the dose response relationship for excess cardiac mortality on the basis of given clinical data. The study showed that a dose reduction to the heart has more importance than a restriction of the irradiated heart volume. In this model, the heart's functional subunits are regarded as an organ with a parallel structure of serially aligned subunits.

The risk of secondary cancer induction in the contralateral breast is also of concern in radiotherapy of breast cancer. Storm et al. (1992) conducted a case-control study in cohort of 56,540 women in Denmark diagnosed with invasive breast cancer from 1943 through 1978. The average age at the time of radiation exposure in this study was 51 years, and 2.51 Gy was the mean radiation dose to the contralateral breast. The result of

their study indicated that the radiation treatment of women with breast cancer does not significantly increase the risk of development of contralateral breast cancer. They attributed the negative finding to the age at radiation exposure. Most published positive findings for radiation-associated risk has been concentrated in young patients, less than 30 years at time of exposure (Hancock et al. 1993).

1.3.4. IMRT

One approach that may solve the problem of normal tissue complications is intensity-modulated radiation therapy (IMRT).Unlike conventional techniques, IMRT utilizes varying intensity beams, which allows more conformal dose delivery to complex PTV shapes while limiting dose to nearby critical structures. IMRT has shown to be a promising approach in a wide range of disease sites (Khan 2003). An increasing body of evidence suggests that IMRT can produce superior conformal treatment plans for head and neck, lung, prostate, and other sites. Published comparisons between conventional PMRT techniques and IMRT are limited in number. After studying treatment plans for ten stage II and III breast cancer patients with left-sided cancers, Krueger et al. (2003) concluded that a nine-field IMRT technique achieves full PTV coverage and improved dose homogeneity while maintaining similar doses to heart and ipsilateral lung as the conventional PWTF technique. In this technique, 6-MV tangential photon fields were used to treat the supraclavicular node. Medial and lateral coplanar tangents using 6-MV photons were used to treat the chest wall and the internal mammary chain node. The inferior medial chest wall was treated with supplemental electrons (6 or 9 MeV). The study also showed contralateral lung and breast receive a larger volume of low dose compared to the PWTF which may increase the chance of secondary cancer induction.

1.4. Hypothesis/Specific Aims

The hypothesis of current study is that TomoTherapy can plan dose distributions for PMRT patients, that a pre-selected radiation oncologist judges to be equal to or better than that of a conventional plan treated with electron beams, alone or in combination with photon beams. To carry out this objective the following specific aims were followed.

Aim 1: Generate a patient database. Generate a patient database by selecting patient data from five chest wall (CW) patients that were previously-treated with electron beams.

Aim 2: Plan each case on the TomoTherapy Hi-Art planning system. Specify planning objectives and weights for the PTVs and critical structures. Use the system's iterative method to minimize the objective function and produce clinically acceptable treatment plan.

Aim 3: Determine treatment plan metrics. Choose and conduct physical plan evaluation metrics for both techniques. Generate dose volume histograms (DVHs) for all involved structures. The metrics will include, the minimal, maximal and mean dose to the planning PTV volumes (PTVs) and organs at risks (OARs), the volume of lung receiving more than 20 Gy ($V20_{lung}$), the volume of heart receiving more than 30 Gy ($V30_{heart}$), and the volume of the contralateral breast receiving more than 5 Gy ($V5_{contralateral\ breast}$). This data will be made available for the radiation oncologist's evaluation and comparison of rival plans (Aim 4) as needed, and to further supplement the comparisons.

Aim 4: Clinically evaluate the conventional and TomoTherapy treatment plans. Have one American Board Radiology (ABR) certified radiation oncologist evaluate both

the TomoTherapy and the conventional treatment plans. Along with the plans,

provide multiple choice questionnaires to the radiation oncologist for this evaluation.

Aim 5: Determine biological treatment plan metrics. Calculate and compare the tumor

control probability (TCP), the normal tissue complication probability (NTCP), and

the secondary cancer complication probability (SCCP) for both techniques. The

purpose of these data is to supplement the comparisons of two rival plans

(conventional and the TomoTherapy plans) with radiobiological modeling of the

impact of the treatment.

Chapter 2
Materials and Methods

2.1. Overview of Study

The first aim was to generate a PMRT patient database on an ADAC Pinnacle workstation version 6.2 (Philips, Inc., Milpitas, California). The planning process is based on Hogstrom algorithm for an electron treatment planning (Hogstrom et al. 1981b) and a superposition-convolution dose calculation engine for photon treatment planning. The patient database included the CT scan data, contoured regions of interests (ROIs) relevant to the study, and several Pinnacle treatment plan trials for plan comparison studies. At least one Pinnacle treatment plan trial contained the original conventional treatment plan used to treat the PMRT patient along with the calculated dose distribution. The database was made to maintain patient confidentiality in accordance with a protocol approved by an institutional review board.

The second goal was to generate a clinically-acceptable, TomoTherapy treatment plan for each case in the PMRT patient database. TomoTherapy Hi-Art System, version 2.1 (TomoTherapy, Inc, Madison, WI) was used to generate a plan for each of the five patients in the PMRT patient database. The planning process is based on a superposition-convolution dose calculation engine (Mackie et al. 2000) and an iterative least square optimization process (Shepard et al. 2000). An iterative process is a process used to minimize the objective function after the user specified the planning objectives and weights for the PTV and critical structures. As a result, appropriate beam pattern, position, and intensity will be calculated by the system. After a suitable plan was developed on the TomoTherapy treatment planning system, the dose distribution was transferred to the PMRT patient database into a separate Pinnacle treatment plan trial.

The third goal was to generate and compare dose-volume metrics from both the TomoTherapy and the conventional electron beam treatment plans.

The fourth goal was to have a radiation oncologist evaluate both plans for clinical acceptability, i.e., is the plan acceptable for treating the patient? The radiation oncologist also was to review both plans side-by-side and determine which plan was better (or if they were similar). A questionnaire was generated to help the radiation oncologist in the decision process.

The fifth goal was to generate and compare the radiobiological impact of the PMRT plans using standard radio-biological models. Radiobiological metrics of interest in this study included:

1. PTV tumor control probability (TCP).

2. normal tissue complication probability (NTCP) for the heart and lung.

3. secondary cancer complication probability (SCCP) for contralateral and ipsilateral lungs, contralateral breast, and for normal tissue.

2.2. Aim 1: Patient Database

A logbook of Pinnacle treatment plans archived since August 2000 maintained by MBPCC group was searched for possible chest wall or breast treatment sites. From that list 22 patients receiving conventional electron beam PMRT to the chest wall were identified. From the 22 patients identified, five were selected for the study; four left-sided and one right-sided chest wall PMRT patients. The basis for the five patients chosen were (1) they were treated by the same radiation oncologist who was asked to evaluate treatment plans for the study, and (2) that the CT scan data was readily available from a separate archive maintained by on-site CT technologists. This was important because CT

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scan data could not be directly exported from a Pinnacle workstation to the TomoTherapy planning system.

The Pinnacle treatment plan was retrieved and imported into the Pinnacle workstation. The patient name and medical record number were stripped from the treatment plan and replaced with a code number. The code number was linked to the patient name and medical record number on a master list kept independently by the project director. This was done to maintain patient confidentiality in accordance with a protocol approved by an institutional review board.

PTVs were generated for each of the PMRT treatment plans in the patient database, as (1) PTVs are typically not contoured for conventional electron beam PMRT planning, and (2), the TomoTherapy treatment planning system (TPS) is strictly an inverse planning system and requires contoured PTVs and OARs.

All OARs were generated except for the spinal cord which was previously contoured in some patients. Both the lungs were contoured separately using Pinnacle's auto contour tool which uses CT thresholds and appropriate edits was made. The heart chambers (left and right atria and left and right ventricles) were contoured starting at the superior extent of the heart chamber and ending at the apex. The contralateral breast was outlined starting at the clavicular head and ending at the inframammary fold. Also, the spinal cord and the 0.5 cm expanded spinal cord were outlined. A structure compromising all normal tissue, excluding specified OARs and PTVs, was auto-contoured. This was defined by subtracting the volumes of PTVs and specified normal tissues from the whole patient volume. The entire contour set was reviewed by a certified dosimetrist and later by the radiation oncologist upon reviewing the dose distributions.

Since the prescribed dose for the chest wall (CW) can differ from prescribed dose for the supraclavicular and axillary (SCl/AX) nodes, separate PTVs are required for TomoTherapy treatment planning. Therefore, two PTVs were generated, one for the CW and the IMN, and a second for the supraclavicular/axillary nodes (SCl/AX). The IMN was considered part of the CW PTV because the dose prescriptions for each were the same in each of the patient cases.

The PTVs were generated from the conventional Pinnacle treatment plans by converting an isodose line to a contour. The isodose line chosen for generating a PTV was 90% of the prescribed dose. The prescribed dose in each case was the maximum dose delivered to water along the central axis. In order to separate the two PTVs, the prescription for SCl/AX was set to zero when contouring CW and vice versa. Pinnacle allows turning individual prescription assigned to filed(s) on/off, when a multiple prescriptions present in a treatment plan. As a result, the dose distribution from individual fields can easily be seen. If the automatically-generated PTV was found broken up into several contours on the same slice resulting in "contour islands," the PTV contours were connected if found in close proximity to each other. PTV contours that protruded into OARs delineating the lung and the heart were pushed outside of the contour delineating the OAR.

Figure 3 shows an example of converting the 90% isodose line to a contour for the CW PTV. Figure 3a shows the Pinnacle-calculated dose distribution of the conventional plan for the CW. The prescribed dose was 50 Gy to 100% of the dose at R_{100} along the central axis of each beam. Note the CW PTV in Figure 3b has excluded the ipsilateral lung, which is an organ at risk.

a)

b)
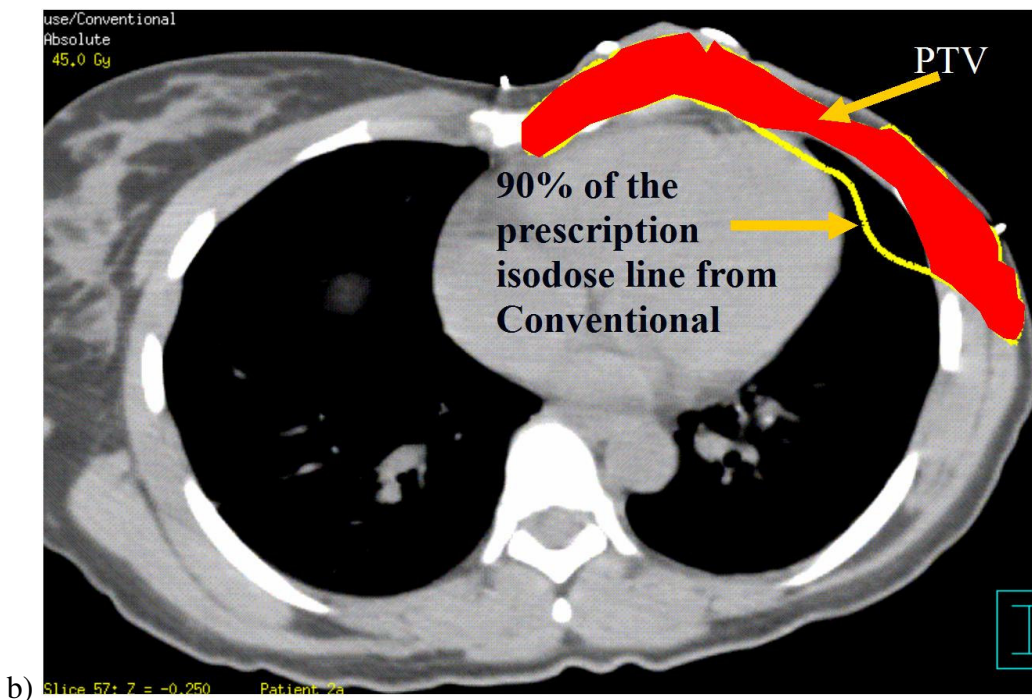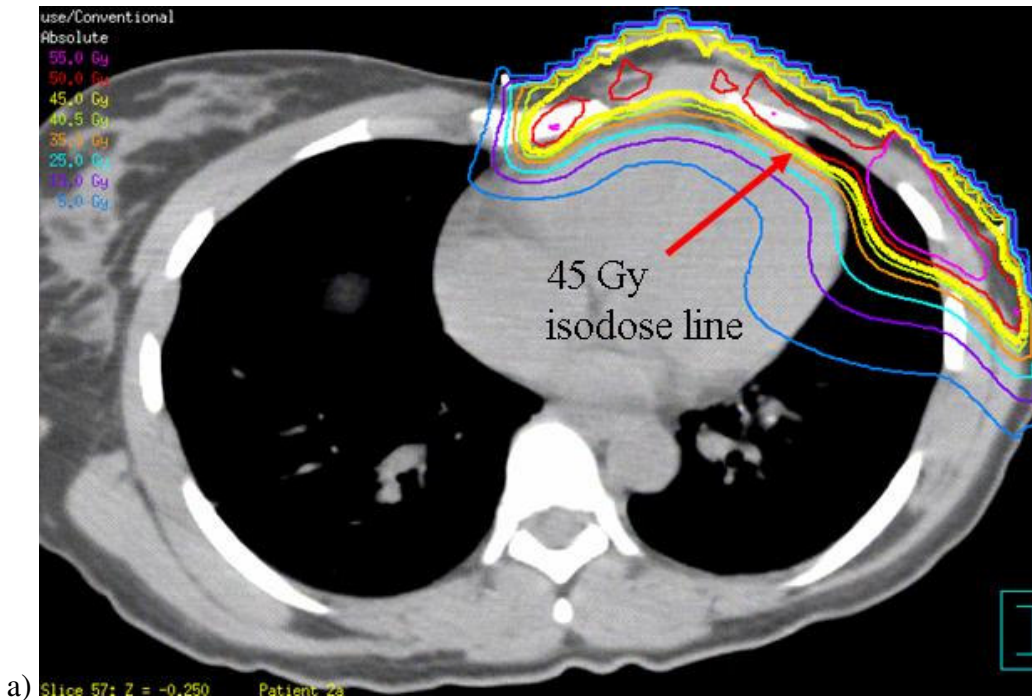
Figure 3 shows an example of converting the 90% isodose line (45 Gy) shown in (a) to a CW PTV (b).The 45 Gy isodose line, 90% of the prescribed dose, is shown as a thick yellow contour. The converted PTV is shown as a solid red area

2.3. Aim 2: TomoTherapy PMRT Treatment Plans

2.3.1. Importing CT Data

The TomoTherapy treatment planning system was used to generate an inverse IMRT plan for 5 patients. CT scan data was imported into the TomoTherapy treatment planning 20workstation from the CT workstation (GE Discovery ST, Model #: 316097CN5) after being retrieved from long term storage. Patient name and medical record number were removed and changed to a code before sending CT images to the TomoTherapy planning system. CT image slices, which were 5-cm or more beyond the superior and inferior extent of the PTVs and did not include OARs, were removed from the CT scan data to reduce dose calculation times with TomoTherapy treatment planning. The CT scan data was down-sampled to a smaller matrix size (128 x 128 matrix) as it was imported into the Tomotherapy treatment planning system. The diameter of the CT scan data field-of-view was 50 cm. Hence, the pixel width of the down-sampled CT image was 3.91 mm. The slice width of the CT scan data in all patient studies was 2.5 mm.

2.3.2. TomoTherapy Dose Prescription

Planning ROIs (PTVs and OARs) were transferred from the Pinnacle workstation to the TomoTherapy planning system. The CW PTV was selected as the primary PTV to receive the TomoTherapy dose prescription. The TomoTherapy dose prescription is specified in terms of percentage volume and dose, i.e., the percentage volume of the primary PTV that receives at least the prescribed dose. The TomoTherapy dose prescription for the CW was specified to be 50 Gy (same as conventional plan), and the percentage volume that received 50 Gy or less was set to match the percentage volume of the CW in the conventional plan that received 50 Gy or less.

2.3.3. TomoTherapy Plan Parameters

Table 1 gives a summary of the plan parameter values used for TomoTherapy treatment planning. To achieve better dose conformality to the PTV in the superior-inferior direction of the patient, the small jaw opening (2.45 cm) was used instead of the large jaw opening (4.98 cm). The pitch, *i.e.,* the fraction of the field width advanced with each revolution, was set to a standard value of 0.3 used in the clinic. The planning modulation factor, the ratio of the highest beamlet intensity to the average intensity of all non-zero beamlets, was set to a maximum of 7 to allow for significant intensity modulation. The dose grid resolution was set to "fine" making the dimensions of the dose grid equivalent to the voxel dimensions of the CT scan data ($3.91 \times 3.91 \times 2.5$ mm^3).

Table 1. TomoTherapy plan parameter specifications

Field width	2.45 cm
Pitch	0.3
Planning modulation factor	7
Dose grid resolution	Fine ($3.91 \times 3.91 \times 2.5$ mm^3)

2.3.4. Dose Limiting Structures

Quite often, dose limiting structures were utilized to better control the TomoTherapy dose distribution. The most common dose limiting structures used was a "ring" (Figure 4) surrounding a PTV, which is also widely utilized for IMRT treatment planning on conventional linear accelerators. Several treatment planning trials were performed to study the effect of using "ring" dose limiting structures on TomoTherapy. The contour expands and contract option on the Pinnacle system was used to auto-contour rings. The procedures followed were as follows:

1. A temporary ROI was generated by expanding the PTV by 1 cm in all directions.

2. Another temporary ROI was generated by expanding the PTV by 1.5 cm in all directions.

3. The final "ring" ROI was generated by subtracting the first ROI from the second.

The ring dose limiting structures were labeled as region at risk (RAR) for TomoTherapy treatment planning.

Other dose limiting structures were utilized in the TomoTherapy treatment plan as needed. A dose limiting structure which acts as a buffer zone was drawn approximately one cm superiorly and inferiorly from the PTVs to limit patient dose outside the PTVs. A directional blocking RAR was utilized to prevent beamlets from coming in the direction where patient anatomy was outside the CT scan field of view (FOV) Figure 5.

2.3.5. TomoTherapy Optimization and Dose Calculation

Once all such constraints were defined, optimization and dose calculation commenced. Table 2 lists typical PTV and RAR constraints upon completion of optimization. Dose constraints such as importance levels and maximum/minimum penalties were specified to all structures (PTVs and RARs). Compared to distal critical structures, a large value was used for the importance and max dose penalty for adjacent ones. In general, OARs dose limits were made as low as possible without degrading dose delivered to the PTV or creating unnecessary dose to large volumes of normal tissue. Also dose to normal tissue peripheral to PTVs was minimized without degrading PTV dose homogeneity or OAR dose sparing.
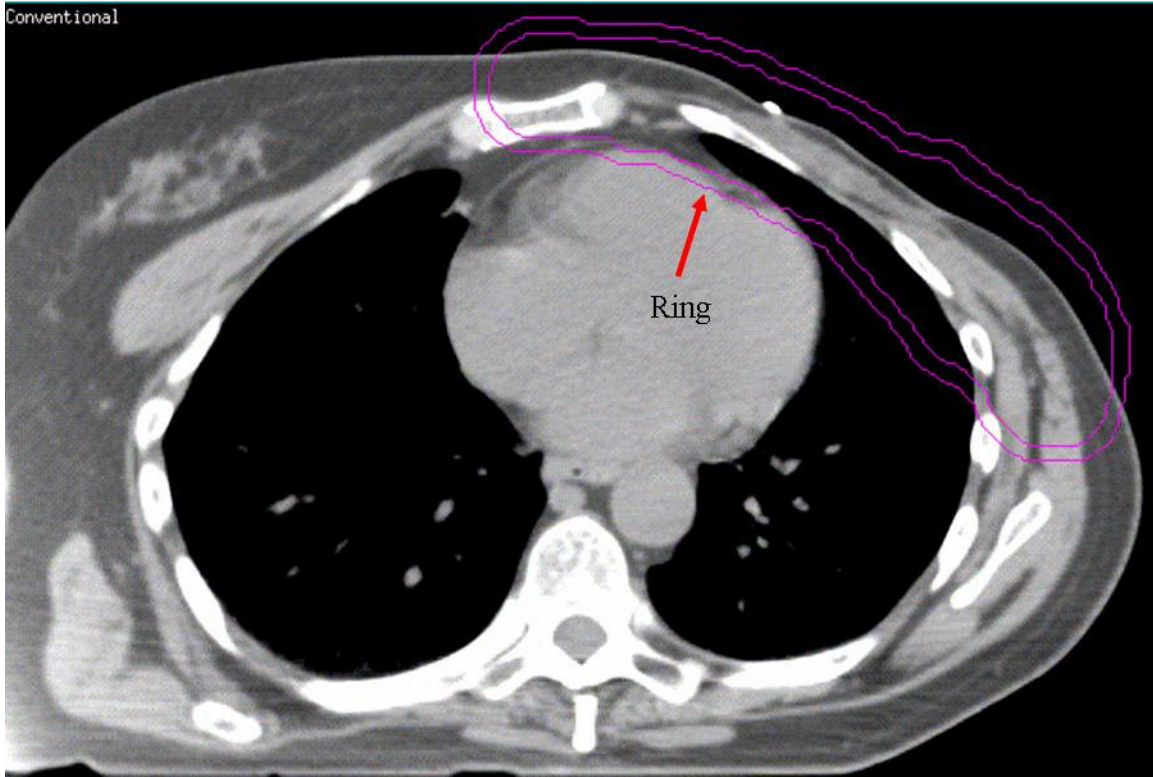
Figure 4. A dose limiting structure called ring
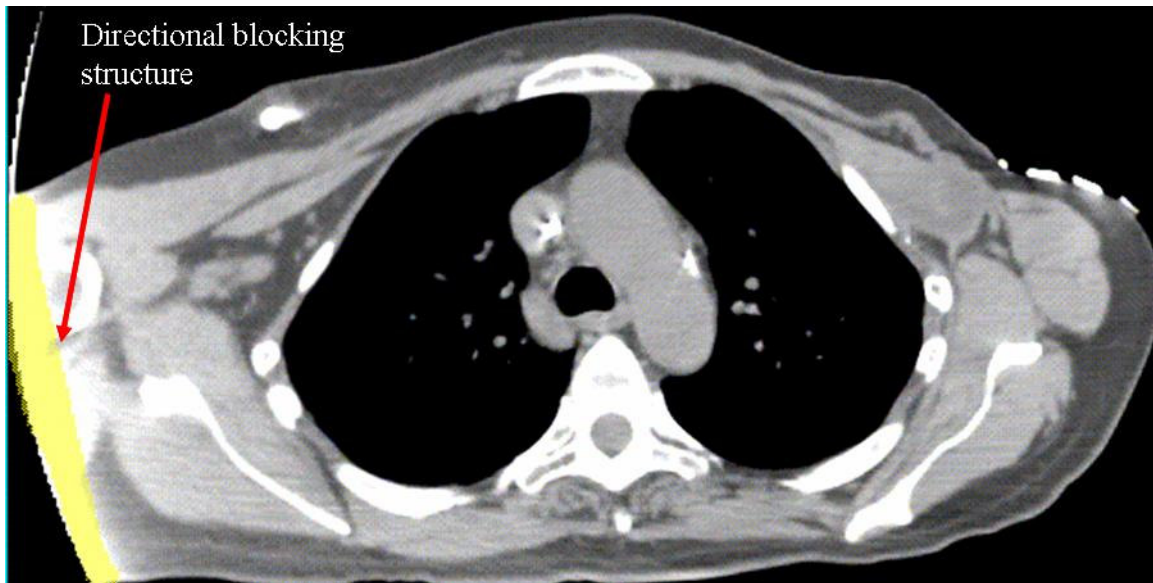
Figure 5. A directional blocking structure (Structure is directional blocked, so that no primary beam should pass through it before passing through the PTV structure)

Table 2. Typical PTV (a) and RAR (b) constraints upon completion of optimization.

(a)

Name	Importance	Max Dose (Gy)	Max Dose Penalty	DVH Vol (%)	DVH Dose (Gy)	Min Dose (Gy)	Min Dose Penalty
CW	100	53	100	50	50	50	250
SC/AX	1200	55	1000	50	50	48	5

(b)

Name	Importance	Max Dose (Gy)	Max Dose Penalty	DVH Vol (%)	DVH Dose (Gy)	DVH Penalty
Cont. Lung	15	14	30	5	5	700
Ips. Lung	21	45	1000	40	5	50000
Cont. Breast	22	3	150	50	1	2000
Heart	16	27	50	20	5	1000
Exp. Cord	8	3	100	10	2	40
Ring	13	48	10000	45	15	400

A plan using TERMA (Total Energy Released per unit Mass) optimization mode was used to generate an estimate of dose deposited from photon interaction. TERMA dose algorithm allows for fast optimization but does not convolve the dose spread kernel with the TERMA interaction point along the central ray of a beamlet. After adjusting the dose constraint parameters and modifying dose limiting structures (RARs), the plan was further optimized using BEAMLET optimization mode to obtain the most accurate dose distribution. Optimization with the beamlet dose algorithm is much more time consuming but the resultant dose distribution is more accurate as it does convolve the dose spread kernel with the TERMA interaction point. On the other hand, BEAMLET optimization takes significant amount of time since the dose distribution from individual beamlets has to be calculated on the first iteration.

Fractionation was applied in all five cases, once an acceptable dose distribution was generated to verify that the TomoTherapy machine could deliver such a treatment.

Fractionation is dividing up the patient's dose prescription into a number of different sessions, all of which add up to the total prescribed dose. The temporary dose distribution file (EOPDose.img) was saved along with the header file into a separate directory on the TomoTherapy workstation and was exported to a separate Pinnacle plan trial in the patient database.

2.4. Aim 3: Generate Dose-Volume Treatment Plan Metrics

Dose-volume treatment plan metrics were generated using (1) ADAC Pinnacle, (2) Matlab version 7.1 (MathWorks, Inc., Natick, Massachusetts), and (3) Microsoft office excel 2003 (Microsoft, Inc., Redmond, Washington). The Pinnacle treatment plan trial dose-volume information was exported to the in-house program as an RTOG file. Differential dose-volume histograms (dDVHs) embedded in the RTOG file were read in by the in-house program to generate relevant dose-volume metrics. The dose-volume metrics of interest in this study included:

1. DVHs for each PTV and OAR.

2. Mean and standard deviation of dose to each PTV.

3. Difference in PTV dose between 10% and 90% of PTV ($D_{90\%}$-$D_{10\%}$).

4. Volume of lung receiving at least 20 Gy or more.

5. Volume of heart receiving at least 30 Gy or more.

6. Volume of heart receiving at least 15 Gy or more.

7. Volume of contralateral breast receiving at least 5 Gy or more.

8. Mean dose to the contralateral breast.

Both the standard deviation of the PTV and the $D_{90\%\text{-}10\%}$, the difference between the dose received by 90% of the PTV volume and the dose received by 10% of the PTV volume.. The percent of the total lung volume exceeding 20 Gy ($V20_{lung}$) to be

statistically significant relative to the development of pneumonitis. Hence, the volume of

lung receiving at least 20 Gy or more was useful in comparing competing treatment plans

to evaluate the risk of pneumonitis (Graham et al., 1999). Studies conducted by Gagliardi

et al. (1996) showed that the probability of excess cardiac mortality due to IHD is less

than 4.5% for the whole heart volume receiving less than 30 Gy. Hence, the percentage of

heart that received 30 Gy or less ($V30_{heart}$) was chosen to compare competing treatment

plans.

Table 3 lists the dose/volume limits specific to our clinic. Published tolerance

doses and irradiated volumes (Emami, et al. 1991) are generally higher those listed on

Table 3. Radiation oncologists at our institution have stricter dose limits than published

tolerance doses, which they feel take into account the patient's prior experience, such as

chemotherapy. The radiation oncologist specifications were taken into consideration

during optimizing the TomoTherapy treatment plans. Also, the volume of the

contralateral breast that received 5 Gy or more ($V5_{contralateral\ breast}$), the volume of the heart

that received 15 Gy or more ($V15_{heart}$), and the volume of the lung that received 20 Gy or

more ($V20_{lung}$) were noted when generating the dose-volume treatment plan metrics.

Table 3. Radiation oncologist specifications

Organ	Dose Limit	Volume
Lung	20 Gy	$\leq$ 15%
Heart	15 Gy	$\leq$ 10%
Spinal Cord	10 Gy	$\leq$ 10%
Contralateral Breast	Max 5 Gy	

2.5. Aim 4: Radiation Oncologist Evaluation of Treatment Plans

In the fourth aim, a radiation oncologist evaluated and compared both

conventional and TomoTherapy plans. The radiation oncologist was presented with a

side-by-side trial comparison of the patient dose distribution and DVHs of both the conventional and TomoTherapy plans on a Pinnacle workstation. The actual worksheet provided to the radiation oncologist is located in Appendix A. First, the radiation oncologist was asked to evaluate the clinical acceptability of each plan on a scale of 1 to 5, 1 being best (acceptable) and 5 being worst (unacceptable). Second, the radiation oncologist was asked to rate the TomoTherapy plan in comparison with the conventional plan on a scale of 1 to 5, 1 being best (superior) and 5 being worst (inferior). The radiation oncologist was then asked to fill out a simple multiple-choice question as to why he preferred a particular plan. Third, a margin was left on questionnaire for additional comments.

2.6. Aim 5: Determine Biological Treatment Plan Evaluation Tools

An "in-house" radiation biological program developed by Dr. Tae Ku Lee, research medical physicist, was used to calculate and compare relevant radiobiological treatment plan evaluation tools. The radiobiological evaluation tools included:

1. PTV tumor control probability (TCP).

2. Normal tissue complication probability (NTCP) for the heart and lung.

3. Secondary cancer complication probability (SCCP) for the both the

contralateral and ipsilateral lungs, contralateral breast, and for normal tissue.

Differential dose-volume histograms (dDVHs) embedded in the RTOG file were imported into the in-house program to evaluate radiobiological treatment plans.

2.6.1. Tumor Control Probability (TCP)

TCP, the probability of tumor control in radiation therapy, for the chest wall PTV was calculated using the Webb and Brenner model [Webb and Nahum 1993 and Brenner et al. 1993], which incorporates a repair mechanism. Since α, β and Tr values for chest wall

are not available in literature, chest wall was considered as a breast to retrieve α and β values and as a skin to retrieve the T_r value. Definitions of α, β and T_r parameters are listed on the following page. The overall probability of tumor control is the product of probabilities of tumor control in each tumor dose bin i of the differential dose-volume histogram:

$$TCP=\prod_i TCP_i. \tag{1}$$

The tumor control probability in each tumor sub-volume is calculated as

$$TCP_i = e^{-N*SF_i}, \tag{2}$$

N in Equation 2 is the product of the number of tumor cells per cm^3 (n) and the volume v_i that receives dose D_i, i.e.

$$N = n\sum_i v_i. \tag{3}$$

SF in Equation 2, the survival fraction (i.e., the probability of cell survival from irradiation), is given by

$$SF_i = \exp\{-\alpha D_i (1+\frac{Gd_i}{\alpha/\beta})\}. \tag{4}$$

G, the dose protraction factor for radiation-induced DNA damage repair, in the Equation 4 is calculated as

$$G = \frac{2}{(\lambda_R T)^2}(\exp(-\lambda_R T) + \lambda_R T - 1) \tag{5}$$

where λ_R, repair rate (hr^{-1}), is calculated as

$$\lambda_R = \frac{\ln 2}{T_r}. \tag{6}$$

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The rest of the parameters in Equations 4, 5, and 6 defined as:

α = cell radio sensitivity (Gy^{-1}).

β = the effectiveness/lethality of radiation (Gy^{-2}).

d_i = D_i/number of fraction (Gy/fraction).

T = treatment time per fraction (hr).

T_r = Repair half-time of cells with sub lethal damage (hr).

The values of the parameters used to calculate TCP for the chest wall are shown in Table 4.

Table 4. Parameters selected to calculate TCP for chest wall

Name	Value	Source
N	2 .0 E 8 cm^{-3}	[Wigg et al. 2001]
α	0.51 Gy^{-1}	[Wigg et al. 2001]
β	0.061 Gy^{-2}	[Wigg et al. 2001]
T	1/3 hrs	Each treatment time is approximated to 20 minutes (Wang et al. 2003)
T_r	1.6 hrs	[Wigg 2001]

2.6.2. Normal Tissue Complication Probability (NTCP) for The Lung

Since lung has a strong dose-volume tissue complication response, it is considered a parallel structure. The NTCP for lung was calculated using Layman-Kutcher-Burman (LKB) model [Layman et al., 1992, Kutcher and Burman, 1989], i.e.,

$$NTCP = \frac{1}{2}(1 + erf(\frac{t}{\sqrt{2}})) \ , \qquad (7)$$

where

$$t(D, V) = \frac{D_{eff} - D_{50}}{m \cdot D_{50}} \ , \qquad (8)$$

and

$$D_{eff} = (\sum_i v_i D_i^{\frac{1}{n}})^n . \qquad (9)$$

D_{eff} is biological mean dose called effective dose (Warkentin et al. 2004). The other parameters in Equations 7, 8, and 9 are defined as:

n = a fitting parameter that accounts for the dose-volume dependence of tissue

v_i = is volume ratio (volume that receives D_i / total volume of the structure)

m = a fitting parameter that control the slope of the dose repose curve

D_{50} = the dose at which there is a 50% chance of complication (Gy) within 5yrs

i = the number of individual bins in the differential DVH data.

Radiation pneumonitis was used as an end point for the current study. The parameters used to calculate NTCP are listed on Table 5.

Table 5. Parameters selected to calculate NTCP for lung.

Name	Value	Source
N	0.87	[Pierce et al. 2002]
M	0.18	[Pierce et al. 2002]
D_{50}	24.5 Gy	[Emani et al. 1991]

2.6.3. Normal Tissue Complication Probability (NTCP) for The Heart

The heart has a low dose-volume complication response, but can be damaged with high dose in small volumes. Therefore, it is appropriate to model it as a serial structure like the spinal cord. The relative seriality model, developed by Kallman et al. (1992), was used to calculate NTCP for the whole heart structure. Cardiac mortality due ischaemic heart disease (IHD) was used as an end point for the current study. NTCP using the relative seriality model is calculated as:

$$NTCP = \{1 - \prod_{i=1}^{n} (1 - P(D_i)^s)^{v_i}\}^{\frac{1}{s}}, \qquad (10)$$

where

$$P(D_i) = 2^{-\exp(e\gamma(1-\frac{D_i}{D_{50}}))}, \qquad (11)$$

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where: P (D) = the NTCP of the organ irradiated homogenously to dose D_i

v_i = is volume ratio (volume that receives D_i / total volume of the structure)

m = a fitting parameter that control the slope of the dose repose curve

D_{50} = the dose at which there is a 50% chance of complication (Gy)

s = seriality of subunits (ratio of number of serial subunits to all subunits)

γ = The maximum relative slope of the dose response curve

i = the number of individual bins in the differential DVH

The parameters used to calculate NTCP are listed on Table 6.

Table 6. Parameters selected to calculate NTCP for heart.

Name	Value	Source
D_{50}	52.3 Gy	[Gagliardi et al. 1996]
S	1.0	[Gagliardi et al. 1996]
γ	1.28	[Gagliardi et al. 1996]

2.6.4. Secondary Cancer Complication Probability (SCCP) for The Lung.

The probability of secondary cancer induction was calculated for lung, contralateral breast, and normal tissue using the Schneider model [Schneider et al. 2005a and 2005b]:

$$SCCP_{org} = In_{org} * OED_{org} \ , \qquad (12)$$

Where OED_{org} is the organ equivalent dose calculated as

$$OED_{org} = \frac{1}{N} \sum_{i=1}^{N} D_i e^{-\alpha D_i} \qquad (13)$$

The parameters of Equations 12 and 13 are listed below:

α = Cellular radio sensitivity (Gy $^{-1}$).

In_{org} = Absolute cancer incidence provided by the International Commission on

Radiological Protection (ICRP 60) and the United Nation Scientific

Committee on the Effects of Atomic Radiation (UNSCEAR).

N= is dose calculation point

i = the number of individual bins in the differential DVH.

D = dose (Gy).

The parameter values used to calculate SCCP for lung are listed in Table 7. The In_{org}

for lung (data is from UNSCEAR) is for the total lung (ipsilateral and contralateral lung).

Hence, the individual ipsilateral and contralateral lungs' SCCP values were corrected by

multiplying the calculated SCCP values with the respective volume ratio. The residual

life expectancy that was used to find the life time SCCP for lung was taken as the

difference between the female life expectancy (79.8 yrs) Arias et al.,(2003) and the onset

age of female patients diagnosis for breast cancer (45 yrs) (SEER, 2006).

The parameter values used to calculate SCCP for the contralateral breast and the

normal tissue are listed in Table 8 and 9 respectively. The In_{org} values (data is from ICRP

60) for both the contralateral breast and the normal tissue are given in life-time risk (50-

yrs) in percent. The In_{org} for normal tissue (Table 9) is taken from the atomic bomb

survivors (whole body irradiation). Hence, normal tissue's SCCP value for each patient

was corrected by multiplying the calculated SCCP values with the respective volume

ratio. The average woman's volume in cm^3 was calculated assuming an average weight

of 74.5 Kg (Ogden et al. 2004) and density of 0.001kg/cm^3.

Table 7. Parameters selected to calculate SCCP for lung.

Name	Value	Source
α	0.129Gy^{-1}	[Schneider et al. 2005a]
In$_{org}$	8.27/(10^4. patients. yr. Gy)	[Schneider et al. 2005a]

Table 8. Parameters selected to calculate SCCP for the contralateral breast.

Name	Value	Source
α	0.085 Gy^{-1}	[Schneider et al. 2005b]
In$_{org}$	0.78 (% Gy^{-1})	[Schneider et al. 2005b]

Table 9. Parameters selected to calculate SCCP for the normal tissue.

Name	Value	Source
α	0.085 Gy^{-1}	[Schneider et al. 2005b]
In$_{org}$	1.76 (% Gy^{-1})	[Schneider et al. 2005b]

Figure 6 shows a plot of cancer incidence per 10^4 patients per year for solid tumor (i.e., an abnormal mass tissue that usually does not contain cysts or liquid areas) induction as a function of dose. Note that the probability is maximum around 11 Gy and decreases for higher dose values because sterilization of already mutated cells becomes more important. According to the Schneider's model, certain tissue receiving dose between 5 and 25 Gy will have a high probability of solid tumors induction (≥ 0.75) with a mean follow up time of 9.5yrs. Therefore, the volume of normal tissue receiving doses between 5 and 25 Gy was also determined for plan evaluation
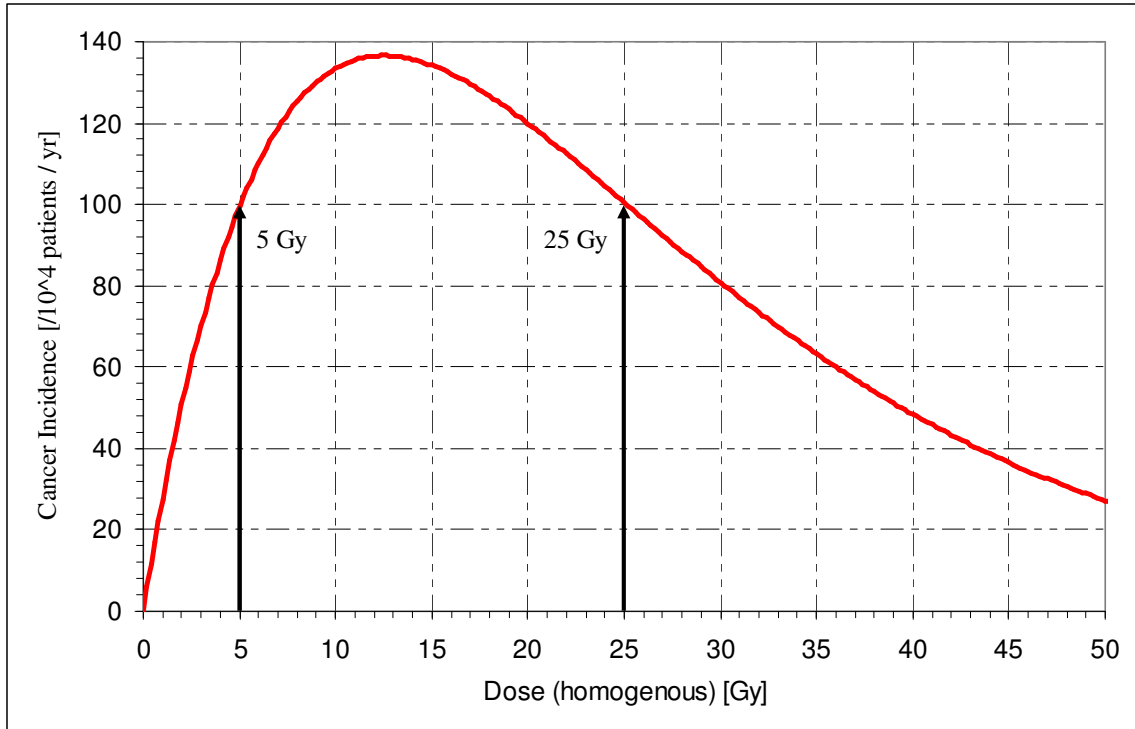
Figure 6. Estimated solid tumors induction as function of homogenous organ dose for normal tissue (based on Schneider's model, Schneider et al 2005a).

Chapter 3
Results

3.1. Format for Presenting Results of Each Patient

The format for presenting the results is the same for all patients. For each patient, the results are presented in the following order:

1. isodose comparison,

2. DVH comparison,

3. radiation oncologist's review of the conventional and TomoTherapy plans, and their comparison,

4. mean and standard deviation of dose to the chest wall PTV, and the resultant TCP,

5. dose to the ipsilateral lung and heart, and the resultant NTCPs, and

6. dose to the contralateral breast and normal tissue, and the resultant SCCPs.

The isodose comparisons between the conventional and TomoTherapy plans are shown on transverse CT image slices for three distinct regions:

1. The supraclavicular nodal region along the beam axis of the parallel-opposed photon beams used in the conventional plan.

2. The region of the chest wall containing the internal mammary chain nodes.

3. A region of the chest wall inferior to (2).

The transverse CT image slice where the isodose comparison is made is delineated by a yellow line in a sagittal midline CT image view in the same figure as the isodose comparison. The isodose lines are displayed in Gy, with dose values of 55, 50, 45, 35, 25, 15, and 5 Gy. In addition, due to change in the prescription for the supraclavicular and axillary nodal region, an additional 40.5 Gy dose line is added for the third and fifth

patients and 43.2 Gy dose line is added for the fourth patient. The color scheme for the isodose lines is consistent for all patients. It should be noted that the TomoTherapy TPS calculates dose in air outside the patient while ADAC Pinnacle TPS sets this dose to zero. This results in isodose lines appearing outside the patient in the TomoTherapy plan.

A cumulative DVH comparison between the conventional and TomoTherapy plans is done for both planning PTVs (chest wall and supraclavicular/axillary nodes) and for the heart, ipsilateral lung, contralateral breast, and normal tissue. In these plots, the y-axis displays the percentage of the total volume of each region of interest; the x-axis displays in Gray. DVHs for both plans are superimposed on one plot for each patient, with a consistent color and line scheme for all patients.

3.2. Patient One

A 74 year old female was diagnosed to have an infiltrating ductal carcinoma of the upper outer quadrant of the left breast, stage T2pN3aM0 carcinoma with 10 out of 12 lymph nodes positive with extra-nodal extension. The conventional electron beam PMRT plan had the following fields:

1. AP/PA 6 MV photon beam SCl/AX fields,

2. 12 MeV electron beam IMN field,

3. 9 MeV electron beam medial CW field, and

4. 9 MeV electron beam lateral CW field.

Both the SCl/AX and CW PTVs were irradiated to 50 Gy in 25 fractions.

3.2.1. Isodose Comparison

Figure 7 shows the isodose comparison between the conventional plan (Figure 7a) and the TomoTherapy plan (Figure 7b) on the transverse CT image slice in the region of the supraclavicular nodes delineated by the yellow line in sagittal midline CT image

shown in Figure 7c. The yellow 45-Gy isodose line represents the 90% isodose line where the TomoTherapy plan was optimized to match the conventional plan. The conventional plan showed a hot spot of 55 Gy (110% of the prescription dose) in the medial, anterior portion of the dose distribution, whereas the TomoTherapy plan showed no similar hot spot in that region.

The conventional plan showed a sharper dose falloff than the TomoTherapy plan along the beam edges of the parallel-opposed photon beams of the conventional plan. Greater dose restriction outside the supraclavicular PTV in the TomoTherapy plan during optimization might have resulted in a sharper dose falloff along the "beam edges" delineated by the conventional plan. The TomoTherapy plan also showed a significant volume of tissue outside the PTV receiving low dose (5 Gy or more).However, the TomoTherapy plan showed a greater dose gradient beyond the 45 Gy isodose line in the anterior-to-posterior (AP) direction. This resulted in lower dose to region posterior to the supraclavicular nodes, including the scapula.

Figure 8 shows the dose distribution for the conventional plan (Figure 8a) and the TomoTherapy plan (Figure 8b) on a transverse CT image slice in the region of the IMN delineated by the yellow line in sagittal image shown in Figure 8c. The yellow 45 Gy isodose line represents the 90% prescription isodose line, where the TomoTherapy plan was optimized to match the conventional plan. The conventional plan showed a hot spot of 55 Gy (110% of the prescription dose) in the IMN region and at the junction of the lateral and medial electron fields. Although in practice this hot spot is reduced (smeared) by moving the match line, this is not reflected in the conventional plan.
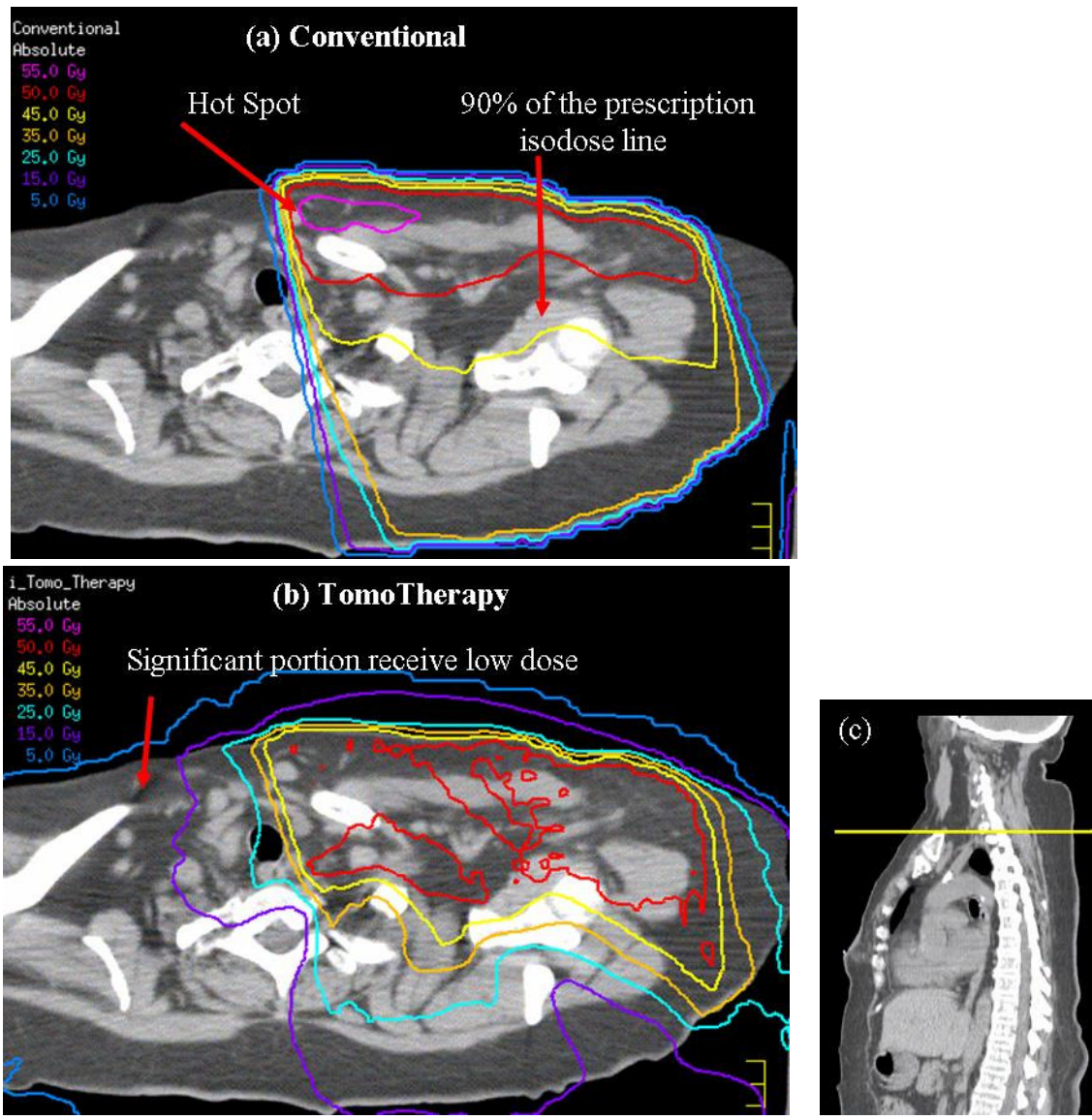
Figure 7. Transverse views of the conventional plan (a) and TomoTherapy plan (b) taken at the supraclavicular nodal region shown on sagittal view (c).
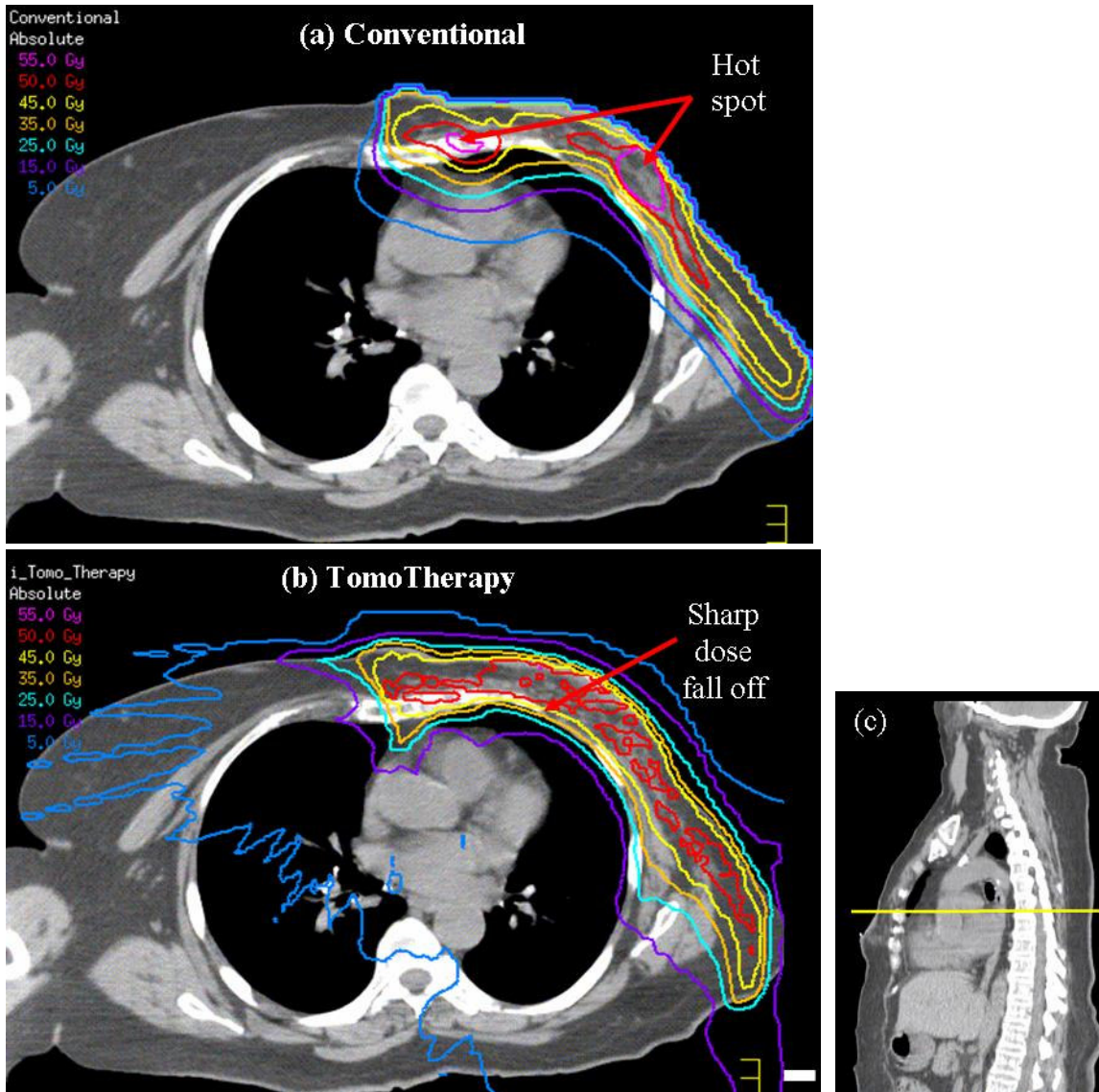
Figure 8. Transverse views of the conventional plan (a) and TomoTherapy plan (b) taken at the IMN region as shown on the sagittal view (c).

Figure 9 shows the isodose comparison between the conventional plan (Figure 9a) and the TomoTherapy plan (Figure 9b) on a transverse CT image slice near the inferior border of the CW PTV, and is delineated by the yellow line in sagittal midline CT image shown in Figure 9c. The yellow 45 Gy isodose line represents the 90% isodose line, where the TomoTherapy plan was optimized to match the conventional plan. The conventional plan showed a hot spot of 55 Gy (110% of the prescription dose at the junction of the lateral and medial electron fields. Although in practice this hot spot is

reduced by moving (smeared) the match line, this is not reflected in the conventional plan.

The conventional plan showed a sharper dose falloff than the TomoTherapy plan along the beam edges of the electron beams for the IMN and the lateral chest wall of the conventional plan. Greater dose restriction outside the chest wall PTV in the TomoTherapy plan during optimization might have resulted in a sharper dose falloff along the "beam edges" delineated by the conventional plan. The TomoTherapy plan also showed a significant volume of tissue outside the PTV receiving low dose (5 Gy or more). However, the TomoTherapy plan showed a greater dose gradient beyond the 45 Gy isodose line in the anterior-to-posterior (AP) direction. This resulted in a lower volume with dose greater than 20 Gy to ipsilateral lung.

3.2.2. DVH Comparisons

The DVH comparisons are shown in Figure 10. The conventional plan showed a small volume of the PTV receiving high dose created by the junction of the medial and lateral chest wall, although in practice this hot spot is reduced by moving (smeared) the junction over the course of treatment. For the TomoTherapy plan, dose homogeneity was better than the conventional plan for both the SCl/AX and CW PTVs. However, low dose ($D \leq 5Gy$) covered a larger volume of normal tissue.

Compared to the conventional plan, the TomoTherapy plan showed less ipsilateral lung volume receiving doses greater than 13 Gy while more ipsilateral lung volume received doses less than 13 Gy. This crossover of DVH lines for OARs was seen in all patients so it will be reported as the crossover dose from here on out. The crossover dose for the heart was 15 Gy.
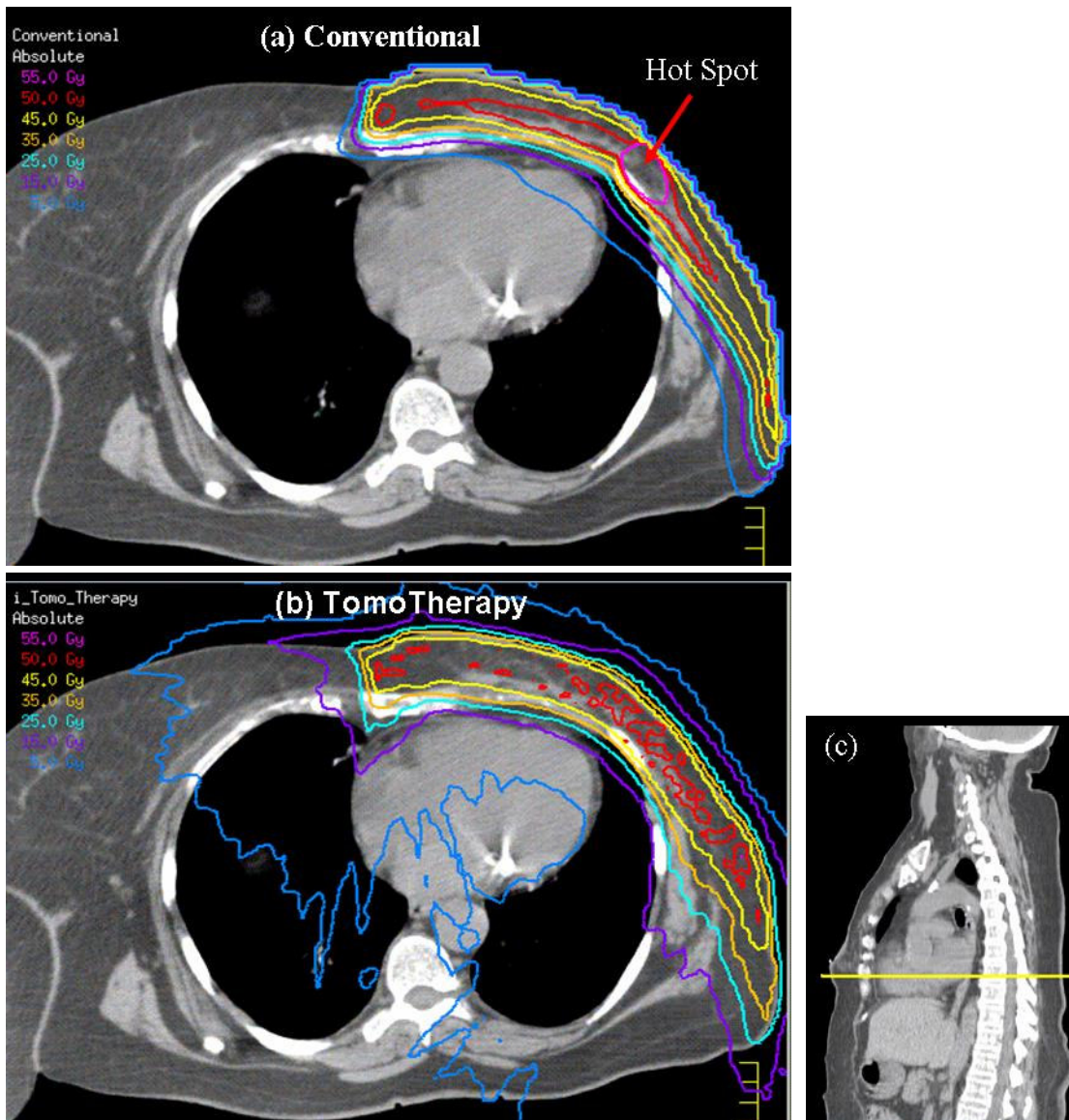
Figure 9. Transverse views of the conventional plan (a) and TomoTherapy plan (b) taken at the chest wall region as shown on the sagittal view (c).

3.2.3. Radiation Oncologist Review

A radiation oncologist evaluated the clinical acceptability of both conventional and TomoTherapy plans and scored both plans acceptable. After reviewing the dose distributions and DVHs for both plans, he ranked the TomoTherapy plan marginally superior. PTVs (CW and SCI/AX) coverage was listed as a reason for preferring TomoTherapy plan over the conventional plan. The radiation oncologist commented that

the dose to the heart was higher in the TomoTherapy plan and may be of concern if the patient was to receive chemotherapy.
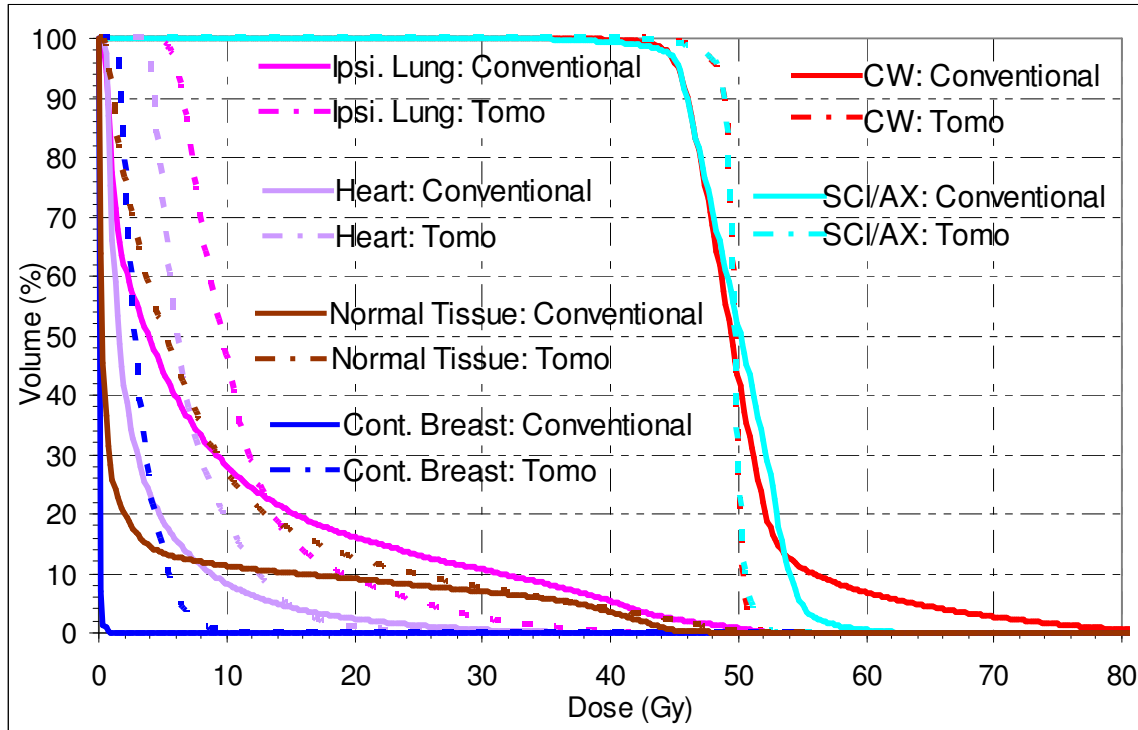
Figure 10. DVHs comparison for distribution shown in Figures 7 to 9. Solid lines – conventional plan, dashed lines –TomoTherapy plan. CW – chest wall PTV; SCl/AX – supraclavicular/axillary PTV; Ipsi – ipsilateral; Cont – contralateral

3.2.4. Chest Wall

The TomoTherapy plan showed a more uniform CW PTV dose, e.g. the standard deviation (σ) of the CW PTV dose on the TomoTherapy plan was lower than that for the conventional plan. The average CW dose ($\pm$ 1σ) was 49.6 $\pm$ 0.9 Gy on the TomoTherapy plan and 50.7 $\pm$ 6 Gy on the conventional plan. The D90%-10% of the CW volume was 9.8 Gy for the conventional plan and 1.4 Gy for the TomoTherapy plan. Even though the CW PTV dose distribution showed better uniformity on the TomoTherapy plan, the TCP values were comparable for both plans (conventional plan = 0.978 and TomoTherapy plan = 0.995).

3.2.5. Ipsilateral Lung

During optimization of the TomoTherapy plan, a high penalty factor was assigned to the ipsilateral lung objective to force photon beams to come in an oblique direction. As a result, TomoTherapy avoided irradiating it with high doses (20Gy). The ipsilateral lung receiving dose above 20 Gy was reduced from 16.1% on the conventional plan to 9.1% on the TomoTherapy plan. The ipsilateral lung in the conventional plan was exposed to higher doses (e.g. 5% of the ipsilateral lung received 40 Gy or more). However, as shown in Figure 10, a large volume of the ipsilateral lung received low dose (5 Gy or more) with the TomoTherapy plan. The average ipsilateral lung dose ($\pm$ 1σ) was comparatively higher on the TomoTherapy plan (conventional plan = 9.4 $\pm$ 12.5 Gy and TomoTherapy plan = 11.3 $\pm$ 6.0 Gy). The reason behind high standard deviation of the conventional plan is due to asymmetric distribution of dose to the ipsilateral lung, shown in Figure 11. A relatively higher NTCP value was observed for the TomoTherapy plan although both values were small (conventional plan = 0.0007 and TomoTherapy plan = 0.0016).

3.2.6. Heart

The heart volume receiving a dose above 30 Gy or more was very low and similar in both plans (0.06% for the TomoTherapy plan and 0.54% for the conventional plan). Also, similar was the value for $V15_{heart}$ (conventional plan = 4.3% and TomoTherapy plan = 4.5%). Like the ipsilateral lung, a larger volume of the heart received low dose (5 Gy or more) with the TomoTherapy plan. The average heart dose ($\pm$ 1σ) was reduced from 7.3 $\pm$ 3.6 Gy on the TomoTherapy plan to 3.5 $\pm$ 5.0 Gy on the conventional plan. A relatively lower NTCP value was observed for the TomoTherapy plan although both values were insignificant (conventional plan = 0.0009 and TomoTherapy plan = 0.0002).
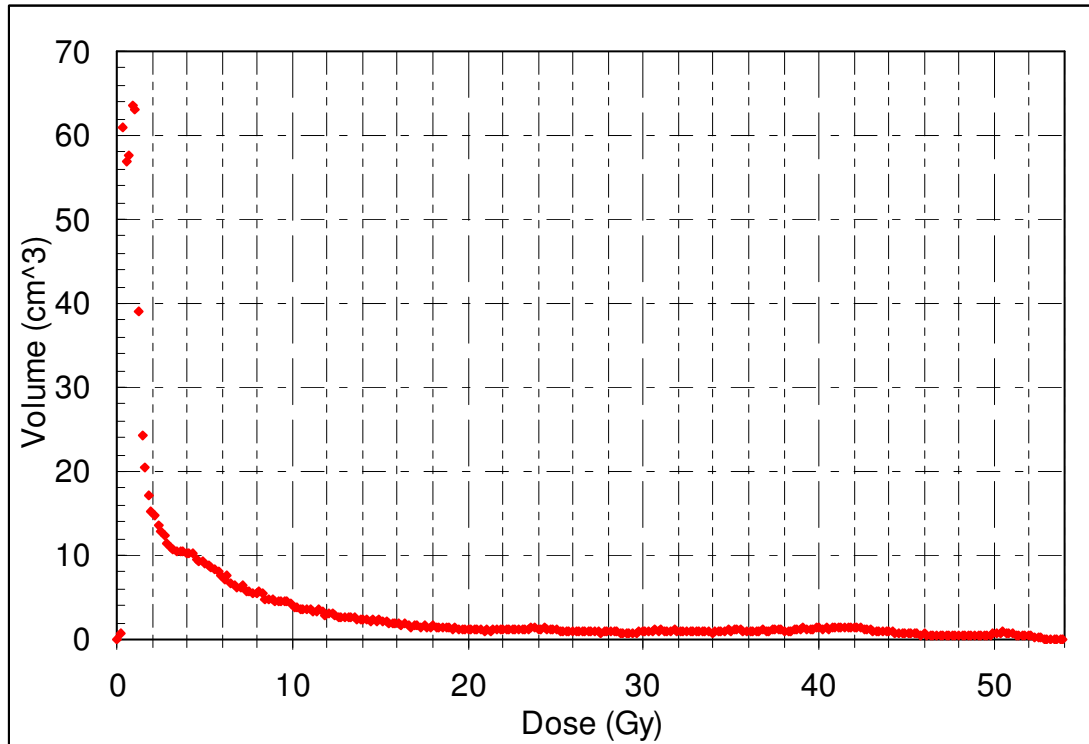
Figure 11. The dDVH of the ipsilateral lung.

3.2.7. Contralateral Breast

In order to stop dose exposure to the contralateral breast, a higher importance factor was assigned compared to other critical structures during optimization of the TomoTherapy plan (Table 2). This helped to bring down the dose to the contralateral breast. However, due to the nature of beam arrangements of TomoTherapy delivery, dose to the contralateral breast was significantly greater than the dose for conventional plan. The average contralateral breast dose ($\pm$ 1σ) was 3.2 $\pm$ 1.6 Gy on the TomoTherapy plan and 0.1 $\pm$ 0.1 Gy for the conventional plan. As shown in Figure 9, a relatively large volume of the contralateral breast was exposed to low dose with the TomoTherapy plan. The percent of volume receiving 5 Gy or more was zero for the conventional plan and 13.1 for the TomoTherapy plan. Age dependence effect of radiation induced breast cancer was ignored when calculating SCCP for patient one (age = 73 yrs). The SCCP was

relatively higher for the TomoTherapy plan (conventional plan = 0.0001 and TomoTherapy plan = 0.0178).

3.2.8. Normal Tissue

The normal tissue volume receiving between 5 and 25 Gy for this patient was 17.6 cm^3 for the conventional plan and 111.7 cm^3 for the TomoTherapy plan. The calculated SCCP value relatively higher on the TomoTherapy plan (conventional plan =0.003 and TomoTherapy plan = 0.012).

3.3.   Patient Two

A 53 – year old female was diagnosed to have an infiltrating ductal carcinoma of the upper outer quadrant of the left breast, stage T3pN2aM0 carcinoma with 4 out of 12 lymph nodes positive with extra-nodal extension. The conventional electron beam PMRT plan had the following fields:

1. AP/PA 6 MV photon beam SCl/AX fields,

2. 12 MeV electron beam IMN field,

3. 6 MeV electron beam medial CW field, and

4. 9 MeV electron beam lateral CW field.

Both the SCl/AX and CW PTVs were irradiated to 50 Gy in 25 fractions.

3.3.1. Isodose Comparison

Figure 12 shows the isodose comparison between the conventional plan (Figure 12a) and the TomoTherapy plan (Figure 12b) on the transverse CT image slice in the region of the supraclavicular nodes delineated by the yellow line in sagittal midline CT image shown in Figure 12c. The yellow 45 Gy isodose line represents the 90% isodose line where the TomoTherapy plan was optimized to match the conventional plan. The conventional plan showed a hot spot of 55 Gy (110% of the prescription dose) in the

medial, anterior portion of the dose distribution, whereas the TomoTherapy plan showed no similar hot spot in that region.

The conventional plan showed a sharper dose falloff than the TomoTherapy plan along the beam edges of the parallel-opposed photon beams of the conventional plan. Greater dose restriction outside the supraclavicular PTV in the TomoTherapy plan during optimization might have resulted in a sharper dose falloff along the "beam edges" delineated by the conventional plan. The TomoTherapy plan also showed a significant volume of tissue outside the PTV receiving low dose (5 Gy or more).However, the TomoTherapy plan showed a greater dose gradient beyond the 45 Gy isodose line in the AP direction. This resulted in lower dose to region posterior to the supraclavicular nodes, including the scapula.

Figure 13 shows the isodose comparison on the transverse slice for the conventional plan (Figure 13a) and the TomoTherapy plan (Figure 13b) on a transverse CT image slice in the region of the IMN delineated by the yellow line in sagittal image shown in Figure 13c. The yellow 45 Gy isodose line represents the 90% prescription isodose line, where the TomoTherapy plan was optimized to match the conventional plan. The conventional plan showed a hot spot of 55 Gy (110% of the prescription dose) in the IMN region and at the junction of the lateral and medial electron fields.

The conventional plan showed a sharper dose falloff than the TomoTherapy plan along the beam edges of the electron beams for the IMN and the lateral CW of the conventional plan. Greater dose restriction outside the CW PTV in the TomoTherapy plan during optimization might have resulted in a sharper dose falloff along the "beam edges" delineated by the conventional plan. The TomoTherapy plan also showed a significant volume of tissue outside the PTV receiving low dose (5 Gy or more).

However, the TomoTherapy plan showed slightly greater dose gradient beyond the 45 Gy isodose line in the AP direction. This resulted in lower volume of dose to ipsilateral lung.
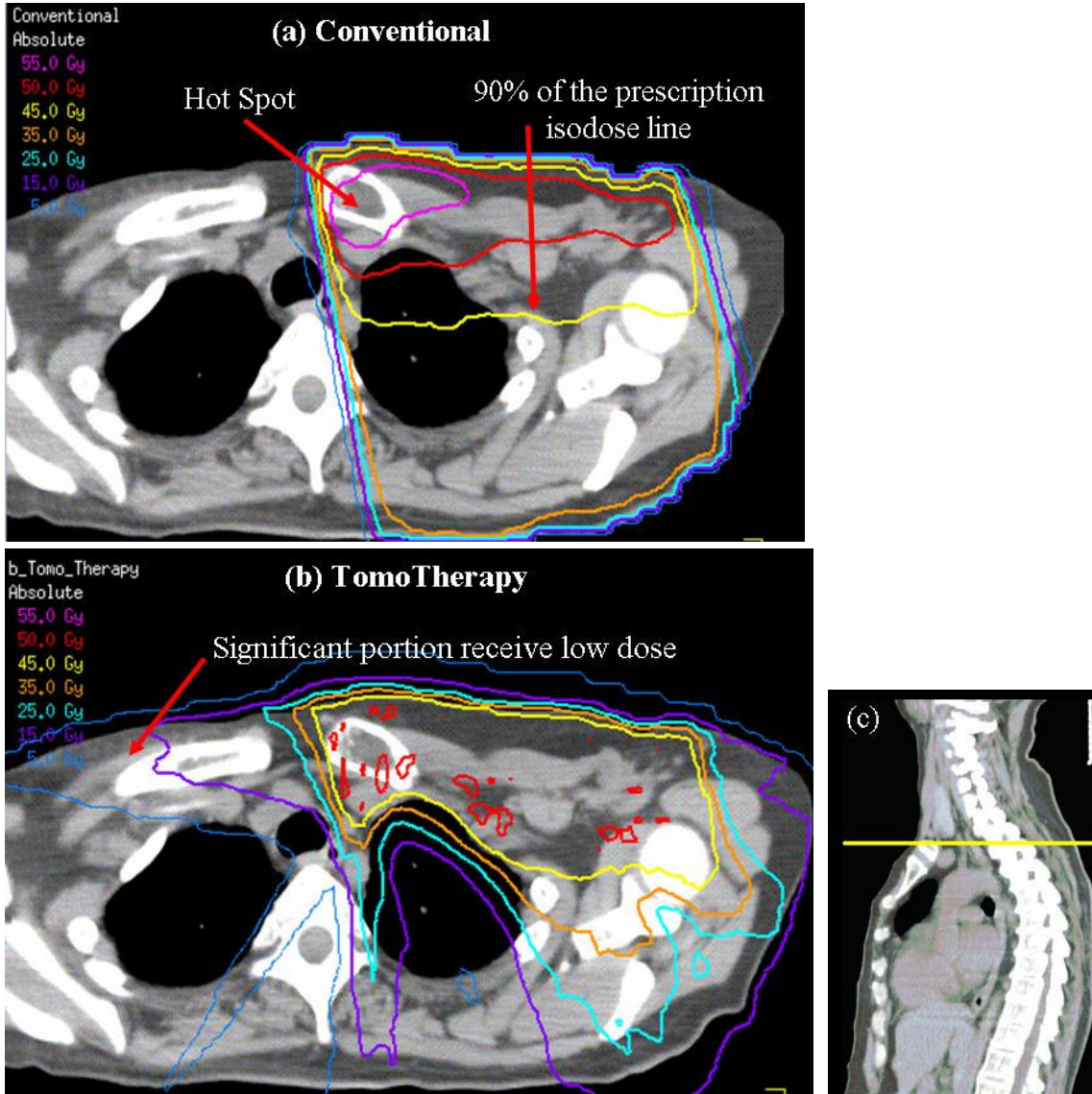
Figure 12. Transverse views of the conventional plan (a) and TomoTherapy plan (b) taken at the supraclavicular nodal region shown on sagittal view (c).
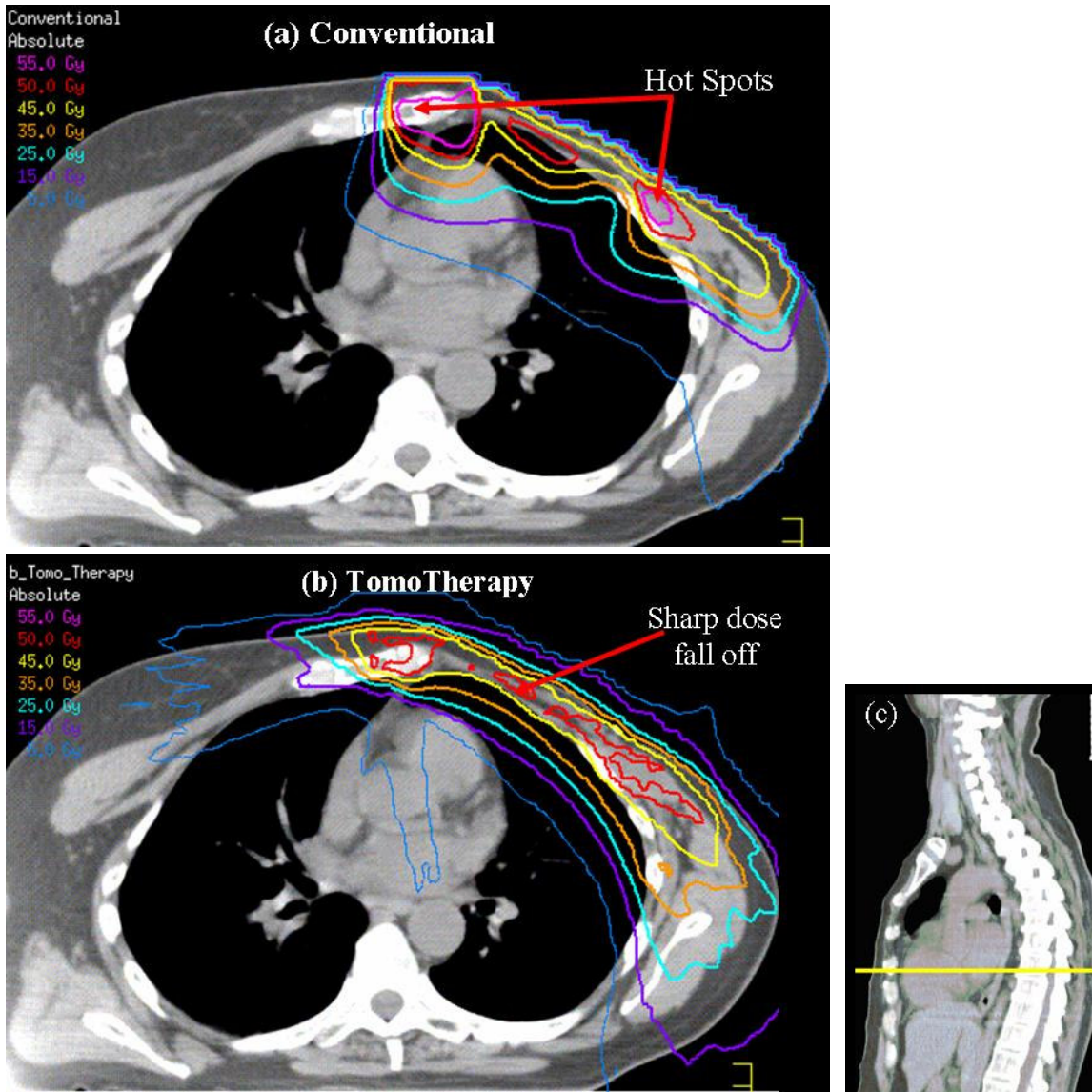
Figure 13. Transverse views of the conventional plan (a) and TomoTherapy plan (b) taken at the IMN region as shown on the sagittal view (c).

Figure 14 shows the isodose comparison between the conventional plan (Figure 14a) and the TomoTherapy plan (Figure 14b) on the transverse CT image slice near the inferior border of the CW PTV, and is delineated by the yellow line in sagittal midline CT image shown in Figure 14c. The yellow 45 Gy isodose line represents the 90% isodose line, where the TomoTherapy plan was optimized to match the conventional plan. The conventional plan showed a hot spot of 55 Gy (110% of the prescription dose) and at the junction of the lateral and medial electron fields.

The conventional plan showed a sharper dose falloff than the TomoTherapy plan along the beam edges of the medial and the lateral CW of the conventional plan. Unlike the conventional plan, the TomoTherapy plan avoided irradiating the ipsilateral lung with high dose (45, 50, and 55 Gy). However, the TomoTherapy plan also showed a significant volume of tissue outside the PTV receiving low dose (5 Gy or more).
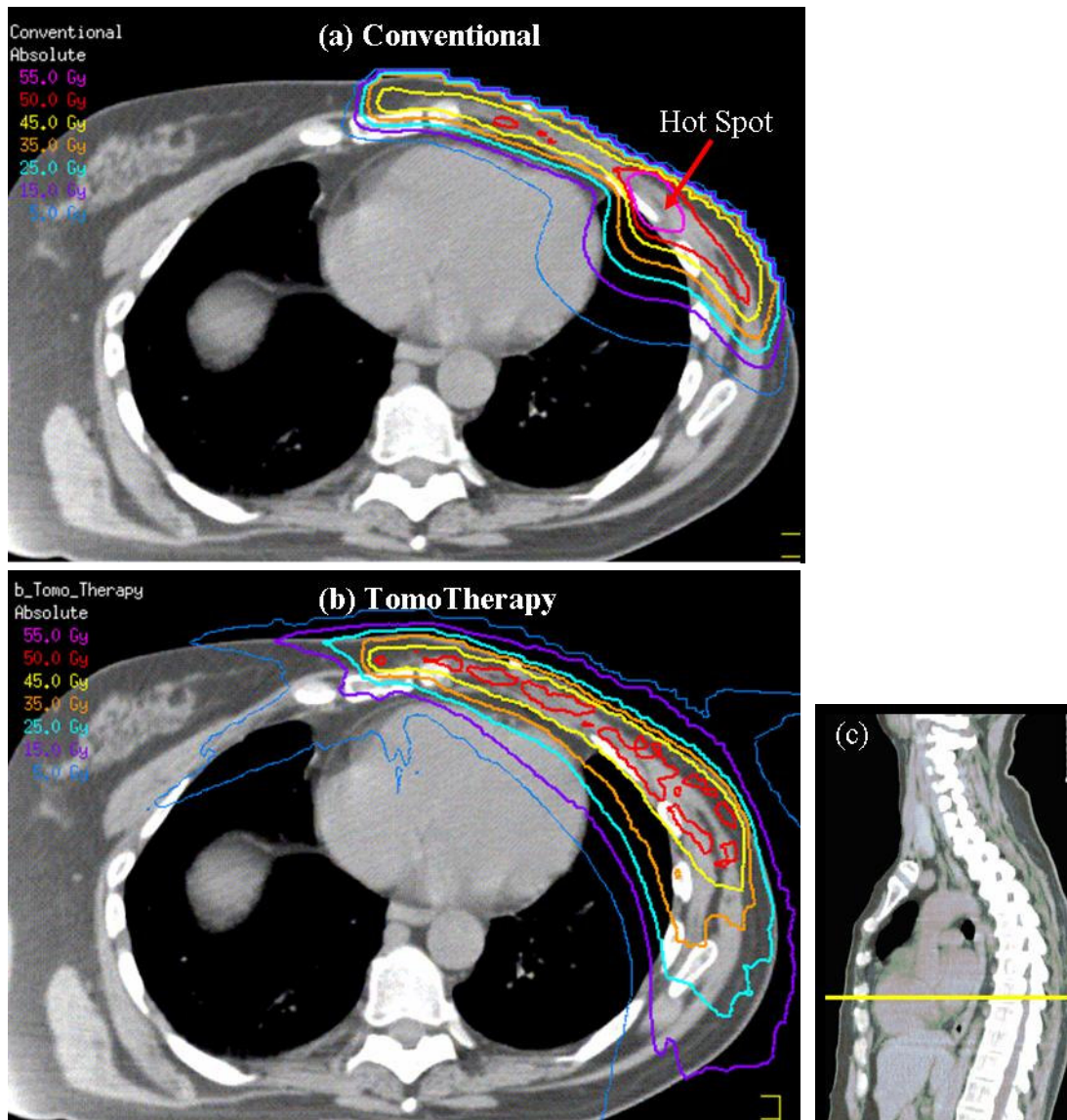
Figure 14. Transverse views of the conventional plan (a) and TomoTherapy plan (b) taken at the CW region as shown on the sagittal view (c).

3.3.2. DVH Comparisons

The DVH comparisons are shown in Figure 15. The conventional plan showed a

small volume of the PTV receiving high dose created by the junction of the medial and

lateral CW. For the TomoTherapy plan dose homogeneity was better than the

conventional plan for both the SCl/AX and CW PTVs. However, low dose (5 Gy or

more) covered a larger volume of the normal tissue not including critical structures. The

crossover dose for the ipsilateral lung was 4.3 Gy, and the crossover dose for the heart

was 6 Gy.
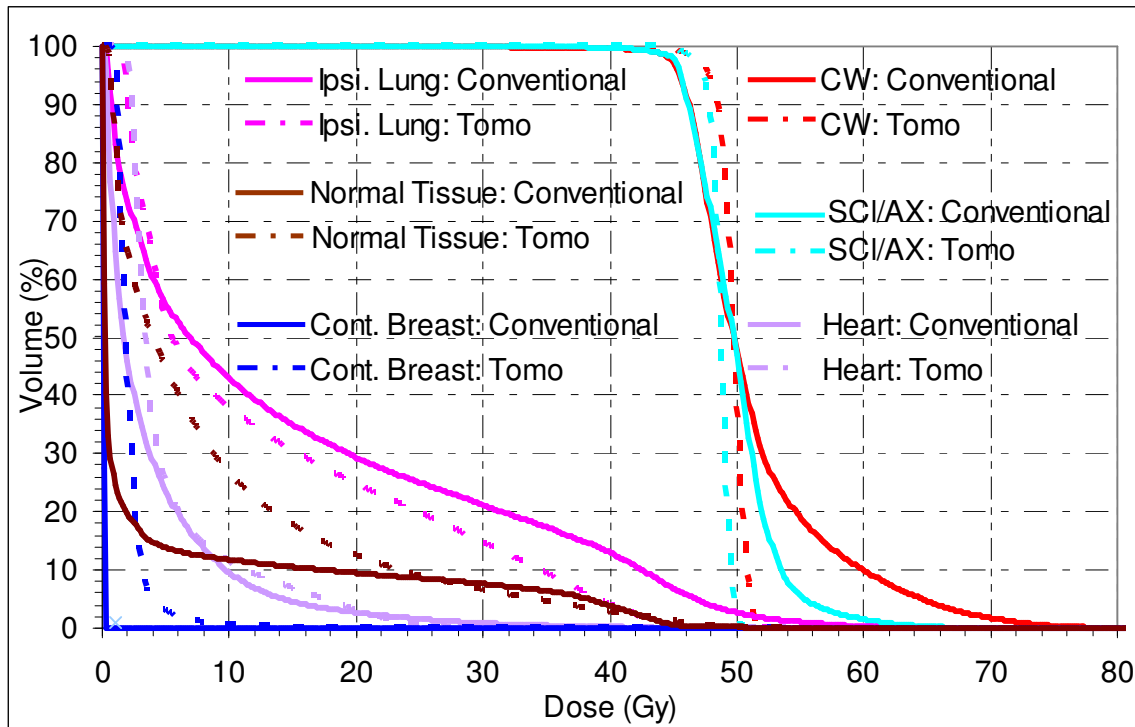
Figure 15. DVH comparisons for distribution shown in Figures 12 to 14. Solid lines –
conventional plan, dashed lines –TomoTherapy plan. CW – CW PTV; SCl/AX –
supraclavicular/axillary PTV; Ipsi – ipsilateral; Cont – contralateral

3.3.3. Radiation Oncologist Review

A radiation oncologist evaluated the clinical acceptability of both conventional and

TomoTherapy plans and scored the conventional plan marginally acceptable and the

TomoTherapy plan acceptable. After reviewing the dose distributions and DVHs for both plans, he ranked the TomoTherapy plan superior. The absence of hot and cold spots on the TomoTherapy plan was listed as a primary reason for preferring TomoTherapy plan over the conventional plan.

3.3.4. Chest Wall

The TomoTherapy plan showed a more uniform dose distribution. The average CW dose ($\pm$ 1σ) was 49.9 $\pm$ 1.1 Gy on the TomoTherapy plan and 51.4 $\pm$ 6.1 Gy on the conventional plan. Dose irradiating 90% to 10% of the CW volume was 13.6 Gy for the conventional plan and was 2.3 Gy for the TomoTherapy plan. Although the CW PTV dose distribution showed better uniformity on the TomoTherapy plan, TCP values were comparable for both plans (conventional plan = 0.989 and TomoTherapy plan = 0.996).

3.3.5. Ipsilateral Lung

During optimization of the TomoTherapy plan, high penalty factor was assigned to the ipsilateral lung objective to force photon beams to come in an oblique direction. As a result, compared to the conventional plan, the TomoTherapy plan showed less volume irradiated. The ipsilateral lung receiving dose above 20 Gy was reduced from 29.4% for the conventional plan to 24.8% for the TomoTherapy plan. Also unlike the TomoTherapy plan, the ipsilateral lung was exposed to high doses with the conventional plan (e.g. 5% of the ipsilateral lung received 40 Gy or more). The average ipsilateral lung dose ($\pm$ 1σ) was comparatively lower on the TomoTherapy plan (conventional plan = 14.7 $\pm$ 16.2 Gy and TomoTherapy plan = 12.3 $\pm$ 12.6 Gy). A relatively lower NTCP value was calculated for the TomoTherapy plan although both values were insignificant (conventional plan = 0.025 and TomoTherapy plan = 0.005).

3.3.6. Heart

The heart volume receiving a dose above 30 Gy or more was very low (0.02% for the TomoTherapy plan and 0.9% for the conventional plan). The heart volume receiving 15 Gy or more was slightly higher on the TomoTherapy plan (conventional plan = 4.6% and TomoTherapy plan = 6.8%). As shown on Figure 15, large volume of the ipsilateral lung received low dose (2.5 Gy) with the TomoTherapy plan compared to the conventional plan. The average heart dose ($\pm$ 1σ) was reduced from 5.1 $\pm$ 4.8 Gy on the conventional plan to 3.9 $\pm$ 5.6 Gy on the TomoTherapy plan. A relatively lower NTCP value was calculated for the TomoTherapy plan although both values were insignificant (conventional plan = 0.0018 and TomoTherapy plan = 0.0003).

3.3.7. Contralateral Breast

The average contralateral breast dose ($\pm$ 1σ) was 2.1 $\pm$ 1.4 Gy on the TomoTherapy plan and 0.1 $\pm$ 0.1 Gy on the conventional plan. As shown in the DVH comparison, a large volume of the contralateral breast was exposed to low dose (2 Gy) with the TomoTherapy plan. Also, the percent of volume receiving 5 Gy or more on the conventional plan was 0.0% and 3.0% on the TomoTherapy plan. Age dependence effect of radiation induced breast cancer was ignored when calculating SCCP for patient two (age = 53 yrs). The calculated SCCP value was relatively higher on the TomoTherapy plan (conventional plan 0.0003 and TomoTherapy plan = 0.0125).

3.3.8. Normal Tissue

The normal tissue volume receiving between 5 and 25 Gy for this patient was 11.6 cm^3 for the conventional plan and 61.9 cm^3 on the TomoTherapy plan. The calculated SCCP value was relatively higher on the TomoTherapy plan (conventional plan = 0.002 and TomoTherapy plan 0.008).

3.4. Patient Three

A 49-year old female was diagnosed to have a squamous cell carcinoma of the upper outer quadrant of the left breast, stage T2N1M0 carcinoma with 2 out of 10 lymph nodes positive with extra-nodal extension. The conventional electron beam PMRT plan had the following fields:

1. AP/PA 6 MV photon beam SCl/AX fields,

2. 9 MeV electron beam IMN field,

3. 9 MeV electron beam medial CW field, and

4. 9 MeV electron beam lateral CW field.

The prescription for the CW was 50 Gy in 25 fractions. The prescription for the SCl/AX was 45 Gy in 25 fractions.

3.4.1. Isodose Comparison

Figure 16 shows the isodose comparison between the conventional plan (Figure 16a) and the TomoTherapy plan (Figure 16b) on the transverse CT image slice in the region of the supraclavicular nodes delineated by the yellow line in sagittal midline CT image shown in Figure 16c. The yellow green 40.5 Gy isodose line represents the 90% prescription isodose line where the TomoTherapy plan was optimized to match the conventional plan. Compared to the conventional plan, the TomoTherapy plan showed small area covered by hot spot of 50 Gy (110% of the prescription dose).

The conventional plan showed a sharper dose falloff than the TomoTherapy plan along the beam edges of the parallel-opposed photon beams of the conventional plan. Greater dose restriction outside the supraclavicular PTV in the TomoTherapy plan during optimization might have resulted in a sharper dose falloff along the "beam edges" delineated by the conventional plan. The TomoTherapy plan also showed a significant

volume of tissue outside the PTV receiving low dose (5 Gy or more). However, the

TomoTherapy plan showed a greater dose gradient beyond the 40.5 Gy isodose line in

AP direction. This resulted in lower dose to region posterior to the supraclavicular nodes,

including the left upper lobe of lung.
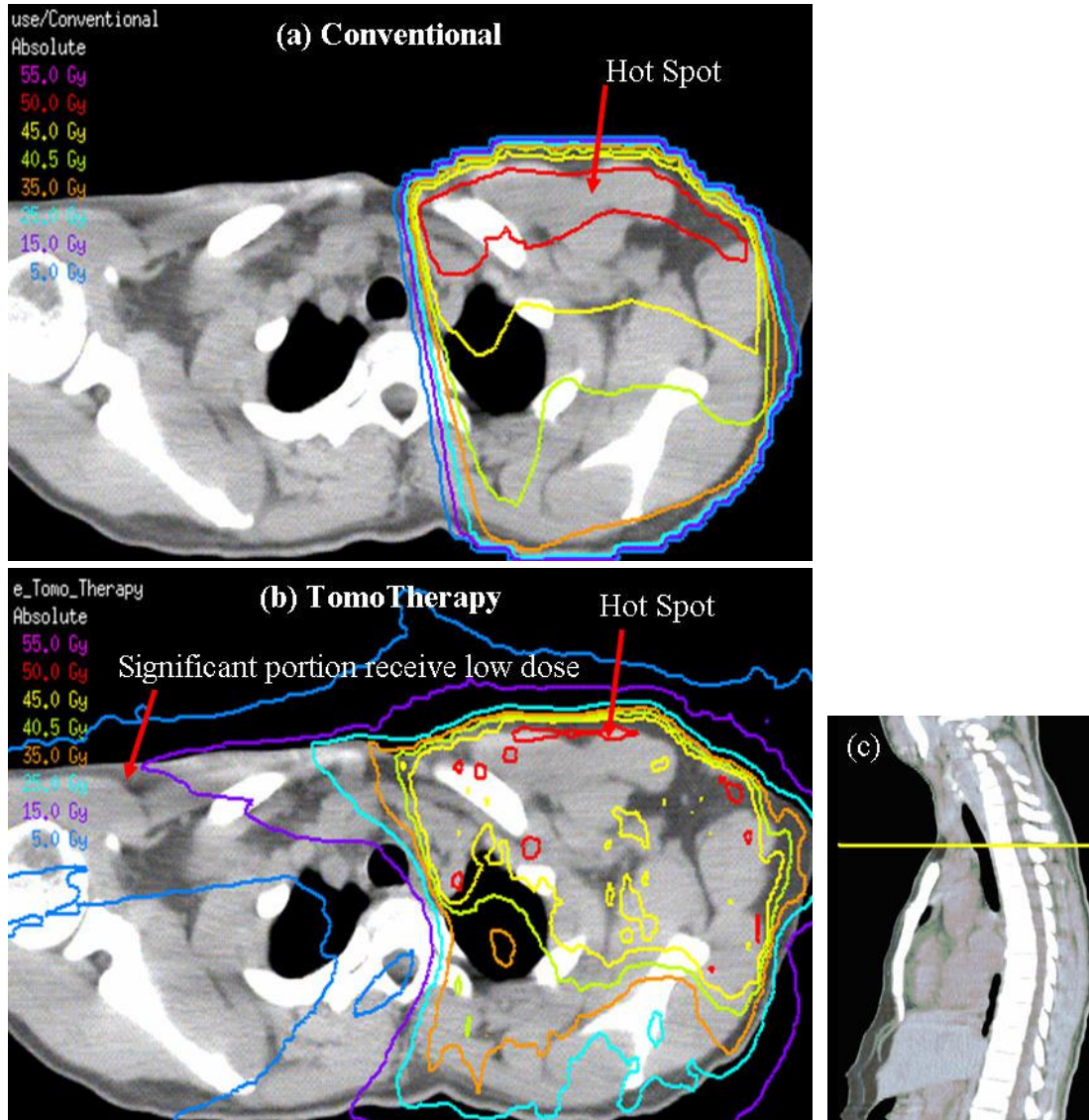
Figure 16. Transverse views of the conventional plan (a) and TomoTherapy plan (b)
taken at the supraclavicular nodal region shown on sagittal view (c).

Figure 17 shows the isodose comparison the conventional plan (Figure 17a) and the

TomoTherapy plan (Figure 17b) on a transverse CT image slice in the region of the IMN

delineated by the yellow line in sagittal image shown in Figure 17c. The yellow 45 Gy

isodose line represents the 90% prescription isodose line, where the TomoTherapy plan

was optimized to match the conventional plan. The conventional plan showed a hot spot

of 55 Gy (110% of the prescription dose) at the junction of the lateral and medial electron

fields. Although in practice this hot spot is reduced (smeared) by moving the match line,

this is not reflected in the conventional plan.

The conventional plan showed a sharper dose falloff than the TomoTherapy plan

along the beam edges of the electron beams for the IMN and the lateral CW of the

conventional plan. The physical location of the IMN, in between the contralateral and

ipsilateral lung at a depth of approximately 2 – 5.5 cm from the surface made it difficult

for the TomoTherapy trying to cover this region with a photon beam. As a result, dose

bleeding toward aorta was observed throughout all five cases. Also, the TomoTherapy

plan showed a significant volume of tissue outside the PTV receiving low dose (5 Gy or

more).

Figure 18 shows the isodose comparison between the conventional plan (Figure 18a)

and the TomoTherapy plan (Figure 18b) on the transverse CT image slice near the

inferior border of the CW PTV, and is delineated by the yellow line in sagittal midline

CT image shown in Figure 17c. The yellow 45 Gy isodose line represents the 90%

isodose line, where the TomoTherapy plan was optimized to match the conventional plan.

The conventional plan showed a hot spot of 55 Gy (110% of the prescription dose) at the

junction of the lateral and medial electron fields. Although in practice this hot spot is

reduced (smeared) by moving the match line, this is not reflected in the conventional
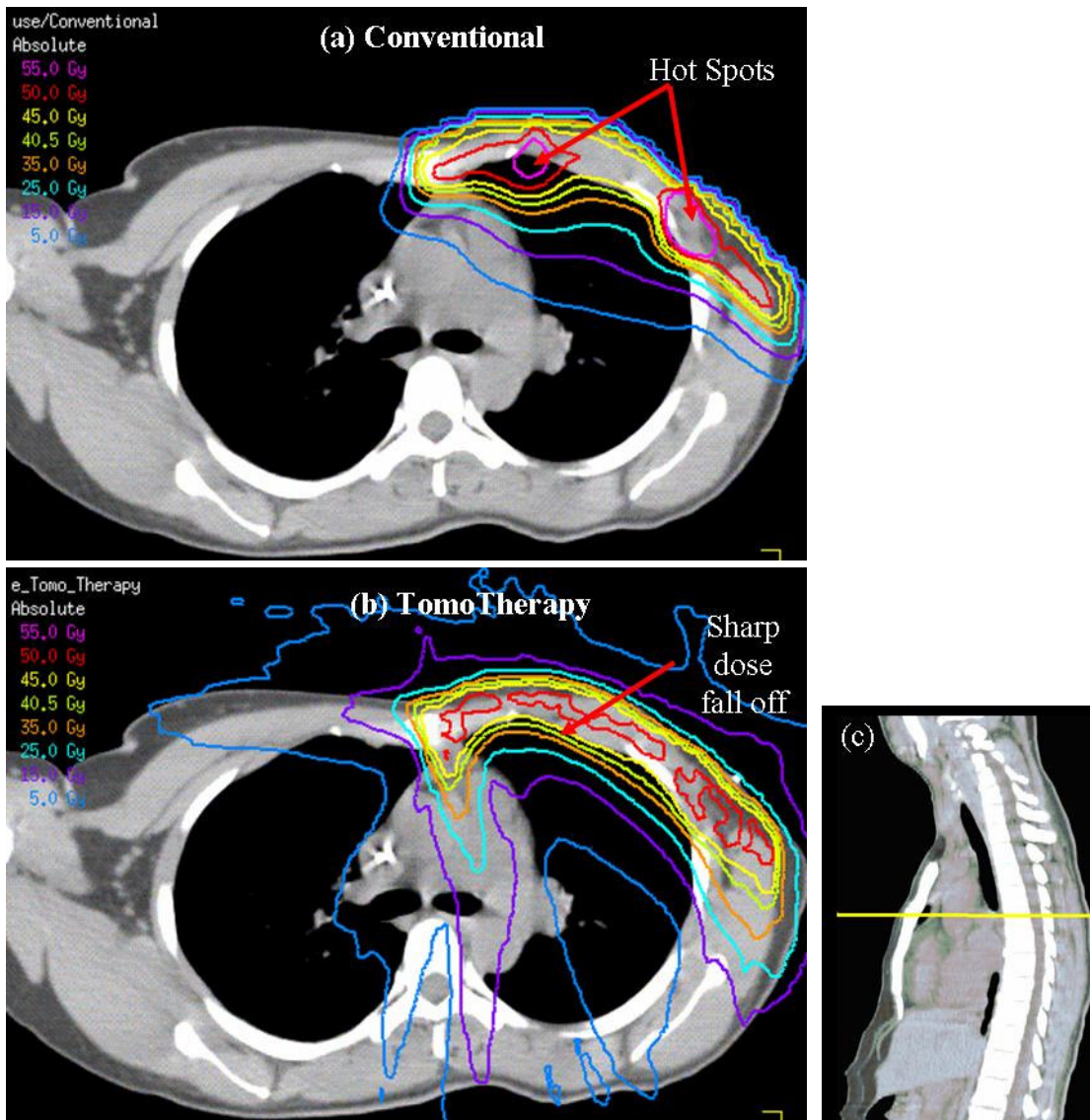
plan.

Figure 17. Transverse views of the conventional plan (a) and TomoTherapy plan (b) taken at the IMN region as shown on the sagittal view (c).
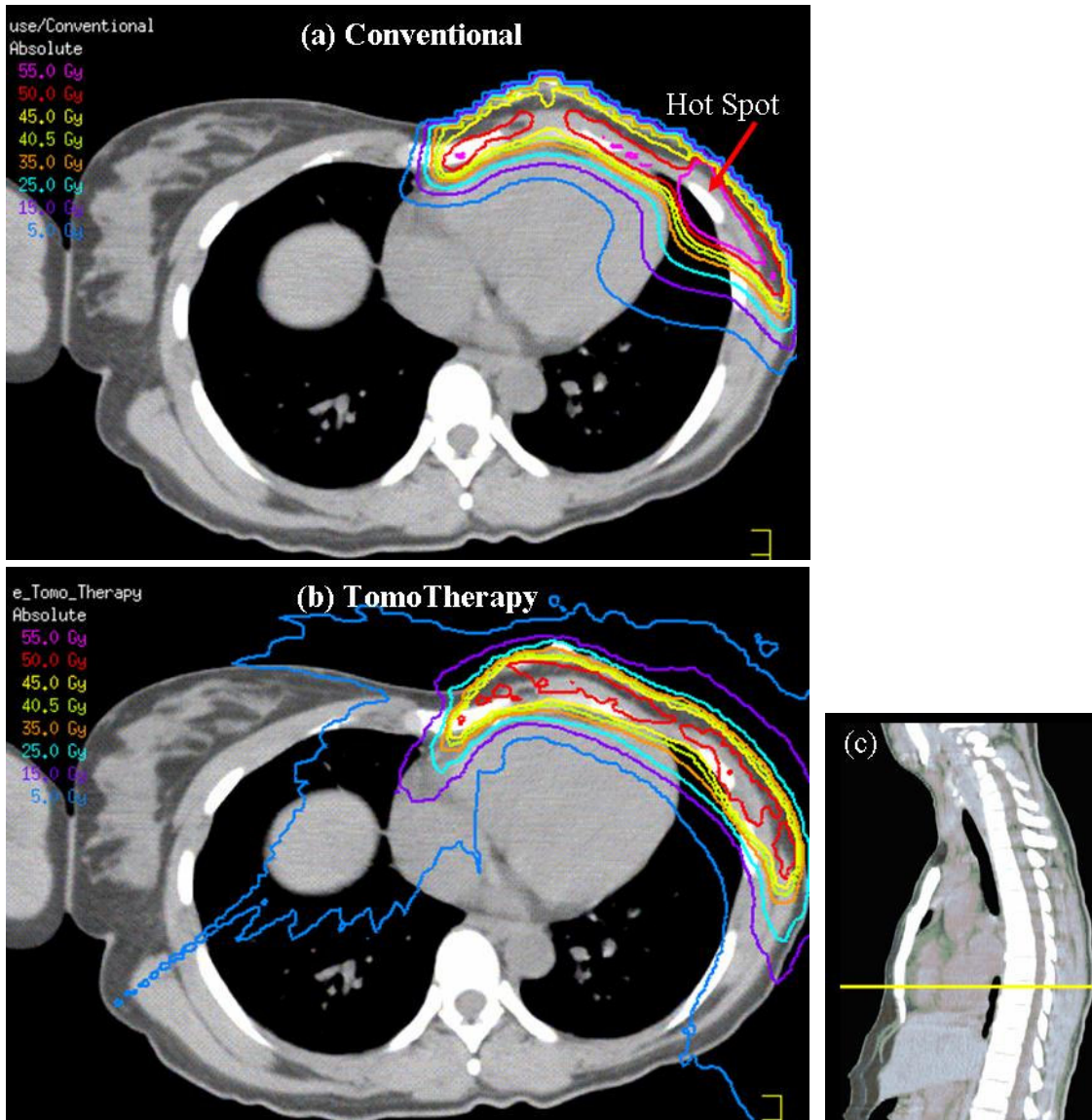
Figure 18. Transverse views of the conventional plan (a) and TomoTherapy plan (b) taken at the CW region as shown on the sagittal view (c).

The conventional plan showed a sharper dose falloff than that of the TomoTherapy plan along the beam edges of the medial and the lateral CW of the conventional plan. Greater dose restriction outside the CW PTV in the TomoTherapy plan during optimization might have resulted in a sharper dose falloff along the "beam edges" delineated by the conventional plan. The TomoTherapy plan also showed a significant volume of tissue outside the CW PTV receiving low dose (5 Gy or more). Both the

conventional and TomoTherapy plans showed similarity when it comes to sparing the lung and heart.

3.4.2. DVH Comparisons

The DVH comparisons are shown in Figure 19. The conventional plan showed small volume of the PTV receiving high dose created by the junction of the medial and lateral CW. For the TomoTherapy plan, dose homogeneity was better than the conventional plan for both the SCl/AX and CW PTVs. However, low dose (5 Gy or more) covered a larger volume of the normal tissue not including critical structures. The crossover dose for the ipsilateral lung was 5.5 Gy. The crossover dose for the heart was 15 Gy.
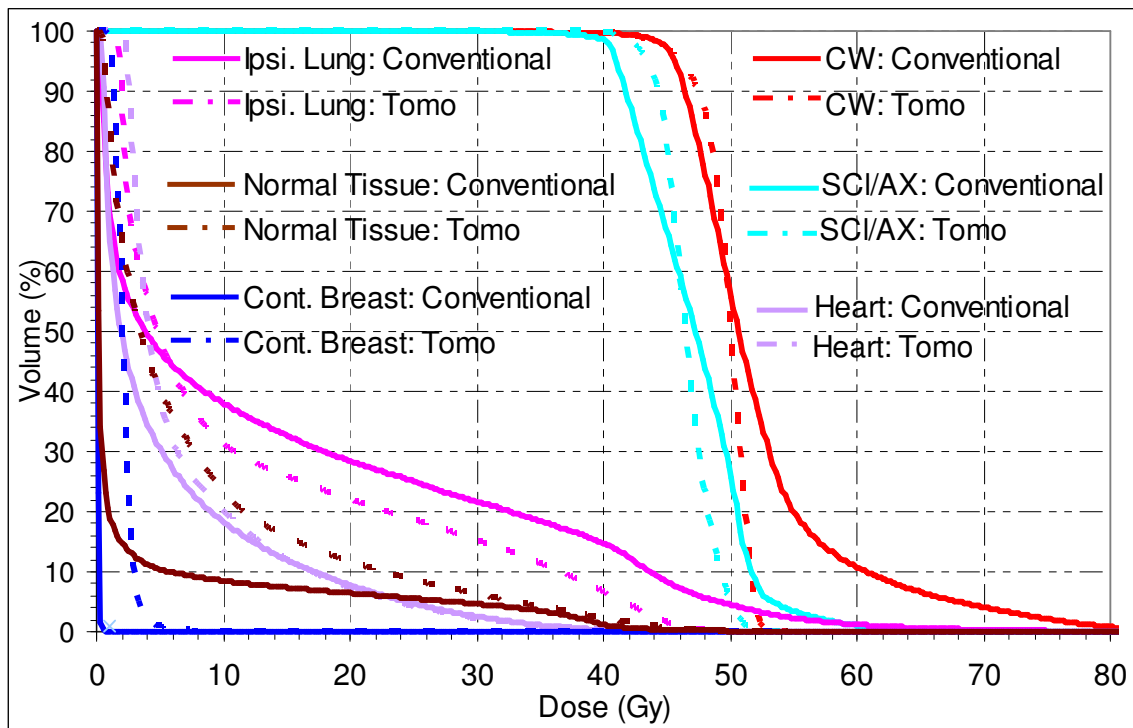
Figure 19. DVH comparisons for distribution shown in Figures 16 to 18. Solid lines – conventional plan, dashed lines –TomoTherapy plan. CW – CW PTV; SCl/AX – supraclavicular/axillary PTV; Ipsi – ipsilateral; Cont – contralateral

3.4.3. Radiation Oncologist Review

A radiation oncologist evaluated the clinical acceptability of both conventional and TomoTherapy plans and scored both plans acceptable. After reviewing the dose distributions and DVHs for both plans, he ranked the TomoTherapy plan superior. No comment was provided on his decision.

3.4.4. Chest Wall

The TomoTherapy plan showed an improved uniform dose distribution. The average CW dose ($\pm$ 1σ) was 49.7 $\pm$ 1.9 Gy on the TomoTherapy plan and 52.4 $\pm$ 7.0 Gy on the conventional plan. Dose irradiating 90% to 10% of the CW volume was 14.3 Gy on the conventional plan and was 4.2 Gy for the TomoTherapy plan. Even though the CW PTV dose distribution showed better uniformity on the TomoTherapy plan, the TCP values were similar for both plans (conventional plan = 0.989 and TomoTherapy plan = 0.991).

3.4.5. Ipsilateral Lung

The TomoTherapy plan showed less volume of ipsilateral lung irradiated. The ipsilateral lung receiving dose above 20 Gy was reduced from 28.4% on the conventional plan to 22.0% on the TomoTherapy plan. Also unlike the TomoTherapy plan, the ipsilateral lung was exposed to high doses with the conventional plan (e.g. 5% of the ipsilateral lung received 40 Gy or more). The average ipsilateral lung dose ($\pm$ 1σ) was comparatively lower on the TomoTherapy plan (conventional plan = 14.0 $\pm$ 17.7 Gy and on the TomoTherapy plan = 11.5 $\pm$ 13.3 Gy). A relatively lower NTCP value was calculated for the TomoTherapy plan although both values were small (conventional plan = 0.02 and TomoTherapy plan = 0.0031).

3.4.6. Heart

The heart volume receiving above 30 Gy or more was similar for both plans (2.2% for the TomoTherapy plan and 2.5% for the conventional plan). Also similar was the heart volume receiving 15 Gy or more (conventional plan = 12 % and TomoTherapy plan = 12.1 %). As shown on Figure 19 large volume of the ipsilateral lung received low dose (2.5 Gy) with the TomoTherapy plan compared to the conventional plan. A higher average heart dose ($\pm 1\sigma$) was observed in the TomoTherapy plan (conventional plan = 5.6 $\pm$ 8.0 Gy and TomoTherapy plan = 7.1 $\pm$ 7.05 Gy). The NTCP values were the same for both plans (conventional plan = 0.004 and TomoTherapy plan = 0.004).

3.4.7. Contralateral Breast

The average contralateral breast dose ($\pm 1\sigma$) was 2.1 $\pm$ 0.8 Gy for the TomoTherapy plan while 0.1 $\pm$ 0.1 Gy for the conventional plan. As shown on in Figure 19, relatively large volume of the contralateral breast was exposed to low dose (2 Gy) with the TomoTherapy plan compared to the conventional plan. Also, the percent of volume receiving 5 Gy or more was similar on both plans (conventional plan = 0% and TomoTherapy plan = 0.9%). Age dependence effect of radiation induced breast cancer was ignored when calculating SCCP for patient three (age = 49 yrs). The calculated SCCP value was relatively higher on the TomoTherapy plan (conventional plan = 0.0004 and TomoTherapy plan = 0.0131).

3.4.8. Normal Tissue

The normal tissue volume receiving dose between 5 and 25 Gy was 9.2 cm^3 on the conventional plan and 52.4 cm^3 on the TomoTherapy plan. The calculated SCCP value per year was relatively higher for the TomoTherapy plan (conventional plan = 0.002 and TomoTherapy plan = 0.007).

3.5. Patient Four

A 39 – year old female was diagnosed to have an infiltrating ductal carcinoma of the upper outer quadrant of the left breast, stage T3pN2aM0 carcinoma with 9 out of 12 lymph nodes positive with extra-nodal extension. The conventional electron beam PMRT plan had the following fields:

1. AP/PA 6 MV photon beam SCl/AX fields,

2. 12 MeV electron beam IMN field,

3. 9 MeV electron beam medial CW field, and

4. 9 MeV electron beam lateral CW field.

The prescription for the CW was 50 Gy in 25 fractions. The prescription for the SCl/AX was 48.25 Gy in 25 fractions.

3.5.1. Isodose Comparison

Figure 20 shows the isodose comparison between the conventional plan (Figure 20a) and the TomoTherapy plan (Figure 20b) on the transverse CT image slice in the region of the supraclavicular nodes delineated by the yellow line in sagittal midline CT image shown in Figure 20c. The yellow green 43.4 Gy isodose line represents the 90% prescription isodose line where the TomoTherapy plan was optimized to match the conventional plan. The conventional plan showed a hot spot of 55 Gy (110% of the prescription dose) in the medial, anterior portion of the dose distribution, whereas the TomoTherapy plan showed a lower hot spot of 50 Gy (104% of the prescription dose) in that region. Unlike the conventional plan, the TomoTherapy plan avoided irradiating the ipsilateral lung with high dose (45 Gy).

The conventional plan showed a sharper dose falloff than the TomoTherapy plan along the beam edges of the parallel-opposed photon beams of the conventional plan. The

TomoTherapy plan also showed a significant volume of tissue outside the PTV receiving

low dose (5 Gy or more).
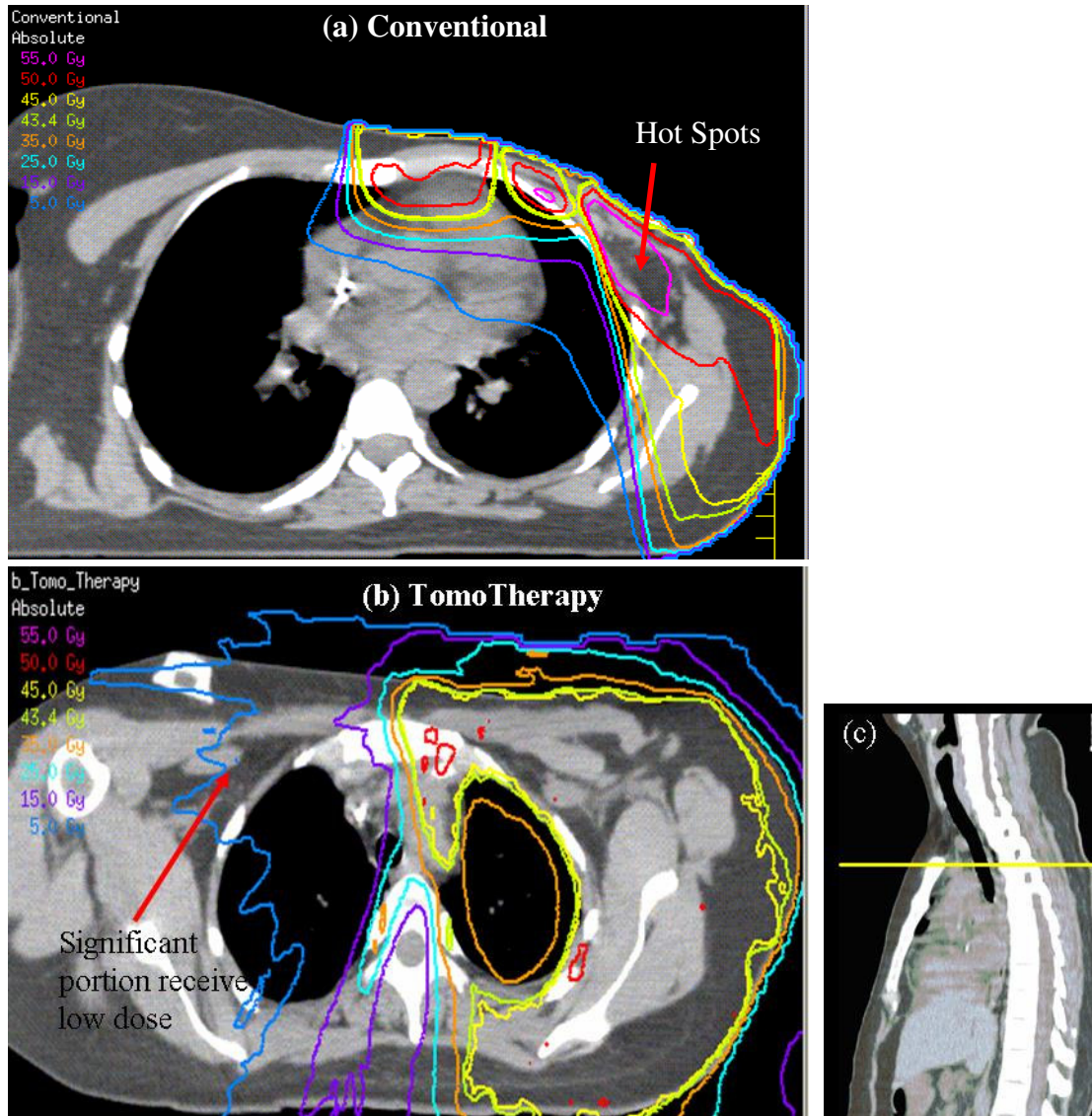
Figure 20. Transverse views of the conventional plan (a) and TomoTherapy plan (b)
taken at the supraclavicular nodal region shown on sagittal view (c).

Figure 21 shows the isodose comparison for the conventional plan (Figure 21a) and

the TomoTherapy plan (Figure 21b) on a transverse CT image slice in the region of the

IMN delineated by the yellow line in sagittal image shown in Figure 21c. The yellow 45

Gy isodose line represents the 90% prescription isodose line, where the TomoTherapy

plan was optimized to match the conventional plan. The Conventional plan showed a hot

spot of 55 Gy (110% of the prescription dose) at the junction of the lateral and medial

electron fields.

The conventional plan showed a sharper dose falloff than that of the TomoTherapy

plan along the beam edges of the electron beams for the IMN and the lateral CW of the

conventional plan. Higher dose near the aorta was observed in the TomoTherapy plan.

The TomoTherapy plan showed a significant volume of tissue outside the PTV receiving

low dose (5 Gy or more).

Figure 22 shows the isodose comparison between the conventional plan (Figure 22a)

and the TomoTherapy plan (Figure 22b) on the transverse CT image slice near the

inferior border of the CW PTV, and is delineated by the yellow line in sagittal midline

CT image shown in Figure 22c. The yellow 45 Gy isodose line represents the 90%

isodose line, where the TomoTherapy plan was optimized to match the conventional plan.

The conventional plan showed a significant region of tissue receiving 55 Gy (110% of the

prescription dose).

The conventional plan showed a sharper dose falloff than that of the TomoTherapy

plan along the beam edges of the medial and the lateral CW of the conventional plan. The

TomoTherapy plan showed a significant volume of tissue outside the PTV receiving low

dose (5 Gy or more).

3.5.2. DVH Comparisons

The DVH comparisons are shown in Figure 23. The conventional plan showed a

small volume of the PTV receiving high dose created by the junction of the medial and

lateral CW. Although in practice this hot spot is reduced by moving (smeared) the match

line. For the TomoTherapy plan showed dose homogeneity was better than the

conventional plan for both the SCl/AX and CW PTVs. However, low dose (5Gy or more) covered a large area of contralateral breast, contralateral lung, and the normal tissue not including critical structures. The crossover dose for the ipsilateral lung was 16 Gy. The crossover dose for the heart was 8.6 Gy.

Figure 21. Transverse views of the conventional plan (a) and TomoTherapy plan (b) taken at the IMN region as shown on the sagittal view (c).
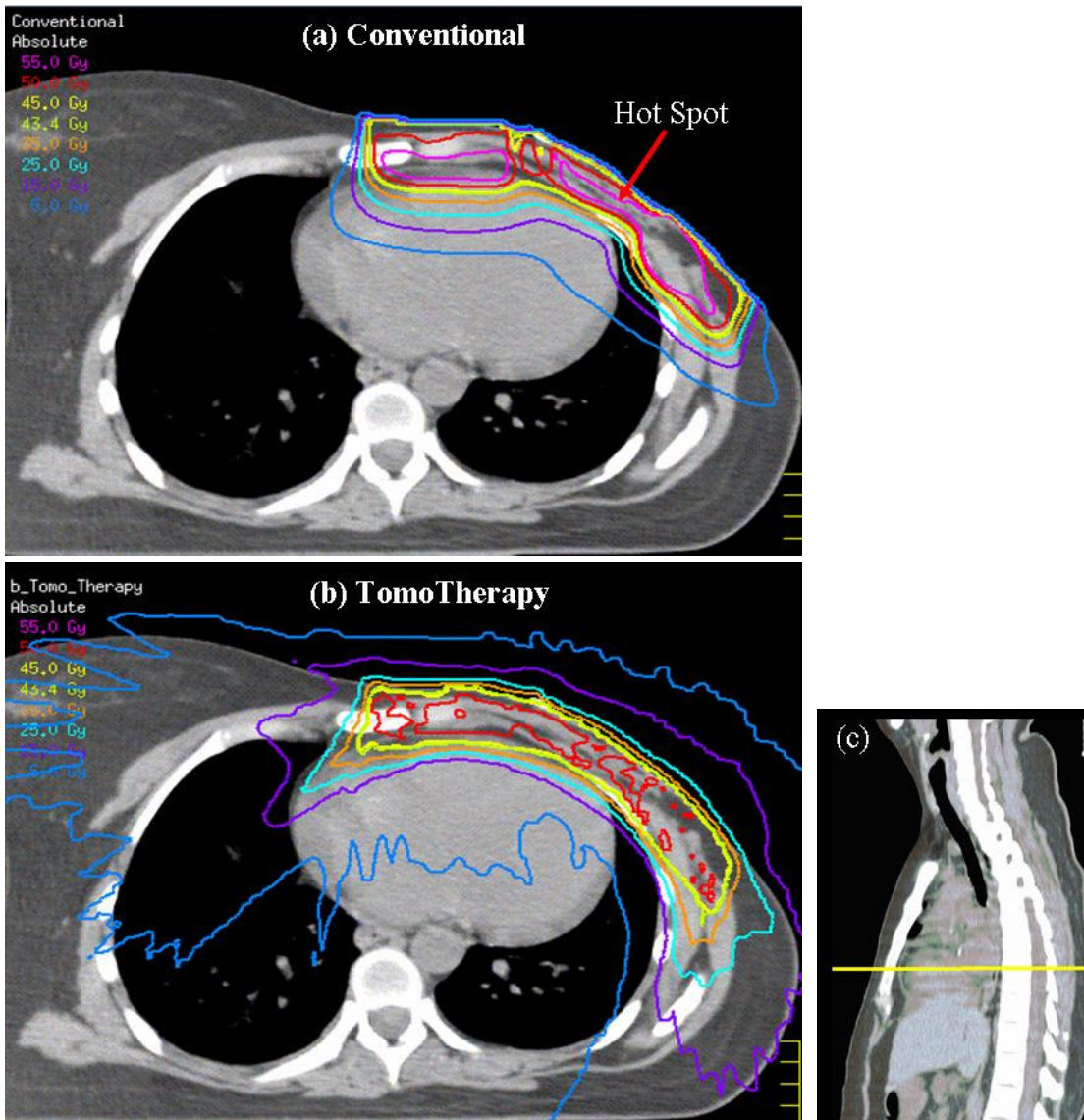
Figure 22. Transverse views of the conventional plan (a) and TomoTherapy plan (b) taken at the CW region as shown on the sagittal view (c).
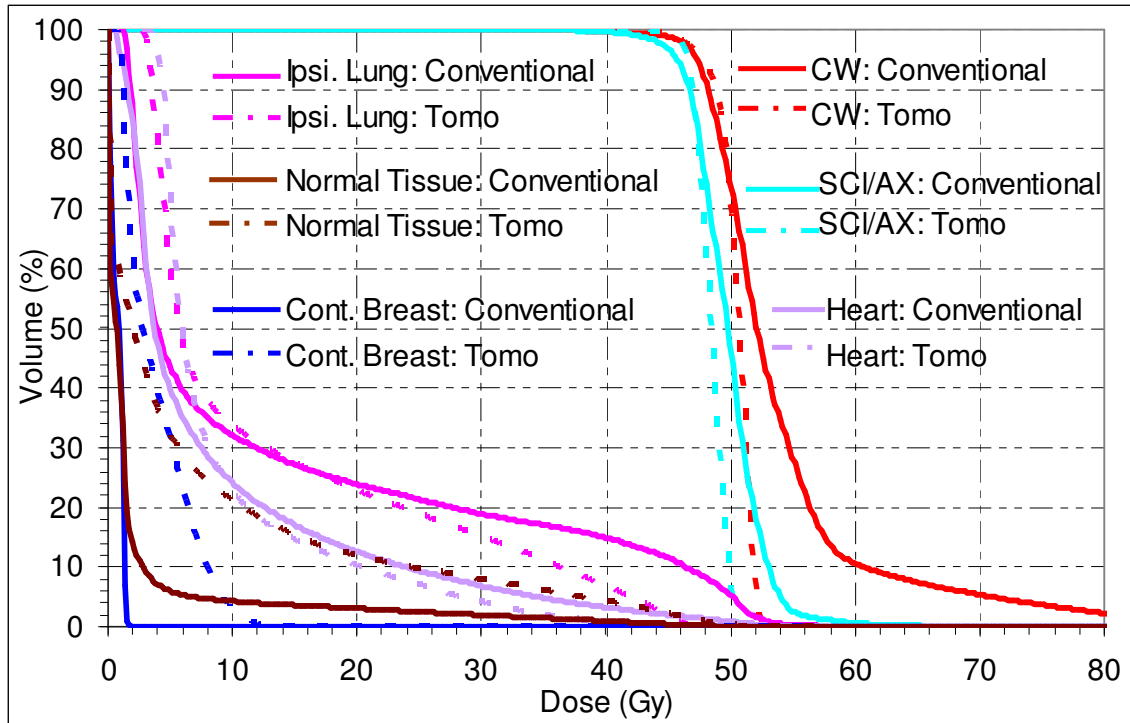
Figure 23. DVH comparisons for distribution shown in Figures 20 to 22. Solid lines – conventional plan, dashed lines –TomoTherapy plan. CW – CW PTV; SCl/AX – supraclavicular/axillary PTV; Ipsi – ipsilateral; Cont – contralateral

3.5.3. Radiation Oncologist Review

A radiation oncologist evaluated the clinical acceptability of both conventional and TomoTherapy plans and scored the conventional plan marginally acceptable and the TomoTherapy plan acceptable. After reviewing the dose distributions and DVHs for both plans, he ranked the TomoTherapy plan superior. Better PTV coverage and fewer hot spots on the TomoTherapy plan was listed as a primary reason for preferring TomoTherapy plan over the conventional plan.

3.5.4. Chest Wall

The TomoTherapy plan showed an improved uniform dose distribution. The average CW dose ($\pm$ 1σ) was 50.4 $\pm$ 1.5 Gy on the TomoTherapy plan and 54.0 $\pm$ 7.5 Gy on the conventional plan. Dose irradiating 90% to 10% of the CW volume was 12.5 Gy for the

conventional plan and was 3.0 Gy for the TomoTherapy plan. Even though, the CW PTV

dose distribution showed better uniformity on the TomoTherapy plan, the TCP values

were similar for both plans (conventional plan = 0.996 and TomoTherapy plan = 0.997).

3.5.5. Ipsilateral Lung

Compared to the conventional plan, the TomoTherapy plan avoided exposing the

ipsilateral lung with high doses (45 Gy). However, as shown in Figure 23, a large

volume of the ipsilateral lung received low dose (5 Gy or more) with the TomoTherapy

plan. Similar values for $V20_{lung}$ was observed for both plans (conventional plan = 23.9%

and TomoTherapy plan = 22.8%). The average ipsilateral lung dose ($\pm$ 1σ) was

comparatively lower on the TomoTherapy plan (conventional plan = 13.3 $\pm$ 16.7 Gy and

TomoTherapy plan = 12.7 $\pm$ 12.7 Gy). A relatively smaller NTCP value was observed for

the TomoTherapy plan although both values were insignificant (conventional plan =

0.0117 and TomoTherapy plan = 0.0059).

3.5.6. Heart

The heart receiving dose above 30 Gy or more was reduced from 6.8% on the

conventional plan to 4.1% on the TomoTherapy plan. The heart volume receiving 15 Gy

or more was reduced from 17.1% on the conventional plan to 14.5% on the

TomoTherapy plan. However, as shown in Figure 23, a large volume of the heart

received low dose (2.5 Gy) with the TomoTherapy plan. Comparable average heart dose

($\pm$ 1σ) was observed in both plans (conventional plan = 8.5 $\pm$ 10.7 Gy and TomoTherapy

plan = 9.1 $\pm$ 7.7 Gy). A lower NTCP value was calculated for the TomoTherapy plan

(conventional plan = 0.020 and TomoTherapy plan = 0.007).

3.5.7. Contralateral Breast

Dose to the contralateral breast was significantly higher in the TomoTherapy plan than in the conventional plan. The average contralateral breast dose ($\pm$ 1σ) was 3.8 $\pm$ 2.8 Gy on the TomoTherapy plan while 0.7 $\pm$ 0.5 Gy on the conventional plan. As shown in Figure 23, a large volume of the contralateral breast was exposed to low dose (2 Gy) with the TomoTherapy plan. Large difference was observed for the percent of volume receiving 5 Gy or more (conventional plan = 0.0% and TomoTherapy plan = 30.6%). Age dependence effect of radiation induced breast cancer was ignored when calculating SCCP for patient four (age = 39 yrs). The calculated SCCP value was relatively higher for the TomoTherapy plan (conventional plan = 0.0046 and TomoTherapy plan = 0.0183).

3.5.8. Normal Tissue

The normal tissue volume receiving between 5 and 25 Gy for this patient was 32.7 cm^3 for the conventional plan and 89.1 cm^3 on the TomoTherapy plan. The calculated SCCP value was relatively higher for the TomoTherapy plan (conventional plan = 0.004 and TomoTherapy plan = 0.009).

3.6. Patient Five

A 49 – year old female was diagnosed to have an infiltrating ductal carcinoma of the upper outer quadrant of the left breast, stage T1scpN1M0 carcinoma with 2 out of 19 lymph nodes positive with extra-nodal extension. The conventional electron beam PMRT plan had the following fields:

1. AP/PA 6 MV photon beam SCl/AX fields,

2. 12 MeV electron beam IMN field,

3. 9 MeV electron beam medial CW field, and

4. 9 MeV electron beam lateral CW field.

The prescription for the CW was 50 Gy in 25 fractions. The prescription for the SCl/AX was 45 Gy in 25 fractions.

3.6.1. Isodose Comparison

Figure 24 shows the isodose comparison between the conventional plan (Figure 24a) and the TomoTherapy plan (Figure 24b) on the transverse CT image slice in the region of the supraclavicular nodes delineated by the yellow line in sagittal midline CT image shown in Figure 24c. The yellow green 40.5 Gy isodose line represents the 90% prescription isodose line where the TomoTherapy plan was optimized to match the conventional plan. Unlike the TomoTherapy plan, the conventional plan showed large area covered by hot spot of 50 Gy (110% of the prescription dose).

The conventional plan showed a sharper dose falloff than the TomoTherapy plan along the beam edges of the parallel-opposed photon beams of the conventional plan. The TomoTherapy plan also showed a significant volume of tissue outside the PTV receiving low dose (5 Gy or more).

Figure 25 shows the isodose comparison between the conventional plan (Figure 25a) and the TomoTherapy plan (Figure 25b) on a transverse CT image slice in the region of the IMN delineated by the yellow line in sagittal image shown in Figure 25c. The yellow green 40.5 Gy isodose line represents the 90% prescription isodose line, where the TomoTherapy plan was optimized to match the conventional plan. The conventional plan showed a hot spot of 55 Gy (110% of the prescription dose) at the junction of the lateral and medial electron fields.
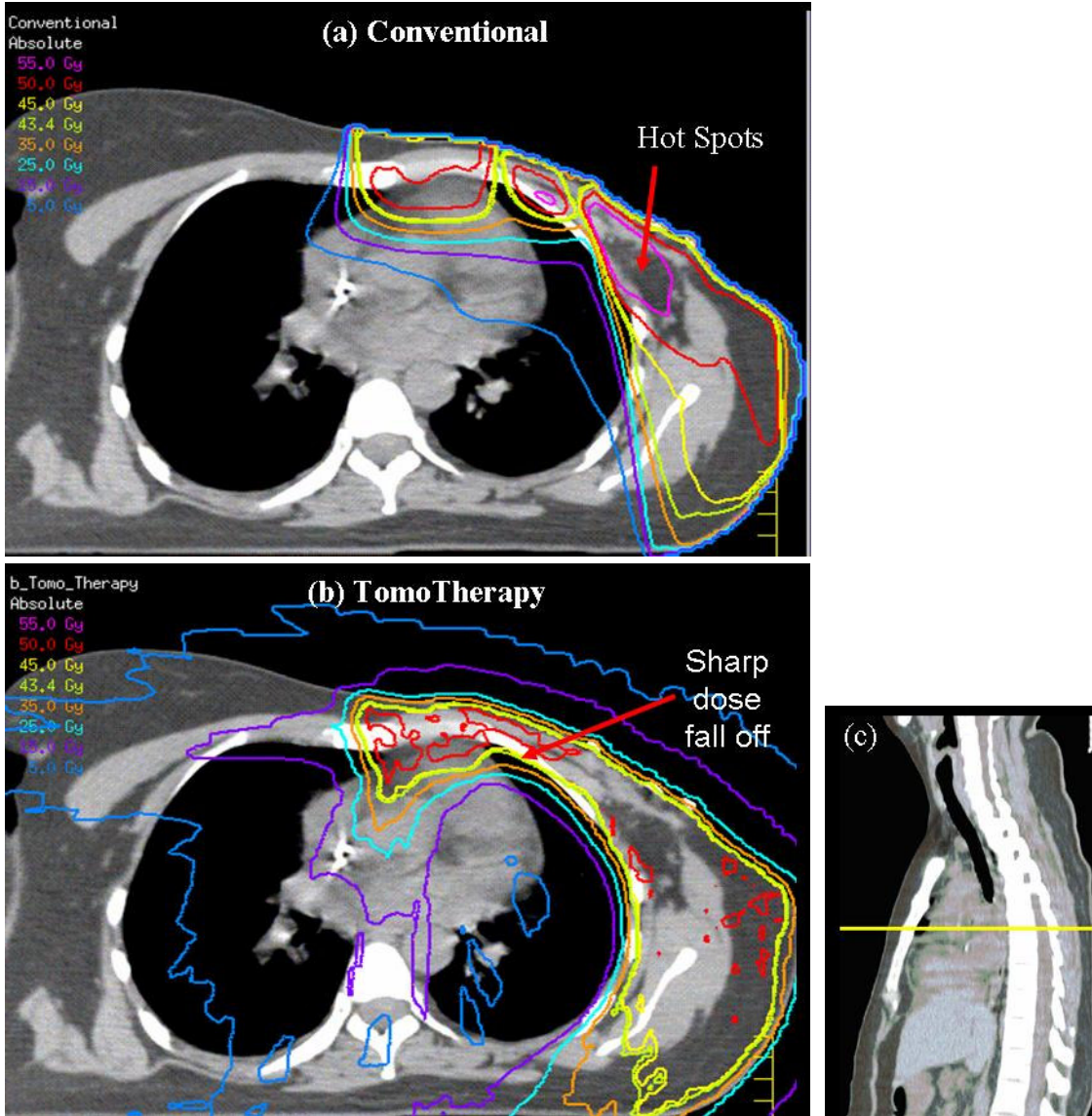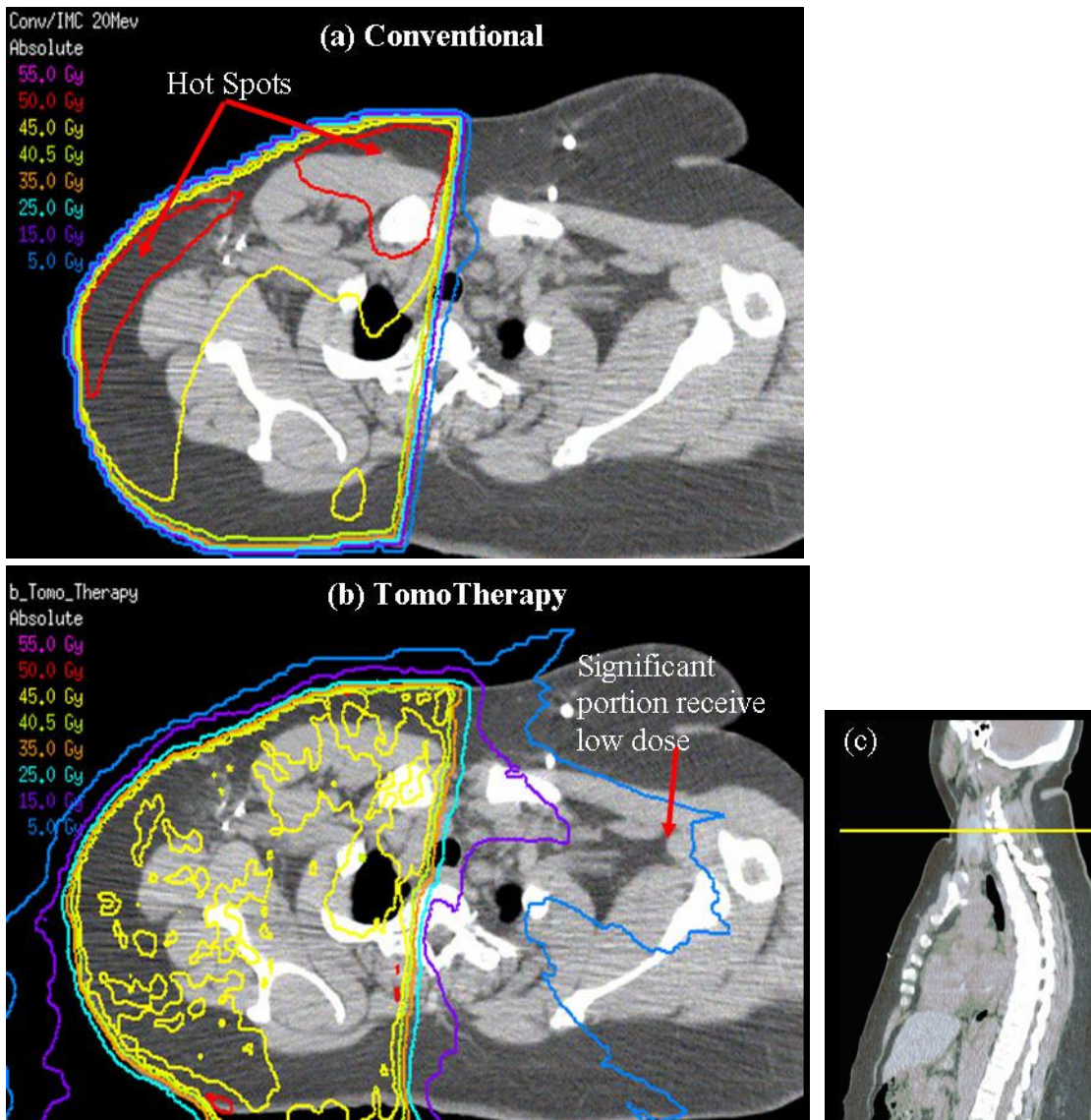
Figure 24. Transverse views of the conventional plan (a) and TomoTherapy plan (b) taken at the supraclavicular nodal region shown on sagittal view (c).

The conventional plan showed a sharper dose falloff than the TomoTherapy plan along the beam edges of the electron beams for the IMN and the lateral CW of the conventional plan. TomoTherapy showed more dose in the region of the aorta. Also, the TomoTherapy plan showed a significant volume of tissue outside the PTV receiving low dose (5 Gy or more).
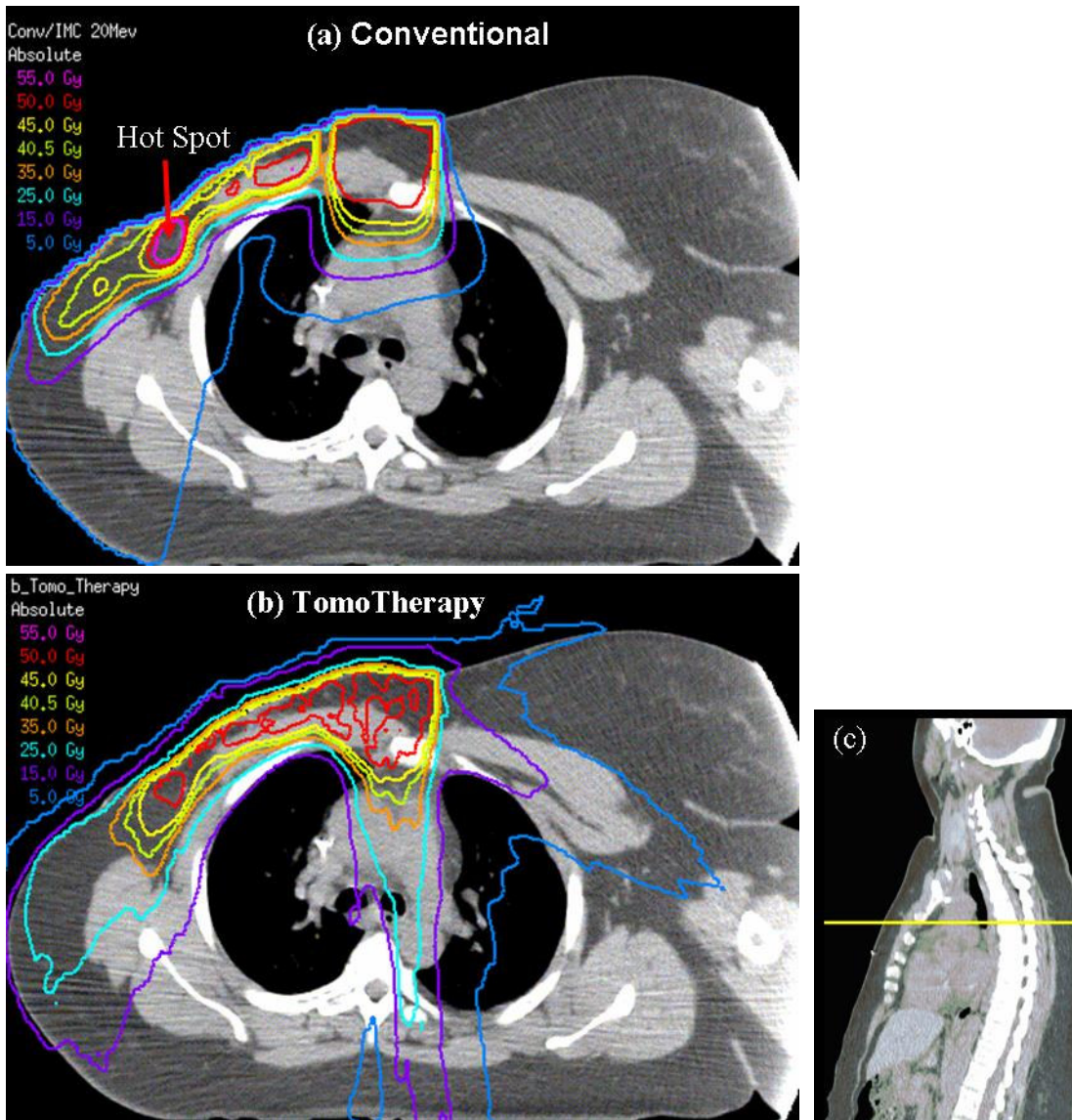
Figure 25. Transverse views of the conventional plan (a) and TomoTherapy plan (b)
taken at the IMN region as shown on the sagittal view (c).

Figure 26 shows the isodose comparison between the conventional plan (Figure 26a)
and the TomoTherapy plan (Figure 26b) on the transverse CT image slice near the
inferior border of the CW PTV, and is delineated by the yellow line in sagittal midline
CT image shown in Figure 26c. The yellow 45 Gy isodose line represents the 90%
isodose line, where the TomoTherapy plan was optimized to match the conventional plan.
The conventional plan showed a hot spot of 55 Gy (110% of the prescription dose) at the
junction of the lateral and medial electron fields.

The conventional plan showed a sharper dose falloff than the TomoTherapy plan along the beam edges of the medial and the lateral CW of the conventional plan. The TomoTherapy plan showed a significant volume of tissue outside the PTV receiving low dose (5 Gy or more).
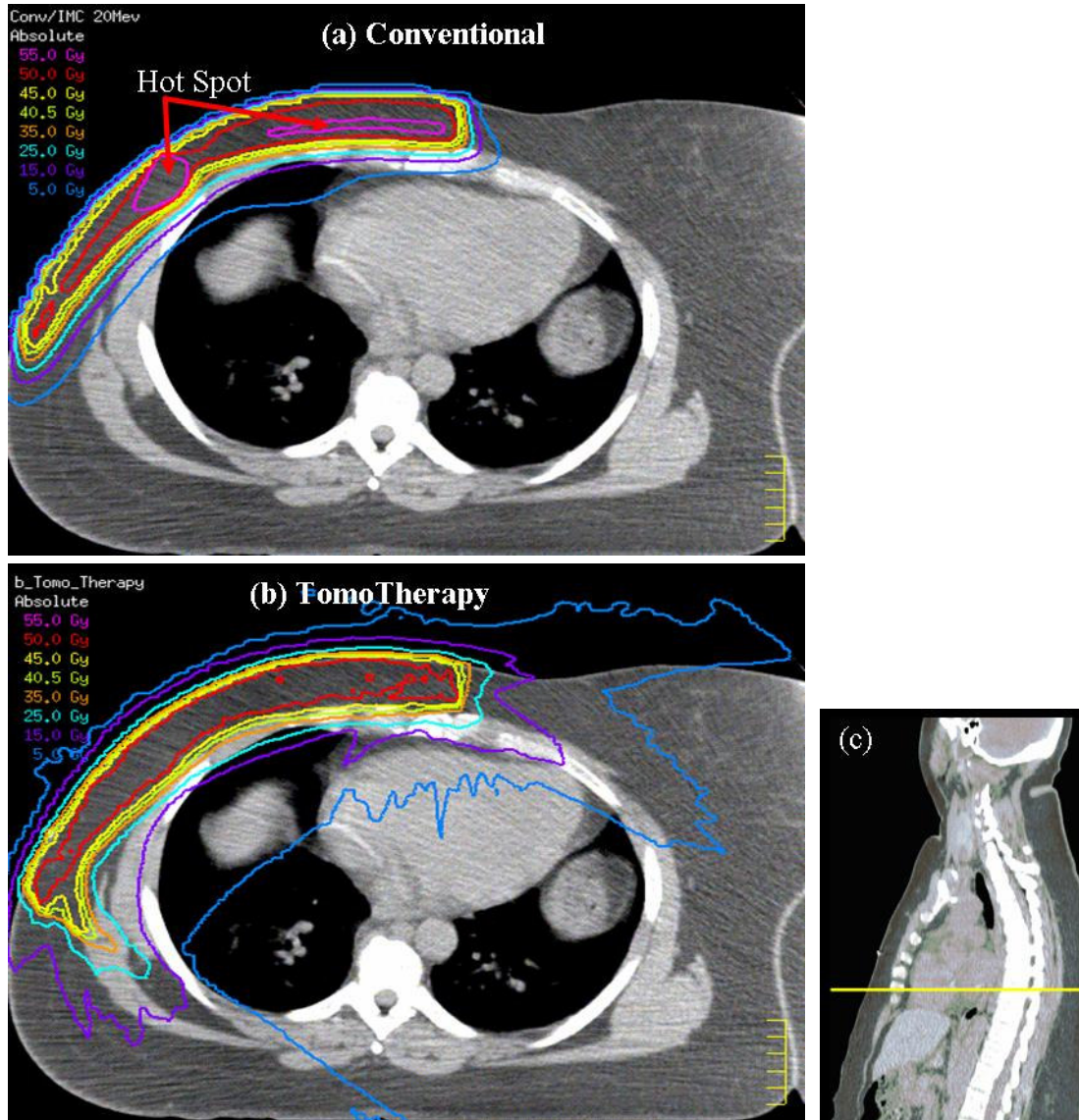
Figure 26. Transverse views of the conventional plan (a) and TomoTherapy plan (b) taken at the CW region as shown on the sagittal view (c).

3.6.2. DVH Comparisons

Figure 27 shows the DVH comparisons between the conventional and TomoTherapy plan. The conventional plan showed small volumes of the PTV receiving high dose created by the junction of the medial and lateral CW. For the TomoTherapy plan, dose homogeneity was better than the conventional plan for both the SCl/AX and CW PTVs. However, low dose (5Gy or more) covered a larger volume of the normal tissue not including critical structures. The crossover dose for the ipsilateral lung was 19 Gy. The cross over dose for the heart was 6.4 Gy.
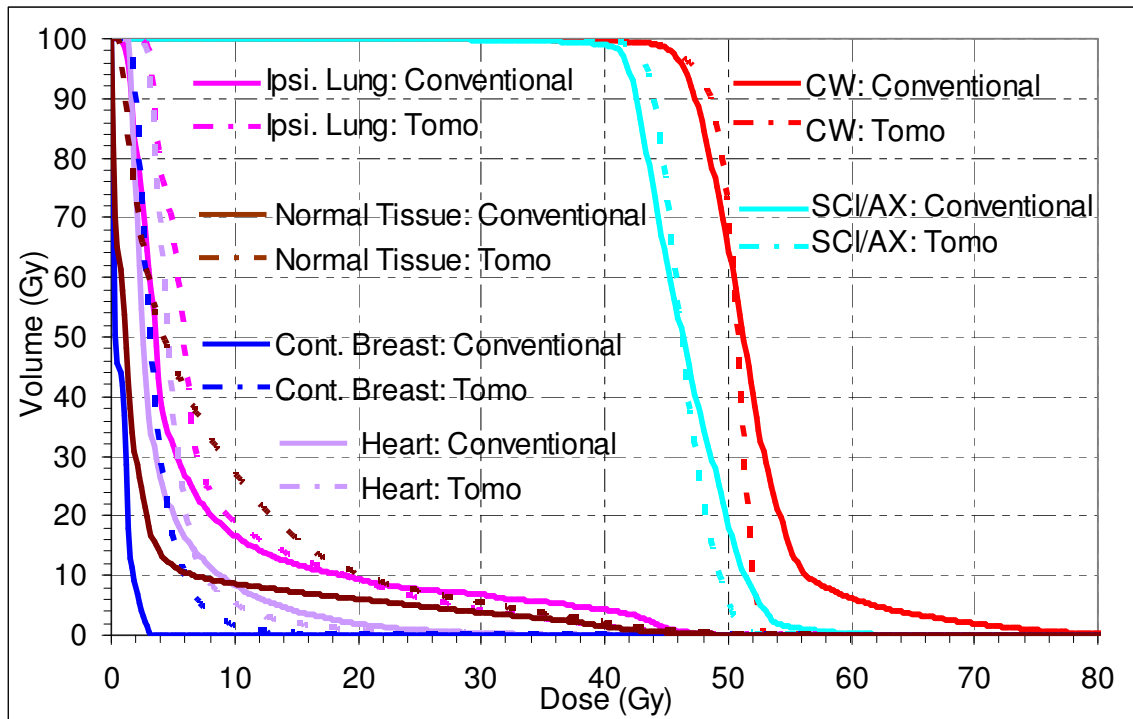
Figure 27. DVH comparisons for distribution shown in Figures 24 to 26. Solid lines – conventional plan, dashed lines –TomoTherapy plan. CW – CW PTV; SUP/AX – supraclavicular/axillary PTV; Ipsi – ipsilateral; Cont – contralateral

3.6.3. Radiation Oncologist Review

A radiation oncologist evaluated the clinical acceptability of both conventional and TomoTherapy plans and scored the conventional plan marginally acceptable and the

TomoTherapy plan acceptable. After reviewing the dose distributions and DVHs for both plans, he ranked the TomoTherapy plan superior. Better PTVs (CW and SCl/AX) coverage and fewer doses to the critical structure on the TomoTherapy plan was listed as a primary reason for preferring TomoTherapy plan over the conventional plan.

3.6.4. Chest Wall

The TomoTherapy plan showed improved dose homogeneity in the CW. The average CW dose ($\pm$ 1σ) was 50.4 $\pm$ 1.7 Gy on the TomoTherapy plan and 52.0 $\pm$ 5.2 Gy on the conventional plan. Dose irradiating 90% to 10% of the CW volume was 9.0 Gy on the conventional plan and was 3.5 Gy on the TomoTherapy plan. The TCP values were similar for both plans (conventional plan = 0.990 and TomoTherapy plan = 0.993).

3.6.5. Ipsilateral Lung

The TomoTherapy plan avoided exposing the ipsilateral lung with high doses (45 Gy). However, as shown in Figure 27, a large volume of the ipsilateral lung received low dose (5 Gy or more) with the TomoTherapy plan. Comparable $V20_{lung}$ was observed for both plans (conventional plan = 9.5% and TomoTherapy plan = 9.2%). The ipsilateral lung dose ($\pm$ 1σ) was lower for the TomoTherapy plan (conventional plan = 7.4 $\pm$ 10.2 Gy and TomoTherapy plan = 8.5 $\pm$ 8.0 Gy). A lower NTCP value was calculated for the TomoTherapy plan (conventional plan = 0.0001 and TomoTherapy plan = 0.0002).

3.6.6. Heart

In this patient the heart is not a proximal critical structure because the CW PTV is located on the right side of the patient's anatomy. The heart volume receiving above 30 Gy or more was similar for both plans (0.1% on the TomoTherapy plan and 0.4% on the conventional plan). The heart volume receiving 15 Gy or more was reduced from 4.1 % on the conventional plan to 1.9 % on the TomoTherapy plan. The average heart dose ($\pm$

1σ) was 5.2 ± 3.0 Gy on the TomoTherapy plan and 4.2 ± 4.4 Gy on the conventional plan. The calculated NTCP slightly higher with the TomoTherapy plan (conventional plan = 0.0005 and TomoTherapy plan = 0.0002).

3.6.7. Contralateral Breast

Dose to the contralateral breast was significantly higher in the TomoTherapy plan than in the conventional plan. The average contralateral breast dose (± 1σ) was 3.6 ± 1.9 Gy on the TomoTherapy plan while 0.8 ± 0.8 Gy on the conventional plan. As shown in Figure 27, a large volume of the contralateral breast was exposed to low dose (2 Gy) with the TomoTherapy plan. The percent volume receiving 5 Gy or more on the conventional plan was 0% and 15.9% for the TomoTherapy plan. Age dependence effect of radiation induced breast cancer was ignored when calculating SCCP for patient five (age = 49 yrs). The calculated SCCP value was relatively higher on the TomoTherapy plan (conventional plan = 0.0047 and TomoTherapy plan = 0.0191).

3.6.8. Normal tissue

The normal tissue volume receiving between 5 and 25 Gy for this patient was 45.7 cm^3 for the conventional plan and 108.0 cm^3 on the TomoTherapy plan. The calculated SCCP was higher for the TomoTherapy plan (conventional plan = 0.006 and TomoTherapy plan =0.014).

3.7.   Summary: Tables of Review

Table 10 shows the summary of the radiation oncologist review of the treatment plans. In all cases both plans were scored to be acceptable for treating the patient, and that the TomoTherapy plan was better than the conventional plan.

Table 10. Summary of the radiation oncologist plan review

Patient	Conventional (Conv.)	TomoTherapy (Tomo)	Conv. Vs. Tomo	Reason for preferring Tomo over Conv.
1	Acceptable	Acceptable	Marginally* Superior	Better PTV coverage; absence of hot or cold spot
2	Marginally Acceptable	Acceptable	Superior	Absence of hot or cold spot
3	Acceptable	Acceptable	Superior	No comment
4	Marginally Acceptable	Acceptable	Superior	Better PTV coverage; less hot spot
5	Marginally Acceptable	Acceptable	Superior	Better PTV coverage; less dose to the critical structure

*Dose to the heart in the TomoTherapy plan was a concern if probability that the patient was to receive chemotherapy.

3.7.1. Chest Wall

Table 11 lists the mean dose and the standard deviation of dose distribution in the CW PTV for each of the treatment plans. Table 12 lists the $D_{90\%}$-$D_{10\%}$ for the CW PTV. Both tables show improved dose homogeneity in the CW PTV with the TomoTherapy plan. A Paired Student 't' test was used for plan comparisons using the values listed on Table 12. There exist a significant difference in the $D_{90\%}$-$D_{10\%}$ for the CW PTV between the conventional and the TomoTherapy plans (p = 0.001). Paired Student 't' test is a statistical analysis method used to evaluate if there exist an actual difference between two small sets of quantitative data when data in each sample set are related. The difference is statistically significant (95% confidence level), if the value of p (probability) < 0.05. On the other hand, the difference is not statically significant, if the value of p > 0.05 (Press et al. 1986). The average value ($\pm$ 1σ) was reduced from 11.8 $\pm$ 2.3 Gy on the conventional plan to 2.9 $\pm$ 1.1 Gy on the Tomotherapy plan.

Table 11. Dmean (Gy) for PTV: CW (Average $\pm$ Standard deviation)

Patient	Conventional	TomoTherapy
1	50.7 + 6.0	49.6 + 0.9
2	51.4 + 6.1	49.9 + 1.1
3	52.4 + 7.0	49.7 + 1.9
4	54.0 + 7.5	50.4 + 1.5
5	52.0 + 5.2	50.4 + 1.7

Table 12. $D_{90\%} - D_{10\%}$ (Gy) for PTV: CW

Patient	Conventional	TomoTherapy
1	9.8	1.4
2	13.6	2.3
3	14.3	4.2
4	12.5	3.0
5	9.0	3.5

Table 13 lists the TCP values of the CW PTV for all patients. There was a slight, but insignificant difference in the calculated TCP values for CW PTV between the conventional and the TomoTherapy plans (p = 0.11).The average TCP value ($\pm$ 1σ) on the conventional plan was 0.988 $\pm$0.007 and 0.994 $\pm$ 0.002 on the TomoTherapy plan.

Table 13. Calculated TCP values for CW PTV

Patient	Conventional	TomoTherapy
1	0.978	0.995
2	0.989	0.996
3	0.989	0.991
4	0.996	0.997
5	0.990	0.993

3.7.2. Lung

Table 14 lists the $V20_{lung}$ for the ipsilateral lung. There was a statistically significant difference in the ipsilateral lung volume receiving $\geq$ 20 Gy between the conventional and the TomoTherapy plans (p = 0.05). The average value ($\pm$ 1σ) of the $V20_{lung}$ for the conventional plan was 21.5 $\pm$8.5 % and 17.6 $\pm$ 7.8 % for the TomoTherapy plan.

Table 14. Percent volume of the ipsilateral lung receiving $\geq$ 20 Gy

Patient	Conventional	TomoTherapy
1	16.1	9.1
2	29.4	24.8
3	28.4	22.0
4	23.9	22.8
5	9.5	9.2

Table 15 lists the calculated NTCP values for the ipsilateral lung. There was no significant differences in the NTCP between the conventional and the TomoTherapy plans (p = 0.13).The average of the NTCP ($\pm$ 1σ) on the conventional plan was 0.012 $\pm$ 0.011 and 0.003 $\pm$ 0.002 on the TomoTherapy plan.

Table 15. Calculated NTCP values for radiation pneumonitis

Patient	Conventional	TomoTherapy
1	0.0007	0.0016
2	0.0250	0.0049
3	0.0200	0.0031
4	0.0117	0.0059
5	0.0001	0.0002

Table 16 shows the $V20_{lung}$ for the total lung (ipsilateral + contralateral) volume. Three out of the five patients listed had $V20_{lung}$ values that were higher than the clinical limit of 15%. There was no significant differences in the volume receiving $\geq$ 20 Gy between the conventional and the TomoTherapy plans (p = 0.4). The average of the $V20_{lung}$ ($\pm$ 1σ) on the conventional plan was 12.4 $\pm$ 4.2 % and 11.4 $\pm$ 3.3 % on the TomoTherapy plan.

Table 17 lists the calculated SCCP values for the ipsilateral lung. There was significant differences in the SCCP between the conventional and the TomoTherapy plans (p = 0.005).The average of the SCCP ($\pm$ 1σ) on the conventional plan was 0.021 $\pm$ 0.007 and 0.029 $\pm$ 0.008 on the TomoTherapy plan.

Table 16. Percent volume of the total lung (ipsilateral + contralateral) $\geq$ 20 Gy

Patient	Conventional	TomoTherapy
1	9.9	7.8
2	17.8	15.1
3	15.2	12.1
4	11.8	13.8
5	7.2	8.2

Table 17. Ipsilateral lung's calculated SCCP values

Patient	Conventional	TomoTherapy
1	0.020	0.033
2	0.019	0.025
3	0.014	0.023
4	0.019	0.024
5	0.032	0.041

Table 18 lists the calculated SCCP values for the total lung. There was significant differences in the SCCP between the total and the TomoTherapy plans (p = 0.004).The average SCCP value ($\pm$ 1σ) on the conventional plan was 0.032 $\pm$ 0.012 and 0.062 $\pm$ 0.010 on the TomoTherapy plan.

Table 18. Total lung's calculated SCCP values

Patient	Conventional	TomoTherapy
1	0.028	0.073
2	0.025	0.046
3	0.019	0.059
4	0.038	0.067
5	0.049	0.066

3.7.3. Heart

Table 19 lists the value of $V30_{heart}$. Since the heart is not in a proximal distance to the CW PTV for the last patient, the fifth patient's $V30_{heart}$, $V15_{heart}$ and NTCP were not considered when calculating either a paired Student's T test or the overall average. There was a difference, although statistically insignificant, in the volume receiving $\geq$ 30 Gy

between the conventional and the TomoTherapy plans (p = 0.14). The average heart

volume receiving dose above or equal to 30 Gy ($\pm$ 1σ) was reduced from 2.7 $\pm$2.9 % on

the conventional plan to 1.6 $\pm$ 2.0 % on the TomoTherapy plan.

Table 19. Percent volume of the heart receiving $\geq$ 30 Gy

Patient	Conventional	TomoTherapy
1	0.54	0.06
2	0.9	0.02
3	2.5	2.2
4	6.8	4.1
5	0.4	0.1

Table 20 lists the value of $V15_{heart}$. Both the conventional and the TomoTherapy plans

showed values of $V15_{heart}$ higher than the clinical limit of 10% for two of the cases. The

average heart volume receiving dose above or equal to V15 ($\pm$ 1σ) on the conventional

plan was 9.5 $\pm$6.2 % and 9.5 $\pm$ 4.6 % on the TomoTherapy plan. There were no

significant differences in the volume receiving $\geq$ 15 Gy was observed between the

conventional and the TomoTherapy plans (p = 0.98).

Table 20. Percent volume of the heart receiving $\geq$ 15 Gy

Patient	Conventional	TomoTherapy
1	4.3	4.5
2	4.6	6.8
3	12.0	12.1
4	17.1	14.5
5	4.1	1.9

Table 21 shows the calculated NTCP values for the heart. There were no significant

differences in the NTCP for excess cardiac mortality after radiotherapy between the

conventional and the TomoTherapy plans (p = 0.31). The average of the NTCP ($\pm$ 1σ) on

the conventional plan was 0.007 $\pm$0.009 and 0.003 $\pm$ 0.003 on the TomoTherapy plan.

Table 21. Calculated NTCP values for excess cardiac mortality due to Ischaemic disease after radiotherapy

Patient	Conventional	TomoTherapy
1	0.0009	0.0002
2	0.0018	0.0003
3	0.004	0.004
4	0.02	0.007
5	0.0005	0.0002

3.7.4. Contralateral Breast

Table 22 lists the average dose to the contralateral breast. The overall average of the mean dose of the contralateral breast on the conventional plan was 0.4 and 2.95 on the TomoTherapy plan.

Table 22. Dmean (Gy) for contralateral breast (Average $\pm$ Standard deviation)

Patient	Age (yrs)	Conventional	TomoTherapy
1	73	0.1 $\pm$ 0.1	3.20 $\pm$ 1.58
2	53	0.1 $\pm$ 0.1	2.07 $\pm$ 1.37
3	49	0.1 $\pm$ 0.1	2.10 $\pm$ 0.76
4	39	0.7 $\pm$ 0.5	3.77 $\pm$ 2.75
5	49	0.8 $\pm$ 0.8	3.60 $\pm$ 1.93

Table 23 lists the V5contralateral breast. There were differences in the contralateral breast volume receiving > 5 Gy between the conventional and the TomoTherapy plans (p = 0.08). The average of the V5contralateral breast ($\pm$ 1σ) on the conventional plan was 0.0 % and 12.7 $\pm$ 11.9 % on the TomoTherapy plan.

Table 23. Percent volume of the contralateral breast receiving $\geq$ 5 Gy

Patient	Conventional	TomoTherapy
1	0	13.1
2	0	3.0
3	0	0.9
4	0	30.6
5	0	15.9

Age dependence effect of radiation induced breast cancer was ignored when calculating the SCCP values (Table 24) for the contralateral breast. There was statistically significant difference in the SCCP after radiotherapy between the conventional and the TomoTherapy plans (p = 0.0001). The average of the SCCP ($\pm$ 1σ) was 0.002 $\pm$ 0.002 for the conventional plan and 0.016 $\pm$ 0.003 for the TomoTherapy plan.

Table 24. Calculated SCCP for the contralateral breast after radiotherapy

Patient	Conventional	TomoTherapy
1	0.0001	0.0178
2	0.0003	0.0125
3	0.0004	0.0131
4	0.0046	0.0183
5	0.0047	0.0191

3.7.5. Normal Tissue

Table 25 lists the percent volume of normal tissue receiving 5 to 25 Gy. There was a statistically significant difference between the rival plans in the percentage of normal tissue volume that received 5 to 25 Gy (p = 0.002). The overall average of on the conventional plan ($\pm$ 1σ) was 23.4 $\pm$15.5 cm^3 and 84.6$\pm$ 26.7 cm^3 on the TomoTherapy plan.

Table 25. Volume of normal tissue (delineated tissue volume except critical structures) receiving between 5 and 25 Gy

Patient	Conventional	TomoTherapy
1	17.6	111.7
2	11.6	61.9
3	9.2	52.4
4	32.7	89.1
5	45.7	108.0

Table 26 lists the SCCP values for normal tissue. There was a statistically significant difference in the SCCP values between the rival plans (p = 0.001). The average of the SCCP on the conventional plan ($\pm$ 1σ) was 0.003 $\pm$ 0.002 and 0.010 $\pm$ 0.003 on the TomoTherapy plan.

Table 26. Calculated SCCP values for normal tissue

Patient	Conventional	TomoTherapy
1	0.003	0.012
2	0.002	0.008
3	0.002	0.007
4	0.004	0.009
5	0.006	0.014

Chapter 4
Discussions

The focus of this study was to show TomoTherapy could deliver dose distributions a radiation oncologist judges to be equal to or better than that of a conventional electron plan. Physical dose-volume and radiobiological metrics were calculated and used to evaluate the treatment plans in addition to the radiation oncologist's critique.

4.1. Similarities Between The TomoTherapy and Conventional Plans

Overall, the TomoTherapy plan was very similar to the conventional electron beam plan in treating the CW PTV while sparing critical structures adjacent to the CW PTV. There was no statistically significant difference in the CW TCP values between the TomoTherapy and conventional plans, although there was considerable difference in PTV dose homogeneity. The values for $V20_{lung}$ and NTCP for the ipsilateral lung were similar (i.e., no significant difference) between the two treatment plans, as was the values for $V15_{heart}$, $V30_{heart}$, and NTCP for the heart. From this study, one can assume with some degree of confidence that TomoTherapy is able to plan a PMRT that is as good as the conventional electron beam PMRT plan so far as TCP and NTCP are concerned.

4.2. Differences Between The TomoTherapy and Conventional Plans

As expected, the Tomotherapy plan showed better PTV dose uniformity compared to the conventional plan (Table 12). Dose uniformity was insured by giving a high importance to the PTVs (CW and SCl/AX), and as a result, the TomoTherapy plan produced a significantly more uniform dose distribution in the PTV. Also, the conventional plan had at least a 10% dose gradient because of the method of generating the PTVs (i.e., the 90% isodose line was utilized to generate the PTV). Hot spots in the

field junctions added to the PTV dose inhomogeneity in the conventional plan. A difference in PTV dose homogeneity, mostly due to the abutting of the electron fields, were slightly over stated as the effect of edge feather were not included in the calculation.

On the other hand, the conventional plan successfully avoided irradiating the contralateral breast. In all five cases, the volume receiving 5 Gy or more was negligible (Table 23). In order to stop dose exposure to the contralateral breast, a higher importance factor was assigned compared to other critical structures during the optimization of the TomoTherapy plan. This helped reduce the dose to the contralateral breast; however, the nature of beam arrangements and modality made dose reduction difficult for the TomoTherapy. As a result, the average dose to the contralateral breast was higher compared to the conventional plan. The average for all five patients was increased from 0.4 Gy on the conventional plan to 2.95 Gy on the TomoTherapy plan. No excess breast cancer risk has been found among woman irradiated at age 40 years or older (Leeuwen et al. 2005*).* Boice et al*, (*1992) showed radiation exposure after the age of 45 years entails little, if any risk (relative risk, 1.01) of radiation-induced breast cancer for population of an average age of 51.7 years woman exposed with mean radiation dose to the contralateral breast be 2.82 Gy (maximum 7.10). Storm et al*, (*1992) also showed little if any risk (relative risk, 1.04) of radiation-induced breast cancer for population of an average age of 51 years woman exposed with mean radiation dose to contralateral breast estimated to be 2.51 Gy. Relative risk is ratio of the probability of the event occurring in the exposed group vs. the control (non-exposed) group. In the current study, the average age for the five patients was 53 years and the overall average mean dose was 2.95 Gy. Given the conclusions of the studies mentioned above, the risk of developing radiation

induced breast cancer is comparable with other PMRT techniques for the five patients studied using the TomoTherapy.

Two assumptions were made when calculating SCCP for the contralateral breast. (1) Age dependence effect of radiation induced breast cancer was ignored and (2) incidence of solid tumor induction in the contralateral breast was only calculated. The SCCP modeling for the TomoTherapy plan indicates a higher prediction of SCCP for the TomoTherapy plan relative to the conventional plan (Table 24). This may be attributed to the increased mean dose observed on the TomoTherapy plan (Table 22). The study recommends that further studies that attempt to reduce dose to the contralateral breast should be done before implementing TomoTherapy clinically as PMRT technique for young patients less than 30 yrs of age who experience long survival times and may be at risk of radiation-induced cancer. Hancock et al. (1993) showed that for women treated for Hodgkin's disease with therapeutic radiation before 30 years of age are at markedly increased risk for breast cancer.

According to Schneider et al. (2005a), solid tumor induction anywhere in the body tends to peak in the dose range of 5 to 25 Gy. Hence the present study noted the volume receiving between 5 and 25 Gy and found larger normal tissue volumes on the TomoTherapy plan compared to the conventional plan. This might be the reason why the SCCP for normal tissue was higher on the TomoTherapy plan compared to the conventional plan, but on the average, the calculated SCCP values for both rival plans were found to be very small. Limiting high dose to critical structures (ipsilateral lung and heart) proximal to the PTVs (CW and SCl/AX) the ipsilateral lung and heart and the nature of TomoTherapy's beam arrangements and modality resulted in low dose spread to normal tissue. Dose limiting structures were used to minimize dose to the normal tissue

but could not eliminate the dose without negatively impacting the treatment plan. As a

result of the low dose spread to a large area of the normal tissue, TomoTherapy showed

relatively higher risk of SCCP. The overall SCCP value when using TomoTherapy plan

for the five studied patients was 0.088 ± 0.012 (total lung = 0.062, contralateral breast =

0.016, and normal tissue = 0.010) compared to the conventional plan 0.037 ± 0.011 (total

lung = 0.032, contralateral breast = 0.002, and normal tissue = 0.003). The influence of

chemotherapy and possible genetic susceptibility are not included in the radio-biological

models (TCP, NTCP and SCCP). Also, there is lack of accuracy in dos reconstruction in

patient treated decade ago. Hence, the absolute values generated by radiobiological

models thus far are not accurate and as a result should not be used to predict response.

However, the models are sufficient to compare rival plans.

4.3. Overview of Doctor's Review

After reviewing the spatial dose distributions and the superimposed DVHs of both the

conventional and the TomoTherapy plans, the radiation oncologist ranked the

TomoTherapy plan to be superior in all cases (marginally superior in one case). The basis

for his judgment was his clinical experience. Absence of hot and cold spots to the PTV

for the TomoTherapy plan was the reason why he chose the TomoTherapy plan over the

conventional plan. He liked (1) the significant improvement in dose uniformity seen in

the PTV on the TomoTherapy plan, (2) the ability of the TomoTherapy to avoid

complexities that arise from matching abutting fields, (3) the absence of necessity for the

use of more than one modality (electrons/photons), and (4) the ability of the

TomoTherapy to spare specified organs at risk (e.g. ipsilateral lung). Also seen as a

bonus feature was the on board megavoltage computed tomography (CT), which verifies

setup in three dimensions rather than in two. On the other hand, he had a concern in the

accuracy of TomoTherapy dose delivery to the skin surface due to the effect of breathing motion. The chest wall is the site at greater risk of recurrence in patient undergoing mastectomy (Recht et al. 1996). For patient with locally advanced disease (stage IIIB), achieving a high skin and subcutaneous dose may be more important (Thomas et al. 1989). It is also the clinical experience of radiation oncologists at MBPCC that most recurrences (failure to control locoregional tumor) occur on the skin.

Both rival plans showed similarity on what the radiation oncologist set as a requirement for the total lung and the heart (Table 16 and Table 20 respectively). However, due to the nature of beam arrangements of the TomoTherapy delivery, only two of the five TomoTherapy plans met his contralateral breast requirement (maximum of 5 Gy), while all five of the conventional plans met his requirement (Table 23).

Chapter 5
Conclusions

The study showed that TomoTherapy can deliver dose distributions the radiation oncologist judges to be equal to or better than that of a conventional electron beam PMRT plan for five CW treatment plans. TomoTherapy showed improved dose homogeneity in the CW PTV with reduced dose to proximal critical structures (ipsilateral lung and heart). However, large volume of critical structures and normal tissue received low doses with TomoTherapy. As a result, SCCP for a contralateral breast and normal tissue were found to be higher with the TomoTherapy plan when compared to the conventional plan. This may be a concern for young patients (< 30 yrs) who experience long survival times and as a result may be at risk of radiation-induced cancer; however, this was not considered a significant factor by the radiation oncologist reviewing the plans.

In conclusion, the ability of the TomoTherapy to avoid complexities that arise from matching abutting fields and to spare specified normal tissue (e.g. ipsilateral lung) while maintaining a uniform dose distribution to the PTV makes it an attractive candidate for PMRT. However, more studies should be done to address issues such as skin dose and the effect of breathing motion on the dose distribution before gaining complete confidence with treating PMRT patients on TomoTherapy.

Chapter 6
Future Works

6.1. Additional Treatment Studies

Additional studies should be conducted to better compare conventional and TomoTherapy PMRT plans. These studies should include junction shift over the course of treatment should be modeled by the treatment planning system to reduce the hot spot seen in the dose distributions and DVHs. Also, surgically-removed tumor beds are typically boosted to 60 Gy in 2Gy/fraction treatments after the CW is treated to 50 Gy. Whether the boosted portion of the CW can be treated at the same time as the rest of the CW, or if an additional TomoTherapy plan has to generated, is yet to be studied.

6.2. Accuracy of Dose Calculation on Surface

The accuracy of the TomoTherapy dose calculate on the skin surface is of interest. The dosimetric uncertainty in the surface and buildup region in IMRT cases has been documented by Chung et al. (2005) for the Pinnacle treatment planning system and by Mutic et al. (1999) for the Peacock treatment planning system (NOMOS Corp., Sewickley, PA). Hence, a careful experimental measurements and comparison to the TomoTherapy treatment planning system's dose calculation in this superficial site are necessary as most breast cancer recur on the skin surface.

6.3. Impact of Breathing Motion

The effect of motion due to breathing may have significant impact on the study. Breathing motion is not so much an issue with conventional electron beam PMRT as the beams are perpendicular to the breathing motion. However, the TomoTherapy plan required greater weighting to beamlets incident on the CW at highly oblique, grazing angles to avoid excessive dose to the heart and lungs. Breathing motions would take the

CW out of the PTV area for a fraction of the treatment, and therefore a margin would have to be added to the CW PTV to account for breathing. Unfortunately expanding the PTV into the air above the CW would have a negative impact on the optimization of beamlet fluence patterns near the skin unless the patient is scanned with bolus allowing expansion of the ROI above the skin.

6.4. Utility of Skin Collimation

Typically when the CW is treated with photon beams, bolus is applied to the skin of the CW to insure adequate skin dose. Such a procedure would be performed for PMRT on the TomoTherapy. However, this study utilized patient CT scan data absent of bolus material and TomoTherapy does not provide an option for adding bolus material to the plan unless the patient is scanned with bolus. Skin dose is of great concern in PMRT as failure of local control is often seen on the skin.

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Appendix A
Radiation Oncologist Evaluation of Treatment Plans

Date   :
Patient:

a. Evaluate the clinical acceptability of plans (scale 1-5)

- How do you evaluate the **TomoTherapy plan**? Please circle
  one value that closely describes your observation.

        1   2   3   4   5

Acceptable	1
Marginally acceptable	2
Indifferent	3
Marginally unacceptable	4
Unacceptable	5

- How do you evaluate the **Conventional plan**? Please circle
  one value that closely describes your observation.

        1   2   3   4   5

Acceptable	1
Marginally acceptable	2
Indifferent	3
Marginally unacceptable	4
Unacceptable	5

b. Compare the TomoTherapy plan with the conventional plan (either
    electron beam alone treatment or mixed beam treatment).
    i. Please circle one value that closely describes your observation,
        after comparing the TomoTherapy plan with the conventional pan.

          1   2   3   4   5

Superior	1
Marginally superior	2
Indifferent	3
Marginally inferior	4
Inferior	5

    ii. Why do you prefer it? Is it,
        a. Better PTV coverage
        b. Less dose to the critical structure
        c. Less whole body dose
        d. other

c. Comment

Appendix B
Acronyms

ABR	American Board of Radiology
AX	axillary
CW	chest wall
CT	computed tomography
DVH	dose volume histogram
dDVHs	differential dose-volume histograms
FOV	field of view
IHD	ischaemic heart disease
ICRP	International Commission on Radiological Protection
IGRT	image-guided radiotherapy
IMRT	intensity-modulated radiotherapy
IMN	internal mammary chain
MVCT	mega-voltage computerized tomography system
MBPCC	Mary Bird Perkins Cancer Center
NTCP	normal tissue complication probability
OAR	organ at risk
PMRT	post-mastectomy radiation therapy
PTV	planning PTV volume
PWTF	partially wide tangent fields
RAR	region at risk
RHS	reverse hockey stick
ROI	region of interest
SCCP	secondary cancer complication probability
SCl	supraclavicular
SEER	Surveillance Epidemiology and End Results
SCl/AX	supraclavicular/axillary nodes
TCP	tumor control probability
TERMA	total Energy Released per unit Mass
UNSCEAR	United Nation Scientific Committee on the Effects of Atomic Radiation

Vita

Michael Ashenafi was born in Addis Ababa, Ethiopia, in 1979. He is the oldest son of Sissay Ashenafi and Birhan Abraham and has two brothers and one sister. He began his education at Saint Joseph school in Ethiopia. After graduation from high school, he was employed by the Crown International Consultants Company. After spending more than a year with this company, he came to the United States of America to further his education and to pursue a degree in physics. First, he joined Southern University at New Orleans (SUNO) and then he transferred to Southern University and A & M College in Baton Rouge (SUBR) to pursue physics.

His research experience has been rich and varied. In the summer of 1999, he worked at the Louisiana Universities Marine Consortium (LUMCON) in Houma, Louisiana. During this same summer, he worked at the Thomas Jefferson Laboratory, a research center managed and operated by the Southern Universities Research Association (SURA). During the summer of 2000, he had the opportunity to work with Dr. Sergey Mirov (patent holder) at the Laser Photonic Research Laboratory in Birmingham, Alabama. He studied the spectroscopic analysis of color center crystal and ultimately succeeded in conducting a spectral hole burning experiment. During the summer of 2001, he had the privilege again to work with Dr. Sergey Mirov and Dr. Marry Zvanut. During the summer of 2002, he had the great privilege to work at the famous CERN Laboratory, a world-renowned facility for Nuclear Physics Research in Geneva, Switzerland.

He began his master's work at the Louisiana State University in 2003. He is now a candidate for the degree of Master of Science in the Department of Medical Physics.