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The impact of imaging modality (CT vs MRI) and patient position (supine vs prone) on tangential whole breast radiation therapy planning

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Abstract

Purpose

The purpose of this study was to evaluate the impact of magnetic resonance imaging (MRI) versus computed tomography (CT)-derived planning target volumes (PTVs), in both supine and prone positions, for whole breast (WB) radiation therapy.

Methods and materials

Four WB radiation therapy plans were generated for 28 patients in which PTVs were generated based on CT or MRI data alone in both supine and prone positions. A 6-MV tangential intensity modulated radiation therapy technique was used, with plans designated as ideal, acceptable, or noncompliant. Dose metrics for PTVs and organs at risk were compared to analyze any differences based on imaging modality (CT vs MRI) or patient position (supine vs prone).

Results

With respect to imaging modality 2/11 whole breast planning target volume (WB_PTV) dose metrics (percentage of PTV receiving 90% and 110% of prescribed dose) displayed statistically significant differences; however, these differences did not alter the average plan compliance rank. With respect to patient positioning, the odds of having an ideal plan versus a noncompliant plan were higher for the supine position compared with the prone position ($P = .026$). The minimum distance between the seroma cavity planning target volume (SC_PTV) and the chest wall was increased with prone positioning ($P < .001$, supine and prone values 1.1 mm and 8.7 mm, respectively). Heart volume was greater in the supine position ($P = .005$). Heart doses were lower in the supine position than prone ($P < .01$, mean doses 3.4 ± 1.55 Gy vs 4.4 ± 1.13 Gy for supine vs prone, respectively). Mean lung doses met ideal dose constraints in both positions, but were best spared in the prone position. The contralateral breast maximum dose to 1cc (D1cc) showed significantly lower doses in the supine position ($P < .001$, 4.64 Gy vs 9.51 Gy).

Conclusions

Planning with PTVs generated from MRI data showed no clinically significant differences from planning with PTVs generated from CT with respect to PTV and doses to organs at risk. Prone positioning within this study reduced mean lung dose and whole heart volumes but increased mean heart and contralateral breast doses compared with supine.

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Abstract:

Purpose: To evaluate the impact of MRI vs CT derived planning target volumes (PTVs), in both supine and prone positions, for whole breast (WB) radiotherapy.

Methods and Materials: Four WB radiotherapy plans were generated for 28 patients, where PTVs were generated based on CT or MRI data alone in both supine and prone positions. A 6MV tangential IMRT technique was used, with plans designated as ideal, acceptable or non-compliant. Dose metrics for PTVs and OARs were compared to analyse any differences based on imaging modality (CT vs MRI) or patient position (supine vs prone).

Results: With respect to imaging modality 2/11 WB_PTV dose metrics (V90% and V110%) displayed statistically significant differences, however these differences did not alter the average plan compliance rank. With respect to patient positioning, the odds of having an ideal plan vs a non-compliant plan were higher for the supine position compared to the prone position ($p=0.026$). The minimum distance between the seroma cavity (SC)_PTV and the chest-wall was increased with prone positioning, ($p<0.001$, supine and prone values 1.1 mm and 8.7 mm respectively). Heart volume was greater in the supine position ($p=0.005$). Heart doses were lower in the supine position than prone ($p<0.01$, mean doses 3.4 ± 1.55 Gy vs 4.4 ± 1.13 Gy for supine vs prone respectively). Mean lung doses met ideal dose constraints in both positions, however best spared in the prone position. The contra-lateral breast D1cc showed significantly lower doses in the supine position, ($p<0.001$, 4.64 Gy vs 9.51 Gy).

Conclusions: Planning with PTVs generated from MRI data showed no clinically significant differences to planning with PTVs generated from CT with respect to PTV and OAR doses. Prone positioning within this study reduced mean lung dose and whole heart volumes but increased mean heart and contra-lateral breast doses, compared to supine.

Introduction:

Radiotherapy is an integral component of breast conserving therapy, which has been shown to have equivalent survival compared to mastectomy [1, 2]. Long term side effects after radiotherapy for breast cancer, include cardiac toxicities [3], radiation fibrosis and second primary cancers [4, 5]. With increasing survivorship, exploration of potential changes in practice that could reduce secondary effects is important.

Routinely, computed tomography (CT) is used to delineate target volumes for radiotherapy [6]. The European Society for Radiotherapy and Oncology (ESTRO) consensus guidelines on target delineation for whole breast (WB) radiotherapy state the target should include all glandular breast tissue [7], however, the extent of glandular breast tissue is not clear on CT scans [8]. Magnetic resonance imaging (MRI) has been shown to better identify breast tumours and allow greater distinction between glandular breast tissue and adipose tissue when compared with CT [6, 9]. Traditionally, breast MRI is performed with the patient lying in a prone position whilst breast radiotherapy is delivered most commonly in the supine position. Previous work demonstrated comparable imaging quality with supine versus prone positioning for breast radiotherapy target delineation purposes [10]. The use of the prone position for breast radiotherapy is increasing with reported improvements in organ at risk (OAR) doses and target dose coverage [11, 12].

Several groups have examined differences in supine and prone positioning for WB radiotherapy [13-24], however few groups have examined the impact of imaging modality on breast radiotherapy planning. Mast et al observed that the mean volume of delineated glandular breast tissue was significantly larger on CT compared to that volumed on co-registered CT- MRI breast radiotherapy planning images acquired with the patient in the supine position [25]. Previous work from our group, incorporating all four elements (CT vs MRI imaging modality and supine vs prone patient positioning) found that WB clinical target volume (CTV) was larger when patients were positioned prone than supine, and that seroma cavity (SC) volumes were smaller on MRI than CT [26].

To our knowledge no planning study has been conducted to evaluate the dosimetric implications of imaging modality and patient position on target and OAR doses in WB radiotherapy plans. Specifically, our aims were to evaluate the impact of differences between MRI and CT derived target volumes, in both supine and prone positions, on target and OAR doses for WB radiotherapy.

Methods and Materials:

Following ethics approval, 33 breast radiotherapy patients were scanned, with both CT and MRI in both supine and prone positions. A breakdown of cohort characteristics is presented in table 1. The patients' actual treatments were planned on the supine CT scans as per departmental protocol. The remaining images were used for the planning study only. The imaging protocols, image registration and clinical target volume (CTV) contour delineation methodology for this planning study has been described previously [26]. Eleven qualified specialists (no trainees; 9 Radiation Oncologists and 2 Radiologists) from 4 different institutions, contoured WB_CTV and SC_CTV, on all data-sets for all patients. No clinical information including pre-operative imaging was supplied to the observers, so that contouring observations were based on image data alone. Supine and prone MRI image sets were rigidly registered to the corresponding CT scans as described previously [26], based on image data where all contoured structures were turned off. The image fusion was visually confirmed in three planes (axial, sagittal, and coronal), by an experienced radiation therapist. Some random and all difficult fusions were checked by another experienced radiation therapist.

Determination of CTVs and PTVs:

Gold standard CTVs for each image set were generated using the Simultaneous Truth And Performance Level Estimation (STAPLE) algorithm [27], with all observers weighted equally. The WB_CTV STAPLE was generated from all 11 observers. As no clinical information was provided to observers, there were some cases where the SC was incorrectly contoured in different locations across the different observers and imaging modalities (for example, an axillary seroma may have been mistaken for a tumour bed seroma in occasional volumes). To ensure SC_CTV STAPLE volumes were clinically relevant for this planning study, they were generated from a variable number of observer contours. The qualitative process to determine which observer contours were utilised in the creation of the SC_CTV STAPLE volume is described in appendix 1. There was one patient case in this study where there was no SC_CTV staple volume determined. The methodology of determining the planning target volumes (PTVs) is described in appendix 2.

Organs At Risk:

Delineated OARs included the ipsi-lateral and contra-lateral lung, the heart and the contra-lateral breast. Auto-threshold tools were used to delineate the lung volumes. The heart was contoured to conform to heart atlas guidelines [28]. The contra-lateral breast was defined by a radiation therapist, based on visible breast tissue between the lateral aspect of the sternum and the latissimus-dorsi muscle postero-laterally, the chest-wall posteriorly and the patient contour anteriorly. All OARs were checked by a second radiation therapist. MRI information was not considered in OAR definitions, all OARs were delineated on CT data.

Planning Technique:

After image registration, the MRI STAPLE CTVs were imported onto the respective CT data-set for planning. Plans were generated for the MRI PTV STAPLE in the supine position, the CT PTV STAPLE in the supine position, the MRI PTV STAPLE in the prone position and the CT PTV STAPLE in the prone position, for all participants. All planning calculations were performed on the CT data-sets, using the OARs derived from the CT data-sets using a 0.25^3 dose grid and the adaptive convolve algorithm in Pinnacle[3] version 9.10 (Philips, Netherlands). A 6MV tangential IMRT technique was used where plans were limited to: a maximum of 8 segments, a minimum segment area of 9 cm^2, and a minimum monitor unit limit of 6. This approach was chosen as it represents current clinical practice [29-31], and allowed automation of planning steps with the use of scripts. In all cases the medial tangential gantry angle selection was based on optimal PTV coverage whilst minimising dose to the surrounding OARs. For supine plans this process was automated through utilisation of a point dose optimiser tool in the treatment planning system; however the option to adjust manually was available for the planner. For prone plans all gantry angles were determined manually. A prescription of 50 Gy in 25 fractions was used for all cases. After the script was finished, if required, the planner spent a further 10 mins adjusting weightings and optimisation parameters with the aim of meeting the dose compliance criteria shown in table 2. This dose compliance criteria used for the target volumes and OARs were based on the RTOG 1005 protocol [32], with a tighter criterion for the acceptable WB_PTV dose designation (V45Gy=95% our study vs V45Gy = 90% RTOG 1005) was used based on current clinical practice of the authors. Plans were designated as ideal, acceptable or non-compliant based on the criteria. Boost doses to the SC_PTV were not considered in this study, however the dose received to the SC from the WB plan was an important part of the plan compliance as outlined in table 2.

Analysis:

In addition to the metrics recorded to assess plan compliance, the following were determined for reporting purposes:

i. Manual measures of SC_PTV distance to the chest-wall (measured using the treatment planning system software),
ii. Patient and tumour characteristics (documented from treatment records),
iii. Homogeneity Index (HI) (determined as HI = (D2% - D98%)/(D50%) where an optimal value = 0 [33],)

Chi square tests were used to test for differences in plan ranks between imaging modality (CT vs MRI) and patient position (supine vs prone). Paired t-tests were used to analyse any differences in OAR volumes with imaging modality. Multilevel models were used to determine whether there were differences in target volumes and the dose metrics between imaging modality and patient position. Normality of residuals was assessed with histograms and quantile-quantile plots. Cook's distance was used to identify patients with relatively large influence on the results. Based on these diagnostics, transformations on the outcome variable and sensitivity analyses were performed. Statistical analysis was conducted using SAS version 9.4. To improve normality of residuals from the multilevel models, inverse hyperbolic sine transformations were performed for WB_PTV_V107%, Ipsi-lateral Lung_V20Gy, Ipsi-lateral Lung_V10Gy, Ipsi-lateral Lung_V5Gy, Heart_V25Gy, Heart_V20Gy, Heart_V10Gy, Heart_mean dose (Gy), Contra-lateral Breast_V1.86Gy, Contra-lateral Breast_D1cc (Gy) due to right skewness of the outcome, to reduce the potential bias of the results.

Results:

Thirty-three patients receiving breast radiotherapy were recruited [26]. From this group, five patients were excluded from the planning study due to inadequate alignment (on either the prone CT or prone MRI scan) of the patients sternum on the prone breast board with respect to the hole for the ipsilateral breast to fall through. This problem has been encountered and described elsewhere [11].

Target and OAR Volume Analysis:

There was no volumetric difference with image modality between WB_PTV, SC_PTV, or the minimum distance between the SC_PTV and the chest-wall. With respect to patient positioning, there was a significant difference in the minimum distance between the SC_PTV and the chest-wall ($p < 0.001$), with supine and prone values 1.1 mm and 8.7 mm respectively (Table 3).

A paired t test analysis showed significant differences in volume between all supine and prone image sets (irrespective of laterality of disease) for the heart (mean supine heart volume = 475.2 cc, mean prone volume = 440.5 cc, $p=0.005$). The volumes of other OARs showed no statistically significant differences between supine and prone positioning (Table 3).

Plan ranking (ideal/acceptable/non-compliant)

Chi Square tests showed significant differences across the plan ranks for patient positioning (p<0.001). Specifically, the odds of having an ideal plan vs a non-compliant plan was higher for the supine position compared to the prone position (p = 0.026) (Figure 1). There were no significant differences with imaging modality. There were 19/112 non-compliant plans in total. In 2/28 patient cases non-compliant plans occurred in all 4 image sets, one left sided case and one right sided case. For the left sided case, all 4 plans failed to meet heart dose compliance criteria. The right sided case had a medial SC_PTV and WB_PTV which extended close to midline, and all 4 plans failed to meet minimum SC_PTV dose criteria as well as contra-lateral breast dose constraints. The remaining 11 non-compliant plans were all prone cases. Details of all non-compliant plans are listed in table 4.

Dose metrics:

Table 5 summarises the comparison of dose metrics. Contra-lateral lung and right-sided heart dose metrics were not analysable with multi-level statistical model analysis due to the prevalence of '0' values. With respect to imaging modality, WB_PTV_V90% and WB_PTV_ V110% metrics displayed statistically significant differences between imaging modalities. With respect to patient position there were several WB_PTV dose metrics that were statistically different and all lung and heart dose metrics showed significant differences. The prone position achieved better sparing of lung tissue compared to supine position, with all ipsi-lateral and combined lung doses significantly lower for the prone position (all p values <0.001). Conversely, mean heart doses were lower in the supine position than prone (p<0.001, mean doses 3.4 ± 1.55 Gy vs 4.4 ± 1.13 Gy for supine vs prone respectively). The contra-lateral breast D1cc showed significant differences with doses lower in the supine position, (p<0.001, 4.64 Gy vs 9.15 Gy for prone).

WB_PTV_HI showed statistically better homogeneity for MRI plans than for CT (HI_MRI =0.19±0.08 HI_CT=0.21 ±0.81 p=0.047). WB_PTV_HI also demonstrated statistically better homogeneity for supine plans than for prone after an outlier was removed (HI_supine = 0.19±0.09 HI_prone=0.22±0.08 p=0.01). SC_PTV_V95% was found to be statistically larger with prone position (difference = -0.91%, p < 0.001). SC_PTV_D1cc, displayed a statistically significant increase in supine position compared with prone (difference = 0.66Gy, p < 0.001).

Discussion:

This is the first study to analyse target and OAR dose compliance differences due to imaging modality (CT vs MRI) for target volume determination, in both supine and prone positions, although several groups have examined differences in supine and prone positioning for WB radiotherapy (Table 6) [13-26].

A requirement for greater margins when determining PTVs for prone position (compared to supine) for reproducibility issues has been demonstrated [35, 36]. In this study the PTV expansion margin were kept the same to allow for a comparison based on imaging modality, this may result in an under-estimation of OAR dosimetric parameters for the prone results of this study.

Whilst there were some statistical differences within WB_PTV metrics for both imaging modality and patient position, the differences were small and within the same band of plan compliance thus limiting clinical impact.

Despite earlier work establishing that the SC_CTVs were smaller on MRI compared to CT [26], there was no difference between CT vs MRI SC_PTV size. However, we did not investigate differences in SC location between CT vs MRI, and this would need to be taken into account, particularly if boost doses or partial breast (PB) radiotherapy scenarios were being considered. Whilst prone positioning did increase the distance between the SC_PTV from the chest-wall, when compared to supine, there was no significant difference in dose metrics for the different imaging modalities. Other groups have reported no difference in breast dose coverage between supine and prone positions [15, 18, 21, 24].

Our study demonstrates that mean lung doses met ideal dose constraints in both positions, however lung was better spared in the prone position. Similar results of prone positioning allowing greater sparing of dose to the lungs have been reported by other groups [15, 18-21, 23, 24].

In this study there was no significant difference in contra-lateral breast dose based on image modality. However with respect to patient positioning, the supine position displayed better contra-lateral breast sparing than prone. For the supine position the mean contra-lateral breast D1cc met the "acceptable" plan ranking, compared to "non-compliant" for the prone position. These results are in contrast to previous groups who have reported no difference in doses to the contra-lateral breast with patient position [17, 21]. These conflicting results may be explained by the differences between CTV/PTV determination. In our study, field sizes and gantry angles were determined by optimal PTV coverage, where the CTV was determined based on imaging alone. In contrast, Griem et al reported no difference to contra-lateral breast dose with patient position where the gantry angles were reported to be placed according to clinically defined borders as opposed to a contoured volume [17]. Similarly, Sethi et al also reported no difference to contra-lateral breast dose with patient position, where the WB target was determined by converting the 50% isodose line from clinically placed tangential beams into a structure, then cropping 5 mm from both the field edge and skin surface, as opposed to a contouring a target based on breast tissue [21]. Another study compared supine free-breathing (FB), supine deep inspiration breath-hold (DIBH) and prone whole breast radiotherapy plans, where the CTV was determined on the CT scans with the assistance of radio-opaque markers placed clinically. In line with our results, they reported that the volume of the contra-lateral breast receiving >5 Gy was significantly lower for the supine position (either DIBH or FB) versus prone [24]. As radiotherapy may increase the incidence of contra-lateral breast cancer [37], further investigations into differences in contra-lateral breast dose with positioning should be considered.

Analysis of left sided cases showed supine heart dose metrics to be less than prone. There has been controversy with respect to best position for reducing heart dose. Some authors report that prone positioning is better at heart dose and/or volume sparing than supine [15-17, 20, 23]. Some have reported no significant difference in heart dose between prone and supine positions [19, 22]. One group identified a significant benefit of prone positioning on heart doses for women where the WB_CTV exceeded 1000 cm^3 for WB radiotherapy [18]. They also reported that heart tissue moves towards chest-wall in patients positioned prone similarly to our study. Other studies report similar findings [13]. Any reported advantages of prone positioning on heart dose for larger patients may be less significant with the more recent uptake of breath-hold techniques. The UK HeartSpare study found that breath hold techniques in the supine position was superior to prone positioning for heart sparing[38].

Results from this study indicate a statistically significant increase in whole heart volume with supine positioning. Another group also reported an increase in heart volume with supine positioning when compared to prone [17]. Veldeman et al reported no difference in heart volumes between supine and prone-lateral patient positioning [23]. We suggest that the anterior surface of the heart may be more difficult to identify and contour in the prone position, or perhaps the cavernous nature of the heart sub-structures may collapse when the patient is in a prone position.

MRI is increasingly being considered for use in radiotherapy planning due to superior soft tissue contrast when compared to CT [39], and the potential for MRI guided radiotherapy [40]. A limitation of MRI, and hence for this study is that patients with a large body habitus are excluded from the cohort due to restrictions of the bore size. As such the results reported here may not be applicable for very large and obese patients (where benefits of prone positioning for breast radiotherapy have been reported). Another limitation is the prone positioning board used for this study (details are described elsewhere [26])was not designed specifically for radiotherapy as at the time of study commencement no MRI compatible board was available. To determine differences between imaging modalities an MRI compatible option was required. We acknowledge that this may limit the applicability of our patient positioning results; however as already discussed our positioning results are not dissimilar to other published data. This study investigated differences between radiotherapy breast plans based on target volume delineation differences to imaging modality used, this knowledge will support understanding with the advance towards MRI only planning and the aim of reducing radiation dose to patients. Previous studies demonstrate that the effect of distortion is minimal for breast radiotherapy planning [41]. Previous work from our group, on the same data-set demonstrated that supine WB CTVs were smaller in volume than prone WB CTVs [26]. This current study demonstrates that when CTV is expanded to PTV and clipped 0.5 cm inside the external skin volume, there is no volume difference in WB_PTV due to either imaging modality or patient position. This is likely to be due to a decreased separation across the volume in prone position (thus decreasing the volume expanded in the prone position) and the increased surface area of the CTV in prone position (due to gravitational pull), thus increasing the effect of clipping the volume to 0.5 cm within the skin edge, when compared to corresponding supine volumes. Our planning study demonstrates that there are no significant differences in doses to OARs when target doses are determined based on imaging information from MRI compared to CT, although we did not investigate differences in SC location between CT vs MRI. Importantly, the choice of patient position, does affect OAR doses. We report that whole heart volumes are reduced with prone positioning. With prone positioning lung doses are reduced, however heart doses and contra-lateral breast doses are increased.

CONCLUSIONS:

Planning with PTVs generated from MRI data showed no differences compared to planning with PTVs generated from conventional CT scans with respect to WB and SC targets and OAR doses, even when seroma cavity volumes were not the same. Prone positioning within this study reduced mean lung dose and whole heart volumes but increased mean heart and contra-lateral breast doses, compared to supine. Clinicians should consider the implications of patient positioning on OAR doses for each individual patient.

Figure Legend:

Figure 1: Comparison of plan compliance ranking (ideal/acceptable/non-compliant). There was a statistically significant difference between supine and prone positioning $p<0.001$ (chi square test).

Table Captions:

Table 1: Patient Characteristics (n= 28)

Table 2: Plan Compliance Criteria

Table 3: Comparison of Mean Target and Mean OAR Volumes and SC to chest-wall Distance.

Table 4: Non-compliant Plan Details

Table 5: Dose Metrics Averages

Table 6: Review of breast radiotherapy planning literature

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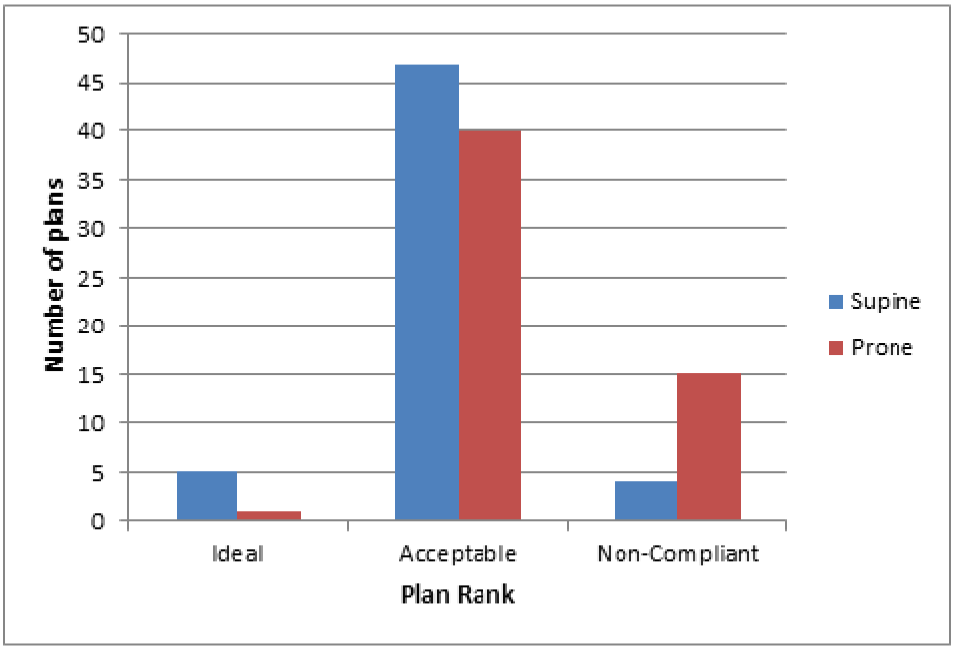
50
45
40
35
30
25
20
15
10
5
0
Number of plans
Ideal
Acceptable
Non-Compliant
Plan Rank
Supine
Prone

Figure 1

Table 1: Patient Characteristics (n= 28)

Patient Characteristics		
Side	Left Right	11 17
Tumour Position	UOQ UIQ LOQ LIQ Overlapping lesion of breast Central portion of breast Intra-ductal breast	13 7 1 1 3 2 1
Age	mean range	58 years 38 – 72 years
Breast size (WB_PTV Volume)	< 500 cc 501 – 1000 cc > 1000 cc	3 7 1

Abbreviations: UOQ = upper outer quadrant, UIQ = upper inner quadrant, LOQ = lower outer quadrant, LIQ = lower inner quadrant, WB = whole breast, PTV = planning target volume, cc = cubic centimetre.

Table 2: Plan Compliance Criteria

Plan Compliance Criteria			
Structure	**Dose Metric**	**Ideal**	**Acceptable**
WB_PTV	**V95%**	>95%	N/A
	V90%	N/A	>95%
	V107%	<5%	N/A
	V110%	N/A	<5%
	D 1cc (Gy)	<53.5 Gy	<57.5 Gy
SC_PTV	**V95%**	>99%	N/A
	V92%	N/A	>99%
	D 1cc (Gy)	<55 Gy	< 57.5 Gy
Combined Lung Volume	**V20Gy**	<10%	<10%
	mean dose (Gy)	<10 Gy	<10 Gy
Ipsi-lateral Lung	**V20Gy**	<15%	<20%
	V10Gy	<35%	<40%
	V5Gy	<50%	<50%
Contra-lateral Lung	**V5Gy**	<10%	<15%
Heart - LEFT SIDED CASES	**V25Gy**	N/A	<5%
	V20Gy	<5%	N/a
	V10Gy	<30%	<35%
	mean dose (Gy)	<4 Gy	<5 Gy
Heart - RIGHT sided cases	**V25Gy**	N/A	<0%
	V20Gy	<0%	N/A
	V10Gy	<10%	<15%
	mean dose (Gy)	<4 Gy	<5 Gy
Contra-lateral Breast	**V1.86Gy**	<5%	N/A
	V3.1Gy	N/A	<5%
	D 1cc (Gy)	<3.1 Gy	<5 Gy

Plans that did not meet either ‘Ideal’ or ‘Acceptable’ criteria were classed as ‘Non-compliant’.

Abbreviations: WB = whole breast, PTV = planning target volume, SC = seroma cavity, cc = cubic centimetre.

Table 1: Comparison of Mean Target and Mean OAR Volumes and SC to chest-wall Distance.

	Imaging Modality			Patient Position		
Anatomical Measure	CT	MRI	p	Supine	Prone	p
Volume WB _PTV (cc)	808 ± 306	795 ± 303	0.96*	799 ± 298	803 ± 310	0.93*
Volume SC_PTV (cc)	94 ± 63	75 ± 62	0.11*	80± 57	88± 689	0.53*
Minimum distance SC_PTV to chest-wall (mm)	4.9 ± 10.9	4.9 ± 11.1	0.98*	1.1 ± 3.4	8.7 ± 14.2	<0.001*
Ipsi-lateral Lung Volume (cc)				1300 ± 312	1343 ± 276	0.195†
Contra - lateral Lung Volume (cc)				1243 ± 310	1274 ± 253	0.368†
Combined Lung Volume (cc)				2544 ± 558	2618 ± 491	0.220†
Heart Volume (cc)				475 ± 81	441 ± 67	0.005†
Contra-lateral Breast Volume (cc)				850 ±342	877 ± 317	0.199†

* p-value refers to multivariable analysis

† p-value refers to the paired t test.

Abbreviations: WB = whole breast, PTV = planning target volume, SC = seroma cavity, cc = cubic centimetre.

Table 4: Non-compliant Plan Details:

ID	Laterality	Plan	ROI dose constraint not met
ID3	Left	MRI_Prone	Heart V25Gy, Heart mean dose, Contra-lateral breast D1cc *
ID8	Left	CT_Prone	Contra-lateral breast D1cc*
ID9	Left	CT_Prone	SC_PTV_SCV92% *
ID14	Right	CT_Prone	Heart V25Gy
	Right	MRI_Prone	Heart V25Gy
ID15	Right	CT_Prone	Contra-lateral breast D1cc#
	Right	MRI_Prone	Contra-lateral breast D1cc#
ID21	Left	CT_Supine	Heart V25Gy, Heart mean dose
	Left	MRI_Supine	Heart V25Gy, Heart mean dose
	Left	CT_Prone	Heart V25Gy
	Left	MRI_Prone	Heart V25Gy, Heart mean dose
ID25	Left	CT_Prone	Contra-lateral breast V 3.1Gy
	Left	MRI_Prone	Heart V25Gy, Heart mean dose & Contra-lateral breast D1cc
ID30	Right	CT_Supine	SC_PTVV92% , Contra-lateral breast V3.1Gy, Contra-lateral breast D1cc
	Right	MRI_Supine	SC_PTV_SCV92% Contra-lateral breast V3.1Gy, Contra-lateral breast D1cc
	Right	CT_Prone	SC_PTV_SCV92% , Contra-lateral breast D1cc
	Right	MRI_Prone	Contra-lateral breast D1cc
ID32	Left	CT_Prone	Heart V25Gy, Heart mean dose
	Left	MRI_Prone	Heart V25Gy, Heart mean dose

*only one of the 2 prone data set plans were non-compliant due to differences in target volumes (the image set with the larger PTV had dose criteria that could not be met).

The prone PTVs came to midline whereas the supine PTVs were 1.2 cm away from midline

Table 5: Dose Metrics Averages

Structure	Metric	Imaging Modality Comparison					Patient Positioning Comparison				
		MRI		CT		P-value	Supine		Prone		P-value
		mean	±SD	mean	±SD		mean	±SD	mean	±SD	
WB_PTV	Dmean (Gy)	50.16	±0.54	50.07	±0.52	0.28	50.23	±0.35	49.99	±0.65	<0.001
	V95% (%)	93.56	±3.20	93.05	±3.37	0.2	94.81	±2.50	91.81	±3.30	<0.001
	V90 (%)	97.57	±1.50	97.23	±1.50	0.05	97.86	±1.57	96.93	±1.28	<0.001
	V107% (%)	1.47	±2.13	1.93	±2.43	0.23	1.49	±1.73	1.91	±2.73	0.83
	V110% (%)	0.05	±0.11	0.18	±0.41	0.02	0.11	±0.30	0.11	±0.32	0.97
	D1cc (Gy)	54.27	±0.97	54.45	±1.08	0.32	54.27	±0.83	54.45	±1.20	0.34
SC_PTV	V95% (%)	99.03	±1.33	98.47	±2.96	0.51	99.03	±2.67	98.47	±1.87	<0.001*
	V92% (%)	99.79	±0.45	99.42	±2.20	0.44	99.63	±2.12	99.58	±0.83	0.34
	D1cc (Gy)	53.07	±1.18	53.18	±1.26	0.28	52.77	±0.95	53.47	±1.35	<0.001*
Combined Lung	V20Gy (%)	4.24	±2.58	4.31	±2.56	0.8	5.99	±1.56	2.57	±2.18	<0.001
	Dmean (Gy)	2.6	±1.27	2.64	±1.29	0.74	3.53	±0.74	1.71	±1.02	<0.001
Ipsi-lateral Lung	V20Gy (%)	8.26	±4.95	8.38	±4.87	0.81	11.75	±2.90	4.89	±3.98	<0.001
	V10Gy (%)	11.55	±6.48	11.76	±6.38	0.72	16.46	±3.40	6.85	±4.92	<0.001
	V5Gy (%)	16.74	±8.82	17.08	±8.66	0.64	23.89	±4.04	9.94	±6.12	<0.001

Heart (Left cases only)	**V25Gy (%)**	4.8	±2.67	4.16	±2.98	0.15	3.26	±2.89	5.7	±2.18	<0.001
	V20Gy (%)	5.07	±2.88	4.54	±3.31	0.30	3.85	±3.15	5.76	±2.74	0.001
	V10Gy (%)	7.97	±3.87	7.5	±4.31	0.43	5.77	±3.88	9.7	±3.24	<0.001
	Dmean (Gy)	4.03	±1.36	3.77	±1.52	0.32	3.4	±1.55	4.4	±1.13	<0.001
Heart (Right cases only)	**V25Gy (%)**	0.16	0.91	0.00	0.00		0.00	0.00	0.16	0.91	
	V20Gy (%)	0.14	0.72	0.00	0.00		0.00	0.00	0.14	0.72	
	V10Gy (%)	0.30	1.60	0.01	0.04		0.00	0.00	0.32	1.60	
	Dmean (Gy)	0.85	0.34	0.88	0.21		0.85	0.17	0.93	0.35	
Contra-lateral Breast	**V1.86Gy (%)**	6.69	±3.91	7.12	±4.08	0.41	6.67	±4.42	7.14	±3.51	0.10
	V3.1Gy (%)	0.88	±1.34	0.97	±1.74	0.67	0.72	±1.40	1.13	±1.67	0.06
	D1cc (Gy)	7.04	±8.39	7.11	±9.15	0.78	4.64	±7.19	9.51	±9.51	<0.001

*significant p-value only achieved after removing outliers.

Abbreviations: SD = standard deviation, WB = whole breast, PTV = planning target volume, SC = seroma cavity, cc = cubic centimetre, D = dose, V = volume, CI = conformity index, CN = conformity number, Hi = homogeneity index.

Table 6: Review of breast radiotherapy planning literature

Study:	n=†	Image Modality		Patient Position		Target determination	Reported results
		CT	MRI	Supine	Prone		
Chino et al [13].	16	√	√	√	√	N/A	heart to chest-wall distance: diagnostic MRI prone < supine planning CT
DeWyngaert et al [14] & Lymberis et al [20].	100	√	X	√	√	clinical	Target dose coverage: no difference detected Lung dose: prone position superior Heart dose: prone position superior in 87% cases
Fernandez-Lizarbe et al [15].	10	√	X	√	√	image	Target dose coverage: no difference detected Lung dose: prone position superior Heart dose: V35Gy – prone superior; mean dose - no difference detected
Formenti et al [16].	400	√	X	√	√	mixed	Lung volume: in-field volume prone < supine Heart volume: in-field volume prone < supine in 85% cases
Griem et al [17].	15	√	X	√	√	mixed	Target dose coverage: prone superior Target volume differences: supine < prone Lung dose: prone position superior Lung volume: ipsi-lateral lung - supine > prone; contra-lateral lung supine < prone Heart volume: whole heart volume - supine > prone; irradiated heart volume - no difference detected Contra-lateral breast dose: no difference detected Contra-lateral breast volume: supine < prone
Kirby et al [18].	65	√	X	√	√	mixed	Target volume differences: no difference detected Lung dose: prone position superior Heart dose: no difference detected across entire sample, however prone better for large breast size

Krengli et al [19]	41	√	X	√	√	image	Target dose coverage: supine superior Lung Doses: prone position superior Heart doses: no difference detected
Sethi et al [21].	12	√	X	√	√	mixed	Target volume differences: no difference detected Lung dose: prone position superior Heart dose: prone superior (n=4) Contra-lateral breast dose: no difference detected
Varga et al [22].	61	√	X	√	√	image	Target dose coverage: supine superior Lung dose: prone position superior Heart dose: no difference detected Contra-lateral breast dose: supine superior initially then no difference after positioning technique changed
Veldeman et al [23].	18	√	X	√	√	image	Target dose coverage: no difference detected Lung dose: prone position superior Lung volume: ipsi-lateral lung - prone > supine Heart dose: prone position superior
Verhoeven et al [24].	34	√	X	√	√	image	Target dose coverage: no difference detected Lung dose: prone position superior Heart dose: supine DIBH superior to prone Contra-lateral breast dose: supine DIBH and supine FB superior to prone
Mast et al [25].	10	√	√	√	X	image	Target volume differences: CT volume > CT co-registered with MRI
XXXXX [26].	33	√	√	√	√	image	Target dose coverage: SC volume: MRI < CT Target volume differences: Prone WB CTVs > supine
Current study:	28	√	√	√	√	image	Target dose coverage: no difference detected Target volume differences: no volumetric difference detected however distance between SC PTV to chest-wall prone > supine Lung dose: prone position superior Lung volume: no difference detected

							Heart dose: supine position superior Heart volume: prone < supine Contra-lateral breast dose: D1cc supine position superior Contra-lateral breast volume: no difference detected

***Target determination method: defined as either image (where the target was determined by contouring target tissue on an image), clinical field (where the target was determined by clinically defined borders) or mixed (where the target was determined by a mix of the previous two methodologies).**

† n=sample size