Dosimetric evaluation of 3 and/or 4 field radiation therapy of breast cancers: clinical experience

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Abstract

Background: Breast cancer is the most commonly diagnosed cancer among women and the second leading cause of cancer-related death in Canadian women. Surgery is often the first line of treatment for low-risk early stage patients, followed by adjuvant radiation therapy to reduce the risk of local recurrence and prevent metastasis after lumpectomy or mastectomy. For high-risk patients with node positive disease or are at greater risk of nodal metastasis, radiation therapy will involve treatment of the intact breast or chest-wall as well as the regional lymph nodes.
Materials and methods: We retrospectively evaluated the treatment plans of 354 patients with breast cancer with nodes positive or were at high risk of nodal involvement treated at our cancer centre. All patients were treated with a prescription dose of 50 Gy in 25 fractions to the intact breast or chest-wall and 50 Gy in 25 fractions to the supraclavicular region and, based on patient suitability and tolerance, were treated either using the deep inspiration breath hold (DIBH) or free-breathing (FB) techniques.
Results: Based on patient suitability and tolerance, 130 (36·7%) patients were treated with DIBH and 224 (63·3%) with FB techniques. There were 169 (47·7%) patients treated with intact breast, whereas 185 (52·3%) were treated for post-mastectomy chest-wall. The mean PTV_eval $V_{92\%}$, $V_{95\%}$, $V_{100\%}$ and $V_{105\%}$ for all patients are $99·4 \pm 0·7$, $97·6 \pm 1·6$, $74·8 \pm 7·9$ and $1·5 \pm 3·2\%$, respectively. The mean ipsilateral lung V_{10Gy}, V_{20Gy} and V_{30Gy} are $30·0 \pm 5·3$, $22·4 \pm 4·7$ and $18·4 \pm 4·3\%$ for intact breast and $30·9 \pm 5·8$, $23·5 \pm 5·4$ and $19·4 \pm 5·0\%$ for post-mastectomy patients with FB, respectively. The corresponding values for patients treated using DIBH are $26·3 \pm 5·9$, $18·9 \pm 5·0$ and $15·6 \pm 4·7\%$ for intact breast and $27·5 \pm 6·5$, $20·6 \pm 5·7$ and $17·1 \pm 5·2\%$ for post-mastectomy patients, respectively. The mean heart V_{10Gy}, V_{20Gy}, is $1·8 \pm 1·7$, $0·9 \pm 1·0$ for intact breast and $3·1 \pm 2·2$, $1·7 \pm 1·6$ for post-mastectomy patients with FB, respectively. The corresponding values with the DIBH are $0·5 \pm 0·7$, $0·1 \pm 0·4$ for intact breast and $1·1 \pm 1·4$, $0·4 \pm 0·7$ for post-mastectomy patients, respectively.
Conclusion: The use of 3 and/or 4 field hybrid intensity-modulated radiation therapy technique for radiation therapy of high-risk node positive breast cancer patients provides an efficient and reliable method for achieving superior dose uniformity, conformity and homogeneity in the breast or post-mastectomy chest-wall volume with minimal doses to the organs at risk. The development and implementation of a consistent treatment plan acceptability criteria in radiotherapy programmes would establish an evaluation process to define a consistent, standardised and transparent treatment path for all patients that would reduce significant variations in the acceptability of treatment plans.

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Introduction

Breast cancer is the most commonly diagnosed cancer among women and accounts for approximately 25% of all new cancer cases and 13% of all cancer deaths in Canadian women.[1,2] In 2020, it is estimated that about 27,400 Canadian women will be diagnosed with breast cancer (an average of 75 new cases per day) and an estimated 5,100 women will die from the disease (an average of 14 deaths per day).[1,2] The most commonly used treatment modalities to effectively treat and control the disease include surgery, systemic therapy and radiation therapy or any combination depending on the stage of the tumour.[3] Surgery is often the first line of treatment for low-risk early stage patients, when the cancer is localised within the breast, followed by adjuvant radiation therapy to reduce the risk of local recurrence and prevent metastasis after lumpectomy or mastectomy.[2,3] This usually implies treatment of the surgical bed or the treatment of the intact

breast or chest-wall and a local radiation boost to the surgical bed. When treating the intact breast or chest-wall for low-risk early stage patients, a pair of opposed tangential fields are usually employed.[4–18] However for high-risk patients with node positive disease or are at greater risk of nodal metastasis, radiation therapy will involve treatment of the intact breast or chest-wall as well as the regional lymph nodes. This is achieved using two tangential fields to treat the intact breast or chest-wall and an anterior and sometimes opposed posterior fields to treat the regional lymph nodes in the upper axillary and supraclavicular regions.[3,19–27]

There are several techniques used for breast radiation therapy including the use of wedges, field-in-field (FIF), hybrid technique (involving open and optimised fields), intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT).[3–27] Several studies have reported that using IMRT, VMAT, FIF or the hybrid technique to treat the breast and regional lymph nodes have greater target coverage, reduced hotspots and reduced doses to the organs at risk (OAR) compared to conventional treatment with wedges.[4,6,7,10,11,14,18,23,27–30] Some studies[6,9,12–14,16,17,21,26,31] that have evaluated and compared the dosimetric parameters of three-dimensional conformal radiation therapy using FIF technique have reported significant maximum dose and hotspots reduction, improved dose coverage and a more homogenous distribution within the target. Other studies[6,8,11,12,15,18,26,27] have also used the hybrid technique for breast radiotherapy and observed similar improved dose coverage, reduced hotspots in the target and less dose to the OARs. The impact of respiratory motion during breast radiation therapy has also been investigated comparing free-breathing (FB) and deep inspiration breath hold (DIBH) techniques.[5,7,11,12,18,20,25,30] Mansouri et al.,[5] Osei et al.[18] and Hjelstuen et al.[20] reported low dose to the heart with the DIBH technique as the heart is pushed out of the high dose region (increased distance from the field edge to the heart) due to increased lung volume during inspiration. Other studies[21,23] have also investigated and evaluated radiation doses to the heart for patients treated in either the supine or prone positions during treatment. Csenki et al.[21] used the 4-field technique to treat patients in either the supine or prone positions and observed that the prone position approach resulted in significantly less dose to the heart and lung compared to the FB supine position although the target dose coverage was similar.

One of the challenges in radiation treatment planning is the lack of consistency among different institutions and individuals with regard to what is considered an acceptable treatment plan in terms of target coverage and doses to the OAR. Clinical trials[32,33] usually resolve this issue by providing well-defined criteria for treatment plans acceptability within the trial whereby any plan fulfilling the criteria is considered acceptable, whereas any plan not fulfilling all the criteria may be considered unacceptable. The availability of these criteria lessens the stress on dosimetrists, as they can present treatment plans to radiation oncologists, which are less likely to be rejected and therefore could potentially improve confidence in dosimetrists, reduce variation in treatment plans and improve workflow and patient care.[18] Despite these benefits, several institutions are yet to develop local institutional criteria for accepting treatment plans. Therefore, there is a growing need for the development of local site-specific treatment plan acceptability criteria in order to minimise significant variations in patient treatment plans.

Aim of study

In a previous study,[18] we described the establishment of well-defined criteria for accepting treatment plans of intact breast and chest-wall for low-risk early stage breast cancer patients' treatment plans. In order to develop similar institutional criteria for accepting volume-based breast radiation therapy treatment plans for high-risk patients with nodal involvement based on our current experiences and resources, we conducted this comprehensive retrospective dosimetric analysis of 3 and/or 4 field radiation therapy plans for high-risk breast cancer patients. This study therefore reports on the dosimetric evaluation of the 3 and/or 4 field technique for high-risk breast cancer treatment at our centre over a 4-year period and suggests criteria for treatment plans acceptability. The implementation of such criteria would establish an evaluation process to define a consistent and transparent treatment path for all patients that reduces significant variations in the acceptability of treatment plans.

Materials and Methods

We retrospectively evaluated the treatment plans of 354 high-risk breast cancer patients with nodal involvement who were treated at our cancer centre over a 4-year period. All patients were treated with a prescription dose of 50 Gy in 25 fractions to the intact breast or chest-wall and 50 Gy in 25 fractions to the supraclavicular region and, based on patient suitability and tolerance, were treated either using the DIBH technique or the FB technique.

Patient positioning for computer tomography scan

The standard protocol for patient positioning during computer tomography (CT) scan for breast cancer patients with nodal involvement at our institution is usually the supine position with both arms raised above the patient's head. The arms are supported in position with a custom made Vac-Lok cushion, and a Kneefix cushion is usually placed under the knees. If breast tissue falls above the second intercostal space as a result of patient positioning, then a breast board is used at an appropriate inclined angle. The use of a head rest is optional but may be used depending on patient comfort and folds in the skin tissue. Usually, the patient's head will be slightly turned to the contralateral side. If the patient cannot be scanned through the CT simulator bore diameter due to the arms positioning, the positioning may be modified such that the ipsilateral arm is raised above the head and the contralateral arm is placed by the patient's side. In some cases, a breast sling may be used to support the breast when a pendulous breast falls too far laterally that result in a large lung volume being included in the treatment field or if the breast falls inferiorly and creates a fold.

Patient CT simulation

The detailed CT scan protocol used for low-risk breast cancer patients at our institution has been described by Osei et al.[18] In addition, for high-risk patients, radio-opaque markers are placed on the scar and the surrounding breast tissue for visualisation on the radiograph. A marker is also placed at the level of the second intercostal space to guide the placement of the isocentric tattoo. All patients are scanned using the institutional 'breast' CT scan protocol with a slice thickness of 3 mm. The scan extends superiorly from the mandible to inferiorly to include the breast and lung
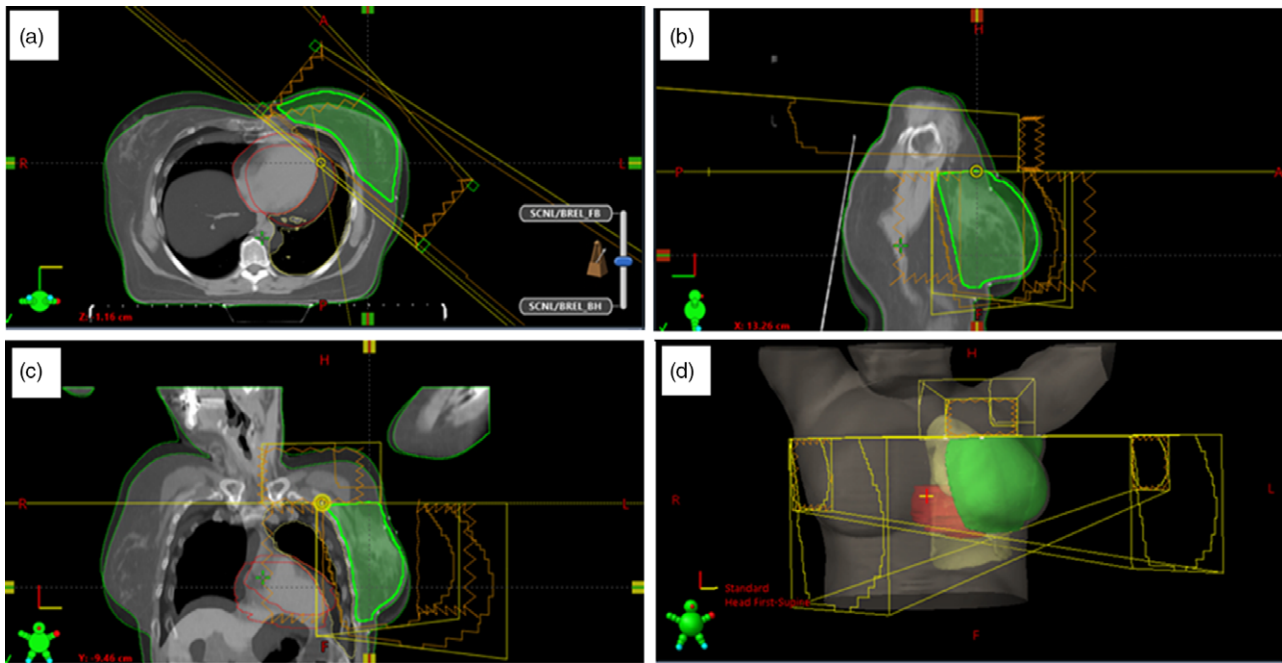
Figure 1. Beams arrangement for a 3 field radiation therapy of the breast and the supraclavicular lymph nodes: two tangential fields to treat the intact breast or chest-wall and a third field to treat the supraclavicular lymph nodes. The figure shows the blended images of the CT datasets for both free breathing and deep inspiration breathe hold for the same patient in the transverse (a), sagittal (b), coronal (c) views and the 3-D visualisation of the breast, lung, heart and the field placements (d).

tissue. A reproducible 3-point setup is marked on the patient for tattoo localisation. Tattoos are placed at the anterior, right lateral and left lateral setup points. Additional tattoos are placed at the isocentre and inferiorly for leveling if the patient's anatomy requires a more stable setup point. The CT scan dataset and all points were then exported into the Eclipse TPS (Version 13·6; Varian Medical Systems, Palo Alto, CA, USA).

Field arrangements and borders for treatment planning

Supraclavicular field(s)

The isocentre is placed at the base of the clavicle. The supraclavicular area is usually treated with a single anterior field (for a 3 field arrangement) which is usually angled slightly away from the vertebral bodies. The superior border of this field is placed at the inferior level of the cricoid cartilage and the inferior border at the isocentre at the base of the clavicle. The lateral borders are placed at the neck of the humeral head and the medial borders at 1 cm from the spinal cord. Multileaf collimators are used to shield the humeral head and larynx (Figure 1). Currently, the lymph nodes in the supraclavicular region are not contoured; therefore, the radiation oncologist will usually examine the isodose lines coverage to ensure adequate coverage of the lymph nodes. Depending on the acceptability of the dose coverage in the axilla, a posterior field (opposed anterior field) may be added to the supraclavicular area creating a 4 field monoisocentric field arrangement.

Tangential fields

The intact breast or chest-wall is treated with an opposing pair of tangential fields, and the detailed description of the field borders for these fields has been described by Osei et al.[18] In summary, the superior field border is set at the level of the second intercostal space but may be adjusted to clinically cover the entire breast tissue. The inferior border is set at 1·5 cm inferior to the

inframammary fold. The medial tangent field border is set medially at midline and the lateral border is set at the mid-axillary line or 1·0 cm posterior to palpable breast tissue (Figure 1).

Target volumes and OAR

The detailed description of the contouring of the targets and OAR volumes has been described by Osei et al.[18] The following structures are usually generated for treatment plan evaluation; the body, the ipsilateral lungs, a treated volume (i.e., 50% isodose line converted to a structure to help create the breast volume), PTV_eval [breast volume for evaluation, which is a contraction of 5 mm (in all directions) of the breast contour] and the heart for left sided breast patients. The ipsilateral lung is usually contoured with autosegmentation with manual verification. Currently, the lymph nodes in the supraclavicular region are not contoured and are therefore not evaluated in this study.

Radiation treatment planning

A 3-field or 4-field monoisocentric plan is generated by the treatment planner using either 6, 10 and 15 MV beam energies or a combination of energies depending on patient breast size or separation to ensure acceptable dose coverage; however, low-energy beams are usually used for the optimised field. All patients were treated with a prescription dose of 50 Gy in 25 fractions to the intact breast or chest-wall using two tangential fields and 50 Gy in 25 fractions to the supraclavicular region with a 3rd and/or 4th fields. Usually, a 0·5 cm or 1 cm thickness of bolus is placed on the chest-wall to ensure adequate skin dose coverage. A hybrid IMRT technique using both 'open' and optimised tangential fields and the dose distribution from the supraclavicular field(s) used as the based dose plan are used for generating the 3-field or 4-field monoisocentric treatment plans. The details of the hybrid IMRT technique have been described elsewhere[18] and the technique
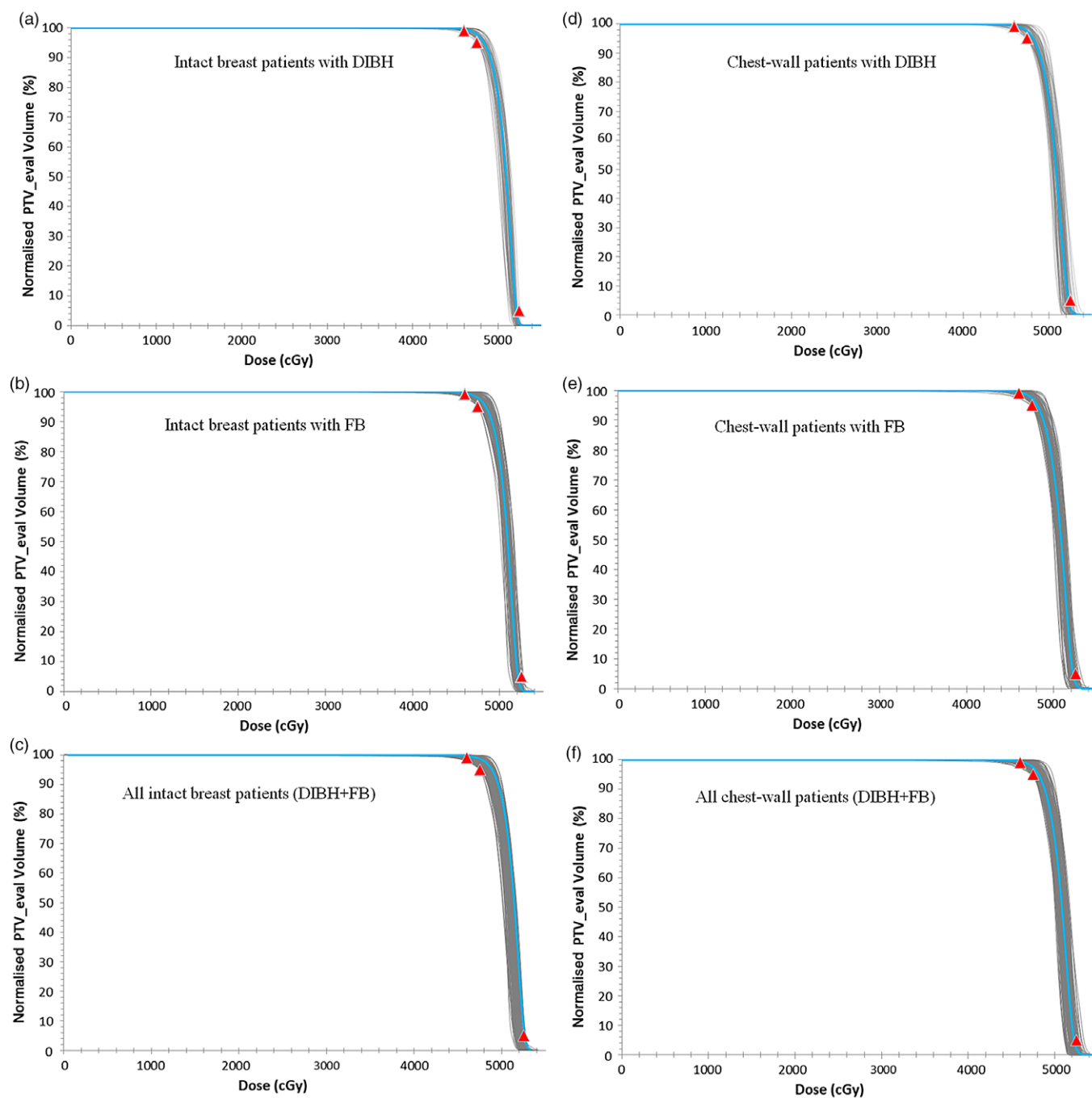
Figure 2. A plot of the dose-volume histogram (DVH) of the intact breast (a, b and c) and chest-wall (d, e and f) PTV_eval for patients treated using either the DIBH technique (a and d) or FB technique (b and e). (c) All treated intact breast patients and (f) all treated chest-wall patients. The grey lines represent individual patients DVH and the blue lines in each plot are the mean DVHs. The red data points are the planning dose objectives of $V_{92\%} \geq 99$, $V_{95\%} \geq 95$ and $V_{105} < 5\%$.
Abbreviations: DIBH, deep inspiration breathe hold; FB, free breathing.

has the potential to produce a homogeneous dose distribution within the breast or chest-wall PTV_eval.

Daily treatment

Patients are set up as per the CT simulation using the tattoos on the patient which were marked during the CT and the in-room lasers as per institutional protocol. Patients are ensured to be straight using a single isocentre and inferior straightening tattoos and the target-to-skin distances and clearance of breast tissue are also checked. Images are taken on Day 1 and weekly thereafter for verification of field portals for all patients: An anterior kV image is taken for supraclavicular field verification and it is matched to bony anatomy and a medial MV image is taken to verify and match lung volume. Although there are standard images taken for all patients, other images may be repeated more often at the discretion of the treating radiation therapists to ensure the correct target is being treated.

Table 1. A summary of the measures of central tendency and dispersion of patient breast separation, PTV_eval volume and normalised PTV_eval volume receiving 90, 92, 95, 100, 101, 102, 103, 104, 105 and 106% of the prescription dose for all patients and stratified by breast separation into small (< 20 cm), medium (20 ≤ x ≥ 25) and large (> 25 cm) main groups

All patients	Breast separation (cm)	PTV_eval volume (cm³)	Normalised PTV_eval volume receiving the percentage of the prescribed dose									
			$V_{90\%}$ (%)	$V_{92\%}$ (%)	$V_{95\%}$ (%)	$V_{100\%}$ (%)	$V_{101\%}$ (%)	$V_{102\%}$ (%)	$V_{103\%}$ (%)	$V_{104\%}$ (%)	$V_{105\%}$ (%)	$V_{106\%}$ (%)
Small: < 20 cm, n = 138												
Mean	18·2	591·1	99·9	99·6	98·2	75·8	62·0	43·2	22·8	7·4	1·2	0·1
Median	18·5	540·4	100·0	99·9	98·7	76·3	62·5	44·2	20·5	4·7	0·2	-
Standard deviation	1·5	274·9	0·3	0·5	1·5	8·3	11·4	14·7	13·6	7·7	2·4	0·4
Maximum	20·0	1721·1	100·0	100·0	99·9	89·9	83·1	70·5	55·5	31·4	14·3	2·6
Minimum	10·3	126·2	98·2	97·2	94·3	52·1	28·0	7·2	0·7	-	-	-
Medium: 20 ≤ x ≥ 25, n = 176												
Mean	22·2	936·0	99·7	99·3	97·6	74·4	62·4	46·2	27·0	9·5	1·5	0·2
Median	22·1	880·6	99·8	99·4	97·2	75·5	63·8	49·0	27·7	6·9	0·2	-
Standard deviation	1·3	447·5	0·6	0·8	1·4	7·8	11·0	13·9	13·8	8·6	3·4	1·2
Maximum	25·0	2573·2	100·0	100·0	99·8	88·4	82·2	71·7	59·1	40·0	25·1	12·8
Minimum	20·0	181·9	92·6	91·9	89·6	47·8	22·1	6·8	0·1	-	-	-
Large: >25 cm n = 40												
Mean	26·9	1532·3	99·5	98·9	96·3	73·1	62·6	48·7	30·9	12·8	2·8	0·5
Median	26·5	1609·9	99·6	99·0	95·9	74·5	64·8	51·4	32·3	11·0	0·7	0·0
Standard deviation	1·7	639·2	0·4	0·7	1·4	6·5	8·6	11·0	12·7	9·7	4·5	1·4
Maximum	31·3	2871·1	100·0	100·0	99·6	85·2	78·2	68·1	56·2	37·8	21·5	7·0
Minimum	25·1	319·6	98·7	97·8	93·8	55·5	34·9	18·3	1·0	-	-	-
All patients, n = 354												
Mean	21·1	868·9	99·7	99·4	97·6	74·8	62·3	45·3	25·8	9·0	1·5	0·2
Median	21·0	718·7	99·9	99·6	97·5	75·6	63·5	46·5	26·1	6·2	0·2	-
Standard deviation	3·1	506·0	0·5	0·7	1·6	7·9	10·9	14·0	13·8	8·5	3·2	1·0
Maximum	31·3	2871·1	100·0	100·0	100·0	90·8	83·1	71·7	59·1	40·0	25·1	12·8
Minimum	10·3	126·2	92·6	91·9	89·6	47·8	22·1	6·8	0·1	-	-	-

'-' Indicates the value is less than 0·1%.

Indices for PTV_eval

The plan quality in this study was quantitatively evaluated by calculating the homogeneity index (HI), uniformity index (UI) and the conformity index (CI) for the PTV_eval. The HI, CI and UI evaluate the dose homogeneity, conformity and uniformity, respectively, within the PTV_eval and are calculated as

$$HI = \frac{D_2 - D_{98}}{DPD}$$

$$UI = \frac{D_5}{D_{95}}$$

$$CI = \frac{V_{RI}}{TV}$$

where D_2, D_5, D_{95} and D_{98} are the doses received by 2, 5, 95 and 98% of the PTV_eval, respectively. DPD is the prescribed dose, VRI is the volume of PTV_eval covered by the reference isodose line (in this case the 95% isodose line) and TV is the target volume (in this case the PTV_eval). The values of CI and UI close to unity indicate greater conformity and uniformity, and values of HI close to zero indicate greater homogeneity.

Treatment plan data analysis

We retrospectively evaluated the treatment plans of 354 high-risk breast cancer patients with nodal involvement or at risk of nodal involvement who were treated at our cancer centre over a 4-year period. For each patient, we determined the mean, median, maximum, minimum and standard deviation of the breast separation, the HI, UI and the CI for the PTV_eval and volumes of the

Table 2. A summary of the measures of central tendency and dispersion of patient breast separation, PTV_eval volume and normalised PTV_eval volume receiving 90, 92, 95, 100, 101, 102, 103, 104, 105 and 106% of the prescription dose for patients treated with intact breast and stratified by breast separation into small (< 20 cm), medium ($20 \leq x \geq 25$) and large (> 25 cm) main groups

All patients	Breast separation (cm)	PTV_eval volume (cm³)	Normalised PTV_eval volume receiving the percentage of the prescribed dose									
			$V_{90\%}$ (%)	$V_{92\%}$ (%)	$V_{95\%}$ (%)	$V_{100\%}$ (%)	$V_{101\%}$ (%)	$V_{102\%}$ (%)	$V_{103\%}$ (%)	$V_{104\%}$ (%)	$V_{105\%}$ (%)	$V_{106\%}$ (%)
Small: < 20 cm, $n = 61$												
Mean	18·3	665·4	99·9	99·8	98·7	77·8	63·3	43·2	21·3	5·6	0·7	0·1
Median	18·5	636·5	100·0	99·9	99·0	76·8	63·5	44·1	18·9	3·7	0·1	0·0
Standard deviation	1·4	292·4	0·1	0·3	1·2	7·2	10·8	13·8	12·4	6·4	1·9	0·3
Maximum	20·0	1575·2	100·0	100·0	100·0	90·8	82·6	69·9	54·4	33·3	10·9	1·9
Minimum	12·0	208·7	99·5	98·4	95·0	61·2	38·1	12·2	3·1	-	-	-
Medium: $20 \leq x \geq 25$, $n = 82$												
Mean	22·1	1155·3	99·8	99·4	97·7	76·9	65·0	48·2	27·8	8·8	0·7	0·0
Median	22·1	1184·7	99·9	99·5	97·5	78·1	65·5	51·0	28·3	6·4	0·1	0·0
Standard deviation	1·2	430·2	0·3	0·5	1·2	6·8	9·9	13·5	13·8	7·8	2·0	0·2
Maximum	24·7	2390·3	100·0	100·0	99·8	88·4	82·2	71·7	55·7	37·2	13·6	1·3
Minimum	20·1	181·9	98·3	97·3	95·1	52·8	33·4	7·3	1·5	0·1	-	-
Large: >25 cm $n = 26$												
Mean	27·1	1809·5	99·4	98·8	96·2	75·4	65·5	51·5	32·1	12·2	2·2	0·3
Median	26·6	1708·0	99·5	98·9	95·9	76·2	66·6	52·2	32·3	8·0	0·3	0·0
Standard deviation	1·9	538·3	0·4	0·6	1·3	5·1	6·0	8·3	11·6	9·8	3·8	1·1
Maximum	31·3	2871·1	100·0	100·0	99·6	85·2	78·2	68·1	56·2	32·8	13·5	5·4
Minimum	25·1	637·0	98·7	97·8	93·8	65·7	52·3	32·4	15·4	0·1	-	-
All intact breast patients, $n = 169$												
Mean	21·5	1079·1	99·8	99·5	97·8	77·0	64·4	46·9	26·1	8·2	1·0	0·1
Median	21·1	964·7	99·9	99·7	98·1	76·9	65·5	48·6	25·2	5·5	0·1	0·0
Standard deviation	3·3	557·2	0·3	0·6	1·5	6·7	9·7	13·2	13·5	8·0	2·4	0·5
Maximum	31·3	2871·1	100·0	100·0	100·0	90·8	82·6	71·7	56·2	37·2	13·6	5·4
Minimum	12·0	181·9	98·3	97·3	93·8	52·8	33·4	7·3	1·5	-	-	-

'-' Indicates the value is less than 0·1%.

PTV_eval, ipsilateral lung and heart (for patients whose left-sided breast was treated and for whom the heart is usually contoured). We also analysed the dose-volume histograms (DVHs) for the PTV_eval and the OARs. We stratified patients into those who received treatment using the DIBH and those who used the FB technique for their treatment. The PTV_eval coverage is evaluated to ensure that the plan meets the following criteria for the normalised PTV_eval receiving 92 ($V_{92\%}$), 95 ($V_{95\%}$) and 105 ($V_{105\%}$) of the prescription dose such that $V_{92\%} \geq 99$, $V_{95\%} \geq 95$ and $V_{105\%} < 5\%$ and adequate dose coverage in the axilla region as determined by the radiation oncologist based on the isodose lines coverage. For the OARs, plan acceptability is determined based on the following organs volume dose constraints: The volume dose constraints used for the ipsilateral lung are $V_{5Gy} \leq 65$, $V_{10Gy} \leq 45$ and $V_{20Gy} \leq 25\%$ (ideal) or $V_{20Gy} \leq 35\%$, (acceptable) and the heart volume dose constraints are $V_{25Gy} \leq 10\%$ and the mean heart dose ≤ 3 Gy (ideal) or $V_{30Gy} \leq 10\%$ and the mean heart dose ≤ 5 Gy (acceptable).[34]

Results and Discussions

The treatment plans of high-risk breast cancer patients treated with the 3 and/or 4 field technique at our cancer centre over a 4-year period using either the FB or the DIBH techniques were evaluated. Figure 1 shows typical beams arrangement for a 3 field radiation therapy of the breast or chest-wall and supraclavicular lymph nodes: two tangential fields to treat the intact breast or chest-wall and a third field to treat the supraclavicular lymph nodes. Based on patients suitability and tolerance, 130 (36·7%) patients were treated using the DIBH technique and 224 (63·3%) were treated with the FB technique. There were 169 (47·7%) patients treated with intact

Table 3. A summary of the measures of central tendency and dispersion of patient breast separation, PTV_eval volume and normalised PTV_eval volume receiving 90, 92, 95, 100, 101, 102, 103, 104, 105 and 106% of the prescription dose for post-mastectomy chest-wall patients and stratified by breast separation into small (< 20 cm), medium ($20 \leq x \geq 25$) and large (> 25 cm) main groups

All patients	Breast separation (cm)	PTV_eval volume (cm³)	Normalised PTV_eval volume receiving the percentage of the prescribed dose									
			$V_{90\%}$ (%)	$V_{92\%}$ (%)	$V_{95\%}$ (%)	$V_{100\%}$ (%)	$V_{101\%}$ (%)	$V_{102\%}$ (%)	$V_{103\%}$ (%)	$V_{104\%}$ (%)	$V_{105\%}$ (%)	$V_{106\%}$ (%)
Small: < 20 cm, $n = 77$												
Mean	18·1	532·3	99·8	99·5	97·9	74·2	61·0	43·1	23·9	8·8	1·6	0·2
Median	18·5	499·9	100·0	99·7	98·4	75·2	61·6	44·5	23·5	5·3	0·4	0·0
Standard deviation	1·6	246·5	0·3	0·6	1·5	8·9	11·9	15·4	14·4	8·4	2·7	0·5
Maximum	20·0	1721·1	100·0	100·0	99·9	89·9	83·1	70·5	55·5	31·4	14·3	2·6
Minimum	10·3	126·2	98·2	97·2	94·3	52·1	28·0	7·2	0·7	-	-	-
Medium: $20 \leq x \geq 25$, $n = 94$												
Mean	22·2	744·6	99·6	99·2	97·0	72·2	60·1	44·4	26·4	10·1	2·1	0·4
Median	22·1	683·7	99·8	99·4	97·0	72·5	61·4	47·6	27·5	7·9	0·4	0·0
Standard deviation	1·5	369·1	0·8	0·9	1·5	8·1	11·4	14·1	13·9	9·2	4·2	1·6
Maximum	25·0	2573·2	100·0	100·0	99·8	87·2	79·4	71·7	59·1	40·0	25·1	12·8
Minimum	20·0	265·3	92·6	91·9	89·6	47·8	22·1	6·8	0·1	-	-	-
Large: >25 cm $n = 14$												
Mean	26·5	1017·5	99·5	99·0	96·4	68·8	57·3	43·5	28·5	14·0	3·9	0·9
Median	26·2	954·2	99·8	99·3	96·1	69·7	59·3	46·4	31·1	13·6	2·4	0·1
Standard deviation	1·3	478·9	0·5	0·8	1·5	6·9	10·3	13·7	14·8	9·8	5·5	1·9
Maximum	28·8	1843·7	100·0	100·0	99·2	77·9	69·2	60·2	50·5	37·8	21·5	7·0
Minimum	25·1	319·6	98·7	97·9	94·5	55·5	34·9	18·3	1·0	-	-	-
All intact breast patients, $n = 185$												
Mean	20·8	676·9	99·2	99·3	97·3	72·8	60·3	43·8	25·5	9·9	2·0	0·3
Median	20·6	611·1	99·9	99·5	97·2	73·4	61·4	45·5	26·5	7·2	0·5	0·0
Standard deviation	3·0	360·7	0·6	0·8	1·6	8·4	11·5	14·6	14·2	9·0	3·8	1·3
Maximum	28·8	2573·2	100·0	100·0	99·9	89·9	83·1	71·7	59·1	40·0	25·1	12·8
Minimum	10·3	126·2	92·6	91·9	89·6	47·8	22·1	6·8	0·1	-	-	-

'-' Indicates the value is less than 0.1%.

breast, whereas 185 (52·3%) were treated for post-mastectomy chest-wall.

Analysis of PTV_eval Dose

Figure 2 shows the DVH plots of the intact breast and chest-wall PTV_eval for patients treated using either the DIBH or FB techniques. A summary of the measures of central tendency and dispersion of patients breast separation, PTV_eval volume and normalised PTV_eval volume receiving 90, 92, 95, 100, 101, 102, 103, 104, 105 and 106% of the prescription dose for all patients and stratified by breast separation into small (< 20 cm), medium ($20 \leq x \geq 25$) and large (> 25 cm) groups are shown in Table 1. A similar summary of the measures of central tendency and dispersion is shown in Tables 2 and 3 when the patients were stratified into those treated for the intact breast and those treated for the

chest-wall post-mastectomy, respectively. The mean patient breast separation and PTV_eval are $21\cdot1 \pm 3\cdot1$ cm and $868\cdot9 \pm 506\cdot0$ cc, respectively (Table 1). When the patients were stratified into those who received treatment to the intact breast (Tables 2) and those who received treatment to the chest-wall post-mastectomy (Table 3), the mean breast separations were $21\cdot5 \pm 3\cdot3$ cm and $20\cdot8 \pm 3\cdot0$ cm and the PTV_eval volumes were $1079\cdot1 \pm 557\cdot2$ cc and $676\cdot9 \pm 360\cdot7$ cc for intact breast and chest-wall patients, respectively. A two tail student *t*-test of the mean breast separations (*p*-value = 0·04) and mean PTV_eval volumes (*p*-value < 0·001) indicates that there is significant difference in the patients breast separations and the PTV_eval volumes when patients were stratified into intact breast and post-mastectomy chest-wall.

The mean $V_{92\%}$, $V_{95\%}$, $V_{100\%}$, $V_{101\%}$, $V_{102\%}$, $V_{103\%}$, $V_{104\%}$ and $V_{105\%}$, for all patients are $99\cdot4 \pm 0\cdot7$, $97\cdot6 \pm 1\cdot6$, $74\cdot8 \pm 7\cdot9$, $62\cdot3 \pm 10\cdot9$, $45\cdot3 \pm 14\cdot0$, $25\cdot8 \pm 13\cdot8$, $9\cdot0 \pm 8\cdot5$ and $1\cdot5 \pm 3\cdot2$,
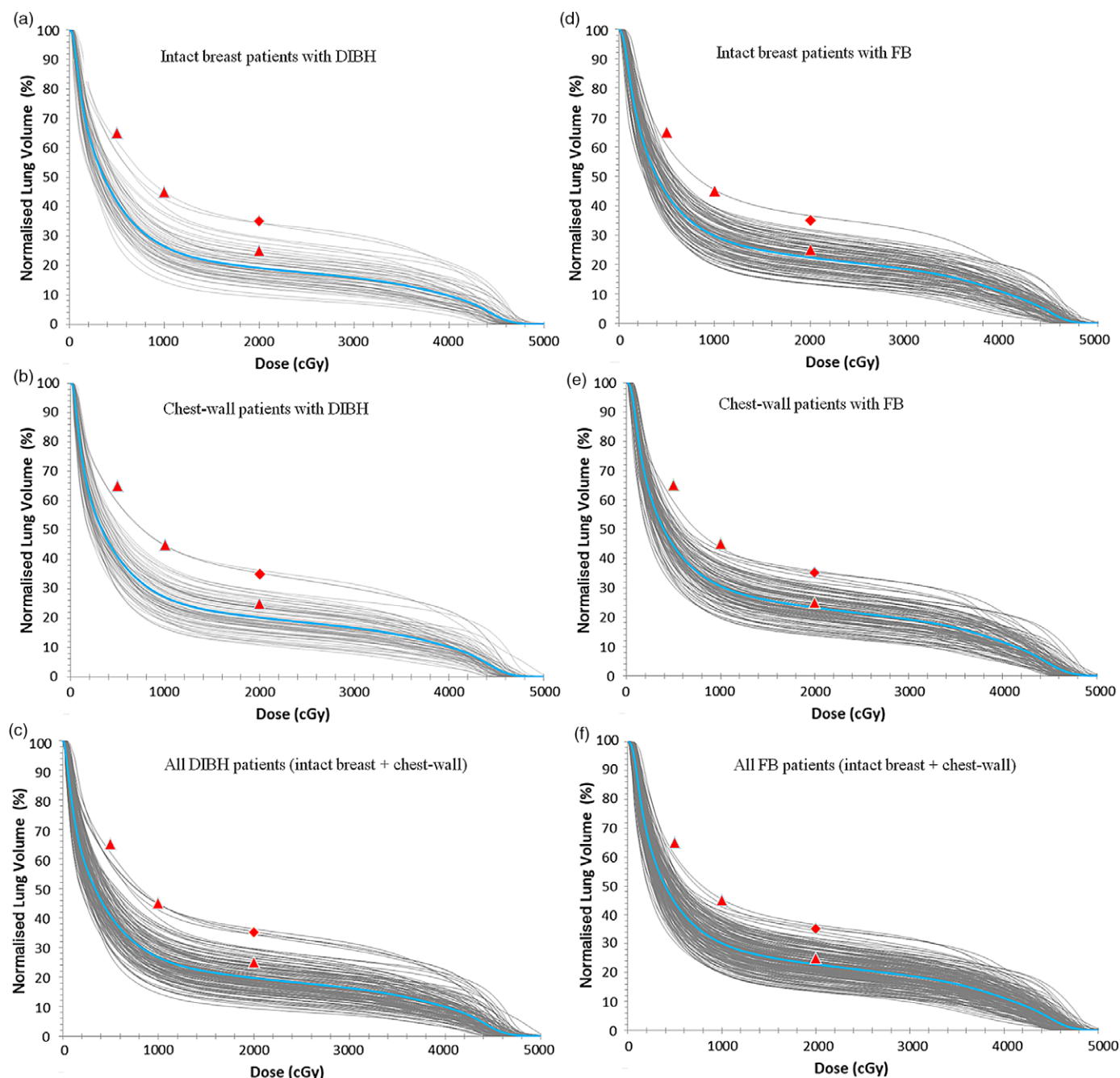
Figure 3. A plot of the dose-volume histogram (DVH) of the ipsilateral lung for patients treated using either the DIBH technique (a, b and c) or the FB technique (d, e and f). (c) All patients treated with the DIBH and (f) all patients treated with the FB techniques. The grey lines represent individual patients DVH and the blue lines in each plot are the mean DVHs. The red data points are the planning dose objectives of $V_{5Gy} \leq 65$, $V_{10Gy} \leq 45$ and $V_{20Gy} \leq 25\%$ (ideal: triangles) or $V_{20Gy} \leq 35\%$ (acceptable: diamonds). Abbreviations: DIBH, deep inspiration breathe hold; FB, free breathing.

respectively. When patients were stratified into the three cohorts based on the breast separation of small (PTV_eval < 20 cm), medium (20 cm ≤ PTV_eval ≤ 25 cm) and large (PTV_eval > 25 cm) groups, the mean $V_{92\%}$ (which is our current minimum dose coverage to the PTV_eval of $V_{92\%} \geq 99\%$) were 99.6 ± 0.5, 99.3 ± 0.8 and $98.9 \pm 0.7\%$ for the small, medium and large breast (Table 1). Furthermore, when patients were stratified based on whether they were treated for intact breast (Table 2) or chest-wall (Table 3), the target coverages were found to meet our current minimum target coverage and the hotspots (V_{106}) were

also very similar. Adequate target coverage is associated with tumour control which leads to improve biochemical relapse-free survival, cancer progression-free survival and cancer-specific survival. Several studies[8–16,20,22,23,26,27,30] have reported similar PTV_eval coverage for breast cancer patients. Tanaka et al.[16] investigated the FIF technique with lung blocks for breast radiotherapy and reported $V_{95\%}$ and $V_{100\%}$ of 93.2 and 62.7% for patients treated with the FB technique. Zheng et al.[27] investigated the dosimetry of seven radiation therapy planning techniques for breast cancer after mastectomy and reported $V_{95\%}$, $V_{100\%}$, $V_{105\%}$ of 95 ± 0.0,
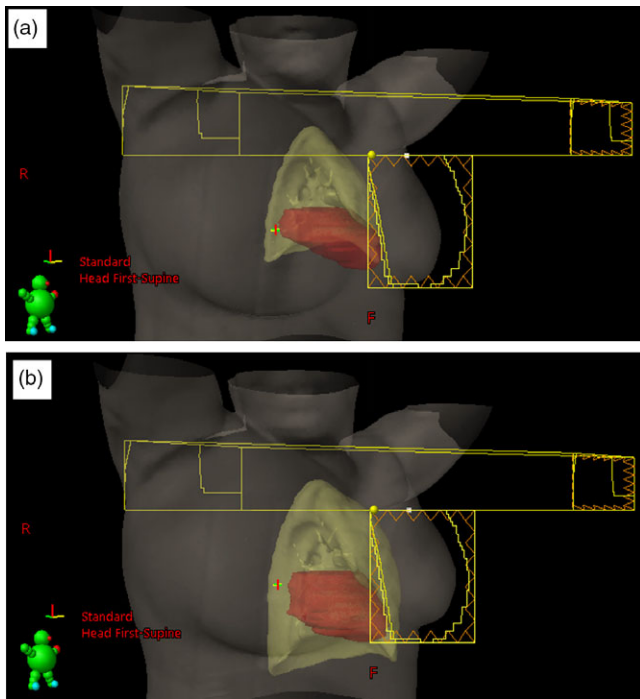
Figure 4. 3-D visualisation of the lung and heart positions and size in the tangential and supraclavicular treatment fields during free breathing (a) and deep inspiration breathe hold (b) for the same patient.

$32 \cdot 0 \pm 14 \cdot 9$ and $0 \cdot 16 \pm 0 \cdot 16\%$ for the hybrid technique and $95 \pm 0 \cdot 0$, $72 \cdot 9 \pm 8 \cdot 2$ and $15 \cdot 7 \pm 12 \cdot 5\%$ for FIF-IMRT. Ma et al.[14] compared radical mastectomy radiotherapy treatment plans for left-sided breast cancer patients using three-dimensional conformal radiotherapy with FIF technique and reported a $V_{95\%}$ of $78 \cdot 2 \pm 4 \cdot 3\%$. Hjelstuen et al.[20] also evaluated the reduction in cardiopulmonary radiation doses using the DIBH technique and reported $V_{95\%}$ of $98 \cdot 9 \pm 0 \cdot 5$ and $98 \cdot 8 \pm 0 \cdot 5\%$ for treatment plans based on patient FB and DIBH techniques, respectively.

Analysis of lung dose

The DVH plots of the ipsilateral lung for patients treated using either the DIBH or the FB techniques are shown in Figure 3, and Figure 4 shows a 3-D visualisation of the ipsilateral lung volume in the tangential and supraclavicular treatment fields during FB and DIBH for the same patient. Table 4 shows a summary of the measures of central tendency and dispersion of the ipsilateral lung volumetric doses for all patients stratified into patients who were treated with the FB and those treated with the DIBH techniques. The mean ipsilateral lung volumes for patients treated with intact breast and post-mastectomy chest-wall are $1413 \cdot 4 \pm 337 \cdot 3$ cc and $1423 \cdot 4 \pm 339 \cdot 0$ cc, respectively, using FB technique, and the corresponding values for patients treated with DIBH are $2164 \cdot 3 \pm 457 \cdot 7$ cc and $2164 \cdot 0 \pm 352 \cdot 3$ cc, respectively. A two tail student t-test of the means of the ipsilateral lung volumes for intact breast and chest-wall patients with FB (p-value $= 0 \cdot 83$) and with DIBH (p-value $= 0 \cdot 99$) techniques shows no significant difference in the mean lung volumes when comparing intact breast and chest-wall patients irrespective of the technique (Table 4). However, there was a significant difference (about 53% increased) in patients mean lung volumes between FB and DIBH techniques for both intact breast and chest-wall patients (Table 4, Figure 3). A two tail

student t-test of the means of the lung volumes with FB and DIBH techniques for intact breast patients (p-value $< 0 \cdot 001$) and for chest-wall patients (p-value $< 0 \cdot 001$) indicates a significant difference in mean lung volumes between FB and DIBH techniques irrespective of the target volume (i.e., intact breast or chest-wall). The dose to the ipsilateral lung was indexed by V_{5Gy}, V_{10Gy}, V_{15Gy}, V_{20Gy}, V_{25Gy} and V_{30Gy} (i.e., the percentage volume of the ipsilateral lung receiving at least the indicated dose). The mean ipsilateral lung V_{5Gy}, V_{10Gy}, V_{15Gy}, V_{20Gy}, V_{25Gy} and V_{30Gy} for patients treated with intact breast and using the FB technique are $44 \cdot 6 \pm 5 \cdot 8$, $30 \cdot 0 \pm 5 \cdot 3$, $24 \cdot 9 \pm 5 \cdot 2$, $22 \cdot 4 \pm 4 \cdot 7$, $20 \cdot 4 \pm 4 \cdot 5$, $18 \cdot 4 \pm 4 \cdot 3$ and $44 \cdot 6 \pm 5 \cdot 8\%$, $30 \cdot 9 \pm 5 \cdot 8$, $26 \cdot 0 \pm 5 \cdot 6$, $23 \cdot 5 \pm 5 \cdot 4$, $21 \cdot 5 \pm 5 \cdot 2$ and $19 \cdot 4 \pm 5 \cdot 0\%$ for post-mastectomy chest-wall patients, respectively. Similarly, the V_{5Gy}, V_{10Gy}, V_{15Gy}, V_{20Gy}, V_{25Gy} and V_{30Gy} for patients treated using the DIBH technique are $41 \cdot 6 \pm 6 \cdot 8$, $26 \cdot 3 \pm 5 \cdot 9$, $21 \cdot 2 \pm 5 \cdot 3$, $18 \cdot 9 \pm 5 \cdot 0$, $17 \cdot 3 \pm 4 \cdot 9$ and $15 \cdot 6 \pm 4 \cdot 7\%$ for patients treated with intact breast and $41 \cdot 3 \pm 6 \cdot 9$, $27 \cdot 5 \pm 6 \cdot 5$, $22 \cdot 9 \pm 6 \cdot 0$, $20 \cdot 6 \pm 5 \cdot 7$, $18 \cdot 8 \pm 5 \cdot 5$ and $17 \cdot 1 \pm 5 \cdot 2\%$ for post-mastectomy chest-wall patients, respectively. The p-values using a two tail student t-test analyses of the means for the V_{5Gy}, V_{10Gy}, V_{15Gy}, V_{20Gy}, V_{25Gy} and V_{30Gy} for the ipsilateral lung comparing the DIBH and FB techniques are well below $0 \cdot 05$ (i.e., $p < 0 \cdot 05$) indicating that there is significant differences in the lung volumetric doses when comparing the two treatment techniques. The reason for the increased dose with DIBH being that during inspiration the lung takes in more air and hence increases in volume, thereby extending into both the tangential and supraclavicular treatment fields (Figure 4). Banaei et al.[22] compared monoisocentric and dual isocentric techniques for mastectomy patients undergoing chest-wall radiotherapy using the 3 field technique and reported ipsilateral lung $V_{10Gy} = 26 \cdot 6$, $V_{15Gy} = 22 \cdot 9\%$ and mean lung dose of $13 \cdot 0$ Gy. Takano et al.[35] compared the dosimetry of TomoDirect, TomoHelical and 3D-CRT plans in left breast cancer patients who received postoperative radiation therapy to the chest-wall and supraclavicular lymph node areas and reported mean ipsilateral lung V_{5Gy}, V_{10Gy}, V_{15Gy}, V_{20Gy} and mean lung dose of $55 \cdot 37 \pm 5 \cdot 37$, $46 \cdot 56 \pm 5 \cdot 98$, $42 \cdot 62 \pm 6 \cdot 25$, $39 \cdot 95 \pm 6 \cdot 34$ and $19 \cdot 64 \pm 3 \cdot 04\%$ for 3D-CRT plans. Ma et al.[14] also reported V_{5Gy}, V_{10Gy} and V_{20Gy} of $49 \cdot 6 \pm 7 \cdot 8$, $37 \cdot 5 \pm 7 \cdot 1$ and $31 \cdot 4 \pm 6 \cdot 0\%$, whereas Hjelstuen et al.[20] reported V_{20Gy} of $44 \cdot 5 \pm 5 \cdot 0$ and $32 \cdot 7 \pm 4 \cdot 8\%$ and mean doses of $21 \cdot 7 \pm 2 \cdot 5$ Gy and $16 \cdot 4 \pm 2 \cdot 3$ Gy for patients treated using the FB and DIBH techniques, respectively. According to Emami's[36] the tolerance of normal tissue to therapeutic radiation revealed that symptomatic radiation pneumonitis is one of the most common toxicities in radiotherapy of patients with breast cancer. Therefore, it is very important to minimise the dose to the lung during radiation therapy of the breast.

Analysis of heart dose

The DVH plots of the heart for patients treated using either the DIBH or the FB techniques are shown in Figure 5. A summary of the measures of central tendency and dispersion of the heart volumetric doses for all patients stratified into patients who were treated with the FB technique and those treated with the DIBH technique is shown Table 5. The mean heart volumes for patients treated with intact breast and post-mastectomy chest-wall are $653 \cdot 1 \pm 139 \cdot 9$ cc and $625 \cdot 4 \pm 134 \cdot 9$ cc, respectively, using FB ,and the corresponding values for patients treated with DIBH are $570 \cdot 5 \pm 94 \cdot 5$ cc and $558 \cdot 5 \pm 90 \cdot 3$ cc, respectively. A two tail student t-test of the means of the heart volume for intact breast and chest-wall patients with FB (p-value $= 0 \cdot 45$) and with DIBH

Table 4. A summary of the measures of central tendency and dispersion of the ipsilateral lung volume dose parameters for both intact breast and chest-wall patients stratified into patients who were treated with the free-breathing (FB) technique and those treated with the deep inspiration breath hold (DIBH) technique. The p value analysis of the tabulated results for the various doses when comparing the DIBH and the FB techniques is also shown in the table

	FB technique ($n = 224$)				DIBH technique ($n = 130$)				
	Minimum	Maximum	Mean	Standard deviation	Minimum	Maximum	Mean	Standard deviation	p-Values
Ipsilateral lung dose parameters for intact breast patients									
	$n = 112$				$n = 57$				
Lung volume (cc)	663·4	2420·2	1413·4	337·3	1188·1	3269·2	2164·3	457·7	<0·001
V_{5Gy} (%)	33·0	60·6	44·6	5·8	27·3	62·1	41·6	6·8	0·005
V_{10Gy} (%)	19·7	45·4	30·0	5·3	14·5	45·0	26·3	5·9	<0·001
V_{15Gy} (%)	15·3	39·5	24·9	5·2	10·9	37·9	21·2	5·3	<0·001
V_{20Gy} (%)	13·3	36·6	22·4	4·7	9·3	34·5	18·9	5·0	<0·001
V_{25Gy} (%)	11·7	34·4	20·4	4·5	8·2	32·7	17·3	4·9	<0·001
V_{30Gy} (%)	9·7	32·0	18·4	4·3	7·1	30·6	15·6	4·7	<0·001
Mean lung dose (cGy)	777·0	1761·2	1172·5	191·7	623·7	1720·7	1039·9	220·7	<0·001
Max lung dose (cGy)	4637·5	5219·3	4907·0	99·8	4665·0	5208·2	4911·1	124·7	0·830
Ipsilateral lung dose parameters for post-mastectomy chest-wall patients									
	$n = 112$				$n = 73$				
Lung volume (cc)	649·2	2359·6	1423·4	339·0	1384·7	2929·5	2164·0	352·3	<0·001
V_{5Gy} (%)	30·5	59·7	44·6	5·8	29·2	63·1	41·3	6·9	0·001
V_{10Gy} (%)	19·4	47·2	30·9	5·8	16·4	49·2	27·5	6·5	0·001
V_{15Gy} (%)	14·7	42·2	26·0	5·6	12·7	42·9	22·9	6·0	<0·001
V_{20Gy} (%)	12·4	39·4	23·5	5·4	10·8	39·6	20·6	5·7	0·001
V_{25Gy} (%)	10·6	37·1	21·5	5·2	9·4	36·8	18·8	5·5	0·001
V_{30Gy} (%)	9·0	34·4	19·4	5·0	7·8	34·1	17·1	5·2	0·002
Mean lung dose (cGy)	721·6	1841·2	1206·0	223·5	664·7	1886·0	1082·7	237·9	0·001
Max lung dose (cGy)	4672·3	5227·7	4923·4	118·8	4643·5	5328·4	4941·4	124·2	0·329

(p-value = 0·43) technique shows no significant difference in the mean heart volumes when comparing intact breast and chest-wall patients (Table 5). However, there was a significant difference in patients mean heart volumes between FB and DIBH techniques for both intact breast and chest-wall patients (Table 5). A two tail student t-test of the means of the heart volumes with FB and DIBH techniques for intact breast patients (p-value = 0·005) and for chest-wall patients (p-value = 0·0025) shows significant difference in mean heart volumes irrespective of the target volume (i.e., intact breast or chest-wall). The dose to the heart was evaluated by estimating the V_{5Gy}, V_{10Gy}, V_{15Gy}, V_{20Gy}, V_{25Gy} and V_{30Gy} values. The mean heart V_{5Gy}, V_{10Gy}, V_{15Gy}, V_{20Gy}, V_{25Gy} and V_{30Gy} for patients using the FB technique are $5·5 \pm 3·5$, $1·8 \pm 1·7$, $1·2 \pm 1·3$, $0·9 \pm 1·0$, $0·7 \pm 0·8$ and $0·5 \pm 0·7\%$ for patients treated with intact breast and $7·5 \pm 3·7$, $3·1 \pm 2·2$, $2·2 \pm 1·8$, $1·7 \pm 1·6$, $1·3 \pm 1·4$ and $1·0 \pm 1·2\%$ for post-mastectomy chest-wall patients, respectively. Similarly, the V_{5Gy}, V_{10Gy}, V_{15Gy}, V_{20Gy}, V_{25Gy} and V_{30Gy} for patients using the DIBH technique are $3·5 \pm 2·0$, $0·5 \pm 0·7$, $0·2 \pm 0·5$, $0·1 \pm 0·4$, $0·1 \pm 0·3$ and $0·1 \pm 0·2\%$ for patients treated with intact breast and $4·8 \pm 3·2$, $1·1 \pm 1·4$, $0·6 \pm 0·9$, $0·4 \pm 0·7$, $0·2 \pm 0·6$ and $0·2 \pm 0·4\%$ for post-mastectomy chest-wall patients, respectively. The p-values obtained using a two tail student t-test analyses of the means for the V_{5Gy}, V_{10Gy}, V_{15Gy}, V_{20Gy}, V_{25Gy} and V_{30Gy} for the heart comparing the DIBH and FB techniques are well less

than 0·05 (i.e., $p < 0·05$) indicating that there is significant difference in heart volumetric doses comparing the two treatment techniques. The reason being that during DIBH the lung takes in more air and hence increases in volume, thereby pushing the heart away from the treatment beams with the corresponding reduction in heart dose (Figure 4, Table 5). Banaei et al.[22] reported heart V_{5Gy}, V_{20Gy} and mean heart dose of 11·5%, 5·1% and 3·5 Gy, respectively, for mastectomy patients who received chest-wall and lymph nodes radiotherapy with a 3 field technique. Ma et al.[24] on the other hand reported V_{5Gy}, V_{10Gy}, V_{20Gy} and V_{30Gy} of $22·1 \pm 8·6$, $15·0 \pm 6·7$, $12·5 \pm 6·4$ and $10·7 \pm 5·9\%$, respectively. Hjelstuen et al.[20] also reported V_{25Gy} of $6·7 \pm 6·8$ and $1·2 \pm 2·8\%$, mean doses of $6·2 \pm 3·6$ Gy and $3·1 \pm 1·9$ Gy, maximum doses of $47·4 \pm 4·1$ Gy and $33·5 \pm 13·9$ Gy for treatment plans using the FB approach and the DIBH technique, respectively. Takano et al.[35] also evaluated dosimetry of 3D-CRT plans in left breast cancer patients who received postoperative radiation therapy to the chest-wall and supraclavicular lymph node areas and reported mean heart V_{15Gy}, V_{25Gy}, V_{30Gy}, V_{35Gy} and mean heart dose of $21·32 \pm 7·6\%$, $18·68 \pm 7·13\%$, $17·47 \pm 6·86\%$ and $16·19 \pm 6·59$ Gy. Deseyne et al.[23] also investigated breast treatment plans for prone and supine positions for whole breast plus lymph node irradiation and reported mean heart V_{5Gy}, V_{10Gy}, V_{20Gy}, V_{30Gy} and mean heart dose of $7·10 \pm 1·93\%$, $3·47 \pm 0·92\%$, $1·04 \pm 0·39\%$, $0·10 \pm 0·18\%$
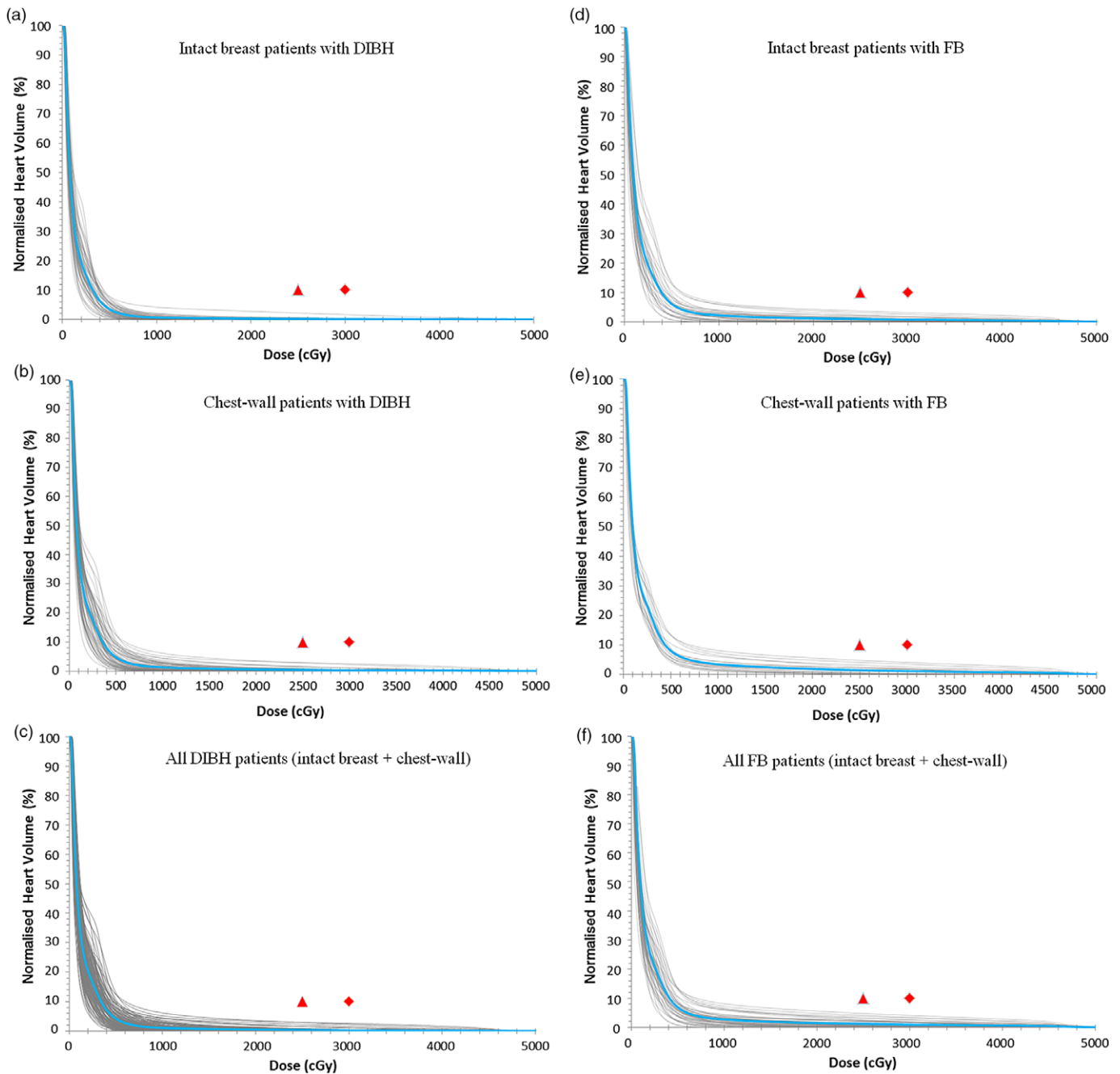
Figure 5. A plot of the dose-volume histogram (DVH) of the heart for patients treated using either the DIBH technique (a, b and c) or the FB technique (d, e and f). (c) All patients treated with the DIBH and (f) all patients treated with the FB techniques. The grey lines represent individual patients DVH and the blue lines in each plot are the mean DVHs. The red data points are the planning dose objectives of $V_{25Gy} \leq 10$ (ideal: triangles) or $V_{30Gy} \leq 10\%$ (acceptable: diamonds).
Abbreviations: DIBH, deep inspiration breathe hold; FB, free breathing.

and $2·38 \pm 0·28$ Gy for prone treatment and $6·83 \pm 3·56\%$, $3·51 \pm 2·35\%$, $1·23 \pm 1·20\%$, $0·06 \pm 0·05\%$ and $2·52 \pm 0·59$ Gy for supine treatment. According to Emami's,[36] radiotherapy of the breast could result in cardiac symptoms such as clinical pericarditis and death from a myocard infarctus due to previous radiotherapy. Therefore, it is of crucial importance to ensure there is very minimal radiation dose to the heart when treating patients with breast cancer.

Evaluation of plan quality

The quality of each plan was quantitatively assessed by calculating the HI, UI and the CI for the PTV_eval for all patients. Table 6

shows a summary of the measures of central tendency and dispersion of the HI, UI and CI calculated for the PTV_eval and stratified into patients treated for intact breast and chest-wall and further grouped by breast separation. The mean HI, CI and UI for all PTV_eval of all patients are $0·09 \pm 0·04$, $1·07 \pm 0·03$, $0·98 \pm 0·02$, respectively (Tables 6). There were similar values of the mean HI, CI and UI values when stratified into patients treated with intact breast and post-mastectomy chest-wall patients and also into the three groups (small, medium and large) by breast separation (Table 6). When values of CI and UI are close to unity, it indicates greater conformity and uniformity and values of HI

Table 5. A summary of the measures of central tendency and dispersion of the heart volume dose parameters for both intact breast and chest-wall patients stratified into patients who were treated with the free-breathing (FB) technique and those treated with the deep inspiration breath hold (DIBH) technique. The p value analysis of the tabulated results for the various doses when comparing the DIBH and the FB techniques is also shown in the table

	FB technique ($n = 58$)				DIBH technique ($n = 130$)				
	Minimum	Maximum	Mean	Standard deviation	Minimum	Maximum	Mean	Standard deviation	p-Values
Heart dose parameters for intact breast patients									
	$n = 31$				$n = 57$				
Heart volume (cc)	405·9	940·5	653·1	139·9	327·7	953·7	570·6	94·5	0·005
V_{5Gy} (%)	-	14·2	5·5	3·5	0·1	7·8	3·5	2·0	0·005
V_{10Gy} (%)	-	6·1	1·8	1·7	-	4·2	0·5	0·7	<0·001
V_{15Gy} (%)	-	4·7	1·2	1·3	-	3·4	0·2	0·5	<0·001
V_{20Gy} (%)	-	3·8	0·9	1·0	-	2·8	0·1	0·4	<0·001
V_{25Gy} (%)	-	3·2	0·7	0·8	-	2·2	0·1	0·3	0·001
V_{30Gy} (%)	-	2·6	0·5	0·7	-	1·7	0·1	0·2	0·001
Mean heart dose (cGy)	49·31	375·99	181·48	69·70	73·81	268·47	138·99	34·69	0·003
Max heart dose (cGy)	502·4	5048·5	3774·6	1413·2	611·5	5062·3	2354·9	1363·4	<0·001
Heart dose parameters for post-mastectomy chest-wall patients									
	$n = 27$				$n = 73$				
Heart volume (cc)	441·5	1111·8	625·4	134·9	394·8	766·0	558·5	90·3	0·025
V_{5Gy} (%)	0·1	13·8	7·5	3·7	0·3	13·0	4·8	3·2	0·002
V_{10Gy} (%)	-	8·1	3·1	2·2	-	6·1	1·1	1·4	<0·001
V_{15Gy} (%)	-	6·6	2·2	1·8	-	4·5	0·6	0·9	<0·001
V_{20Gy} (%)	-	5·6	1·7	1·6	-	3·5	0·4	0·7	<0·001
V_{25Gy} (%)	-	4·8	1·3	1·4	-	2·9	0·2	0·6	0·001
V_{30Gy} (%)	-	4·1	1·0	1·2	-	2·6	0·2	0·4	0·002
Mean heart dose (cGy)	68·79	389·53	223·76	81·24	73·13	321·13	158·01	51·31	0·001
Max heart dose (cGy)	618·9	5055·1	4118·8	1287·0	708·6	4971·9	2751·3	1396·8	<0·001

'-' Indicates the value is less than 0.1%.

close to zero indicate greater homogeneity; therefore, our data show superior dose conformity, uniformity and homogeneous to the PTV_eval for breast 3 and/or 4 field treatment plans irrespective of target (i.e., intact breast or post-mastectomy chest-wall) or the size of the intact breast or chest-wall (Table 6). Current data show that using the hybrid IMRT technique for tangential intact breast radiation therapy plus a supraclavicular field to treat the lymph nodes can result in smaller 'hotspots' while maintaining improved dose coverage and dose uniformity throughout the whole breast or chest-wall. Hotspots and dose inhomogeneity can lead to poor cosmetic outcomes and more skin reactions, especially in women with larger breasts. One of such reaction, moist desquamation, has been correlated with increased pain and reduction in quality of life.[37] Zheng et al.[27] in their study reported CI of 0·59 ± 0·10, HI of 1·08 ± 0·01 using the hybrid planning technique and CI of 0·42 ± 0·06 and HI of 1·12 ± 0·03 when the FIF-IMRT technique is used. Ma et al.[14] on the other hand reported HI of 0·24 ± 0·02 and CI of 0·27 ± 0·07. Hjelstuen et al.[20] also reported HI values of 0·10 ± 0·01 and 0·11 ± 0·01 for treatment based on

patient FB and DIBH, respectively, and corresponding CI values 0·99 ± 0·00 and 0·99 ± 0·00 for FB and DIBH, respectively.

Dosimetric Comparison of 2 field and 3 and/or 4 field Techniques

In a previous study,[18] we retrospectively evaluated the treatment plans of 623 low-risk breast cancer patients and reported the mean DVHs for PTV_eval, ipsilateral lung and heart for all patients. In Figure 6, we have plotted a comparison of the mean DVHs in the current study for treatment of high-risk breast cancer patients with nodes positive or risk of nodal involvement using 3 and/or 4 field technique with the mean DVHs derived from the previous study[18] for low-risk patients with node negative using a 2-field tangential treatment technique. In Table 7, we have presented a comparison of the mean volume dose parameters for ipsilateral lung and heart for the 2-field tangential technique[18] and 3 and/or 4 field technique (current study) stratified into patients who were treated with FB technique and those treated with DIBH technique. We observed

Table 6. Summary of the measures of central tendency and dispersion of the homogeneity index (HI), uniformity index (UI) and conformity index (CI) for the PTV_eval for all patients and stratified by breast separation of small (< 20 cm), medium (20 ≤ x ≥ 25) and large (> 25 cm) and by intact breast or chest-wall treatment

	Mean	Standard deviation	Minimum	Maximum
Patients treated with intact breast				
Small < 20 cm				
HI	0·08	0·02	0·01	0·13
CI	1·06	0·02	1·01	1·11
UI	0·99	0·01	0·95	1·00
Medium 20–25 cm				
HI	0·08	0·04	0·01	0·01
CI	1·06	0·03	1·00	1·00
UI	0·98	0·01	0·95	0·95
Large > 25 cm				
HI	0·10	0·04	0·01	0·01
CI	1·08	0·03	1·00	1·00
UI	0·96	0·01	0·94	0·94
All intact breast patients				
HI	0·08	0·03	0·01	0·15
CI	1·06	0·03	1·00	1·12
UI	0·98	0·01	0·94	1·00
Patients treated post-mastectomy chest-wall				
Small < 20 cm				
HI	0·09	0·02	0·06	0·15
CI	1·08	0·01	1·05	1·12
UI	0·98	0·02	0·94	1·00
Medium 20–25 cm				
HI	0·10	0·05	0·01	0·58
CI	1·08	0·03	1·01	1·31
UI	0·97	0·02	0·90	1·00
Large > 25 cm				
HI	0·11	0·02	0·07	0·13
CI	1·09	0·01	1·06	1·11
UI	0·96	0·01	0·95	0·99
All chest-wall patients				
HI	0·10	0·04	0·01	0·58
CI	1·08	0·02	1·01	1·31
UI	0·97	0·02	0·90	1·00
All patients combined				
Small < 20 cm				
HI	0·09	0·02	0·06	0·15
CI	1·07	0·02	1·05	1·12
UI	0·98	0·01	0·94	1·00
Medium 20–25 cm				
HI	0·09	0·05	0·01	0·58

(Continued)

Table 6. (*Continued*)

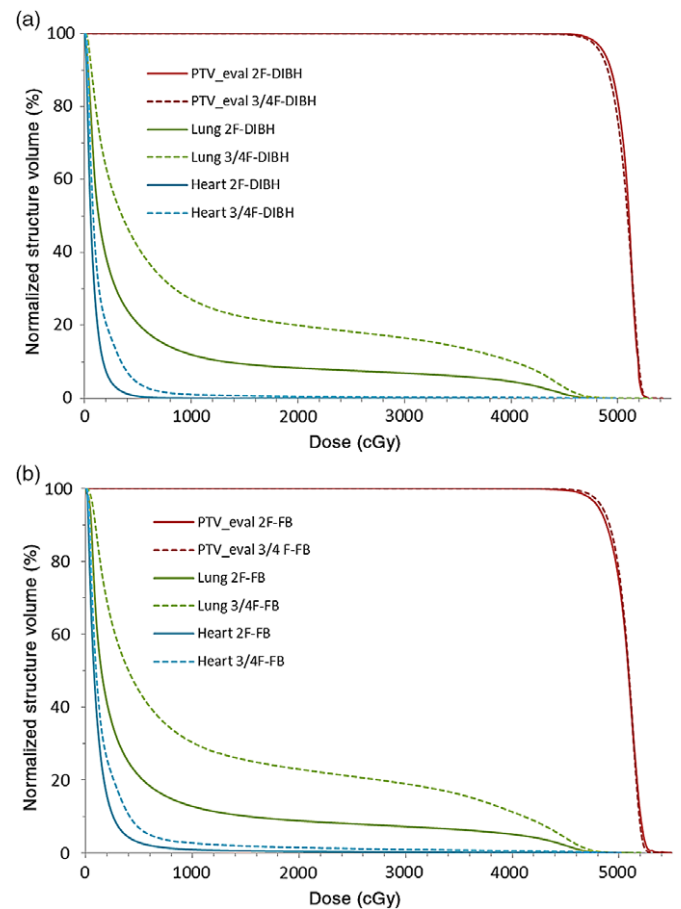|	Mean	Standard deviation	Minimum	Maximum
CI	1·07	0·03	1·00	1·31
UI	0·97	0·01	0·90	1·00
Large > 25 cm				
HI	0·11	0·03	0·01	0·14
CI	1·09	0·03	1·00	1·12
UI	0·96	0·01	0·94	1·00
All patients				
HI	0·09	0·04	0·01	0·58
CI	1·07	0·03	1·00	1·31
UI	0·98	0·02	0·90	1·00

Figure 6. Comparison of dose-volume histograms (DVHs) for 3 or 4 fields (2 tangential fields plus supraclavicular fields) radiotherapy (this work) with 2-field tangential radiotherapy of the breast[18] for patients treated at 50 Gy in 25 fractions using the deep inspiration breathe hold technique (a) and free breathing technique (b).

similar target coverage based on the mean DVH plots for the PTV_eval for both treatment techniques; however, there is significant difference in the mean DVHs for the ipsilateral lung and the heart DVHs also vary slightly in the low dose region (2–6 Gy) for both FB and DIBH techniques (Figure 6). The volume dose parameters (V_{5Gy}, V_{10Gy}, V_{15Gy}, V_{20Gy} and V_{30Gy}) for both ipsilateral lung

Table 7. A comparison of the mean volume dose parameters for ipsilateral lung and heart for 2-field tangential technique[18] and 3 and/or 4 field technique: 2 tangential fields plus supraclavicular field(s) (current study) stratified into patients who were treated with free-breathing (FB) technique and those treated with deep inspiration breath hold (DIBH) technique

| | FB technique | | DIBH technique | |
| | Mean ± SD | | Mean ± SD | |
	3–4 field technique (current study)	2 field technique[18]	3–4 field technique (current study)	2 field technique[18]
Ipsilateral lung				
V_{5Gy} (%)	44·6 ± 5·8	21·57 ± 5·15	41·6 ± 6·8	20·72 ± 3·71
V_{10Gy} (%)	30·0 ± 5·3	13·09 ± 3·95	26·3 ± 5·9	12·13 ± 2·31
V_{15Gy} (%)	24·9 ± 5·2	10·31 ± 3·48	21·2 ± 5·3	9·48 ± 1·93
V_{20Gy} (%)	22·4 ± 4·7	8·89 ± 3·22	18·9 ± 5·0	8·40 ± 1·75
V_{30Gy} (%)	18·4 ± 4·3	7·3 ± 2·96	15·6 ± 4·7	6·99 ± 1·62
Maximum lung dose (cGy)	4907·0 ± 99·8	4868·5 ± 106·0	4911·1 ± 124·7	4818·0 ± 147·0
Heart				
V_{5Gy} (%)	5·5 ± 3·5	2·53 ± 1·48	3·5 ± 2·0	0·54 ± 0·39
V_{10Gy} (%)	1·8 ± 1·7	0·7 ± 0·5	0·5 ± 0·7	0·03 ± 0·07
V_{15Gy} (%)	1·2 ± 1·3	0·37 ± 0·31	0·2 ± 0·5	0·01 ± 0·04
V_{20Gy} (%)	0·9 ± 1·0	0·23 ± 0·22	0·1 ± 0·4	0·01 ± 0·02
V_{30Gy} (%)	0·5 ± 0·7	0·09 ± 0·12	0·1 ± 0·2	0 ± 0·01
Maximum heart dose (cGy)	3774·6 ± 1413·2	3779·0 ± 1142·5	2354·9 ± 1363·4	1307·5 ± 1231·5

and heart are significantly different between the 2-field and 3 and/or 4 field treatment techniques (Table 7). For a 2-field treatment of low-risk patients, the prescription dose is 50 Gy in 25 fractions to treat the intact breast or chest-wall, whereas for high-risk patients the prescription dose is 50 Gy in 25 fractions to treat the intact breast or chest-wall and a 50 Gy in 25 fractions to treat the supra-clavicular region. The increased lung and heart doses observed with the 3 and/or 4 field technique (approximately a factor of 2) could potential be due to scatter radiation dose contributions from the 3rd and/or 4th fields treating the supraclavicular region. Therefore, whereas a plan acceptability criteria used for the PTV_eval (i.e., intact breast or chest-wall) can be used for both the 2-field and 3 and/or 4 field hybrid IMRT treatment techniques as the target coverages are very similar, the OARs should have different plan acceptability criteria for the two techniques due to the differences in the mean volumetric doses. It is possible to develop 3 and/or 4 field hybrid IMRT treatment plan for high-risk patients with nodal involvement or risk of nodal involvement that aim to achieve the mean volumetric doses presented in this study for both the ipsilateral lung and the heart with no imposition on resources and time constraints. Predefined dose-volume constraints and objectives can be achieved and can result in improved dose coverage of target breast tissue, reduction in breast volume receiving high doses and dose to adjacent normal tissue, and therefore with the potential to reduce the rate of acute skin reaction, decrease pain and improve quality of life. The results of this study would enable the development of local criteria for treatment plans acceptability for this technique based on available resources and technology.

Conclusions

The use of 3 and/or 4 field hybrid IMRT for radiation therapy of high-risk node positive breast cancer patients provides an efficient and reliable method for achieving superior dose uniformity, conformity and homogeneity throughout the whole breast or post-mastectomy chest-wall volume and the nodal regions with minimal doses to the OAR. Based on current data, it is possible to develop breast treatment plans that aim to achieve dose coverage for the PTV_eval volume of 92% ($V_{92\%}$) and 95% ($V_{95\%}$) of the prescribed dose to at least 99 and 97% of the normalised volume, respectively, while at the same time, restricting the normalised volume of the PTV_eval receiving a hotspot of 105% ($V_{105\%}$) of the prescribed dose to less than 5%. Treatment planning for intact breast or post-mastectomy chest-wall with lymph nodes involvement should also aim to achieve ipsilateral lung $V_{5Gy} \leq 50$, $V_{10Gy} \leq 35$, $V_{15Gy} \leq 30$, $V_{20Gy} \leq 25$, $V_{30Gy} \leq 20\%$ for FB technique and $V_{5Gy} \leq 45$, $V_{10Gy} \leq 30$, $V_{15Gy} \leq 25$, $V_{20Gy} \leq 20$, $V_{30Gy} \leq 15\%$ for DIBH technique. Similarly, the criteria for the heart should aim to achieve $V_{5Gy} \leq 10$, $V_{10Gy} \leq 4$, $V_{15Gy} \leq 3$, $V_{20Gy} \leq 2$, $V_{30Gy} \leq 1\%$ and mean heart dose of 5 Gy for FB technique and $V_{5Gy} \leq 5$, $V_{10Gy} \leq 2$, $V_{15Gy} \leq 1·5$, $V_{20Gy} \leq 1$, $V_{30Gy} \leq 0·5\%$ and mean heart dose of 3 Gy for DIBH. The clinical implementation of this technique for high-risk breast cancer patients with nodal involvement can be achieved with minimal or no imposition on resources and time constraints.

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