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Original Article

Which simultaneous-integrated boost (SIB) intensity-modulated radiotherapy (IMRT) technique is dosimetrically superior in the treatment of breast cancer; volumetric-modulated arc therapy (VMAT) or fixed field (ff) IMRT?

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Abstract

Background and purpose: To determine which concomitant boost technique is dosimetrically superior in the treatment of breast cancer; volumetric-modulated arc therapy (VMAT) or fixed field intensity-modulated radiotherapy (ff-IMRT).

Materials and methods: In total, 30 breast patients were re-planned with both VMAT and fixed field concomitant boost intensity-modulated radiotherapy techniques. A hybrid technique was used delivering 80% of the dose through tangential beams and 20% through an integrated boost. A two-tailed *t*-test sample for means was used to compare the dosimetric differences between the techniques.

Results: Maximum dose was statistically lower for VMAT; 103·2 versus 103·7% for ff-IMRT along with statistically lower V2 Gy doses to the contralateral lung (0·7 versus 1·6%) and heart for both left- (19·0%/22·6%), and right- (5·5%/8·8%) sided patients, respectively. ff-IMRT boasted significantly lower ipsilateral lung V20, V18 and V10 Gy (7·9/8·6/13·1 versus 8·1/8·8/13·4%) than VMAT, respectively. No differences were found with minimum coverage, mean dose and V5 Gy to all organs at risk (OARs).

Conclusion: VMAT and ff-IMRT techniques demonstrate excellent target coverage and OAR sparing facilitated by the hybrid planning technique and deep inspiration breath hold. There is no obvious dosimetrically superior option between the two techniques. Reduced treatment times with VMAT make it more desirable to implement clinically.

Keywords: breast cancer; dosimetry; IMRT; simultaneous-integrated boost; VMAT

INTRODUCTION

The benefits of post-operative breast radiotherapy are well documented.[1,2] Further boosting of the tumour bed has shown to improve local control yet has also been associated with poor cosmetic outcome.[2] Furthermore, the degree of cardiac exposure from breast irradiation is linked to major coronary events.[3]

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A tumour bed boost is typically delivered using an appositional electron beam following whole breast irradiation (WBI) sparing the underlying heart and lungs due to the steep dose fall off.[4] The drawbacks associated with electron breast boosts are numerous; localisation based on a surgical scar misses 50% of the target in average cases.[4,5] Electrons are not always penetrative enough and may be unsuitable in eight out of nine breast boost cases.[6] Electrons are not as standard modelled in treatment planning systems (TPS).[4,7,8] Difficulties verifying the set up require large planning margins.[9]

Despite advances in imaging techniques for staging and improving treatments, the breast technique has not developed at speed as in the case of other tumour sites.[7] Yet, breast cancer is the most common cancer in women[10] and over 78% of patients survive over 10 years.[11]

Several studies looking at the use of intensity-modulated radiotherapy (IMRT) for breast tumour bed boosts,[12,13] highlight the ability to deliver multiple-dose prescriptions to the breast and tumour bed namely the simultaneous-integrated boost (SIB). The benefits of this technique are three-fold; first, the doses can be modelled correctly by the TPS. Second, concomitant dose delivery with hypofractionated doses reduces course lengths by around 1 week[14] in turn reducing the inconvenience to the patient and costs to the department. Third, the conformity and uniformity of dose across the targets are improved which is associated with an improved cosmesis; a number of SIB studies[12,14,15] report good or excellent breast cosmesis from 6 months to 3 years in nearly 100% of patients.

Locally, a sequential computed tomography (CT) planned electron boost technique is the treatment of choice although often for deep-seated targets, an alternate method is sought. This prompted the evaluation of two IMRT systems already in departmental use; volumetric-modulated arc therapy (VMAT) and fixed field intensity-modulated radiotherapy (ff-IMRT).

The dosimetric comparison of VMAT with ff-IMRT in breast cancer has been reviewed in previous SIB planning studies; the first[16] revealed both techniques to be equivalent; faster treatment times associated with VMAT were considered preferential. In the second study[13] ff-IMRT was determined to be the superior option based on reduced organ at risk (OAR) toxicities. The third[17] found ff-IMRT to be preferential for the majority of cases. All papers included ten patients and the first[16] women with A and B cup size breasts. As there appears to be little consensus or a standard technique for breast SIB radiotherapy, for this study a larger planning study was proposed and undertaken. In all, 30 previously treated patients were re-planned with both VMAT and ff-IMRT, where target coverage and OAR doses to the heart, lungs and contralateral breast were statistically analysed.

METHOD AND MATERIALS

A retrospective study was undertaken. Patients were selected via a random number generator from a pool of 342 breast patients previously treated in 2014. Previous treatment consisted of tangential field radiotherapy followed by an electron boost or reduced tangent boost to the tumour bed. Each patient was re-planned incorporating a SIB with both VMAT and ff-IMRT techniques using deep inspiration breath hold (DIBH) or free breathing. The sample included 30 patients due to this being larger than in similar studies[6,13,16] and representative of planning projects of this nature.

Ethical considerations and data protection

The study was approved by both governance teams at GenesisCare (Spire Hospital, Southampton) and Sheffield Hallam University, as the study was retrospective there were no risks to the patient. Confidentiality and privacy was maintained throughout. All patients provided written consent for their medical information in the clinic's database to be used and stored for the purpose of this study.

Delineation of the target volume and OARs

The breast target volume was generated from the tangential field placement as per similar studies,[6] planning target volume 4,000 cGy (PTV 4000).

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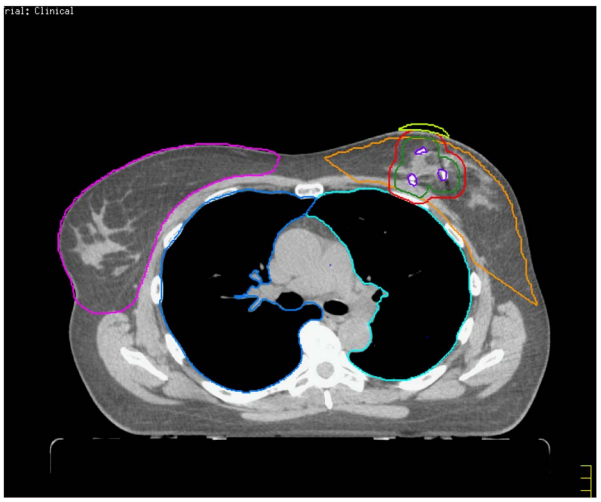

Figure 1. Target volume delineation example.
Notes: Orange = PTV 4000 cGy; purple = surgical clips; green = CTV 4800 cGy; red = PTV 4800 cGy; pink = contralateral breast; yellow = virtual bolus.
Abbreviations: PTV, planning target volume; CTV, clinical target volume.

The delineation of the tumour bed involved outlining the surgical clips and any changes noted in the surrounding tissue. Clinical target volume 4,800 cGy (CTV 4800) was created by expanding the tumour bed by1 cm and avoiding the exterior of PTV 4000. PTV 4800 was created by expanding CTV 4800 by 0·5 cm uniformly.

Treatment planning

Dose prescriptions were selected based on similar studies,[6,15,18] 48 Gy in 15 fractions to the tumour bed and 40 Gy in 15 fractions to the whole breast based upon local practice and the standardisation of breast radiotherapy trial B outcomes.[19]

For both trials (VMAT and ff-IMRT), the original tangential forward planned IMRT plan was copied reducing the original total prescription of 40–38 Gy to serve as the base plan. In the ff-IMRT trial, the boost portion consisted of five beams; the two tangent beams were copied along with adding a further three equally spaced beams. The VMAT boost portion consisted of one partial arc starting and finishing between the tangent angles.

Approximately 20% of the total dose was delivered through the boost portion of the plan, and ~80% was prescribed to the breast through the base plan. Dose constraints for planning were taken from the IMPORT HIGH trial;[20] treatment planning was performed using Pinnacle Version 9.8, Phillips, USA, TPS.

Inclusion/exclusion criteria

Early stage I–II breast cancer patients were randomly selected, that is, patients that did not receive nodal irradiation. Only patients with surgical clips in situ were included to define the tumour bed accurately. All left breast patients were offered DIBH, and ~90% of patients currently receive this technique after assessing eligibility and capability. Free-breathing left breast patients were still included in the study to reflect the general population.

Data collection

Target coverage was reported as per International Commission on Radiation Units and Measurements 83 recommendations;[21] the volume of the PTV receiving 98% of the target dose (D98%) and the volume of the PTV receiving 2% of the target dose (D2%) for both PTVs. With reference to the QUANTEC review[22] and other breast SIB studies[6–8,12–17] a variety of (V) values (V5 = volume of organ receiving 5 Gy) were recorded including the mean dose to each organ and a range of V measurements.

Statistical analysis

A two-tailed *t*-test sample for means was used to compare the dosimetric differences between the techniques using excel software. Statistical significance was defined as $p < 0{\cdot}05$.

All 30 plans were completed successfully and results were summarised in Table 1 (15 right breast and 15 left breast patients, 12 under DIBH).

Target coverage

Maximum doses were found to be statistically lower in the VMAT trials for both PTVs. Mean D2% and D2 cc parameters for both PTV 4800 were 103·3%/103·3% with VMAT and 103·7%/103·7% with ff-IMRT, respectively.

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Table 1. *Results table*

Target/organ at risk	Dosimetric parameter	VMAT (mean ± SD)	ff-IMRT (mean ± SD)	*p* value
PTV 4800 cGy	D2% (%)	103·25 ± 1·02	103·65 ± 1·19	0·027
	D2 cc (%)	103·30 ± 1·09	103·67 ± 1·14	0·036
PTV 4800 evaluation	D98% (%)	94·12 ± 0·50	94·08 ± 0·81	0·728
	V95% (%)	96·38 ± 0·70	96·54 ± 0·93	0·356
PTV 4000 evaluation	D2% (%)	107·43 ± 1·00	108·29 ± 1·39	<0·001
	V105% (%)	6·95 ± 2·95	7·95 ± 3·54	0·048
PTV 4000 cGy	D98% (%)	94·64 ± 0·98	94·60 ± 1·04	0·849
	V95 (%)	97·60 ± 1·01	97·32 ± 1·28	0·289
Ipsilateral lung	V20 (Gy)	8·08 ± 2·37	7·92 ± 2·31	<0·001
	V18 (Gy)	8·75 ± 2·47	8·58 ± 2·42	<0·001
	V10 (Gy)	13·40 ± 3·01	13·07 ± 2·96	0·004
	V5 (Gy)	24·21 ± 4·36	24·37 ± 4·98	0·635
	Mean (Gy)	5·45 ± 0·88	5·40 ± 0·82	0·297
Contralateral lung	V2 (Gy)	0·73 ± 1·59	1·64 ± 1·89	0·040
	Mean (Gy)	0·47 ± 0·14	0·48 ± 0·14	0·677
Heart (left breast)	V10 (Gy)	0·15 ± 0·26	0·12 ± 0·23	0·086
	V5 (Gy)	1·33 ± 1·69	1·18 ± 1·46	0·446
	V2 (Gy)	18·95 ± 11·51	22·58 ± 13·31	0·004
	Mean (Gy)	1·42 ± 0·39	1·45 ± 0·45	0·483
Heart (right breast)	V5 (Gy)	0·003 ± 0·01	0·04 ± 0·09	0·105
	V2 (Gy)	5·45 ± 6·26	8·84 ± 9·54	0·023
	Mean (Gy)	0·93 ± 0·24	0·98 ± 0·33	0·172
Contralateral breast	Mean (Gy)	0·55 ± 0·28	0·57 ± 0·28	0·313

Abbreviations: VMAT, volumetric-modulated arc therapy; ff-IMRT, fixed field intensity-modulated radiotherapy; PTV, planning target volume.

V105% values were 7·0 versus 8·0% in favour of VMAT and the D2% was 107·4% with VMAT and 108·3% with ff-IMRT. Minimum doses to the targets were so similar that significance was not reached.

Ipsilateral lung dose

V5 Gy and the mean dose to the ipsilateral lung were comparable in both trials and significance was not reached; the mean ipsilateral lung dose was 5·5 Gy (±0·9 Gy) with VMAT and 5·4 Gy (±0·8 Gy) with ff-IMRT, and V5 Gy doses were 24·2% (±4·4%) with VMAT and 24·4% (±5·0%) with ff-IMRT. V20, V18 and V10 Gy doses were found to be statistically lower with ff-IMRT; mean values 7·9%/8·6%/13·1% versus 8·1%/8·8%/13·4% with VMAT, respectively.

Contralateral breast

No significant differences were found with contralateral breast mean dose; both arms demonstrated low doses of 0·55 Gy (±0·28 Gy) with VMAT and 0·57 Gy (±0·28 Gy) with ff-IMRT.

Contralateral lung

VMAT resulted in a statistically significant lower V2 Gy to the contralateral lung of 0·7 Gy (±1·6 Gy) versus 1·6 Gy (±1·9 Gy) with ff-IMRT, however, mean contralateral lung dose was almost identical at 0·47 Gy with VMAT and 0·48 Gy with ff-IMRT, and the same standard deviation for both (±0·14).

Heart

For both left and right breast patients the mean heart dose, V5 and V10 Gy (left side only) significance was not reached between the two techniques yet VMAT revealed lower V2 Gy doses of 19·0% (±11·5%) for left and 5·5% (±6·3%) for right breast patients, whereas ff-IMRT demonstrated V2 Gy doses of 22·6% (±13·3%) for left breast patients and 8·8% (±9·5%) for right breast patients, respectively.

DISCUSSION

The use of a SIB technique is a well-established technique for a variety of tumour sites and this study has demonstrated some very promising

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dosimetric results when used for breast cancer. The results did not highlight an obvious superior technique, but they did demonstrate the high-quality plans that can be achieved with a SIB using either VMAT or ff-IMRT. The reduced treatment times associated with VMAT make it a desirable treatment of choice and the increase in calculation time may be offset by finding a planning solution in fewer optimisations.

Target coverage

First, it was not surprising that minimum doses to PTV 4800 were similar in both techniques because the PTV coverage was pushed to tolerance to achieve the lowest possible OAR doses. Minimum dose to PTV 4000 was in all cases higher than the target constraints due to prescribing 95% of the whole breast dose in the base plan. Maximum dose was statistically lower with VMAT for both target volumes, and always well below specified constraints with the majority of D2% and D2 cc values with PTV 4800 were <105%. In addition, D2% and D2 cc values were always within 0·5% of each other highlighting that either value is a good representation of maximum dose. In addition to maximum dose, measuring the homogeneity index (HI) and conformity index (CI) have been used to assess plan quality and are linked to skin toxicity.[2,23] Although not measured in our study, similar publications report the improved CI and HI of IMRT techniques; Wu et al.[13] found an improved CI with VMAT (0·91) compared with ff-IMRT (0·84) and reported an improved HI for the breast PTV of 1·16 (ff-IMRT) versus 1·13 with VMAT, although their study used a 100% inverse planned IMRT.

OAR DOSES

Heart

Keeping the heart dose as low as possible is important due to late radiation-induced side effects which may not be noticed until over 20 years after radiotherapy; Darby et al.[3] determined a 7·4% increased risk of a major coronary event per mean gray to the heart with no upper threshold. The incorporation of DIBH combined with the low-weighted inverse planned boost demonstrated very low heart doses such that V13 and V10 Gy were zero and near zero, respectively. The IMPORT HIGH planning study[6] similarly documented V13 Gy heart values of <1% except for tomotherapy-based plans which exhibited mean heart V13 Gy of 5%.

The mean heart dose reported in our study was incredibly low; 1·4/1·5 Gy for left breast patients and 0·9/1 Gy for right breast patients for VMAT and ff-IMRT, respectively. The similar study by Wu et al.[13] revealed mean heart doses of 5 Gy with ff-IMRT and 7·6 Gy with VMAT comparable with Scorsetti et al.[15] reporting 5·4 Gy with VMAT. Again, it should be noted that both studies used 100% inverse planned IMRT so it is difficult to establish if the higher OAR doses are due to inverse planning or the lack of DIBH. Interestingly, in a free-breathing 30 patient study,[8] a 100% inverse planned, a 25% inverse planned and a conformal forward planned SIB technique were compared. The authors documented the limited benefit of inverse planned IMRT compared with their conformal forward plan approach, highlighting cases where there is a significant amount of heart (>1·4 cm) in the field or patients with large boost volume (>12 5 cc) to benefit the most from inverse planning. Regarding mean heart dose, the conformal arm exhibited 4·1 versus 3·4 Gy and 3 Gy in the 25% IMRT and 100% IMRT trials, respectively, indicating that it is not necessarily the inverse planning capability that increases OAR doses but the treatment technique. For instance, in our Centre, treating 1·4 cm of heart would be considered unacceptable and shielded using micro-leaf collimator's or a DIBH technique adopted. Jeulink et al.[17] recently conducted a planning study to identify a preferred IMRT SIB technique for left breast patients. The ten-patient study determined a hybrid ff-IMRT plan similar to ours, preferential due to achieving the lowest OAR doses overall yet it delivered larger high-end doses to the heart, whereas their arc technique spared the high doses to the heart and increased doses at the lower end of the spectrum. Mean heart, V5 and V20 Gy were reported as 3·8 Gy/23%/2·9% (hybrid IMRT), 4·8 Gy/28·1%/1·6% (ff-IMRT), 5 Gy/31·8%/1·4% (VMAT two arcs), 3·9 Gy/25·5%/0·5% VMAT (six arcs).

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A literature search[24] revealed ten studies advocating the benefits of DIBH for left breast patients, demonstrating a statistically significant reduction in cardiac dose compared with free-breathing plans. Mean heart doses ranged from 1·3 to 3·9 Gy in DIBH plans demonstrating mean dose reductions up to 3·4 Gy, whereas stricter heart doses are adhered to in our Centre. More modest heart dose reductions were reported between free-breathing and breath-hold plans in a previous publication;[25] the retrospective analysis on 275 left breast patients reported mean heart doses of 1·02 Gy compared with 1·69 Gy for free-breathing cases. As previously mentioned, our current planning system does not model electrons, however, other breast boost studies report higher heart doses of 1·5[4] and 5 Gy[13] supporting recommendations to implement a VMAT SIB as the new standard breast boost technique. In future SIB studies, it may prove useful to separate DIBH and free-breathing patients into different groups to increase the veracity of the results.

Skin dose

The cosmetic outcome after breast conserving therapy is important; investigators have found multiple factors affecting overall cosmesis such as radiation dose, boost volume, homogeneity, volume of excision, infection, chemotherapy and tumours arising in the lower quadrants of the breast.[2]

There is limited data on toxicities and clinical outcomes from breast SIB studies, in particular, inverse planned IMRT or hybrid studies, however, the literature suggests acute toxicity is acceptable although longer follow-up is still necessary to assess late effects. Scorsetti et al.[15] measured the superficial 3 and 5 mm of skin reporting mean doses of 21 and 23 Gy, respectively, theV40 Gy for the first 5 mm was 6%. This 50-patient VMAT analysis used the same dose regime as in our study and measured toxicity in the first 12 months' post-radiotherapy. One case experienced a grade 3 skin reaction, all other cases were grade 0 or grade 1 (Radiation Therapy Oncology Group scoring criteria) and after 3–6 months, all patients were scored as good or excellent cosmesis.

A concomitant versus sequential study[26] reported a lower incidence of ≥ grade 2 skin toxicity of 4% in the accelerated dose regime of 40·5 Gy WBI and 45 Gy to the boost PTV in 15 fractions versus 24% in their conventional regimen of 46·8 Gy in 26 fractions followed by 14 Gy in 7 fractions to the boost PTV. Likewise, Teh et al.[27] reported just one case of ≥ grade 2 skin toxicity using an accelerated regime of 42·4 Gy WBI and 52·4 Gy to the boost PTV in 16 fractions. Similarly, 98% of patients had good or excellent cosmesis in a 55 SIB patient study[12] after 1 year with an accelerated schedule of 45 Gy WBI and 60 Gy to the tumour bed in 25 fractions. One of the largest SIB breast studies[14] reported good or excellent cosmesis in 96·5% of 354 patients after 3 years with doses of 45 Gy WBI and 59·92 Gy to the boost PTV in 28 fractions.

Lung dose

Reduced lung V20–V10 Gy with ff-IMRT appears to be offset by the increased V2 Gy contralateral lung and heart doses. These results contrast with other studies reporting VMAT to increase low-end radiation doses; Wu et al.[13] describe V5, V10, V20 Gy ipsilateral lung doses with VMAT of 40%/25%/12% versus 18%/13%/9% with ff-IMRT, respectively. The large differences are partly due to the modest increase in dose prescription (50·4 Gy to the breast and 64·4 Gy to the boost PTV in 28 fractions), and as previously mentioned the planning technique was fully inversely planned. Furthermore, the VMAT plan consisted of two partial arcs, whereas the ff-IMRT plan consisted of three sets of tangential fields which appears to be the preferential option when using a 100% inverse planned SIB technique. Likewise, Scorsetti et al.[15] reported much higher lung doses in their fully inverse planned VMAT SIB trial; the same doses were used as in our study, yet the ipsilateral lung dose was higher at each dose constraint revealing mean, V5 and V20 Gy doses of 9 Gy/62%/9% versus ours of 5·5 Gy/24%/8%. The study resulted in no short-term lung toxicities reported in the first year, and they are awaiting longer follow-up data although symptomatic radiation pneumonitis (SRP) usually develops 4–12 weeks after radiotherapy.[10] A 93-patient ff-IMRT study similar to ours[28] determined an increased risk of SRP in the elderly and patients with a low body mass index recommending a dose constraint V20 Gy to the ipsilateral lung

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<37% to keep risks of developing SRP <20%. V5–V50 Gy doses were also measured in the study but the V20 Gy appeared to be the most predictive factor. These doses are much higher than those delivered in any of the breast studies reviewed and is probably the reason for the low incidence of SRP noted in breast patients in published SIB toxicity studies. Reporting the lung V20 Gy in breast cases would create standardisation as it is a common parameter quoted in lung cancer radiotherapy, yet as this value is so low in breast radiotherapy, it may not be the most effective parameter to review during planning, whereas V10 and V5 Gy constraints may prove useful for planning purposes.

Regarding the contralateral lung, mean dose was on average 0·5 Gy for both techniques, identical to the hybrid ff-IMRT study,[17] whereas the V2 Gy was statistically lower with VMAT; 0·7 Gy ± 1·6 versus 1·6 Gy ± 1·9 with ff-IMRT.

Contralateral breast dose

Mean doses of 0·6 Gy were recorded for both techniques with most cases <1 Gy; similar to other hybrid studies.[6,8] Fully inverse planned SIB studies report increased mean contralateral breast doses of 1·2 Gy in the VMAT study by Wu et al.[13] and 3 Gy in the VMAT SIB study by Scorsetti et al.[15] A hybrid technique like ours boasts the improved conformity of an IMRT technique combined with the OAR sparing of a tangential approach.

CONCLUSION

The benefits of a SIB technique are indisputable; improved target coverage, conformity, homogeneity accurate dose reporting, improved target localisation not to mention the reduced treatment course length. There are many treatment techniques available with varying merits in particular, the hybrid technique used in this study combines the OAR sparing of tangential field delivery while incorporating inverse planning to provide sufficient modulation to conform to different dose levels. VMAT demonstrated reduced maximum doses to both targets, and exhibited lower V2 Gy doses to the heart and contralateral lung, whereas ff-IMRT reduced ipsilateral lung V20–V10 Gy doses. Mean organ doses were comparable, which highlighted when high-end OAR doses were improved it was at a compromise of the low-end OAR doses. The incorporation of DIBH resulted in very low heart doses for both VMAT and ff-IMRT. As no obvious technique presented as dosimetrically superior, the reduced treatment times associated with VMAT make it a more desirable technique to implement into practice.

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Conflicts of Interest

None.

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