

Original Article

Cite this article: de la Llana V, del Castillo Á, Andrés C, Gómez L, Agulla M, del Valle ML, Iglesias M, and Torres R. (2021) Breast boost vector: a new metric proposed to optimise isocentre location in an fIMRT-VMAT hybrid technique for a simultaneous integrated boost in breast radiotherapy. *Journal of Radiotherapy in Practice* 20: 158–163. doi: [10.1017/S1460396920000242](https://doi.org/10.1017/S1460396920000242)

Received: 22 January 2020

Revised: 19 March 2020

Accepted: 21 March 2020

First published online: 20 April 2020


Key words:

breast radiotherapy; hybrid technique; isocentre position; simultaneously integrated boost; VMAT

Author for correspondence:

Víctor de la Llana, Servicio de Radiofísica y Protección Radiológica, Hospital Clínico Universitario de Valladolid, Valladolid, Spain. Tel: +34687683864. E-mail: Victor_llg@hotmail.com

Breast boost vector: a new metric proposed to optimise isocentre location in an fIMRT-VMAT hybrid technique for a simultaneous integrated boost in breast radiotherapy

Víctor de la Llana¹ , Ángel del Castillo¹, Carlos Andrés¹, Laura Gómez², Manuel Agulla¹, María Luisa del Valle², María Iglesias² and Ricardo Torres¹

¹Servicio de Radiofísica y Protección Radiológica, Hospital Clínico Universitario de Valladolid, Valladolid, Spain and

²Servicio de Oncología Radioterápica, Hospital Clínico Universitario de Valladolid, Valladolid, Spain

Abstract

Purpose: Evaluating the improvements of placing the treatment isocentre at the boost centre of mass (CoM) in a hybrid treatment for breast cancer radiotherapy.

Material and methods: Twenty-two patients were planned in two isocentre locations with two forward intensity-modulated radiation therapy (fIMRT) tangentials to the breast and a volumetric-modulated arc therapy (VMAT) to the boost. A simultaneous integrated boost technique was used. Breast Boost (BB) Vector was investigated as a criterion for selecting an appropriate isocentre placement. Various metrics for boost, breast and hybrid plans were analysed using analysis of variance statistics.

Results: Comparing hybrid plans at the boost CoM vs. hybrid plans at the breast CoM, no significant differences were found. Analysis of relative variations of planning target volume (PTV) boost coverage vs. BB Vector indicated an upgrade in boost CoM isocentre strategy. Dose to organs at risk was comparable: V_{5Gy} (26.24 vs. 25.69%, $p = 0.8$), V_{20Gy} (14.66 vs. 14.58%, $p = 0.959$) and the mean dose (7.37 Gy vs. 7.26 Gy, $p = 0.879$) to ipsilateral lung; V_{5Gy} (15.60 vs. 15.22%, $p = 0.903$), and the mean dose (4.91 Gy vs. 4.86 Gy, $p = 0.950$) to heart and dose to free breast of boost (46.71 Gy vs. 46.62 Gy, $p = 0.408$).

Findings: The hybrid fIMRT-VMAT technique centred at the boost CoM resulted equivalent to plans centred at the breast CoM, while benefiting from an enhancement in PTV boost coverage for patients with BB Vector superior to 5.

Introduction

Breast cancer is the most frequent neoplasm in women. Due to improved screening programmes, early diagnosis approach and higher quality of treatments, the overall survival rate has increased in recent years.¹ It is known that 80% of women with breast cancer may benefit from radiation therapy.² Regarding radiotherapy for breast conserving treatment, studies show an improved breast control rate when additional dose to the tumour bed is given after conventional whole breast radiotherapy.³

For years, breast radiotherapy technique has remained intact: two opposed tangential fields to optimise planning target volume (PTV) coverage while avoiding exposure to ipsilateral lung and other organs at risk (OAR). Nevertheless, planning dynamic techniques such as field in field (FIF)⁴ have evolved into more complex planning and the shortening of overall treatment times with simultaneously delivered boost dose³ introducing a wide range of possibilities for breast treatment.

Currently, a gold standard boost does not seem to be established [different techniques were evaluated such as intensity-modulated radiation therapy (IMRT), electron boost and non-coplanar photon fields⁴]. To overcome potential issues such as adjoining nodes irradiation or additional dose escalation of the tumour bed in a simultaneous integrated boost (SIB) scheme, volumetric-modulated arc therapy (VMAT) is being implemented to whole breast irradiation or for partial arcs in hybrid techniques.⁵⁻⁷

Standard of care for boost breast radiotherapy is to administer radiation sequentially to the whole breast and then to the tumour bed. Nevertheless, SIB techniques are currently under study whether they are more or equally effective compared to conventional schemes. Advantages of this method are, for example, the ability to increase boost dose while keeping the remaining volume of breast with an acceptable dose, studied in a VMAT-SIB hypofractionation treatment by Scorsetti et al.⁸ Moreover, this technique reduces visits to the radiotherapy department, therefore making adjuvant radiotherapy a more comfortable process for these patients.⁹

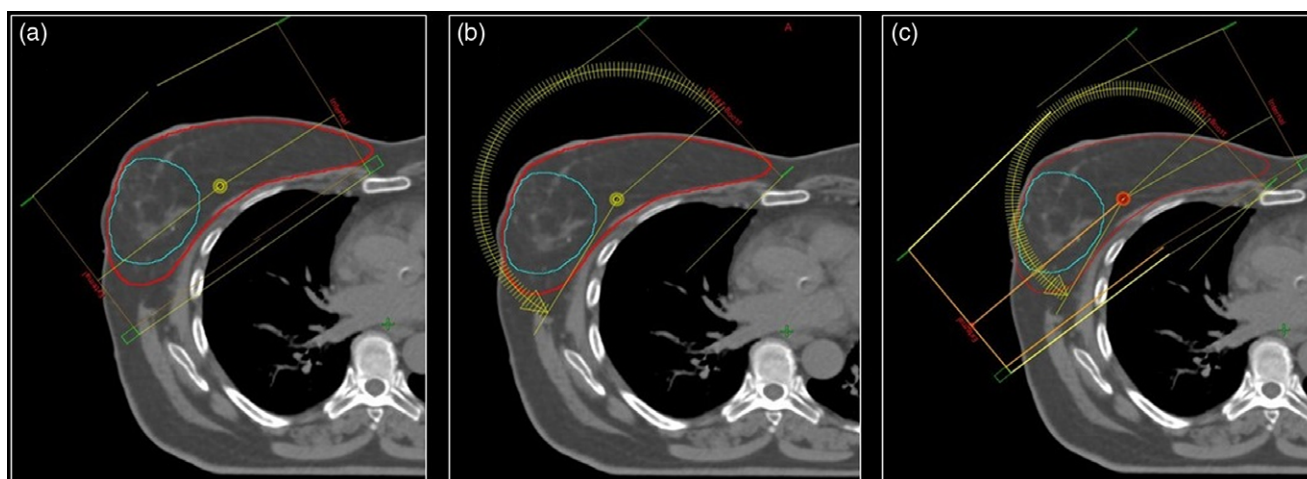


Figure 1. (a) fIMRT tangentials, (b) VMAT boost, (c) hybrid technique (a) + (b). Red contour: PTV_{breast}, blue contour: PTV_{boost}.

A comparison study of this variety of techniques (tangential fields, IMRT and VMAT) included in an SIB configuration for breast radiotherapy is still being carried out.¹⁰⁻¹²

One of the difficulties in SIB treatment is locating the isocentre position for both boost and breast volumes. Boost conformity could be dependent on this election as the majority of hybrid breast radiotherapy approaches were placed on the breast centre of mass (CoM). Field experts have not reached an agreement in the optimum technique for an SIB breast treatment or boost technique. The aim of this study is to propose a metric Breast Boost Vector (BB Vector), which could help in the election of the isocentre placement in a breast hybrid forward IMRT (fIMRT)–VMAT technique.

Material and Methods

Study setup

A random selection of 22 female patients with breast carcinoma from March 2019 to September 2019 (12 left side and 10 right side), already treated in our Radiation Therapy Department, were included retrospectively in this study. Patients with positive axillary lymph nodes and distant metastasis were excluded.

A volumetric scan was performed with a CT scanner Aquilion LB (Canon Medical Systems, Otawara, Japan) in decubitus supine with a slice thickness of 3 mm. A breast board BreastSTEP (Elekta AB, Stockholm, Sweden) was used for patient immobilisation and comfort. Both arms were positioned above the head in a free breathing technique.

Structure contouring was made by a radiation oncologist specialised in breast radiotherapy following the Radiation Therapy Oncology Group breast cancer atlas¹³ as a guideline for delineation of the clinical target volumes (CTVs). CTV breast (CTV_{breast}) includes the apparent CT glandular breast tissue, and PTV breast (PTV_{breast}) was created adding 5 mm isotropically to the CTV_{breast} but limited to 3 mm within the skin surface. The gross tumour volume (GTV) was delineated including the clips placed in the tumour bed during surgery. PTV boost (PTV_{boost}) was generated with the depth, width and height of the tumour bed, including GTV + 1 cm. PTV_{breast} volume for patients in the study has a mean and standard deviation of $1,184 \pm 488 \text{ cm}^3$, whereas for PTV_{boost} volume, $92 \pm 41 \text{ cm}^3$. In addition, OAR were contoured: heart, both lungs and contralateral breast.

For planning evaluation, Eclipse v13.6 software was used (Varian Medical Systems, Palo Alto, CA, USA).

Only one scheme of fractionation was applied to the set of patients. The hypofractionation adopted for SIB treatment in our centre involves a dose of 45.9 Gy to the breast and 51.3 Gy to the tumour bed, simultaneously during 18 sessions (equivalent dose in 2 Gy fractions: EQD₂ = 50.5 Gy to breast, 59.2 Gy to tumour bed, with $\alpha/\beta = 3.5 \text{ Gy}$ ¹⁴). The contribution of VMAT therapy to the tumour bed was 5.40 Gy, which is 0.3 Gy per session.

Treatment planning

PTV_{breast} plan used two 6-MV tangential fields with multi-leaves collimator (MLC) conforming to the PTV, the internal jaws aligned to minimise dose to OAR and exceeding 3 cm beyond contour in external jaws to account for small changes in size and position of the target due to breathing motion. Supplementary FIF was used to achieve desired homogeneity and reduces hot and cold spot areas, resulting in an fIMRT plan (an iterative process through a manual fluence optimisation).

For PTV_{boost}, a VMAT plan was created as the same isocentre as the first plan and comprised a partial arc travelling from internal field to external field angulation with jaws restricted to PTV_{boost} to avoid healthy tissue irradiation. During PTV_{boost} optimisation, the previous PTV_{breast} plan was used as a base dose plan for keeping OAR and PTVs homogeneity into desired values.¹⁵

The hybrid technique convoluted two plan sets resulting in a three dynamic field plan (Figure 1).

Plans were accomplished using Analytical Anisotropic Algorithm with a calculation grid of 2.5 mm, and they were developed for a Varian Clinac 21iX (Varian Medical Systems) equipped with a Millennium 120 MLC and RapidArc technology. The results of both plans were merged into a hybrid plan designed for treatment.

BB vector

In order to analyse the position of the CoM of the tumour bed and to characterise boost position in reference to PTV_{breast}, we define a metric: BB Vector, which measures the distance between the centres of mass of the two PTV volumes involved.

Table 1. Metrics

Boost analysis	Breast analysis	Hybrid analysis
$CI = \frac{V_{5.4Gy}}{V_{PTV_{boost}}}$ ^a	$QI = \frac{D_{98\%}}{45.9 \text{ Gy}}$ ^b	MUs ^c
$HI = \frac{D_{2\%}}{5.40 \text{ Gy}}$ ^a	$HeI = \frac{D_{2\%}}{D_{98\%}}$ ^b	$DI = \frac{V_{51.3Gy}}{V_{45.9Gy}}$ ^c

^a $V_{5.4Gy}$ is the volume with a dose of 5.4 Gy, $V_{PTV_{boost}}$ is the volume of the boost and D2% is the dose that receives the 2% of the boost volume.

^bD2% is the dose that receives the 2% of the breast volume and D98% is the dose that receives the 98% of the breast volume.

^c $V_{51.3Gy}$ is the volume with a dose of 51.3 Gy, $V_{45.9Gy}$ is the volume with a dose of 45.9 Gy, MU_Boost are the unit monitors of the arc and MU_Breast are the unit monitors of the fIMRT tangentials.

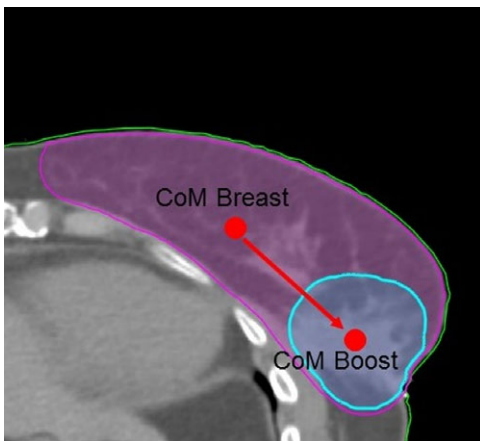


Figure 2. BB Vector: distance from CoM of PTV_{breast} to CoM of PTV_{boost}.

$$BB \text{ Vector} = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2}, \quad (1)$$

where (x_1, y_1, z_1) and (x_2, y_2, z_2) are the coordinates (in centimetres) of the CoM of the PTV_{breast} and PTV_{boost}, respectively. Figure 2 shows a plot of a BB Vector example for a patient of this study.

Variations with isocentre placements and their influence over dose distribution were examined for each patient using hybrid plans with different isocentre locations. One placed at the breast CoM (*Iso_CoM_Breast*) and another at the boost CoM (*Iso_CoM_Boost*) (Figure 3).

Figure 4 shows an example of the hybrid plan isodoses for one of the patients in the study: 55 Gy (107% of the boost prescription dose), 51.3 Gy (100% of the boost prescription dose), 48.7 Gy (95% of the boost prescription dose), 45.9 Gy (100% of the breast prescription dose) and 43.6 Gy (95% of the breast prescription dose).

Data analysis

Table 1 shows the metrics analysed in order to evaluate plan quality. Conformity index (CI) and homogeneity index (HI) were defined for the boost treatment, quality index (QI) and heterogeneity index (HeI) for breast and dose index and total monitor units (MU) for the hybrid plan.

For evaluating the coverage of PTV_{boost} of the two hybrid plans, relative differences between CI versus BB Vector were represented as

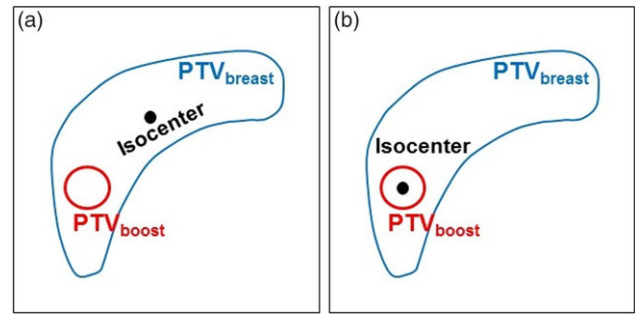


Figure 3. Schematic presentation of isocentre placements: (a) isocentre at the breast CoM and (b) isocentre at the boost CoM.

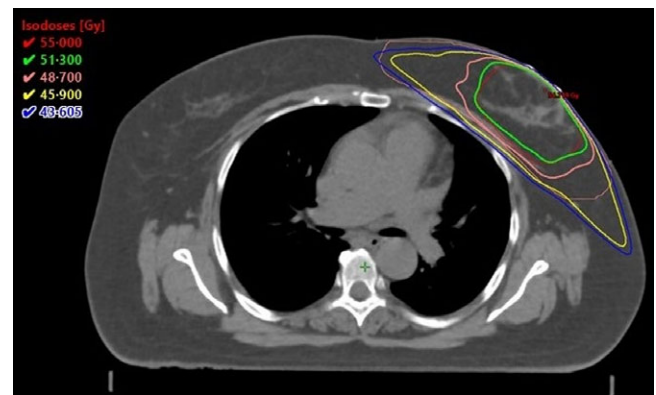


Figure 4. Isodoses of the SIB technique.

$$\Delta CI = \frac{CI_1}{CI_2}, \quad (2)$$

where CI_1 was the boost CI for plans centred at the breast CoM and CI_2 was the boost CI for plans centred at the boost CoM.

Ipsilateral lung and heart were accounted as OAR. An additional auxiliary organ, free breast of boost (FBB), defined as PTV_{breast} – PTV_{boost} was analysed to characterise the influence of the boost arc on the hybrid plan. Dose spillage metric was used for FBB evaluation considering the volume of the isodose of 95% of the dose divided by PTV_{boost} volume:

$$Dose \text{ spillage} = \frac{V_{95\%PTV_{boost}}}{V_{PTV_{boost}}}. \quad (3)$$

Statistical analysis

Descriptive statistics of the results were presented as the mean values ± standard deviations. The difference between the mean values for the two sets of planning was compared by one-factor analysis of variance analysis using Minitab Statistical software v18.1 (Minitab, LLC, www.minitab.com). Statistically significant findings were assumed for a significance level of $p < 0.05$.

Results

The values of the BB Vector for the 22 patients under study are shown in Figure 5. The mean value and standard deviation were 4.5 ± 1.6 cm.

Table 2. Metrics for RapidArc boost

Boost + Breast	Metrics	<i>Iso_CoM_Breast</i>	<i>Iso_CoM_Boost</i>	<i>p</i> Values
VMAT boost	CI	0.85 ± 0.12	0.87 ± 0.12	0.675
	HI	1.07 ± 0.03	1.07 ± 0.03	0.929

Results and standard deviation of CI and HI.

Table 3. Metrics for fIMRT breast

Boost + Breast	Metrics	<i>Iso_CoM_Breast</i>	<i>Iso_CoM_Boost</i>	<i>p</i> Values
fIMRT breast	QI	0.88 ± 0.03	0.88 ± 0.02	0.578
	Hel	1.19 ± 0.04	1.18 ± 0.03	0.552

Results and standard deviation of QI and Hel.

Table 4. Analysis for hybrid plan comparison

Hybrid plan	Metrics	<i>Iso_CoM_Breast</i>	<i>Iso_CoM_Boost</i>	<i>p</i> Values	
SIB ^a	MUs	360 ± 10	360 ± 16	0.895	
	Dose index	9 ± 4%	8 ± 4%	0.319	
	Dose spillage	2.76 ± 0.58	2.48 ± 0.64	0.139	
OAR ^b	Ipsilateral lung	<i>V</i> _{5Gy} (%)	26.24 ± 7.33	25.69 ± 7.00	0.800
		<i>V</i> _{15Gy} (%)	14.66 ± 6.28	14.58 ± 5.28	0.959
	<i>D</i> _{mean} (Gy)	7.37 ± 2.30	7.26 ± 2.20	0.879	
Heart ^c	<i>V</i> _{5Gy} (%)	15.60 ± 5.78	15.22 ± 6.60	0.903	
	<i>D</i> _{mean} (Gy)	4.91 ± 1.80	4.86 ± 2.00	0.950	
FBB	<i>D</i> _{mean} (Gy)	46.71 ± 0.35	46.62 ± 0.42	0.408	

Results with standard deviation were added.

^aMUs, DI and dose spillage are used to SIB isocentre comparison.

^bOAR dose analysis included *V*_{5Gy}, *V*_{15Gy} and *D*_{mean}: mean dose for ipsilateral lung, *V*_{5Gy} and *D*_{mean} for heart and *D*_{mean} for FBB.

^cHeart dose analysed for left-side pathology.

Table 2 presents the evaluation parameters of the RapidArc technique. For VMAT Boost plan, CI and HI were, respectively, 0.85 ± 0.12 and 1.07 ± 0.03 when placing in the *Iso_CoM_Breast*. Whereas at the *Iso_CoM_Boost*, metric results were 0.87 ± 0.12 and 1.07 ± 0.03, respectively.

Figure 6 shows relative variations in CI vs. BB Vector for both hybrid plans (*Iso_CoM_Breast* and *Iso_CoM_Boost*) of the 22 patients under study. ΔCI values close to one mean no differences between a boost planned at the boost CoM or at the breast CoM. Whereas for patients with high BB Vector, Figure 6 suggests a correlation between values, showing an enhancement of CI for VMAT plan centred at the boost CoM.

Table 3 presents metric parameters of the fIMRT tangentials. QI and Hel were 0.88 ± 0.03 and 1.19 ± 0.04 at the *Iso_CoM_Breast*. Whereas at the *Iso_CoM_Boost*, metric results were 0.88 ± 0.02 and 1.18 ± 0.03.

Table 4 shows SIB analysis results and OAR dosimetric parameters. Both hybrid plans used the same MUs: 360 ± 10 (*Iso_CoM_Breast*) and 360 ± 16 (*Iso_CoM_Boost*). Dose index values are also close between them: 9 ± 4% at the *Iso_CoM_Breast* plans and 8 ± 4% at the *Iso_CoM_Boost* plans. The mean dose spillage is about 11% higher at the *Iso_CoM_Breast* plan, 2.76 ± 0.58 vs. 2.48 ± 0.64.

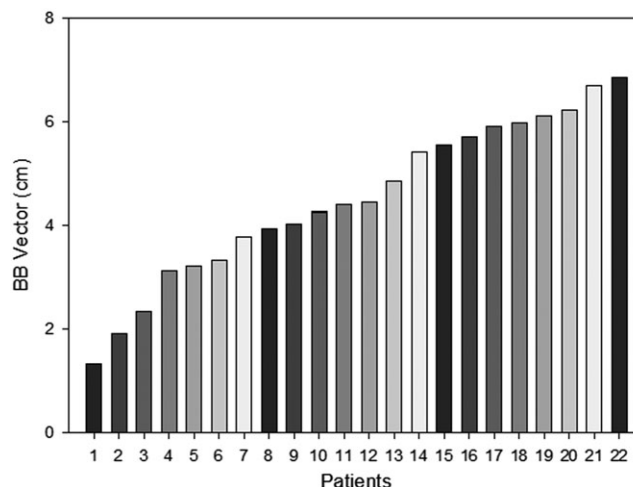


Figure 5. Values of the BB vector for the 22 patients under study.

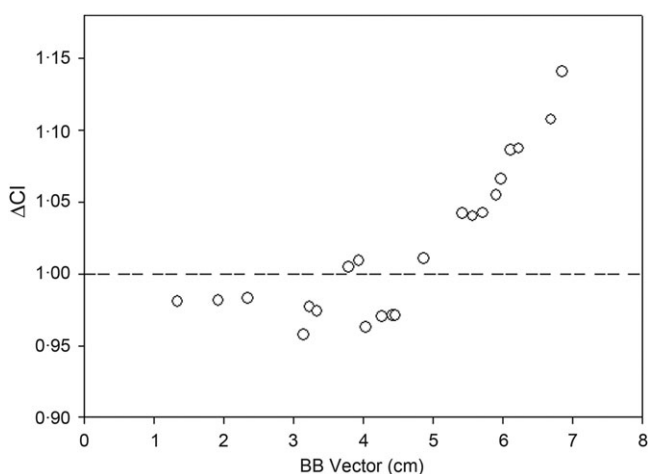


Figure 6. Relative CI variations vs. BB Vector.

All OAR dose constraints of our protocols were respected in the two techniques. Hybrid plans were able to record *V*_{5Gy} < 30%, *V*_{15Gy} < 15% and the mean dose < 8 Gy in ipsilateral lung, *V*_{5Gy} < 16% and the mean dose < 5 Gy in heart and the mean dose of 46 Gy for FBB. No substantial differences were noted between the two arms.

Discussion

Nowadays, linacs are able to deliver high-dose distributions and mixing techniques with the robustness of conventional radiotherapy and advantages of dynamics techniques. Nevertheless, the implementation of hybrid modalities needs to be simultaneously optimised to avoid possible conflicts. These hybrid approaches for SIB treatments are being investigated to reduce heart dose¹⁶ or in comparison with other techniques.^{12,17}

Although volume contouring is carried out by a single radiation oncologist specialised in breast cancer treatment following international guidelines, extending this study to a wide variety of Radiation Oncology Departments could be interesting to address potential sources of bias.¹⁸

In this study, we analysed isocentre positions when using boost arc for hybrid SIB radiotherapy. Viability of different treatment

isocentre placements was also analysed in other studies.¹⁹ Plans treated from the breast CoM may lead to a reduction of boost conformity and overdose PTV_{breast} with PTV_{boost} dose prescription. Therefore, planning was strongly influenced by the location of PTV_{boost} inside PTV_{breast}. Outer boosts could be treated differently, an isocentre placed in the PTV_{boost} CoM. In that sense, our BB Vector metric proposal might be a tool for these peripheral boosts. Figure 6 suggests that there is a point when PTV_{boost} conformity in plans centred at the boost CoM starts to increase in comparison with plans centred at the breast CoM. This point starts to be noticeable for patients with high BB Vector, superior to 5 cm.

This hybrid technique is highly based on tangential robustness and slightly on dose delivered to tumour bed (5.4 Gy). Nevertheless, exposing boost to higher doses (16 Gy²⁰) improves local control despite decreasing the overall treatment time for patient convenience. Hence, in an examination of optimal SIB treatment, VMAT was incorporated into our scheme⁶ to solve boost issues. This technique was implemented in other studies, for example, SIB treating the whole breast with radiotherapy²¹ or a study by Fogliata et al. about dosimetric trade-offs in breast planning with VMAT.²² Potential downsides of low-dose bath were limited with this hybrid approach; VMAT is 10.5% of the overall treatment. In addition, the use of inverse planning helps to supply a higher boost CI.

Arc travelling influences PTV_{boost} conformity and overdose to healthy tissue (FBB). In this study, VMAT partial arc was limited into the medial and lateral beam angles. This may become an issue when an isocentre placed at the breast CoM causes a spillage of VMAT boost dose which in turn inhomogeneities into PTV_{breast}. Moreover, PTV_{boost} location in breast volume influences dose spillage to FBB; consequently, it had made to investigate little modifications in VMAT boost keeping the benefits of this technique. Placing the isocentre close to boost CoM hardly decreases the mean dose to FBB (46.71 ± 0.35 vs. 46.62 ± 0.42). In addition, results of CI and HI showed no significant differences between isocentres (0.85 ± 0.12 vs. 0.87 ± 0.12, $p = 0.675$; 1.07 ± 0.03 vs. 1.07 ± 0.03, $p = 0.929$). Dose to OAR was highly dependent in tangential fields. Boost dose is a small percentage of the total prescript SIB dose and can slightly weight in the treatment. Hybrid plans centred at different CoMs show no significant differences in OAR dose analysis.

Considering the study results, it seems that the use of individual BB Vector could help in choosing the optimal technique. It will allow us to distinguish which plans would benefit from a change of isocentre, and with this planning variation, conformity of these marginal boosts will be enhanced without compromising the strength of the hybrid plan. Nonetheless, small size of this sample leads us to conclude that these results should be interpreted with caution and investigated in depth in further studies.

Conclusions

BB Vector has been defined as a metric that helps to modify the choice of the isocentre in hybrid plans for breast cancer treatments.

Two isocentre positions have been evaluated: *Iso_CoM_Boost* and *Iso_CoM_Breast*, and we have verified that, when the BB Vector is greater than 5 cm, it could improve PTV_{boost} coverage by placing the isocentre in the *Iso_CoM_Boost*, while in the rest of the cases, the difference is not noticeable. Regarding metrics

and OAR dose analysis, there are no statistical differences between the isocentre approaches.

Acknowledgements. The author would like to thank Sean Cerezo McGee for his constructive criticism on the manuscript.

Conflict of Interest. The authors declare that they have no conflict of interest.

References

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet* 2005; 366: 2087–2106.
2. Poortmans P. Optimal approach in early breast cancer: radiation therapy. *EJC Suppl* 2013; 11 (2): 27–36.
3. Franco P, Cante D, Sciacero P et al. Tumor bed boost integration during whole breast radiotherapy: a review of the current evidence. *Breast Care* 2015; 10: 44–49.
4. Fournier-bidoz N, Kirova YM, Campana F, Dendale R, Fourquet A. Simplified field-in-field technique for a large-scale implementation in breast radiation treatment. *Med Dosim* 2012; 37 (2): 131–137.
5. Orton J, Halle J, Chang S, Artor C. EComparison of three concomitant boost techniques for early-stage breast cancer. *Int J Radiat Oncol Biol Phys* 2006; 64 (1): 168–175.
6. Byrne M, Archibald-Heeren B, Hu Y, Fong A, Chong L, Teh A. Comparison of semiautomated tangential VMAT with 3DCRT for breast or chest wall and regional nodes. *J Appl Clin Med Phys* 2018; 19 (5): 684–693.
7. Vaegler S, Scheibner M, Hartwig C et al. Evaluation of a new hybrid VMAT simultaneous integrated boost technique for breast radiotherapy. *Curr Dir Biomed Eng* 2017; 3 (2): 335–337.
8. Virén T, Heikkilä J, Myllyoja K, Koskela K, Lahtinen T, Seppälä J. Tangential volumetric modulated arc therapy technique for left-sided breast cancer radiotherapy. *Radiat Oncol* 2015; 10: 7–9.
9. Scorsetti M, Alongi F, Fogliata A et al. Phase I-II study of hypofractionated simultaneous integrated boost using volumetric modulated arc therapy for adjuvant radiation therapy in breast cancer patients: a report of feasibility and early toxicity results in the first 50 treatments. *Radiat Oncol* 2012; 7 (1): 1–8.
10. Nitsche M, Hermann RM. Emerging role of hypofractionated radiotherapy with simultaneous integrated boost in modern radiotherapy. *BreastCare* 2015; 10: 320–324.
11. Askoxylakis V, Jensen AD, Häfner MF et al. Simultaneous integrated boost for adjuvant treatment of breast cancer- intensity modulated vs. conventional radiotherapy: the IMRT-MC2 trial. *BMC Cancer* 2011; 11: 249–257.
12. Aly MMOM, Glatting G, Jahnke L, Wenz F, Abo-Madyan Y. Comparison of breast simultaneous integrated boost (SIB) radiotherapy techniques. *Radiat Oncol* 2015; 10 (1): 139–147.
13. Smith SK, Estoesta RP, Kader JA et al. Hybrid intensity-modulated radiation therapy (IMRT) simultaneous integrated boost (SIB) technique versus three-dimensional (3D) conformal radiotherapy with SIB for breast radiotherapy: a planning comparison. *J Radiother Pract* 2016; 15 (2): 131–142.
14. White J, Tai A, Arthur D et al. Breast cancer atlas for radiation therapy planning: consensus definitions collaborators. Radiation Therapy Oncology Group (RTOG): 1–71. <https://www.rtog.org/CoreLab/ContouringAtlases/BreastCancerAtlas.aspx>. Accessed on 18th December 2019.
15. Leeuwen CM Van, Oei AL, Crezee J et al. The alfa and beta of tumours: a review of parameters of the linear-quadratic model, derived from clinical radiotherapy studies. *Radiat Oncol* 2018; 13: 96.
16. A Phase III trial of accelerated whole breast irradiation with hypofractionation plus concurrent boost versus standard whole breast irradiation plus sequential boost for early-stage breast cancer (NRG ONCOLOGY RTOG 1005). <https://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?action=openFile&FileID=9366>. Accessed on 19th December 2019.
17. Jöst V, Kretschmer M, Sabatino M et al. Heart dose reduction in breast cancer treatment with simultaneous integrated boost: comparison of

- treatment planning and dosimetry for a novel hybrid technique and 3D-CRT. *Strahlentherapie und Onkol* 2015; 191 (9): 734–741.
18. Mourik AMV, Elkhuisen PHM, Minkema D, Duppen JC. Multiinstitutional study on target volume delineation variation in breast radiotherapy in the presence of guidelines. *Radiother Oncol* 2010; 94 (3): 286–291.
 19. Moragues S, Pozo M, Casals J. Dosimetric feasibility of an “off-breast isocenter” technique for whole-breast cancer radiotherapy. *Reports Pract Oncol Radiother* 2019; 21 (6): 500–507.
 20. Armpilia C, Antypas C, Zygogianni A, Balafouta M, Sandilos P. A review on radiotherapy hypofractionation schedules for breast cancer treatment. *J Radiother Pract*. 2011; 10 (3): 201–208.
 21. De Rose F, Fogliata A, Franceschini D et al. Phase II trial of hypofractionated VMAT-based treatment for early stage breast cancer: 2-year toxicity and clinical results. *Radiat Oncol* 2016; 11 (1): 1–9.
 22. Fogliata A, Seppälä J, Reggiori G et al. Dosimetric trade-offs in breast treatment with VMAT technique. *Br J Radiol* 2017; 90: 20160701.