

# A Dosimetric Analysis of Incidental Radiation to the Internal Mammary Nodes with a Three-field Chest Wall Technique



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## ABSTRACT

**Objectives:** The authors' aim was to conduct a dosimetric analysis of the incidental radiation dose to the internal mammary node (IMN) region using a three-field chest wall technique (TFCWT).

**Methods:** This retrospective study utilized 3D-conformal radiotherapy plans of 50 post-mastectomy patients (25 left-sided and 25 right-sided). All plans used the TFCWT, composed of narrowed tangents matched medially to an AP electron field, and prescribed a total dose of 50 Gy in 28 fractions. The IMNs were not intentionally treated in all included plans.

**Results:** The mean dose to the IMN-planning target volume (IMN-PTV) was 45.1 Gy (26.4 - 55.6, SD 6.5). Minimum doses received by 95% and 90% of the IMN-PTV were 29.3 Gy (8 - 49, SD 10.0) and 34.0 Gy (10.0 - 52.0, SD 8.6), respectively. The percent volume of IMN-PTV receiving 100%,

95%, 90%, and 80% were 47.4% (3 - 94, SD 21.6), 55.6% (6 - 97, SD 22.4), 61.92% (7 - 98, SD 22.2), and 72.61% (18-100, SD 20.2), respectively. The average ipsilateral lung V20 Gy (with supraclavicular fields) was 25.0% (16 - 29, SD 3.4), and the average heart mean dose was 2.5 Gy (0.5 - 7.9, SD 1.58).

**Conclusion:** Although the results suggest increased IMN radiation doses with the TFCWT when compared historically to standard tangents, the incidental doses are comparatively less than that traditionally prescribed to the IMNs in high-risk patients. It is unknown whether this incidental IMN dose confers any clinical benefit.

**Key words:** breast cancer; dosimetry; internal mammary nodes

## INTRODUCTION

Regional nodal irradiation (RNI) as part of radiotherapy (RT) for breast cancer has been a topic of much debate in recent years. Components of RNI include axillary node irradiation, supraclavicular irradiation (SCV), and internal mammary node (IMN) irradiation. Of these, irradiation of the IMNs has been most challenged due to the low incidence of IMN failures, the uncertain clinical benefit of irradiating the IMNs, and the technical difficulties in delivering it safely.[1-7] The commonly used

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techniques in irradiation of the IMNs are: (1) partial wide tangents, (2) a separate IMN anterior posterior (AP) field (photon, electron, or mixed) to complement opposing tangential fields, and more recently, (3) deep inspiration breath hold (DIBH) techniques.[6-14] Results from previous dosimetric studies have shown that wide tangents or supplementary AP fields may cover the target prescription for the IMNs. However, there was some increased radiation dose to the organs at risk (OAR) with these techniques, specifically for left-sided breast cancer. DIBH techniques have been shown to safely deliver target prescription doses to the IMNs even for left-sided breast cancer.[13,14] However, DIBH has been known to be quite resource intensive and may still not be widely available in developing countries.[15]

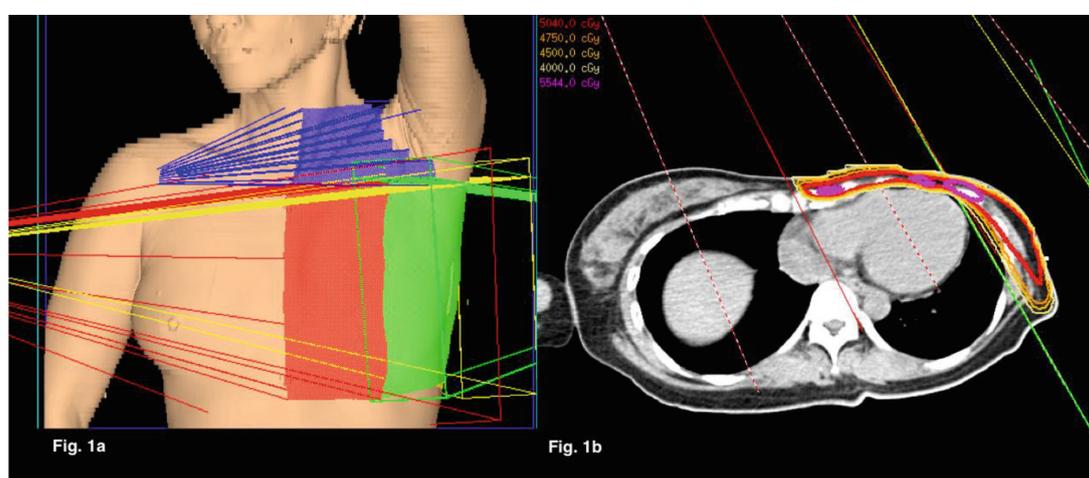
Dosimetric studies investigating incidental dose to the axillary lymph nodes found the radiation dose to be insufficient with standard tangential fields.[16-21] The ACOSOG Z0011 study, however, indirectly suggested that incidental radiation to the axilla may already be capable of providing significant clinical benefit.[22] Data is more limited for incidental dose to the IMN, but a retrospective American study reported inadequacy of incidental radiation using standard tangents.[23]

Approximately 200 breast cancer patients receive adjuvant RT at our institution annually, the majority (96%) of which are delivered in the post-mastectomy setting. These numbers are in accordance with our national data, highlighting the slow uptake of breast conservation surgery in local practice.[24] In the post-mastectomy setting, our institution makes use

of a three-field chest wall technique (TFCWT) with narrowed tangents matched to a medial anterior electron field. This technique is quite similar to the techniques used in large studies which investigated IMN RT.[8-11] However, our primary intent in using this technique is to potentially decrease the lung volume and contralateral breast irradiated without increasing the mean heart dose. Although the IMNs of patients included in this study were not intentionally treated, there is a possibility that the incidental radiation dose to the IMNs using this RT technique is sufficient. The purpose of this study is to conduct a dosimetric analysis of the incidental radiation dose to the IMNs using the TFCWT used at our institution.

## METHODS AND MATERIALS

This is a retrospective dosimetric study of consecutive breast RT plans at the Benavides Cancer Institute - University of Santo Tomas Hospital from 2016-17. A total of 50 (25 left-sided and 25 right-sided) plans were used in this study. The eligible plans were CT-based, 3D conformal RT plans used for post-mastectomy patients. All plans utilized the TFCWT composed of (1) narrowed 6 MV tangential fields set at angles that included a maximum of 1 cm of lung tissue, matched medially to (2) a 6 to 9 MeV anterior electron field (Figure 1A and 1B). The anterior electron field borders extended medially to the midsternal line, laterally to the medial edge of the tangential fields, and were matched superiorly and inferiorly to the corresponding border of the



**Figure 1.** **a:** 3D beam arrangement; **b:** Axial slice of a sample CT simulation plan of the TFCWT used by the authors' institution. The beam colors are as follows: **red** - AP electron field, **yellow** - medial tangential field, **green** - lateral tangential field, **blue** - supraclavicular field.

tangents. The TFCWT was matched superiorly to a 6 MV anterior photon supraclavicular field. Being in a limited resource setting, breath hold techniques were not used in any of our patients. The involved chest wall and supraclavicular regions were treated to a total dose of 50 Gy in 28 fractions without intentional irradiation of the IMNs. The Phillips Pinnacle Treatment Planning System version 7.6c was used to plan all radiation treatments using the adaptive convolve treatment algorithm.

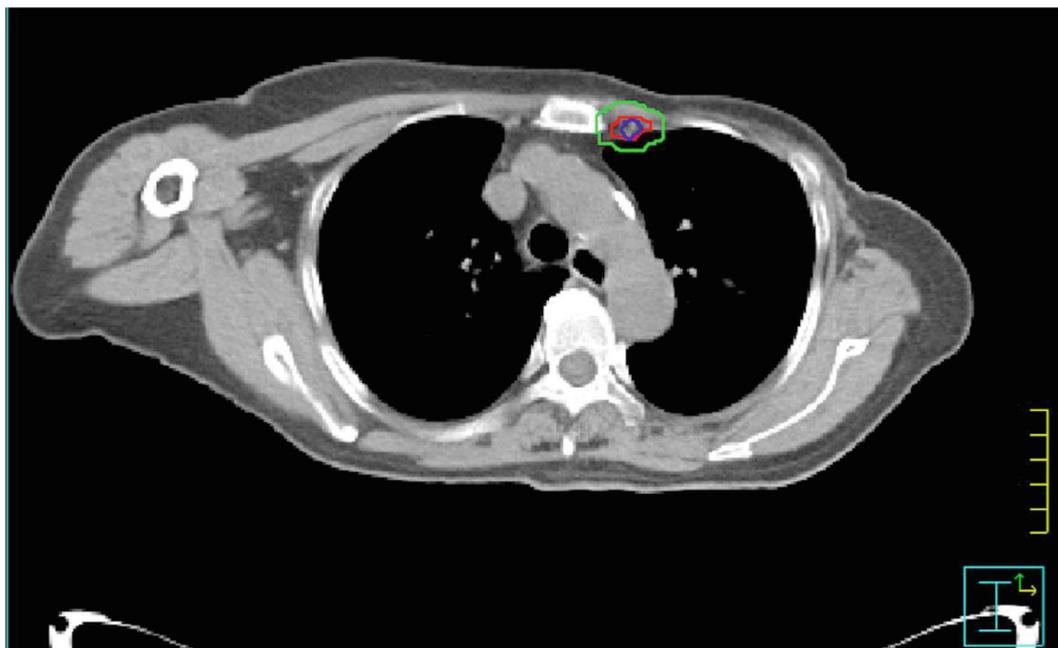
Prior CT simulation images of eligible patients were uploaded on the treatment planning computer and the IMN clinical target volumes (IMN-CTV) were contoured by two radiation oncologists. The target volumes, isodose lines, and beam arrangements of the original plans were turned off prior to contouring of the IMN-CTVs to minimize bias. The authors contoured the IMN-CTV based on the updated European Society for Radiotherapy and Oncology (ESTRO) contouring guidelines for breast cancer. [25] As per our institutional protocol, an additional 5 mm margin was added to the IMN-CTV to form the IMN planning target volume (IMN-PTV) (Figure 2). Although a paper published in 2004 suggested using 7 mm margins for the PTV, there are currently no recommendations for the specific size of PTV margins for the IMN. [26] We followed the latest ESTRO recommendation to base the size of the PTV margins from actual measurements of set-up performance. [25]

Dose volume histograms (DVH) were evaluated for the following variables: (1) mean IMN-PTV dose, minimum dose received by (2) 95% (D95) and (3) 90% (D90) of the IMN-PTV, volume of IMN-PTV receiving 100% (IMN-PTV 100%), (3) 95% (IMN-PTV 95%), (4) 90% (IMN-PTV 90%), (5) 80% (IMN-PTV 80%) of the prescribed dose, (6) heart mean dose, and (7) ipsilateral lung volume receiving 20 Gy (V20 Gy). IMN-PTV100%, IMN-PTV 95%, IMN-PTV 90%, and IMN-PTV 80% corresponded to volumes receiving 50 Gy, 47.5 Gy, 45 Gy, and 40 Gy, respectively. We reported the ipsilateral lung V20 Gy with and without the supraclavicular photon field due to its possible significant contribution to the volume of lung irradiated. [27]

Data was encoded using Microsoft Excel and data analysis was done using the Statistical Package for the Social Sciences (SPSS) Statistics version 22. Quantitative variables were summarized and presented as mean, median, range, and standard deviation (SD). Comparison of values between right-versus left-sided breast cancer plans was done using the Wilcoxon Rank Sum Test. Statistical significance was defined as a p-value of less than 0.05.

## RESULTS

The results of the IMN-PTV are listed in Table 1. The mean dose of the IMN-PTV was 45.1 Gy (26.4 - 55.6, SD 6.5), which corresponded to 90% of the



**Figure 2.** Sample contour of the IMN-PTV (green) and IMN-CTV (red), created around the internal thoracic vessels (blue).

**Table 1.** IMN-PTV Dosimetric Parameters

	Left (N=25)	Right (N=25)	Entire group (N=50)	Left vs Right p-value
IMN-PTV Mean Dose				
Mean ± SD	43.9 Gy ± 7.4	46.3 Gy ± 4.6	45.1 Gy ± 6.5	0.19
Median (min-max)	42.2 Gy (26.4 - 53.8)	46.1 Gy (34.9-55.6)	45.6 Gy (26.4-55.6)	
IMN-PTV D95				
Mean ± SD	28.6 Gy ± 10.7	30.0 Gy ± 9.3	29.3 Gy ± 10.0	0.33
Median (min- max)	30.0 Gy (8.0 – 48.0)	30.0 Gy (13.0 – 49.0)	30.0 Gy (8.0 – 49.0)	
IMN-PTV D90				
Mean ± SD	32.9 Gy ± 9.7	31.9 Gy ± 10.7	34.0 Gy ± 8.6	0.28
Median (min- max)	33.0 Gy (10 – 50)	33.0 (19.0 – 52.0)	33.0 Gy (10.0 – 52.0)	
IMN-PTV 100% (50Gy)				
Mean ± SD	44.4% ± 24.0	50.4% ± 18.5	47.4% ± 21.6	0.13
Median (min-max)	33.0% (3.0-90.0)	47.0% (22.0-94.0)	45.5% (3.0-94.0)	
IMN-PTV 95% (47.5Gy)				
Mean ± SD	52.0% ± 24.8	59.2% ± 19.1	55.6% ± 22.4	0.12
Median (min-max)	44.0 (6.0-96.0)	54.0 (29.0-97.0)	53.5 (6.0-97.0)	
IMN-PTV 90% (45Gy)				
Mean ± SD	58.3% ± 24.9	65.6% ± 18.5	61.9% ± 22.2	0.13
Median (min-max)	51.0% (7.0-97.0)	64.0% (33.0-98.0)	63.5% (7.0-98.0)	
IMN-PTV 80% (40Gy)				
Mean ± SD	68.8% ± 23.4	76.4% ± 15.5	72.6% ± 20.2	0.14
Median (min-max)	65.0% (18.0 -100.0)	76.0% (43.0-100.0)	75.5% (18.0-100.0)	

Analyzed via Wilcoxon Rank Sum Test; IMN-PTV – Internal Mammary Node Planning Target Volume; D95 – minimum dose received by 95% of IMN-PTV; D90 – minimum dose received by 90% of IMN-PTV; IMN PTV 100%, 95%, 90%, 80% - volume of IMN PTV receiving 100%, 95%, 90%, and 80% of prescription dose  
SD - Standard Deviation

prescription dose. The D95 and D90 of the IMN-PTV were 29.3 Gy (8 – 49, SD 10.0) and 34.0 Gy (10.0 – 52.0, SD 8.6), respectively. The IMN-PTV 100%, IMN-PTV 95%, IMN-PTV 90%, and IMN-PTV 80% were 47.4% (3 - 94, SD 21.6), 55.6% (6 - 97, SD 22.4), 61.92% (7 - 98, SD 22.2), and 72.61% (18 - 100, SD 20.2), respectively. Although right-sided plans had slightly higher dosimetric values than left-sided plans, all parameters failed to reach statistical significance.

Radiation dosimetric parameters to the OAR are reported in Table 2. The average heart mean dose was 2.5 Gy (0.5 – 7.9, SD 1.58), with left-sided plans having significantly higher doses than right-sided plans, 3.7 Gy (2.5 - 7.9, SD 1.3) versus 1.3 Gy (0.5 - 2.9, SD 0.6) ( $p < 0.01$ ), respectively. The average ipsilateral lung V20 Gy was 25.0% (16 - 29, SD 3.4) with the supraclavicular field and 17.5% (9 – 28, SD 4.7) without the supraclavicular field. The average ipsilateral lung V20 Gy failed to

show significant difference between left- and right-sided plans whether or not a supraclavicular field was used (with supraclavicular field: left 24.3% versus right 25.6%,  $p = 0.18$ ; without supraclavicular field: left 16.4% versus right 18.7%,  $p = 0.11$ ).

## DISCUSSION

Results of the study reveal that even with the TFCWT, the incidental IMN-PTV radiation dose does not attain the IMN prescription dose (48-50 Gy) used by the studies reporting benefit with IMN-RT.[8-10] Although the mean dose of our plans translated to 90% of the prescription dose, the mean D95 (29.3 Gy) and D90 (34.0 Gy) were only 58.6% and 68.0% of the prescription dose, respectively. Only 54% (27/50) of the plans had a mean dose to the IMN-PTV of at least 45 Gy (90% of the dose), and 16% (8/50) had at least 90% of their IMN-PTVs receiving 90% of the total dose (data not shown). Importantly, if we look specifically at our IMN-CTVs, only 28%

**Table 2.** Dosimetric Parameters for the Organs at Risk

	Left (N=25)	Right (N=25)	Entire group (N=50)	Left vs Right p-value
Heart				
Mean $\pm$ SD	3.7 Gy $\pm$ 1.3	1.3 Gy $\pm$ 0.6	2.5 Gy $\pm$ 1.6	< 0.01*
Median (min-max)	3.3 Gy (2.5-7.9)	1.2 Gy (0.5-2.9)	2.6 Gy (0.5-7.8)	
Ipsilateral Lung V20 Gy (with the supraclavicular field)				
Mean $\pm$ SD	24.3% $\pm$ 3.1	25.6% $\pm$ 4.8	25.0% $\pm$ 3.4	0.18
Median (min-max)	25.0% (18.0 - 29.0)	26.0% (16.0 - 29.0)	25.0% (16.0-29.0)	
Ipsilateral Lung V20 Gy (excluding the supraclavicular field)				
Mean $\pm$ SD	16.4% $\pm$ 4.7	18.7% $\pm$ 4.4	17.5% $\pm$ 4.7	0.11
Median (min-max)	16.0 (9 - 28)	19 (9 - 27)	18.0 (9 - 28)	

SD - Standard deviation; Analyzed via Wilcoxon Rank Sum Test; \* statistically significant  
Lung V20 Gy - volume of lung receiving 20 Gy

(14/50) achieved the prescription target used by the MA.20 study (IMN-CTV covered by at least 80% isodose).[9] The results imply that the incidental IMN dose with the TFCWT does not always achieve target prescription levels, a finding in line with the results of the study by Arora et al.[23] When our results were compared with that of Arora et al., we found a near doubling of almost all dosimetric parameters with our plans utilizing the TFCWT versus their plans which used standard tangents (Table 3). Of note, the study of Arora et al. used a different contouring guideline (RTOG) from our study.

Will this increase in dosimetric coverage compared to standard tangents be enough

to provide clinical benefit? Another important question is the minimum radiation dose needed to meaningfully treat subclinical disease. The Withers' study on dose response relationship for subclinical disease showed that locoregional control benefit may already be achieved by lower doses using standard fractionation.[28] However, breast cancer patients included in that study were treated to more standard doses of 46-48 Gy. Despite several trials showing inadequate dose coverage to the axillary lymph nodes with the use of standard tangents, the ACOSOG Z0011 study suggested that incidental radiation may be enough to make up for the lack of axillary dissection in selected patients.[22]

**Table 3.** Comparison of dosimetric parameters between the TFCWT and other RT techniques by Arora et al. and Thorsen et al.

Dosimetric parameters	Current study (n = 50)	Arora et al.[23] (n = 50)	DBCG-IMN; Thorsen et al. [30] (n=68)
<b>Technique</b>	TFCWT	Standard tangents	Left-sided: standard tangents Right-sided: anterior electron field or partial wide tangents
<b>Mean IMN-PTV</b>	45.1 Gy (SD 6.5)	25.0 Gy (SD 16.0)	-
<b>IMN-PTV 100 %</b>	47.4% (SD 21.6)	22.5% (SD 20.6)	-
<b>IMN-PTV 95 %</b>	55.6% (SD 22.4)	32.2% (SD 24.7)	-
<b>IMN-PTV 90 %</b>	61.9% (SD 22.2)	38.4% (SD 27.0)	
<b>IMN-CTV 90%</b>		<b>Left-sided only</b>	
	61.4 (SD 27.4) (n = 25)	-	35.2 % (SD 27.7) (n = 30)
		<b>Right-sided only</b>	
	64.6% (SD 22.1) (n = 25)	-	73.2 % (SD 26.9) (n = 38)

TFCWT - Three field chest wall technique; IMN-PTV - Internal Mammary Node Planning Target Volume;  
IMN-PTV 100%, 95%, 90%, 80% - volume of IMN-PTV receiving 100%, 95%, 90%, and 80% of prescription dose  
IMN-CTV 90% - volume of Internal Mammary Node Clinical Target Volume receiving 90% of prescription dose;  
SD = Standard Deviation

It is important to highlight that around half of the patients included in that study were treated with high tangents (19% receiving intentional RNI) as reported in a separate analysis by Jagsi et al.[29] Hence, similar to patients in our study, a proportion of their patients were treated with techniques that may sometimes deliver significant incidental radiation to the regional nodes of interest. However, the population (T1-T2, 1-2 positive SLN, post-breast conservation surgery) included in the ACOSOG Z0011 study had a relatively low risk of regional nodal failure. Assuming that this hypothetical clinical benefit translates to most post-mastectomy patients may not be prudent.

As part of the DBCG-IMN study, Thorsen et al. conducted a dosimetric study reporting the volume of IMN-CTV receiving 90% (IMN-CTV 90%) of the prescribed dose in one-tenth of their patients.[30] We compared the IMN-CTV 90 in our plans with the data they presented (Table 3). For left-sided breast cancers, there was still a doubling of the V90 with our plans (61.4%, SD 27.4) compared with the DBCG-IMN plans (35.2%, SD 27.7). Left-sided breast cancers were treated with standard tangents in the DBCG-IMN study and these results are consistent with our prior comparison of the Arora et al. study.[23] For right-sided breast cancers, the average V90 from our plans was 64.6% (SD 22.1), which is somewhat lower than the average V90 of the DBCG-IMN study (73.2%, SD 26.9), although no statistical comparison was made. Thus, although the DBCG-IMN study showed significant improvement in clinical outcomes with a mean IMN-CTV 90 of only 73.2%, relying solely on incidental irradiation may not generate the same results.

The ICRU-62 recommends a heterogeneity allowance of +7% and -5% of the prescription dose inside the PTV.[31] This limit for hotspots has been reported to be quite difficult to achieve for breast RT as described in a study by Salem et al.[27] Authors of that study used a more liberal maximum limit of  $\leq 120\%$  of the prescribed dose, which may be too high with modern RT techniques. Currently, contemporary studies use the volume receiving 110% of prescription dose as the monitoring variable for hotspots.[32,33] At our institution, every effort is made to minimize areas of hotspots with the aid of field-in-field techniques. However, areas receiving 110% of the dose are still inevitably present, particularly because of the use of combined

photon and electron fields (Figure 1b). This is a recognized problem with mixed beams due to the potential overlaps and gaps between the fields. Areas of overdosage or underdosage at the photon-electron junction with the use of this technique must be carefully monitored.

An important area of controversy with RT to the IMNs is the potential for increased radiation doses to the OAR. All the large trials that included IMN-RT did not demonstrate increased incidence of toxicity, although none of these had sufficient follow-up to adequately assess long-term effects.[8-11] The results of our study showed that the overall average radiation dose to the lungs was within the dose constraints set by the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) (V20Gy < 30%), even when the TFCWT was combined with a supraclavicular field.[34] The mean heart dose (2.5 Gy) in our plans was lower than the mean dose in the study by Darby (4.9 Gy).[35] However, it is important to emphasize that left-sided plans in our study showed a significantly higher mean heart dose compared to right-sided plans. In fact, the top end of the range of mean heart dose for our left-sided plans reached a relatively high dose (7.9 Gy). This may potentially have clinical implications as the Darby study showed a 7% increased risk of heart complications per Gy of increase in mean dose. While our numbers are typical of left-sided plans, vigilance must be practiced to decrease the mean heart dose in these patients as much as possible. DIBH techniques have been reported in dosimetric studies to achieve prescription IMN doses without increasing the mean heart dose.[13,14] However, DIBH may still not be widely available in centers located in developing countries. Therefore, the utility of traditional 3DCRT techniques for breast irradiation which includes TFCWT are of relevance in this setting.

Probably the greatest debate concerning IMN-RT is quantifying the actual benefit it lends to oncologic outcomes, especially for lower risk breast cancer. The updated reports of the contemporary EORTC 22922 and the MA.20 intergroup trials have augmented the information on the clinical value of RNI.[8,9] Both studies showed a significant but modest disease-free survival benefit with RNI even for low-risk breast cancer. Both trials treated the SCV, axillary lymph nodes, and the IMNs in their experimental arms, which raises a doubt on

whether the benefit was from IMN-RT or from the other components of RNI. A French phase III study published in 2013 tried to isolate the benefit of IMN-RT but showed no significant difference in oncologic outcomes.[11] On the other hand, the more recently completed DBCG-IMN study found a significant benefit in overall survival and breast cancer mortality with the effect being more pronounced in patients at higher risk for IMN metastasis (medial/central location, N2 disease).[10] The European Society for Medical Oncology (ESMO) clinical practice guidelines for breast cancer concur with the results of the Danish study and recommends inclusion of the IMN in adjuvant RT for such high-risk patients.[36] Thus, it is important to intentionally target the IMNs regardless of the radiotherapy technique used, as incidental doses may be inadequate even with the TFCWT. However, the benefit of IMN-RT for low-risk patients is a lot less clear. Whether the increase in radiation dose to the IMN-PTV seen in our plans with the use of the TFCWT results is a clinical benefit to these low-risk patients is beyond the scope of this paper, and therefore a dedicated study investigating clinical outcomes may be warranted.

This report is limited by the purely dosimetric nature of the study. Assumptions generated from dosimetric studies should be cautiously applied in clinical settings. The lack of use of techniques incorporating DIBH may also limit the applicability of

findings in modern RT facilities routinely using DIBH. However, for practitioners in low-resource settings, there are still meaningful insights to be gleaned from these findings.

## **CONCLUSION**

The results of our study suggest a possible increase in radiation dose coverage to the IMN-PTV with the TFCWT when compared historically to standard tangential field techniques. Whether this increase in incidental radiation dose will be enough to improve oncologic outcomes is still in question, as it may not always fall within the target prescription dose for intentional IMN irradiation. It is therefore recommended to intentionally treat the IMNs in high-risk patients, regardless of the technique used.

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## **Conflict of Interest**

The authors declare no conflict of interest.

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