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Retrospective dosimetric comparison of VMAT versus t-IMRT for patients with carbon dioxide tissue expanders undergoing left sided PMRT using the recent ESTRO-ACROP target volume delineation

Abstract

Introduction: The Aeroform tissue expander device (ATED) is a novel alternative system for patients who have had mastectomy for breast cancer (BC) and require adjuvant radiation therapy (RT), and investigations are required when used during RT. We aim to compare RT dosimetry outcomes using volumetric modulated arc therapy (VMAT) versus tangential intensity-modulated radiation therapy (t-IMRT) techniques when planning post-mastectomy RT (PMRT), using the recent European Society for Radiation Oncology – Advisory Committee on Radiation Oncology Practice (ESTRO-ACROP) target volume delineation consensus guideline.[1]

Methods: Five patients with left-sided BC undergoing PMRT with ATED in-situ were identified. Retrospectively, their CT-simulation scans were utilised to delineate the chest wall (CW) and nodal target volumes. A dose of 50.4Gy in 28 fractions was prescribed and four plans generated. Dosimetry for all target volumes and organs at risk were extracted, with paired means compared.

Results: When comparing VMAT with t-IMRT techniques, there was no statistically significant difference in the PTV50.4 D95% or D2% coverage. Within t-IMRT plans, excluding internal mammary nodes (IMN) leads to higher D95% coverage. The heart mean dose and V25 were significantly lower with VMAT than t-IMRT. There was no significant difference to the heart dose whether IMN was included or not. The ipsilateral lung V20 was significantly lower with VMAT than t-IMRT, but not the V5. Within t-IMRT plans, excluding IMN leads to lower ipsilateral lung V20. The t-IMRT plans had lower contralateral lung V5, and even lower when IMN was not included. The contralateral breast mean dose was not significantly different between VMAT and t-IMRT. Within t-IMRT plans, the right breast mean dose was lower if IMN was excluded.

Conclusion: We have not shown a clear advantage of VMAT over t-IMRT techniques when prescribing PMRT for left-sided BC patients with ATED in-situ.

Keywords: breast neoplasms, mastectomy, radiation oncology, radiotherapy, intensity-modulated, tissue expansion devices

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Janice Yeh,[1] Margaret Cokelek,[2] Mark Tacey,[1,3,4] Emily Holt,[2] Huong Ho,[2] Tai Tran,[2] Brindha Subramanian,[2] Farshad Foroudi,[1] Michael Chao[1,2]

[1]Department of Radiation Oncology, Olivia Newton-John Cancer Wellness & Research Centre, Austin Hospital, Victoria, Australia
[2]Department of Radiation Oncology, GenesisCare, Ringwood, Victoria, Australia
[3]Office of Research, Northern Health, Epping, Victoria, Australia
[4]Melbourne School of Population and Global Health, University of Melbourne, Carlton, Victoria, Australia

Correspondence: Janice Yeh, Department of Radiation Oncology, Olivia Newton-John Cancer Wellness & Research Centre, Austin Hospital, 145 Studley Road, Heidelberg, VIC 3084, Australia, Telephone +613 9496 2800, Facsimile +613 9496 2826, Email Janice.Yeh@austin.org.au

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Abbreviations: 3DCRT, 3D-conformal radiation therapy; ATED, aeroform tissue expander device; BC, breast cancer; CT, computed tomography; CTV, clinical target volume; CW, clinical target volume; DIBH, deep inspiration breath hold; ESTRO-ACROP, european society for radiation oncology – advisory committee on radiation oncology practice; IMN, internal mammary node; OAR, organs at risk; PMRT, post-mastectomy radiation therapy; RNI, regional nodal irradiation; RT, radiation therapy; t-IMRT, tangential intensity-modulated radiation therapy; VMAT, volumetric modulated arc therapy

Introduction

Post-mastectomy radiation therapy (PMRT) is considered an important aspect in the overall management for many women with locally advanced breast cancer. Meta-analysis of individual patient data performed by the Early Breast Cancer Trialists' Collaborative Group[2] found that radiation therapy (RT) following mastectomy and axillary dissection surgery lead to reduced locoregional recurrence, overall recurrence, and breast cancer mortality in groups of women with one or more involved lymph nodes, even when systemic therapy was given.

For some patients, post-mastectomy reconstruction is sought after to improve psychosocial quality of life.[3] Despite there being studies which have shown that RT after immediate reconstruction does not significantly compromise cosmesis,[4] the majority of clinicians still prefer a two-stage approach with immediate tissue expander placement, followed by autologous reconstruction or implant placement after completion of radiation therapy due to reported loss in reconstruction cosmesis. Retro-pectoral tissue expanders allow gradual stretching of the pectoralis major muscle and overlying skin, to create the implant envelope, preparing for the eventual reconstruction procedure.[5]

The Aeroform (carbon dioxide) tissue expander device (AirXpanders, San Francisco, USA) (ATED) is a novel system

introduced in recent years as an alternative to the traditional saline tissue expanders.[6] Rembert et al.[7] confirmed that the electronic components inside this device is able to continue to function properly after exposure to radiation levels beyond the standard PMRT doses. However, the metallic reservoir within the device poses a significant impact on radiation therapy dosimetry while treating the chest wall area with this tissue expander in-situ.[8]

Motwani et al.[9] found that optimal PMRT plans can be more challenging to achieve in patients who underwent immediate reconstruction following mastectomy, than those who did not have reconstruction. Compromises to the plan in the domains of target coverage or dose constraints to organs at risk (OAR) was most prevalent in those with left-sided cancers.

Tangential intensity-modulated radiation therapy (t-IMRT) and volumetric modulated arc therapy (VMAT) techniques have been shown and widely accepted as being more likely to achieve reasonable target coverage especially when treating left sided breast cancers and locoregional nodes, while minimising dose to OARs.[10-12]

The European Society of Radiation & Oncology and Advisory Committee on Radiation Oncology Practice (ESTRO-ACROP) in 2019 published a consensus guideline for target volume delineation of the chest wall for PMRT in the setting of immediate breast reconstruction, tailored to the location of the implant,[1] which will likely be increasingly utilised in the future, especially in the setting of modern RT planning techniques. It has been shown by Chang et al.[13] to lead to VMAT plans with significantly lower dose to heart and left anterior descending coronary artery when compared to conventional target volume delineations which include the whole implant. The decision to include or exclude internal mammary node (IMN) in the treatment volumes continues to be a topic of clinical controversy in node positive breast cancer.[14]

The aim of this study is to compare RT dosimetry outcomes using VMAT or t-IMRT techniques when planning PMRT to chest wall and at risk nodal regions on patients with ATED in-situ, using the relatively new ESTRO-ACROP target volume delineation consensus guideline. This is a retrospective dosimetric evaluation and these new target volumes were not used to clinically treat the patients.

Material and methods

Ethics approval was obtained from our Institutional review board prior to commencement of the study.

Patient selection

Five patients who had ATED in-situ following mastectomy surgery and axillary dissection for left sided breast cancers for locally advanced breast cancer were identified. The devices were all placed in the retro-pectoral position.

Details regarding the components and use of the device has been previously reported.[8] In brief, the device was expanded incrementally after surgery, during adjuvant chemotherapy period by the patient, using the Aeroform dosage controller, as instructed by their plastic surgeons. The ATEDs were expanded to their full capacity prior to commencement of RT planning.

Image acquisition and volume definition

All patients underwent computed tomography (CT) simulation with Phillips CT scanner (Amsterdam, Netherlands) in a supine position with arms up using a vacuum bag immobilisation device as per institutional protocol for their clinical treatment plan. They were scanned in deep inspiration breath hold (DIBH) position. 3mm slice thickness images were obtained and transferred to MIM Maestro® software (Ohio, USA), which was used to contour the structures of interest.

Target volumes for this study was retrospectively generated by one experienced breast radiation oncologist. The clinical target volumes (CTV) included the left chest wall (denoted as CTVp_chest wall), left supraclavicular fossa and level III axilla (denoted as CTVn_L4 and CTVn_L3), and left internal mammary nodes (denoted as CTVn_IMN).

The CTVp_chest wall was contoured using the 2019 ESTRO-ACROP consensus guideline,[1] while the CTVn_L4, CTVn_L3, and CTVn_IMN were contoured using the 2015 ESTRO consensus guideline.[15] As the ATEDs were placed in the retro-pectoral position, the CTVp_chest wall included the rim of tissue ventral to the ATED and pectoralis major muscle, except where the muscle may extend closer to the chest wall, hence the ATED is largely not included in the CTVp_chest wall.

The planning target volumes (PTV) were generated after expansion of CTVp_chest wall by 7mm isotropically, and 5mm for the nodal CTVs in all directions except medially where only 3mm was used.

The organs at risk (OAR) included the heart, left and right lung, contralateral right breast, ipsilateral left chest wall (ribs and intercostal muscles). These were contoured as per institutional guidelines.

Different components of the Aeroform device were also contoured and assigned appropriate densities as described by Tran et al.[8]

Treatment planning

Four plans per patient were generated retrospectively by one experienced radiation dosimetrist purely to assess dosimetry, and not delivered to the patient. Pinnacle treatment planning system (Philips, Amsterdam, Netherlands) was used to generate plans with a prescribed dose of 50.4Gy in 28 fractions with 1.0 cm thick bolus material applied over the chest wall region.

A. VMAT to the left chest wall, nodal levels 3, 4, and IMN (denoted as VMAT to all PTVs including IMN)

B. VMAT to the left chest wall, nodal levels 3 and 4, not IMN (denoted as VMAT to all PTVs excluding IMN)

C. t-IMRT to the left chest wall, nodal levels 3, 4, and IMN (denoted as t-IMRT to all PTVs including IMN)

D. t-IMRT to the left chest wall, nodal levels 3 and 4, not IMN (denoted as t-IMRT to all PTVs excluding IMN).

The VMAT plans consisted of two arcs rotating from 310-30 to 70-150 degrees and reverse, with collimator setting of 15 degrees. The optimization was Smart Arc, and dose distribution was calculated with convoluted collapsed cone algorithm with 3 mm dose grid resolution and 3° control point spacing.

The tangential IMRT plans were based on two tangential fields, with beam angles entering from 310 degrees and 130 degrees. The jaws of all fields were fixed to fit the whole PTV, plus 2.0cm margin above the bolus into air, like standard tangents, and the collimator angle was set to 0 degrees. Direct machine parameter optimization (DMPO) was used to optimize the plans, and jaw motion was allowed. The max iterations were 80, and the convolution dose iteration was 40. The minimum field size and monitor units of subfield were restricted as 5 cm2 and 5 MU, respectively.

Dosimetry for all target volumes and OARs were extracted from each plan and evaluated. These include PTV D95% and D2%, heart mean dose and V25Gy, ipsilateral lung V20Gy and V5Gy, contralateral lung V5Gy, contralateral breast mean dose, ipsilateral chest wall (ribs and intercostal muscles) maximum and minimum dose.

Table 1 displays the institutional planning criteria for PTV coverage and dose constraints to OARs.

Table 1 Institutional planning criteria

Structure	Parameter	Goal
PTV	D95%	>95% prescribed dose
	D2%	<105% prescribed dose
Heart	Mean dose	<3Gy
	V25Gy	<5% prescribed dose
Lung – ipsilateral (left)	V20Gy	<15% prescribed dose
	V5Gy	<50% prescribed dose
Lung – contralateral (right)	V5Gy	<10% prescribed dose
Breast – contralateral (right)	Mean dose	ALARA
Chest wall – ipsilateral (left)	Max dose	ALARA
	Min dose	ALARA

Statistical analysis

Descriptive statistics were calculated to summarise and compare the dosimetry measurements across the four plans for the five patients. Results were presented as means and medians (and range). Due to the minimal sample size, all measurements were considered to be normally distributed and thus results presented as means (and range: minimum to maximum), with each plan compared using paired Student's t-tests. Multi-level mixed effects linear models were used to consider the clustered nature of the data with repeated measurements for the same patient, when assessing the independent effects of VMAT or t-IMRT and IMN. Data was prepared in Microsoft Excel and Stata version 15.1 (StataCorp, College Station, Texas, USA) used to conduct the statistical analysis. A p-value of less than 0.05 was considered to indicate statistical significance.

Results

Representative axial dose distributions with VMAT and t-IMRT to the left chest wall, nodal levels 3, 4, and including IMN are shown in Figure 1. Representative axial dose distributions with VMAT and t-IMRT to the left chest wall, nodal levels 3, 4, but excluding IMN are shown in Figure 2.

Table 2 displays the medians and range (minimum to maximum), with accompanying charts in Figures 3 and 4. As shown in Figure 3, the mean prescribed dose percentage that 95% of the PTV50.4 is at least receiving (D95%) was 92.9%, 93.0%, 93.6%, 94.8%, for VMAT to all PTVs including IMN, VMAT to all PTVs excluding IMN, t-IMRT to all PTVs including IMN, t-IMRT to all PTVs excluding IMN, respectively. The mean prescribed dose percentage that 2% of the PTV50.4 is at least receiving (D2%) was 105.9%, 105.3%, 105.5%, and 105.5%, respectively. There was no statistically significant difference between the PTV50.4 coverage of the prescribed dose for when comparing VMAT with t-IMRT (p=0.122 for D95%, p=0.816 for D2%). However, when assessing t-IMRT plans alone, excluding IMN lead to a significantly higher D95% coverage than including IMN (p=0.002).

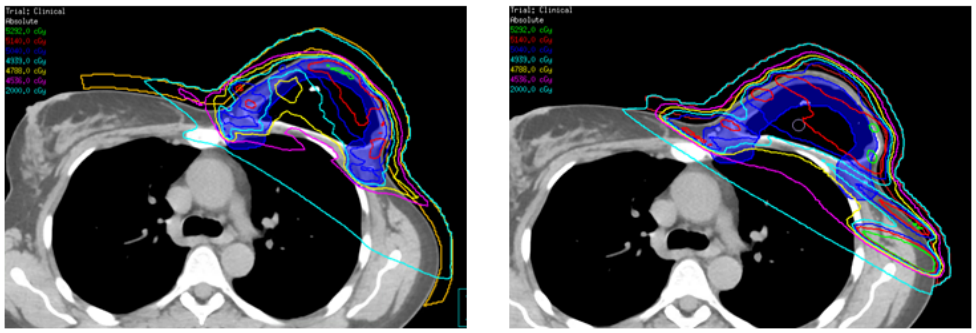

Figure 1 Comparison of dosimetry between VMAT (A) and t-IMRT (B) to all PTVs including IMN. The filled in blue area represents the PTV, while dosimetry is represented as multi-coloured isodose lines.

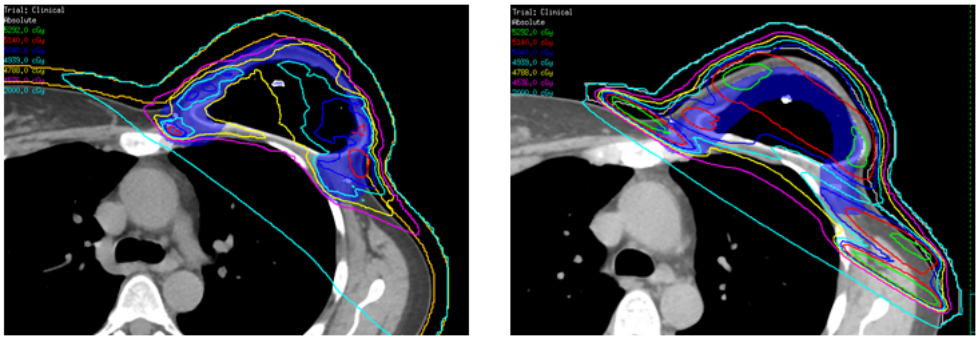

Figure 2 Comparison of dosimetry between VMAT (C) and t-IMRT (D) to all PTVs excluding IMN. The filled in blue area represents the PTV, while dosimetry is represented as multi-coloured isodose lines.

Citation: Yeh J, Cokelek M, Tacey M, et al. Retrospective dosimetric comparison of VMAT versus t-IMRT for patients with carbon dioxide tissue expanders undergoing left sided PMRT using the recent ESTRO-ACROP target volume delineation. *Int J Radiol Radiat Ther.* 2022;9(1):6–12.
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Table 2 Comparisons of the Median values (range) of each dose parameter

Structure	Parameter	VMAT to all PTVs including IMN value median (range)	VMAT to all PTVs excluding IMN value median (range)	t-IMRT to all PTVs including IMN value median (range)	t-IMRT to all PTVs excluding IMN value median (range)
PTV50.4	D95%	93.2% (87.4 – 96.7)	93.4% (90 – 95.2)	94.2% (89.7 – 95.6)	95.4% (91.4 – 96.4)
	D2%	105.2% (103 - 110)	105.4% (103.7 – 105.8)	105.4% (104 – 107.1)	105.4% (104.7 – 106.6)
Heart	Mean dose (Gy)	2.7 (2.5 – 4.8)	2.8 (2.4 – 3.8)	4.0 (3.4 – 5.5)	3.4 (2.8 – 5.7)
	V25Gy	0.3% (0.1 – 2.8)	0.3% (0.1 – 0.8)	3.6% (2.8 – 8.7)	2.6% (1.8 – 9)
Ipsilateral (Left) Lung	V20Gy	21.6% (19.9 – 23.2)	21.6% (20.1 – 26.5)	34.5% (26 – 35)	25.7% (23 – 28.9)
	V5Gy	45.5% (42.8 – 50.2)	47% (43.7 – 48.4)	48.1% (32.5 – 53.9)	42.6% (39.9 – 45.5)
Contralateral (Right) Lung	V5Gy	2.9% (1.4 – 10.5)	3.1% (2 – 12)	0.4% (0.1 – 0.7)	0.0% (0 – 0.1)
Contralateral (Right) Breast	Mean dose	3.6Gy (3 – 6.7)	3.7 (2.9 – 7.1)	4 (0.7 – 6.7)	2.1 (0.8 – 3.2)
Ipsilateral (Left) Chest wall (ribs and intercostal muscles)	Max dose	52.4Gy (51.1 – 55.2)	51.9 (50.1 – 53.4)	51.9 (51.7 – 53.9)	51.8 (51.1 - 53)
	Min dose	39Gy (34.7 - 40)	38.8 (38.3 – 42.3)	42.3 (40.9 – 44.5)	42.7 (40.9 – 45.3)

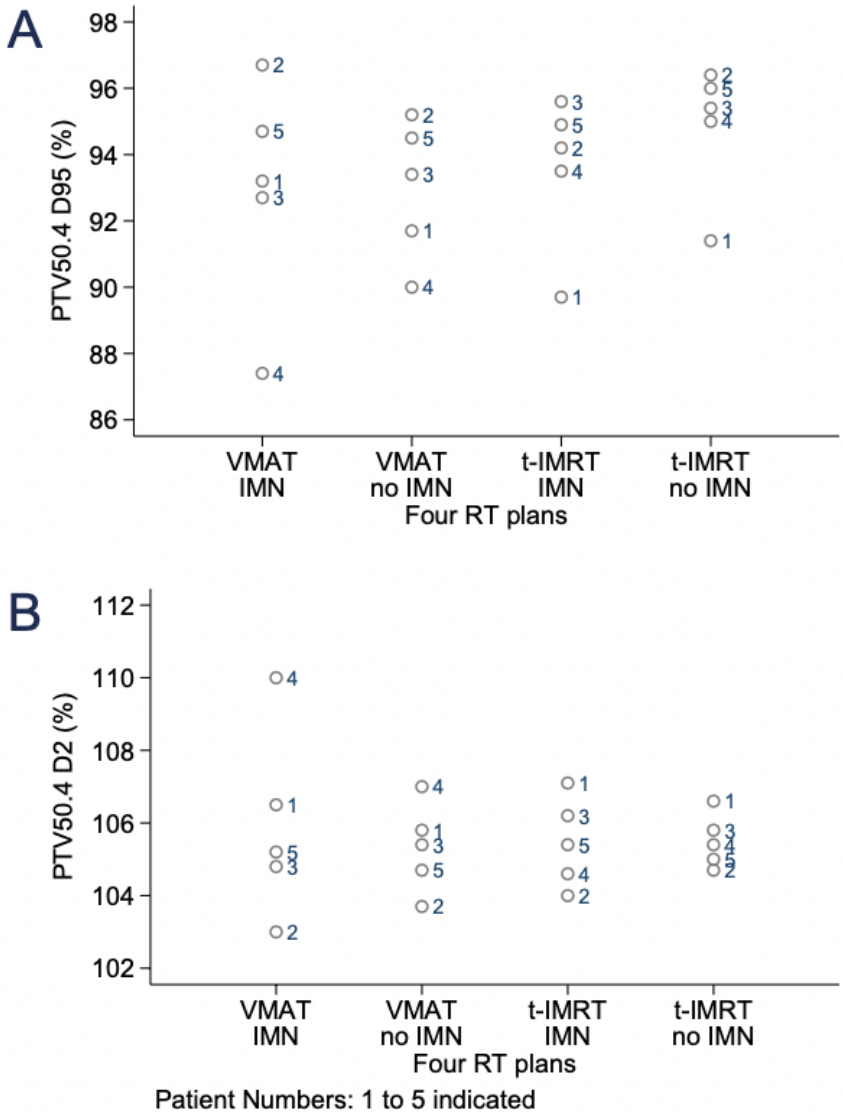

Figure 3 Dot plots of PTVs, Panel A– PTV50.4 D95 (%), Panel B – PTV50.4 D2 (%).

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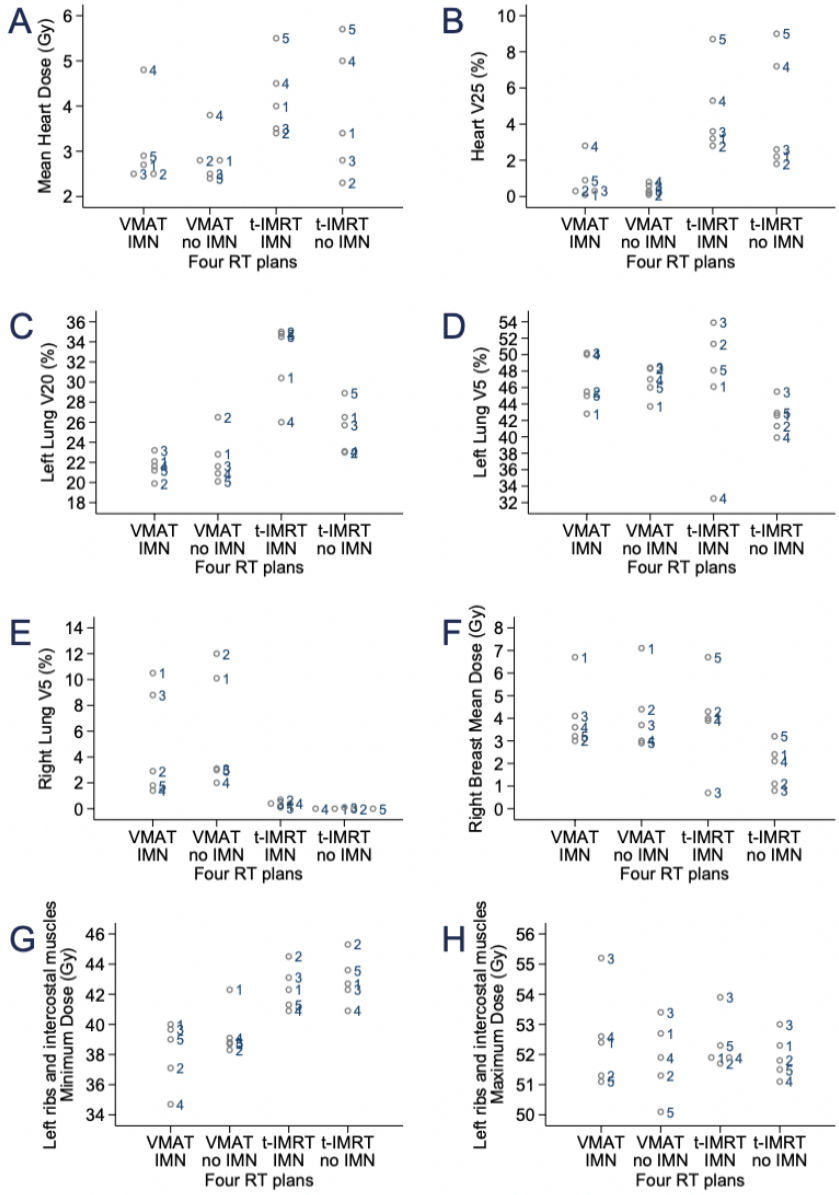

Figure 4 Dot plots of OARs, Panel A - Mean Heart Dose (Gy), Panel B - Heart V25 (%), Panel C - Left Lung V20 (%), Panel D - Left Lung V5 (%), Panel E – Right Lung V5 (%), Panel F - Right Breast Mean Dose (Gy), Panel G - Left ribs and intercostal muscles Minimum Dose (Gy), Panel H - Left ribs and intercostal muscles Maximum Dose (Gy).

With regards to OARs, the mean heart dose as well as V25 (heart volume that is receiving 25Gy) was lower with VMAT than t-IMRT technique ($p=0.001$ and $p\leq0.001$ respectively). IMN coverage had no significant effect on the mean heart dose or V25 ($p=0.369$ and $p=0.642$, respectively) (Figure 4, Panel A and B).

The ipsilateral lung volume that is receiving 20Gy (V20) dose was lower with VMAT technique than t-IMRT technique ($p<0.001$). Amongst the t-IMRT plans, excluding IMN resulted in lower ipsilateral lung V20 value ($p<0.001$) (Figure 4, Panel C).

There was no statistically significant difference in the ipsilateral lung V5 value amongst the different techniques ($p=0.246$, Figure 4, Panel D).

The contralateral lung V5 was significantly lower with t-IMRT technique than VMAT ($p<0.001$). The impact of IMN coverage was only significant in the t-IMRT group with lower values in the no IMN group ($p=0.001$) (Panels E and F, Figure 4).

The contralateral breast mean dose was not significantly different between VMAT and t-IMRT ($p=0.073$). Within t-IMRT plans, the right breast mean dose was lower if IMN was excluded ($p=0.002$) (Figure 4, Panel F).

The VMAT plans had lower minimum doses to the ipsilateral ribs and intercostal muscles ($p<0.001$), while the maximum dose was not significantly different ($p=0.837$) There was no statistically significant difference to the dose to ipsilateral ribs and intercostal muscles whether IMN was included or not ($p=0.165$ and $p=0.075$, respectively) (Panels G and H, Figure 4).

Discussion

The ATED system in the setting of two-stage approach of post mastectomy reconstruction for breast cancer has been shown to be

Citation: Yeh J, Cokelek M, Tacey M, et al. Retrospective dosimetric comparison of VMAT versus t-IMRT for patients with carbon dioxide tissue expanders undergoing left sided PMRT using the recent ESTRO-ACROP target volume delineation. *Int J Radiol Radiat Ther.* 2022;9(1):6–12.
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safe, efficacious, and comparable to the more traditional saline tissue expanders.[6,16] The design of the device allows patients to gradually fill the expander via a remote-control system, and removes the need for intermittent saline injections, which has been shown to be associated with high patient and clinician satisfaction. It also meant that women who were undergoing adjuvant chemotherapy and developed leukopenia, did not need to interrupt their carbon dioxide expansion process, when they would have for saline expansion.

Due to the potential impact of the metal cylinder on RT dosimetry, ATEDs are generally avoided in women whom adjuvant RT is anticipated.[16] Despite best efforts, there will be cases where patients who opt to have the ATED inserted, have unforeseen pathological findings after surgery, with subsequent recommendations for adjuvant RT to achieve the best oncological outcomes.

The device itself has undergone physical testing to ensure its tolerability to therapeutic doses of RT in the post-mastectomy setting.[7] as well as feasibility (albeit with challenges) with regards to the RT dosimetry within phantom models.[8,17]

In the XPAND trial,[16] 2 of 98 patients in the ATED arm received adjuvant RT given their surgical pathological findings. The RT treatment was completed and both patients also completed their reconstruction after RT successfully. The XPAND II study[6] also included patients who had a history of receiving RT or planned to have RT with the ATED in-situ. The one patient who was planned to undergo RT with the ATED in-situ withdrew from the study before commencement of treatment. In the smaller, non-randomised ASPIRE study,[18] 3 of 21 patients received adjuvant RT with the ATED in-situ, receiving up to 50Gy, with no adverse events reported.

With the introduction of the 2019 ESTRO-ACROP consensus guidelines for volume delineation when treating PMRT after implant-based immediate reconstruction,[1] we envisage there may be clinicians who are keen to implement this when presented with a patient who has this ATED in-situ, given the potential to significantly reduce dose to cardiac structures when compared to conventional target volumes.[13] Minimising RT dose to the heart is well known to be beneficial when it comes to reducing the risk of major coronary or other cardiac events.[19,20]

This study shows that acceptable RT plans can be generated if needing to treat left sided PMRT, targeting the chest wall and regional nodes, using DIBH and VMAT or t-IMRT technique. The lower heart, ipsilateral lung and minimum ribs and intercostal muscle dose shown in this study's VMAT plans can be explained by VMAT technique's ability to "sculpt" RT dosimetry to the PTV, which in this study population, would have had increased distance from the ipsilateral OARs. On the other hand, due to the arc component of VMAT, the contralateral lung and breast dose is understandably higher. Although technically there was no statistically significant difference between the mean right breast dose in VMAT versus t-IMRT plans, the absolute doses were higher in the VMAT plans (range 2.9 – 7.1Gy in VMAT plans versus range 0.7 – 6.7Gy in t-IMRT plans). This can lead to concerns of increased risk of contralateral breast cancer development, especially in those aged under 40 years.[21,22] However, given this patient cohort would have been diagnosed with locally advanced, likely node positive disease warranting adjuvant PMRT and regional nodal irradiation (RNI), the risk of developing a second primary malignancy may be less clinically relevant.

Other published studies attempting to compare different RT techniques for treatment of left sided breast or chest wall RT and regional nodal irradiation (RNI), understandably did not show similar OAR dosimetry outcomes to our study,[23,24] given they did not use the new 2019 ESTRO-ACROP volume delineation guidelines.

Several inherent limitations apply to this small retrospective study. As it was a planning study focused on the evaluation of dosimetry, no clinical data is collected or presented. Other RT techniques such as 3D-conformal RT (3DCRT) or non-DIBH planning scans were not included in this study. The analysis was conducted on paired data for five patients, which did not allow for the testing of the assumption of normally distributed measures. The limited sample size may also have reduced the ability to detect statistically significant differences.

Ultimately, there are both pros and cons to both type of RT techniques in this study cohort. Therefore, the decision of which technique to use should be made on an individual basis, balancing relevant benefits and risks, together with appreciation of each patient's anatomy.

Conclusion

VMAT technique can lower the mean heart dose, ipsilateral lung V20 dose, ipsilateral ribs, and intercostal muscle minimum dose, when treating left sided post mastectomy chest wall and regional nodes with ATED in-situ using the 2019 ESTRO-ACROP volume delineation guidelines. However, it is also associated with higher absolute dose values to contralateral lung and right breast, when compared to t-IMRT technique, whilst maintaining similar target volume coverage. Each patient should be considered individually by their risk factors when deciding which planning technique to use.

Conflicts of interest

Nil.

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