## **Original Research Article**

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## Dosimetric study of hypo fractionated adjuvant post mastectomy radiotherapy with and without bolus and assessment of acute toxicity of treatment: a single institution study

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## ABSTRACT

**Background:** Moderate hypo fractionated PMRT is convenient for patients and is particularly beneficial in busy radiotherapy department like in developing nations. Furthermore, PMRT can be given with or without bolus as per institution protocol. The purpose of this study was to do dosimetric comparison of with and without bolus plans in patient undergoing hypo fractionated PMRT and to assess acute toxicity of treatment.

**Methods:** Our study is single institution prospective study done at DMCH cancer center Ludhiana, Punjab, India. Study period was from March 2020 to October 2020 and we included post mastectomy patients irradiated by hypo fractionated regime. After CT simulation and contouring, rapid arc radiotherapy plans were evaluated and DVH analysis was done for PTV and OARs. Acute toxicity was assessed during treatment and 1 month post radiotherapy treatment. Ethical approval was not taken due to COVID 19 pandemic emergency, but also hypofractionated PMRT is standard of care. Statistical analysis was done on SPSS, Version 20.0

**Results:** A total of 30 patients were analyzed which received mean PTV dose of 42.3Gy in 16 fractions (8 fractions with and 8 without bolus). We were able to achieve adequate PTV coverage in plan sum which included both bolus and non-bolus plan. However, use of bolus resulted in statistically significant increase in low dose volume mainly V4Gy of ipsilateral lung in left sided breast cancer cases. Despite use of bolus no patient had above grade I skin toxicity.

**Conclusions:** Moderate hypo fractionated PMRT with and without bolus is well tolerated with minimal acute side effects. It is important to note that use of bolus results in higher V4Gy volume of ipsilateral lung more precisely in left side breast cancer cases.

Keywords: Intensity modulated radiotherapy, Post astectomy radiotherapy, Regional node irradiation

## **INTRODUCTION**

Post mastectomy radiation therapy (PMRT) has shown to improve breast cancer survival in patients with lymph node positive disease and is important component of multidisciplinary management of locally advanced breast cancer.<sup>1,2</sup> As per NCCN guidelines PMRT is also recommended for node negative tumor  $\leq 5$  cm and with  $\geq 1$  mm margin with multiple high risk factors.<sup>3</sup> Modest hypofractionation improves convenience for patients and is particularly beneficial in busy RT department mainly in developing nations.<sup>4</sup> More over recent reports have shown that hypo fractionated nodal radiotherapy was not associated with increased arm stiffness, lymphedema or

brachial plexopathy compared to conventional fractionated radiotherapy.<sup>5</sup> Result of recently published trial from Beijing, China which treated 820 patients with either a standard fractionation of 50 Gy in 25 fractions or 43.5 Gy in 16 fractions after mastectomy support safety and efficacy of hypo fractionated PMRT.<sup>6</sup> When chest wall is treated, a tissue- equivalent material known as bolus is frequently placed on skin too reduce the skinsparing effects of megavoltage photons and to increase dose to skin, subcutaneous tissue and dermal lymphatics. The bolus techniques used by radiation oncologists when treating the chest wall in postmastectomy setting is heterogenous. As per international survey published in 2006 the use of bolus is frequently determined by personal preference of treating radiation oncologist.7 Currently there is no randomized or prospective clinical evidence to support the use of bolus with regard to frequency of application, distribution of bolus on chest wall and thickness of bolus As yet, there is no research on dosimetric comparison of with and without bolus in PMRT Consequently, it remains unknown what the answer is. In our department we routinely use conventional fractionation for PMRT but in view of COVID-19 pandemic as per institution policy we started using hypofractionation regime for post-operative breast cancer patients which needed adjuvant radiotherapy. Chest wall bolus was used in phase I of prescribed dose. In this study we did dosimetric comparison of hypo fractionated adjuvant PMRT with and without bolus and assessed acute skin reactions during and after treatment.

#### **METHODS**

Single institution prospective study was done at DMCH cancer center Ludhian, Punjab, India. Study was conducted from March 2020 to October 2020. Last follow up of patient was in November 2020. All post mastectomy patients irradiated by hypo fractionated regime were included in study.

#### Inclusion criteria

Patients with invasive breast cancer who underwent mastectomy, non-metastatic disease and who received adjuvant irradiation to chest wall, no restrictions on regional nodal irradiation.

## Exclusion criteria

Patients excluded were those older than 70 years, patients with loco-regionally recurrent tumours, a history of connective tissue disorders and/or cardiac and pulmonary morbidities.

### Procedure

#### Set up and treatment planning

All patients were immobilized while 'free breathing' in supine position on breast board of All-in-One-

immobilization system with both arms abducted and externally rotated. Radiopaque wires were placed on chest wall scar area non-contrast computed tomography (CT) images were taken from lower neck to upper abdomen at 2.5 mm-slice thickness. CT images were imported and contoured in Eclipse planning system version 16.1 (Varian Medical System, Palo Alto, CA).

For clinical target volume (CTV) delineation we followed the Radiation Therapy Oncology Group (RTOG) contouring atlas for breast cancer.8.Regional lymph nodal irradiation was done as per institution protocol. Planning target volume (PTV) was generated by adding 3mm margin around CTV. Organ at risk delineated were ipsilateral and contralateral lung, esophagus, opposite breast, spinal cord and heart.

Lung was contoured in pulmonary window, with inclusion of all inflated, collapsed, fibrotic, emphysematous lung and small vessels extending beyond the hilar region. Hila, trachea and main bronchus were excluded from the lung volume. Heart was delineated as described by Feng et al. Superiorly heart starts just inferior to left pulmonary artery and inferiorly it extends up to the diaphragm.<sup>9</sup>

Treatment plans were generated using the Eclipse planning system, version 16.1 (Varian Medical System, Palo Alto, CA). All patient underwent half beam rapid arc planning. Whole chest wall bolus was placed during first phase of radiotherapy for up to 8 fractions. Whole chest wall bolus was defined as bolus placed on whole chest wall. Thickness of bolus was 1cm. Plans were generated separately for bolus and non-bolus phases. Patient underwent treatment on True Beam Linear accelerator (Varian Medical System, Palo Alto, CA). Daily CBCT was done as per institute protocol daily for patients.

#### Table 1: Plan evaluation parameters.

Structure	Parameter	Preferred objective	Acceptable limits
PTV	D <sup>95%</sup> (%)	≥95% of P.D	≥ 90% of P.D
	$V^{116\%}$ (%)		<3% of PTV
Ipsilateral lung	V <sub>8Gy</sub> (%)	<40%	≤50%
	$V_{16Gy}(\%)$	<35%	≤40%
Heart	Mean dose (Gy)	<4	<6
Opposite breast	Mean dose (Gy)	≤2	≤3Gy

Prescribed dose to PTV was 42.5 Gy in 16 fractions (2.65 Gy/fraction). Photon optimizer, version 13.7.16 was used for inverse optimization with 2.5mm optimization resolution. For calculation, anisotropic analytical

algorithm (version 13.7.16) was used and calculation grid was 2.5mm. Jaw-tracking option was selected to reduce the MLC leakage dose and inhomogeneity correction was applied for all plans. The isocenter was placed at center of PTV volume. The couch angle was set at 0 degree. The collimator angles were set at 350, 10 and 0 degrees. For left and right breast rapid arc plans 2 to 3 arcs were used with gantry angle ranging from 179-to 300 degree and 181-to-60-degree, vise-versa respectively. Our institution treatment planning objective are summarized in (Table 1).

These objectives were determined according to several sources, including recommendations from the Royal College of Radiologists.<sup>10</sup> Objectives from the Alliance A221505 clinical trial of hypo fractionated PMRT.<sup>11</sup>

## Target volume

For PTV, D95% and V 116% were analyzed for all plans.D95% is minimum dose received by 95% of PTV, which indicates the dose coverage.V116% is volume of PTV receiving 116% of prescribed dose, which indicates the maximum dose within PTV.

## Organ at risk

For ipsilateral lung, the parameters V4Gy, V8Gy, V16Gy and mean dose were analyzed. For opposite lung V4Gy was analyzed. Ipsilateral lung V16Gy was calculated to be an approximate biological equivalent dose to evaluating V20Gy in standard fractionation.

Heart constraints were V4Gy, V8Gy, V16Gy and mean heart dose for left sided tumors and mean heart dose for right sided tumor. V XGy represents the volume of organ receiving x Gy dose and D X% represents the minimum dose received by X % of target/OAR.

## Indices

## Homogeneity index

The homogeneity index (HI) has been defined in several ways in literature.<sup>12,13</sup> We used the following formula to calculate the homogeneity index.<sup>14</sup>

 $HI = (D2\% - D98\%/Dp) \times 100$ 

Where, D2% represents the minimum dose received by 2% of PTV (maximum dose), D98% represents the minimum dose received by 98% of PTV (minimum dose) and Dp represents the prescribed dose. The value HI close to zero indicates a more homogenous dose within the PTV.

## Conformity index

Conformity index (CI) has been defined in RTOG as 15.

## CI RTOG = V95% RI/TV

Where V95% RI represents the volume encompassed by 95% of prescription dose and TV represents the target volume.

All the patients underwent baseline clinical examination before start of radiotherapy, and on weekly basis while on treatment followed thereafter by monthly evaluation for at least one months for assessment of acute toxicities. During clinical visits, patients were assessed for development and severity of any acute toxicity including haematological and skin toxicities. All acute toxicity was graded according to Common Terminology Criteria for Adverse Events (CTCAE), version 5.16.

## Ethical approval

Ethical approval was not taken as hypo fractionated chest wall adjuvant radiotherapy is already established protocol 6. In addition we started it as an emergency measure during COVID19 pandemic to reduce number of visits of patients in department.

## Statistical analysis

All data was analyzed using SPSS Statistics for Windows, Version 20.0(IBM Corp., Aemonk, NY, USA).

## RESULTS

## Target volume

A total of 30 patients meeting inclusion and exclusion criteria were analysed out of these 50% (N=15) were left side breast cancer and 50% (N=15) were right side breast cancer The median age of the patients was 53 years (range: 34-66 years). The details of the patients are shown in (Table 2).

All the patients were treated using hypo fractionated PMRT without boost Treatment volume included chest wall with axillary RNI in 93.3.%.(N=28).First 3 intercostal space internal mammary nodal irradiation was done in 83.3%(N=25.).All node positive patients received ipsilateral supraclavicular fossa irradiation.

Mean dose of irradiation to PTV was 42.3Gy in 16 fractions. Phase I of treatment was done with chest wall bolus and in phase II no bolus was used.

Mean dose of radiotherapy with bolus was 21.15Gy in 8 fractions and mean dose of radiotherapy without chest wall bolus was 21.15Gy in 8 fractions. Dosimetric comparison of PTV are shown in (Table 3 and 4).No patient had hot spot within PTV which was 116% of prescribed dose.

For left breast cancer, paired sample t test showed that as compared to non-bolus plan PTV dose coverage

(M=18.14, S.D=2.83) was better with bolus plan (M=20.78, S.D=1.44) t (14) = 5.25, p=001, which is statistically significant and further comparison of bolus plan with plan sum showed that as compared to bolus plan (M=20.42, S.D=0.44) PTV dose coverage was better in plan sum of both bolus and non-bolus plan (M=38.30, S.D=0.44) t (13) = 36.5, p=001, which is statistically significant.

For right breast cancer, paired sample t test showed that as compared to non-bolus plan PTV dose coverage (M=, S.D=19.03, S.D=4.5) was better with bolus plan (M=20.49, S.D-0.39) t (13)=1.25, p=0.23, which is not statistically significant and further comparison of bolus plan with plan sum showed that as compared to bolus plan (M=20.49, S.D=0.39) PTV dose coverage was better in plan sum of both bolus and non-bolus plan (M=38.25, S.D=2.33) t (13)=28, p=001, which is statistically significant.

#### Organ at risk

Detailed lung constraints are shown in (Table 5). T test showed that for left sided breast cancer, as compared to bolus plan, low dose volume mainly V 4Gy of ipsilateral lung (M=45.91,S.D=6.94) was less with non-bolus plan (M=44.04, S.D=7.39), t (14)=2.74, p=0.01, which is statistically significant. Further low dose volume mainly V4Gy of ipsilateral lung was less in non -bolus plan (M=49.0, S.D=13.73) compared to plan sum which included both bolus and non-bolus plan (M=77.9, S.D=14.5) t (15)=5.58, p=0.01, which is statistically significant. Low dose volume and mean dose to heart was not statistically different in bolus and non-bolus plan for left sided breast cancer as shown in (Table 6).

In plan sum which included both bolus and non-bolus plan mean dose to heart was 4.2Gy,to esophagus was 13 Gy and to opposite breast was 2.4Gy

#### Monitor units

Monitor unit used are show in (Table 7).

We found no significant difference in monitor unit used in bolus and non-bolus plans for both left and right sided breast cancer patients

### Table 2: Demographic details of patients.

Patient related variable	Number (%)		
Histology			
Infiltrating ductal carcinoma	29 (96.7)		
Others	1 (3.3)		
Grade of tumor			
Gx	3 (10)		
G1	6 (20)		
G2	16 (53.3)		
G3	5 (16.7)		
Pathological T stage			
Тх	1 (3.3)		
pT0	2 (6.7)		
T1	4 (13.3)		
T2	20 (67.7)		
Т3	2 (6.7)		
T4	1 (3.3)		
Pathological N stage			
Nx	1 (3.3)		
N0	6 (20)		
N1	4 (13.3)		
N2	8 (26.7)		
N3	11 (39.7)		
Final post op HPT stage			
pCR	2 (6.7)		
ĪA	2 (6.7)		
IIA	3 (10)		
IIB	4 (13.3)		
IIIA	7 (23.3)		
IIIB	2 (6.7)		
IIIC	10 (33.3)		
Hormone receptor positivity			
Positive	18 (60)		
Negative	12 (40)		
Her2/neu status			
Positive	9 (30)		
Negative	21 (70)		
Chemotherapy prior to			
radiotherapy			
Neoadjuvant	9 (30)		
Adjuvant	28 (93.3)		

#### Table 3: Dosimetric comparison of PTV with and without bolus of left and right sided breast cancer.

Variables	Left side		Right side	
	With bolus	Without bolus	With bolus	Without bolus
PTV D95%	20.78±1.44	18.14±2.83	20.49±0.39	19.03±4.5
HI	$0.24 \pm 0.04$	0.41±0.16	0.24±0.03	0.35±0.17
CI	1.21±0.04	1.06±0.14	1.06±0.30	1.04±0.06

## Table 4: Dosimetric comparison of PTV with bolus and in plan sum (combined with and without bolus) of left and right sided breast cancer.

Variables	Left side		Right side	
	With bolus	Plan sum	With bolus	Plan sum
PTV D <sub>95%</sub>	$20.42 \pm 0.44$	38.30 ±0.44	20.49±0.39	38.25±2.33
HI	$0.24 \pm 0.04$	0.11±0.09	0.24±0.03	0.11±0.08
CI	1.21±0.16	1.04±0.39	1.06±0.30	1.04±0.06

## Table 5: Dosimetric comparison of lung dosage with and without bolus of left and right sided breast cancer.

Variables	Left breast			Right breast		
	With bolus	Without bolus	P value	With bolus	Without bolus	P value
Ipsilateral lung						
V <sub>4Gy</sub>	45.91±6.94	44.04±7.39	0.01	45.02±4.3	47.21±8.24	0.36
V <sub>8Gy</sub>	24.13±2.12	23.70±2.45	0.10	22.70±2.13	23.81±3.69	0.34
V 16Gy	9.45±3.05	9.16±3.05	0.30	8.35±1.51	8.96±2.96	0.41
Mean	5.92±0.46	5.79±0.45	0.11	5.83±0.34	61.15±1.16	0.35
<b>Contralateral lung</b>						
$V_{4Gy}$	16.39±7.84	16.37±6.67	0.97	8.32±5.08	12.32±11.19	0.21
Mean	2.22±0.77	2.19±0.73	0.62	1.79±0.31	2.03±0.17	0.26

## Table 6: Dosimetric comparison of heart dosage with<br/>and without bolus of left sided breast cancer.

Left breast cancer				
	Bolus	Non-bolus	P value	
V <sub>4Gy</sub>	$17.6 \pm 16.1$	$16.5 \pm 14.8$	0.43	
V <sub>8Gy</sub>	$7.8 \pm 10.1$	6.7±8.8	0.47	
V <sub>16Gy</sub>	$1.9{\pm}2.6$	$0.75 \pm 1.1$	0.50	
Mean	3.2±1.7	2.0±81.2	0.50	

# Table 7: Mean value of MU used in with and withoutbolus plan for left and right sided breast cancer.

Monitor units		P value
Left breast		
With bolus	942.7±215	0.73
Without bolus	935.5±190	
Right breast		
With bolus	1036±396.4	0.46
Without bolus	1022.79±113.3	

## Acute toxicities of treatment

Prior to radiotherapy, 16.7% (N=5) had grade I anemia, 16.7% (N=5) had grade II and 6.7% (N=2) had grade III anemia. In addition all these patients had received prior adjuvant chemotherapy. At end of radiotherapy 20% (N=6) had grade I anemia and 6.7% (N=2) had grade II anemia. There was no grade III anemia at end of radiotherapy. Also, no patient had worsening of anemia while on radiotherapy. At one-month post radiotherapy 4 patients had grade I anemia and 1patient had grade II anemia. Before start of radiotherapy 10% (N=3) had grade II eukocytopenia and 3.3% (N=1) had grade II

leukocytopenia. Again, all these patients had received adjuvant chemotherapy.

## Table 8: Hematological toxicity following hypofractionated chest wall radiotherapy.

Acute hematological toxicity	At completion	One month after radiotherapy
Anemia		
Grade 0	16	25
Grade I	7	4
Grade II	5	1
Grade III	2	0
Grade IV	0	0
Leukocytopenia		
Grade 0	22	28
Grade I	6	2
Grade II	2	0
Grade III	0	0
Grade IV	0	0
Thrombocytopenia		
Grade 0	30	30
Grade I	0	0
Grade II	0	0
Grade III	0	0
Grade IV	0	0

At end of radiotherapy 20% (N=6) had grade I leukocytopenia and 3.3% (N=1) had grade II anemia. Chi square test suggested that there is no significant difference in grade I and II of leukocytopenia after completion of radiotherapy,  $X^2$  (1) = 2.0, p=0.15. At one-

month post radiotherapy 2 patients had grade I leucopoenia patient had thrombocytopenia Acute hematological toxicity of group are shown in (Table 8).

All patients were observed for skin toxicity as per acute Radiation Therapy and Oncology Group (RTOG) morbidity scoring criteria.76.7% (N=23) has grade 0 skin reaction and 20% (N=6) had grade I skin reaction. One patient did not come on follow up during radiotherapy. It is important to note that there was no grade II or III skin toxicity seen in our study. After 1-month post radiotherapy 93.3% (N=28) had grade 0 toxicity and 3.3% (N=1) had skin I toxicity Paired sample t test showed that as compared to skin toxicity after completion of radiotherapy, the recovery in dermatological toxicity at one-month post radiotherapy was better (M=0.17, S.D=0.39) t (28)=2.4, p=0.023, which is statistically significant. Bar diagram of acute skin reactions are shown in (Figure 7).





#### DISCUSSION

The superiority of hypofractionation PMRT in terms of PTV coverage, normal tissue sparing and dose homogeneity has been demonstrated in previous studies.<sup>17,18</sup> Moreover, there is no established consensus regarding the use of bolus for delivery of chest wall PMRT. Furthermore, there is a significant clinical variation in use of bolus, often at the discretion of individual clinician. Likewise, regimes have been developed with bolus application for a proportion of radiotherapy fractions. Most importantly, these regimes have been shown to be effective in increasing surface and skin dose in overall treatment, even though a bolus is not used for every fraction.<sup>19</sup> Presently there is paucity of data which has compared hypo fractioned chest wall irradiation with and without bolus. It is important to note that our study has shown that target coverage is better with hypo fractionated plan sum PMRT which included both with and without bolus plan with HI of 0.11±0.09 for left sided and 0.11±0.08 for right sided plan along with CI of 1.04±0.39 and 1.04±0.06 for left and right side respectively as compared to plans with only bolus or no bolus used. Likewise, Camarota et al study has also demonstrated that hypo fractionated radiation techniques offered superior dose homogeneity PTV coverage.<sup>20</sup>

Studies have shown that target coverage tends to decrease in PTV with RNI, so was with our study. The PTV D 95% was 91% of prescribed dose in plan sum PMRT which included both bolus and non-bolus plan.<sup>21</sup> Most importantly, this underdosing is a result of geometric miss of PTV chest wall at the medial or lateral ends, as attempting to cover the entire PTV leads to beam passing through the contralateral breast, or excessive dose to lung and heart. Similarly, Tanaka et al., also showed the mean V90 and V95 seen with free breathing technique were 96.2% and 91%, respectively

The addition of RNI does potentially increase the rate of pneumonitis as more lung is exposed to treatment fields and was noted to increase pneumonitis rates in the MA-20 trial compared to WBI without RNI (1.3% vs. 0.2%, p = 0.01).<sup>22</sup> While limited prospective data exist regarding hypo fractionated chest wall with RNI and pneumonitis risk. However, a small study from Belgium demonstrated a reduced risk of pneumonitis with hypofractionated RNI compared with standard fractionation RNI which was confirmed by non-randomized data from Thailand and Greece.<sup>23,24</sup> It is important to note that we in our study was able to achieve ipsilateral lung V 16Gy 23.4 % ,S.D 2.1 in plan sum PMRT which included both bolus and non-bolus plans.

Chang et al reported that no significant changes were found in cardiac function (ejection fraction,summed stress defect scores) after radiotherapy with mean heart dose of <5Gy. We were able to achieve 4.2Gy mean heart dose of plan sum PMRT which included both bolus and non-bolus plans.<sup>25,26</sup>

Hypofractionation does not appear to pose a higher risk of cardiac complications when compared to conventional RT. For example, in the report by Chan et al., with a median follow up of more than 14 years, the excess death due to cardiac causes was similar between conventional and HFRT (4.8 and 4.2%, respectively).<sup>27</sup> On the other hand, there is a potential increase in risk of late cardiotoxicity with more extreme hypofractionation. Likewise, a report by Tjessem et al., suggested that severe hypofractionation (43 Gy in 10 daily fractions) could increase the risk of cardiac injury.<sup>28</sup> Thus caution must be exercised in adopting a more aggressively hypo fractionated regimen more precisely, for left sided breast cancer.

On comparing with and without bolus plans we found that bolus plan resulted in significant (p value 0.01) higher ipsilateral lung dosage mainly the low dose volume (V 4Gy) in left breast cancer patients but no significant change was seen in V8Gy, V 16Gy and mean dosage. In sum, we found that application of bolus is the cause of increase in low dose volume regions of ipsilateral lung in left sided breast cancer patients. In our study haematological toxicity secondary to RT was generally low, moreover, it is at least partially the result of prior chemotherapy received by the patient. Similarly, Deshmukh et al conducted an observational prospective study on 56 patients with breast cancer who underwent mastectomy and adjuvant chest wall with or without axillary lymph nodes irradiation (2.66 Gy/fr., 5 fractions per week, total dose 42.5 Gy), and found the incidence of acute haematological toxicity to be very low.<sup>29</sup> Furthermore, the reported toxicities may have been the result of prior chemotherapy received by patients, and thus their association with radiotherapy is not justified.

Acute skin toxicity experienced by our patients was generally mild, specifically, none of patient experiencing moist desquamation at the completion of treatment. In contrast, there were only grade I reactions at the completion of treatment, which resolved in 93.3% of patients over subsequent one month follow up. Likewise, in a similar report by Nandi et al., none of the patients developed grade IV acute reactions.<sup>30</sup> It is important to note that in a study by Arti et al, moist desquamation (MD) was higher in patient undergoing conventional (10.9%) compared with hypo fractionated therapy (1.8%; P=0.05) PMRT.<sup>31</sup> Similarly, another study comparing conventional with hypo fractionated radiotherapy reported that conventional fractionation was associated with significantly higher rates of grade  $\geq 2$  dermatitis.<sup>32</sup> Most importantly ,acute skin toxicity with hypo fractionated PMRT appears to be moderate and is usually self-limited, provided care is taken to avoid significant dose inhomogeneity. Futhermore, data from retrospective studies suggest that large dose inhomogeneity (V>107%) predisposes to more severe acute skin reactions.<sup>33</sup> Likewise. two randomized trial has shown that IMRT compared to two-dimensional radiotherapy resulted in decreased acute skin reactions.<sup>34,35</sup> Some studies have shown that the use of a bolus is associated with greater acute and late effects including moist desquamation and skin telangiectasia.<sup>36</sup> On the other hand Soong et al reported no difference in acute toxicity was seen between the bolus and no-bolus groups.<sup>37</sup> It is important to note that in this study thickness of bolus used was 0.5cm and was applied on alternate days. Most importantly, the reason why we did not have moist desquamation reported in our study could by that we used 0.5cm bolus only for first eight fractions of our hypo fractionated PMRT regime. In addition, there was no dose inhomogeneity in all our rapid arc plans.

## Limitation

Limitation of our study was that we was not able to report on late toxicity. However our study results suggest that acute side effects were minimal with use of 0.5cm bolus for first 8 fractions of moderate hypo fractionated PMRT regime. More precisely, especially for left sided breast cancer patients bolus use resulted in significant higher low dose volume in ipsilateral lung. Consequently, clinicians can take into consideration the indications for use of bolus after PMRT as highlighted by Vu et al, which include skin involvement, inflammatory disease, close or positive margin or LVI-positive tumours. Other limitation of our study was that sample size was less.

## CONCLUSION

The conclusion of our study is that PTV coverage is statistically significant better in plan sum PMRT of both bolus and non-bolus compared to non-bolus and bolus plans. Respectively in both left sided breast and right sided breast cancer patients. In contrast, use of bolus result in statistically increase in low dose volume mainly V 4Gy of ipsilateral lung in left sided breast cancer patients. Acceptable acute tolerance is seen with moderate hypo fractionated PMRT and it should be considered a viable option in chest wall and regional irradiation.

Further large RCT in this area would be helpful in clarifying the role of bolus in post mastectomy patients undergoing moderate hypo fractionated regime radiotherapy.

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#### REFERENCES

- 1. Overgaard M, Hansen P, Overhaard J. Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. N Engl J Med. 1997;337:949-55.
- 2. Overgaard M, Jensen M, Overgaard J. Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82C randomized trial. Lancet. 1999;353:1641-8.
- Oncology. NCCN clinical practice Guidlines in. Breast cancer. Available at https: //www. nccn. org/professionals/physician\_gls/pdf/breast.pdf. Accessed on 12 September 2020.
- 4. Khan AJ, Rafique R, Zafar W, Shah C, Haffty BG, Vicini F. Nation-scale adoption of shorter breast radiation therapy schedules can increase survival in resource constrained economies. Markov Chain Analysis. 2017;97:287-95.
- Leong N, Truong PT, Tankel K, Kwan W, Weir L, Olivotto IA, et al. Hypofractionated nodal radiation therapy for breast cancer was not associated with increased patient-reported arm or brachial

plexopathy symptoms. Int J Radiat Oncol Biol Phys. 2017;99:1166-72.

- 6. Wang SL, Fang H, Song YW, Hu C, Liu YP. Hypofractionated versus conventional fractionated post mastectomy radiotherapy for patients with high-risk breast cancer: a randomised, noninferiority, open-label, phase 3 trial. Lancet Oncol. 2019;20:352-60.
- 7. Pignol JP, Rakovitch E, Paszat L. Variability in radiation oncologists' opinion on the indication of a bolus in post-mastectomy radiotherapy: an international survey. Clin Oncol. 2007;19:115-9.
- 8. RTOG. Breast cancer atlas for radiation therapy planning; consensus defination. 2018.
- 9. Feng M, Moran JM, Koelling T, Chughtai A, Chan JL, Freedman L, et al. Development and validation of a heart atlas to study cardiac exposure to radiation following treatment for breast cancer .Int J Radiat Oncol Biol Phys. 2011;79:10-8.
- Postoperative radiotherapy for breast cancer: UK consensus statements. The Royal College of Radiologist, London. 2016. Available at https://www.rcr.ac.uk/system/files/publication/field \_publication\_files/bfco2016\_breast-consensusguidelines.pdf. Accessed on 12 October 2020.
- 11. Poppe M. Hypofractionated radiation therapy after mastectomy in preventing recurrence in patients with stage IIa-IIIa breast cancer.2017. Available at https://clinicaltrials.gov/ct2/show/record/NCT03414 970. Accessed on 20 September 2020.
- Shaw E, Kline R, Gillin M, Souhami L, Hirschfeld A, Dinapoli R, et al. Radiation therapy oncology group: radiosurgery quality assurance guidelines. Int J Radiat Oncol Biol Phys. 1993;27:1231-9.
- Commission on radiation units and measurements. Measurements report prescribing, recording and reporting photon-beam intensity-modulated radiation therapy (IMRT). Bethestha Oxford University Press. 2010.
- Wu Q, Mohan R, Morris M, Lauve A, Ullrich SR. Simultaneous integrated boost intensity-modulated radiotherapy for locally advanced head-and-neck squamous cell carcinomas dosimetric results. Int J Radiat Oncol Biol Phys.2003;56:573-85.
- 15. Bethesda MD. International Commission on Radiation Units and Measurements, Prescribing, Recording and Reporting Photon Beam Therapy (Supplement to ICRU Report 50), ICRU Report 62: International Commission on Radiation Units and Measurements. 1999.
- 16. Common Terminology Criteria for Adverse Events (CTCAE), version 5: U. S. department of health and human services, 2017.
- Hijal T, Bidoz FN, Pena CP, Kirova YM, Zefkili S, Bollet MA, et al. Simultaneous integrated boost in breast conserving treatment of breast cancer: a dosimetric comparison of helical tomotherapyand three-dimensional conformal radiotherapy. Radiother Oncol. 2010;94:300-6.

- Zhou GX, Xu SP, Dai XK, Ju ZJ, Gong HS, Xie CB, et al. Clinical dosimetric study of three radiotherapy techniques for postoperative breast cancer: Helical Tomotherapy, IMRT and 3D-CRT. Technol Cancer Res Treat. 2011;10:15-23.
- 19. Pierce LJ, Lichter AS. Defining the role of postmastectomy radiotherapy: the new evidence. Oncology. 1996;10:991-1002.
- 20. Camarota F, Giugliano FM, Iadanza L, Cutillo L, Muto M, Toledo D, et al. Hypofractionated breast cancer radiotherapy. Helical tomotherapy in supine position or classic 3D-conformal radiotherapy in proneposition: which is better? Anticancer Res. 2014;34:1233-8.
- 21. Chitapanarux I, Nobnop W, Tippanya D, Sripan P, Chakrabandhu S, Klunklin K, et al. Clinical outcomes and dosimetric study of hypofractionated Helical Tomo Therapy in breast cancer patients. PLoS ONE.2019.
- 22. Whelan TJ, Olivotto IA, Parulekar WR, Ackerman I, Chua BA, Nabid A, et al. Regional nodal irradiation in early-stage breast cancer. N Engl J Med. 2015;373:307-16.
- 23. Koukourakis MI, Panteliadou M, Abatzoglou MI, Sismanidou K, Sivridis E, Giatromanolaki A, et al. Postmastectomy hypofractionated and accelerated radiation therapy with (and without) subcutaneous amifostine cytoprotection. Int J Radiat Oncol Biol Phys. 2013;85:7-13.
- 24. Pinitpatcharalert A, Chitapanarux I, Euathrongchit J, Tharavichitkul E, Lorvidhaya V. A retrospective study comparing hypofractionated radiotherapy and conventional radiotherapy in postmastectomy breast cancer. J Med Assoc Thai. 2011;94:94-102.
- 25. Chang E ,Corbett JR, Moran JM, Griffith KA, Marsh RB, Feng M, et al. Is there a dose-response relationship for heart disease with low-dose radiation therapy? Int J Radiat Oncol Biol Phys. 2013;85:959-64.
- 26. Tanaka H, Hayashi S, Hoshi OK. Impact of respiratory motion on breast tangential radiotherapy using the field-in-field technique compared to irradiation using physical wedges. Radiol Oncol. 2014;48(1):94-8.
- 27. Chan EK, Woods R, Virani S, Speers C, Wai ES, Nichol A, et al. Long-term mortality from cardiac causes after adjuvant hypo-fractionated vs.conventional radiotherapy for localized left-sided breast cancer. Radiother Oncol. 2015;114(1):73-8.
- 28. Tjessem KH, Johansen S, Malinen E, Reinertsen KV, Danielsen T, Fossa SD, et al. Long-term cardiac mortality after hypofractionated radiation therapy in breast cancer. Int J Radiat Oncol Biol Phys. 2013;87(2):337-43.
- 29. Deshmukh S, Sharan K, Fernandes DJ, Srinivasa VM, Yathiraj PH, Singh A, et al. A Study on dosimetric outcomes and acute toxicity of post mastectomy adjuvant hypofractionated radiotherapy for breast cancer. J Clin Diagn Res. 2016;10:5-8.

- Nandi M, Mahata A, Mallick I, Achari R, Chatterjee S. Hypofractionated radiotherapy for breast cancers - preliminary results from a tertiary care center in Eastern India. Asia Pac J Cancer Prev. 2014;15(6):2505-10.
- 31. Parekh A, Dholakia AD, Zabranksy DJ, Asrari F, Camp M, Habibi M, et al. Predictors of radiationinduced acute skin toxicity in breast cancer at a single institution: role of fractionation and treatment volume. Adv Radiat Oncol. 2018;3:8-15.
- 32. Ali EM, Khalil M, Mageed A. Post-mastectomy hypofractionation radiotherapy in breast cancer patients. Cancer Oncol Res. 2014;2:87-93.
- Chen MF, Chen WC, Lai CH, Hung CH, Liu KC, Cheng YH et al. Predective factors of radiationinduced skin toxicity in breast cancer patients. BMC Cancer. 2010;10:508.
- 34. Donovan E, Bleakley N, Denholm E, Evans P, Gothard L, Hanson J, et al. Randomised trial of standard 2D radiotherapy (RT) versus intensity modulated radiotherapy (IMRT) in patients prescribed breast radiotherapy. Radiother Oncol. 2007;82:254-64.
- 35. Barnett GC, Wilkinson J, Moody AM, Wilson CB, Sharma R, Klager S, et al. A randomized controlled

trial of forward-planned radiotherapy (IMRT) for early breast cancer: baseline characterisics and dosimetry results. Radiother Oncol. 2009;92:34-41.

- 36. Pignol JP, Vu TTT, Mitera G, Bosnic S, Erkooijen HM, Verkooijen HM, et al. Prospective evaluation of severe skin toxicity and pain during postmastectomy radiation therapy. Int J Radiat Oncol Biol Phys. 2015;91:157-64.
- 37. Soong IS, Yau TK, Yeung RW, Sze WM, Lee AWM. Post-mastectomy radiotherapy after immediate autologous breast reconstruction in primary treatment of breast cancers. Clin Oncol. 2004;16:283-9.

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