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Hypofractionated volumetric modulated arc therapy with SIB adjuvant to breast preservation surgery: retrospective experience from a Regional Cancer Centre in Eastern India

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Original Article

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Abstract

Background: The incidence of breast cancer has surpassed cervical cancer in India and it has now become the most common cancer in women. Multiple randomised studies have reported low α/β value in the range of 3–4 for breast cancer, which predict a potential radiobiological advantage for hypofractionated radiotherapy resulting in such schedules becoming standard in many centers with reduction in overall treatment time. Volumetric modulated arc therapy (VMAT) is a novel technique of delivering radiotherapy that reduces treatment delivery time, requires less monitor units (MU) and offers good conformity. The mean dose to normal tissue may be minimised using this technique although there will be inferior sparing if we consider the low-dose volume such as V_5, the effect of which is not quantifiable yet.

Aim: Reporting acute toxicity, cosmetic effects, and quality of life in patients of early breast cancer treated with adjuvant hypofractionated VMAT with SIB.

Material and Methods: The records of 44 patients registered at the hospital between August 2014 and December 2015 were included in this analysis. Acute toxicities were analysed using CTCAE v4.03. Cosmetic outcomes were assessed using Harvard scale, while quality of life outcomes were assessed using EORTC scales and Health Related quality of life (HRQOL) questionnaires (QLQ-C30 and QLQ-BR23).

Results: No grade ≥2 skin toxicities were recorded. Breast pain was recorded as Grade 1 in 13·8% patients and Grade 1 fatigue in 18·2%. The maximum haematological abnormality grade recorded was Grade 1. Cosmesis was assessed at the baseline, 6 months, 1 year and 2 years. A total of 88·6% of the patients had an Excellent or good cosmesis at the baseline, which was similar even at 6 months, at 88·7%, improved further at 1 year to 90·9%. At 6 months post radiotherapy, high functional scale QOL scores were noted.

Conclusion: The technique is associated with minimum acute toxicity, good to excellent cosmesis and acceptable quality of life.

Introduction

The most common cancer diagnosed in women worldwide is breast cancer, and even in Indian women, the incidence rate of breast cancer has surpassed cervical cancer.[1] Randomised clinical trials in early stage breast cancer patients have demonstrated that adjuvant irradiation lowers the relative risk of ipsilateral breast tumour recurrence by approximately 70% at 5 years with a 5% absolute improvement in 15-year overall survival, following breast conserving surgery.[2] Multiple randomised studies have also reported low α/β value in the range of 3–4 for breast cancer that predict a potential radiobiological advantage for hypofractionated radiotherapy.[3–5] Recently, there has been a renewed interest worldwide in hypofractionated radiotherapy schedules for breast cancer,[3,4,6–8] which reduce the overall treatment time and consequently are resource sparing and beneficial, both for the patients, as well as for the hospitals with heavy patient load that can treat larger number of patients. These schedules have now become standard of care in many centers across the world. Intensity Modulated Radiation Therapy (IMRT) technique has been successfully used for radiation treatment of many disease sites and has also been found to improve the dose distribution between the target and non-target tissues in breast cancer patients with decrease in the dose to critical normal tissues such as heart and lung, which come in the path of radiation beams.[9] IMRT also provides the possibility to integrate the boost [simultaneous integrated boost (SIB)] in daily radiation sessions by increasing the dose per fraction within the boost volume with added advantage of completion of treatment schedule within a short period of three weeks.[10,11] Volumetric modulated arc therapy

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(VMAT) is a novel technique of delivering radiotherapy that reduces treatment delivery time, requires less monitor units (MU) and offers good conformity. The mean dose to normal tissue may be minimised using this technique although there will be inferior sparing if we consider the low-dose volume such as V_5, the effect of which is not quantifiable yet.[12]

This report analyses data of 44 patients of early breast cancer who underwent breast conserving surgery (BCS), treated in this hospital with adjuvant hypofractionated VMAT and SIB, in the context of toxicity, cosmetic effects and quality of life.

Material and Methods

This retrospective, observational study was done at the Department of Radiation Oncology, Chittaranjan National Cancer Institute (CNCI), Kolkata, which is a Regional Cancer Center of Eastern India located in the state of West Bengal. The treatment records of 44 eligible Breast Cancer (Infiltrating Duct Carcinoma/other subtypes) patients registered at the Radiation Oncology Department between August 2014 and December 2015 for adjuvant radiation therapy with hypo-fractionated VMAT and SIB, after margin negative BCS, with pTNM T1–T3 and/or N0–N1, aged between 18 and 60 years with ECOG performance status 0–2, baseline hematological and biochemical parameters within normal limit and having no pulmonary or cardiac morbidity were included in the present analysis. Due approval of the institutional Ethical Committee was obtained and informed consent was taken from all the eligible patients before analysing their data. Data collection from patient follow-up data was done up to March 2018.

Radiation therapy

The CT-Simulation was performed with the patient lying in supine position on a breast board, with both arms raised above the head. Radio-opaque wires were placed to identify the outline of the clinically palpable breast. CT dataset was acquired with 3-mm-thick adjacent slices. No respiratory gating was adopted.

The breast Clinical Target Volume (CTV_{WB}) included the palpable breast tissue demarcated with radio-opaque markers at CT Simulation and was delineated in accordance with Radiation Therapy Oncology Group (RTOG) Breast Cancer Atlas[13] and consensus guidelines. It was limited anteriorly within 3 mm from the skin and posteriorly to the anterior surface of the pectoralis major and serratus anterior muscles excluding the chest wall.

The breast Planning Target Volume (PTV_{WB}) was created by 3D expansion of the CTV by 7 mm (excluding heart and did not cross midline) and anteriorly covering up to skin.

The boost Clinical Target Volume (CTV_{BOOST}) was defined as 1 cm of breast tissue beyond the delineated surgical cavity to include possible microscopic disease, and was limited posteriorly at anterior surface of the pectoralis major and antero-laterally 3 mm from the skin.

PTV_{BOOST} was created by 7 mm 3D expansion of CTV_{BOOST}. Figure 1 displays the dose distribution in target volumes in different planes.

VMAT treatment planning using a 3D treatment planning system (CMS MONACO v.5.00.04, ELEKTA, Stockholm, Sweden) was performed. One or two partial arcs were used for a particular plan. The plans were approved when at least 90% of the PTV_{WB} received at least 90% of the prescription dose (40 Gy/15#), although the goal was to deliver minimum 95% of the prescription dose to 95% of the PTV_{WB}. For PTV_{BOOST}, the goal was to deliver the 95% of the prescription dose (48 Gy/15#) to minimum 98% of the PTV. Figure 2 is a representative Dose Volume Histogram (DVH) from our study series.

Dose prescriptions and constraints

Prescribed doses to different target volumes and dose constraints for organ at risk (OAR) are summarised in Table 1.

Before each treatment, the set-up reproducibility was checked daily with the patients' position being verified using Image-guided radiotherapy (IGRT) with kV cone beam CT.

External skin localising marks, which included permanent tattoos, were used for radiation localization and for set-up accuracy.

Radiation-induced acute toxicities were reported and analysed using CTCAE v4.03[14] during treatment and follow-up period by history taking and clinical examination by the physicians. All patients were called for monthly follow-up for first 3 months and thereafter 3 monthly as per institutional protocol. Cosmetic outcomes were assessed using Harvard scale, while quality of life outcomes were assessed using EORTC scales and Health-Related quality of life (HRQOL) questionnaires (QLQ-C30[15] and QLQ-BR23[16]) at baseline and at 6 months, 1 year and 2 years post treatment by the physicians.

Results

Clinical profile

The median age of our study population was 48·5 years. Among 44 total patients, 28 patients presented with stage II disease, 27 patients had left-sided breast cancer and 43 patients had invasive ductal carcinoma. The clinical profile is depicted in Table 2.

Dose distribution

Satisfactory target coverage was achieved with optimal sparing of organ at risks.

Table 3 shows the doses received by heart, ipsilateral and contralateral lung.

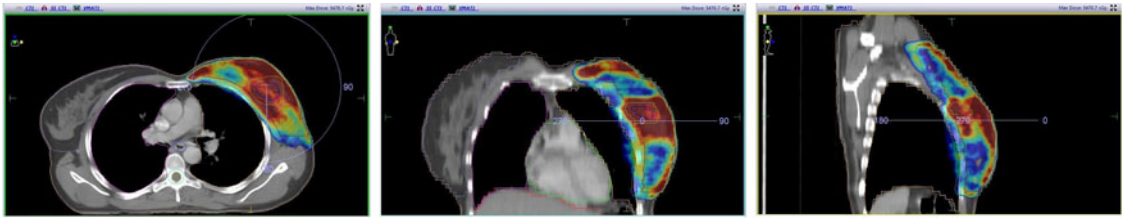

Figure 1. Dose distribution in target volumes in axial, coronal and sagittal planes.

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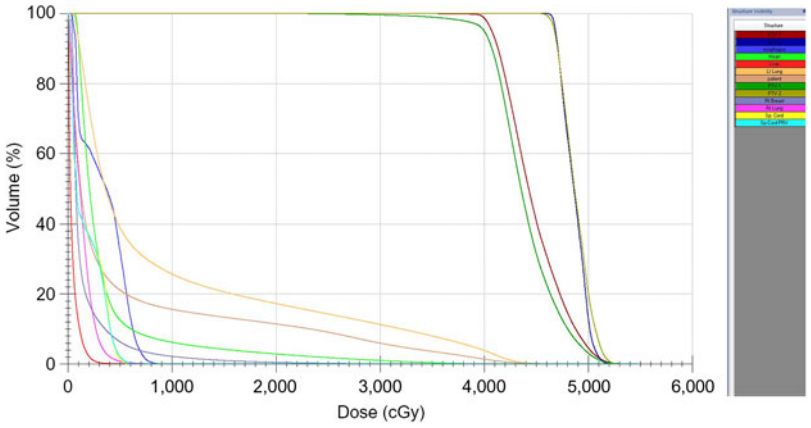

Figure 2. DVH.

Table 1. Dose prescription

$PTV_{WB\ (whole\ breast)}$	40 Gy/15#
PTV_{BOOST}	48 Gy/15#
I/L (ipsilateral) lung	$V_{16} \leq 20\%$, $V_8 \leq 40\%$, $V_4 \leq 55\%$
C/L (contralateral) lung	$V_4 \leq 15\%$
C/L (contralateral) breast	D_{MEAN} 1·5–2 Gy
Heart (for left sided breast cancer)	$V_{20} \leq 5\%$, $V_8 \leq 35\%$, $D_{MEAN} \leq 4$ Gy
Heart (for right sided breast cancer)	$V_{20} = 0\%$, $V_8 \leq 15\%$, $D_{MEAN} \leq 4$ Gy

Table 2. Clinical profile

Age (in years)	Mean ± SD Median	45·11 ± 6·76 48·5 (24–60)
TNM stage	Stage I	10
	Stage IIA	8
	Stage IIB	20
	Stage IIIA	6
Laterality	Left	27
	Right	17
Histological subtype	IDC Other	43 1
Grade	Grade 1 Grade 2 Grade 3	4 34 6
Immunohistochemical	ER +	32
Profile	ER −	12
	PR +	27
	PR −	17
	Her2neu +	18
	Her2neu −	26
Margins status	Free Positive	44 Nil

Acute toxicity

Acute toxicity was graded according to CTCAE criteria v4.03.[14] The parameters taken into account were skin toxicity (dermatitis), breast pain, fatigue and hematological abnormalities. Skin toxicity was the most common acute toxicity followed by hematological toxicity and fatigue. Table 4 demonstrates the distribution of different toxicities with grades.

Cosmetic outcome

Cosmetic outcomes were assessed according to Harvard scale at baseline and at 6 months, 1 year and 2 years post treatment. Most patients had good or excellent cosmesis. Table 5 demonstrates the cosmetic outcomes observed in our patients.

Quality of life

In the present study, Quality of life (QOL) was assessed using EORTC QLQ-C30[15] and EORTC QLQ-BR23[16] questionnaires validated in Hindi or Bengali languages. Table 6 summarises the QOL assessment results.

Discussion

Acute toxicity

In this study, Grade 2 or higher skin toxicity was not recorded and Grade 1 Breast Pain was recorded in only 13·8% of patients. Scorsetti et al.[11] conducted a study with over 50 patients with early breast cancer post BCS. A hypofractionated VMAT with SIB was used and the dose used was 40·5 Gy in 15 fractions to the whole breast with SIB of 48 Gy in 15 fractions over 3 weeks. Grade 2 skin toxicity was not found in any patients. In that study, a single Grade 3 skin toxicity was recorded, which was one of the three cases where a bilateral breast irradiation was performed. Formenti et al.[17] had already confirmed the feasibility of hypofractionated breast radiotherapy using a 3-week schedule with similar results. In a study published by Chadha et al.,[18] there was no significant difference in acute toxicities between the conventional arm and the hypofractionated arm (40·5 Gy in 2·7 Gy per fraction to whole breast with a concomitant surgical bed boost of 4·5 Gy in 0·3 Gy per fraction in 15 total fractions). In the hypofractionated arm of Chadha et al., Grade 2 or higher skin toxicity was seen in 4% of the patients and breast pain of Grade 1 or higher was recorded in 32% patients. Fatigue is one of the most bothersome symptoms

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Table 3. Dose to OAR

Organ	Parameter	Value (%)
Heart	Mean V_{16}	1·44
	Mean of mean doses	3·49Gy
Ipsilateral lung	Mean V_{16}	14·20
	Mean V_8	24·50
Contralateral lung	Mean V_4	1·93

Table 4. Acute toxicity profile

	Grade 0		Grade 1		Grade 2		Grade 3	
Acute toxicities	Number	%	Number	%	Number	%	Number	%
Skin toxicity	15	34·1	29	65·9%	0	0	0	0
Breast pain	38	86·4	05	11·4%	1	2·3%	0	0
Fatigue	36	81·8	08	18·2%	0	0	0	0
Haematological	35	79·5	09	20·5%	0	0	0	0

Table 5. Cosmesis at different time period

Cosmesis grade	Cosmesis at baseline (no. of patients)	Cosmesis at 6 months (no. of patients)	Cosmesis at 1 year (no. of patients)	Cosmesis at 2 years (no. of patients)
Excellent	23	19	21	20
Good	16	20	19	22
Fair	5	4	3	1
Poor	0	1	1	1

Table 6. QOL assessment

QLQ-C30 version 3.0 Questionnaire		QLQ-BR23 Questionnaire
QL2 (global health status/ QoL-revised)		BRBI (body image)
Mean ± SD	82·57 ± 6·44	88·07 ± 4·92
PF2 (physical functioning-revised)		BRSEF (sexual functioning)
Mean ± SD	93·02 ± 5·36	14·01 ± 19·99
RF2 (role functioning-revised)		BRSEE (sexual enjoyment)
Mean ± SD	91·65 ± 8·45	18·94 ± 27·29
EF (emotional functioning)		BRFU (future perspective)
Mean ± SD	86·55 ± 4·86	80·32 ± 19·44
CF (cognitive functioning)		BRST (systemic therapy side effects)
Mean ± SD	94·31 ± 8·01	11·14 ± 3·07
SF (social functioning)		BRBS (breast symptoms)
Mean ± SD	89·75 ± 8·23	3·97 ± 5·82
FA (fatigue)		BRAS (arm symptoms)
Mean ± SD	1·01 ± 3·22	4·79 ± 8·08
NV (nausea and vomiting)		BRHL (upset by hair loss)
Mean ± SD	3·03 ± 9·68	10·60 ± 15·69
PA (pain)		
Mean ± SD	5·69 ± 8·01	
DY (dyspnoea)		
Mean ± SD	3·78 ± 10·69	
SL (insomnia)		
Mean ± SD	12·10 ± 16·20	
AP (appetite loss)		
Mean ± SD	10·60 ± 15·69	
CO (constipation)		
Mean ± SD	4·54 ± 11·56	
DI (diarrhoea)		
Mean ± SD	2·27 ± 8·49	
FI (financial difficulties)		
Mean ± SD	6·05 ± 12·99	

during radical breast radiotherapy. Fatigue persists due to an uncertain etiology. There is no identified method to assign the patients at high risk of developing significant fatigue after the completion of treatment. Cancer-related fatigue generally runs a self-limiting course.[19] Jagsi et al.[20] compared acute toxic effects including fatigue, in patients receiving hypofractionated radiotherapy and conventional fractionation following BCS. Patients treated in hypofractionated arm of the above study had presented with a fatigue of 18·9%, which was almost similar to the present study showing fatigue in order of Grade 1 or higher in 18·2% of patients. Grade 2 fatigue was not recorded. The proportion of patients with no fatigue was 81·8%. Haematological abnormality was Grade 0 in 79·5% and Grade 1 in 20·5%, which was easily manageable.

Cosmesis

The most widely used scaling method in most of the published papers following breast conservative procedure till today is the Harvard Scale,[21] introduced in 1979 by Jay Harris. The Harvard scale classifies cosmesis into excellent, good, fair and poor to compare the treated breast with the contralateral or untreated breast. Based on this scale, the cosmetic outcome was assessed by a panel of observers independently. The outcomes at baseline, 6 months, 1 year and at 2 years were compared. In this study, 88·6% of the patients had an excellent or good cosmesis at the baseline which was similar even at 6 months at 88·7%, improving to 90·9% at 1 year and it further improved to 95·4% at 2 years. Fair cosmesis in 11·4% (5) patients was registered at the baseline, and poor cosmesis was seen in one patient (2·3%), which continued to be poor at 1 year and at 2 years as well although the incidence of fair cosmesis decreased to 2·3% at the end of 2 years. Whelan et al.[8] had already reported a non-significant relation in cosmetic outcomes between conventional radiotherapy arm (50 Gy in 25 fractions) and hypofractionated arm (42·5 Gy in 16 fractions) at 10 years, being a 71·3% in conventional arm and a 69·8% in the hypofractionated arm, with a good or excellent cosmetic outcome. Mc Donald et al.[22] had reported a 3 year outcome of global breast cosmesis in early stage breast cancer patients as 96·5% in good to excellent category using IMRT-SIB technique. Scorsetti et al.[11] reported all

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patients with an excellent to good cosmesis compared with baseline. Ghannam and Khedr[23] used accelerated hypofractionated radiotherapy with concomitant boost to 122 patients who had undergone breast conserving surgery. The proportion of excellent or good cosmesis was 95% at 6 months compared to 97% at 1 year.

Quality of life

QOL assessment in breast cancer patients has been the focus of clinical practice and research in recent times and also for assessing treatment outcomes. The reason could be the dismal effect of multi-modality therapy with respect to QOL, seen in various parts of the world.

EORTC QLQ BR 23 consisted of 23 questions that assessed four functioning scores (body image, sexual functioning, sexual enjoyment and future perspective) and four symptom scores (systemic side effects, upset by hair loss, breast symptoms and arm symptoms). Patients were given the option to or not to answer the questionnaires regarding sexual functioning and sexual enjoyment.

Both of the questionnaires were graded on a four-point response scale (not at all, a little, quite a bit and very much) to assess every functional or symptom item, and a seven-point response scale was used to assess global health status from very poor to excellent. Raw scores were linearly transformed to a score of 0–100 for processing according to the EORTC scoring manual. Higher the scores in the functioning and global health status scales, better the QOL, whereas higher the scores in the symptom scales, greater the problems. Patients usually completed the HRQOL questionnaires during their hospitals visits, but if they did not have time, they were asked to return them by mail or were attended by individual house visit. The mean (± standard error) of each score was calculated. The higher scores in functional scales and lower scores in symptom scales correlated to a better QOL outcome.[24] Multi-centric START trials[4,7] had already shown assessment of QOL post radiotherapy in early stage breast cancer. In this study, QOL when reviewed at 6 months post radiotherapy, high functional scale scores were noted which could be attributed to shorter duration of treatment causing less fatigue, which also decreased with time but the low score in social functioning can be related purely to the individual background and psycho-social environment. Fatigue was found to be a strong predictor of quality of life in this present study, throughout the first three months of treatment schedule. At 6 months of assessment, the fatigue scores had subsequently decreased, although persistent fatigue was prevalent in a few. Exercise was advised to patients during radiotherapy and advised to be followed post radiotherapy to overcome fatigue. Patients who had continued exercise after radiotherapy as well were found to have higher functional scores with lesser fatigue, sleep disturbances, depression and anxiety than those who did not, similar to certain studies.[25] These four parameters had a close inter-relation, which could be correlated to the present study. Fatigue that was persistent at 6 months could not be related to any treatment involved factors, although the possible reason may be early induction of menopause due to prior chemotherapy which was found in some of the patients in our study. It could also have had a relation with anemia or related haematological abnormalities, which is quite common in an Indian scenario. Breast symptoms were less, owing to lesser proportion of acute toxicity. These symptoms were found to be transient. Arm symptoms such as lymphoedema of the ipsilateral arm and reduced range of mobility were slightly higher compared to literature. The sexual functioning and sexual enjoyment scores were assessed only if the patients were willing to answer the 2 specific questions related to it. Body image differences had a high score relating to higher satisfaction in cosmesis at 6 months. Future perspective worries were to a lesser extent. Versmessen et al.[26] concluded that hypofractionated tomotherapy patients had a clinically significant increase in role and social functioning scores and decrease in fatigue, which was clinically significant when compared to conventional arm and the functioning scores particularly physical, cognitive and emotional function post radiotherapy, improved faster in tomotherapy arm.

A Randomised Multicenter Phase III Clinical Trial (*RTOG 1005*, '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') is underway since late 2013, and the results of this trial will likely confirm benefits of whole breast Radiotherapy with concurrent/simultaneous integrated boost.

Conclusion

This study showed that hypofractionated radiotherapy using VMAT with SIB is quite feasible for the treatment of early stage breast cancer with breast conserving approach in Indian scenario where not many radiation oncologists are practicing this novel technique as routine as of now. It is associated with the achievement of minimum acute toxicity, good to excellent cosmesis, acceptable quality of life and more convenience to the patients. Lower doses to OAR, could be achieved by VMAT, which would be highly beneficial as the incidences of late toxicities would be restricted to a lower level. A longer period of follow up will be required to assess the real impact with respect to late toxicities and survival data. No Grade 3 or more late toxicities were reported till the last follow up although we have not yet analysed the late toxicity profile of our patients.

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References

1. Bray F, Ferlay J, Soerjomataram I, Siegel R, Torre L, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68 (6): 394–424.
2. Clarke M, Collins R, Darby S et al. 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 (9503): 2087–2106. doi: 10.1016/S01406736(05)67887-7.
3. Yarnold J, Ashton A, Bliss J et al. Fractionation sensitivity and dose response of late adverse effects in the breast after radiotherapy for early breast cancer: long-term results of a randomized trial. Radiother Oncol 2005; 75 (1): 9–17. doi: 10.1016/j.radonc.2005.01.005.
4. START Trialists' Group, Bentzen S M, Agrawal R K et al. The UK Standardisation of Breast Radiotherapy (START) Trial A of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. Lancet Oncol 2008; 9 (4): 331–341. doi: 10.1016/S1470-2045(08)70077-9.
5. Hennequin C, Dubray B. [Alpha/beta ratio revisited in the era of hypofractionation]. Cancer Radiother 2013; 17 (5–6): 344–348. doi: 10.1016/jcanrad.2013.06.035.
6. Owen J R, Ashton A, Bliss J M et al. Effect of radiotherapy fraction size on tumour control in patients with early stage breast cancer after local tumour

https://doi.org/10.1017/S1460396919000165 Published online by Cambridge University Press

excision: long-term results of a randomised trial. Lancet Oncol 2006; 7 (6): 467–471. doi: 10.1016/S14702045(06)70699-4.
7. START Trialists' Group, Bentzen S M, Agrawal R K et al. The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. Lancet 2008; 371 (9618): 1098–1107. doi: 10.1016/S0140-6736(08)60348-7.
8. Whelan T J, Pignol J P, Levine M N et al. Long- term results of hypofractionated radiation therapy for breast cancer. N Engl J Med 2010; 362 (6): 513–520. doi: 10.1056/NEJMoa0906260.
9. Borghero Y O, Salehpour M, McNeese M D et al. Multileaf field-in-field forward- planned intensity-modulated dose compensation for whole-breast irradiation is associated with reduced contralateral breast dose: a phantom model comparison. Radiother Oncol 2007; 82 (3): 324–328. doi: 10.1016/j.radonc.2006.10.011.
10. Teh A Y, Walsh L, Purdie T G et al. Concomitant intensity modulated boost during whole breast hypofractionated radiotherapy-a feasibility and toxicity study. Radiother Oncol 2012; 102 (1): 8995. doi: 10.1016/j.radonc.2011.10.015.
11. 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): 145. doi: 10.1186/1748-717X-7-145.
12. Teoh M, Clark C H, Wood K, Whitaker S, Nisbet A. Volumetric modulated arc therapy: a review of current literature and clinical use in practice. Br J Radiol 2011; 84 (1007): 967–996. doi: 10.1259/bjr/22373346.
13. White J, Tai A, Arthur D et al. Breast cancer atlas for radiation therapy planning: consensus definitions. Radiat Ther Oncol Group, 2011. http://www.rtog.org/CoreLab/ContouringAtlases/BreastCancerAtlas.aspx.
14. Anon. 2019. https://www.eortc.be/services/doc/ctc/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf.
15. EORTC– Quality of Life. Quality of life of cancer patients | EORTC – quality of life, 2019. https://qol.eortc.org/questionnaire/eortc-qlq-c30.
16. EORTC– Quality of Life. Breast cancer (update of QLQ-BR23) | EORTC – quality of life, 2019. https://qol.eortc.org/questionnaire/update-qlq-br23.
17. Formenti S C, Gidea-Addeo D, Goldberg J D et al. Phase I-II trial of prone accelerated intensity modulated radiation therapy to the breast to optimally spare normal tissue. J Clin Oncol 2007; 25 (16): 2236–2242. doi: 10.1200/JCO.2006.09.1041.
18. Chadha M, Vongtama D, Friedmann P et al. Comparative acute toxicity from whole breast irradiation using 3-week accelerated schedule with concomitant boost and the 6.5-week conventional schedule with sequential boost for early-stage breast cancer. Clin Breast Cancer 2012; 12 (1): 57–62. doi: 10.1016/j.clbc.2011.09.002.
19. Goldstein D, Bennett B K, Webber K et al. Cancer-related fatigue in women with breast cancer: outcomes of a 5-year prospective cohort study. J Clin Oncol 2012; 30 (15): 1805–1812. doi: 10.1200/JCO.2011.34.6148.
20. Jagsi R, Griffith K A, Boike T P et al. Differences in the acute toxic effects of breast radiotherapy by fractionation schedule: comparative analysis of physician assessed and patient-reported outcomes in a large multicenter cohort. JAMA Oncol 2015; 1 (7): 918–930. doi: 10.1001/jamaoncol.2015.2590.
21. Harris J R, Levene M B, Svensson G, Hellman S. Analysis of cosmetic results following primary radiation therapy for stages I and II carcinoma of the breast. Int J Radiat Oncol Biol Phys 1979; 5 (2): 257–261. doi: 10.1016/03603016(79)90729-6.
22. McDonald M W, Godette K D, Whitaker D J, Davis L W, Johnstone P A S. Three-year outcomes of breast intensity-modulated radiation therapy with simultaneous integrated boost. Int J Radiat Oncol Biol Phys 2010; 77 (2): 523–530. doi: 10.1016/j.ijrobp.2009.05.042.
23. Ghannam A A, Khedr R A. An accelerated hypofractionated schedule with a daily concomitant boost after breast conservation surgery: the feasibility and toxicity. J Egypt Natl Canc Inst 2016; 28 (1): 39–44. doi: 10.1016/j.jnci.2016.01.002.
24. Fayers P M, Aaronson N K, Bjordal K et al. The EORTC QLQ-C30 Scoring Manual, 3rd edition. Brussels: European Organisation for Research and Treatment of Cancer, 2001.
25. Mock V, Dow K H, Meares C J et al. Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. Oncol Nurs Forum 1997; 24 (6): 991–1000.
26. Versmessen H, Vinh-Hung V, Van Parijs H et al. Health-related quality of life in survivors of stage I-II breast cancer: randomised trial of post-operative conventional radiotherapy and hypofractionated tomotherapy. BMC Cancer 2012; 12 (1):495.

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