Oncology
and Radiotherapy ©
Vol.15 Iss.3: 28-33 • Research Article

Cosmetic outcomes of hypofractionated partial breast irradiation in early breast cancer

Arun Thimmarayappa[1], Karthik Srevatsa[2], Uday Krishna AS[3], Lokesh V[3], Varathraj C[4]

[1] Department of Radiotherapy, Gujarat Cancer Research Insitute, Asarwa, Ahmedabad, India
[2] Sri Shankara Cancer Hospital, Basavanagudi, Bengaluru, India
[3] Department of Radiotherapy, Kidwai Memorial Institute of Oncology, Bangalore, India
[4] Department of Medical Physics, Kidwai Memorial Institute of Oncology, Bangalore, India

SUMMARY

Introduction: Breast conservative surgery is the standard of care in early breast cancer. Although, conventional fractionation whole breast irradiation followed by cavity boost is the current standard of practice; limiting the volumes to the cavity alone with additional margins with hypofractionation has yielded comparable results with local control. However, question of late toxicities is not addressed. The objective of the study was to evaluate and assess the late toxicities and cosmetic outcome of hypofractionated partial breast irradiation in early breast cancer.

Patients and Methods: Twenty histologically proven early breast cancer patients underwent breast conservation surgery with sentinel lymph node biopsy. They received adjuvant radiation of 40Gy in 15fraction via 3-Dimensional Conformal Radiotherapy (3DCRT) or Intensity Modulated Radiotherapy (IMRT) technique. Post radiotherapy they were followed up for assessment of late toxicities-breast cosmesis-reported by patient and radiation oncologist.

Results: At the end of three years 70% of the patients had excellent cosmesis. There was no difference between the radiation oncologist and patient assessment of cosmesis. Patients with resected specimen of < 220 cc, breast separation of ≤ 21cm had better cosmesis (p=0.024) and with whole breast V20%(8 Gy) ≤ 474.582 cc had better cosmesis (p=0.05).

Conclusion: Hypofractionated PBI without acceleration is a safe alternative for WBI preserving the cosmesis of the irradiated breast.

Key words: breast cancer, hypofractionation, PBI, cosmesis

Address for correspondence:

Arun Thimmarayappa, Department of Radiotherapy, Gujarat Cancer Research Insitute, Asarwa, Ahmedabad, India, email: 47arunt@gmail.com

Word count: 4487 **Tables:** 06 **Figures:** 00 **References:** 27

Received: - 18 February, 2021

Accepted: - 20 March, 2021

Published: - 26 March, 2021

INTRODUCTION

Breast Conserving Surgery (BCS), is an alternative for mastectomy in Early Breast Cancer (EBC). Following BCS, Whole Breast Irradiation (WBI) is the current standard practice. Radiotherapy has shown to improve local control and provide survival benefit in patients with EBC [1]. It reduces the risk of death by 9% to 12% and reduces the risk of Ipsilateral Breast Tumor Recurrence (IBTR) up to 70%. Whole breast is treated for 50Gy in 25 fractions, at 2 Gy per fraction over a period of 5 weeks. This long duration radiotherapy is associated with poor compliance. Further studies [2, 3] have shown that breast cancer is a slow growing tumour with a lower α/β of 3 to 3.5. Such tumours respond well for hypofractionated radiotherapy. Therein, hypofractionated radiotherapy schedules have evolved, reducing the overall treatment time, improving patient compliance, and reducing financial burden to the patient and patient load in the radiation facilities.

Patterns of failures after radiotherapy have shown that nearly 75% to 90% occur within 1.5 cm for the lumpectomy cavity [4-6]. Limiting the radiation to cavity with margins avoids radiation to the remaining part of the breast. With results of similar loco regional control, Partial Breast Irradiation (PBI) is a practice of interest. Multiple studies have established the safety and efficacy of PBI [7-9].

Few studies have raised concern regarding the late toxicities and cosmetic concerns of hypofractionated PBI [10,11]. This study was an institutional pilot study conducted to address local control rates, late toxicities and cosmesis after hypofractionated PBI. In this study we intend to report the cosmetic outcomes of Hypofractionated Partial breast irradiation in early breast cancer.

PATIENTS AND METHODS

This study was approved by the institute scientific review board and ethical committee and was carried out in accordance with the code of ethics of the world medical association (Declaration

of Helsinki). After informed consent, twenty histologically proven early breast cancer patients were recruited for this study, conducted between December 2014 to December 2016. Inclusion criteria were: T1-2 tumors with size <3cm, axillary node negative, her-2 neu negative, age >35 years, grade 1 or 2 invasive ductal carcinoma or ductal carcinoma *in-situ*. Patients with multifocal or multicentric or bilateral breast cancer, previous thoracic irradiation, positive margins, node positive, her-2 neu positive, grade 3 tumor, in-situ or invasive lobular carcinoma, extensive intra ductal component of >25%, neoadjuvant chemotherapy were excluded.

Radiation planning and treatment

Treatment planning and delivery was done using supine breast board (R611-5SDCF supine breast board ® Klarity). Patients underwent contrast enhanced Computer Tomography (CT) scan with supine breast board from mandible to lower border of L1. Intravenous contrast was administered at 1 to 2 cc per kg body weight. Initially the lumpectomy cavity was delineated with the help of surgical clips placed. The Clinical Target Volume (CTV) was defined by cavity with 2.5 cm isotropic margins. The Planning Target Volume (PTV) was created with additional 1 cm isotropic expansion. A PTV_Eval was generated for dosimetric evaluation by cropping the PTV 5 mm from the skin and the chest wall. Organs at Risk (OARs) were bilateral lungs, heart, and contralateral breast.

Treatment was planned on Eclipse Treatment planning system (® Varian Medical System, Pal Alto, USA). PTV was planned for a dose of 40 Gy in 15 fractions at 2.67 Gy per fraction. The plans were either 3-Dimensional Conformal Planning (3DCRT) or forward-Intensity Modulated Radiation Therapy (IMRT). Treatment position verification was done on day 1 to 3, followed by twice a week using Electronic Portal Imaging Device (EPID).

Assessment of late toxicities

Pulmonary toxicities were assessed for with Contrast Enhanced Computer Tomography (CECT) of thorax, pulmonary function test and Diffusion Capacity For Carbon Monoxide (DLCO) every 6 monthly after the completion of radiotherapy. Cardiac Toxicities were assessed for with 2D-Echocardiography every 6 monthly after the completion of radiotherapy.

Cosmesis assessment

Cosmesis was assessed by the radiation oncologist and the patient. The assessment was done at 3rd month, 6th month and then every 6 monthly for 3 years and then annually. Harvard four-point breast cosmesis scale was used to assess breast cosmesis. This scale used 4 grades of breast cosmesis-excellent when there was no or minimal changes in size, shape or texture of the treated compared to untreated breast, good when there was slight or mild changes in size, shape or texture of the treated breast compared to the untreated, fair when there was moderate to obvious changes in size, shape or texture involving one fourth or less of the treated breast compared to the untreated, poor when there was marked or obvious changes in shape or texture involving more than one fourth of the treated breast compared to untreated. Patients were allowed to score the cosmesis of the treated breast by using Harvard four-point breast cosmesis scale. Breast Induration, Telangiectasia and Shrinkage were graded according to RTOG/EORTC Late Radiation Morbidity Scoring Schema [12].

Statistical analysis

Sample size was estimated using non-inferiority tests-exact test, with samples being drawn from population of infinite size. The power of the study was taken as 80% and an alpha of 0.05, a non-inferiority proportion (p0) with respect the ipsilateral breast tumor recurrence rate, was taken from literature for standard conventional fractionated whole breast radiotherapy as 0.13 [13,14]. Actual proportion (p1) was obtained from pilot studies was ipsilateral breast tumor recurrence rate of 0.011 [15]. Using Fischer exact test, a sample size of 20 was established to show non inferiority for the current study. Harvard 4-point scale was used to assess the cosmetic outcome. Patients were dichotomized into tumors of ≤ 20 mm and > 20 mm. Breast was divided into 5 quadrants-upper outer, lower outer, upper inner, lower inner and central. No patient had lump in central quadrant. During segmentation, the glandular component and fatty component of the WBV were contoured separately. Breast Composition Ratio (BCR) was defined by ratio of fatty component of the breast and WBV [16]. The BCR was stratified as -0.26-0.5, 0.51-0.75 and ≥ 0.76. The resected specimen size was dichotomized into <220cc and ≥220cc. The distance between the central axis of Medial and lateral tangential beams at the beam entry points was documented stratified as ≤21 cm and >21 cm. Patients were treated on Dual energy Linac, higher energy beam was used in some patients to achieve better dose conformity. Patient and treatment parameters were compared with cosmesis using non-parametric test-Fischer's Exact t test. Dosimetric parameters were compared with cosmesis using Independent sample t-Test and spearman correlation coefficient. Statistical analysis was done using SPSS v24.0 (®IBM, New York, USA). Probability value (p value) of less than 0.05 was considered significant (Table 1).

Tab. 1. Patient characteristics

Patient parameter		N
Age	> 45 yrs	7
	≤ 45 yrs	13
Menopausal status	premenopausal	9
	postmenopausal	11
Tumor size	≤ 20 mm	10
	>20 mm	10
Breast quadrant	Upper outer	12
	Lower outer	3
	Upper inner	4
	Lower inner	1
Side	Right	9
	Left	11
Resection specimen size	<220 cc	11
	≥ 220 cc	9
Breast composition ratio	0.26 to 0.50	7
	0.51 to 0.75	10

RESULTS

Twenty patients were recruited for the study. The median age at the time of diagnosis was 42 years (range, 30 to 63 years). The median follow-up duration was 50 months (range, 44.1 to 64.3 months). Patient age and menopausal were analysed. Seven patients were aged, more than 45 years and 13 patients were aged 45 years and less. Nine patients were pre-menopausal and 11 were post-menopausal. There was no significant difference in breast cosmesis between the two groups for age and menopausal status. Patient characteristics are tabulated in table 1.

Dose received by PTV_Eval, Whole Breast Volume (WBV), Volume of the treated breast receiving 5%, 20%, 50% and 100% of the prescribed dose was documented. V5/WBV, V20/WBV, V50/WBV, V100/WBV and PTV_Eval/WBV were generated. The median PTV_Eval was 115.767cc and median WBV was 850.764cc. Median V20% was 474.582cc which was 50.025% of WBV. Hundred percent of the prescribed dose was received by a median volume of 123.0725cc slightly higher than PTV_Eval showing the PTV_Eval was optimally covered by 100% of prescribed dose (Table 2).

Table 3 shows the tabulated cosmetic data of the treated breast assessed by the radiation oncologist and the patient at 6th month, 1st year, 2nd year and 3rd year after treatment. None of the patients had fair or poor cosmesis during the follow up. By Radiation oncologist assessment, at the end of 6 months 90% of the patients had excellent cosmesis, which dropped to 85% at 1st year, 75% at 2nd year and to 70% at 3rd year. During patient self-assessment, 90% of patients had excellent cosmesis at the end of 6 months remaining same at 1st year followed by dropping to 80% at 2nd year and 70% at 3rd year. There was no difference between the radiation oncologist and patient assessment of cosmesis. Cosmesis was categorized into breast induration, skin telangiectasia, and breast shrinkage. No patient had grade 2 or above toxicity and none grade 1 telangiectasia (Table 4).

Tab. 2. Treatment dosimetric parameters

Parameter	Median (95%CI)
PTV_Eval (cc)	115.767 (102.523-124.293)
WBV (cc)	850.764 (810.538-1043.049)
V5% (2Gy) (cc)	640.8055 (550.185-743.979)
V20% (8Gy) (cc)	474.582 (402.966-549.702)
V50% (20Gy) (cc)	343.991 (288.622-380.464)
V100% (40Gy) (cc)	123.0725 (110.248-142.444)
V5/WBV	74.905 (63.843-76.109)
V20/WBV	50.025 (46.343-57.788)
V50/WBV	35.24 (31.969-43.093)
V100/WBV	11.99 (11.672-17.653)
PTV_Eval/WBV	12.065 (10.633-15.142)

Cosmesis and tumor parameters

Tumor size, breast quadrant, breast composition ratio and resected specimen size were analysed. Patients with resected specimen of <220cc had better cosmesis. With excellent and good cosmesis clubbed there was no statistically significant difference among the parameters. Ten patients had excellent cosmesis compared to 4 patients (p=0.024). Seven patients with BCR of 0.26 to 0.5 and 6 patients with BCR of 0.51 to 0.75 had excellent cosmesis compared to those who had BCR of ≥ 0.76. The difference between the two groups was in the trending significant (p=0.067). However, the difference between the group 0.26 to 0.5 and 0.51 to 0.75 was not significant (Table 5).

Cosmesis and treatment parameters

Beam energy and breast separation were analysed. Eleven patients had excellent cosmesis among the patients with separation ≤ 21 cm compared to 4 patients among those with separation >21cm (p= 0.024). With excellent and good cosmesis clubbed there was no statistically significant difference among the parameters. There was no correlation between late toxicities of breast and dosimetric parameters.

Cosmesis and dosimetric parameters

Various dosimetric parameters were analysed for effect on breast cosmesis. Nine patients had excellent cosmesis compared to 5 patients in the dosimetric parameter Whole breast V20%, which was statistically significant (p=0.05). None of the other dosimetric parameters were statistically significant. With excellent and good

Tab. 3. Breast cosmesis at serial intervals assessed by radiation oncologist and patient

Radiation oncologist	6 months		1 year		3 year	
	N	%	n	%	n	%
Excellent	19	90	17	85	14	70
Good	1	10	3	15	6	30
Fair	0	0	0	0	0	0
Poor	0	0	0	0	0	0
Patient	**6 months**		**1 year**		**3 year**	
	n	**%**	**n**	**%**	**n**	**%**
Excellent	19	90	18	90	14	70
Good	1	10	2	10	6	30
Fair	0	0	0	0	0	0
Poor	0	0	0	0	0	0

Tab. 4. Late breast toxicities

Toxicity	1 year		3 years	
	Grade 0	Grade 1	Grade 0	Grade 1
Induration	19 (95%)	1 (5%)	18 (90%)	2 (10%)
Telangiectasia	20 (100%)	0 (100%)	20 (100%)	0 (100%)
Shrinkage	18 (80%)	2 (10%)	18 (80%)	2 (10%)

Tab. 5. Patient and tumour parameters compared against cosmesis

Patient and tumor parameter	n	P value	Cosmesis score by Radiation oncologist at 3 yrs. Excellent (n)	Good (n)
Age				
> 45yrs	7	0.919	5	2
≤ 45yrs	13		9	4
Menstrual status				
Premenopausal	9	0.769	6	3
Postmenopausal	11		8	3
Tumor size				
≤20mm	10	0.329	6	4
>20mm	10		8	2
Breast quadrant				
Upper outer	12	0.468	8	4
Lower outer	3		3	0
Upper inner	4		2	2
Lower inner	1		1	0
Breast composition ratio				
0.26 to 0.50	7	0.067	7	0
0.51 to 0.75	10		6	4
≥0.76	3		1	2
Specimen size				
<220cc	11	0.024	10	1
≥220cc	9		4	5
Beam Energy				
6MV	11	0.202	9	2
18MV	9		5	4
Separation				
≤21cm	11	0.024	10	1
≥22cm	9		4	5

Tab. 6. Dosimetric parameter compared against cosmesis

Dosimetric parameter dichotomized at median	n	p value	Cosmesis score by Radiation oncologist at 3 yrs. Excellent (n)	Good (n)
PTV_Eval (cc)				
≤ 115.767	10	0.329	8	2
>115.767	10		6	4
WBV (cc)				
≤ 850.764	11	0.202	9	2
>850.764	9		5	4
V5%(2Gy) (cc)				
≤ 640.8055	10	0.329	8	2
>640.8055	10		6	4
V20%(8Gy) (cc)				
≤ 474.582	10	0.05	9	1
>474.582	10		5	5
V50%(20Gy) (cc)				
≤ 0.26 to 0.50	10	0.329	8	2
>0.51 to 0.75	10		6	4
V100%(40Gy) (cc)				
≤123.0725	10	0.329	8	2
>123.0725	10		6	4
V5/WBV				
≤ 74.905	11	0.769	8	3
>74.905	9		6	3
V20/WBV				
≤ 50.025	10	0.329	8	2
>50.025	10		6	4
V50/WBV				
≤35.24	10	0.329	8	2
>35.24	10		6	4
V100/WBV				
≤ 11.99	10	1.0	7	3
>11.99	10		7	3
PTV_Eval/WBV				
≤ 12.065	9	0.769	6	3
>12.065	11		8	3

cosmesis clubbed there was no statistically significant difference among the parameters (Table 6).

DISCUSSION

Radiotherapy in breast cancer has evolved over time from conventional fractionation to hypofractionation; acceleration; and whole breast to partial breast irradiation. With APBI being commonly used in early breast cancer, brachytherapy was the most common technique used. With technical advancement External Beam Radiotherapy (EBRT) is becoming popular technique of APBI. Acute and late toxicity outcome is of concern with external beam APBI. We intent to study this technique in BCS patients in an Indian setup. We treated our patients with hypofractionated partial breast irradiation without acceleration.

Early external beam APBI results were reported by Rodriguez N et al. [17]. One hundred and two patients were randomized between Whole Breast Irradiation (WBI) (51 patients) and APBI (51 patients). The WBI arm patients received 48Gy in 24 fractions with or without boost of 10Gy and APBI arm received 37.5Gy in 10fractions with 2 fractions per day. Excellent/Good cosmesis was reported >75% in APBI arm and >84% in WBI arm. The V10 ipsilateral lung received 6.5 ± 3.3% in WBI arm compared to 3.8 ± 3.3% in APBI arm (p=0.001). Interim results on cosmetic outcomes of RTOG-0413/NSABP-B039 was presented at ASTRO 2019 [18]. This was a randomized control trial comparing WBI of 50Gy in 25 fractions or 50.4Gy in 28 fractions with PBI of 34Gy in 10fraction with 2 fractions per day via interstitial brachytherapy or mammosite or 38.5Gy in 10 fractions with 2 fractions per day *via* 3DCRT. Nine hundred and seventy-five patients were enrolled between March 2005 to May 2009. The cosmesis was assessed using global cosmesis scale of four points: 1-Excellent, 2-Good, 3-Fair and 4-Poor *via* digital photos by patients, treating physician and central review. The Excellent/good cosmesis reported by patients, treating physician and central review was 79%, 84%, and 78% for WBI and 73%, 72% and 80% for PBI. IRMA is a phase III randomized study comparing WBI of 50Gy in25 fractions versus APBI of 38.5Gy in 10 fractions, 2 fractions per day [19]. Between March 2007 to December 2013, 983 patients were recruited. The interim results showed fair/poor cosmesis among patients treated by APBI versus WBI as assessed by physicians was 20% *vs* 21% at 1 year, 20% *vs* 19% at 3 years and by patients was 14% *vs* 16% at 1 year, 14% *vs* 14% at 3 years. APBI with 3DCRT resulted with similar excellent/good cosmesis compared to WBI.

IMPORT LOW was a 3 arm, phase III randomized control trial with patients randomly assigned (1:1:1) to receive 40 Gy whole-breast radiotherapy (control), 36 Gy whole-breast radiotherapy and 40 Gy to the partial breast (reduced-dose group), or 40 Gy to the partial breast only (partial-breast group) in 15 daily treatment fractions [20]. They dichotomized the cosmesis of the treated breast as none or mild versus moderate or marked. Thirty three out of 472 (33%) had moderate or marked breast shrinkage in PBI arm compared to 41 out of 452 (9%) in WBI arm (p=0.165). Breast induration at the index site was seen in 24/471 (5%) patients in PBI arm compared to 21/453 (5%) in WBI arm (p=0.310). Similarly, telangiectasia was seen in 4/465 (1%) patients in PBI arm versus 4/465 (1%) of the WBI arm (p=0.401). A system review was done from Cochrane database group comparing PBI/APBI versus WBI [21]. The late toxicity results showed that there was no difference in late skin toxicity with PBI/APBI versus WBI (OR 0.21, 95% CI 0.01 to 4.39; p value=0.31). Telangiectasia was worse in PBI/APBI group compared to WBI group (OR 26.56, 95% CI 3.59 to 196.51; p value=0.001). Radiological fat necrosis was increased in PBI/APBI compared to WBI (OR 1.58, 95% CI 1.02 to 2.43; p value= (0.04). The subcutaneous fibrosis was higher PBI/APBI versus WBI (OR 6.58, 95% CI 3.08 to 14.06; p value <0.00001). Although, our study shows no patient having fair or poor cosmesis after PBI, and low percentage of grade 1 and no grade 2 or above toxicity, the small number of patients and assessment as early as at 3 years must be considered.

Our study showed breast induration of 10% and breast shrinkage of 5% at the end of 3 years. Yadav B S et al. [22] reported Grade 1 induration and shrinkage of 18% respectively over a median follow up of 60 months. Shah C et al. [23] reported grade 1 induration of 45% and grade 1 volume reduction of 27% at the end of 5 years. There was no statistically significant correlation with dosimetric parameters. Taylor M E et al. [24] evaluated cosmesis records of 458 patients. They analysed various patient, tumor and treatment factors for cosmesis. Patients >60 years of age (p=0.001) and post-menopausal patients (p=0.02) had lower proportion of excellent cosmetic scores compared to their counterpart. Patients with resection volume of >100cc had lower proportion of excellent cosmetic scores (p= 0.0001). With increase in breast tissue lateral separation (>22cm *vs* ≤22cm) the cosmesis worsen. This was more evident in patients treated with 4 MV photons (p= 0.072). The results of our study are concordant with literature data. American Society for Radiation Oncology (ASTRO) updated the selection criteria for APBI in 2017 [25]. Patients below 40 years were unsuitable for APBI. With evolving data of comparable IBTR of PBI with WBI from studies by Stull T S et al. [26], Shah S et al. [27], patients younger than 40 years were included in the study.

Our study had few limitations. Firstly, this was a single arm study without a standard treatment arm for comparison. Secondly, the number of patients in the study was small. The sample size was calculated based on the power to detect ipsilateral breast tumor recurrence rate. Cosmetic outcome was not the outcome used to calculate the sample size, leaving the study underpowered. Thirdly, the follow up duration was short to draw early conclusions on the cosmetic outcome. Inclusion of patients <40 years was another limitation as younger patients tend to have poorer prognosis. However, many studies [26, 27] have shown comparable IBTR of PBI with WBI in this age group. Our study shows that PBI is a safe alternative for WBI preserving the cosmesis of the irradiated breast. With phase III external beam APBI studies results still pending (ISRCTN19906132) hypofractionated PBI without acceleration would be a reasonable option to go with.

AUTHOR DECLARATION

The manuscript titled 'Cosmetic outcomes of hypofractionated

partial breast irradiation in early breast cancer' was not previously published in any other journal and/or under consideration for publication elsewhere in the future. The study was conducted with the ethical and scientific review committee of the institute in accordance with the ethical standards laid down in an appropriate version of the 1964 Declaration of Helsinki.

REFERENCES

1. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, Clarke M, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. Lancet. 2011;378:1707-1716.
2. START Trialists' Group, Bentzen SM, Agrawal RK, Aird EG, Barrettt JM, 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;9:331-341.
3. START Trialists' Group, Bentzen SM, Agrawal RK, Aird EG, Barrettt JM, 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;371:1098-1107.
4. Fisher B, Anderson S, Bryant J, Richard G, Deutsch M, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med. 2002;347:1233-1241.
5. Veronesi U, Marubini E, Mariani L, Galimberti V, Luini A, et al. Radiotherapy after breast-conserving surgery in small breast carcinoma: long-term results of a randomized trial. Ann Oncol. 2001;12:997-1003.
6. Holli K, Saaristo R, Isola J, H Joensuu, M Hakama, et al. Lumpectomy with or without postoperative radiotherapy for breast cancer with favourable prognostic features: results of a randomized study. Br J Cancer. 2001;84:164-169.
7. Lewin AA, Derhagopian R, Saigal K, Panoff JE, Abitbol A, et al. Accelerated partial breast irradiation is safe and effective using intensity-modulated radiation therapy in selected early-stage breast cancer. Int J Radiat Oncol Biol Phys. 2012;82:2104-2110.
8. Ribeiro GG, Magee B, Swindell R, Marris B, Banerjee S. The christie hospital breast conservation trial: an update at 8 years from inception. Clin Oncol. 1993;5:278-283.
9. Shah C, Antonucci JV, Wilkinson JB, Wallace M, Ghilezan M et al. Twelve-year clinical outcomes and patterns of failure with accelerated partial breast irradiation versus whole-breast irradiation: results of a matched-pair analysis. Radiother Oncol. 2011;100:210-214.
10. Hepel JT, Tokita M, MacAusland SG, Evans SB, Hiatt JR, et al. Toxicity of three-dimensional conformal radiotherapy for accelerated partial breast irradiation. Int J Radiat Oncol Biol Phys. 2009;75:1290-1296.
11. Jagsi R, Ben-David MA, Moran JM, Marsh RB, Griffith KA, et al. Unacceptable cosmesis in a protocol investigating intensity modulated radiotherapy with active breathing control for accelerated partial-breast irradiation. Int J Radiat Oncol Biol Phys 2010;76:71-78.
12. https://www.rtog.org/ResearchAssociates/AdverseEventReporting/RTOGEORTCLateRadiationMorbidityScoringSchema.aspx.
13. Mariella M, John R. Yarnold. Shorter fractionation schedules in breast cancer radiotherapy: Clinical and economic implications. Eur J Cancer. 2009;45:730-731.
14. Stegman LD, Beal KP, Hunt MA, Fornier MN, McCormick B. Long-term clinical outcomes of whole-breast irradiation delivered in the prone position. Int J Radiat Oncol Biol Phys. 2007;68:73-81
15. Shelley W, Brundage M, Hayter , Paszat L, Zhou S, et al. A shorter fractionation schedule for post lumpectomy breast cancer patients. Int J Radiation Oncology Biol Phys 2000;47:1219-1228.
16. Juneja P, Bonora M, Haviland JS, Harris E, Evans P, et al. Does breast composition influence late adverse effects in breast radiotherapy? Breast. 2016;26:25-30.
17. Rodriguez N, Sanz X, Dengra J, Foro P, Membrive I, et al. Five-year outcomes, cosmesis, and toxicity with 3-dimensional conformal external beam radiation therapy to deliver accelerated partial breast irradiation. Int J Radiat Oncol Biol Phys. 2013;87:1051-1057.
18. White J. (IL): The American society for Radiation Oncology. c2019.
19. Meduri B, Baldissera A, Galeandro M, Tolento G, Giacobazzi P, et al. OC-0568: Accelerated PBI VS standard radiotherapy (IRMA trial): interim cosmetic and toxicity results. Radiother Oncol. 2017;123:S303.
20. Coles CE, Griffin CL, Kirby AM. Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results from a multicentre, randomised, controlled, phase 3, non-inferiority trial. Lancet 2017;390:1048-1060
21. Hickey BE, Lehman M, Francis DP, See AM. Partial breast irradiation for early breast cancer. Cochrane Database Syst Rev. 2014.
22. Yadav BS, Loganathan S, Sharma SC, Singh R, Dahiya D, et al. Comparison of toxicity and cosmetic outcomes after accelerated partial breast irradiation or whole breast irradiation using 3-dimensional conformal external beam radiation therapy. Adv Radiat Oncol. 2019;5:171-179.
23. Shah C, Wilkinson JB, Lanni T, Jawad M, Wobb J, et al. Five-year outcomes and toxicities using 3-dimensional conformal external beam radiation therapy to deliver accelerated partial breast irradiation. Clin Breast Cancer. 2013;13:206-211.
24. Taylor ME, Perez CA, Halverson KJ, Kuske RR, Philpott GW, et al. Mortimer Je et al. Factors influencing cosmetic results after conservation therapy for breast cancer. Int J Radiat Oncol Biol Phys. 1995;31:753-764.
25. Correa C, Harris EE, Leonardi MC, Smith BD, Taghian A, et al. Accelerated partial breast irradiation: executive summary for the update of an astro evidence-based consensus statement. Pract Radiat Oncol. 2017;7:73-79.
26. Stull TS, Catherine Goodwin, Chernick MR, Carella RJ, et al. A single-institution review of accelerated partial breast irradiation in patients considered "cautionary" by the American Society for Radiation Oncology. Ann Surg Oncol. 2012;19:553-559.
27. Shah S, Kyrillos A, Kuchta K, Habib H, Tobias M, et al. A single institution retrospective comparison study of locoregional recurrence after accelerated partial breast irradiation using external beam fractionation compared with whole breast irradiation with 8 years of follow-up. Ann Surg Oncol. 2017;24:2935-2942.