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SIMULTANEOUS INTEGRATED BOOST BY INTENSITY MODULATED RADIATION THERAPY IN CARCINOMA LEFT BREAST AFTER BREAST CONSERVATION SURGERY-A PRELIMINARY EXPERIENCE

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Abstract

Aim of study-Breast conservation surgery followed by radiotherapy has become the standard of care for early breast cancer. Total treatment time extends from6½ to 7 weeks. In radiotherapy such a long treatment duration is always worrisome. Simultaneous treatment of cavity and breast can reduce treatment time but we should consider acute and late toxicities.

Materials and methods- In this study we are presenting data of 14consecutive patients of carcinoma left breast which were treated between March 2010 and June 2012.Dose prescribed to clinical target volume breast was 50 Gy in 25 fractions and CTV boost was 60 Gy in 25 fractions. **Results**-Clinical target volume for cavity ranged from 34.81cc to 369.8cc. Two patients (14.2%) had acute grade 2 skin toxicity and all other (85.7%) grade 1. Higher dose in boost region did not produce differential fibrosis or edema of breast. Median follow up is 26 months. None of our patients has experienced cardiac or pulmonary toxicity till date and all are in regular follow up. **Conclusion-**With simultaneous integrated boost in carcinoma breast patients, overall treatment time can be reduced without increasing early and late toxicities. Accrual of more patients is continuing.

Keywords: Simultaneous integrated boost, Carcinoma breast,Radiotherapy after breast conservation surgery

In 2011, the American Cancer Society predicted more than 230,480 new cases of breast cancer in women. They estimated that roughly 50,430 of these women would be younger than 50 years (American Cancer Society, 2011).In 2005 study conducted by the International Association of Cancer Research, based in Lyon, France, projected that there would be 250 000 cases of breast cancer in India by 2015, a 3% increase per year (Bagchi, 2008)). Diagnosis and treatment of breast cancer affects women physically as well as psychologically. Women, in general, are concerned about their appearance, their weight, and their body. A greater overall body satisfaction and a less negative body image has been shown in various studies in patients with breast conservative treatment compared to those who have undergone mastectomy(Lasry *et al.*, 1987).For younger women, this issue becomes more important. Based on the mature data from the well-conducted randomized trials, breast-conserving therapy is equivalent to modified radical mastectomy for women with early stage invasive breast cancer and ductal carcinoma in situ (Clarke et. al., 2005). Radiotherapy is an integral part of breast conservation therapy. Breast conservation has become the standard of care in western countries for early breast cancer (Bland *et al.*, 1998). India although the trend is increasing but still it is less common. Among various reasons, long distance to radiation center and long treatment duration also play a role (Nattinger *et al.*, 2001).

Current recommendation is to treat whole breast by 45-50 Gy followed by 10 -16Gy boost to lumpectomy cavity. Total treatment time extends from 6½ to 7 weeks. In radiotherapy such a long treatment duration is always worrisome for the patient and it also increases patient load to the machine. Simultaneous treatment of cavity and breast can reduce treatment time but we should consider acute and late toxicities. Various planning studies and clinical trials have demonstrated favorable results with breast intensity modulated radiotherapy with simultaneous integrated boost (Mc Donald *et al.*, 2010; Guerrero *et al.*, 2004; Singla *et al.*, 2006).Here we are presenting our clinical experience with SIB -IMRT .

Materials and Methods

In this study we are presenting data of 14 consecutive patients of carcinoma left breast which were treated between March 2010 and June 2012.Those left sided breast cancer patients who underwent breast cancer conservation surgery were included in the study. To minimize data heterogeneity, patients with right sided

breast cancer were excluded. Before surgery all patients underwent metastatic work up. After excluding metastases, patients underwent breast conservation surgery followed by chemotherapy according to standard guidelines. After completion of chemotherapy, patients were planned for adjuvant radiotherapy.

Planning process for all the patients was same that follows the steps as described. For immobilization, both thermoplastic mould and VACLOC of chest were made. Patient was kept in supine position with both arms abducted alongside of head and head turned towards opposite side .For CT simulation, radiation technologist accompanied the patient. Same positioning as during immobilization of patient was followed. During CT simulation radio opaque markers were placed over scar mark, medial, lateral and lower border of palpable breast. A planning CT scan of the area of interest was taken with 2 mm slice thickness without intravenous contrast .Area of interest extended from mandible till umbilicus.

The radiotherapy equipment used was dual energy linear accelerator (ClinaciX, Varian Oncology System) incorporating asymmetric X and Y collimators, 120 leaf millenium-multileaf collimator , amorphous silicon based electronic portal imaging , kilovoltage cone beam CT scanner ,3D beam planning computer workstation (EclipseTPSver 8.6.17) and networking (ARIA network).

Target volumes and organ at risk both were contoured by radiation oncologist. All the organs at risk were contoured according to RTOG guidelines. Breast clinical target volume (CTV) included all glandular breast tissue that is included in the CT scan and also the clinical breast volume marked by radio opaque markers. Breast CTV excluded skin, pectoralis muscles, chest wall muscles and ribs. For planning target volume 0.5 cm margin anteroposterior, mediolateral and 0.8 cm magincraniocaudal were taken and this was limited to 5mm within skin surface .Cavity boost volume was delineated with the help of surgical clips seroma, surgery induced changes and preoperative radiological findings. For clinical target volume boost three dimensional margin of one cm around cavity boost was taken. This volume was kept 5mm inside skin surface and was not encroaching in lung and not outside the breast PTV. Node positive patients also received radiation to supraclavicular region. Right lung, left lung and whole lung were auto contoured. Contralateral right breast was contoured similar to left breast clinical target volume. Heart was contoured from apex to pulmonary artery also involved pericardium. Esophagus, trachea and left humeral head were also contoured.

All patients were treated with intensity modulated image guided radiotherapy by seven to nine beams in between medial and lateral tangential fields.Skin flash tool was used during planning. Dose prescribed to clinical target volume breast was 50 Gy in 25 fractions and CTV boost was 60 Gy in 25 fractions. DVH constraints for left lung were set at less than 25% of lung volume to be treated over 20Gy and less than 10% over 40 Gy. For contra lateral lung V 10 Gy should be less than 3 % and for contralateral breast V 5 Gy less than 10 %.For heart constraints were set at less than 10 % of heart volume to be treated over 25 Gy and less than 5 % over 40 Gy.

According to dose prescription and organ at risk constraints various radiotherapy plans were generated. Plans were evaluated by radiation oncologist. During treatment, weekly review of each patient was done to monitor treatment related toxicities. Acute and late toxicities were scored according to the Radiation Therapy Oncology Group (RTOG) morbidity scoring scale. Acute toxicity was defined as as an occurrence of toxicity during or within three months of completion treatment.

After completion of treatment, first follow up visit was done at 15 days, subsequently three monthly visits were performed for two years then 6 monthly upto 5 years. Clinical examination was done at every visit.

Results

This was a prospective single arm study. Demographic characteristics of patients are presented in Table 1. Median age of our patients was 51 years. All patients had Karnofsky performance score 90 or more. Pathological T stage was either T1 or T2. Histopathology of all our patients was invasive ductal carcinoma.64.3% patients had grade 3 disease , 28.5% grade 2 and 17.2% grade 1 disease.

All patients received five fractions per week. Volume of cavity ranged from 10.96cc to 143.02cc and clinical target volume for cavity ranged from 34.81cc to 369.8cc. Clinical target volume for breast ranged from 450.8cc to 1935.6cc. Volume of target and organ at risk and dose achieved by organ at risk are described in Table 2 and 3 respectively. Acute skin toxicity was evaluated according to RTOG acute skin radiation morbidity scoring criteria. Two patients (14.2%) had acute grade 2 skin toxicity and all other (85.7%) grade 1.Eight (57%) patients had late grade zero and 6(42.8%) grade 1 skin reactions. Median follow up is 26 months. None of our patients has experienced cardiac or pulmonary toxicity till June 2013 and all are in regular follow up.

Discussions

Several randomized trials have documented that breast conservation surgery followed by radiotherapy is standard of care in patients with stage I and II breast

cancer (Fisher *et al.*, 2002). Radiotherapy to the breast is an integral part of BCT (EBCTCG, 2005).

Earlier standard opposed tangential fields with appropriate use of wedges was the most commonly used method for radiation delivery. IMRT reduces dose inhomogeneity and improves dose distribution. In their review article JP Pignol et al concluded that there is level 1 evidence that IMRT reduces acute dermatitis and improves long term cosmetic results.[12] Randomized trials have demonstrated a decrease in in-breast recurrence with an additional boost dose of radiation to tumor bed (Pignol*et al.*, 2006; Whelan *et al.*, 2002)). That boost can be delivered by either photons,brachytherapy or electrons. All dose schedules are given five fractions per week. The standard radiotherapy treatment including boost takes about 6 ½ to 7 weeks.

Table 1- Demographic Characteristics of patients

Age(years) Median Range	 51 29-65
Pathological T Stage T1 T2	 4 (28.5%) 10(71.4%)
Pathological N Stage N0 N1a N2a	 7(50%) 6(42.8%) 1(7.2%)
ER receptor Positive Negative	 9(64.3%) 5(35.7%)
PR receptor Positive Negative	 8(57.2%) 6(42.8%)
Her 2 neu receptor Positive Negative	 4(28.5%) 10(71.5%)

Table 2-Volume of target and organ at risk

Target /Organ at risk	Mean Volume(cc)	Median Volume(cc)
Left Lung	869.28	857.13
Contra lateral breast	804.23	718.14
Heart	455.90	447.48
Cavity volume	45.64	32.71
CTV cavity (boost)	118.65	74.65
CTV breast	930.32	926.95

Table 3- Dose achieved by organs at risk

Organs at risk		V20 Gy(%)	V40 Gy(%)	Mean Dose (Gy)
Ipsilateral Left lung	Mean	30.61	11.16	17.16
	Median	30.81	11.64	17.06

		V10Gy(%)	Mean Dose (Gy)
Opposite right lung	Mean	2.43	4.8
	Median	3.0	3.4

		V25 Gy(%)	V40 Gy(%)
Heart	Mean	12.97	4.60
	Median	11.49	4.58

		V5Gy(%)	Mean Dose (Gy)
Contra lateral breast	Mean	11.99	3.29
	Median	9.27	2.76

Literature regarding simultaneous integrated boost has been published in many cancers such as carcinoma lung, carcinoma prostate and head and neck carcinoma. With SIB, treatment time was reduced without increase in normal tissue toxicity (Bos *et al.*, 2002; Dirkx *et al.*, 2004; Wu *et al.,* 2003)

Gurrero et al reported that conventional treatment of 45 Gy (1.8 Gyx25) to the whole breast and then a boost of 20 Gy(2 Gy X 10) is equivalent to an alternative plan of 1.8 Gy x 25 to the whole breast with a 2.4 Gy x 25 SIB to the tumor bed. They also concluded that from dosimetric point of view, for patients with deep seated tumor, SIB IMRT plans provided good target volume coverage with reduced dose to normal breast as compared to conventional plan.

Hurkmans et al developed simultaneously integrated boost (SIB) technique for a phase 3 trial. The intended normalized total dose was produced by 31 fractions of 1.66 Gy to the whole breast and 2.38 Gy to the boost volume. SIB resulted in a more conformal irradiation of the boost volume. Thevolume of the PTV which received a dose higher than 95% of the boost dose could be reduced significantly (p=0.01) using SIB compared with the sequential treatment. During sequential treatment, volume was 129 cm3 (range, 48 –262 cm3) while during simultaneous treatment, volume was 55 cm3 (range, 30–102 cm3).

On this back ground, we are treating our breast patients with 60 Gy and 50 Gy dose by IMRT technique from March 2010. For left breast cancer patients, mean cavity volume was 45.64 cc and mean CTV cavity volume was 118.65 cc. By simultaneous boost, dose to normal tissues (contralateral breast) remain almost similar or significantly decreased (lungs and heart) in comparison to sequential treatment. The mean heart dose and mean lung dose were both reduced by approximately 10% (van der Laan *et al.*, 2007).

In our study, mean ipsilateral lung volume was 869.28cc while median volume of ipsilateral lung receiving 20 Gy or more was 30.61%. Mean heart volume was 455.90cc and median volume of heart receiving 25 Gy or more was 11.49%.The RTOG and European Organization for Research and Treatment of Cancer constraints are in widespread use and normally accepted. Our doses to normal tissues (ipsilateral and contralateral lung, heart, opposite breast)are within dosimetric limits (Feng-Ming *et al.*, 2011).

Sparse data is available in literature for comparison .In 2010 Mcdonald et al reported their 3 year outcomes of SIB -IMRT. The median ipsilateral lung volume receiving 20 Gy or more (V20) was 10.6% (range, 0–27%). Analyzing left breast cases only (n = 168), the median volume of heart receiving 15 Gy or more (V15) was 2.9% (range, 0–17.4%).This difference may be due to difference in volume of organs at risk or body curvature. Grade 2 acute toxicity was noted in 43% patients and global breast cosmesis was good or excellent in 96.5% patients.None of our patients had acute grade 3 skin toxicity and grade 2 toxicity was noticed in 14.% patients. Higher dose in boost region did not produce differential fibrosis or edema of breast. According to RTOG late toxicity criteria our 8 (57%) patients had grade zero and 6(42.8%) grade 1 skin reactions.

Conclusion

With simultaneous integrated boost in carcinoma breast patients, overall treatment time can be reduced without increasing early and late toxicities. Accrual of more patients is continuing.

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