

Organ at risk doses in hypo fractionated three dimensional conformal radiotherapy in carcinoma breast following breast conservation surgery

Joneetha Jones, Vinin NV, Geetha Muttath, Nabeel Yahiya, Shoaib Nawaz, Arun P Narendran, Ayisha Reja

Department of Radiation Oncology, Malabar Cancer Centre, Kerala, India

SUMMARY

Breast cancer is the most frequently diagnosed cancer globally and is the leading cause of cancer-related death in women. Adjuvant radiation forms an integral component in the treatment of patients following breast conservation surgery. Techniques for radiation has evolved from conventional 2D dimensional techniques to 3D conformal radiotherapy and Intensity modulated radiotherapy. The survival of breast cancer has improved because of advances in treatment and hence toxicities are of major concern as far as quality of life is concerned. In breast radiotherapy, organ at risk include lungs, heart, contra lateral breast and spinal cord. When compared to conventional 2D dimensional RT techniques 3DCRT can improve dose homogeneity and can better reduce the organ at risk doses. Hypo fractionated RT has gained significant popularity as adjuvant treatment post breast conserving surgery, based on the results of several randomized trials. This study aims to find out the organ at risk doses and dosimetric parameters in post breast conservation surgery treated with a hypo fractionated schedule at our centre.

Materials and Methods: Dosimetric details of 32 patients treated with 3DCRT during the period from 01/01/2016 to 01/01/2018 were retrospectively analysed. All patients received EBRT dose of 40 Gy in 15 fractions followed by photon boost of 10 Gy in 5 fractions. Dose volume Histograms were analysed from the Eclipse treatment planning system and necessary data was collected.

Results: A total of 32 patients were included. 17 patients had right sided tumours whereas 15 had left sided lesions. All patients were treated with 2 tangential fields, medial and lateral tangents. In addition 17 patients had radiation to supra clavicular fossa and 5 patients received radiation to axilla in addition. The mean ipsilateral lung dose in our study was found to be 11.05 Gy (Standard Deviation 2.55). The mean v20 of ipsilateral lung was found to be 21.27% (standard deviation 6.38). The mean contra lateral lung dose was 0.549 Gy (standard deviation 0.458). The mean heart dose was 6.51 Gy (SD 3.23) for left sided tumours. 15 patients had right sided tumours. The mean heart dose was 1.50Gy (SD 1.69) %. In our study the mean V25 was 7.2% for heart for left sided tumours which was within acceptable limits. The mean Dmax to spinal cord achieved was 23.5 Gy (SD 16.53). The mean homogeneity index was 1.17 (sd-0.05). The mean conformity index was 0.89(SD-0.03).

Conclusion: 3 Dimensional conformal radiotherapy technique can effectively reduce the organ at risk doses in breast radiotherapy. Also it can yield better dose distribution and better dose homogeneity.

Key words: OAR doses, 3DCRT, hypo fractionation, carcinoma breast

INTRODUCTION

Globally breast cancer is the most frequently diagnosed cancer in women and a leading cause of cancer associated deaths [1]. The treatment of breast cancer requires multimodality therapy aimed at eradicating all disease in the loco-regional area and preventing distant disease recurrence. These goals are best achieved through the use of combined-modality treatments that include chemotherapy, surgery, and radiation. Breast conservation surgery is the standard surgical option in early stage breast cancer [2]. Literature has shown that hypo fractionated radiation therapy in the adjuvant setting have equivalent outcomes with respect to tumour recurrence rate and toxicities when compared with conventional radiation treatments [3-5]. Following breast conservation surgery, breast is treated in most radiation centres by using two simple tangential beams. This can be done by using either 2D or 3D treatment planning. The use of Multi-Leaf Collimator (MLC) and fields segments allows for better plan optimization in 3DCRT and IMRT and is being employed in majority of treatment centres and it can reduce acute toxicity and provide better cosmesis [6,7].

3D-CRT is still preferred over IMRT for its lower cost [8], no differences in overall survival [9], and reduced treatment planning time. Especially in high volume centres hypo fractionated RT delivered using 3DCRT is the preferred method. With 3DCRT it is possible to have a better dose distribution, target coverage and reduced organ at risk doses. The purpose of this study is to find out the organ at risk doses and the dosimetric parameters of hypofractionated 3DCRT post breast conservation surgery.

METHODS

Study design

Retrospective cross sectional record based study

Setting: Malabar Cancer Centre, Thalassery is a major cancer care provider in Northern district of

Kerala. It is a tertiary care cancer centre under Government of Kerala. It caters to Northern districts of Kerala and the neighbouring states like Karnataka, Tamilnadu and Pondicherry. Around 6000 new cancer cases are registered annually as per the data from our cancer registry. This study

Address for correspondence:

Geetha Muttath, Department of Radiation Oncology, Malabar Cancer Centre, Thalassery, Kerala, India, email: joneetha14@gmail.com

Word count: 2687 Tables: 0 Figures: 0 References: 17

Received: - 01 May, 2020

Accepted: - 22 May, 2020

Published: - 30 May, 2020

was conducted in the Department of Radiation Oncology, Malabar Cancer Centre, Thalassery.

Study population: All patients treated with 3DCRT for adjuvant radiation post breast conservation surgery from 1st January 2016 to 1st January 2018, were included in the study.

Exclusion criteria

- Those patients treated with conventional 2D planning and those treated with IMRT (Intensity Modulated Radiotherapy) was excluded
- Patients who received bilateral breast irradiation and patients who received boost with electrons were also excluded

Procedure

The data pertaining to patients were derived from record review of case records available in the medical records department of MCC. Data regarding details of radiation was collected from the treatment planning system. Thus, routinely reported data was abstracted into the structured study instrument. Principal Investigator and Co-Investigators were responsible for data abstraction. Abstraction and coding was done by taking the Hospital records and entered into the study data sheet. Double entry was done to avoid any errors.

Simulation

Patients were placed in the supine position on a wing board combi fix system with both arms raised above the head and face turned to opposite side. Lead wires were placed to locate breast, scar and skin marks on the CT images. Patients were scanned from the level of the larynx to the level of the upper abdomen, including left and right lungs, with a 2.5 mm slice thickness and slice separations. Non contrast CT scans were taken.

Target volumes

The delineation of target and critical structures for all patients was done by radiation oncologist according to RTOG guidelines [10]. The breast target volume was defined as the glandular tissue apparent on CT scan, with a 3-mm rim of the skin removed. The retraction of the breast contour 3 mm from the skin surface was to account for dose build-up during dose calculation. The Planning Target Volumes (PTVs) were generated by expanding the CTVs by 10 mm. The PTV was then modified so that it was no closer than 3 mm to the skin surface and was no deeper than the lung-chest wall interface. For all cases, the Clinical Target Volumes (CTVs) for boost was the lumpectomy cavity plus a margin of 15 mm.

Critical structures

The critical structures contoured included the left and right lungs, the heart and contra lateral breast and spinal cord.

Treatment planning

All plans were designed using 6 MV photon beams of varian linear accelerator. The treatment plans for all patients used two standard tangential fields shaped by jaws in X and Y direction. Wedge angles and beam weights were chosen to yield the dose

distributions that met the prescription requirements. Axilla was included in the field if there was extracapsular spread in the nodes. Supraclavicular fossa was covered in all node positive cases. The dosage schedule employed was 40 Gy in 15 fractions followed by boost dose of 10 Gy in five fractions. Treatment was carried out in Varian Clinic ix.

Dose Volume histogram from eclipse treatment planning system was analysed and organ at risk doses were recorded. HI (Homogeneity Index) and conformity indices were calculated as per the RTOG definition.

Statistical analysis

The data was entered and analysis was carried out in Statistical Package for Social Sciences (SPSS) version 20.3. Descriptive statistics like frequency, percentage and mean with standard deviation were used wherever appropriate.

RESULTS

A total of 32 patients underwent breast radiotherapy with 3DCRT during the study period. 17 patients had right sided tumours whereas 15 had left sided lesions.

All patients were treated with 2 tangential fields, medial and lateral tangents. In addition 17 patients had radiation to supraclavicular fossa and 5 patients received radiation to axilla.

Organ at risk doses

Ipsilateral lung dose: The mean ipsilateral lung dose in our study was found to be 11.05 Gy (standard deviation 2.55). The mean v20 of ipsilateral lung was found to be 21.27% (standard deviation 6.38).

Contralateral lung dose: The mean contralateral lung dose was 0.549 Gy (standard deviation 0.458).

Heart dose: Heart dose will vary depending on the side of treatment of breast cancer. In our study 15 patients had left sided tumours. The mean heart dose was 6.51 Gy (SD 3.23) in left sided lesions. The mean heart dose was 1.50 Gy (SD-1.69) in right sided lesions.

Spinal cord: The mean D_{max} to spinal cord achieved was 23.5 Gy (SD 16.53).

Contralateral breast dose: The mean contralateral breast dose was 1.92 Gy (SD-2.8).

Homogeneity index and conformity index

The mean homogeneity index in our study was found to be 1.13 (SD-0.05). The mean conformity index was 0.96 (SD-0.03). Both were found to be within acceptable limits.

DISCUSSION

The recent advances in technology and knowledge in radiotherapy had driven attempts of minimizing toxicity. The techniques for radiation has evolved from conventional 2D fields to 3DCRT and IMRT techniques. A number of studies have demonstrated dosimetric benefit of IMRT compared to 3DCRT for the whole breast in early breast cancer patients.

Many studies have reported lower doses to the ipsilateral lung, contralateral lung, contralateral breast, heart, and left anterior descending artery using IMRT technique for whole breast radiotherapy. But in high volume treatment centres and those with limited resource it may not be feasible to do IMRT for all cases. Moreover 3DCRT has been used for long and it is able to provide good dose distribution with acceptable normal tissue toxicities when compared to two dimensional conformal RT.

A total of 32 patients underwent radiation to whole breast following breast conservation surgery with 3DCRT techniques at our centre during the study period. All patients were treated with tangential breast fields and an anterior field for supraclavicular fossa in node positive patients. The organ at risk doses which were assessed included dose to ipsilateral lung, heart, spinal cord and dose to contralateral lung.

Radiation pneumonitis is one of the most common side effects following radiation to breast. For patients treated with 3DCRT, the volume of lung receiving 20 Gy i.e., V20 has been found to predict the risk of symptomatic radiation pneumonitis in literature. However, there is no absolute safe dose below which there is no pneumonitis. If the V20 of the ipsilateral lung was <30% for breast cancer patients, clinically significant pneumonitis should be rare [11, 12]. In our study the mean ipsilateral lung dose was found to be 11.05 Gy (standard deviation 2.55). The mean v20 of ipsilateral lung was found to be 21% which was well in accordance with literature. The mean contralateral lung dose was 0.549 Gy in our study.

Increase in the rates of cardiac morbidity and mortality following radiation has always been an area of significant concern. It has been established that adjuvant RT to left sided breast cancers has a small but significant increase in the risk of both cerebrovascular and cardiac deaths [13]. Clinical effects

of radiation induced heart disease have been observed with therapeutic doses of ≥ 35 Gy to partial volumes of the heart [14]. There is potentially no threshold dose below which risk of cardiotoxicity does not exist. Therefore, it is intended that the irradiated heart volume be minimized to the greatest possible degree without compromising the target coverage. Heart dose will vary depending on the side of treatment of breast cancer. In our study 15 patients had left sided tumours. The mean heart dose was 6.51 Gy in left sided tumors. 17 patients had right sided tumours. The mean heart dose was 1.50 Gy in them. The dose constraint that we follow is V25 should be less than 10%. In our study the mean V25 was 7.2% for heart for left sided tumours which was within acceptable limits.

The dose to the contralateral breast is another critical factor to consider, especially for younger patients [15]. Stovall et al. [16] found an elevated long-term risk of developing secondary contralateral breast cancer, with the D_{mean} of 3.2 Gy to the contralateral breast. In our study the mean contralateral breast dose was 1.92 Gy (SD-2.8).

Regarding dose homogeneity, Neal et al. [17] showed in their studies the only way to truly appreciate the dose inhomogeneity within the clinical target volume is to devise a 3D plan, perform a 3D dose calculation, and display the result in the form of a Dose Volume Histogram (DVH). The homogeneity and conformity indices for our treatment plans were within acceptable limits.

CONCLUSION

Three dimensional conformal radiotherapy in breast cancer provides uniform dose distribution and target coverage with better sparing of organ at risk and thus reducing acute and long term radiation induced morbidities.

CONFLICT OF INTEREST

Authors declares, there is no conflict of interest.

REFERENCES

- Mohammad H, Forouzanfar KJF, Allyne MD, Rafael L, Alan D, et al. Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. *Lancet*. 2011;6736:61351-61352.
- Morrow M, Strom EA, Bassett LW, Dershaw D, Fowble B, et al. Standard for breast conservation therapy in the management of invasive breast carcinoma. *CA Canc J Clin*. 2002;52:277-300.
- Whelan TJ, Pignol JP, Levine MN, Julian J, Mac Kenzie R, et al. Long-term results of hypofractionated radiation therapy for breast cancer. *N Engl J Med*. 2010;362:513-520.
- Bentzen SM, Agrawal RK, Aird EG. The UK standardisation of breast radiotherapy trial a (START) of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. *Lancet Oncol*. 2008;9:331-341.
- Bentzen SM, Agrawal RK, Aird EG. The UK standardisation of breast radiotherapy trial b (START) of radiotherapy hypofractionation for treatment of early breast cancer: A randomised trial. *Lancet*. 2008;371:1098-1107.
- Pignol JP, Olivetto I, Rakovitch E. A multicenter randomized trial of breast intensity-modulated radiation therapy to reduce acute radiation dermatitis. *J Clin Oncol*. 2008;26:2085-2092.
- Donovan E, Bleakley N, Denholm E. Randomized trial of standard 2D Radiotherapy (RT) versus Intensity Modulated Radiotherapy (IMRT) in patients prescribed breast radiotherapy. *Radiother Oncol*. 2007;82:254-264.
- Kofke-Egger H, Udow-Phillips M. Intensity modulated radiation therapy for breast and lung cancer: a review of use, cost, clinical evidence and safety. 2012.
- McDonald MW, Godette KD, Butker EK, Davis LW, Johnstone PA. Long-term outcomes of IMRT for breast cancer: a single-institution cohort analysis. *Int J Radiat Oncol Biol Phys*. 2008;72:1031-1040.
- Radiation Therapy Oncology Group (RTOG). Breast cancer atlas for radiation therapy planning: consensus definitions. 2015.
- Movsas B, Raffin TA, Epstein AH, Link J. Pulmonary radiation injury. *Chest*. 1997;111:1061-1076.
- Blom Goldman U, Wennberg B, Svane G, Bylund H, Lind P. Reduction of radiation pneumonitis by V20-constraints in breast cancer. *Radiat Oncol*. 2010;5:99.
- Goddu SM, Chaudhari S, Mamalui-Hunter M, Pechenaya OL, Pratt D, et al. Helical tomotherapy planning for left-sided breast cancer patients with positive lymph nodes: comparison to conventional multiport breast technique. *Int J Radiat Oncol Biol Phys*. 2009;73:1243-1251.
- Fogliata A, Nicolini G, Alber M, Asell M, Dobler B, et al. IMRT for breast: a planning study. *Radiat Oncol*. 2005;76:300-310.
- Hoening MJ, Aleman BM, Hauptmann M. Roles of radiotherapy and chemotherapy in the development of contralateral breast cancer. *J Clin Oncol*. 2008;26:5561-5568.
- Stovall M, Smith SA, Langholz BM, Boice Jr JD, Shore RE, et al. Dose to the contralateral breast from radiotherapy and risk of second primary breast cancer in the WECARE study. *Int J Radiat Oncol Biol Phys*. 2008;72:1021-1030.
- Neal AJ, Torr M, Helyer S. Correlation of breast dose heterogeneity with breast size using 3DCT planning and dose volume histograms. *Radiother Oncol*. 1995;34:210-218.