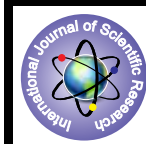


Comparative Study of Imrt V/S 3Dcrt in Postmastectomy Breast Cancer Patients



Medical science

KEYWORDS : IMRT, 3DCRT, Post mastectomy

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ABSTRACT

Introduction

This study evaluates the dose distribution of reversed planned tangential beam intensity modulated radiotherapy (IMRT) compared to standard wedged tangential beam three-dimensionally planned conformal radiotherapy (3D-CRT) of the chest wall in unselected post mastectomy breast cancer patients

Methods

For 20 unselected subsequent post mastectomy breast cancer patients tangential beam IMRT and tangential beam 3D-CRT plans were generated for the radiotherapy of the chest wall. The prescribed dose was 50 Gy in 25 fractions. Dose-volume histograms were evaluated for the PTV and organs at risk. Parameters of the dose distribution were compared using the Student 't' test.

Results

Tangential beam IMRT statistically significantly reduced the ipsilateral mean lung dose by an average of 21% (1129 cGy versus 1437 cGy). In all patients treated on the left side, the heart volume encompassed by the 70% isodose line (V70%; 35 Gy) was reduced by an average of 43% (5.7% versus 10.6%), and the mean heart dose by an average of 20% (704 cGy versus 877 cGy). The PTV showed a significantly better conformity index with IMRT; the homogeneity index was not significantly different.

Conclusions

Tangential beam IMRT significantly reduced the dose-volume of the ipsilateral lung and heart in unselected post mastectomy breast cancer patients.

Introduction

Breast cancer is the most common cancer diagnosed in women worldwide (30). In India the majority of the patients present in advanced stage of disease at diagnosis, and mastectomy is the most common treatment followed by adjuvant radiotherapy of the chest wall. In western world as patients presents in earlier stages so breast conserving surgery followed by adjuvant radiotherapy is the treatment of choice.(1)

Most mastectomy series show that more than 50% of LRF occur on the chest wall, with the mastectomy scar at greatest risk for recurrence. (59, 34, 58) Therefore, treatment to the chest wall is recommended for almost all post mastectomy patients. The second most common site of LRF is the supraclavicular/intraclavicular (axillary apex) region. As many as 33% of LRF occur in this region, with absolute rates of first failure reported in up to 18% of patients, depending upon extent of axillary involvement and tumor size.(59,20,50) While supraclavicular/axillary apex failures are uncommon in patients with one to three positive axillary nodes, failure rates increase in patients with \geq four positive nodes. Therefore, post mastectomy radiotherapy, including a supraclavicular field, is recommended in patients with \geq four positive axillary nodes. (53, 26) Post mastectomy radiotherapy included treatment to the chest wall and draining lymphatics. The most commonly used technique to treat the whole breast is currently called a tangent beam. This field arrangement is designed to minimize radiation exposure of the intra thoracic structures, the heart, and particularly lung. However, due to the curvature of the breast and chest wall, some volume of lung (and the heart in left-sided breast cancers) is included in the radiation beam. In many studies, inclusion of the internal mammary nodes in a comprehensive chest wall field was standard, although today routine inclusion of this nodal region is controversial. The anatomical location of the internal mammary nodes, lying in the intercostal spaces of the first five ribs and crossing the patient's midline, increases the volume of the treatment field and the vol-

ume of heart at risk for exposure in both right-and left-sided patients. Several studies have demonstrated a higher risk of cardiac disease when the internal mammary nodes were included in the treatment fields. (39, 40, 52, 31)

Several Randomized trials have shown that the radiotherapy of the chest wall is associated with a significantly increased risk of developing ipsilateral radiation pneumonitis and lung carcinomas, radiation carditis, soft tissue and bone sarcomas. (56, 19, 18, 14, 57, 37, 38, 41) Radiation pneumonitis is directly related to the volume of lung tissue irradiated. The likelihood of pneumonitis increases when the tangential fields are combined with the axillary –supraclavicular field and adjuvant chemotherapy. (55) Left sided post mastectomy patients have significantly increased risk of cardiac toxicity. Radiation related pericarditis occurs when the dose to heart is above of 35Gy. (42) Anthracycline based chemotherapy also predisposes heart to radiation toxicity. (24)

A variety of dosimetric studies have suggested that intensity modulated radiotherapy (IMRT) potentially leads to a more favourable dose distribution compared to three-dimensional planned conformal radiotherapy (3D-CRT) for the radiotherapy of the whole breast after breast conserving surgery. (13, 25, 2, 7, 15, 16, 21, 22, 23, 29, 35, 36, 45, 46, 47, 48, 51, 54, 61, 27, 8, 9, 10, 11) Radiotherapy treatment planning for the chest wall are complex due to missing tissue and the presence of lung tissue within the treatment field. Accurate dose distribution is important as doses to neighbouring organs at risk, such as heart, lungs and contralateral breast, needs to be minimized. (3,4,5) There are many differences between the target volume of the chest wall and the whole breast. The shape of the target volume of the chest wall is usually shallower compared to the whole breast. In addition, in stage I-IIa patients the pectoralis muscle, chest wall muscles, and ribs may be excluded in the target volume of the whole breast, whereas these structures are included in the

target volume of the chest wall. Due to these differences in the target volume, results of a dosimetric study of the radiotherapy of the whole breast may not be completely applicable to the radiotherapy of the chest wall. Dosimetric study of the chest wall is required to compare IMRT with 3DCRT in post mastectomy patients.

This study evaluates the dose distribution of tangential beam IMRT of the chest wall in post mastectomy breast cancer patients compared to tangential beam 3D-CRT.

Material and methods

Patient data

20 consecutive post mastectomy breast cancer patients coming to a tertiary care center were included in the study. A tangential beam IMRT plan and a standard tangential beam 3D-CRT plan were generated for the chest wall radiotherapy. Thirteen patients had right-sided breast cancer and seven left-sided. The target volumes and the dose prescribed according to the (International Commission on Radiation Units and Measurement) ICRU Reports 50 and 62 recommendations. According to this target volume should be surrounded by the 95% isodose line. The planning target volume for chest wall was defined according to the breast cancer atlas for radiation therapy planning consensus definitions of the Radiation Therapy Oncology Group (RTOG). The chest wall with the pectoralis muscle, chest wall muscles, and ribs, were included in planning target volume (PTV) and excluded the outermost 3 mm from the superficial skin surface. The heart was defined as all visible myocardium, from the apex to the right auricle, atrium, and infundibulum of the ventricle. The pulmonary trunk, root of the ascending aorta, and superior vena cava were excluded.

Treatment techniques

A NCCT-simulation was done in order to optimize target delineation in the supine position on a carbon breast board with the ipsilateral arm up and head turned to the contralateral side. Radio-opaque wires were placed on the mastectomy scar and the clinical boundaries (inferior aspect of clavicular head, mid sternum, mid axillary line, 2cm below the level of the contralateral infra-mammary sulcus). A CT scan was performed using 5 mm slice thickness. The CT scanning reference point and target volumes (PTV) were defined. The 3D-CRT and IMRT plans were generated using the treatment planning system LinaTech. A Siemens Oncor linear accelerator with dual photon energy of 6 MV and 15 MV and multileaf collimator was used for the treatment. The dose calculation was determined using the "Superposition/convolution" algorithm. 50 Gy in 25 fractions was prescribed dose. The beam energy of 6 MV was used for all 3D-CRT and IMRT plans because of the better dose coverage of the chest wall due to the lower penetration power compared to 15 MV.

Tangential beam 3D-CRT

The dose was prescribed to the ICRU reference point which was usually located at the centre of the PTV or at the intersection of the beam axes. Two tangential parallel opposed beams, physical wedges (usually 15° or 30°), and a MLC (multileaf collimator) were used for 3D-CRT. The beam angles, wedge angles, and beam weighting (usually minimal) were chosen to optimize coverage of the PTV, while causing less exposure to the ipsilateral lung, heart and contralateral breast. Gantry angles ranged from 44 to 56° for the medial fields and from 225° to 235° for the lateral fields for patients treated on the right side, and from 307° to 325° for the medial fields and from 132° to 146° for the lateral fields for patients treated on the left side. The fields extended 1.8 cm anteriorly of the chest to provide coverage of the "flash" region.

IMRT technique

The beam orientations and angles of the 3D-CRT plan were used same for the tangential beams of the corresponding IMRT plan. The PTV for IMRT was the same as used for the 3D-CRT plans plus an extension into the air anteriorly of the chest of 1.5 cm to ensure appropriate opening of the multileaf collimator. The dose was prescribed to the PTV, and as initial dose volume constraints the IMRT prescription table provided by the Linatech

treatment planning system (Table A). Tissue inhomogeneities were considered in the treatment planning optimization process, and the dose calculation was done by using superposition/convolution method. A step-and-shoot technique was used.

Dose volume histograms (DVH) of the PTV and organs at risk (OAR) of the 3D-CRT and IMRT plans were generated and dose parameters compared. The Homogeneity index (HI) was defined as the fraction of the PTV with a dose between 95% and 105% of the prescribed dose ($V_{95\%} - V_{105\%}$). The Conformity Index (CI) was defined as the fraction of the PTV surrounded by the reference dose (V95%) multiplied by the fraction of the total body volume covered by the reference PTV dose ($(PTV_{95\%}/PTV) \times (PTV_{95\%}/V_{95\%})$).

Statistics

IMRT and 3D-CRT plan parameters derived from the same patient were tested for statistically significant difference using the student "t"

P-Value is 0<.05 if Value of t >2.1009 i.e. the difference is significant.

Results

Table B (about here?) compares plan parameters of opposed tangential beam IMRT with conventional 3D-CRT for the adjuvant radiotherapy of the chest wall in 20 consecutive breast cancer patients after mastectomy.

Figure 1 (about here?) demonstrates typical dose distributions of an IMRT and 3D-CRT plan of the same patient.

In comparison to 3DCRT the maximum and mean dose for chest wall (PTV) was higher in tangential beam IMRT Plan. Tangential beam IMRT also improved the conformity index compared to 3D-CRT. The Homogeneity Index was not significantly different between the IMRT and 3D-CRT plans.

Left side treated patients showed a reduction of the V70% (percentage of volume encompassed by the 70% isodose line; corresponding to the volume receiving ≥ 35 Gy) of the heart with an average of 46% ($P < 0.05$). The mean heart dose was reduced by an average of 20%. The ipsilateral mean lung dose was statistically significantly reduced by an average of 21%.

The mean volume and the standard deviation (1SD) of the PTV (chest wall) was 622.0 cm³ (176.7 cm³), of the heart 534.2 cm³ (130.5 cm³), and of the ipsilateral lung 1150.7 cm³ (254.4 cm³).

Discussion

Several studies have shown a dosimetric benefit of IMRT compared to 3D-CRT for the whole breast in early breast cancer patients. Comparison of IMRT with 3DCRT in respect to post mastectomy radiotherapy has not done. In our country patients come in advanced stages when breast conserving surgery is not possible. So mastectomy is the treatment of choice here. There are distinct geometric differences between the target volume of the chest wall and the whole breast, and these differences might have an impact on the resulting dose distribution. This study was undertaken to evaluate the dose distribution of tangential beam IMRT of the chest wall compared to tangential beam 3D-CRT in unselected post mastectomy breast cancer patients.

In our study tangential beam IMRT of the chest wall compared to 3D-CRT significantly reduces the ipsilateral lung dose-volume (D30% by 43%), and heart dose-volume in patients treated on the left side (V70% by 46%). Clinically it is not possible to estimate the effect of heart dose volume reduction by the tangential beam IMRT. Radiation associated heart disease involves a spectrum of clinical diagnosis including pericarditis, pericarditis, cardiomyopathy and coronary heart disease with ischemic heart disease. Clinical presentations of radiation induced heart disease have been observed in patients who received therapeutic doses of about ≥ 35 Gy to partial volumes of the heart. Predisposing factors for radiation induced heart disease are pre-existing cardiovascular disease, smoking, obesity, and hypertension

as well as the use of cardiotoxic agents such as anthracyclines, paclitaxel and trastuzumab. (42, 24) To prevent radiation toxicity of the heart all measures should be attempted to reduce cardiac radiation exposure.

Increased irradiated volume of the lung causes radiation pneumonitis. Clinically, radiation pneumonitis is characterized by a chronic cough, fever, and nonspecific infiltrate on chest x-ray. It usually develops in the first few months after radiotherapy and (for breast cancer patients) is usually self-limited, with symptoms lasting an average of 4 weeks. Few patients require any specific treatment. Changes on x-ray may persist after the resolution of symptoms. (55)

Chemotherapy may cause pulmonary toxicity independently of radiotherapy, and hence combining these modalities may result in enhanced lung damage. (6) Both the sequencing of chemotherapy and radiotherapy, radiotherapy treatment technique (which affects the volume of lung treated), and the drugs used may be important in determining this effect. Thus, careful treatment planning to limit the volume of treated lung is warranted. When this is done, the risk of pneumonitis is low and should not restrict the use of PMRT.

An increased risk of secondary tumours has been observed in breast cancer patients treated with older radiation techniques, which combined higher radiation dose and larger tissue volumes. The carcinogenic effects of radiotherapy used for the treatment of breast cancer patients have recently been reviewed. Second malignancies develop in the radiation field in a small number of cases. The two types of potentially lethal malignancy that appear in the radiation field most often are soft tissue and bone sarcomas and lung cancer. (62)

Sarcomas develop an average of 10 years after irradiation. Therefore, the frequency of sarcomas developing in the radiation fields is especially difficult to ascertain for patients treated with current radiotherapy techniques and equipment. (17) Two Swedish registry studies have suggested that an increase in the "integral dose" (a combination of radiation dose and treatment volume) increases the risk of sarcoma development. (43, 44) Women with breast cancer are at a 0.3% to 1% per year risk of developing a contralateral breast cancer. (49, 32) The risk of contralateral breast cancer in several cancer registry case-control studies was increased slightly in women treated with radiation, probably a result of the small dose of "scatter" radiation to the opposite breast. (33, 60, 12, 28) This increased risk seems confined to patients younger than 40 to 45 years old at treatment. In an analysis of data from the Connecticut Tumor Registry, patients age 45 or younger at exposure had an increased relative risk of 1.59 (95% confidence interval, 1.07 to 2.36); at an average dose of 1 Gy delivered to the contralateral breast, the estimated relative risk was 1.21. (61)

Modern radiotherapy techniques as IMRT are likely to reduce the secondary cancer risk by reducing the lung dose-volume. Smoking has been shown to significantly increase the risk of second lung cancer in radiotherapy patients even if modern radiation techniques were used. Prospective studies with long follow-up times are needed to fully evaluate the cardiac toxicity and secondary lung cancer risk in breast cancer patients treated with tangential beam IMRT.

We treat right sided breast cancer patients with 3DCRT and left sided breast cancer with IMRT as IMRT is much costlier than 3DCRT and most patients coming to our department cannot afford IMR.

Conclusions

In post mastectomy patients tangential beam IMRT significantly reduces the dose-volume of the ipsilateral lung and dose-volume of the heart in left sided patients compared to tangential beam 3D-CRT.

Abbreviations

DX%: Dose to X% of the volume (PTV or Organs at risk); IMRT: Reversed planned intensity modulated radiotherapy; PTV: Planning target volume; VX%: Percentage of tissue encompassed by the X% isodose line, representing the volume of tissue that receives at least 95% of the prescribed dose; 3D-CRT: Three-dimensionally planned conformal radiotherapy

Legends:

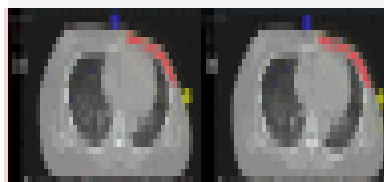


Figure 1: Dose distribution (V107%, V95%, V90%, V70%) for (a) conformal three-dimensional (3D-CRT) and (b) intensity modulated radiotherapy (IMRT) plans.

Table A

Dose Structure	Type	Volume Objective	Constraints for IMRT Plan
PTV	Target	Maximum	5300
PTV	Target	Minimum	5000
Ipsilateral Organ at risk	Maximum	2100	
Ipsilateral Organ at risk	Minimum	1300	
Heart Organ at risk	Maximum	4400	

Organ parameter	Mean	1SD	Mean	1SD	Difference	Difference%	P value
Isilateralchestwall(PTV)	5530	78	5202	81	328	6.3%	<.05
Maximum dose (cGy)	5183	66	4920	165	263	5.3%	<.05
Conformity index	0.33	.03	.26	0.13	.07	26%	<.05
Heart	4060	1210	4530	180	470	-10.37%	>.05(ns)
Maximum dose(cGy)	704	295	877	272	-173	-20%	<.05
Mean dose(cGy)	5.71	3.40	10.61	3.68	-4.9	-46%	<.05
Ipsilateral lung	1129	88	1447	204	308	-21%	<.05
Mean dose(cGy)							
Homogeneity index	.72	.14	.76	.12	.04	-5.2%	<.05

Table B. Relevant plan parameters of tangential beam IMRT versus tangential beam 3D-CRT of the adjuvant radiotherapy of the chest wall in post mastectomy breast cancer patients.

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