Original Article Open Access

Archives Of Breast Cancer

DOI: 10.19187/abc.20163114-18

Assessment of Dose Delivery to Supraclavicular and Axillary Lymph Nodes in Adjuvant Breast Cancer Radiotherapy, with or without Posterior Axillary Boost in Relation to BMI

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ARTICLE INFO

Received:
12 December 2015
Revised:
2 February 2016
Accepted:
28 February 2016

Keywords:
Dosimetry,
breast cancer,
posterior boost,
axillary lymph nodes,
supraclavicular lymph nodes

ABSTRACT

Background: The axillary and supraclavicular nodal volume treatment results in improvement of local control and survival after breast conserving surgery (BCS) or modified radical mastectomy (MRM). Studies on the depth of these nodes have questioned the consistent use of standard fields for all patients. This study was done to assess the dose delivery to these lymph nodes with conventional treatment techniques according to body mass index (BMI).

Methods: Twenty six patients with breast cancer undergoing breast surgery were included and computed tomography (CT) simulation was done. Their axillary and supraclavicular nodal volumes were contoured for planning target volume (PTV). Supraclavicular and posterior axillary fields were generated for each patient with digital reconstruction radiography (DRR) technique. Then the dose distribution of the two conventional methods - anterior-posterior field (AP), and anterior field with posterior boost (AP+PA boost) - for total dose of 5000 cGy, was examined with radiotherapy dose plan program. An AP planned field suitable for PTV, was designed and compared to AP+PA boost. The diameter of axilla was measured at the center of AP field in CT scan. Data were analyzed in relationship to BMI.

Results: PTV coverage and excessively irradiating normal tissues (hot points), proved to have significant differences in each method ($p < 0.001$ to 0.01). Axillary and supraclavicular LNs were in 1.6 to 10 and 0.5 to 6.3 cm depth, respectively. Depth of the prescribed dose, which was gained from planned field, had a significant statistical association with BMI ($p < 0.05$).

Conclusions: Current standard fields are not appropriate for all patients, because of poor coverage of PTV. To sum up, 3D CT planning is strongly recommended for patients with high BMI.

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Introduction

Breast cancer with annually 1.5 million new cases, is the most common cancer among women all over the world.[1] In early stages, tumor will be resected and depending on the stage of the disease and lymph node involvement, adjuvant radiation therapy might be necessary. Adjuvant radiation in patients with lymph node involvement, would increase local control and survival in patients who

have sustained either breast conserving surgery (BCS) or modified radical mastectomy (MRM).[2-4] Since 2012, American Society of Clinical Oncology (ASCO) highly recommends radiotherapy in lymph node positive patients even with less than 3 positive nodes. In a systematic review by Veronesi *et al*. and a recent study by van Wely *et al*. it has been shown that radiation of nodes decreases recurrence rate, even in patients with clear nodes.[5, 6] These data show the importance of adequacy of dose distribution for the lymph nodes in this region. On the other hand, radiation side effects like upper limb lymph edema, brachial plexopathy, radiation-induced pneumonitis, cardiac complications and radiation-induced malignancies necessitate reduction of normal tissues dose delivery.[3,4,7]

Some studies have shown variability in depth of these groups of nodes, which raise doubt regarding application of a unique and standard method for all patients. In fact, level 3 axillary lymph nodes depth varies between 14 to 76 mm. Meanwhile, some have shown a relation between body mass index (BMI) and depth of axillary nodes.[8-10] Thus, inappropriate field or depth of dose prescription for treatment planning, leads to higher or lower dose delivery than optimal leading to inadequate dose in tumoral site or excessive dose delivery in normal tissues that in turn might lead to higher recurrence rate and side effects, respectively.

Most of these problems can be overcome by computed tomography planning. Treatment planning software can calculate and choose appropriate field and assay dose distribution in each part.[7, 8, 11, 12] Today, for almost all patients in advanced radiotherapy centers, application of a treatment planning software and computed tomography rather than a unique clinical delineation is accepted as the standard practice. Recent studies have focused on details of CT planning. An important issue that should be taken into consideration is that, sometimes clinicians do not contour lymph nodes as planning target volume (PTV) and still use the standard clinical fields, without computerized planning. In this state, the overall organs dose intake cannot be accurately assessed. Posterior axillary field is one of the most common fields used in breast cancer adjuvant radiotherapy, in order to improve dose delivery, especially in patients with multiple nodes involvement or extra-capsular extension. This study aims to assess the dose delivery to axillary and supraclavicular lymph nodes with conventional treatment techniques according to body mass index (BMI).

Methods

Patients treated with breast conserving surgery (BCS) or modified radical mastectomy (MRM) and referred for adjuvant radiation to Cancer Institute of Tehran University of Medical Sciences, were included from March to November 2011 and a CT simulation for treatment planning was performed. Patients lied down in supine position on a flat board and a specific breast board was used with ipsilateral hand rise up and head tilt to contralateral site of involvement. CT scanning was carried out from the angle of mandible bone to 5 cm below infra-mammary fold and in 5 mm intervals of slices.

For determination of fields and delineation of nodes, RtDosePlan (Math Resolution, LLC 5975 Gales Lane, Columbia, MD 21045) program was used. An assistant delineated supraclavicular and axillary nodes as a PTV; from cricothyroid notch to lower border of head of clavicle according to radiotherapy oncology group RTOG criteria and two radiation oncologists supervised and corrected it.[13]

A physicist planned the field which was desired by the radiation oncologist as a supraclavicular and axillary field with digital reconstruction radiography (DRR) technique base on skeletal and skin landmarks which was used in our clinic without attention to PTV. Supraclavicular field borders in DRR planning are medial border (lateral border or head of ipsilateral clavicle), lateral border (axillary fold), inferior border (lower border of head of clavicle), superior border (cricothyroid notch), and posterior axillary field in posterior, designed similar to supraclavicular field, with a limitation in medial border as only 2 to 3 cm of lung would be in the field.

Dosimetry

According to planned DRR, with RtDosePlan treatment planning software, for linear accelerator and energy of 6 mv, three methods were applied. The first one was AP method. In this method, an anteroposterior field for 50Gy/25f in the center of supraclavicular field and in depth of 3 cm was used. The second one was AP-Boost method. In this method, an AP field for 50Gy/20f in depth of 1.5 cm (d max) was applied, with a posterior axillary field to compensate dose up to 50Gy/25f in depth of 5.5 cm (point we spot as middle of axilla in conventional fields). In the third method (3D CT planning method) a plan was designed to irradiate breast tissue, skin folds, lung, cricothyroid cartilage, etc according to PTV and ignoring skeletal markers such as the humorous head. In this plan, a field was designed to cover PTV with 1-cm margin, by multi-leaf collimators. The treatment planning program chose the suitable depth of the prescribed dose, automatically, and according to isodoses coverage this point was corrected manually to achieve for PTV coverage by 90% of the prescribed dose. This point is known as the depth of prescribed dose. Dose calculations were done for 50Gy/25f in the depth of prescribed dose. In all plans after drawing the Dose Volume Histogram (DVH), the following dosimetric parameters was defined and measured:

V45: Volume which receives 45 Gy or 90% of the prescribed dose.

V45 body: Volume of body and normal tissue which receive 45 Gy in cc

D100: The isodose which covers all of PTV.

Hot point: The volume (cc) of the body that receives more than 107% of the prescribed dose (the dose that is known as the unfavorable).

Hot point Minimum 2cc: The maximum dose which is more than 107% and covers more than 2 cc of tissue in the body.

Global Max: The maximum dose delivery, regardless of the volume.

Axillary diagonal: The anteroposterior diagonal, measured in the center of axillary field in CT scan.

Supraclavicular nodes depth: The maximum depth of supraclavicular nodes from the skin in the center of AP field in sagittal view measured in CT scan according to PTV.

Axillary nodes depth: The highest depth of axillary nodes from the skin in the center of AP field in axial view of axilla in CT scan, according to PTV.

Results

Twenty six breast cancer patients treated in the Cancer Institute of Tehran University of Medical Sciences were recruited in this study. Eleven patients had left sided and 15 had right sided breast cancer. MRM was performed for 10 patients and 16 were treated by BCS. Lymph node dissection was performed for 21 patients, 3 others underwent SLNB and the remaining 2 patients no surgical assessment for lymph nodes was performed. In patients receiving lymph node dissection, the number of involved lymph nodes ranged from 0 to 27 (N0 to N3).

The average, Min, and Max of axillary diameter, axillary and supraclavicular nodes depth for patients are demonstrated in Table 1.

The min, max and mean of BMI and depth of dosed description is demonstrated in Table 2. These two variables showed a significant association and in regression curve analysis this formula was obtained: Depth of prescribed dose = 0.117 x BMI + 0.551

Table 1. Axillary diameter, axillary (AX) nodes depth and supraclavicular (SC) nodes depth (cm)

	Mean±SD	Minimum	Maximum
Axillary diameter	1.56±14.9	12	18
SC node depth	0.8±4.71	3.2	6.3
Ax node depth	1.2±7.2	5.0	9.7

Table 2. Body mass index (BMI) and depth of dose prescription (DEPTH in cm)

	Mean±SD	Minimum	Maximum
BMI	26.96±3.71	20.76	33.98
DEPTH	4.78±0.88	3.5	6.4

In AP method and AP+Boost method, patients' contribution curve about dose sufficiency was similar. There was a significant difference between the mean volume of PTV that receives 90% of prescribed dose in AP and AP+Boost method, which was 72.2% and 87% and the minimum volume of PTV covered by 90% isodose was 30% and 60%, respectively (figures 1 and 2).

In Table 3, dosimetry findings in three methods were compared.

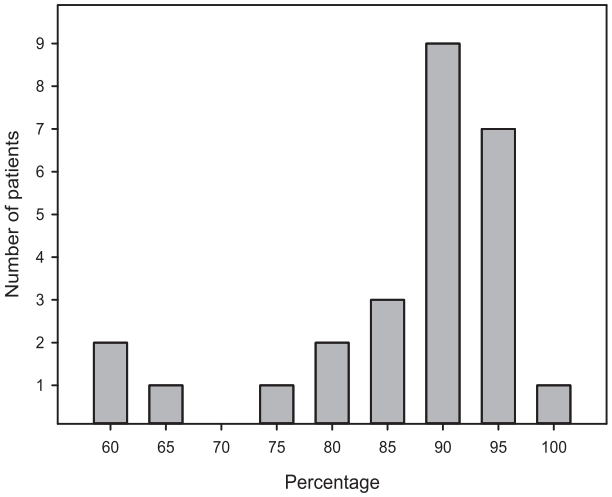

Figure 1. V90 coverage percentage in AP method

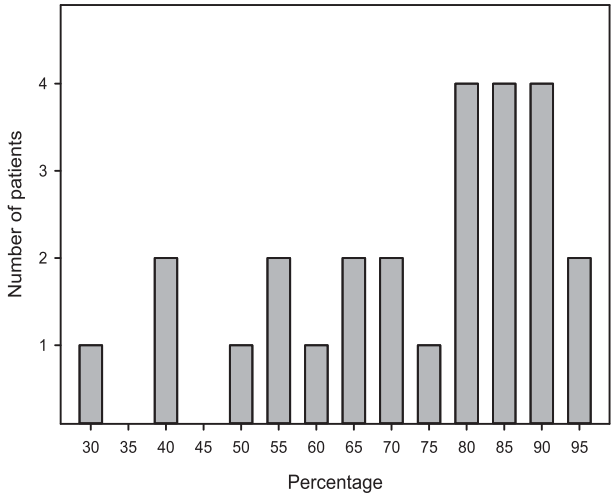

Figure 2. V90 coverage percentage in AP +Boost method

Table 3. Comparison of dosimetry findings in 3 methods

RT technique	Mean±SD	P-value
V45PTV (%)		< 0.001
AP+Boost	87.8±11.26	
AP	72.25±18.35	
PLAN	97.59±3.99	
V45BODY (cc)		< 0.01
AP+Boost	608.3±149.27	
AP	434.5±105.07	
PLAN	613.7±274.77	
D100 (cGy)		< 0.001
AP+Boost	1578.85±1421.74	
AP	1330.58±1190.237	
PLAN	4047.35±810.13	
Hot point > 107% (cc)		< 0.001
AP+Boost	104.08±81.22	
AP	24.12±17.12	
PLAN	181.26±78.48	
Hot point (min 2cc cGy)		< 0.001
AP+Boost	5666.15±133.23	
AP	5462.31±55.41	
PLAN	6027.31±272.45	

Discussion

Radiation is an integral part of nodal treatment in breast cancer. Efficacy of dose delivery and avoiding excessive does are the most important criteria for planning an appropriate field; and in this regard, the position and depth of axillary and supraclavicular nodes are important determinants. The depth of axillary nodes is variable in patients, Kirova *et al*. reported it to be between 19 to 64 mm.[8] Liengsawangwong *et al*. found that level III axillary nodes and supraclavicular nodes depth to be between14 to 67 mm, and it is related with BMI. In that study in patients with higher BMI, the prescribed dose for these nodes were targeted deeper.[10] Bentel *et al*. showed an association between depth of these nodes and the axillary diameter.[14] Goodman evaluated dose and location of posterior axillary nodes and recommended that if we have no 3D planning, axillary nodes should be identified by CT scanning at first.[15] In this study, the depth of supraclavicular nodes ranged from 3.2 to 6.3 cm and axillary nodes in supra clavicular field was from 5 to 9.7 cm.[15] This variation in depth of nodes, leads to variation in dose delivery; however method of treatment influences dose delivery, as well.

Very low amount of D100 in both AP and AP+Boost method shows lack of coverage in these two methods indicating that a part of PTV is out of the treatment field. It could be due to two reasons according to the review of the plans. Head rotation to the contralateral direction might put part of supraclavicular nodes out of treatment field. The other reason could be due to the deep location of level II and III axillary lymph nodes.

According to these findings, it seems that conventional radiotherapy methods are not suitable for satisfactory lymph nodes coverage in treatment of breast cancer. In AP+Boost method, more patients can receive sufficient dose. However in this approach, volume is significantly larger than AP method. After assessment of CT scan of 60 patients with breast cancer, Wang *et al* mentioned that AP+Boost method is an unfavorable method. In comparison, oblique supraclavicular field with Posterior Axillary Boost (PAB) or anterior axillary boost with intensity modulated radiotherapy (IMRT), the latter method had better dose distribution. In that study, the authors found that part of treatment volume that receives 105% of dose has a linear relation with maximum depth of PTV.[16] Jephcatt *et al*. evaluated CT scans of 10 patients with 4 types of fields in 2004 which included AP field alone, AP-PA field, AP field+post axillary boost (PAB), and AP + PAB with tissue compensator.[4] In that study, AP field alone had PTV coverage in only 60% of cases and the overall results were unsatisfactory. AP+Boost method had a good coverage and minimal hot spot; but, posterior neck and lung tissue were exposed to a very excessive dose. In the third method, dose of PTV was sufficient and dose of posterior neck and lung was low. In all methods, hot spot was less than 120%, and hot spot in AP+PAB technique was more than AP alone, too.[4]

According to our findings, regarding use of conventional techniques and the association between depth of prescribed dose and BMI, and considering that the diameter of axilla varies in different patients, use of a unique and fixed field with consistent depth of prescribed dose in all patients is not a suitable technique. This is due to the fact that a part of lymph nodes will not receive the sufficient dose and on the other hand, single AP field (usually 6 mv photon, in the depth of 4cm or less of prescribed dose), creates hot spots with high volume and dose leading to normal tissue injury and acute or chronic side effects. In the 3D planning method, higher depth of the prescribed dose was equivalent to more and larger hotspots. This effect is more distinctive with low energies.

Based on the study findings, 3D planning and if not possible, defining the suitable depth of prescribed dose with CT scan or using the formula is highly recommended. According to the location of axillary lymph nodes which are deep located, especially in patients with high BMI, use of high energy beams for prevention of side effects and delivering sufficient dose to breast regional lymph nodes is recommended. Indications to use posterior axillary boost need more assessment. Since many patients are not planned to undergo any types of surgery for axillary area and radiation therapy is the sole treatment modality for this region, this decision regarding the prescribed dose would be of utmost importance.

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