The importance of radiation optimization using CT-planning for supraclavicular irradiation in breast cancer patients

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Abstract

Introduction: For breast cancer patients, routine prescription of the dose to supraclavicular (SC) region at depth of 2.5-3 cm may underdose these regions due to differences in the depth of SC and axillary lymph nodes (AXLI-III).
Aim: to determine whether radiation optimization using CT-planning should be used for SC irradiation for breast cancer or routine prescription of the dose to 2.5-3cm achieves adequate coverage for SC and AXLI-III lymph nodes for all patients.
Methods: Ten breast cancer patients with post mastectomy radiation that included a SC field were selected. The planning target volume (PTV) of the chest wall, SC region, AXLI-III, contra-lateral breast (CB), heart and both lungs were contoured. Three plans were generated for each patient by prescribing the dose at 2.5cm, 3cm and 5cm depth for anterior SC field. The three plans were compared and analyzed statistically. A correlation was tested between the depth of the SC and of AXLI-III lymph nodes, their minimum dose, $D_{95\%}$, dose inhomogeneity & body maximum dose.
Results: Significant improvement in different target volumes coverage when the dose is prescribed to 3 or 5cm compared with 2.5cm. There is a significant positive relationship between the depth of SC and AXLI-III lymph nodes. A correlation was found between depth of different target volumes and its min dose, $D_{95\%}$ and dose inhomogeneity.
Conclusion: CT simulation and generation of optimized treatment plan for each patient should be the standard way for radiation treatments of SC and AXLI-III lymph nodes in breast cancer patients.

I declare that there is no conflict of interest with any financial organization regarding the material in this manuscript

Introduction

Breast cancer is the most common malignancy among women. Breast-radical or conservative surgery followed by radiotherapy is a major choice for breast cancer treatment. Post mastectomy radiotherapy routinely includes two tangential fields to irradiate the chest wall. If AXLI-III lymph nodes are positive, SC region is irradiated using a direct anterior 6 MV photon field.[1,2]

The dose of 50Gy in 25 fractions is commonly prescribed to the center of PTV for tangential fields and to 2.5-3 cm depth for anterior SC field.[1,3] The anatomical locations of the SC and AXLI-III beds vary according to patient's position and body built; they are deeper for those who are thicker or heavier. Because of the more lateral position of AXLI/II lymph nodes, they have a much deeper location. Prescription of dose to a standard depth of 2.5- 3 cm does not take into account the fore mentioned difference and so the dose may not properly cover the target nodal areas in all patients.[1,3,4]

The variation in lymph nodes depth needs CT simulation to accurately define the target volumes and normal tissues based on anatomical features of individual patient. CT customized radiation treatment planning is also needed to evaluate the dose distribution and to improve the target coverage, dose homogeneity and conformality within SC and AXLI-III beds.[1,3] If they are not properly covered when the dose is prescribed to 2.5-3cm, the plan can be modified by using a posterior axillary boost field [3] or by prescribing the dose to a deeper depth which can vary depending on the dose distribution in the target volumes and the dose to adjacent critical structures and the maximum body dose.[1,3]

Aim

To determine whether radiation optimization using CT-planning should be used for SC irradiation for breast cancer or routine prescription of the dose at 2.5-3 cm achieves adequate coverage for SC and AXLI-III lymph nodes for all patients.

Material and methods

CT simulation was performed for ten post-mastectomy breast cancer patients with the patient supine in breast board with the ipsilateral arm above the head. The CT data were transferred to Precise Elekta treatment planning system at the Clinical Oncology and Nuclear Medicine department, Alexandria University Hospital, from January 2011 to March 2012.

The PTV of the chest wall and SC region were contoured according to the breast cancer atlas for radiation therapy planning consensus definitions of the Radiation Therapy Oncology Group (RTOG) [5,6]. Organs at risk (OARs) including contra-lateral breast, heart and both lungs were also contoured. The maximum depth of AXLI-III and SC region was measured vertically from the skin surface as Bentel et al[4] did in their work.

3DCRT plans were generated using Precise Elekta treatment planning system. Optimized plans were carried out using medial & lateral wedged tangential photon fields and anterior SC field. The matching between the tangential and SC fields was adjusted. SC field extended superiorly to thyroid cartilage, inferiorly to clavicular head, medially to trachea, posterolaterally to anterior scalene muscle and posteromedialy to carotid artery. To optimize coverage of the target volumes, to reduce the dose to the lung and heart and to avoid CB irradiation; beam angles, wedge angles, and beam weighting were adjusted. For tangential fields, gantry angles ranged from 300° to 319°& 120° to 146° for the medial fields and the lateral fields respectively. Collimator and couch rotation of 8^0-30^0 & 6^0-28^0 respectively was done. Wedge angles of 10°, 15° & 35° were used as needed. For SC field, gantry angle of 341^0-353^0 with 1^0-2^0 collimation rotation and 90^0 couch rotation were used. Multi-leaf collimator (MLC) was used to shield ipsilateral humeral head. A tissue equivalent bolus of 1-1.5 cm thickness was used in tangential and supraclavicular fields to improve target coverage in build up region.

A dose of 50 Gy in 25 fractions was prescribed to the center of the PTV for tangential fields and to 2.5, 3 and 5cm depth for anterior SC field. Different dose prescription points of SC field generated three plans for each patient. For each plan, the added dose plan function was used to check the dose coverage of the tangential and SC fields. The target coverage, dose inhomogeneity, hot spot of different target volumes and maximum body dose of the three plans were compared. Target coverage was compared using minimum dose & $D_{95\%}$ of PTV, SC and axillary level I-III lymph nodes. Hot spot was compared using maximum dose, and $D_{5\%}$ of the target volumes. Dose homogeneity was calculated as the ratio of $D_{5\%}/D_{95\%}$.

This study had approval of Institutional Review Board as a retrospective one in which confidentially of records was considered.

Statistical Analysis

DVPs for the three plans were listed and analyzed statistically using Wilcoxon signed Rank test of SPSS (version 18). A P value of less than 0.05 was taken as statistically significant. A correlation was tested between the depth of the SC and the depth of AXLI-III. The differences between the depth of SC and the depth of each axillary lymph node level (I-III) were calculated and correlated to each other. A correlation was tested between the maximum depth of different target volumes and their min dose, $D_{95\%}$, dose inhomogeneity and body maximum dose.

Results

Figure 1 shows an example of the contours of SC and AXLI -III nodal beds. The maximum depth of SC lymph nodes ranged from 4.5 cm to 8 cm (mean, 6cm). The depth of AXLI -III lymph nodes ranged from 5.5cm to 9.5cm, 4cm to 10cm and 4 to 9.5cm (mean, 7cm, 6cm & 6cm) respectively.

Table I shows the comparison of DVPs of SC and AXLI-LIII lymph nodes irradiated by three different dose prescription methods. The comparison was based on target coverage, hot spot and dose inhomogeneity within the target and the body maximum dose. There is a statistically significant increase in most DVPs for different target volumes when the dose is prescribed to a point deeper than 2.5cm (3cm & 5cm).

SC coverage was adequate when the dose prescribed to 2.5cm depth for one patient, to 3cm for 5 patients and to 5cm for 4 patients. AXLI coverage was adequate when the dose prescribed to 2.5cm depth for 5 patients, to 3cm for 3 patients and to 5cm for 2 patients. AXL II & AXL III coverage was adequate when the dose was prescribed to 3cm for 6 patients and to 5cm for 4 patients. Figure 2; DVH shows coverage for different target volumes for one patient with the dose prescription to 3cm depth.

The hot spot within different target volumes was evaluated by maximum point dose and $D_{5\%}$. The average of the maximum dose within SC, AXL I, AXL II and AXL III when the dose prescribed to 3cm was 111%, 105.5%, 104 % and 107.5%. It increased to 122%, 107.5%, 108% and 115% respectively when the dose prescribed to 5cm depth. The average of $D_{5\%}$ of different target volumes was 107%, 102%, 102% and 104% when the dose prescribed to 3cm and 118%, 104%, 105% and 112% when the dose prescribed to 5cm; removing the bolus reduced the hot spot (for 5 cm depth).

The average of dose inhomogeneity within SC, AXL I-III was comparable for the three prescription points except for inhomogeneity within AXL II which was significantly lower when the dose prescribed to 3cm than to 2.5cm (table 1)

The average of body max dose was 118% (range 108% - 126%) for 2.5cm prescription point, 121.5% (range, 113%-131%) for 3cm and 132% (range, 122%- 148%) for 5cm prescription point.

As shown in figure 3, there is a significant positive linear relationship between the depth of SC and the depth of level II & III lymph nodes (R=0.77 and 0.96).

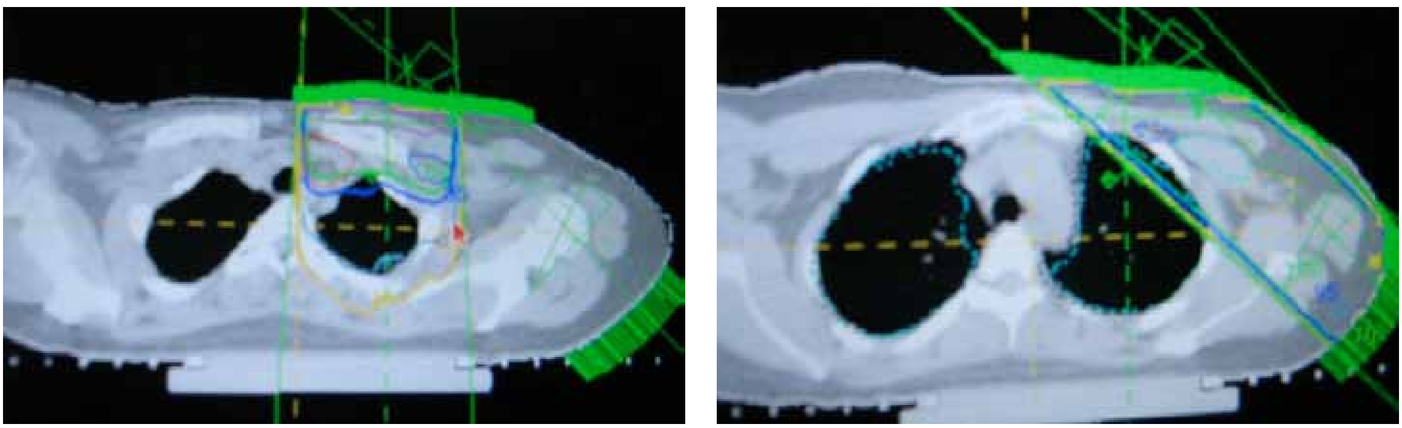
The differences between the depth of SC and the depth of AXL I-III nodes were calculated, its average was 0.75cm, 0.2cm & 0.05 cm respectively. The AXL I, II and III were deeper than the SC in 7, 4 and 2 patients respectively; however these differences were not statistically significant (P=0.112, 0.887 & 0.915). The differences in the minimum dose and $D_{95\%}$ between that of SC lymph nodes and that of AXLI, AXLII & AXLIII were calculated. SC min dose was 5% higher than that of AXLI and 4% and 2.5% lower than that of AXLII and AXLIII. SC $D_{95\%}$ was lower than that of AXL I- III lymph nodes by 1.5, 2.3 and 1.1 respectively. However these differences in min and $D_{95\%}$ were not significant (P= 0.859, 0.168, 0.257, 476, 0.308 & 0.528).

To find how the variation in depth of different target volumes affects the dose distribution and so the depth of prescription point, a correlation was done between the depth of different target volumes and its min dose, $D_{95\%}$, dose inhomogeneity and body max dose.

As shown in figure 4 there is a negative correlation between the depth of SC, AXLI, LII & LIII and $D_{95\%}$ of each (R= -0.80,-0.57,-0.85 &-0.78) (R2= 0.65, 0.33, 0.72 & 0.61), however this correlation is not significant between depth of AX LI and $D_{95\%}$ (P=0.005, **0.08**, 0.002, 0.007 respectively). Also there is a significant negative correlation between the depth of SC, AX II & III and min dose of each (R= -0.65,-0.908, &-0.91) (R2= 0.42, 0.82 & 0.83) (P=0.04, <0.001 & <0.001). (Figure 5)

There was a positive correlation between the depth of SC, AXLI, LII and dose inhomogeneity within corresponding target (R=0.77, 0.54 & 0.70) (R^2=0.59, 0.30 & 0.49), however this correlation was not significant for AXLI (P=0.009, **0.104**, 0.02).

There was a week positive correlation between the depth of SC, AX LII & LIII and body max dose (R=0.60, 0.49 & 0.61) (R^2= 0.36, 0.24 & 0.37), however this correlation was not significant (P=0.06, 0.159 & 0.06 respectively)



a

b

Fig 1: (a) Axial CT from CT simulation showing the supraclavicular nodes outlined in red and AX LIII nodes in blue (b) Axial CT showing AXL I outlined in yellow & LII nodes in green. 95% isodose line displayed in blue covers SC and LI-III lymph nodes.

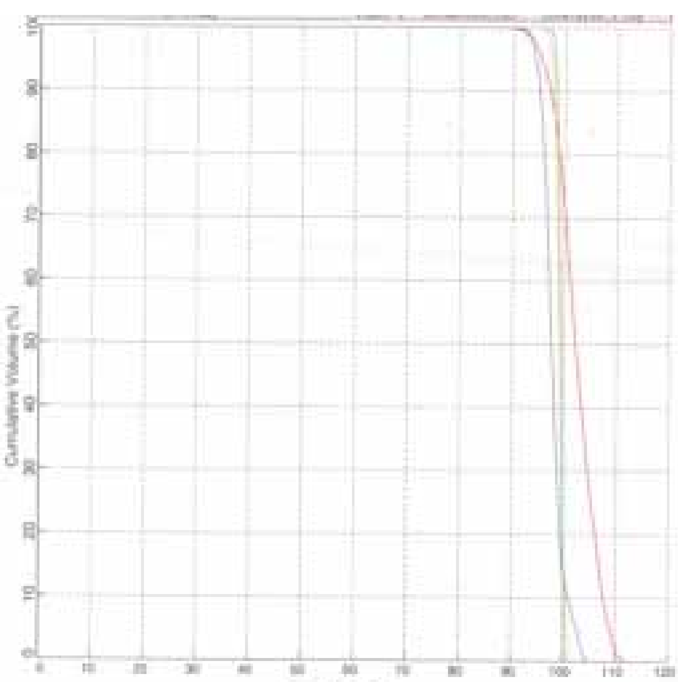


Fig 2: Dose volume histograms in % for SC lymph nodes in red, AX LI in yellow, AX LII in green and AX LIII lymph nodes in blue for a typical case of supraclavicular irradiation for breast cancer. It shows that 95% of their volumes covered by ≥ 95 % of the dose.

Table 1: Comparison of target volume DVPs irradiated by three different dose prescription points (2.5cm, 3cm5 & cm (in postoperative supraclavicular radiation therapy for breast cancer .P values for the difference between plans are also shown.

DVPs	2.5 cm	3cm	5cm	P (2.5, 3cm)	P (2.5, 5cm)	P (3, 5cm)
SC						
Min	81 (75-89)	85.5 (78-94)	92 (79-107)	0.008	0.005	0.014
Max	107 (101-111)	111 (103-119)	122 (104-138)	0.012	0.005	0.005
$D_{95\%}$	88 (80-95)	92 (85-98)	100.5 (83-122)	0.007	0.007	0.011
$D_{5\%}$	104 (100-108)	107 (100-112)	118 (101-132)	0.016	0.002	0.002
Dose inhomogeneity	1.18	1.17	1.18	0.859	0.878	0.445
AXI						
Min	77 (20-97)	79.5 (21-98)	82 (20-101)	0.011	0.011	0.036
Max	103 (94-110)	105.5 (96-114)	107.5 (95-126)	0.006	0.007	0.232
$D_{95\%}$	90 (73-99)	92 (80-100)	94 (80-108)	0.017	0.008	0.050
$D_{5\%}$	101(90-108)	102(92-110)	104 (92-119)	0.453	0.070	0.453
Dose inhomogeneity	1.13	1.12	1.11	0.285	0.139	0.445
AXII						
Min	85.5 (69-96)	88 (74-97)	92.5 (74-101)	0.007	0.008	0.031
Max	102 (93-110)	104 (93-111)	108 (94-124)	0.011	0.008	0.082
$D_{95\%}$	90.5 (75-99)	94 (80-99)	95 (79-108)	0.011	0.008	0.232
$D_{5\%}$	101 (90-110)	102 (90-110)	105 (90-119)	0.070	0.453	0.289
Dose inhomogeneity	1.13	1.09	1.1	0.038	0.203	0.959
AXIII						
Min	84 (69-91)	87 (71-96)	92 (71-104)	0.005	0.005	0.018
Max	105 (100-114)	107.5 (101-120)	115 (102-123)	0.075	0.005	0.009
$D_{95\%}$	89 (75-97)	92 (78-98)	96 (78-108)	0.073	0.008	0.017
$D_{5\%}$	102 (95-110)	104 (95-112)	112 (97-119)	0.070	0.002	0.008
Dose inhomogeneity	1.17	1.14	1.17	0.241	0.878	0.169

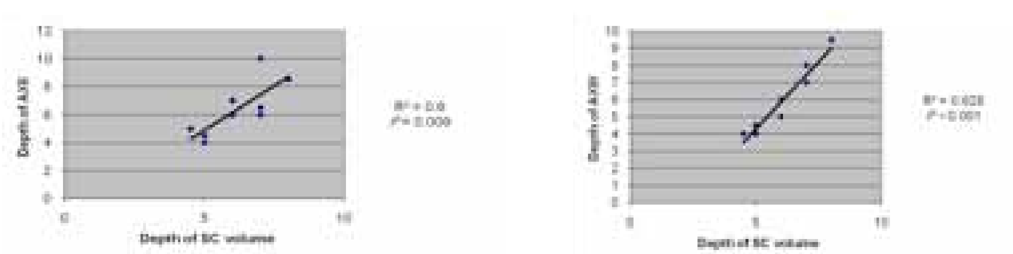
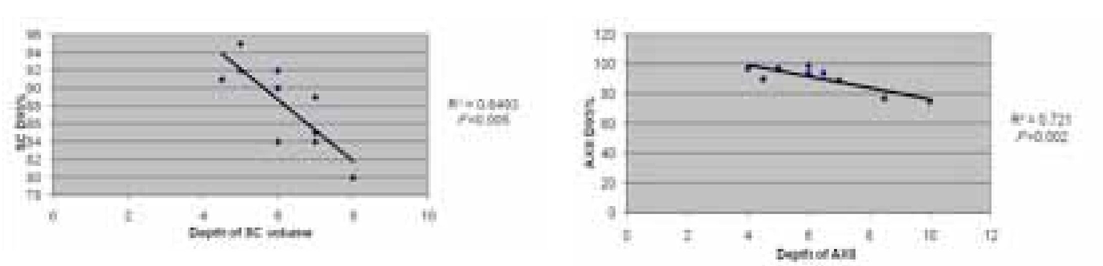


Fig 3: The graph shows that the depth of AXLII & III is significantly correlated with the depth of SC nodal region.



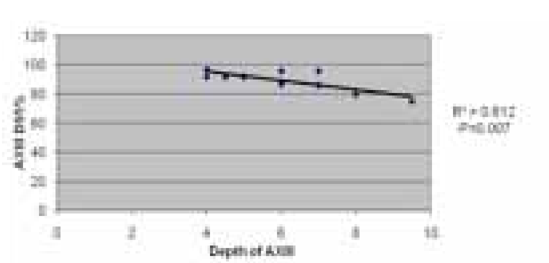
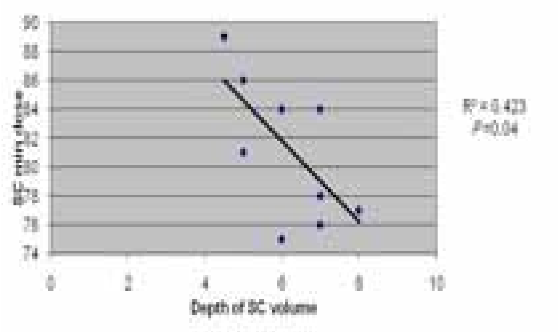
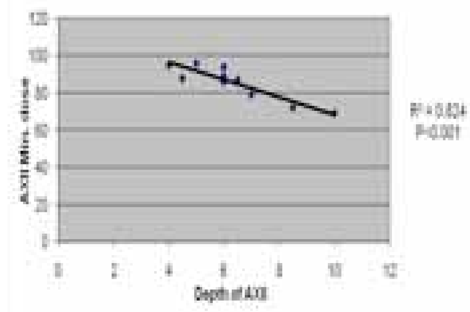


Fig 4: The relationship of the maximum depth of SC and AXLII & AXLIII to its $D_{95\%}$. This graph shows that $D_{95\%}$ is significantly correlated with the depth of the supraclavicular (SC), the axillary level II, and level III nodal region.





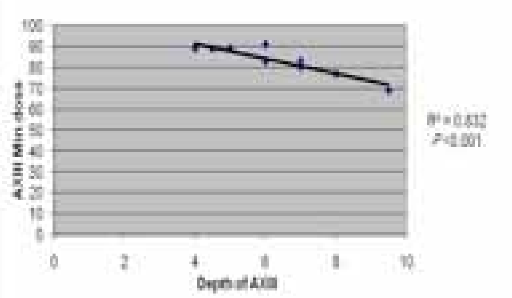


Fig 5: The relationship of the maximum depth of SC and AXLII & AXLIII to its min dose in %. This graph shows that the min dose is significantly correlated with the depth of the supraclavicular (SC) and the axillary lymph nodes level II & level III.

Discussion

For breast cancer patients; radiotherapy after radical mastectomy is a common treatment strategy. Although in most of the departments CT optimization is the standard technique for all patients, however in some departments in developing countries some patients are treated using routine prescription of the dose of SC volume to 2.5cm.

In this study, irradiation of SC fields with prescription of radiation dose to depths of 2.5 cm-3cm leads to suboptimal coverage of SC and AXL I-III, and dose inhomogeneity in a group of patients (40 %). In this group, prescription of the dose to 5cm with addition of a bolus leads to adequate coverage however; it results in an increase in the hot spots within the target volumes, dose inhomogeneity in AXLIII lymph nodes and an increase in the body maximum dose. These findings are in accordance with Liengsawangwong et al[1]. Our findings agree with Cavey et al[7] who showed that using 6MV photons with routine prescription to the depth of 3 and 5 cm produced significant inadequate target coverage and dose heterogeneity. Liengsawangwong et al[1] overcame suboptimal coverage and hot spots by using a combination of 6MV and 18MV AP approach and individualized calculation point. Cavey et al[7] overcame these by using AP/PA fields. In current work, we overcame these by changing the point of dose prescription of SC region to 2.5cm in 10%, 3cm in 50% and 5cm depth in 40% of the patients without using a bolus.

Comparing SC $D_{95\%}$ with AXLI-III, the average of SC $D_{95\%}$ was less than that of AXLI-III by 1.5%, 2.3% and 1.1% respectively. However these differences in $D_{95\%}$ were not significant (P=0.779, 0.497 & 0.944). $D_{95\%}$ of AXLI was lower than SC in 20% of the patients by a maximum of 16% in this patient SC was shallower by 2.5cm. AXLI $D_{95\%}$ was higher than SC in 70% of the patients by a max of 15%, in this patient SC was deeper by 1.5cm. $D_{95\%}$ was comparable in 10% of the patients. We found also that $D_{95\%}$ of AXLII was lower than that of SC in 40% of the patients by a maximum of 14%, in this patient SC was shallower by 3cm. $D_{95\%}$ of AXLII was higher compared to SC in 60% of the patients by a max of 15%, in this patient the SC and AXlII was at same depth. $D_{95\%}$ to AXLIII was lower than SC in 30% of the patients by a maximum of 9% in this patient the SC was shallower by 1cm. $D_{95\%}$ of AXLIII was higher in 50% of the patients with max of 11% in this patient the SC and AXLIII was at same depth. In 20% of the patients there was no difference, in these patients SC was deeper by 1cm.

Bentel et al[4] found the AX dose was 90% of the dose delivered in the SC in 90% of the patients. In these patients the difference in depth ranged from 2.4 to 4.8 cm (median, 3.0 cm). In the patient with the largest depth difference (5cm), the AX dose was 80% of the SC dose. They considered using higher beam energy and/or opposed SC and axillary fields to achieve adequate coverage for axillary lymph nodes.[4]

Lower doses to AX lymph nodes is explained as Level I and II nodes is located more lateral and deeper than SC nodes, so they often receive an inadequate dose from the SC field[3] using the standard SC field at 2.5cm/3cm; therefore, either supplementary dose is required from PAB field [1,3,4] or the dose prescribed at 5cm.

Several investigators measured the depth of the LN vertically from the surface of the skin and attributed the difference in the coverage of different target volume among patients to large variations in location and depth of the SC and AX nodes among different patients with different arm positions.[7–11]

Liengsawangwong et al[1] found that the mean maximum depth of SC and AXL I-III nodal beds was 3.2 cm (range, 1.4–6.7 cm) and 3.1 cm (range, 1.7–5.8 cm) respectively. Bentel et al[4] confirmed the variation in depth of SC and AX lymph nodes, in their study, the maximum depth of SC lymph nodes ranged from 2.4 to 9.5 cm (median, 4.3 cm). The depth was less than 3 cm in 4 patients (8%), 3–6 cm in 39 patients (80%) and greater than 6 cm in 6 patients (12%). The depth of the axillary lymph nodes ranged from 1.4 to 8 cm (median, 4.3 cm). The depth was less than 3 cm in 8 patients (16%), 3–6 cm in 32 patients (65%), and greater than 6 cm in 9 patients (18%). Wang et al[3] found that the mean maximum depth of the treatment target of the Level I/II axilla was 5.7 cm (range, 4.7–7.1

cm). Other investigators found that the mean depth of SC nodes was 3.9–6 cm (range, 2.1–8.3 cm), and the mean depth of the AXL III nodal bed was 3.6–6.7 cm (range, 1.9–7.4 cm) [7–11].

Our study confirms that patients vary considerably in the depth of SC and the AXL I/III lymph nodes; the maximum depth of the SC ranged from 4.5cm to 8 cm (mean, 6cm). The depth was 6cm in 30% of the patients, less than 6 cm in 30% of the patients and greater than 6 cm in 40% of the patients. The depth of the AXLI-III ranged from 5.5cm to 9.5cm, 4cm to 10cm and 4 to 9.5cm (mean, 7cm, 6cm & 6cm) respectively. The depth of AXLI, II and III was 6cm in 20%, 30% & 20% of the patients, less than 6 cm in 30%, 30% & 40% of the patients and greater than 6 cm in 50%, 40% & 40% of the patients respectively.

As some investigators showed the anatomical correlations between depth of SC nodes and other nodal chains, the current study found a positive relationship between the depth of the SC and the depth of the Level I-III lymph nodes (R=0.49, 0.77 & 0.96) (R^2=0.24, 0.60 & 0.93) respectively. This correlation was significant between the depth of the SC and the depth of the level II & III lymph nodes (P= 0.009 & <0.0001) but it was not significant between depth of AXI and depth of SC region. (P=0.147). On the other hand, Bentel et al[4] found no relationship between the depth of the SC and AX lymph nodes and Liengsawangwong et al[1] found a significant correlation between body mass index and the depth of SC and LIII (p value <0.0001).

The differences in figures of the SC and AXI-III lymph nodes compared to others investigators might be related to either position variation or variation of the direction of measurement from the skin whether vertical or with an angle.[4] Bentel et al[4] found that SC depth measured at a 15° angle ranged from 2.4 to 8.6 cm (median, 4.8 cm) compared to 2.4 –9.5 cm (median, 4.3 cm) when measured vertically. The AX node depth measured at a 15° angle ranged from 1.4 to 9.5cm (median, 5.2 cm) compared to 1.4 to 8 cm (median,4.3 cm) when measured vertically.

We found a significant linear relationship between maximum depth of the SC and AX nodes in the SC region and min dose, $D_{95\%}$, and inhomogeneity within target volumes. Wang et al[3] found a significant correlation between $V_{105\%}$ and the maximum depth of the target (p < 0.0001).

Conclusion

As the depth of nodal beds varies from patient to patient; the routine use of 2.5- 3 cm depth for irradiation of SC region and axillary lymph nodes is not optimal. CT simulation and generation of optimized treatment plan for each patient should be the standard way for radiation treatments of supraclavicular and axillary lymph nodes in breast cancer patients.

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