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Regional lymph node radiotherapy in breast cancer: single anterior supraclavicular field vs. two anterior and posterior opposed supraclavicular fields

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Abstract

Background: The treatment of lymph nodes engaged in breast cancer with radiotherapy leads to improved locoregional control and enhanced survival rates in patients after surgery. The aim of this study was to compare two treatment techniques, namely single anterior posterior (AP) supraclavicular field with plan depth and two anterior and posterior opposed (AP/PA) supraclavicular fields. In the study, we also examined the relationships between the depth of supraclavicular lymph nodes (SCLNs) and the diameter of the wall of the chest and body mass index (BMI).

Methods: Forty patients with breast cancer were analyzed using computed tomography (CT) scans. In planning target volume (PTV), the SCLNs and axillary lymph nodes (AXLNs) were contoured, and, with the attention to PTV, supraclavicular (SC) depth was measured. The dosage that reached the aforementioned lymph nodes and the level of hot spots were investigated using two treatment methods, i.e., 1) AP/PA and 2) AP with three-dimensional (3D) planning. Each of these methods was analyzed using the program Isogray for the 6 MV compact accelerator, and the diameter of the wall of the chest was measured using the CT scan at the center of the SC field.

Results: Placing the plan such that 95% of the target volume with 95% or greater of the prescribed dose of 50 Gy (V95) had ≥95% concordance in both treatment techniques. According to the PTV, the depth of SCLNs and the diameter of the wall of the chest were 3-7 and 12-21cm, respectively. Regression analysis showed that the mean SC depth (the mean Plan depth) and the mean diameter of the wall of the chest were related directly to BMI ($p<0.0001$, adjusted $R^2=0.67$) and ($p<0.0001$, adjusted $R^2=0.71$), respectively.

Conclusion: The AP/PA treatment technique was a more suitable choice of treatment than the AP field, especially for overweight and obese breast cancer patients. However, in the AP/PA technique, the use of a single-photon, low energy (6 MV) caused more hot spots than usual.

Keywords: Breast cancer; Supraclavicular; Axillary; Lymph node; Body Mass Index (BMI)

1. Introduction

Axial computed tomography (CT) scan simulation and three-dimensional conformal radiation therapy (3DCRT) are now acceptable for use in planning radiation treatment for breast cancer patients (1). Many clinical trials have shown the benefits of postoperative regional radiotherapy for women with breast cancer in decreasing locoregional breast

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cancer recurrence and increasing overall survival. After breast-conserving surgery (BCS), all patients will need adjuvant radiotherapy to the entire breast, and they also will need radiation therapy to AXLNs and SCLNs if they showed involvement in the patients' final pathologic results. It is clear that, after modified radical mastectomy (MRM), breast cancer patients will need adjuvant radiotherapy to the chest wall and to AXLNs and SCLNs if the latter are involved or if the size of the tumor is 5 cm or there were T4 tumors in their final pathologic results (2-5).

Images from CT simulation are very important to radiation oncologists for contouring AXLNs and SCLNs. Fifteen years ago, the most common method for delivering radiation therapy to SCLNs was to use of single photon, low-energy source (Cobalt 60 or 6MV) empirically prescribed to the depth of maximum dose (Dmax) or D = 3 cm (1-6). However, previous studies found that, in well-developed countries, when radiation oncologists used a single AP to SCLNs and the radiation dose was calculated and delivered to the PTV, 66% of the radiation therapy treatments had a specific depth (not D = 3 cm) in 67.5% of the patients and to the midplane in 17% of the patients (1). It seems that empirical prescription depth points may not cover the target nodal basin properly in all patients who previously showed large variations in the position and depth of SC and AXLNs (7). Therefore, optimal CT techniques are needed to improve dose homogeneity and dose conformality (8-11). There is a particular challenge among radiation oncologists in treating AXLNs and SCLNs to optimize the treatment with different planning techniques.

The purpose of this study was to compare the different treatment techniques for treating the axillary level II/III and SC using different choices of two treatment plans for the AXLNs and SCLNs regions, i.e., by offering optimal dose homogeneity and by planning target volume (PTV) coverage.

2. Materials and methods

2.1. Research Design and Setting

This was a cohort-analytic study. We investigated the plans that had been developed and/or used for the breast cancer patients who were referred to the radiation-oncology ward at Shohada-e-Tajrish Hospital in Tehran, Iran, in 2014. Because all 40 breast cancer patients had already received radiation therapy to their regional lymph nodes before our study, any changes that were made to their treatment plans did not have any effect on their cure rate.

2.2. Sampling

The required sample size for this research was determined to be 40. The following formula was used to calculate the sample size:

$n=Z^2p\ (1-p)/d^2$,

Where:

n=Sample size

Z=Normal distribution percentile

p=Probability

d=Confidence interval

2.3. Data collection

Forty breast cancer patients, who were treated at Shohada-e-Tajrish Hospital in 2014 with post-surgery radiation that included a SC field, were selected for the study. The plans were generated using a three-dimensional (3D) planning system and a 6MV Compact machine. Each patient underwent CT-simulation for radiation treatment planning. The patients were immobilized on a breast board while they were in supine position with 90-degree abduction of the ipsilateral arm, and a trained technician conducted the CT simulation by taking a slice with a thickness of 3 mm. Treatment target volumes, including SC and axillary Level II and Level III (LII and LIII) lymph nodes, were contoured by a radiation oncologist according to the radiation therapy oncology group 8 (RTOG 8) protocol. We planned to treat each patient by two techniques, i.e., 1) direct anterior-posterior (AP) field alone and 2) an anterior-posterior parallel pair (AP/PA). A 10-degree external gantry rotation was used to reduce unnecessary radiation dosage to the spinal cord. The treatment plans were generated using Isogray treatment planning software (version 4.1.3.23L). For the technique with a single field, the calculation of SC depth was measured vertically from the surface of the skin to cover LII, LIII, and the SC nodal bed as PTV. The diameter of the wall of the chest was measured vertically in center of the SC field.

One hundred and twenty plans were evaluated by a radiation oncologist and a radiation physicist (two plans for each of the AP/PA fields and 1 plan for each single AP field). We determined optimal coverage of 95% of the target volume with 95% or greater of the prescribed dose (V95). We tried to reduce hot spots that did not have more than

7% of irradiated volume but received more than 105% of the prescribed dose (V105) as low as possible. It was reasonable that the improvements in the accuracy of the CT simulation and 3DCRT depended on BMI. Therefore, we had to calculate BMI for each patient. The patients were divided into four groups, i.e., thin (BMI=18.5-22.5); normal (BMI=22.6-24.9); overweight (BMI=25.0–29.9); and obese (BMI≥30.0).

2.4. Ethical considerations

The ethical regulations dictated in the act provided by Shahid Beheshti University of Medical Sciences were strictly observed. Because the patients had completed treatments before the study, theoretical alterations to their plans had no effect on their care. The data were preserved anonymously.

2.5. Statistical analyses

The data were analyzed using simple linear regression analysis for the SC depth and the diameter of the wall of the chest with respect to the patient`s BMI. The scores of V95, V105, and V110 were correlated with the patients' BMIs using the chi-squared test. The data were analyzed using SPSS version13.

3. Results

Forty patients with breast cancer were included in the study, and their weights ranged from 44 to 110 kg, with an average weight of 63.5 kg. Their heights ranged from 148 cm to 175 cm, with an average of 163.5 cm. The patients were divided into four groups based on their BMI values. The groups consisted of 10 patients with BMIs in the range of 18.5-22.5 kg/m^2; 10 patients with BMIs in the range of 22.6-24.9 kg/m^2; 10 patients with BMIs in the range of 25-29.9 kg/m^2; and 10 patients with BMIs ≥ 30 kg/m^2. The patients who were selected ranged in age from 22 to 70, with a mean age of 46. Twenty-six patients had undergone modified radical mastectomy (MRM), and 14 patients had received breast conserving therapy (BCT). The sizes of tumors in the pathology ranged from 1.0 to 8.6 cm (T1-T3), with an average of 3.5 cm. The number of women in whom lymph nodes were involved was 0-18, with a mean of 4 (Nx-N3). Table 1 summarizes the baseline characteristics and the clinical-pathological features of the patients.

Table 1. Baseline characteristics and clinical-pathological features of patients

Characteristics	Range	Mean
Age (year)	22-70	46
Weight (kg)	44-110	63.5
Height (cm)	148-175	163.5
BMI (kg/m^2)[a]	18.5-22.5	10
	22.6-24.5	10
	25-29.9	10
	≥30	10
MRM[b]	26	26
BCT[c]	14	14
Size of tumors (cm)	1.0-8.6	3.5
The number of involved lymph nodes	0-18	4

[a]Body mass index, [b]Modified radical mastectomy, [c]Breast conserving therapy

In the center of SC field, the diameter of the wall of the chest was measured, and these measurements ranged from 12 to 21 cm, with an average of 14.2 cm and a standard deviation 2.36 cm (Table 2). The mean diameter was related directly related to BMI using a simple linear regression analysis with a significance of $p<0.0001$ (adjusted $R^2=0.71$). Plan depth ranged from 3 to 7 cm with a mean of 4 cm, and the standard deviation was 1.3 cm (Table 2). The Plan depth was related directly related to BMI using simple linear regression analysis with a significance of $p<0.0001$ (adjusted $R^2=0.67$).

In patients with BMIs in the range of 18.5-22.5 include units (thin) with an anterior field with an average depth of 3.27 cm and standard deviation of 0.26 cm, V95 was an average of 96% of all lymph nodes, and, at the volume that received ≥105% of the dose in the lymph nodes II and III was acceptable, but the goal of treatment in patients with V105<7% was not achieved in SC, while this percentage in the AP/PA technique was much lower than the AP. This difference was statistically significant ($p<0.001$) (Table 3).

Table 2. Mean diameter of the wall of the chest and the mean depth of supraclavicular lymph nodes (the Mean Plan depth) according to BMI

BMI [a] (kg/m^2)	Mean diameter of the wall of the chest	SD [b]	Mean Plan depth (cm)	SD [b]
18.5-22.5	12.09 cm	0.30	3.27	0.26
22.6-24.5	13.50 cm	0.40	4.5	0.41
25-29.9	15.17 cm	0.53	5.43	0.41
≥30	18.02 cm	2.04	6.60	0.54
Total	14.2 cm	2.36	4	1.3

[a] Body mass index, [b] Standard deviation (cm)

Table 3. Results of dosimetry according to BMI

BMI range (kg/m^2)		Level II			Level III			Supraclavicular		
		V95 [a]	V105 [b]	V110 [c]	V95	V105	V110	V95	V105	V110
18.5-22.5	AP	95.81± 0.7	3.25± 1.4	0.00±0	98.90± 0.3	2.22± 0.8	0.00±0	98.63± 1.2	63.63± 1.3	31.08±7
	AP/PA	98.63± 1.2	0.00±0	0.00±0	100.00± 0	0.00±0	0.00±0	96.81± 0.6	0.00±0	0.00±0
	p-value	0.09	0.07	0.1	0.1	0.2	0.1	0.08	<0.001	<0.001
22.6-24.9	AP	96.00± 0.8	16.50± 3.1	14.25± 3.5	96.50±1	5.37± 0.5	1.50±1	98.25±1	76.00± 0.8	38.75±1
	AP/PA	97.00± 2.3	0.00±0	0.00±0	98.75±1 .9	0.00±0	0.00±0	97.50± 0.6	0.00±0	0.00±0
	P-value	0.08	<0.001	<0.001	0.09	0.06	0.07	0.09	<0.001	<0.001
25-29.9	AP	99.12± 1.1	28.12± 5.7	29.87± 6.4	96.75±1	15.37±5	7.00± 3.8	99.75± 0.5	85.25±5	47.75± 0.8
	AP/PA	98.37± 2.1	0.62± 0.7	0.25± 0.7	99.62± 0.5	0.00±0	0.00±0	98.62± 1.7	0.00±0	0.00±0
	P-value	0.09	<0.001	<0.001	0.09	<0.001	<0.001	0.09	<0.001	<0.001
≥30	AP	98.20± 2.2	52.40±2	41.00± 2.3	97.60±2	28.20± 2.9	13.54±2	98.8± 0.8	91.00± 1.6	48.50± 0.9
	AP/PA	96.00± 1.7	3.80± 0.8	0.00±0	99.80± 0.4	3.40± 1.9	0.00±0	97.60± 1.1	2.68± 1.5	0.00±0
	P-value	0.09	<0.001	<0.001	0.08	<0.001	<0.001	0.09	<0.001	<0.001
Total	AP	97.21± 1.9	21.02± 18.4	17.89± 16.9	97.71± 1.5	11.07± 10.2	4.63± 5.6	98.93± 1.1	76.50± 11.7	40.05±8
	AP/PA	97.86± 2	0.86± 1.5	0.07± 0.4	99.68± 0.8	0.61± 1.5	0.00±0	97.57± 1.3	0.48± 1.2	0.00±0
	P-value	0.09	<0.001	<0.001	0.08	<0.001	<0.001	0.09	<0.001	<0.001

[a] 95% of target volume with 95% or greater of the prescribed dose 50 Gy
[b] Irradiated volume received more than 105% of the prescribed dose
[c] Irradiated volume received more than 110% of the prescribed dose

Patients with a BMI of 22.6-24.9 units (normal) with an anterior field with an average depth of 4.5 cm and a standard deviation0.41 cm, volumes that covered 95% (V95) of the dose in the lymph levels II, III, and SC were 96%, 96.5%, and 98.2%, respectively. In these cases, the V105 at level II and SC was >7%, which did not fulfill our goal of treatment, while this number for the AP/PA technique was <7%. This difference was statistically significant (p<0.001) (Table 3). In patients with BMIs in the range of 25-29.9 units (overweight) with an average depth of 5.43 cm and a standard deviation 0.41 cm in V95 at the AP field with LII, LIII and SC were 99%, 96%, and 99%, respectively. In this group V105 at all three lymph levels was >7% and, using the AP/PA technique, V105 Was <7%.This difference was statistically significant (p<0.001) (Table 3). In patients with BMIs ≥30 (kg/m^2) (obese) with an average depth of 6.60 cm and a standard deviation 0.54 cm, in V95 at the AP field with lymph LII, LIII, and SC were appropriate, but, in this group, V105 at all three lymph levels was very high, and, using the AP/PA technique, V105 was<7%. This difference was statistically significant (p<0.001) (Table 3).

In all patients, with an average depth of 4 cm and standard deviation of 1.3 cm, in V95 at the AP field with level II, III, and SC was 97%, 97%, and98%, respectively. Overall, V105 at all three lymph levels was>7%, and, using the AP/PA technique, V105 was <7%. This difference was statistically significant (p<0.001) (Table 3).

4. Discussion

In the patients with breast cancer, the depths of the SC and AX lymph nodes were significantly different. In our study, the mean depths of SCLNs were 2.7-5.3 cm (with a range of 3-7 cm) and the mean depths of the chest wall diameter were 11.8-16.5 cm (with a range of 12-21 cm). These findings were comparable to those in previous reports that showed that the mean depths of SCLNs were3.2-5.5 cm (with a range of 2.7-7.5 cm) (9-11), and the mean depths of the chest wall diameter were12.2-16.8 cm (with a range of 11.2-22.7 cm) (10-11).

Our study also showed a significant linear relationship between BMI and the mean SC depth (the mean Plan depth) and the mean diameter of the wall of the chest ($p < 0.0001$) (adjusted R^2=0.67) and (p<0.0001) (adjusted R^2 = 0.71), respectively. There was a direct relationship between higher BMI and deeper nodal beds. This result was comparable with Bentel and colleagues' findings in which SCLNs depths were estimated to be 19-64 mm. They showed the relationship between the depths of the nodes and patients' BMIs (7). Liengsawangwong and colleagues concluded that the depth of the third level of axillary lymph nodes and SC varied between 14 and 67mm and depended on BMI (8). This finding was consistent with our study that showed that the mean depths of SCLNs were 2.7-5.3 cm (with a range of 3-7 cm). Liengsawangwong et al. found that using single AP for radiation therapy of SC fields with Dmax or D=3 cm usually provided inadequate coverage of PTV, dose inhomogeneity, and more hot spots. Especially, with using single photon low-energy to treat Dmax in SC fields with single AP, the optimal PTV coverage was achieved only in some of the breast cancer patients with BMIs <30 (kg/m^2) (8). This finding was inconsistent with our study that showed all patients in the thin, normal, overweight, and obese groups with an anterior field, V95 of the dose in the lymph levels II, III, and SC were appropriate, with no difference between the AP/PA and AP techniques. However, our findings were consistent with their results in that both studies showed that the AP/PA treatment technique had fewer hot spots in the SC fields than the AP technique.

In our study, V95 in the AP field and AP/PA fields, at level II, at level III, and in SCLNs, did not have any significant differences statistically (p>0.05) (Table 3). V105 in the AP field and the AP/PA fields, at level II, at level III, and in SCLNs, had statistically significant differences (p<0.001) (Table 3). So, it seems that the AP/PA treatment technique is the better choice of treatment, especially for overweight and obese breast cancer patients to avoid hot spots in LII, LIII, and SCLNs, and it is reasonable to avoid hot spots in SCLNs for thin and normal breast cancer patients as well. Goodman's evaluation showed that the lymph node dose made a significant difference in the posterior axillary lymph nodes (11). This finding was comparable with our study that showed all patients in the thin, normal, overweight, and obese groups with an AP field or AP/PA fields, V95 in the lymph levels II and III were appropriate. In 2004, Jephcott and colleagues, studying CT among 10 patients, compared four techniques of radiation therapy in SC fields, i.e., 1) single AP field, 2) AP/PA fields, 3) anterior field with posterior axillary boost, and 4) anterior field with posterior axillary boost with compensator. In this study, a single AP field had a poor result in 60% of the cases. The second method had good coverage as there at least were hot spots, but the medial of neck and chest received excessive doses. In the third method, an adequate dose reached the PTV, and the medial of the neck and chest received a low dose, but 120% more hot spots were created in 90% of the patients. The fourth method, achieved a good dose to the PTV and a low dose to the posterior neck and chest, but it showed less than 120% of hot spots in all patients (12). In that study, using the AP technique also displayed poor results in 60% of the cases. The AP/PA method resulted in good coverage and the hot spots were minimal. This finding was inconsistent with our study that showed all patients in the thin, normal, overweight, and obese groups with an anterior field, V95 in the lymph levels II, III and SC was appropriate. But it was consistent with our study that showed AP/PA treatment technique had fewer hot spots than the AP technique. Jabbari and colleagues found that AP/PA in SC field appears much better than a single AP because of the better coverage of PTV. However, the mean and maximum unnecessary radiation dose to lungs and skin were increased by a few percentage points in AP/PA over that of a single AP (13). This finding was totally inconsistent with our study, which indicated that all patients in the thin, normal, overweight, and obese groups with an anterior field, V95 in the lymph levels II, III and SC was appropriate, and there was no difference between the AP/PA technique and AP technique. Comparing the results in plans computed according to depth for best coverage, the AP method showed the most hot spots. This effect will be especially magnified if low energy equipment, such as Cobalt 60 or Compact 6 MV, is used. Therefore, we suggest that the best method is to use 3D CT planning with AP/PA for treatment. This is due to the difference in SC depth among patients. CT is the best for specifying depth of regional lymph nodes if 2D plans are used. More studies are required to investigate dosage absorbed by endangered organs and to identify ways to reduce the exposures. Only such additional results can prove conclusively whether the AP/PA method is superior to other methods or not.

There were some limitations in our study. First, treatment planning depends on the individual design practice, and perhaps different radiation oncologists have different results in treatment planning or in their calculations. In all patients, the procedure was conducted by a radiation oncologist and a radiation physicist, and we used the standard defined fields, so the difference may be minimal. Second, we did not consider the average and maximum dosages received by the lungs, heart, and skin, which might be increased to a greater extent in the AP/PA technique than in the AP technique.

5. Conclusions

In this paper, various SC fields techniques were compared. The AP-PA technique, due to its having fewer hot spots, was better than a single AP, especially for overweight and obese breast cancer patients. However, in the AP/PA technique, the usage of single photon low-energy (Cobalt 60 or 6 MV) causes more hot spots than usual. To confirm that the field AP/PA is better than those of other methods, further studies are needed to determine the dose to at-risk organs, as the lungs and the heart. Ways to reduce these excessive doses also must be developed, and the various methods must be compared, e.g., using a single high-power field and boosting the dose to the posterior axilla.

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Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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