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Comparison of Photon-electron and Photon Radiotherapy for Supraclavicular Lymph Nodes of Mastectomy Patients with Left-sided Breast Cancer

Mehran Mohseni[1], Fatholah Mohaghegh[2], Nasrin Robatmili[1], Mohammad Reza Bayatiani[2], Fatemeh Seif[2], Nayyer Sadat Mostafavi[3]

[1]Department of Medical Physics, School of Paramedical Sciences, Kashan University of Medical Sciences, Kashan, [2]Department of Medical Physics and Radiotherapy, Arak University of Medical Sciences and Khansari Hospital, Arak, [3]Department of Medical Physics, School of Paramedical Sciences, Isfahan University of Medical Sciences and Khansari Hospital, Isfahan, Iran

The aim of radiotherapy is to deliver the highest possible radiation dose to the tumor and the lowest radiation to normal tissues surrounding the tumor. In the present study, lymph nodes of the supraclavicular region were treated using two therapeutic techniques, namely photon technique (PT) and combinatory photon-electron technique (CPET). We recruited 50 patients with local lymph node metastasis. The photon energies were 6-15 MV. Furthermore, the electron beam energy was 18 MeV in CPET. The study findings revealed that the mean delivered dose to target volume was 41.12 ± 2.98Gy for PT and 44.56 ± 1.90Gy for CPET. The percentage of the target volume irradiated to 90% of the prescribed dose (V90) was calculated as 74.61% ± 9.30% and 82.06% ± 9.70% for PT and CPET, respectively. The mean dose delivered to the heart and lungs was not significantly different between the two groups. Furthermore, the maximum doses delivered to the spinal cord were 12.55Gy in PT and 8.89Gy in CPET. The mean doses delivered to the thyroid gland were 39.26 and 34.89Gy in PT and CPET. According to the study results, the maximum doses delivered to the spinal cord, head of the humerus bone, and thyroid were reduced significantly as measured the CPET technique. In contrast, no significant difference was observed regarding the dose delivered to the heart and lung. The dose delivered to the supraclavicular region determined by the CPET was significantly augmented. Furthermore, the coverage of the tumor mass was optimized using the new method.

Key Words Breast cancer, Treatment planning, Supraclavicular region dose, Thyroid dose

INTRODUCTION

Breast cancer has been reported as the second fatal malignancy after lung cancer among women worldwide. The studies performed during 1989-2012 indicated that the number of patients affected by breast cancer increased up to 36% [1]. The common therapeutic techniques for breast cancer include surgery, chemotherapy, radiotherapy, and hormone therapy. It is noteworthy that approximately 60% of all patients worldwide are treated by radiotherapy [2,3].

During the course of treating cancerous cells, surrounding healthy tissues also get exposed to the radiated beam. Consequently, it is of considerable importance to concentrate the dose on the target mass, so that sensitive and healthy organs, such as the heart (especially, in left-sided breast cancers), lungs, spinal cord, thyroid, and the other breast, would be minimally exposed.

As a result, a proper treatment plan is one of the most important key components of effective therapy of breast cancer. For this, the type and intensity of radiation, beam direction, field measurements, and anatomical condition of the patient should be considered [4]. Due to the possibility of changes in anatomical regions, different therapeutic techniques are considered for different disease stages, among which the techniques of common three-dimensional tangential fields and combinatory fields could be plausible options. In these techniques, electron fields, photons, or a combination of both fields are utilized [5-9].

The most common radiotherapy method for breast cancer uses two opposing medial and lateral tangential fields of photon along with the wedge in chest wall region and the single-field photon in the supraclavicular region [10]. In the

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Correspondence to Nasrin Robatmili, E-mail: robatmilyn@yahoo.com, https://orcid.org/0000-0001-9276-3029

common method, the chest wall region is half-beamed from both sides of the lungs and supraclavicular region. Next, the dose distribution is optimized using a wedge filter and different beam energies.

The current study aimed to evaluate a therapeutic method in which two tangential opposing fields along with the wedge are used for the chest wall region, which are similar to the common three-dimensional method. A posterior-anterior (PA) photon field and an anterior-posterior (AP) electron field opposing each other were considered for the supraclavicular region. The PA photon and the AP electron fields were selected because of the substantially high and low penetration depths of photons and electrons, respectively.

In the present study, the absorbed doses of supraclavicular lymph nodes of planning treatment volume (PTV) and the normal tissues surrounding the PTV were assessed. Finally, a comparison was made between the results of the two therapeutic techniques including the photon technique (PT, the common therapeutic technique) and the combinatory photon-electron technique (CPET), which were applied for the lymph nodes of the supraclavicular region [10]. In the common method, the chest wall region is half-beamed from both sides of the lungs and supraclavicular region. Next, the dose distribution is optimized using a wedge filter and different beam energies.

MATERIALS AND METHODS

This study was approved by the ethics committee of the Kashan University of Medical Sciences, Iran (code number: IR.KAUMS.REC.1395.151). In this study, data of 50 mastectomy patients with left breast cancer and with local lymph node metastasis were used. The study was performed in the Radiation Oncology Department at Ayatollah Khansary Hospital (Arak, Iran) between 2016 and 2017. Informed consent was obtained from all individuals participating in this study.

Computer treatment planning

Prior to the computed tomography (CT)-simulation procedure, the patient was laid on the breast board in a suitable angle. The angle was chosen, so that the chest wall was located parallel to the horizon. Afterwards, a marker was considered as the point of coordinates (x, y, z) and the wires specifying the entrance of medial and lateral fields, as well as the lower and upper borders of the breast were located on the patient's body by the doctor.

The ipsilateral hand of the patient was positioned above his/her head, and the head was rotated toward the contralateral breast. The entrance point of the medial tangent was regarded as the midline, and the entrance point of the lateral tangent was considered 2 cm from the point of breast tissue touch. The initial data were recorded in the planning system after CT-simulation and preparation of CT images. The radiation dose was planned to be 50 Gy in 25 sessions.

Patient sampling was performed using the normal distribution function and simple random method. The total number of samples used was 50.

All the patients underwent radiation therapy including single PT for supraclavicular region using two opposing tangential fields along with the wedge for the chest wall region. To plan CPET for chest wall region using the ISOgray Treatment Planning System, two opposing tangential fields along with the wedge similar to the common three-dimensional technique were used.

On the other hand, the field for the supraclavicular region was planned as two-sided opposing fields of PA photon and AP electron with 15 MeV and 18 MeV energies, respectively. This system can plan treatment by various methods, such as three-dimensional conformal radiation therapy.

The delivered dose and the dose volume histogram (DVH) of the covered volume were obtained for each healthy organ and tissue in addition to the tumoral tissue using the ISOgray software. Two samples of dose distribution resulting from the two therapeutic methods for the tumoral tissue are demonstrated in Figure 1. The hot and cold parts, as well as the DVH, were extracted and analyzed clinically and physically by comparing with the standard protocols.

Dosimetric parameters

Some parameters, including V95 (%) and V90 (%) (the percentage of the target tissue volume irradiated to 95 and

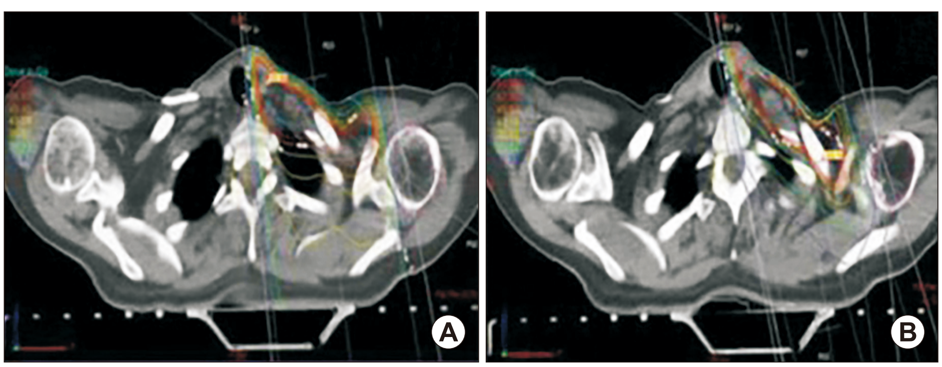

Figure 1. An example of dose distribution in the supraclavicular region with the photon technique (A) and combinatory photon-electron technique (B).

90% of the prescribed dose, respectively); V30 (%), V25 (%), and V5 (%) (the percentage of the heart volume receiving 30, 25, and 5 Gy dose, respectively); and V40 (%) and V20 (%) (the percentage of the ipsilateral lung volume receiving 40 and 20 Gy dose, respectively), needed to be evaluated for dose distribution and were assessed using DVH. The DVH for all exposed organs (the heart, lungs, head of the humerus bone, thyroid, and spinal cord) and PTV (supraclavicular and chest wall) after performing both therapeutic methods are indicated in Figure 2. Moreover, parameters of maximum, minimum, and mean dose delivered to all exposed organs and PTV were determined using the aforementioned software. A sample of the data extracted from the ISOgray software is presented in Figure 3.

Statistical analysis

All statistical analyses were performed by SPSS ver. 16 (SPSS Inc., Chicago, IL, USA). The one-way ANOVA test was applied to compare the results obtained by dosimetric parameters of the two therapeutic methods. $P < 0.05$ was considered significant.

RESULTS

Figure 1 illustrate the extracted isodose curves for tumoral tissue, and Figure 2 shows the DVH for all organs (both tumoral and healthy tissues) using both techniques in a patient. Furthermore, Table 1 and 2 demonstrate the calculated dose parameters for the supraclavicular lymph nodes and normal tissues in both methods. The parameters, including maximum dose, mean dose for target volume (supraclavicular) and exposed organs (thyroid, spinal cord, lungs, heart, and head of the humerus bone); V95 and V90 for the target volume (supracla-vicular region); V40 and V20 for the lungs; and V5, V25, and V30 for the heart, were calculated and compared between the two methods.

Doses delivered to organs at risk

Table 1 lists the maximum and mean doses delivered to the spinal cord, thyroid, head of the humerus bone, lungs, and heart for 50 patients with left-sided breast cancer. The results of both the treatment plans were compared (Fig. 4 and 5). Compared with PT, CPET resulted in a reduction in the maximum and mean doses delivered to the spinal cord, thyroid, and head of the humerus bone. The maximum and mean doses delivered to the lungs and heart were not

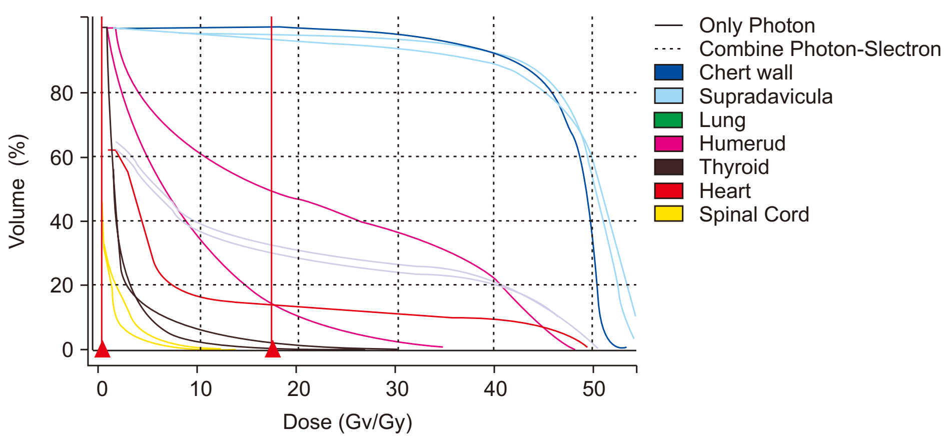

Figure 2. An example of the dose volume histogram of the target tissue and organs at risk calculated for one of the patients treated with combinatory photon-electron technique and photon technique.

	1	2	3	4	5	6	7
Structure	SKIN	HEART	HUMERUS HEAD	LT LUNG	PTV	Spinal cord	SUPR
Geom. Vol. (cm3)	29990.2	958.1	58.1	1189.9	1278.1	28.3	374.
Random points	11144	7617	4998	7957	8078	4564	647
Min. dose (Gy)	0.00	0.00	0.34	0.00	4.62	0.00	0.0
Max. dose (Gy)	54.68	49.49	35.24	51.82	54.67	1.92	52.6
Med. dose (Gy)	0.00	2.46	1.82	10.37	49.00	0.00	43.5
Mean dose (Gy)	5.35	7.33	4.05	20.09	46.18	0.31	40.3
Standard deviation	13.38	13.81	6.02	19.42	8.32	0.45	11.1
Bound min. dose (Gy)	0.00	0.00	0.00	0.00	0.00	0.00	0.0
Bound max. dose (Gy)	48.67	48.67	48.67	48.67	48.67	48.67	48.6
Selection vol. (cm3)	29044.7	948.0	58.1	1076.6	584.6	28.3	325.
Selection vol. (%)	96.8	99.0	100.0	90.5	45.7	100.0	86.
Dose at 95% (Gy)	0.02		0.43		26.46		10.4

Figure 3. An example of the statistical data table of the target tissue and organs at risk calculated by the ISO-gray software.

significantly different.

As shown in Table 2, the mean V25 (%) values for the heart are 4.37% ± 8.36% and 4.41% ± 7.07% in CPET and PT, respectively. Moreover, V30 (%) and V5 (%) were 3.82% ± 7.92% and 32.07% ± 9.75% in CPET, respectively, and 3.71% ± 6.81% and 31.41% ± 9.76% in PT, respectively. The *P*-value was not significantly different between the two techniques. Furthermore, as shown in Table 2, the mean V40 (%) values for the lung were 9.43% ± 7.81% in CPET and 10.29% ± 10.10% in PT, whereas V20 (%) values were 25.23% ± 10.78% and 26.98 ± 10.52% in CPET and PT, respectively.

Doses for planning treatment volume (supraclavicular nodal)

The mean of the maximum dose delivered to the supra-clavicular region and the *P*-values for the differences of this parameter between the two techniques are shown in Table 1. It should be noted that there was no significant difference between the two methods regarding the maximum doses for the supra-clavicular region ($P = 0.086$). Moreover, the mean doses delivered to the supraclavicular region were 44.56 ± 1.90 and 41.12 ± 2.98 Gy for CPET and PT, respectively. According to the results of one-way ANOVA, the latter parameter (the mean doses) was significantly different between the two groups ($P = 0.007$). The maximum and mean doses delivered to the supraclavicular region increased in CPET compared with those in PT (Fig. 4 and 5). In addition, the dose delivered to the supraclavicular region was augmented (Fig. 6).

Based on Table 2 and Figure 6, the mean V95 (%) values were 65.80% ± 13.10% and 55.53% ± 12.31% for CPET and PT, respectively. Furthermore, as mentioned in Table 1, the two groups were significantly different with respect to V95 (%) ($P = 0.002$). Likewise, the mean V90 (%) values for the two methods are shown in Table 2 and Figure 6, and the difference between the two techniques with respect to this parameter was statistically significant ($P = 0.031$).

DISCUSSION

Electron beam therapy (EBT) is currently one of the commonly used radiotherapy methods. EBT has some benefits, including dose homogeneity in the target volume as well as dose reduction in deeper tissues [4,11].

The standard technique currently being used at our hospital for treating breast cancer includes opposing tangential beams of photon for the whole chest wall region in addition to an interior photon beam for the supraclavicular lymph nodes. To elevate the dose for PTV (supraclavicular lymph nodes) and reduce the dose for healthy and sensitive

Table 1. Dosimetric parameters and statistical analysis obtained by one-way analysis of variance test for the two therapeutic methods

	Plan	Number	Mean	SD	SEM	Sig-value
D_{max} Cord	PT	50	12.55	6.2	1.30	0.014*
	CPET	50	8.89	4.68	0.66	
D_{max} Heart	PT	50	47.95	5.96	0.84	0.787
	CPET	50	47.62	6.45	0.91	
D_{max} Lung	PT	50	51.2	1.89	0.28	0.629
	CPET	50	50.98	2.52	0.36	
D_{max} Thyroid	PT	50	39.26	14.03	1.98	0.042*
	CPET	50	34.89	11.54	1.63	
D_{max} Humerus	PT	50	35.58	8.02	1.13	0.004*
	CPET	50	31.00	7.25	1.026	
D_{max} Supra	PT	50	51.89	2.71	1.37	0.086
	CPET	50	54.30	1.59	0.22	
D_{mean} Cord	PT	50	1.18	0.808	0.11	0.111
	CPET	50	1.51	1.24	0.18	
D_{mean} Heart	PT	50	5.51	3.28	0.46	0.949
	CPET	50	5.47	3.29	0.47	
D_{mean} Lung	PT	50	12.99	4.24	0.60	0.429
	CPET	50	12.33	4.12	0.58	
D_{mean} Thyroid	PT	50	6.19	5.55	0.78	0.679
	CPET	50	5.78	4.43	0.63	
D_{mean} Humerus	PT	50	7.27	5.45	0.77	0.508
	CPET	50	7.94	4.77	0.67	
D_{mean} Supra	PT	50	41.12	2.98	0.85	0.007*
	CPET	50	44.56	1.90	0.27	

Sig-value, significant value; PT, photon technique; CPET, combinatory photon-electron technique; D_{max}, max dosimetry; D_{mean}, mean dosimetry. *Results showing significant differences ($P < 0.05$) of dosimetric parameters between CPET and PT performed for mastectomy patients undergoing supraclavicular nodal irradiation.

Table 2. Vx (%) parameters for different organs determined by PT and CPET

	Plan	Number	Mean	SD	SEM	Sig-value
Heart V5 (%)[a]	PT	50	32.07	9.75	1.38	0.934
	CPET	50	31.41	9.76	1.38	
Heart V25 (%)[a]	PT	50	4.41	7.07	1	0.842
	CPET	50	4.37	8.36	1.18	
Heart V30 (%)[a]	PT	50	3.82	6.81	0.96	0.948
	CPET	50	3.71	7.92	1.12	
Lung V40 (%)[b]	PT	50	9.43	7.81	1.10	0.797
	CPET	50	10.29	10.10	1.67	
Lung V20 (%)[b]	PT	50	26.98	10.52	1.49	0.415
	CPET	50	25.23	10.78	1.53	
Supra V95 (%)[c]	PT	50	55.53	12.31	1.74	0.018*
	CPET	50	65.80	13.10	1.85	
Supra V90 (%)[c]	PT	50	74.61	9.30	1.31	0.031*
	CPET	50	82.06	9.70	1.37	

PT, photon technique; CPET, combinatory photon-electron technique; Sig-value, significant value. *Means and statistical analysis results showing significant differences ($P < 0.05$) of dosimetric parameters between CPET and PT performed for mastectomy patients undergoing supraclavicular nodal irradiation. [a]The percentage of the heart volume receiving 5, 25, and 30 Gy dose, respectively. [b]The percentage of the ipsilateral lung volume receiving 40 and 20 Gy dose, respectively; [c]The percentage of the target tissue volume irradiated to 95 and 90% of the prescribed dose, respectively.

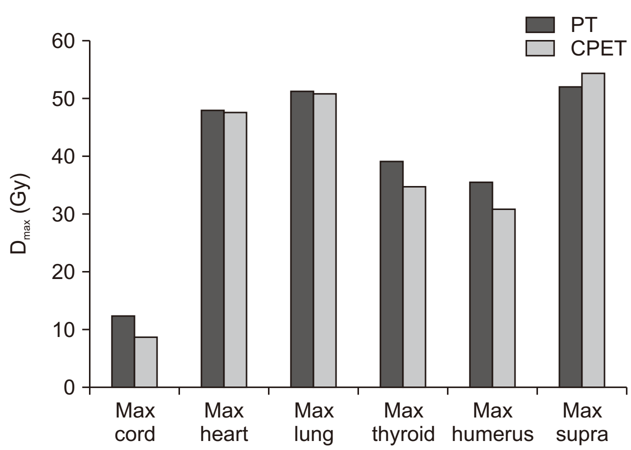

Figure 4. Chart of the maximum delivered doses (D_{max}) to the organ at risk and supraclavicular lymph nodes determined by the two techniques. PT, photon technique; CPET, combinatory photon-electron technique.

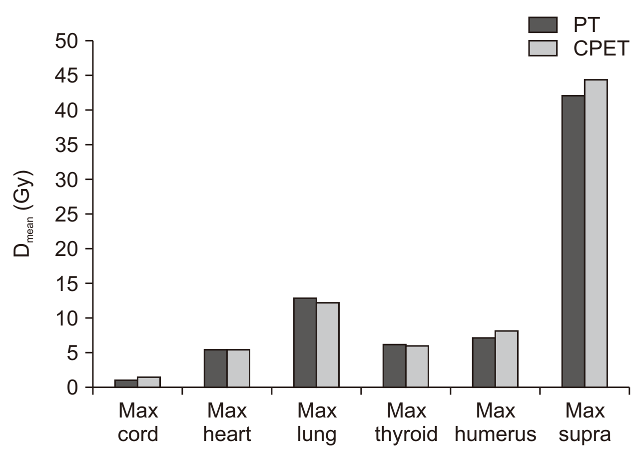

Figure 5. The mean delivered doses (D_{mean}) to the organs at risk and supraclavicular lymph nodes determined by the two techniques. PT, photon technique; CPET, combinatory photon-electron technique.

surrounding organs, we used a new method. In the newly proposed method, we used two photon-electron combinatory beams (the PA photon beam and AP electron beam) for the supraclavicular region and performed the same process for the chest wall region.

Dose to organs at risk

According to our study, the maximum dose delivered to the spinal cord, head of the humerus bone, and thyroid declined significantly with CPET. The deep penetration of photon (being forward due to high energy) led to less disseminated beams, thus accounting for the lower dose delivered to these organs. The spinal cord is regarded as an organ of the series; therefore, reduction in the maximum dose for this organ is of considerable importance.

Radiotherapy might be accompanied by some side effects for the thyroid gland, including hypothyroidism and thyroid cancer. The mean dose of > 20 Gy for neck and vertebral column can be associated with hypothyroidism and thyroid cancer [12,13]. Recent studies reported the occurrence of hypo- or hyper-thyroidism during the first 3-5 years [12-14]. Consequently, it is noteworthy that the dose delivered to the thyroid was < 20 Gy in the present study.

The dose delivered to the heart and lungs was not significantly different between the two methods. In the current study, the mean V25 (%) values were 4.37% ± 8.36% and 4.41% ± 7.07% for CPET and PT, respectively, confirming the optimized result using the combinatory method.

Considering the studies performed on radiotherapy for breast cancer patients, the risk for coronary artery stenosis

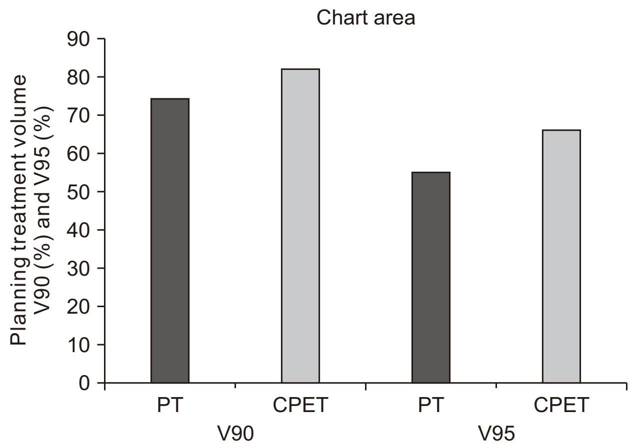

Figure 6. The total planning treatment volume V90 (%) and V95 (%) determined by photon technique (PT) and combinatory photon-electron technique (CPET).

and heart failure disorders is higher in patients with left-sided cancer than for those with right-sided malignancies. Heart-related side effects are more probable after 6-12 months from dose reception. Absorbance of doses > 40 Gy by the mediastinal region is associated with an elevated incidence of heart failure and myocardial disorder. For V25 < 10% (with possibility of 1%), coronary artery stenosis may develop after 10-15 years [15]. In this study, the dose absorbed by the heart was lower than the aforementioned doses, and this result is consistent with the findings of Salem et al. [16].

As shown in Table 2, the V20 (%) values of the lung were 25.23% ± 10.78% and 26.98% ± 10.52% for CPET and PT, respectively. Signs of pulmonary fibrosis might be observed for mean doses of > 10-20 Gy and V20 (%) > 30%, and this was reported to be less with CPET than with PT [15]. Likewise, Salem et al. [16] revealed that the V20 (%) value for the lung needed to be optimized for the photon-electron method. Jabbari et al. [17] reported that the dose for the heart was lower in CPET compared with PT. Furthermore, the dose for the lung was elevated in CPET compared with PT.

Dose to planning treatment volume (supraclavicular nodal)

The mean and maximum doses delivered to the supraclavicular lymph nodes increased significantly by the new therapeutic method. Moreover, tumor volume coverage improved using CPET compared with PT. The *P*-value for V90 was obtained as 0.031, which is indicative of a significant difference between the two techniques.

The aforementioned results demonstrate that CPET has an enhanced coverage compared with PT. Salem et al. [16] also concluded that the coverage was optimized using CPET compared with PT. Likewise, Jabbari et al. [17] stated that the coverage for the supraclavicular lymph nodes was better using CPET than using PT.

Considering our study findings, parallel and opposing fields might lead to homogeneous distribution of beams from the surface to the tissue depth, and the maximum dose will be optimized in the center of PTV. Regarding the thickness of the supraclavicular tissue in the examined patients (< 4 cm) and the penetration depth of the electron beams (< 5 cm), it seems suitable to use AP electron field for these patients.

In addition, using photons with energy of 15 MV and penetration depth higher than PA could account for reduced absorbed doses in the spinal cord and thyroid. However, com-binatory field techniques have some disadvantages, inclu-ding longer treatment process, high treatment costs, and lack of required hardware facilities (multi leaf collimator shortage and fixation methods) [16,18].

In the current study, the use of combinatory fields was associated with reduced doses delivered to exposed organs volume (the spinal cord, thyroid, and head of the humerus bone), favorable coverage of the target volume, and enhanced dose in the supraclavicular lymph nodes. The dose delivered to the heart and lung was not significantly different between the two therapeutic techniques. Homogenous dose distribution and delivery of the maximum dose to the tumoral tissue by increasing the therapeutic fields have driven the efforts toward using these combinatory techniques.

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CONFLICTS OF INTEREST

No potential conflicts of interest were disclosed.

ORCID

Mehran Mohseni,
https://orcid.org/0000-0002-6685-1743
Fatholah Mohaghegh,
https://orcid.org/0000-0003-3645-0540
Nasrin Robatmili,
https://orcid.org/0000-0001-9276-3029
Mohammad Reza Bayatiani,
https://orcid.org/0000-0002-7300-063x
Fatemeh Seif,
https://orcid.org/0000-0002-1532-293x
Nayyer Sadat Mostafavi,
https://orcid.org/0000-0002-1160-8965

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