

Is Pulmonary Function Test Insensitive to Possible Pulmonary Complications after Tangential Radiotherapy of Breast Cancer?

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Abstract

Background: Pulmonary complications of radiation to breast are inevitable, while its incidence and severity are not clear. One of the methods to assess pulmonary complications is spirometry. The influence of radiotherapy on pulmonary function test and the factors affecting it have been assessed in this study.

Methods: Breast cancer patients with stage II and III (based on TNM staging), underwent six courses of chemotherapy, and the total mastectomy was included in this study. Smokers, chronic pulmonary patients, cardiac patients, and those who suffered from anatomic chest malformations were excluded. Sample size was 75 and data collection was conducted by the spirometer device.

The total tumor dose varied between 4800 to 5040 cGy with fraction of 180 or 200 cGy. Spirometry was performed before and 3 months after radiotherapy; the patients were examined at the same time by a specialist for respiratory complications. The measured parameters were FEV₁ (Forced Expiratory Volume in 1 second) and FVC (Forced Vital capacity) which were normalized by age and sex.

Results: The average age of the patients was 45.6 ± 7.92 . Average length and widths of tangential fields were determined 18.2 ± 1.8 and 6.7 ± 1.37 respectively. Average central lung distance was measured 2 ± 1.07 cm. The mean of FEV₁% prior to and following radiotherapy was measured 74.9 ± 15.59 and 78.86 ± 12.55 respectively ($p=0.09$). The mean of FVC% before and after radiation treatment was measured 72.17 ± 14.26 and 74.6 ± 11.36 ($p=0.07$). No abnormal signs were observed in the patients after radiotherapy.

Conclusion: It seems that three months is a short period for appearance of pulmonary changes after radiotherapy with cobalt machine. Moreover, minimizing CLD through planning might lower the probability of pneumonitis due to radiation.

Keywords: Tangential Radiotherapy, Breast Cancer, Spirometry, Pulmonary Complications

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Introduction

Radiotherapy of breast cancer can enhance the local control rate and survival of patients.

Pulmonary complication of radiotherapy is inevitable while its severity and incidence remains unclear [1, 2]. Lung damage due to radiotherapy is one of the complications which may develop to pneumonitis and fibrosis [3, 4].

Pulmonary changes due to radiation have been surveyed by different imaging techniques such as HCRT and nuclear medicine. Shratteer-sehn et al. and Bell et al. have observed some changes in CT images of breast cancer patients who were treated by radiotherapy [5, 6].

Lung clearance is one of the earliest functions that changes after radiation, which has been studied by Soga et al. and others [7, 8].

Furthermore, Groth et al. and Lin et al. have surveyed these changes by DTPA-99m Tc [8, 9]. One of the methods to assess pulmonary complications is spirometry. Radiation pneumonitis usually appears 2 to 6 months after radiotherapy [1, 2].

Lund et al., Lind et al. and Tukatli et al. have reported the reduction of respiratory volumes following radiotherapy [10, 11, 12]. Based on Lind's report [10], FEV₁ mean before and three months after radiotherapy was obtained 1.85 and 1.75 Lits respectively. Kwa and his colleagues, based on a large clinical data set, observed a dose-effect

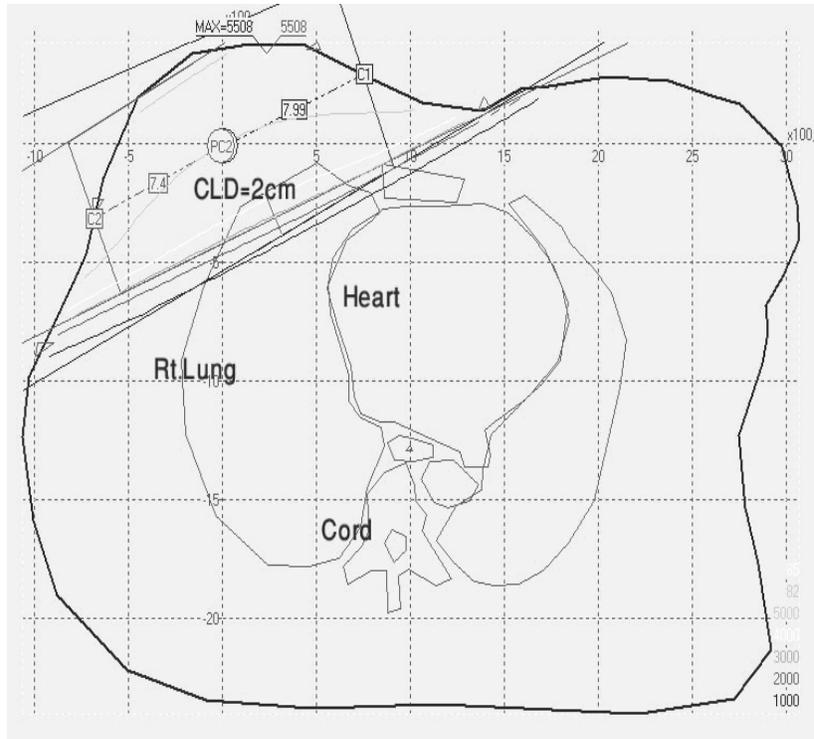


Figure 1. A two dimensional planned image of right breast, showing doses received by breast and lung (Tumor dose was 50 Gy). Moreover CLD (=2 cm) has been delineated on the planned image.

relation between the mean lung dose and the incidence of radiation pneumonitis. They worked on 540 patients with lung cancer, esophagus and 59 breast cancer patients. Observed pneumonitis incidence in the breast group was obtained 1.4 % [13].

The influence of radiotherapy on pulmonary function tests and the factors affecting it have been examined in this study. Moreover, the influence of irradiated lung volume on PFTs has been assessed.

Materials and Methods

Female patients with II and III breast cancer stages (based on TNM staging) underwent both six courses of chemotherapy, and the total mastectomy was examined in this study. Smokers, chronic pulmonary patients, cardiac patients, and those who suffered from anatomic chest malformations were excluded. Sample size was 75 and data collection was conducted by spirometer (SPIROLAB II made in Italy) device of endoscopy section of the 5th Azar hospital of Gorgan, Iran.

The patients were examined by radiotherapists, and radiation fields were drawn on their skin, and after putting some markers on radiation fields'

borders, the patients were referred to CT dept to take planning slices. Patients lied on the special wedge with an adjustable height to make sternum surface parallel to the table top of radiotherapy machine and also CT scanner (for simulation).

CT films were digitized and images were transferred to two dimensional treatment planning software called ALFARD. Dose Volume Histogram was not produced as the software was two dimensional.

In addition to treatment planning, central lung distance (CLD) was measured on the images. CLD is defined as vertical distance between leading edge of tangential field and posterior edge of the chest wall (fig 1). Before the initiation of radiotherapy treatment, patients were referred to spirometry department. All the patients received loco regional radiotherapy fields including two tangential, one supraclavicular and one post axillar fields. Right arm was placed behind the patients' head, the same position taken during CT imaging.

The total tumor dose varied between 4800 to 5040 cGy with fraction of 180 or 200 cGy. Patients were treated by SSD method using Phoenix cobalt machine. Spirometry was performed before

Table 1. Principle Statistical indices of studied population

Index	mean	Standard deviation
Age	45.6	7.92
Length of tangential field	18.2	1.18
Width of tangential field	6.7	1.37
Central lung distance	2	1.07

Table 2. Values of FEV1% and FVC% before and 3 months after radiotherapy

Parameter	Before radiotherapy		3 months after radiotherapy		t	P- Value
	Mean	SD	Mean	SD		
FEV1%	74.9	15.59	77.86	12.55	2.454	0.09
FVC%	72.17	14.26	74.6	11.36	-0.817	0.07

radiotherapy and 3 months thereafter, while patients were examined by a specialist on respiratory complications at the same day. Measured parameters were forced expiratory volume in 1 second (FEV1 %) and forced vital capacity (FVC %) was defined as the percentage of measured value to the predicted value (regarded to age and sex) and was automatically calculated by spirometer software.

Data analysis was performed using statistical indices including standard deviation, standard error, prevalence percentage and chi square. Considering kolmogorov –smirnov results, student t-test was used to compare the means.

Results

Average age was 45.6 ± 7.92 . Average length and width of tangential field were 18.2 ± 1.8 and 6.7 ± 1.37 respectively. Average central lung distance was measured 2 ± 1.07 corresponding to 22% of the total lung volume at max (Table 1). This value has been obtained based on DAS et al. results in which the ratio of irradiated lung volume to CLD was 0.6%/mm and 0.5%/mm for the left and right lungs [14]. The mean of FEV1% before and after radiotherapy were measured 74.9 ± 15.59 and 78.86 ± 12.55 respectively showing no significant difference ($p=0.09$). The mean of FVC% before and after radiotherapy were measured 72.17 ± 14.26 and 74.60 ± 11.36 respectively showing no significant difference ($p=0.07$) (Table 2). No abnormal signs were observed in patients after radiotherapy.

Discussion

Among the adjuvant therapies for the breast, radiotherapy after mastectomy can reduce the risk of local recurrence .Adjuvant radiotherapy can

reduce local recurrence in patients without nodal involvement and can lower far metastasis risk and increase the survival of patients with nodal involvement.

Radiation pneumonitis may emerge 2 to 6 months after radiotherapy and can appear randomly in chest radiographs. In case of respiratory signs, shortness of breathing after exercise, coughing and fever are usual. Based on Moiseenko results, dose-response curves for complications that included radiographic changes were less steep than for symptomatic complications. The volume dependence for symptomatic fibrosis was more pronounced compared to all fibrosis. A strong correlation was observed between developing pneumonitis and developing fibrosis [15]. Moreover, Alena Novakova-Jiresova et al. on an experimental survey concluded that the severity of respiratory dysfunction after partial thoracic irradiation is likely to be governed by an interaction between pulmonary and cardiac functional deficits [16].

At first, Groover reported pneumonitis and fibrosis as the radiation complications [17]. Muosas et al. reported radiation pneumonitis in 34% of the patients with chest radiation; fibrosis, 6 to 12 months after radiation has also been reported [18].

The releases of cytokines and direct damage to pneumocyte type II are the first events reported in radiation pneumonitis which will be replaced gradually by fibrotic and leucocytes infiltration around capillary of alveolus and bronchioles [19].

Despite the irradiation to 22% of lung volume, there was no change of pulmonary function test results which is in contrast with the results of Lund et al. [10]; Toukatli et al. [12], Ameri et al. [20], and Linder et al. [11].

However, some authors showed that pulmonary changes up to 50 Gy after tangential radiation to the chest wall are relatively small and reversible [21, 22]. Moreover, Butherman et al. suggest insignificant alteration in pulmonary function when less than one third of the total lung volume is irradiated; and this is in conformity with our results [23]. Liges et al. have shown one percent probability for pneumonitis if CLD is less than three cm, the same condition in our study in which CLD was 2 ± 1.07 .

Study of Coeffman et al. showed reversible and/or irreversible reduction of pulmonary function test by 3-22% within 3-4 months after radiotherapy [24].

Comesi et al. reported early but transient reduction of pulmonary function tests within 1-4 months after radiation being resolved after 2 years [25].

Concerning the obtained results, it seems that three months is not enough for pulmonary changes to appear after cobalt 60 gamma radiation, while the role of treatment planning to minimize CLD might be critical to lower the risk of pneumonitis resulting from radiation; this is in accordance with the result of Butherman and Linges [23, 25].

Moreover, the absence of any abnormal signs in the examination of lung by specialists is in accordance with the results of pulmonary function test. It seems obeying primary treatment planning principle to lower the irradiated volume of lung was effective. Additional time to detect pulmonary complications and more sensitive diagnostic procedure could lead to more credible conclusions.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

Author's Contribution

KKA was the main executor of the study, programmer of the study, radiation therapy planner

and the study supervisor; in addition, he summarized the study for publication.

BA examined the patients for their respiratory status, interpreted spirometry reports and summarized the study.

HA selected the breast cancer patients, examined and referred them for the study. He also prescribed tumor dose and supervised radiation therapy.

BMT was consulted for interpretation of spirometry results and performing statistical analysis.

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