Patient Setup Variations in Computed Tomography-Based Treatment Planning for Left-Sided Breast Cancer Using Electronic Portal Images

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Abstract

Background and Aim: This study deals with isocentric variations along with the setup reproducibility and determines the random and systematic errors in a cohort of 25 (females) left-sided breast cancer patients treated with megavoltage X-rays using an online electronic portal imaging (EPI) protocol. Materials and Methods: This is a hospital-based cross-sectional observational study which was carried out on 25 female patients of carcinoma breast (left sided) who had undergone modified radical mastectomy. After completion of the planned chemotherapy, all patients underwent virtual three-dimensional (3D) computed tomography (CT) simulation, and an external beam radiotherapy treatment was planned on these 3D CT images on a treatment planning system (TPS) using two (coplanar)/conventional tangential fields for a total dose of 50 Gy in 25 fractions. Analysis of 150 EPIs determined changes in the treatment fields during setup of these 25 patients. The online assessment included setup deviations in all the three directions (anteroposterior [AP], superoinferior [SI], and mediolateral [ML]) and variations in central lung distance (CLD) during the first three fractions. Results: Random errors ranged from 1 to 5 mm for the chest wall (medial and lateral) tangential treatments and 1 mm for the anterior supraclavicular nodal field. Systematic errors ranged from 2.5 to 4.5 mm in the AP direction for the tangential fields and from 2.5 to 7.5 mm in the SI and Mediolateral directions for the anterior supraclavicular nodal field. For 25 (left-sided) patients, the CLD (TPS) was 20–30 mm, CLD (EPIs) was 25–40 mm showing variations of 5–10 mm, V20 was 1.0–6.0 Gy, maximum total lung dose was 43 Gy, V30 was 2.0–4.0 Gy, maximum heart dose was 52 Gy, and maximum spine dose was 45 Gy. Conclusions: Online assessment of patient position with matching of EPIs with digitally reconstructed radiographs is a useful method in evaluation of interfraction reproducibility of tangential fields in breast irradiation, thereby improving upon the quality of treatment delivery for our patient population.

Keywords: Central lung distance, digitally reconstructed radiographs, electronic portal imaging, random errors, setup reproducibility, systematic errors/setup errors, three-dimensional computerized tomography images

INTRODUCTION

The International Agency for Research on Cancer, the specialized cancer agency of the World Health Organization, has published updated estimates for 28 types of cancer in 184 countries, giving a comprehensive overview of the global cancer burden indicating a substantive increase of 19.3 million new cancer cases by 2025. Globally, the five most common cancers considered in both sexes were cancers of the lung (1,824,701; 13%), breast (1,676,633; 11.9%), colorectum (1,360,602; 9.7%), prostate (1,111,689; 7.9%), and cervix uteri (527,624; 3.7%), comprising 46.2% of the 28 cancers reported. In women, cancer of the breast tops the list of cancers, and on the Indian scene, the five most common cancers in both sexes were cancers of the breast (144,937; 14.3%), cervix uteri (122,844; 12.1%), lip-oral (77,003; 7.6%), lung (70,275; 6.9%), and colorectum (64,332; 6.3%), comprising 47.2% of the 28 cancers reported.[1] Both globally and on the Indian scene, breast cancer is the most commonly diagnosed cancer in women (24.2%, i.e., about one in four of all new cancer cases diagnosed in women worldwide).
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and deaths among women (521,817 deaths in 2012) and in GLOBOCAN 2018 is the most common cancer in women in 154 of 185 countries worldwide.[2] For the first time, breast cancer is leading cancer in Indian women and cause of cancer death, surprising cervix uteri cancer.

Radiation therapy is an integral component in the management of patients who have undergone breast conservation surgery or mastectomy. During treatment setup, inaccuracies may seep in which may lead to increased dose to organs at risks (OARs), namely the underlying heart and lung leading to increased toxicities/side effects, thereby affecting disease outcome in terms of local control, morbidity, mortality, and quality of life.[3-8]

The study was conducted to determine isocentric variations and setup reproducibility and errors in a cohort of 25 (females) with left-sided breast cancer using 6 MV photons on linear accelerator equipped with onboard electronic portal imaging (EPI) device.

**Materials and Methods**

A prospective study was carried out after obtaining permission from the hospital ethics committee. Written informed consent was obtained from all patients included in the study. A total of 25 (female) patients with Locally advanced breast cancer (LABC) left sided between the age groups of 30 and 60 years (mean age of 45 years) treated with external beam radiotherapy (EBRT) for a period of 1 year between January 2018 and December 2018 at a tertiary care oncology center were included in the study.

**Patient inclusion criteria**

A sample size of 25 patients aged between 30 and 60 years with biopsy-proven breast cancer were enrolled in the prospective study. All patients underwent detailed history and physical examination, hematological and biochemical investigations, chest radiograph, and mammography prior to treatment to determine locoregional spread and to rule out distant metastasis (positron emission tomography/computed tomography (CT) scan was considered optional and performed only on selected group of patients who were symptomatic) and were clinically staged as per tumor–node–metastasis classification.

**Treatment scheme/protocol**

All 25 patients enrolled in the prospective study underwent left-sided modified radical mastectomy and chemotherapy as per initial protocol. On completion of chemotherapy, postoperative irradiation was initiated within 3–4 weeks. The patients underwent CT simulation, and the CT images acquired were uploaded on treatment planning system (TPS) (Oncentra, version 4.3, Elekta). EBRT planning was done and the radiation treatment was delivered to the chest wall (left) using standard opposing medial and lateral tangential fields, and a single anterior field was used to treat the supraclavicular fossa (in patients requiring supraclavicular nodal irradiation) using 6 MV photons on linear accelerator (Primus HI, Siemens) machine to a total dose of 50 Gy in 25 fractions. Standard fractionation (2 Gy/fraction) was used. All fields were treated once a day, for 5 days in a week, and for 5–6 weeks.

**Simulation and treatment planning**

All patients underwent CT simulation in supine position with arm abducted and head rotated toward the opposite side of affected breast. An appropriate inclined breast board (Orfit) was used so as to make the chest wall flat. These patients underwent surface anatomical markings for chest wall field borders and supraclavicular field for nodal irradiation using fiducial radiopaque ball markers (lead). The fiducial markers were placed at the central axis of the chest wall field, and CT lasers were matched with this central axis. Two straight lines meeting the superoinferior (SI) and mediolateral (ML) field borders and joining the central marker were drawn, and four reference markers were placed one each at the midline of the SI and ML field borders and distances from the upper, lower, and lateral borders with respect to this central marker were noted as (SI) and (ML) distance [Figure 1]. Slice thickness of 5 mm was selected as per institutional protocol. The patients were scanned in the abovementioned position with free breathing on 16-slice CT scanner (Somatom Scope, Siemens). The whole chest wall was scanned with a margin of at least 5 cm (50 mm) in craniocaudal direction. The 5-mm axial CT image data set acquired was uploaded on the TPS (Oncentra, Elekta); slice-by-slice delineation of the tumor (chest wall) and OARs (combined lung, heart, esophagus, and spine) was done, and the treatment was delivered using three-dimensional (3D) conformal technique [Figure 1].

For each patient, treatment plans were generated using 6 MV photon beam on Siemens Primus HI dual energy linear accelerator with a total number of a 29-leaf pair multileaf collimator. The prescribed dose of 50 Gy (2 Gy/fraction), 5 fractions/week, was delivered to chest wall (left) using two coplanar tangential fields at two gantry angles (usually between 120° and 300°). For each plan, cumulative dose–volume histograms (DVHs) were generated and analyzed keeping the dose to target as homogeneous as possible and minimizing OAR doses. The estimation of the mean doses to the total lung volume (V20) receiving 20 Gy and volume of the heart (V30) receiving 30 Gy was done. Linear measurements, namely setup source-to-surface distance (SSD) (distance of the perpendicular drawn from isocenter to the upper skin border) and were named as anteroposterior (AP) distance, and SI and ML distances with respect to central marker and central lung

![Figure 1: (a and b) The markers and field borders of a left-sided chest wall irradiation patient](image)
distance (CLD) on isocentric slice were calculated for each case on this 3D reference approved treatment plan [Figure 2]. This 3D approved plan generated by TPS Oncentra along with the reference digitally reconstructed radiograph (DRR) image was exported to Prime view 3i workstation. EPIs were acquired for both medial and lateral tangential fields on 3 consecutive days using OptiVue 500 (amorphous silicon flat-panel detector, Siemens). The EPIs were compared with reference DRR images, and setup deviations were noted in all the three directions (AP, SI, and ML). The deviations in CLD were recorded. The shifts in superimposed EPIs and the DRR images generated were re-uploaded on the TPS 3D treatment plan, and the plans were re-evaluated. The setup errors and the dosimetric variations for OARs were re-assessed on TPS. The patients were thereafter re-aligned and checked for CLD measurement on EPIs before radiation treatment delivery [Figure 3].

The reported setup deviations in this study are thus the uncorrected random and systematic errors since patient setup was not adjusted during the first three fractions.

Statistical analysis of the data generated was carried out for a total of 25 patients. Random and systematic deviations were calculated in accordance with previously published definitions. Random error is the measurement caused during daily setup reproducibility of treatment fields for matching of coordinates. It is calculated as the standard deviation of the mean, whereas the systematic error is the measurement relative to patient (respiration) motion due to the heart and lungs which vary from 1st-day position to consecutive days. It is defined as deviations between the planned position and the average position over the treatment course, in the individual means of differences between the planned DRRs and the EPIs.

**RESULTS**

A total of 25 patients (left sided) of LABC attending the radiotherapy clinic at our center were taken consecutively who met the inclusion criteria for the study. They were included for statistical analysis. A total of 150 EPI (left sided) chest wall patients for medial and lateral tangential fields were obtained and evaluated for random and systematic errors.

**Random and systematic errors (isocentric variations)**

A shift in setup SSD (shift in AP direction) was found from 5 to 10 mm, and a shift of 2–5 mm was seen for both SI and ML directions. Table 1 depicts the range of deviation in setup SSD and displacements in all three directions (AP, SI, and ML) on 3 consecutive treatment days for all patients. The random and systematic errors regarding isocentric deviations (shifts in AP, SI, and ML directions) have been statistically analyzed in Table 2. For the anterior supraclavicular nodal treatments, the random errors were found to be 1 mm. For the chest wall (medial and lateral) tangential treatments, random errors were in range from 1 to 5 mm. Similarly, systematic errors for AP supraclavicular field were found in the range of 2.5–4.5 mm, and for the chest wall (medial and lateral) tangential fields, the values were 2.5–7.5 mm [Tables 1 and 2].

**Deviations in central lung distance and dose variations in organs at risks due to setup errors (dosimetric variations)**

One hundred and fifty EPIs and DRRs were analyzed for deviation in CLD. The CLD actual measured on TPS was between 20 and 30 mm, and CLD measured on EPIs was between 25 and 40 mm showing the variation of 5 mm–10 mm. The same was analyzed for dose variations in OARs due to setup errors measured on TPS. The DVHs were analyzed; mean total lung dose V20 was between 1.0 and 6.0 Gy, and maximum lung dose was 43 Gy. Mean heart dose V30 was between 2.0 and 4.0 Gy, and maximum heart dose measured was 52 Gy and maximum esophagus and spine doses were 45 Gy, as shown in Table 3.

**DISCUSSION**

Setup errors are an inherent part of radiation treatment process. Coverage of target volume is a direct function of setup margins, which should be optimized to prevent inadvertent irradiation of adjacent normal tissues. Recent advances in CT-based and intensity-modulated radiotherapy planning have the potential to spare normal tissues, particularly the OARs (particularly lung and heart).[9-20]

The International Commission on Radiation Unit and Measurement (50 and 62) guidelines[21] have been used to estimate the lung and heart doses in patients undergoing
radiotherapy for carcinoma breast. Truong et al.[22] and Hurkmans et al.[14] reported in their article that the setup accuracy varies depending on the site of treatment, type and method of immobilization used, and institution protocol. In 90% of all patients, the variation of CLD was <10 mm on 3D-simulated plan.[14,22] Other studies have reported random or interfractional setup errors using measurements in three directions.[13,18,23,24]

Various fixation techniques/immobilization devices were used such as hemibody cradles,[16,25] foam cushions,[24] cellulose casts,[18] fixed arm support,[23] and breast boards.[26] In these studies, the random or interfraction setup errors reported were in the range of 1–14.4 mm. Among the studies using EPI,[15,17,26–28] Lirette et al. reported systematic errors of 3.9 mm and random errors of 3.4 mm in the SI direction among 20 patients receiving tangential breast irradiation with no immobilization.[17] Van Tienhoven et al. reported systematic and random errors of 4.7 and 1.8 mm, respectively, in the SI direction among 12 patients who also received breast RT without immobilization.[26] Pradier et al. reported that the variation in CLD of 3.9 mm was the largest setup error and that 90% of all setup errors were <10 mm.[29]

In our study, the range of random errors was found to be 1–5 mm in all three directions. The range of systematic errors was found to be between 2.5 and 7.5 mm in all three directions. These results are consistent with the findings of the other studies done in this field.[14,22,30,31] Chest wall motion during normal respiration resulted in the large magnitude of random errors in the treatments of tangential fields which fall within the tolerance limit of 5 mm.

In this study, the dosimetric variation which occurred due to setup variations in CLD has been estimated using DVH. The present study was planned to evaluate dose to OARs due to setup errors of EBRT of the breast to generate data for our patient population. The doses to the OARs are correlated with toxicity associated with radiation therapy and tolerance tables which have been published for various organs. The tolerance dose (TD) (Gy)/volume (%) parameters to the lung and heart, i.e., volume receiving 20 Gy (V20) of the lung should be ≤30% and volume receiving 30 Gy (V30) of the heart should be ≤46% for symptomatic radiation pneumonitis and pericarditis (cardiac failure), respectively.

Marks et al. using Normal Tissue Complication Probability (NTCP) models have demonstrated that the mean dose of 7–27 Gy to the lung has been found to correlate with a rate of symptomatic pneumonitis between 5% and 40% and the mean dose to the pericardium (heart) <than 26 Gy has also been found to correlate with rates of pericarditis of <15%.[32] Lorenzen et al.[33] estimated heart doses using 2D tangential technique. The study highlighted that the mean heart dose varied from <1–8 Gy and the maximum dose from 5 to 50 Gy for left-sided breast cancer. Kong et al.[14] have studied the impact of CLD on volumetric doses of lung and heart for breast radiation. Their study has shown that when CLD variation was ≤5 mm, the increase in mean dose to the lung was not ≥2 Gy. Our data correlated well with the published literature with mean lung dose V20 (Gy) between 1.0 and 6.0 Gy for the left side (7%) and mean heart dose V30 (Gy) between 2.0 and 4.0 Gy for the left side with CLD variation

| Number of patients | Number of EPIs evaluated on 3 days | Setup SSD (actual on TPS plan) (mm) | Setup SSD (measured on EPIs) (mm) | Deviation in AP (mm) | Deviation in SI (mm) | Deviation in ML (mm) |
|--------------------|-----------------------------------|-----------------------------------|-----------------------------------|---------------------|---------------------|---------------------|
| 25 (left sided)    | 150                               | Between 15 and 70                 | Between 20 and 80                 | Between 5 and 10    | Between 2 and 3     | Between 4 and 5     |

AP: Anteroposterior, SI: Superoinferior, ML: Mediolateral, TPS: Treatment planning system, EPI: Electronic portal imaging, SSD: Source-to-surface distance

| Table 2: Shifts in anteroposterior, superoinferior, and mediolateral directions (random and systematic errors) |
|----------------------------------------------------------------------------------------------------------|
| Magnitude and directions of random and systematic errors in LABC breast radiotherapy                     |
|----------------------------------------------------------------------------------------------------------|
| Anterior supraclavicular nodal field                                                                     |
| Medial tangential chest wall field                                                                        |
| Lateral tangential chest wall field                                                                       |
| SI                                                  | ML                                  | SI                          | AP                         | SI                          | AP                         |
| Random errors (mm)                                    | 1.0                                 | 1.0                         | 5.0                        | 1.0                         | 5.0                        |
| Systematic errors (mm)                                 | 2.5                                 | 4.5                         | 7.5                        | 2.5                         | 7.5                        |
| AP: Anteroposterior, SI: Superoinferior, ML: Mediolateral, LABC: Locally advanced breast cancer         |

| Table 3: Range of deviation in central lung distance and mean dose variations in organs at risks for 25 patients on 3 consecutive treatment days as per dose-volume histograms |
|----------------------------------------------------------------------------------------------------------|
| Number of patients                                      | Number of EPIs and DRRs evaluated on 3 days | CLD (actual on TPS plan) (mm) | CLD (measured on EPIs) (mm) | Mean total lung dose V20 (Gy) | Mean heart dose V30 (Gy) | Max lung dose (Gy) | Max heart dose (Gy) | Max esophagus and spine dose |
| 25 (left sided)                                         | 150                                   | Between 20 and 30            | Between 25 and 40           | Between 1.0 and 6.0 Gy       | Between 2.0 and 4.0 Gy  | 43.0 Gy            | 52.0 Gy            | 45.0 Gy               |

CLD: Central lung distance, EPI: Electronic portal imaging, DRRs: Digital reconstructed radiographs
10 mm (left sided). Hence, CLD is an acceptable surrogate to the total volume of the lung and heart receiving high doses and hence for long-term toxicity associated with radiotherapy to the chest wall and thoracic cavity.

**Conclusions**

This study has highlighted the probable range of systematic and random errors that occur in the field setup during radiotherapy treatment at our institution. The data demonstrated that the random and systematic deviations are within 5–10 mm with our planning and institutional protocol. Due to these setup errors, the mean and maximum doses to OARs have been found within the acceptable dose constraints resulting in less morbidity and mortality in the patients.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

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