ORIGINAL RESEARCH

Assessment of the shifting margins and setup margins for planning target volume in breast, neck, and head cancer

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ABSTRACT

Background: It is vital to precisely evaluate the setup errors to ensure quality assurance in the subjects undergoing radiation therapy for various cancers. **Aim:** The present cross-sectional clinical study was aimed to assess the random, systematic, PTV (planning target volume) margin errors in subjects with breast, head, and neck cancer. **Methods:** The study assessed 100 subjects with breast cancer and 96 subjects with head and neck cancer. EPIDs (electronic portal imaging) were used to perform the treatment setup followed by the irradiation. The Herk formula was used to assess the errors in the treatment and the results were formulated. **Results:** The PTV margin shifting error was 1.41, 2.31, and 1.48 mm for breast cancer and was 2.77, 1.53, and 4.36 mm for head and neck cancer on the x, y, and z-axis respectively. The random error was 0.64, 0.70, and 0.77 mm for breast cancer and 0.80, 0.66, and 0.92 mm for head and neck cancer. However, the systematic error was 0.37, 0.72, and 0.36 mm for breast cancer and 0.87, 0.41, and 1.47 mm for head and neck cancer on the x, y, and z-axis respectively. **Conclusion:** The study, within its limitations, concludes that setup errors change in cancer depending on the location of the tumors. The present study points to the potential advantages of using electronic portal imaging devices to reduce the uncertainties for the procedures of setup verifications.

Keywords: breast cancer, head cancer, neck cancer, planning target volume, shifting margins

INTRODUCTION

Carcinomas results from abnormal cell growth and division secondary to genetic mutations in the DNA of the cells. The use of radiation therapy has been considered a gold-standard treatment modality for treating carcinoma that usually involves the process of delivering high-energy radiation to the tumor to kill the cancer cells.[1] It is vital to attain the appropriate position of the patient before every fraction in the radiotherapy modality to ensure that maximum radiation dose reaches the PTV (planning target volume) with maximum exposure of radiations to the organs which are at risk which is the main aim of the radiotherapy.[2]

The vital organs in proximity to the tumors of head and neck regions that often make it necessary to have stringent PTV margins include the cochlea, brain stem, and optic nerves. The margin is multiplied by the CTV (clinical target volume) to attain the imperfections in PTV concerning the beam alignment, patient positioning, and organ movements signifying internal margin and setup margin. It is vital to attain setup margins to avoid unnecessary irradiation.[3]

Organs at risk (OAR) pose a significant impact inadvertently on the total dose being delivered to the target organ. The two types of errors seen in radiotherapy treatment positioning include random error and systematic error.[4] Random errors can result in displacement of the cumulative dose from its proper position, whereas, systematic errors can lead to dose distribution that leads to deviation from the target area intended. Systematic errors cause concern particularly as they can be consistent during multiple treatment sessions and can lead to severe organ injuries and tumor recurrence, whereas, random errors are less commonly seen.[5]

EPIDs (electronic portal imaging devices) are usually used for 3D conformal radiotherapy planning to improve patient positioning and accuracy in the localization of the target. EPIDs are considered effective tools to evaluate and reduce setup errors.[6] The present clinical study was aimed to assess the random, systematic, PTV (planning target volume) margin errors by assessing PTV shifts in subjects with breast, head, and neck cancer.

MATERIALS AND METHODS

The present cross-sectional clinical study aimed to assess the random, systematic, PTV (planning target volume) margin errors by assessing PTV shifts in subjects with breast, head, and neck cancer. The study was done at Department of Otorhinolaryngology and head and neck surgery of the institute. Informed consent was taken from all the subjects in written and verbal form before study participation.

To attain the 3D anatomical image of the affected region, all the subjects underwent stimulation by CT (computed tomography) for the treated site. For subjects having head and neck tumors, for immobilization, a 5-point thermoplastic mask was used, and the CT stimulation was done 1 week before the first radiotherapy fraction. The subjects were placed in the supine position with the head facing forward during the Ct scan procedure. The thermal guide layer was placed in the thermoplastic material having the radiopaque markers that helped in the localization of the target and appropriate patient positioning during the CT simulation and planning. The 3D anatomical image retrieved following the stimulation by CT showed a 3 mm slice thickness. The images obtained were transferred to software for treatment planning to recontour with the 3DCRT technique.

The radiation oncologist, an expert in the field, delineated the tumor which is also termed GTV- CTV (gross target volume-clinical target volume) along with organs that were at risk including the organs nearby and surrounding the tumor to optimize the dose of the radiation to the target area and to reduce the radiation exposure to healthy surrounding tissue that defines the PTV (planning target volume). In head and neck plans, planning target volume was generated with a 7mm isotropic margin added around the defined clinical target volume (CTV). The dose prescribed was given to the subject y=using 10 MV and 6 MV photon beam energies using Synergy linear accelerator.

Before every therapy session, the subjects were immobilized with accurate positioning devices, and the position was confirmed using mask markings, skin markings, or laser alignment in the treatment area. An amorphous silicon digital portal imaging system having a flat panel and a high-resolution of 1024 x 768 pixels was used to attain the Orthogonal portal images. The obtained images were compared to DRRs (digitally reconstructed radiographs) obtained from orthogonal portal images taken at 90^0 (lateral) and 0^0 (anterior) TPS with the software used for treatment planning. To study the patient setup errors, three translational axes namely X, Y, and Z implying lateral, vertical, and longitudinal axes respectively were employed.

To assess the random and systematic errors, translational displacement was assessed in three directions. Σ or systematic error for breast and head and neck cancer were evaluated when the planned position for the subject was different from the individual subject position by an SD (standard deviation) between the individual subject position and planned subject position for every treatment fraction, or the standard deviation of all subjects means for every direction. Σ or random errors were defined as deviations between different treatment fractions taken weekly during the treatment. Random errors were assessed by calculation of the mean root square of the individual standard deviations of all subjects.

The study also assessed the 3D vector lengths and calculated their size. To quantify the systematic errors (Σ), the standard deviation of the mean value of individual mean setup error for lateral, longitudinal, and horizontal directions was included. For random errors (σ), the mean root square of all standard deviations was calculated in all lateral, longitudinal, and vertical axes. The herk formula used for calculating the PTV margin in the study was as:

PTV margin= $2.5\ \Sigma + 0.7\ \sigma$.

The formula provides an analytic description of the effect of systematic and random geometric deviation on the target dose to get the margin rules.

RESULTS

The present cross-sectional clinical study aimed to assess the random, systematic, PTV (planning target volume) margin errors by assessing PTV shifts in subjects with breast, head, and neck cancer. In 96 subjects having head and neck cancer, the mean age of the study subjects was 49.2±2.22 years with an age range of 34 years to 80 years. There were 29.16% (n=28) females and 70.83% (n=68) males in the head and neck cancer group. The tumor of stage I, II, III, and IV was seen in 29.16% (n=28), 20.83% (n=20), 33.3% (n=32), and 16.6% (n=16) study subjects respectively. Chemotherapy was administered to 75% (n=72) study subjects and not administered to 25% (n=24) study subjects as shown in Table 1.

S. No	Characteristics	Number (n=96)	Percentage (%)
1.	Mean age (years)	49.2±2.22	
2.	Age range (years)	34-80	
3.	Gender		

a)	Females	28	29.16
b)	Males	68	70.83
4.	**Tumor stage**		
a)	I	28	29.16
b)	II	20	20.83
c)	III	32	33.3
d)	IV	16	16.6
5.	**Chemotherapy**		
a)	Treated	72	75
b)	Not treated	24	25

Table 1: Demographic and disease characteristics of study subjects with head and neck cancer

For the demographic and disease characteristics of study subjects with breast cancer, there were 98% (n=98) females and 2% (n=2) males in the present study. The mean age of the subjects in this group was 47.4±3.12 years and the age range of 31 years to 74 years. The tumors of stages I, II, III, and IV were seen in 34% (n=34), 42% (n=42), 14% (n=14), and 10% (n=10) study subjects respectively. For breast cancer, 84% (n=84) subjects were treated with chemotherapy, whereas, 16% (n=16) subjects were not treated with chemotherapy as depicted in Table 2.

S. No	Characteristics	Number (n=100)	Percentage (%)
1.	**Mean age (years)**	47.4±3.12	
2.	**Age range (years)**	31-74	
3.	**Gender**		
a)	Females	98	98
b)	Males	2	2
4.	**Tumor stage**		
a)	I	34	34
b)	II	42	42
c)	III	14	14
d)	IV	10	10
5.	**Chemotherapy**		
a)	Treated	84	84
b)	Not treated	16	16

Table 2: Demographic and disease characteristics of study subjects with breast cancer

Pairs of orthogonal images were obtained EPIs (electronic portal imaging) for all the subjects with a total of 1600 image pairs for breast cancer and 576 image pairs for head and neck cancer. The images obtained were corrected and measured for random and systematic errors (Table 3).

S. No	Site	Breast			Head and neck		
1.	**Direction**	**longitudinal**	**lateral**	**vertical**	**longitudinal**	**lateral**	**vertical**
2.	**Random error (mm)**	0.77	0.70	0.64	0.92	0.66	0.80
3.	**Systematic error (mm)**	0.36	0.72	0.37	1.47	0.41	0.87

Table 3: Radiotherapy characteristics of study subjects with head and neck and breast cancer

It was seen that systematic errors were significantly higher compared to the random errors in both breast and head and neck cancer in all directions. However, in the lateral direction, random errors were higher than systematic errors. On comparing breast cancer to head and neck cancer, systematic and random errors were higher for head and neck cancers compared to breast cancer in the longitudinal and vertical directions and lower in the lateral direction. In the longitudinal direction, a lower systematic error was seen for breast cancer than was seen in the vertical direction.

The setup error threshold was kept at either 2 mm or more than 2 mm for head and neck as well as breast cancer. The study results showed that 4% of the subjects showed no movement of >2 mm in all three studied directions following the IEC (International Electrotechnical Commission) and 2% of study subjects showed >2 mm motion in two directions studies and <2 mm in the third direction. In head and neck cancer subjects, 0%, 2%, and 4% of study subjects depicted more than 2 mm movements in longitudinal, lateral, and vertical directions respectively. On the contrary, breast cancer subjects had a higher percentage of subjects showing the movement of >2mm in longitudinal, lateral, and vertical directions with 2%, 8%, and 6% subjects respectively.

Hank's formula was used to assess PTV margin shifts. It was seen that in head and neck cancer, the greatest

shift in PTV margins was seen in the longitudinal or supero-inferior axis with 4.36 mm followed by the vertical (anteroposterior) axis with 2.77 mm, and least in lateral (mediolateral) axis with 1.53 mm. However, in breast cancer cases, the highest PTV margin shift was seen in the lateral (mediolateral) axis with 2.33 mm followed by 1.48 mm for the longitudinal or supero-inferior axis, and the least 1.43 mm for the vertical (anteroposterior) axis respectively as shown in Table 4.

S. No	Direction	Breast	Head and neck
1.	Longitudinal (supero-inferior)	1.48	4.36
2.	Lateral (mediolateral)	2.33	1.53
3.	Vertical (anteroposterior)	1.43	2.77

Table 4: Shifted PTV margins (mm) for head and neck and breast cancer study subjects

DISCUSSION

Among 96 subjects having head and neck cancer, the mean age of the study subjects was 49.2±2.22 years with an age range of 34 years to 80 years. There were 29.16% (n=28) females and 70.83% (n=68) males in the head and neck cancer group. The tumor of stage I, II, III, and IV was seen in 29.16% (n=28), 20.83% (n=20), 33.3% (n=32), and 16.6% (n=16) study subjects respectively. Chemotherapy was administered to 75% (n=72) study subjects and not administered to 25% (n=24) study subjects. These reports were in line with Menzel HG[7] in 2010 and Anjanappa M et al[8] in 2017 where authors assessed subjects with demographic data comparable to the present study.

The study data showed that for the demographic and disease characteristics of study subjects with breast cancer, there were 98% (n=98) females and 2% (n=2) males in the present study. The mean age of the subjects in this group was 47.4±3.12 years and the age range of 31 years to 74 years. The tumors of stages I, II, III, and IV were seen in 34% (n=34), 42% (n=42), 14% (n=14), and 10% (n=10) study subjects respectively. For breast cancer, 84% (n=84) subjects were treated with chemotherapy, whereas, 16% (n=16) subjects were not treated by chemotherapy. These findings agreed with Oh SA et al[9] in 2016 and Van Herk M[10] in 2004 where subjects with comparable demographics were assessed as having breast cancer.

For the present study, the Pairs of orthogonal images were obtained EPIs (electronic portal imaging) for all the subjects with a total of 1600 image pairs for breast cancer and 576 image pairs for head and neck cancer. The images obtained were corrected and measured for random and systematic errors. It was seen that systematic errors were significantly higher compared to the random errors in both breast and head and neck cancer in all directions. However, in the lateral direction, random errors were higher than systematic errors. On comparing breast cancer to head and neck cancer, systematic and random errors were higher for head and neck cancers compared to breast cancer in the longitudinal and vertical directions and lower in the lateral direction. In the longitudinal direction, a lower systematic error was seen for breast cancer than was seen in the vertical direction. These results were consistent with the studies of Kim SH et al[11] in 2019 and Pehlivan B et al[12] in 2009 where authors reported similar errors in breast and head and neck cancer in the three axes as in the present study.

The study results showed that the Setup error threshold was kept at either 2 mm or more than 2 mm for head and neck as well as breast cancer. The study results showed that 4% of the subjects showed no movement of >2 mm in all three studied directions following the IEC (International Electrotechnical Commission) and 2% of study subjects showed >2 mm motion in two directions studies and <2 mm in the third direction. In head and neck cancer subjects, 0%, 2%, and 4% of study subjects depicted more than 2 mm movements in longitudinal, lateral, and vertical directions respectively. On the contrary, breast cancer subjects had a higher percentage of subjects showing the movement of >2mm in longitudinal, lateral, and vertical directions with 2%, 8%, and 6% subjects respectively. These results were in agreement with the studies of Rudat V et al[13] in 2011 and Gupta T et al[14] in 2007 where authors suggested a similar proportion of subjects having >2 mm movements in any direction.

It was seen that in head and neck cancer, the greatest shift in PTV margins was seen in the longitudinal or supero-inferior axis with 4.36 mm followed by the vertical (anteroposterior) axis with 2.77 mm, and least in lateral (mediolateral) axis with 1.53 mm. However, in breast cancer cases, the highest PTV margin shift was seen in the lateral (mediolateral) axis with 2.33 mm followed by 1.48 mm for the longitudinal or supero-inferior axis, and the least 1.43 mm for the vertical (anteroposterior) axis respectively. These findings were comparable to the studies of Madlool SA et al[15] in 2020 and Delishaj D et al[16] in 2018 where authors reported comparable PTV margin shifts in head and neck and breast cancer cases in their respective studies.

CONCLUSION

Considering its limitations, the present study concludes that setup errors change in cancer depending on the location of the tumors. The present study points to the potential advantages of using electronic portal imaging devices to reduce the uncertainties for the procedures of setup verifications which can further decrease the complication risks.

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