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Radiotherapy Treatment Plan Quality Metrics for Postmastectomy Breast Cancer Patients Using Conformal Planning Techniques

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ABSTRACT

Introduction: The purpose of this study is to evaluate and compare treatment plan quality metrics for postmastectomy breast cancer patients using 3-Dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT) planning techniques.

Material and Methods: The current study included 50 postmastectomy breast cancer patients out of which 24 were planned with 3DCRT and 26 with IMRT technique. Treatment plan quality metrics, namely homogeneity index (HI), conformity index (CI), conformation number (CN), uniformity index (UI) and spillage index (R_{50}), volume receiving 110% and 95% of the prescribed dose ($V_{110\%}$ and $V_{95\%}$) were calculated and compared for the two planning techniques.

Results: IMRT plans have better conformity, homogeneity indices, and lower $V_{110\%}$ than 3DCRT plans with an almost similar $R_{50\%}$ and $V_{95\%}$.

Conclusion: Quantitative values of radiotherapy treatment plan quality metrics for the target are found in favour of the IMRT technique rather than 3DCRT. Implementation of these five parameters is helpful for evaluating treatment plans along with slice by slice and DVH analysis.

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Introduction

Treatment for breast Cancer (Ca) involves a multidisciplinary approach including surgery, chemotherapy, radiotherapy, and hormonal therapy [1]. Radiotherapy, in postmastectomy breast cancer patients, helps in providing significant locoregional control with reduced recurrence rate and improved overall survival [2,3]. Radiotherapy is given through various advanced planning techniques namely, three Dimensional Conformal Radiotherapy (3DCRT), Intensity Modulated Radiotherapy (IMRT), Image-Guided Radiotherapy (IGRT), and Volumetric Arc Therapy (VMAT) [4-7] to achieve homogeneous dose distribution in the target with minimum doses to normal structures at risk. With advancements in imaging modalities, treatment planning systems (TPSs), and accurate dose calculation algorithms, it has become possible to achieve the goals of radiotherapy with proper visualization of three-dimensional dose distributions in the target and organs at risk.

For the analysis of dose distribution, isodose curves and dose volume histograms (DVH) were used. DVH generated from each plan was used for calculating certain parameters which helped in making quantitative as well as qualitative analysis of the generated treatment plans. Among the different planning techniques, the best planning technique for a particular site of treatment with a particular diagnosis is considered based on the different dosimetric parameters related to target dose homogeneity, conformity, and spillage along with doses to normal structures.

The main objective of the present prospective comparative study was to calculate and evaluate treatment plan quality metrics related to target dose coverage, namely Homogeneity index (HI), conformity index (CI), conformation number (CN), uniformity index (UI), spillage index ($R_{50\%}$), Volume receiving 110% and 95% of the prescribed dose ($V_{110\%}$ and $V_{95\%}$) for the 3DCRT and IMRT plans generated for

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postmastectomy breast cancer patients. The novelty of the study is that the calculated treatment plan quality metrics tell about the overall plan dose homogeneity and conformity quantitatively and are found helpful in plan evaluation in addition to dose volume histogram (DVH) and slice by slice analysis.

Materials and Methods

Patients

The current prospective study involved 50 postmastectomy breast cancer patients who had completed chemotherapy treatment, out of which 24 patients were enrolled under the 3DCRT technique and 26 under the IMRT technique.

CT Simulation

For the treatment planning purpose, computed tomography (CT) images of slice thickness 2.5 mm were taken using a 16 slice Optima CT 580W CT Simulator machine (Wipro GE Hanwei Medical Systems Co. Limited, China) in a supine position immobilized with carbon fiber breast board (Quest) & thermoplastic orfit cast (Humo Healthcare Pvt. Ltd.) with free-breathing technique for all the patients. Standard CT parameters for the chest region of 120KV and 80 mA were chosen for CT acquisition. The Adaptive Statistical Iterative Reconstruction (ASIR) method was used for the reconstruction of CT images. A universal superflab bolus (Radiation Products Design, Inc.) of 1cm thickness and dimensions of 30cm x 30cmwas placed above the patient's skin and under the thermoplastic orfit cast at the time of CT acquisition as well as at the time of treatment. CT images were transferred to contouring station Monaco (Elekta Medical Systems Pvt. Ltd.) through DICOM.

Delineation of target volume and organs at risk

The clinical target volume (CTV) including the chestwall along with supraclavicular, axillary lymph nodes, and internal mammary nodes was contoured by the radiation oncologists according to Radiation Oncology Treatment Group (RTOG) guidelines. The planning target volume (PTV) was generated by the addition of a 5mm margin in all the directions to the CTV. The planning organs at risk (OAR's), namely RT lung, LT lung, Ipsilateral Humeral head, Trachea, Spinal Cord, and Heart, and Left descending coronary artery (LAD) were also contoured for all the patients.

Dose Prescription and Treatment Planning

The prescription dose of 50 Gy in 25 fractions over five weeks was done to the PTV for all the patients. Twenty-four patients were planned with the 3DCRT technique and 26 patients were planned with the IMRT technique using CMS XiO (version 5.1, Computerized Medical Systems, USA) treatment planning system (TPS). 3DCRT plans were generated using 6 MV, 15 MV photon beam or with the combination of both energies, however, IMRT plans were generated using 6MV photon beam. The superposition algorithm was used for dose calculation with grid size calculation settings of 2mm.

Field Arrangements

In 3DCRT plans, 3 to 4 fields were used with a single isocenter while 5 to 6 fields were used for generating IMRT plans. Mainly three gantry angles, one anterior for supraclavicular and two tangential beams for chest wall (with no physical/motorized wedges) were used for 3DCRT planning. One additional posterior field for the supraclavicular region was used in some patients to produce adequate tumour dose coverage and better dose homogeneity. Optimum target coverage with homogeneous dose distribution and acceptable hotspots was achieved by adjusting beam weights, using varying beam energies (6MV, 15MV). For IMRT, gantry angles were placed such that two to three angles were near to medial tangential, two near to lateral tangential, and one near the anterior for supraclavicular nodes. Beams were placed by considering minimum contralateral breast and ipsilateral lung irradiation. Dose weightage from each gantry angle was done with the aim of achieving better tumour coverage and minimal healthy tissue damage.

Plan Comparison metrics

Optimal treatment plans were evaluated on the basis of coverage of the tumor by 95% of the prescribed dose ($V_{95\%}$), hot spot and other dose volume limiting parameters for OARs using DVH, slice by slice dose evaluation, and for maximum and minimum doses. Additionally, other quality metrics like HI, CI, CN, UI, and $R_{50\%}$ were calculated using DVH generated from each plan. Also, volumes $V_{110\%}$ and $V_{95\%}$ for the target were analyzed for all the plans. There are different definitions and formulae of radiotherapy plan quality metrics by different authors and organizations but none has been described as an ideal or near-ideal [2].

The various treatment plan quality indices were calculated using the following formulae [7, 8].

Homogeneity Index

$$HI = (D_{2\%} - D_{98\%})/ D_P \quad (1)$$

Where D_2 and D_{98} are the doses received by 2% and 98% of the PTV volume, respectively, and D_p is the prescribed dose. The value of HI close to 0 indicates better homogeneity of dose distribution [8].

Conformity Index (CI)

The conformity index is one of the radiotherapy treatment plan analysis tools which help in comparing various treatment plans generated for the same patient. As per RTOG, it is defined as

$$CI= V_{RI} / TV \quad (2)$$

Where V_{RI} is the volume covered by the reference (95%) isodose line and TV is the target volume [8]. The ideal value of CI is 1.The acceptable range of CI for a treatment plan is between 1 and 2.If CI comes between 2-2.5 and 0.9-1, a treatment plan is considered acceptable with minor violations. However, values beyond the range (0.9 - 2.5) are considered under major violation.

Conformation Number (CN)

As per Van't Riet *et al*., CN is defined as

$$CN = TV_{RI} / TV \times TV_{RI} / V_{RI} \quad (3)$$

Where TV_{RI} is the target volume covered by the reference (95%) isodose, TV is the target volume, and V_{RI} volume of 95% isodose line. Values of these parameters have been noted from the DVH statistics to calculate CN. Irradiation of both the target volume and the normal healthy structures are taken into account simultaneously in this parameter [7].

Uniformity Index (UI)

$$UI = D_5/D_{95} \quad (4)$$

Where D_5 and D_{95} are minimum doses received by 5% and 95% of the planning target volume (PTV) [7]. A value closer to one signifies better uniformity of the target dose. Both HI and UI tell about the dose distribution inside the target volume. However, both have different formulae.

Dose spillage index ($R_{50\%}$)

For the estimation of dose fall-off outside the target, RTOG recommended metrics called the Dose spillage index ($R_{50\%}$). It is defined as:

$$R_{50\%} = 50\% \text{ isodose volume/ target volume.} \quad (5)$$

Lower the $R_{50\%}$, the less will be the spillage and vice versa. Hence, better dose conformity around the target volume with greater dose fall-off is achieved in treatment plans with a less $R_{50\%}$ value [7]. RTOG has also given other parameters like low dose spillage, high dose spillage, gradient index, etc for monitoring dose spillage. These parameters tell about how steeply the dose falls outside the target is achieved. Mostly, these parameters have been evaluated in SBRT and VMAT planning techniques. The value of these parameters varies depending upon the target volume. Ranges have been given according to different RTOG protocols. As per RTOG 0813, a range from 2.9 to 5.9 has been given (3.7-7.5 for minor deviations).

Statistical analysis

The student's t-test was used for assessing the difference observed in treatment quality metrics values from two planning techniques. The reported p-value is two-tailed. P-values < 0.05 were considered statistically significant or else non- significant (NS). Also, statistical analysis of data was performed by calculating mean values, standard deviation, and standard error, maximum and minimum values.

Results

The mean values for all the calculated quality metrics are outlined in Table 1 for both the planning techniques. Figure 1 shows the graphical representation of HI values for 3DCRT and IMRT plans. Observed differences in dose distribution achieved in IMRT plans and 3DCRT plans in terms of dose homogeneity are not statistically significant. A graphical representation of CI values for 3DCRT and IMRT plans is shown in Figure 2.

The difference in mean CI values for 3DCRT and IMRT plans is statistically significant with a p-value of 0.0068, which shows that higher conformal dose distribution is achieved in IMRT plans than in 3DCRT plans. The DVH of the plans having the highest and lowest CI among the selected cases in this study has been shown in figures 3 and 4 respectively.

The CN and UI values for 3DCRT and IMRT plans for all the patients are presented in figure 5 and figure 6 respectively. There is again a statistically significant difference observed in CN and UI values showing a higher degree of dose conformity and more uniform dose distribution in target volume in IMRT plans than in 3DCRT plans.

Table1. Descriptive Statistical Analysis of radiotherapy treatment plan quality metrics in postmastectomy breast cancer patients from 3DCRT and IMRT treatment planning techniques.

Quality Parameter	Planning Technique	Mean value ±SD	SD Error	max-min	p-value
Homogeneity index (HI)	3DCRT	0.204 ± 0.05	0.01	0.29 - 0.13	0.18 (Insignificant)
	IMRT	0.187± 0.04	0.007	0.26 - 0.12	
Conformity index (CI)	3DCRT	2.06 ± 0.054	0.011	3.5 - 1.4	0.0068 (Significant)
	IMRT	1.68 ± 0.40	0.078	2.9 - 1.3	
Conformation number (CN)	3DCRT	0.47 ± 0.09	0.018	0.62 - 0.27	0.00068 (Significant)
	IMRT	0.58 ± 0.12	0.023	0.97 - 0.34	
Uniformity index (UI)	3DCRT	1.16 ± 0.04	0.008	1.26 - 1.11	0.049 (Significant)
	IMRT	1.14 ± 0.03	0.006	1.2 - 1.09	
Dose Spillage index (R50%)	3DCRT	3.35 ± 0.86	0.18	5.46 - 2.23	0.803 (Insignificant)
	IMRT	3.41 ± 0.90	0.17	5.36 - 1.54	
V110%	3DCRT	12.4 ± 12.2	2.54	40 – 0	0.0076 (Significant)
	IMRT	5.19 ± 4.60	0.90	21.6 – 0	
V95%	3DCRT	95.7 ± 2.39	0.50	99.03 – 90	0.65 (Insignificant)
	IMRT	96.0 ± 1.98	0.39	99.9 - 92.8	

3DCRT: Three-dimensional conformal radiotherapy; IMRT: intensity-modulated radiotherapy; SD: standard deviation

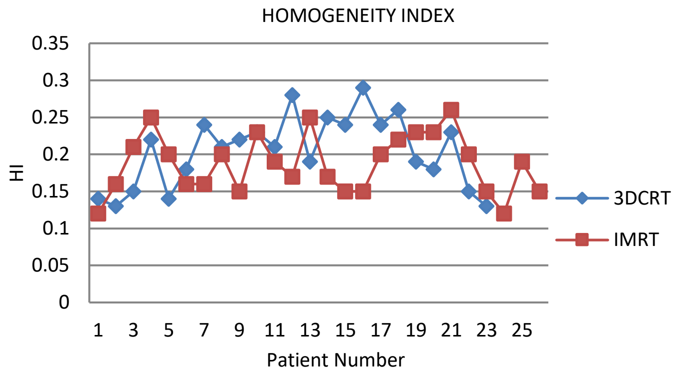

Figure 1. Graphical representation of homogeneity index in 3DCRT and IMRT plans

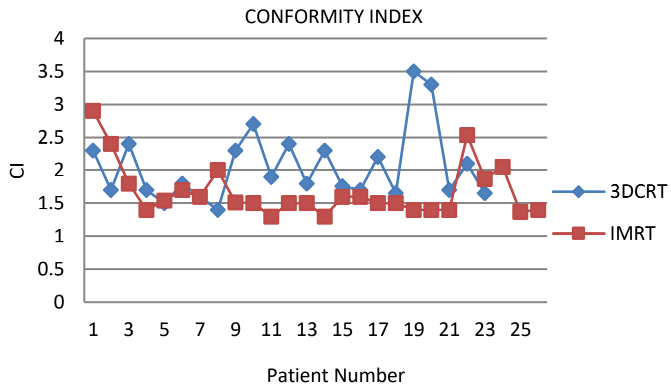

Figure 2. Graphical representation of Conformity Index in 3DCRT and IMRT plans

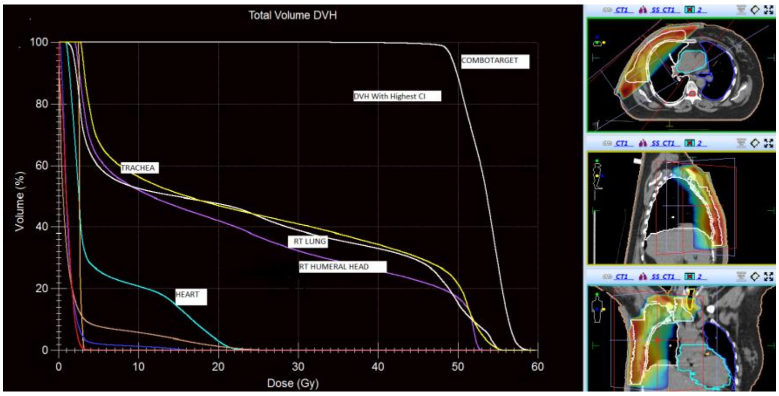

Figure 3. DVH of patient with Highest CI.

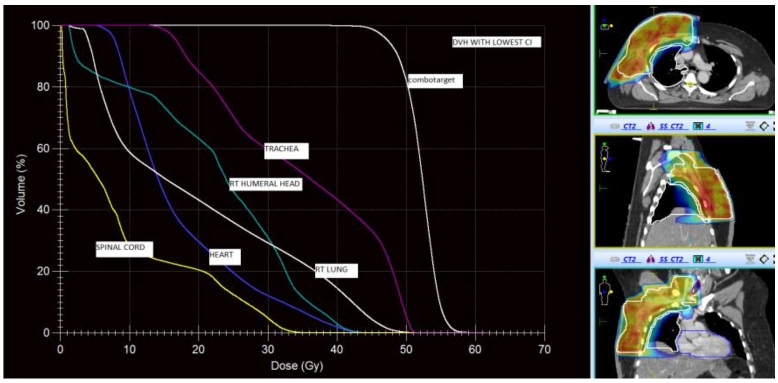

Figure 4. DVH of patient with lowest CI

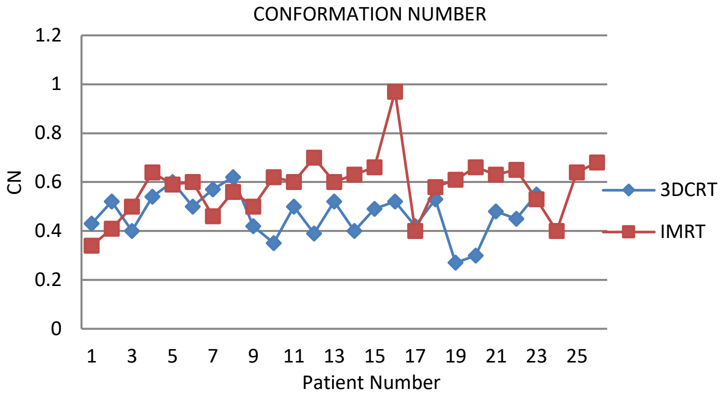

Figure 5. Graphical representation of Conformation Number in 3DCRT and IMRT plans

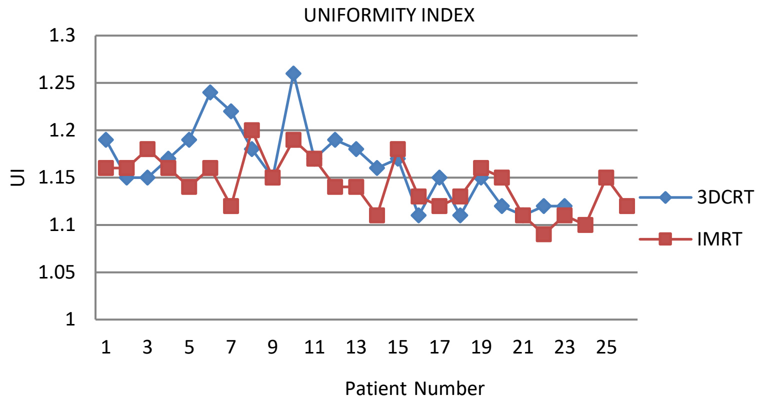

Figure 6. Graphical representation of Uniformity Index in 3DCRT and IMRT plans

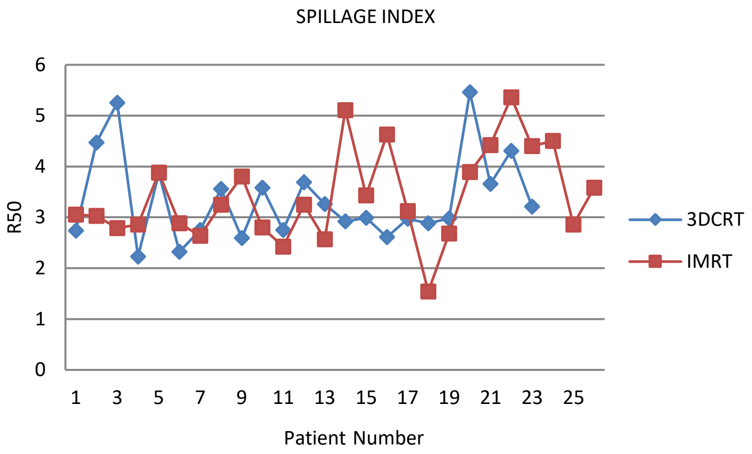

Figure 7. Graphical representation of Dose Spillage Index in 3DCRT and IMRT plans

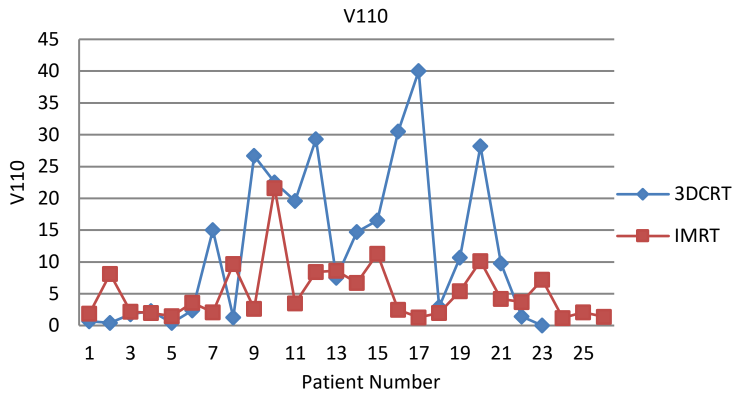

Figure 8. Graphical representation of V_{110} in 3DCRT and IMRT plans

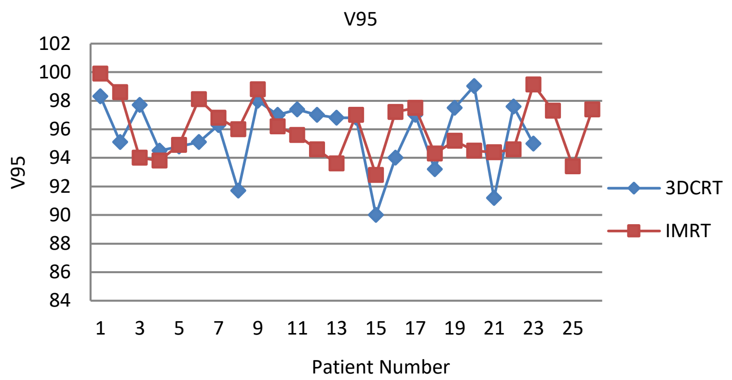

Figure 9. Graphical representation of V_{95}in 3DCRT and IMRT plans

A statistically significant difference (p-value< 0.01) is observed in the high dose volume regions. Lower high dose volumes are obtained in IMRT plans than 3DCRT as shown in figure 8. The V_{95} values achieved in 3DCRT and IMRT plans are presented in figure 9. Almost similar tumor dose coverage with 95% of the prescribed dose has been obtained from both planning techniques with statistically insignificant differences.

Discussion

There are various methods for evaluating a treatment plan. In a busy department, mostly slice by slice view of axial CT sections having isodose lines is being used along with the dose-volume parameters from DVH statistics. Slice by slice analysis has its own importance and is of upmost choice to radiation oncologists as it clearly shows which part of the target is not being covered with reference isodose and which part is receiving high doses. The clinical feasibility of achieved isodose distribution can be easily checked by slice by slice analysis. However, for comparison of the number of plans for the same patient, other treatment plan quality parameters are helpful. These metrics are additional tools for analyzing or comparing the various treatment plans of the same patient but can't replace qualitative analysis of the plan, slice by slice, as well as the detection of illogical high or low doses.

As per RTOG, CI equal to 1 is considered to be an ideal value with the highest dose conformity. A value of CI less than 1 indicates under dosage of the target volume.CI value between 1 and 2 is acceptable with negligible normal tissue covered by reference isodose. But values more than 2, point that even coverage of target is acceptable but healthy tissue included in the reference volume is not negligible. From the present study results, it can be seen that none of the patient plans has a CI value less than 1. However, even if CI is 1, it doesn't mean that a high level of conformity has been achieved [9]. CI value can come 1 only when both target volume and reference isodose volume are same in number. Ideally, they both should overlap otherwise maybe the volume of reference isodose could be shifted out of the target volume. However they are overlapped or not, is the matter of concern i.e reference isodose volume of 4750 cGy dose can cover most of the target volume with a possibility of covering a little bit of normal tissue while sparing a small amount of target volume. This is the drawback of CI that it does not take into account the degree of spatial intersection of the two volumes or their shapes.

To overcome this defect with CI, Van't Riet *et al* proposed an index called conformation number (CN). Conformation number quantifies the degree of conformality in a single numerical value. The formula to calculate CN contains two fractions, out of which the first fraction is related to the dose coverage of target volume with the prescribed reference isodose line (95% of the prescribed dose) and the other fraction tells about the irradiation of normal healthy tissue with a dose equal to or more than the prescribed reference dose. The ideal value of CN is between 0 and 1.

In the present study, a statistically significant difference was observed in CI values for both 3DCRT and IMRT techniques. Better CI was achieved with IMRT compared to 3DCRT ($p<0.05$). However, no significant difference was observed in HI values for both the planning techniques ($p>0.05$). Similar results have been reported in various studies by Rastogi *et al.* [9], Moorthy *et al.* [10], and Rudat *et al.* [11]. However, Li *et al.* [12] reported an insignificant difference in the values of CI and HI between IMRT and 3DCRT. Beckham *et al.* [13] observed significant improvement in both CI and HI in IMRT plans as compared to 3DCRT plans ($p<0.05$). Many other studies have compared advanced techniques like Rapid Arc and VMAT for dosimetric and OAR doses. According to them, the conformity of dose distribution to target is better in Rapid Arc compared with IMRT [14-17].

Conclusion

In this study, a comparison in terms of a few treatment quality parameters has been done for the two planning techniques possible at the research institute. However, the comparison is too vast if done by including normal structure doses and radiobiological differences from both techniques. In the present study, IMRT plans have been found better in conformity, homogeneity of dose distribution and low high dose volumes than 3DCRT plans with an insignificant difference in dose spillage index and target volume coverage. Results show that HI, CI, CN, UI, and $R_{50\%}$ are important tools for the analysis of treatment plans for postmastectomy breast cancer patients apart from DVH. Dose Spillage index and uniformity index are other parameters related to conformal and homogeneous dose distribution, which is rarely discussed for IMRT and 3DCRT techniques in ca breast. These tools can be used as a supplement after a sufficient plan based on good target coverage and normal structure sparing has been reached.

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