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Variation In Mean Heart Dose By Treatment Plan Optimization During Radiotherapy For Left Sided Breast Cancer

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Abstract-
Introduction: Radiotherapy (RT) plays a major role in the management of breast cancer. Cardiac Toxicity is an important late complication of radiotherapy for left sided Breast cancer. Cardiac morbidity can be minimized through careful treatment planning.
Aim: To study the variation of dose to the heart by change in the depth of normalization point during Radiotherapy planning.
Settings and design: Prospective , dosimetric evaluation study.
Materials & Methods: Twenty patients who underwent Left sided Breast Conservation Surgery and registered for Radiotherapy (RT) were simulated on CT Simulator and the Computed tomography images were transferred to the treatment planning system. Target volume and the organ at risks were contoured. Radiotherapy Planning for whole breast was done with tangential fields with additional loco-regional nodal radiotherapy where indicated. The tangential fields were optimized with change of normalization points (P1, P2, P3 and P4) in four different RT plans. Dose to the whole breast and heart was compared for all plans. Patients under went pretreatment cardiac assessment and echocardiography
Results: In optimization of the tangential field for whole breast RT all plans have shown adequate coverage of Planning Target Volume (PTV). The mean heart dose received was 5.07 Gray (Gy), 4.85 Gy, 5.0 Gy and 5.86 Gy by normalization at P1, P2, P3 and P4 respectively. Simple optimization can vary mean heart dose by 17% with absolute decrease in mean heart dose by 1.01Gy.
Conclusion: Optimization of tangential fields can be a useful and easy tool to decrease mean dose to the heart for treating left sided breast cancer especially at centers with limited resources.

Index Terms- Breast cancer, cardiac toxicity, plan optimization, radiotherapy.

I. Introduction

Breast cancer is the most commonly diagnosed cancer in women. The number of estimated new cases of breast cancer in 2016 as per American cancer society is approximately 246,660 and estimated death is 40,450[1]. The treatment strategy for breast cancer patients includes surgery (radical or breast-conserving), radiotherapy, chemotherapy, endocrine therapy and targeted therapy. Historically mastectomy was the standard surgery but in recent years breast conservation surgery (BCS) followed by Radiotherapy has demonstrated equivalent loco-regional control in a large number of randomized trials [2,3].

Cardiac Toxicity is an important sequel of breast radiotherapy, particularly among patients treated for left sided disease [4-6]. The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) reports an increased rate of mortality from heart disease with RT (Risk Ratio=1:27) [7].With improved therapies patients are often cured and survive long enough for late toxicities to become apparent [8].Exposure of heart to radiation during radiotherapy for breast cancer, increases the subsequent risk of ischemic heart disease and cardiomyopathy[9]. To reduce the risk of cardiac toxicity, three-dimensional conformal radiotherapy (3DCRT), Intensity Modulated Radiotherapy (IMRT), Breath Controlled or Gated treatment techniques have been used. But these are resource and labor intensive techniques, not available in all the centers.

Thus we undertook this study to see the variations in dose to the heart by optimization during radiation planning in patients who have undergone Breast conservation surgery for Left sided Breast cancer.

II. RESEARCH ELABORATIONS

Twenty patients who underwent Left sided Breast Conservation Surgery were registered for RT were simulated on Computer Tomography (CT) Simulator and the CT images were transferred to the treatment planning system. Patients under went pretreatment cardiac assessment and echocardiography. Target volume and the organ at risks were contoured by radiation oncologist using Radiation Therapy Oncology Group (RTOG) contouring guidelines (Figure1). Radiotherapy Planning for whole breast was done on a linear accelerator with 1 cm multileaf collimator (Elekta Infinity/synergy). Wedged tangential fields with additional locoregional nodal radiotherapy where indicated were used. The tangential fields were optimized with change of normalization points (P1, P2, P3 and P4) in four different RT plans (Figure 2). Dose to the whole breast and heart was compared for all plans (Figure3).

All patients received a dose of 50 Gy prescribed in 25 fractions to the whole breast and a boost of 10-16 Gy to the tumor bed. In order to avoid hot spots and achieve more homogeneity for the tangential fields, two wedges with 15-30° angles were used when required. Forward IMRT with field in field technique was done to achieve homogenous dose distributions.

In this study variation in dose distribution to heart, left lung and planning target volume (PTV) was studied by changing the depth of the normalization point. The normalization point is a point that is supposed to receive 100% of the prescription dose.

The Treatment planning system (TPS) alters the amount of radiation until this point receives the prescribed dose. The normalization point is positioned in four various locations.
The locations of the four points were as follows:

- P1: Below the skin surface.
- P2:Isocenter
- P3: Middle of isocenter and chest wall.
- P4: Border between the lung and chest wall.

The dose distributions with these points were compared. The dose distribution and Dose Volume Histogram (DVH) was calculated for PTV, mean lung (D mean lung), V20 of lung (V20 is the percentage of lung volume that has received a dose of 20 Gy or more) and mean dose to heart for each of the four plans. In this study for data analyses, SPSS statistical software, version 20 was used.

III. FINDINGS

The average PTV dose received by optimization at P1, P2, P3&P4 was 49.46 Gy, 49.61Gy, 49.11Gy & 52.01Gy respectively. As depicted in table 1 Points P1, P2 and P3 have almost similar mean dose to PTV, which is acceptable as per International Commission for Radiological Units (ICRU 62).

The average of mean heart dose received by all patients was 5.07 Gy in P1, 4.85 Gy in P2, and 5.0 Gy in P3and 5.86 Gy in P4 (Table 2). The variation in mean heart dose between these points was 17% with 1.01 Gy absolute decrease in mean heart dose by simple method of optimization. The same fact is illustrated for lung dose. The mean lung dose was 10.17 Gy to P1, 9.97 Gy to P2, 10.62 Gy to P3 and 10.63 Gy to P4 respectively.WhileV20 for P1 was 18.93%, P2 18.63%, P3 19.84% and P4 19.60 %.(Table 3). The mean lung dose and the V20 lung have both decreased at P2 by 6.20% and 1.21%

IV. DISCUSSION

Following BCS in early stage breast cancer, for all risk groups RT halves the rate of local recurrence and decreases breast cancer mortality by one sixth. For every four women prevented to have local recurrence, one woman is saved 4:1 ratio [3].The mean heart and left anterior descending coronary artery doses are greatest when left breast is treated ,causing an increased risk of cardiac mortality when compared to right breast [10].

To decrease risk of cardiac toxicity, three-dimensional conformal radiotherapy (3DCRT), Intensity Modulated Radiotherapy (IMRT), Breath Controlled or Gated treatment techniques have been used. Several studies have demonstrated that IMRT planning provides better homogeneity and improved dose coverage to target volume with reduced dose in cardiac, lung and contralateral breast than 3DCRT [11,12]. Previous use of cardio toxic chemotherapy, and targeted therapy further add to cardiac morbidity [13].Organ movements secondary to respiratory motion are one of the main concerns during RT.IGRT is especially helpful to manage inter and intra fraction motion thereby protecting normal tissues. Breath hold strategies like Deep Inspiratory Breath Hold (DIBH) have shown greatest promise in reducing heart doses. DIBH can reduce the projected increased risk of heart disease by 13.6% and reduce projected percentage increase in the rate of major coronary events by 25% [14].

Exposure to Radiotherapy for breast cancer increase the rate of major coronary events linearly with mean dose received by heart, i.e. 7.4% per Gray with no apparent threshold [9]. The increased risk of cardiac mortality and morbidity due to radiation exposure is reported to be dose dependent [9, 15] .It is estimated that there is a 4% increase in the risk of heart disease for each 1 Gy increase in mean heart dose [15]. Hence the mean dose to the heart has to be given priority during radiotherapy planning. Even subtle decrease in the mean dose to the heart can decrease major coronary events, thereby transforming into long term gain for patients. If it is important for the physician to reduce the dose received by the lung and heart, optimization of plan by normalizing at various points is suggested since in this method average received dose to heart and lung have been reduced in comparison to other methods. In optimization of tangential field all methods cover PTV. Thus selection of normalization point in radiotherapy planning, which is done regularly in day to day practice should be done carefully to minimize mean heart dose without compromising target volume.

V. CONCLUSION

Optimization of tangential fields by normalization at suitable point in the target volume can be a useful tool for decreasing mean heart dose during breast radiotherapy especially at recourse constrained centers.

REFERENCES

[1] Siegel R, MillerKD,Jemal A. Cancer Statistics, 2016. CA Cancer J Clin 2016;66:7-30

[2] Fisher B, Jeong JH, Anderson S, Bryant J, Fisher ER, Wolmark N. Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. N Engl J Med. 2002;347:567–75.

[3] Early Breast Cancer Trialists' Collaborative Group(EBCTCG). Effect of radiotherapy after breast conservation surgery on 10 year recurrence and 15 year breast cancer death: meta-analysis of individual patient data for 10.801 women in 17 randomised trials.Lancet 2011;378:771-84

[4] Hooning MJ, Botma A, Aleman BM, et al. Long-term risk of cardiovascular disease in 10 yearsurvivors of breast cancer. J Natl Cancer Inst 2007;99:365–375.

[5] Harris EE, Correa C, Hwang WT, et al. Late cardiac mortality and morbidity in early-stage breastcancer patients after breast-conservation treatment. J ClinOncol 2006;24:4100–4106.

[6] Jagsi R, Griffith KA, Koelling T, et al. Rates of myocardial infarction and coronary artery diseaseand risk factors in patients treated with radiation therapy for early-stage breast cancer. Cancer2007;109:650–657.

[7] Clarke M, Collins R, Darby S, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of randomised trials. Lancet. 2005;366:2087-2106.

[8] Mary Feng, Jean M. Moran, Todd Koelling, AamerChughtai, June L. Chan, Laura Freedman ,et al. Development and validation of a heart atlas to study cardiac exposure to radiation following treatment for breast cancer. Int J RadiatOncolBiol Phys. 2011 January 1; 79(1): 10–18.

[9] Sarah C. Darby, Marianne Ewertz, Paul McGale, Anna M. Bennet, Ulla Blom-Goldman, DortheBrønnum ,et al . Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer. N Engl J Med 2013;368:987-98.

[10] Darby SC, McGale P, Taylor CW, Peto R. Long-termmortality from heart disease and lung cancer afterradiotherapy for early breast cancer: prospective cohortstudy of about 300,000 women in US SEER cancerregistries. Lancet Oncol2005; 6: 557–65.

[11] Hurksman CW,ChoBC,DamenE,etal.Reduction of cardiac and lung complication probabilities after breast irradiation using conformal radiotherapy with or without intensity modulation.Radiother Oncol.2002;62:163-71

[12] Kruger EA ,FraassBA,PierceLJ.Clinical Aspect of intensity modulated radiotherapy in the treatment of breast cancer.SeminRadiat Oncol.2002;12(3):250-9.

[13] Offersen B ,Hojris I, Overgaard M. Radiation heart morbidity after adjuvant radiotherapy of early breast cancer-is it still an issue?Radiother Oncol.2011:100:157-9.

[14] L.M Smyth et.al. The cardiac dose sparing benefits of deep inspiration breath hold in left breast irradiation :a systemic review.J Med Radiation Sci 62(2015)66-73.

[15] Sardaro A, Petruzzelli MF, D'Errico MP, Grimaldi L, PiliG, Portaluri M. Radiation-induced cardiac damage in early left breast cancer patients: risk factors, biological mechanisms, radiobiology, and dosimetric constraints.RadiotherOncol 2012; 103: 133–42.

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Figure 1:Digitally Reconstructed Radiograph of a patient with left sided Breast Conservative Surgery in treatment position showing target volume and organs at risk in heart and lung.

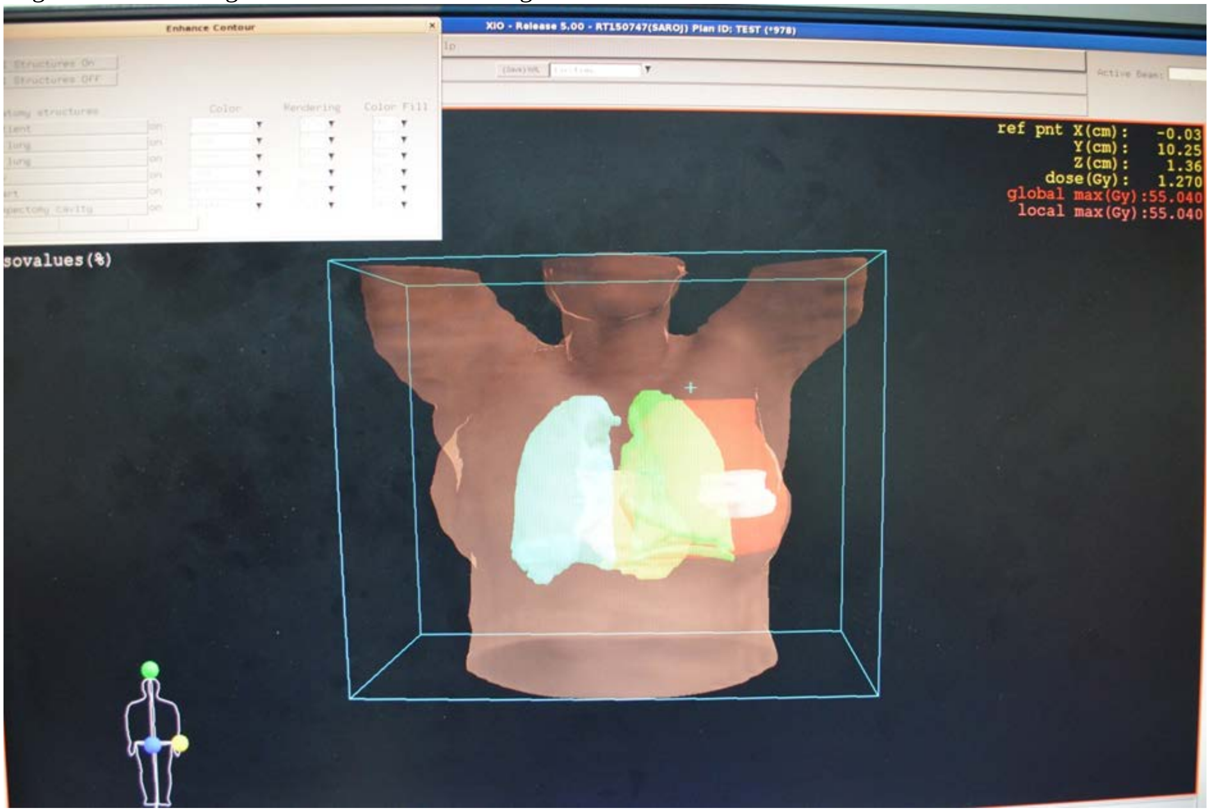

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Figure 2: Wedged Tangential field RT plan optimized at various points P1,P2,P3,P3,P4.

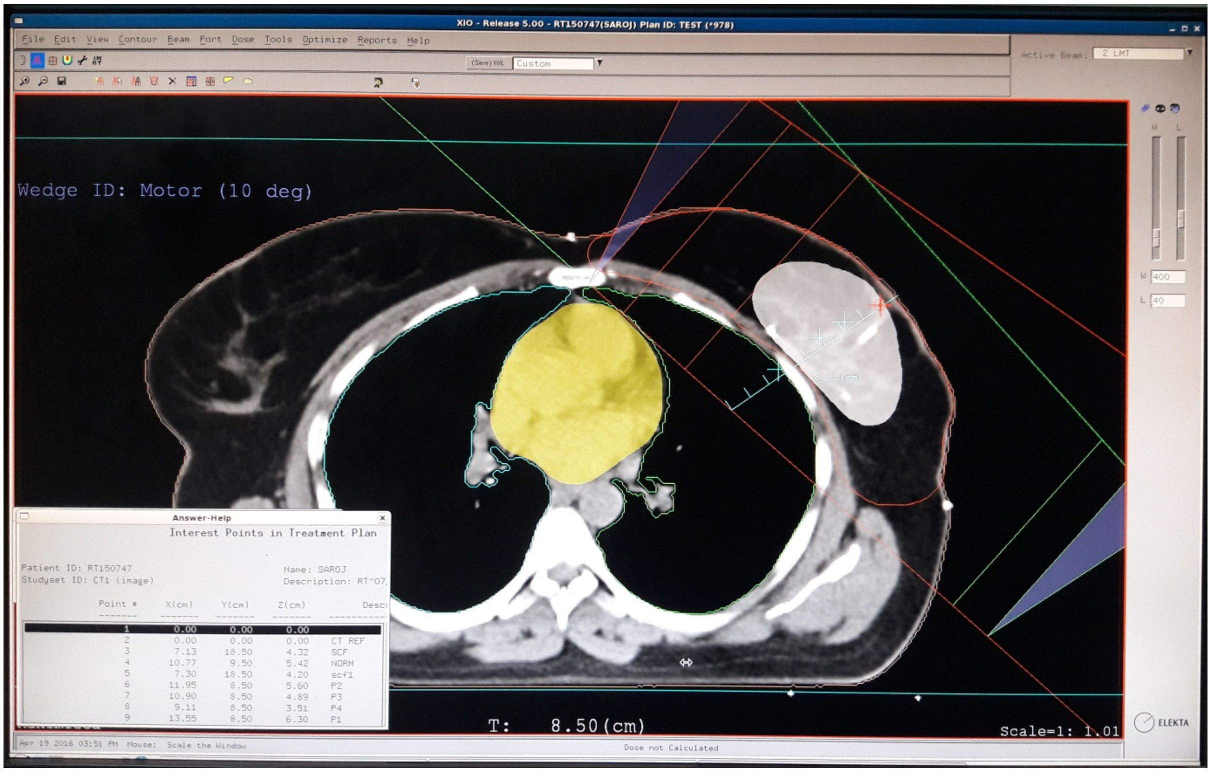

Figure 3: Comparison of two plans in terms of dose to target and heart as depicted with solid and dotted line on DVH.

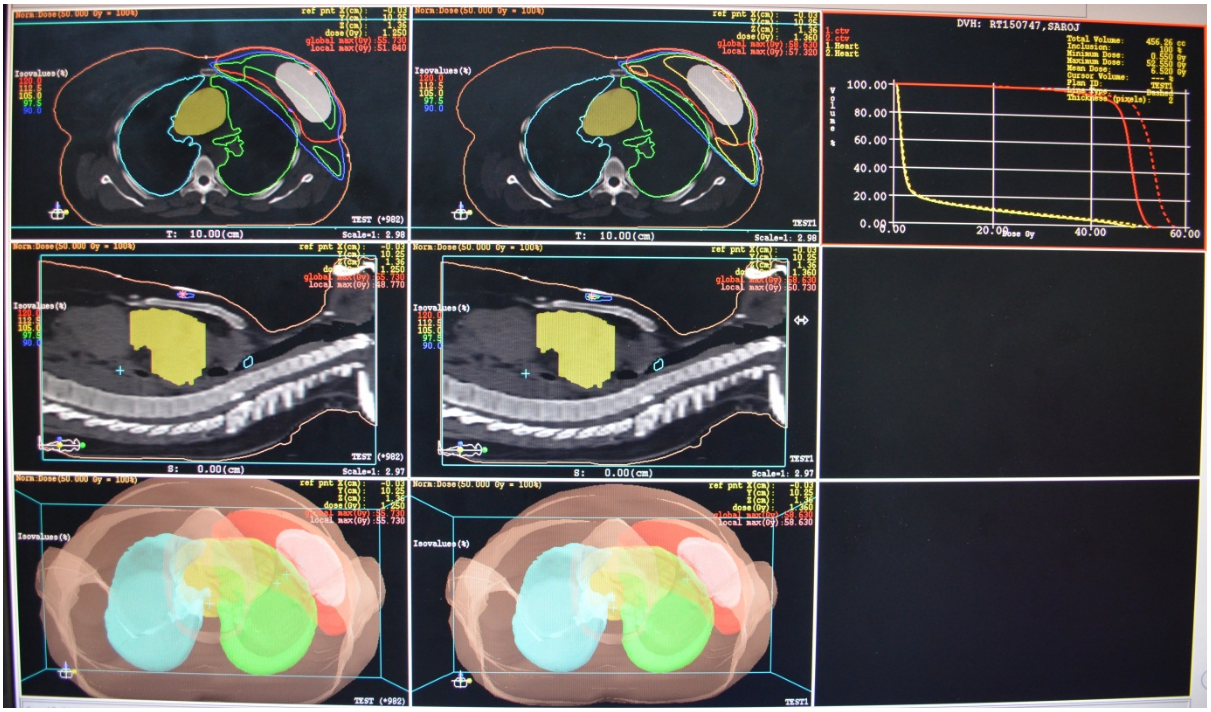

Table 1: Showing Average of mean PTV dose received by 20 pts at various points of normalization

Optimization Point	Mean Dose to PTV(Gy)
P1	49.46
P2	49.61
P3	49.11
P4	52.01

Table 2:Showing Average of mean heart dose received by 20 pts at various points of normalization.

Optimization Point	Average Mean Dose to the Heart(Gy)
P1	5.07
P2	4.85
P3	5.0
P4	5.86

Table 3: Showing Average of mean Lung dose (D mean) and V20 received by 20 pts at various points of normalization

Optimization Point	D mean Lung(Gy)	V20 Lung(%)
P1	10.17	18.93
P2	9.97	18.63
P3	10.62	19.84
P4	10.63	19.60