Analysis of chest wall breathing motion, setup accuracy and dosimetric stability of VMAT technique radiation therapy in breast cancer patients

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Abstract

Background: measuring the extent to which the breast setup error contributed to the total delivered dose discrepancies in all patients treated with Volumetric modulated arc therapy (VMAT) both in deep inspiration breath-hold technique (DIBH) and free breathing (FB) and to compare the dosimetric stability of each technique.

Methods: the dose distribution parameters of the mean of 90 cone-beam computer tomographies (CBCTs) reshaped by deformable image registration (DIR) compared to the mean of their reference plan (RP) in left (Lt) sided breast cancer (BC) patients treated with adjuvant loco-regional radiation. 50 CBCTs in the first group treated in DIBHT and 40 CBCTs in the second group treated in FB compared also to the mean of their RP. Deviations in the delivered from the planned dose distributions have been analyzed. The average of this difference has been calculated for all cases and in each group of patients.

Results: 1% reduction in PTV-total D95% caused by -4% decrease in the PTV-supraclavicular (supra). 13% and 3% increase in Dmean of heart and Lt lung, respectively. 8% and 6% increase in spinal cord Dmax and right (Rt) breast D2%, respectively. The difference between both techniques was significant in heart with its sub-volume, Rt breast and spinal cord.

Conclusions: The dosimetric impacts of breast setup errors during Lt BC loco-regional radiation by VMAT technique using DIR was significant for the heart with its sub-volume in the FB group only.

Keywords CBCT, VMAT, Breast setup error, deformable image registration

Introduction:

Adjuvant radiation therapy (RT) to the left (Lt) sided breast cancer (BC) with regional lymph nodes (RLNs) including the internal mammary chain (IMC) requires best sparing of adjacent organs at risks (OARs) such as heart, lungs and Rt breast. Compared to the three-dimensional conformal RT (3DCRT), the Intensity-modulated RT (IMRT) increases the dose conformity and homogeneity, and reduces high dose to ipsilateral lung and heart for Lt sided BC patients, but also increases the delivery time [1].

VMAT is capable of combining a geometrical rotation and beam shaping fulfilled by continuous modulation of multi-leaf collimator (MLC) in addition to optimizing the gantry speed and the dose rate [2], therefore VMAT is effective for improving the dose conformity, sparing OARs like IMRT, however the treatment time for VMAT is significantly lower [3]. In VMAT FB, respiratory induced motion can result in substantial intra-fractional dosimetric variation during delivery, while VMAT in DIBH can control the respiratory movement decreasing the dosimetric uncertainty and achieve more OARs sparing [3].

On the other side the dosimetric quality of the VMAT plan is negatively affected by mispositioning of the patient, breast shape changes and deformation of the breast, which can lead to a critical decrease in the target coverage and an increase in the dose to OAR, therefore the dosimetric quality of the VMAT treatment is maintained by ideal patient and breast positioning.

Image-guided Radiation therapy (IGRT) using surface scanners (SIGRT) and/or CBCT before each fraction (FX) facilitates accurate position of the patient and improves the setup accuracy, however the extent to which the breast setup error leads to difference in the planned dose distribution is not clear. Recalculation of the Fractional dose distributions, including the breast setup error source, allow for an accurate estimation of the delivered dose distribution.

The aim of this work is to study the effect of breast setup errors on the planned dose distribution in Lt sided BC patients, who have been divided into two groups; one group has been treated with VMAT in DIBH and

the other with VMAT in FB and both have been verified with CBCT as IGRT. The emphasis is to analyze the dosimetric deviations and represent the stability of each technique with its verification in a movable organ like breast and compare the difference between these two techniques in the dosimetric stability throughout the treatment period. This evaluation aims to support the clinicians in choosing the optimal planning dose and technique to be implemented in the clinical routine.

Patients and Methods:

Patients and scans

All cases, who meet the following criteria: female patients with Lt sided BC that have been treated after Breast-conserving surgery (BCS) with adjuvant RT to whole breast (WB) including supra, axillary LN and IMC have been chosen within the period of our study. The planning CT (PCT) scans for these patients have been already done in the supine position using the breast board. For each patient, a daily SIGRT and CBCT have been done during the treatment course for online setup verification representing the daily variations in the breast shape and position. Setup patient errors between the PCT scan and the CBCT scans have been further corrected using rigid registration (RR) on the ribs and sternum. Patients with at least 10 available CBCTs distributed within the treatment period have been selected. Patients with once weekly CBCTs as well as those that had insufficient CBCT scans for re-planning have been excluded. These cases have been chosen for the current research with 10 CBCT scans for each patient representing the entire treatment, so our research has been done on 90 CBCTs, 50 CBCTs in the first group treated in DIBHT and 40 CBCTs in the second group treated in FB.

Contour delineation

In the PCT of each patient, the clinical target volumes (CTVs), the planning target volumes (PTVs) and the OARs have been contoured according to the radiation therapy oncology group (RTOG) guidelines as well as BC patterns of nodal recurrence and contouring recommendations [4][5]. CTVs consisted of WB, supra, axillary LNs and IMC. OARs included both lungs, Rt breast and heart including the Lt, Rt ventricles and the Lt anterior descending coronary artery (LADCA). The PTV have been defined as a 1 cm expansion of CTV-WB and 0.5 expansion of the rest of the CTVs. PTVs used for planning and dose evaluation have been all cropped to within 0.5 cm of the skin to disregard the dose build-up region.

Treatment planning technique

The cases in the first group have been treated with DIBHT-VMAT for which breathing volume was monitored using a surface scanner (Catalyst system from C-RAD, Uppsala, Sweden), while the cases in the second group have been treated with FB-VMAT treatment planning techniques. VMAT plans have been created in Monaco treatment planning system on an Elekta Synergy linear accelerator with a dose of 50 gray (Gy) in 25 FX using a partial 6 mega volt (MV) dual arc that spanned along the affected side of the body.

IMRT constraint

For different structures, the following cost functions have been used as shown in Table 1.

Table (1): Used IMRT constraint for different structures

Structure	Cost functions
PTV total and IMC	a) Target equivalent uniform dose: with reference dose 5000 cGy. b) Quadratic overdose: with reference dose 5000 cGy and isoconstraint ranged from 80 to100. c) Quadratic underdose: with reference dose 5000 cGy and isoconstraint ranged from 80 to 100.
Heart	a) Parallel: with reference dose ranged from 600 to 800 cGy and isoconstraint ranged from 20 to 38. b) Serial: with reference dose ranged from 900 to 1100 cGy.
Lt ventricle	a) Parallel: with reference dose 500 cGy and isoconstraint ranged from 21 to 150
Lt lung	a) Parallel: with reference dose ranged from 1350 to1400 cGy and isoconstraint ranged from 25 to 31. b) Serial: with reference dose ranged from 1670 to1780 cGy.
Rt lung	a) Parallel: with reference dose ranged from 500 to 520 cGy and isoconstraint ranged from 28 to 40.
Rt breast	a) Quadratic overdose: with reference dose 620 cGy and isoconstraint ranged from 150 to 200. b) Serial: with reference dose ranged from 550 to 650 cGy.
Spinal cord	a) Quadratic overdose: with reference dose ranged from 1400 to 1500 and isoconstraint 50.

Velocity model for DIR

The stability of VMAT due to setup errors has been evaluated on CBCTs as they contain the variations in the form and position of the target volume (TV). However, CBCTs are not Hounsfield unit (HU) calibrated, they may contain image artifacts and lack relevant anatomy due to a limited field of view. These modality differences would cause problems in the dose calculations. Therefore, a reshaped CTs have been

created by velocity, which is a B-spline deformable model using mutual information. these reshaped CTs had the anatomy of the CBCT and the properties of the PCT. Firstly, the PCT have been imported with its structures and 10 CBCTs for each patient to velocity then the deformation vector field has been used to map the voxels from the PCT scan to each CBCT to fit the anatomy of the CBCTs after selecting the area of interest. This allowed mapping the entire PCT for dose recalculation. The planning structures and isocenter have been deformed together with the PCT; yielding contours that were consistent with the reshaped CT and did not require further verification. Thus, 10 modified reshaped CT scans have been generated for each patient, each containing the anatomy of the CBCT and the image properties of the PCT scan. In Monaco, the reshaped CTs with their deformed structures and isocenter have been imported then the plan has been copied to each reshaped CT then recalculated (without MLC or fluence re-optimization) creating a set of 10 VMAT plans for each patient and the dose has been calculated, and then compared to the RP.

Plan evaluation and statistical analysis

We have measured the extent to which the breast setup error contributed to the total delivered dose discrepancies by comparing the dose distribution parameters of the RP to the mean of the 10 virtual reshaped CTs in each patient. Deviations in the delivered from the planned dose distributions have been analyzed. Results have been shown as difference between the resultant and the RP for all cases and in each group of patients, DIBH and FB groups. We have evaluated the dose that covered 95 % of the PTV (D95%), the dose that covered 2 % of the PTV (D2%) and the TV mean dose (Dmean) for all PTVs. For OARs we have analyzed the percent of volume receiving ≥20 Gy (V20), the percent of volume receiving ≥5 Gy (V5) and Dmean for the ipsilateral Lt lung, Dmean for the heart, V20 and Dmean for the LADCA, V5 and Dmean for Lt ventricle and D2% for the Rt breast, the TV maximum dose (Dmax) for the spinal cord. Results have been then tested for statistical significance.

Statistical methods

Statistical Package for the Social Sciences (SPSS) version 23.0 has been used for data management and analysis. Mean and standard deviation (SD), with median and range have been used for dose description of all values: (Volume (V)-parameters in (%), Dose (D)-parameters in (Gy). Comparison of related groups has been done using Wilcoxon signed rank test (non-parametric paired t-test) and comparison of independent groups (DIBH vs FB) has been done using Mann Whitney test (non-parametric t-test).

Results:

PTVs coverage

There was significant decrease in the average of D95% to the PTV-total by -1% (-0.43 Gy), caused mainly by significant decrease in the PTV-supra by -4% (-1.72 Gy) then the PTV-IMC by -1% (0.6 Gy). The Dmean to all PTVs was almost unchanged except in PTV-supra with insignificant decrease -1% (-0.6 Gy). In addition, there was an increase in the D2% to the PTV-total by 1% (0.32 Gy) caused mainly by 1% increase in the PTV-breast (0.37 Gy) and both were statistically insignificant. Our study showed that, there was no statistically significant difference in all PTVs doses (D95%, Dmean and D2%) between DIBH and FB groups. Comparison of all PTVs dose difference between the RP and the virtual reshaped CTs in the whole study group and the Percent of changes in the mean of all PTVs doses in the two groups and in the average of all cases are displayed in Table 2 and Figure 1, respectively.

Table (2): Comparison of values of all PTVs dose difference in the whole study group

	Mean (Gy)	**SD (Gy)**	**mean difference (Gy)**	**p value ***
PTV-total				
RP D95%	47.39	0.430	-0.43	**0.05***
CBCTs D95%	46.96	0.627		
RP Dmean	49.828	0.082	0.058	0.953
CBCTs Dmean	49.887	0.607		
RP D2%	52.351	0.349	0.324	0.260
CBCTs D2%	52.675	0.819		
PTV-IMC				
RP D95%	45.162	2.485	-0.598	0.236
CBCTs D95%	44.563	2.819		
RP Dmean	49.406	0.887	-0.065	1.00
CBCTs Dmean	49.341	0.922		
RP D2%	52.350	0.456	0.168	0.767
CBCTs D2%	52.518	0.994		
PTV-breast				
RP D95%	47.748	0.422	-0.065	0.214
CBCTs D95%	47.683	0.607		
RP Dmean	49.974	0.058	0.103	0.953
CBCTs Dmean	50.077	0.597		
RP D2%	52.415	0.317	0.373	0.155
CBCTs D2%	52.788	0.085		
PTV-axilla				
RP D95%	47.782	0.597	-0.084	0.859
CBCTs D95%	47.697	0.921		
RP Dmean	49.858	0.123	0.022	0.812
CBCTs Dmean	49.881	0.683		
RP D2%	52.133	0.350	0.172	0.594
CBCTs D2%	52.305	0.922		
PTV-supra				
RP D95%	47.497	0.786	-1.727	**0.008***
CBCTs D95%	45.77	1.245		
RP Dmean	49.991	0.786	-0.597	0.110
CBCTs Dmean	49.393	0.742		
RP D2%	52.178	0.729	0.107	0.767
CBCTs D2%	52.286	0.824		

p value* is significant ≤0.05

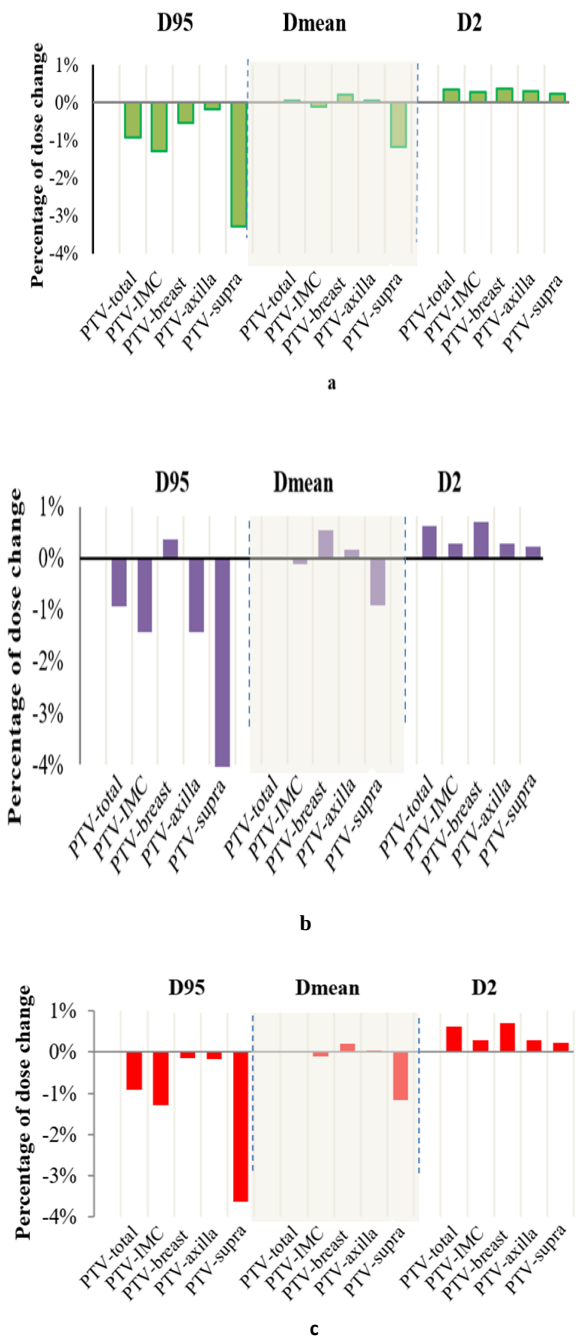

Fig. (1): The percent of changes in the mean of all PTVs doses a) in DIBH group b) in FB group c) in the average all cases.

OARs coverage

The Dmean to the ipsilateral Lt lung showed a mean increase by 3% (0.46 Gy, p= 0.066), while the increase was 1% in both V20% and V5% with p= 0.119 and 0.302, respectively. Comparing the Lt lung analyzed parameters (V20%, V5%, Dmean) between DIBH and FB groups, the differences were small and statistically not significant.

The average significant increase in the heart Dmean was 13% (0.53 Gy, p= 0.024). This difference was 24% (1.08 Gy, p= 0.068) in FB group, 3% (0.1Gy, p= 0.279) in DIBH group. The increase in the LADCA Dmean was 33% (1.93 Gy, p= 0.138). This difference was 71% (4.54 Gy, p= 0.068) in FB group and -3% (-0.15 Gy, p= 0.498) in DIBH group. The percent of increase in the V20 to LADCA was 6% (p= 0.066). This difference was 13% (p= 0.109) in FB group and 0% (p= 0.317) in DIBH group. The increase in the Lt ventricle Dmean in all cases was 13% (0.45 Gy, p= 0.110). This difference was 29% (1.04 Gy, p= 0.068) in FB group and -0.3% (-0.01 Gy, p= 0.686) in DIBH group. The percent of increase in the V5 to Lt ventricle was 3% (p= 0.182). This difference was 8% (p= 0.066) in FB group and -1% (p= 0.194) in DIBH group. The increase in D2% to the Rt breast was 6% (0.65 Gy, p= 0.021). This difference was 9% (1.03 Gy, p= 0.068) in FB group, and 4% (0.35 Gy, p= 0.138) in DIBH group. The increase in Dmax to the spinal cord was 8% (1.30 Gy, p= 0.011). This difference was 10% (1.68 Gy, p= 0.068) in FB group, and 6% (0.99 Gy, p= 0.080) in DIBH group. The OARs difference between both techniques was statistically significant only in whole heart and its sub-volumes except LADCA V20%. Comparison of values of OARs dose difference among both study groups and the percent of changes in the mean of all OARs doses in the two groups and in the average of all cases are displayed in Table 3 and Figure 2, respectively.

CTV breast volume

The percentage of the CTV breast volume shrinkage in the average of all cases was significant (p=0.008), however there was no significant correlation between the size of the breast and the percentage of deformation and between the CTV breast volume and the dose differences in all cases.

Discussion:

Our study is the first study to evaluate the dosimetric impacts of breast setup errors to the TV and OAR using DIR during the radiation treatment of Lt BC with RLNs including the IMC using VMAT technique both in DIBHT and FB. It has been found that dose evaluation in the CBCT scan is impractical due to the presence of large degree of artifacts caused by scattered photons, beam hardening and unmatched HU with the PCT. Many studies, that used CBCT for dose calculations found that the variation in the dose can reach to 3-4 % between CBCT and PCT based treatment plans using Catphan calibration curves and the largest difference of 14.5% was observed for head and neck patients [6], therefore a reshaped CT has been created in this study based on the CBCT anatomy using DIR in velocity. This registration distorts the PCT image via deformation field which detect the motion of each image voxel to take the shape of the CBCT image and produce a virtual reshaped CT having the anatomy of CBCT and the prosperities of PCT [7].

Table (3) Comparison of values of OARs dose difference among both study groups

Diff**	Group						P value*
	DIBHT (N=50 CBCTs)			FB (N=40 CBCTs)			
	Median	Maximum	Minimum	Median	Maximum	Minimum	
Lt lung							
Dmean (Gy)	0.51	0.87	-0.13	0.76	1.27	-0.75	0.730
V20 (%)	1.00	2.00	-1.00	1.50	3.00	-2.00	0.905
V5 (%)	2.00	4.00	0.00	-1.50	3.00	-2.00	0.190
whole heart							
Dmean (Gy)	0.07	0.35	-0.07	0.99	2.08	0.25	**0.032***
LADCA							
Dmean (Gy)	-0.29	0.57	-0.45	3.45	10.03	1.23	**0.016***
V20%	0.00	1.00	0.00	8.500	34.00	0.00	0.111
Lt Ventricle							
Dmean (Gy)	0.06	0.14	-0.10	0.56	2.81	0.21	**0.016***
V5 (%)	-1.00	1.00	-2.00	5.00	18.00	3.00	**0.016***
RT breast							
D2 (%)	0.21	1.36	-0.20	0.67	2.64	0.12	0.286
Spinal cord							
Dmax (Gy)	0.77	3.14	-0.26	1.59	2.84	0.71	0.413

diff** is the difference between the RP and CBCTs.

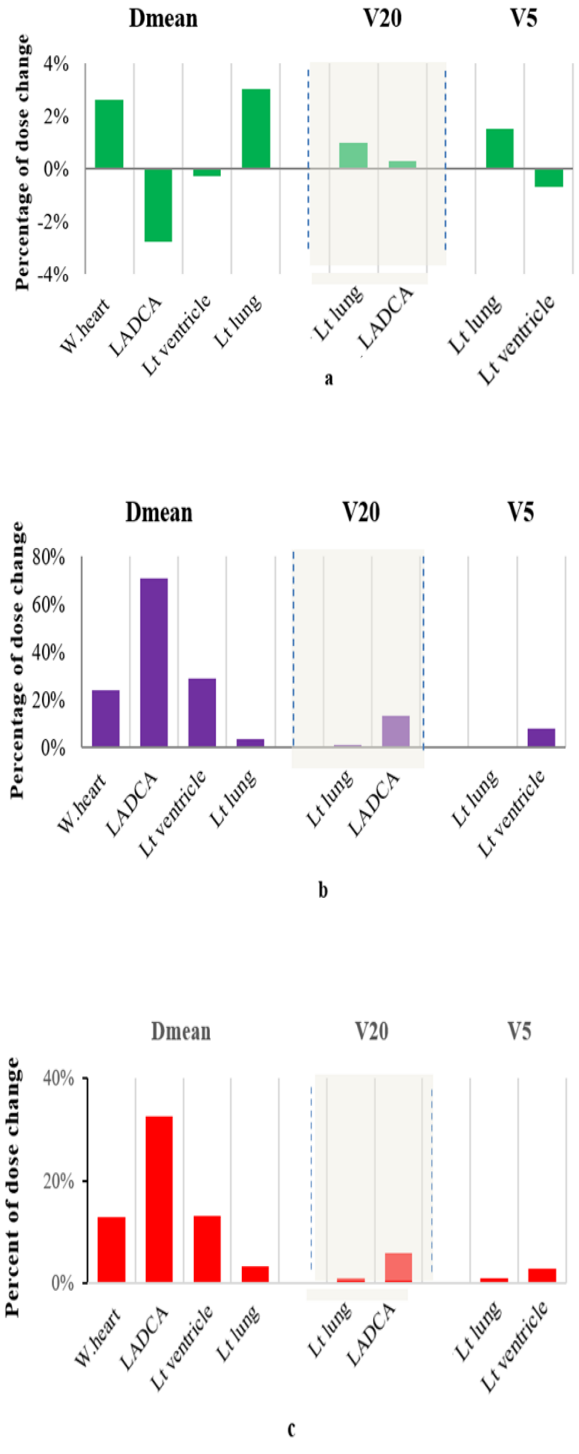

Figure (2): The percent of changes in the mean of all OARs doses a) in DIBH group b) in FB group c) in the average of all cases.

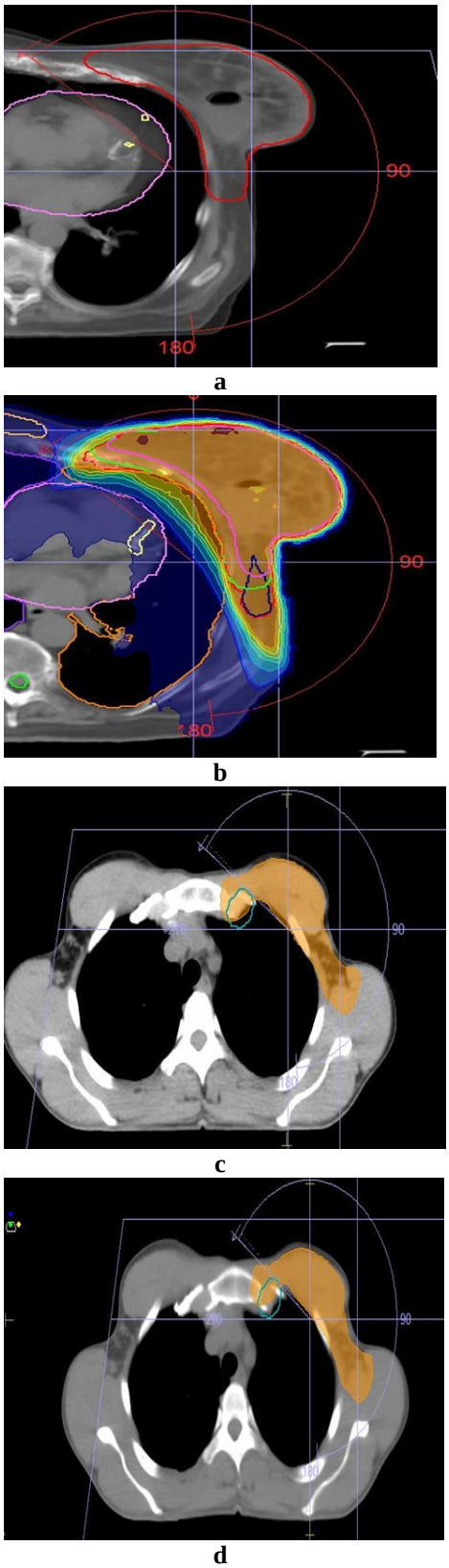

Figure (3): a) Axial CT Diffusion image between PCT (white) and CBCT (gray) in case 3, showing the proximity of the cardiac position to the radiation field in the CBCT more than that in PC, b) Dose distribution in the same CBCT explaining more heart exposure to the dose of radiation, c) IMC coverage in the PCT of Case 4 d) Decrease of the IMC coverage in the CBCT of Case 4.

Batumalai et al. study reported that, the effect of breast deformation setup error was more pronounced in the DIR than the RR [8]. Van Mourik et al. measured the influences of patient setup errors using RR and breast errors using DIR and dose accumulation on the TV dose distributions for 3 types of WB-RT treating plans; wedge, simple IMRT, and full IMRT and reported that the dose distributions from full IMRT planning technique were more seriously affected by the breast errors with -2% loss of coverage near the dorsal field edge and -4% near the skin as the full IMRT plans are more susceptible on the side of the skin to the shape changes of the breast because of absence of glancing open fields [9].

Hasan et al. evaluated the sufficiency of dose delivered by external beam accelerated partial breast irradiation (EB-APBI) using CBCT and DIR and reported an average decrease in the percentage of the PTV that received 90% of the prescribed dose (PTV V90%) by 3% , 4 patients had a maximum 3% increase in the ipsilateral lung volume receiving ≥30 Gy (V30%) and 1patient had an increase in the heart V5 by 1% [10].

Our significant results about the target indicate that, there was average decrease in the D95% to the PTV-total by -1%, caused mainly by decrease in the PTV-supra by -4% then the PTV-IMC by -1%. In our PCTs the mean D95% to all PTVs was minimal above 95% except the PTV-IMC where the mean D95% was 90%, therefore 1% decrease in the PTV consider clinically significant as the International Commission on Radiation Units and Measurements (ICRU) 83 recommends the dose that covered 98% of the PTV volume (D98%) to cover 95% of the PTV for IMRT plans and ICRU50 recommends D95% to cover 95% of the PTV for 3DCRT plans [11].

As for OAR, Lind et al. established that, the incidence and grade of radiation pneumonitis (RP) was significantly correlated with the lung Dmean ($p < 0.001$) and in Zsusana Kahan's study, there was RP with lung Dmean 15 Gy while 12 Gy expressed no RP, therefore considered an increase from 14 Gy to 14.46 Gy in the average Dmean to the ipsilateral Lt lung clinically not significant. In Wennberg et al. reported that treatments techniques with ipsilateral Lt lung V20% less than 20% had lower incidence in RP than V20% with more than 20% [12]. In our PCTs the average ipsilateral Lt lung V20% was already higher than 28% as we treat the RLNs, therefore an increase by1% may increase the risk of RP, even though it was statistically insignificant.

The heart Dmean increased from 4.13 to 4.67 Gy, 4.51 to 5.59 Gy and 3.83 to 3.93 Gy in the average of all cases, FB group and DIBH group, respectively. Darby et al. reported that the degree of risk of a major coronary heart disease was 7.4% per Gy, with no evident threshold below which there was no risk [13]. Jacobse et al. found a linear dose-response relationship between myocardial infarction (MI) risk and the heart Dmean, which means that there is no evident threshold dose below which this risk decreased [14]. Therefore, any increase in the heart Dmean during the treatment considered clinically significant.

Piroth et al. stressed the importance of including cardiac sub-volumes constraints such as Lt ventricle and LADCA besides the heart Dmean. Analyzing the myocardial perfusion in the cardiac apex by Marks et al. showed that 60% of the Lt sided BC patients treated with 50 Gy using tangential photon beam will have myocardial perfusion defects if the radiation portals included more than 5% of the Lt ventricle. The expert panel recommendations of German society for radiation oncology (DEGRO) for the constraints of cardiac sub-volumes developed for adjuvant WB-RT are less than 3 Gy, 17% and 10 Gy for Lt ventricle Dmean, Lt ventricle V5% and LADCA Dmean, respectively.

In our results, there was statistically insignificant increase in the LADCA Dmean in the average of all cases by 33% (1.93 Gy) from 5.92 Gy to 7.85 Gy. In the subgroup analysis the FB group showed significant increase by 71% (4.54 Gy) from 6.99 Gy to 10.99 Gy, which is clinically significant according to the DEGRO recommendation as it > 10 Gy. However, this dose showed insignificant decrease in the DIBH by -3% (-0.15 Gy) from 5.50 Gy to 5.34 Gy and the difference between both techniques was statistically significant [15].

The Dmean to the Lt ventricle increased from 3.45 to 3.91 Gy, 3.58 to 4.61 and 3.36 Gy to 3.35 Gy in the average of all cases, FB group and DIBH group, respectively. This increases in the average of all cases and in the FB group were clinically significant according to the DEGRO recommendation as the dose > 3 Gy from the start. The V5% to the Lt ventricle increased from 13% to 16% in the average of all cases. In the FB group, it increased from 15% to 23%, which considered clinically significant according to the DEGRO recommendation as it > 17%. However, it decreased in the DIBH from 12% to 11%.

The D2% to the Rt breast increased from 10.63 to 11.28 Gy, 11.48 to 12.51 Gy and 9.95 to 10.30 Gy in the average of all cases, FB group and DIBH group, respectively. Although all patients with a diagnosis of BC are at increased risk for developing a contralateral BC, the additional risk contributed by RT with modern techniques appears to be minimal 1.18 (p= .002). Stovall et all. reported that, the risk of second primary BC in the contralateral breast following RT for first BC was dose dependent, therefore any increase in the dose is considered clinically significant and we need to maintain the dose to the contralateral breast as low as possible [16].

The Dmax to the spinal cord increased from 16.06 to 17.35 Gy, 17.11 to 18.80 Gy and 15.21 to 16.20 Gy in the average of all cases, FB group and DIBH group, respectively. Jian-Yue Jin et all. reported that the alpha/beta (α/β) ratio of the human spinal cord was 3.7 and the biological equivalent dose (BED) that induces 5% chance of RIM (D5) was calculated to be 83.9 Gy, which correspond to 55.4 Gy in 2 Gy/FX, therefore considered these differences insignificant clinically [17].

Toyosi Fatunase et al. study, which assessed the consequences of the residual setup error on the dose distribution based on soft-tissue registration provided

by CBCT imaging for APBI patients, reported that there was an average reduction in the PTV Dmean by 1%, the mean difference in the percentage of the PTV that received 95% of the prescribed dose (PTV V95%) was 4% and there was an increase in the heart Dmean by 2% but these dosimetric results were thought to be clinically modest [18].

Batumalai et al. study, which assessed the effect of the day-to-day setup uncertainties on the delivered dose distribution based on soft-tissue and DIR for APBI patients, reported that, the average reduction in the PTV V95% were 7% and 5% for soft-tissue and DIR, respectively. The average increase in the heart Dmean were 9% and 18% for soft-tissue and DIR, respectively, whereas the average increase in the Dmax to the contralateral breast were 20% and 28%, respectively. The study concluded that this effect based on the DIR was greater for OARs and smaller for TVs [8].

Gijs J. van der Veen evaluated the robustness of the 3 planning techniques (tangential field IMRT, conventional VMAT (cVMAT) and VMAT with simulated swelling breast, followed by a segment weight optimization (VMAT + SWO)) by simulating the expansion and contraction of the breast as well as setup errors and recalculating the dose distributions on CBCT in breast and axillary nodal irradiation patients. The study approved that, robustness of cVMAT was inferior to IMRT and the target coverage of VMAT + SWO was proved to be more stable compared to cVMAT, against setup errors. The CTV V95% differed by up to 7% for cVMAT of the PCT, whereas it stayed within 2.5% for VMAT + SWO. The CTV V95% sensitivity to expansion for cVMAT, IMRT and VMAT + SWO was -22%/cm, -5.0%/cm and -5.3%/cm respectively, and its sensitivity to contraction for all techniques was 3%/cm. The effect of expansions/contractions on CTV D1% was low and similar among the 3 techniques as well as the OAR sensitivity to setup error was minimal and planning technique independent [19].

Although the percentage of CTV shrinkage in the average of all cases was significant, there was a wide variation in the percentage of breast shrinkage in all cases ranged from 3% to 21%, moreover there was no significant correlation between the CTV breast volume and the percentage of breast shrinkage and between the change in the breast size and the dose differences in all case. However, it has been detected that the case with the largest breast size (case 3 with 897 cm^3) has the largest percentage of CTV shrinkage (21%) and higher percentage of increase in the most measured doses; PTV-IMC D95%, lung, heart, LADCA and Lt ventricle Dmean, V20% LADCA,V5% Lt ventricle and D2% Rt breast while the Case with the smallest breast size (case 4 with 191 cm^3) has the smallest percentage of CTV shrinkage (3%) and higher percentage of decrease in the PTV-total D95%, PTV-IMC D95% and Dmean, PTV-supra, Lt lung V20%,V5% and Dmean, lower percentage of increase in the heart, LADCA, Lt ventricular Dmean for the FB group and lower percentage of increase in the D2% Rt breast. This conclusion does not apply to other cases; therefore, this result needs more cases to find whether there is a relationship between the breast size changes and the dose difference. Batumalai et al showed that five of the patients who had larger breast size, had a greater difference in the dose distribution. The study suggested that patients with larger breasts may have greater breast deformation than others, but it was not statistically proven due to the small number of patients. They called for a new study with more cases to prove or deny this relationship [8]. Examples of image diffusion between PCT and CBCT and dose distribution in case 3 and case 4 are displayed in Figure 3.

Conclusion:

The dosimetric impacts of breast setup errors during Lt BC with RLNs irradiation including the IMC by VMAT technique using DIR was small for the TVs, Lt lung in both DIBH and FB groups and for the heart with its sub-volume, Rt breast and spinal cord only in the DIBH group while is larger in the FB group. As the significant effect in the average of all cases appeared only in D95% to the PTV-total with average reduction -1% and caused mainly by difference in the D95% to the PTV-supra -4% then D95% to the PTV-IMC -1% so we recommend considering this increase in the IMRT constraint and creating a reasonable margin to the PTV-supra. For the ipsilateral Lt lung, the borderline significant effect in the average of all cases appeared only in the Dmean with an average increase 3%, so we recommend considering this increase in the Lt lung Dmean constraint. We recommend also using DIBH as it has more dosimetric stability throughout the treatment period on the heart and its sub-volumes.

List of abbreviations:

3DCRT	Three-dimensional conformal RT
BC	Breast cancer
BCS	Breast-conserving surgery
BED	biological equivalent dose
CBCTs	Cone-beam computer tomographies
CTVs	Clinical target volumes
D	Dose
DEGRO	German society for radiation oncology
DIBH	Deep inspiration breath-hold technique
DIR	Deformable image registration
EBAPBI	external beam accelerated partial breast irradiation
FB	Free breathing
FX	Fraction
Gy	Gray
HU	Hounsfield unit
ICRU	International Commission on Radiation Units and Measurements
IGRT	Image-guided Radiation therapy
IMC	Internal mammary chain
IMRT	Intensity-modulated RT
LADCA	Lt anterior descending coronary artery
Lt	Left

MI	Myocardial infarction
MLC	Multi-leaf collimator
MV	Mega volt
OARs	Organs at risks
PCT	planning CT
PTVs	Planning target volumes
RLNs	Regional lymph nodes
RP	Reference plan
RR	Rigid registration
Rt	Right
RTOG	Radiation therapy oncology group
SD	Standard deviation
SIGRT	Surface scanners
SPSS	Statistical Package for the Social Sciences
supra	Supraclavicular
SWO	Segment weight optimization
TV	Target volume
VMAT	Volumetric modulated arc therapy
WB	Whole breast

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