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Dosimetric Evaluation of Intact Breast Radiotherapy in Early Stages Breast Cancer Patients using Field-in-Field and 3D-CRT Enhanced Dynamic Wedge Techniques: Experience at a Tertiary Hospital in Tanzania

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ABSTRACT

Introduction: Dose planning is one of the important steps for the effective implementation of radiotherapy. As recommended, 95% to 107% of the prescribed dose should cover the target volume. Thus, radiotherapy cannot improve patient outcomes unless the desired dose delivery accuracy is achieved. The study was performed to evaluate field-in-field (FIF) technique (Forward intensity-modulated radiotherapy) compared with 3D-conformal radiotherapy enhanced dynamic wedge (EDW) technique.

Material and Methods: Two plans with opposed tangential fields; FIF and EDW for each breast cancer patient were created.

Results: The two techniques were comparable as far as the D_{max} , $D_{2\%}$, and $D_{5\%}$ were concerned. However, the FIF plan was slightly superior to EDW as far as $D_{95\%}$ and $D_{98\%}$ were concerned. The V95% was slightly higher in favor of FIF technique. The superiority of the FIF technique was further demonstrated by the lower mean dose (*D*mean) and the volumes receiving 10 Gy (V10Gy) and 20 Gy (V20Gy) of the prescribed dose for the heart. The *D*mean, V5Gy, V10Gy, and V20Gy for ipsilateral and contralateral lungs were comparable between the two techniques. However, the FIF technique demonstrated higher Dmean to the contralateral breast than EDW technique.

Conclusion: These results along with experiences elsewhere show the dosimetric benefits of the FIF technique for the optimal dose that should cover the target volume. However, the higher Dmean to the contralateral breast was a substantial shortcoming for the FIF technique. It can be recommended that the two planning techniques can be combined and used together to cover their drawbacks.

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Introduction

Radiotherapy is useful in the curative management of patients with breast cancer either as radiotherapy after conserving surgery or chemo-radiotherapy. In principle, radiotherapy aims to deliver a homogeneous therapeutic dose to a tumor volume while sparing the normal tissues. Thus, achieving dose homogeneity in target volume is paramount for the effective implementation of radiotherapy. To achieve the desired homogeneity, computed tomography (CT)-based techniques of varying sophistication are employed. The simple and commonly used technique is three-dimensional conformal radiation therapy (3D-CRT). The dose homogeneity obtained from this technique has improved over the years with beam-modifying contrivances like wedge filters especially enhanced dynamic wedges (EDW) [1]. The more sophisticated techniques include intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT) and field-in-field (FIF), also known as forward intensity-modulated radiotherapy. Among these techniques, the 3D-CRT has a wide application largely because of its simplistic nature. This feature makes it suitable for developing countries.

In Tanzania, FIF and 3D-CRT with EDW has been the choice techniques at Ocean Road Cancer Institute (ORCI) when the system for dose calculation and optimization had been implemented. Knowing the varying dosimetric benefits and deficits among the planning techniques, effective implementation of radiotherapy requires the selection of optimal techniques for accurate dose delivery and or cover their weak points. Many studies have compared the

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3D-CRT with FIF, IMRT and VMAT techniques. These studies have vouched for the superiority of IMRT and VMAT techniques to 3D-CRT [2-8]. However, despite these advanced technological opportunities in recent years, IMRT and VMAT are not implemented in many developing countries like Tanzania. This is largely because, the use of these modulation techniques requires significant resources and extensive quality assurance. While efforts are been made to initiate the implementation of these superior techniques, the current interest remains in 3D-CRT with EDW and FIF techniques. Several studies have vouched for an improved dose homogeneity to the PTV and lower doses to OAR in favor of the FIF technique compared to EDW [9]. Even so, there have been some contradictory conclusions in some previous studies regarding these dosimetric benefits of FIF over the EDW technique [3, 9, 10]. Considering the variability among algorithms of planning systems, the skill of the planner to meet the specified plan objective, and challenges in planning to vary between patients [11], it would be important to evaluate the influence of these two planning techniques. Although the FIF technique has been practiced regularly in many parts of the world, the use of FIF is still new in our context. However, experience with these techniques and comparable studies in countries of lower healthcare levels is little documented. Thus, FIF and EDW techniques were compared and the results were presented. Such comparison would be important to identify the weak points between the two techniques for improved dose delivery in breast cancer patients in clinical routine at ORCI. Moreover, the foreseen results could provide the first experience in the country on the subject and additional experience elsewhere.

Materials and Methods

In our study, 3D-CRT plans with EDW and FIF (f-IMRT) were evaluated and compared based on doses in the PTV and OARs. To achieve this objective, CT datasets from sixteen (16) patients with fairly early stages (T1 or T2) breast cancer from ORCI hospital were studied for comparison. The entire breast and thorax were scan with 5 mm slice with normal free-breathing on CT-simulator (SIEMENS, Healthineer Somatom, USA). The study observed confidentiality, guidelines, and compliance with regulations of personal electronic data protection and the Declaration of Helsinki. Since the information such as age, weight, length, and BMI do not influence doses of PTV and OAR, such demographic data were of no interest. The breast sizes were not classified. The PTV for selected patients ranged from 302.6 to 4346.7 cm^3. The median PTV volume for 16 patients was 1508.05 cm^3. The prescribed dose for ten patients was 50 Gy in 2 Gy dose per fraction and 42.50 Gy in 2.656 Gy for the remaining six patients.

The clinical target volume (CTV), PTV, and OAR for each CT-image were contoured by the radiation oncologist as per the guidelines of the International Commission of Radiation Units and Measurements (ICRU) Reports 50 and 62 [12, 13] According to ICRU Report 50 (1), the superficial edges of the beam extended 2 cm beyond the anterior skin surface of the breast in consideration of the movement of the breast during breathing. The OAR of interest in this study were the heart (HT), ipsilateral lung (IPSL), contralateral lung (CONTL), and contralateral breast (CONTB). After contouring, CT images were transferred through DICOM to the Varian's Eclipse treatment planning system (TPS). The TPS utilizes Anisotropic Analytical Algorithm (AAA) for dose calculation. This is a convolution-superposition algorithm, which takes into account the presence of tissue heterogeneity by convolutional energy distribution [14]. Two plans with opposed tangential fields (EDW and FIF) techniques for each patient were made. The plans were created using a 6 MV simulated photon beam of Varian TrueBeam (Varian Medical System, Palo Alto, CA). The plans were created such that the prescribed dose was normalized to cover 95% of the PTV as required by ICRU. For the sake of consistency, all plans were created by the same medical physicist using the institutional protocol and to the planner's experience. With EDW, two tangential beams (medial and lateral) were set depending on the need to meet the specified plan objective in the PTV. The weight for each field was adjusted to meet the same requirement. The enhanced dynamic wedges were selected in both fields and the wedge angles used were 15° and 20°. In the FIF-RT planning technique, the plan was modified based on the original tangential EDW. Additional subfields with varying field weight were used to optimize dose homogeneity within the PTV using varying beam energies (6 MV, 15 MV). Appropriate tangent angles were selected to minimize the dose to OAR without compromising the PTV coverage. Figures 1 and 2 show a sample of plans created for one of the cases using EDW and FIF techniques, respectively. From the figures, three views of transverse, sagittal, and front along with dose-volume histograms (DVH) are presented.

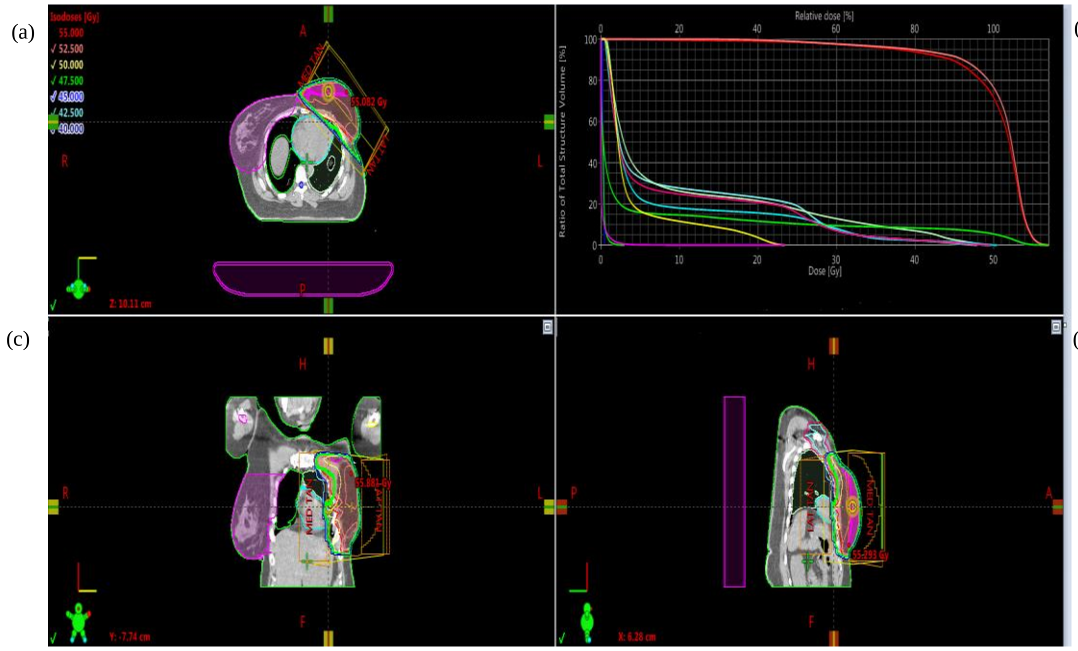

Figure 1. EDW plan (a) Transverse slice (b) DVH (c) Frontal slice (d) Sagittal slice.

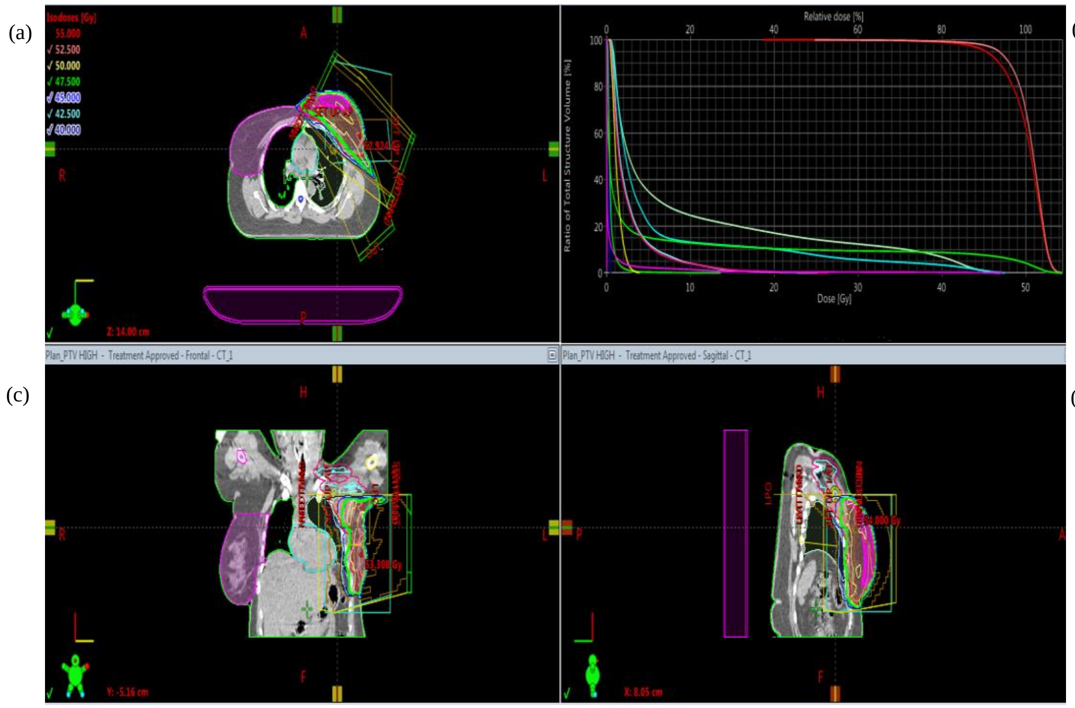

Figure 2. FIF-RT plan (a) Transverse slice (b) DVH (c) Frontal (d) Sagittal slice.

Treatment plans evaluation

In practice, several quantitative indices such as dose homogeneity index (DHI), conformity index (CI), and gradient index (GI) are used to define the 3-D dose distribution in the PTV. Out of these indices, DHI and CI are the commonly used indices. In this study, treatment plans were evaluated based on the DHI and CI values. Along with DHI and CI values, the dose in the PTV based on the maximum dose (D_{Max}), the minimum dose received by 95% of the PTV$\left(D_{95}\right)$, the dose received by 5% of the PTV$\left(D_{5}\right)$, and volume of the PTV covered by the 95% isodose (V95%) and monitor units (MU) were compared.

While several definitions of DHI have been proposed elsewhere, DHI values for each technique were obtained according to Equation 1 [14, 15]. Similarly, the CI values for each technique were obtained based on the formula by the Radiation Therapy Oncology Group (RTOG) in Equation 2 [16].

Dose Homogeneity Index,

$$DHI_{ICRU83} = \frac{D_2 - D_{98}}{D_{50}} \times 100 \quad (1)$$

Conformity Index,

$$CI_{RTOG} = \frac{V(RI)}{\text{Volume of TV}} \quad (2)$$

According to equation (1), D_{98} (often considered the minimum dose) indicates the dose to the 98% of the PTV. This implies that 98% of the PTV receives this dose. D_2 (Considered the maximum dose) is the dose to the 2% of the PTV and indicates that only 2% of the PTV receives this dose. D_{50} is the dose reached in 50% of the PTV. Based on equation (2), $V(RI)$ represent the volume covered by the reference isodose and TV indicates the target volume. To facilitate the determination of DHI and CI, the parameters D_{98}, D_2 and D_{50} to the PTV were obtained for each plan. For OAR, the mean dose (*D*mean) and the volumes receiving 5 Gy (V5Gy), 10 Gy (V10Gy) and 20 Gy (V20Gy) of the prescribed dose to the HT, IPSL, CONTL and CONTB for each plan were obtained. For comparison purposes, the paired t-test was used, with p-values < 0.05 considered to be significant.

Results

The comparison of doses of PTV between plans with EWD and FIF are presented in Table 1 and Figure 3. According to the table, the average D_{max} in plans with EDW and FIF were 55.16 ± 4.08 Gy and 54.46 ± 3.53 Gy, respectively. This observation shows that the mean D_{max} were comparable between the two techniques. As also observed in Figure 3, the two techniques were 109.72 ± 2.07 and 109.14 ± 1.97 and therefore comparable as far as the D_2 and D_5 values was concerned, respectively. However, the FIF technique was superior to the plan with EDW as far as D_{95} and D_{98} are concerned. The mean V95%, on absolute values, was slightly higher in FIF (88.36 ± 2.23%) compared to the EDW plan with 84.42 ± 3.40%. However, this difference was not statistically significant (p-value > 0.05).

Considering that D_{95} is the minimum dose that should cover 95% of the PTV, the FIF technique had a more favorable coverage of 90.24 ± 1.67% compared to 79.56 ± 7.54% for EDW. Similarly, D_{98} in the FIF plan had favorable coverage of the PTV (82.32 ± 5.18%) compared to EDW (64.06 ± 14.41%). Although the doses were more homogeneous in the FIF plan (0.26 ± 0.060) than that of EDW plans (0.44 ± 0.15), the difference is not statistically significant (p-value; 0.0551).

Table 1. The PTV dose parameters between EDW and FIF plans

Parameter	EDW Mean ± SD	FIF Mean ±SD	p-value
D_{Max} (Gy)	55.16 ± 4.08	54.46 ± 3.53	0.4103[n]
D_2 (%)	109.72 ± 2.07	109.14 ± 1.97	0.6175[n]
D_5 (%)	108.62 ± 2.11	108.14 ± 1.96	0.6707[n]
D_{95} (%)	79.56 ± 7.54	90.24 ± 1.67	0.0369[s]
D_{98} (%)	64.06 ± 14.41	82.32 ± 5.18	0.0423[s]
V95%	84.42 ± 3.40	88.36 ± 2.23	0.1730[n]
DHI	0.44 ± 0.15	0.26 ± 0.06	0.0551[n]
CI	0.92 ± 0.24	0.77 ± 0.10	0.0975[n]
MU_{Total}	261.70±10.7	253.30±8.34).	0.1530[n]

[n] p-value > 0.05, statistically insignificant; [s] p-value < 0.05, statistically significant.

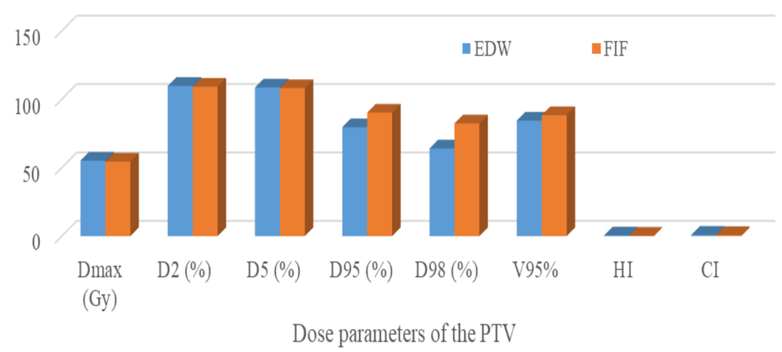

Figure 3. Comparison of dose parameters for plans with EDW and FIF

For CI value, although the differences were not significant, it was evident that the absolute mean CI value for EDW plans was slightly higher (0.92 ± 0.24) compared to FIF plans (0.77 ± 0.10), indicating fairly better conformity. When the total monitor units were compared, the mean MU value required for the EWD was slightly higher (261.70 ± 10.7) compared to the FIF techniques (253.30 ± 8.34). However, the difference in the average MU values used in the EDW and FIF techniques was not statistically significant (p-value; 0.1530)

The comparison of average Dmean, V5Gy, V10Gy, and V20Gy to the HT, IPSL, CONTL, and CONTB for each technique is presented in Table 2 and Figure 4. From the table, it is evident that the Dmean, V5Gy, V10Gy, and V20Gy absolute values for HT and IPSL were generally lower in FIF than in the EDW technique. This observation was also evident in Figure 4. However, with exception of V5Gy, the largest dose reduction in FIF correspond to the HT. For IPSL, the differences between the techniques were not statistically significant for the Dmean, V5Gy, V10Gy, and V20Gy. While the Dmean, V5Gy, V10Gy, and V20Gy for CONTL were comparable, the FIF plan showed a significantly higher Dmean to the CONTB compared to EDW (p-value; 0.0289). However, although on absolute values, the mean V5Gy, V10Gy, and V20Gy to the CONTB were slightly higher in FIF plans, the differences were not statistically significant between the plans.

For HT, with exception of V5Gy, statistically significant differences were found between the two techniques. The Dmean, V10Gy, and V20Gy were significantly lower (p-values; 0.0021, 0.0499, and 0.0034, respectively) in favor of the FIF technique. Despite the higher value of V5Gy for HT in EDW plans, the difference was not statistically significant. For IPSL, it is important to remark that the FIF technique had lower Dmean, V5Gy, V10Gy, and V20Gy on absolute values. This perhaps demonstrates the slight reduction of Dmean, V5Gy, V10Gy, and V20Gy to the IPSL when using the FIF technique. However, the differences were not statistically significant. On the other hand, the Dmean (Gy), V5Gy, V10Gy, and V20Gy were comparable between the two techniques for CONTL. For CONTB, the Dmean (Gy) was higher (2-fold) in the FIF technique compared to EDW. It was important to remark that, on absolute values and as observed in Figure 4, the V5Gy, V10Gy, and V20Gy were slightly higher in FIF than EDW technique. However, the difference was not statistically significant.

Table 2. Comparison of parameters of OAR between EDW and FIF techniques

OAR	Parameters	EWD	FIF	p-value
HT	Dmean (Gy)	7.26 ± 1.81	5.43 ± 1.77	0.0021[s]
	V5Gy (%)	21.86 ± 6.00	18.86 ± 6.71	0.1841[n]
	V10Gy (%)	16.82 ± 5.75	12.04 ± 4.72	0.0499[s]
	V20Gy (%)	13.02 ± 4.39	8.76 ± 3.38	0.0034[s]
IPSL	Dmean (Gy)	12.30 ± 4.30	10.32 ± 1.30	0.2763[n]
	V5Gy (%)	39.20 ± 12.93	36.08 ± 5.37	0.4825[n]
	V10Gy (%)	30.48 ± 11.34	26.14 ± 3.93	0.3518[n]
	V20Gy (%)	25.36 ± 10.39	19.86 ± 3.13	0.2217[n]
CONTL	Dmean (Gy)	0.20 ± 0.06	0.22 ± 0.15	0.7357[n]
	V5Gy (%)	0.00 ± 0.00	0.04 ± 0.09	0.3739[n]
	V10Gy (%)	0.00 ± 0.00	0.00 ± 0.00	-
	V20Gy (%)	0.00 ± 0.00	0.00 ± 0.00	-
CONTB	Dmean (Gy)	0.27 ± 0.13	0.45 ± 0.11	0.0289[s]
	V5Gy (%)	0.5 ± 0.48	1.26 ± 0.80	0.1126[n]
	V10Gy (%)	0.2 ± 0.28	0.72 ± 0.53	0.1424[n]
	V20Gy (%)	0.12 ± 0.18	0.24 ± 0.26	0.5012[n]

[n] p-value > 0.05, not significant; [s] p-value < 0.05, significant

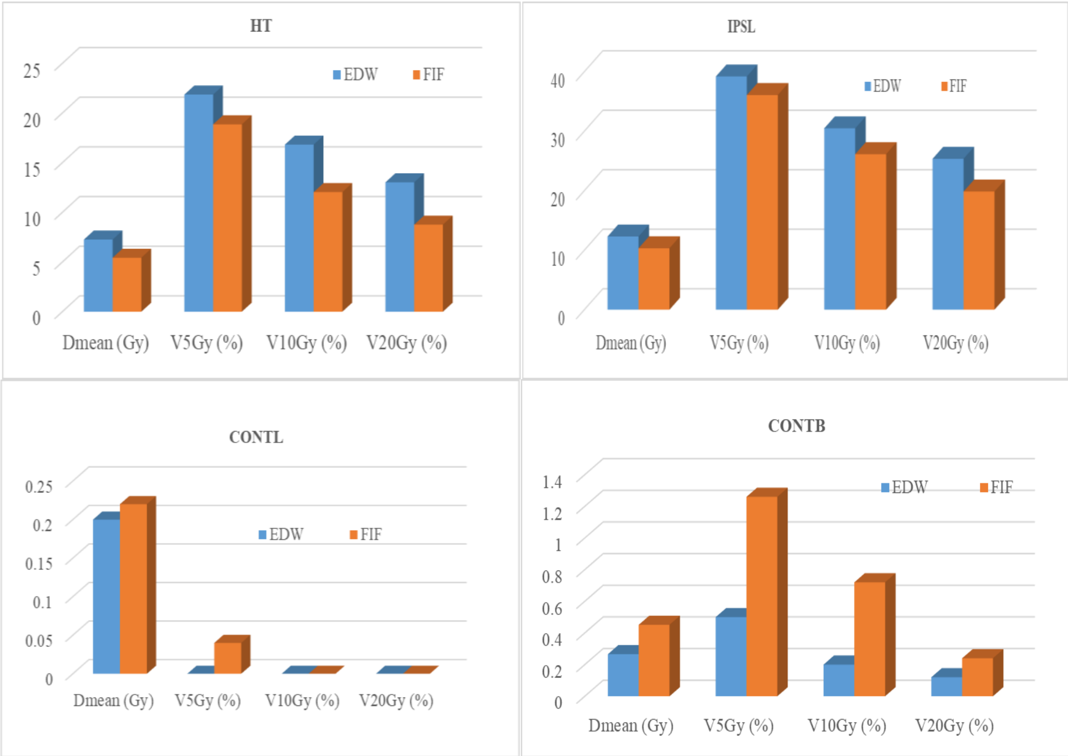

Figure 4. Comparison of dose parameters of the OAR between EDW and FIF

Discussion

Regardless of the technique, the primary objective of radiotherapy is to deliver the highest possible dose to the PTV while simultaneously sparing the critical organs. Thus, effective implementation of radiotherapy requires dose homogeneity within the PTV for tumor control and reduced late complications. Knowing that one of the important steps for the effective implementation of radiotherapy is dose planning, selecting the optimal technique would be important for improved dose delivery accuracy in breast cancer patients. As previously reviewed in the cited publications, the FIF-RT technique has had a more favorable dose homogeneity within the PTV and lower doses to OAR compared to the wedge technique [3, 9]. Although the results in this work confirm in part this assertion, some differences have been observed. The current study shows the D_{max} from the EDW plan were comparable to FIF plans as there was no significant difference between the two techniques. This was also evident from the $D_{2\%}$ of 109.72 ± 2.07 and 109.14 ± 1.97 for EDW and FIF techniques, respectively. According to the ICRU recommendation, 95% to 105% of the prescribed dose should cover the PTV. Based on this reference, one can recall that $D_{95\%}$ is the minimum dose and $D_{5\%}$ is the maximum dose that should cover the PTV. The results of $D_{95\%}$ showed both techniques were below the minimum limit of 95%, where the lowest value was obtained in EDW plan. However, the plan with FIF had a PTV coverage of 90.24 ± 1.67% of the prescribed dose compared to 79.56 ± 7.54% for EDW. This explains in part the superiority of FIF to the EDW technique. This result is in line with the study by D'Avenia et al. (2018). Meanwhile, the results of $D_{5\%}$ showed comparable values between the techniques and exceeded the maximum tolerance level of 105%. Implicit in this observation is that, both techniques can cause a large high dose volume. For DHI values, the absolute CI value of 0.26 ± 0.060 in FIF was lower compared to 0.44 ± 0.15 of EDW plans. Yet, this difference was not statistically significant. In practice, DHI = 0 indicates the ideal dose homogeneity within the PTV. This means, that the closer the DHI value to 0 implies the ideal homogeneity. The observed lower DHI value in the FIF technique compared to EDW suggests a slightly better dose homogeneity compared to EDW as reported in some studies [17]. On the other hand, EDW produced a slightly higher CI value (0.92 ± 0.24) than FIF plans (0.77 ± 0.10) on absolute values. According to RTOG guidelines, the ideal conformity corresponds to a CI value of 1. The CI value exceeding 1, implies the irradiated volume is greater than the PTV whereas the CI value of less than 1 means, not the whole PTV was covered by the reference dose. Thus, the closer the CI value to 1, the better the conformity. The observed CI values seem to suggest that the EDW plans have slightly better conformity than FIF plans. Nevertheless, the difference in CI values between the two techniques was not statistically significant.

While dose homogeneity and conformity within the PTV are important, they may undermine the benefits of treatment if the protection of critical organs is not taken. When the parameters of OAR were compared, the results suggest that the FIF plans were superior to EDW as far as the reduction of Dmean, V10Gy, and V20Gy to the OAR is concerned. This superiority was demonstrated by significantly lower Dmean, V10Gy, and V20Gy for the HT in FIF than EDW plan. The reduction of dose to the HT implies the risks associated with such doses were also reduced in the FIF technique. This observation in part explains the benefit of FIF compared to the EDW plans as confirmed in earlier studies [3, 9, 17, 18]. For IPSL, although there was no statistically significant differences between the two techniques, it would be important to remark that the Dmean, V5Gy, V10Gy and V20Gy were slightly lower for the FIF technique when the absolute values are considered.

On the contrary, the claim reported in some studies that the FIF technique results in lower doses of the CONTB were not valid in our study. The observed results indicated some differences compared to earlier studies. The lower Dmean to the CONTB favors the EDW plan compared to FIF. This implies that the CONTB is over-irradiated in the FIF technique than EDW does. For this reason, effective measures to protect the CONTB are more important from the radiation protection point of view when using the FIF technique. Since the FIF technique has demonstrated some benefits over EDW and the fact that it is easier to protect the CONTB than the HT and IPSL, it would be valuable to identify effective interventions to protect CONTB. This is particularly important because the dose of CONTB has been implicated in the risk of secondary malignancies in longer follow-ups. Additionally, the results showed that the differences between the two techniques for V5Gy, V10Gy, and V20Gy for CONTB were not statistically significant. However, looking at the absolute mean values in Table 2 and Figure 4 for CONTB, the V5Gy, V10Gy, and V20Gy were higher (2-fold) in the FIF technique compared to the EDW plan. This observation is inconsistent with previous studies [3,9,17,18,19] However, the discrepancy in terms of the dose to the CONTB in this study could have been attributed to the influence of the planner's skill on dosimetry, type of wedges and the difficulties in planning to vary between patients pointed out earlier.

Conclusion

The comparison of FIF and 3D-CRT plan with EDW concerning the doses within the PTV and OAR showed that, the two techniques are comparable as far as the D_{max}, $D_{2\%}$ and $D_{5\%}$ was concerned. However, the FIF technique was slightly superior to EDW as far as $D_{95\%}$ and $D_{98\%}$ are concerned. In parallel, the results demonstrated that the FIF plans had significantly lower Dmean, V10Gy, and V20Gy to the HT than EDW does. However, the higher *D*mean to the CONTB was a substantial shortcoming for the FIF technique. Consequently, in order to take advantages of the reduced dose to HT, the FIF technique is the ideal technique in clinical routine. However, since the reduction of dose in HT was obtained at the expense of increased dose to CONTB, it would be important to identify effective practices to reduce doses to CONTB when FIF is used. To conclude, it is the opinion of the authors that even using a larger number of patients would lead to a similar conclusion. Further parameters like PTV Dose improvement (PDI) and geometric conformity index can be used to demonstrate the benefits of FIF technique. Thus, the results of this study set a starting point for the envisaged endeavour. As well, efforts for implementing advanced techniques should be made in Tanzania for improved dose delivery accuracy in breast cancer radiotherapy. However, the use of advanced techniques cannot improve treatment outcome unless a mass of skilled human resources in radiation oncology and medical physics has been created. This is an important aspect where the technical assistance from the IAEA and elsewhere would be greatly appreciated in Tanzania to fulfil the gap.

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