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ORIGINAL ARTICLE

Dosimetric Investigation of FIF, VMAT, IMRT, H-VMAT, and H-IMRT Planning Techniques in Breast Cancer Radiotherapy

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OBJECTIVE

It is aimed to compare the hybrid radiotherapy (RT) plans according to three-dimensional field-in-field (FIF), intensity-modulated RT (IMRT), and volumetric-modulated arc therapy (VMAT) techniques in RT applied to the whole breast volume after breast-conserving surgery.

METHODS

Based on the simulation images of 31 consecutive patients who received whole breast RT, a dose of 50 Gy (25 fractions) was prescribed to the planned treatment volume (PTV) with 6 MV X-rays, five new plans were created, respectively (FIF, VMAT, IMRT, H-VMAT, and H-IMRT). Homogeneity criteria for PTV, volume-dose criteria for peripheral critical organs, and MU values of the plans were evaluated separately for each plan. Subgroup analyses were performed for the left- and right-sided patients.

RESULTS

Both hybrid plans produced a more homogeneous plan at the target volume compared to the other three techniques (HI; 0.14, 0.14, 0.16, 0.12, and 0.13, $p<0.001$, respectively). Again, smaller values for D2% were obtained with both hybrid techniques (53.25, 53.24, 53.8, 52.41, and 52.47 Gy, respectively, $p<0.001$). The mean heart dose for the left-sided irradiations was 3.54, 3.40, 4.33, 3.49, and 3.79 Gy for the five techniques, respectively ($p=0.029$). Compared with FIF with the other four techniques for the left-sided irradiations, the LAD D 10% value was significantly reduced ($p<0.001$).

CONCLUSION

Hybrid plans provide a more homogeneous dose distribution compared to the use of other techniques alone, while at the same time, it allows reducing the ipsilateral lung and heart doses.

Keywords: Breast cancer; field-in-field; hybrid planning technique; intensity modulate; radiotherapy; volumetric-modulated arc therapy.

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INTRODUCTION

Radiotherapy (RT) is a part of multimodal treatment for breast cancer. Equivalent results to mastectomy have been obtained with the application of RT after breast-conserving surgery in early-stage breast cancer.[1,2] Today, the 15-year survival rate for early-stage breast cancer is reported to be 80%.[1] This makes it more important to keep critical organ doses to a minimum in breast cancer RT. Because long-term side effects of RT, such as bad cosmetics due to skin fibrosis, secondary cancers, and coronary diseases, are more likely to occur.[3]

The breast is an organ that shows great geometrical variations on a patient basis. Many factors, such as breast size, shape, surface irregularities, and chest wall structure, directly affect RT planning.[4] This makes it difficult to provide a homogeneous dose distribution during RT planning. Classically, two tangential fields with mutual wedges were used in the three-dimensional period in whole breast RT planning. It was not entirely possible to control hotspots with this technique. However, with the development of the field-in-field (FIF) technique, it has become feasible to close the hotspots in the tangential areas with multi-leaf collimator (MLC) leaves and to provide dose modulation. Subsequently, it has been shown that dose homogeneity is increased with the intensity-modulated RT (IMRT) technique, and thus, a significant reduction in acute and chronic side effects is achieved.[5,6] It has been reported that there is a decrease in acute skin reactions and better long-term cosmetic results are obtained with IMRT.[5] Similarly, it was found that volumetric-modulated arc therapy (VMAT) provides dose homogeneity equivalent to IMRT and is better at protecting critical organs.[7] However, in IMRT and VMAT techniques, a more homogeneous dose distribution is achieved and adjacent critical structures are better preserved, while the volume of the low-dose area and the amount of dose received by the contralateral organs increase compared to the FIF technique. Increasing the low-dose area is associated with an increased risk of secondary cancer in the long term.[8] On the other hand, since IMRT and VMAT are much more complex techniques than tangential irradiation, they cause an increase in workload during both planning and treatment implementation. Considering that 30% of patients treated in radiation oncology clinics have breast disease, the importance of this situation is better understood.[9] To overcome these problems and to combine the good points of each technique, the idea of hybrid planning was introduced. In this way, it aims to make more optimal and balanced RT plans by combining the FIF technique with IMRT or VMAT.[8–10]

In light of this information, the goal of our study was to compare FIF, VMAT, IMRT, H-VMAT (hybrid VMAT), and H-IMRT (hybrid IMRT) techniques in terms of dosimetric and treatment duration (MU) in all breast irradiations (without boost) using conventional fractionation.

MATERIALS AND METHODS

Considering the difference in breast anatomy in the study, target volumes on computed tomography sections taken in the treatment position of 31 breast cancer patients (15 right and 16 left) with breast volumes in the range of 391.4–1901.6 cc, such as CTV, planned treatment volume (PTV), and critical organs; contralateral breast, ipsilateral lung, contralateral lung, and heart were contoured in accordance with Radiation Therapy Oncology Group protocols. Plans were made by ensuring that the 95% volume of the PTV received the 95% treatment dose (50 Gy [2 Gy/fr]). The 6 MV photon energy was calculated using the Analytical Anisotropic Algorithm (AAA) in the Eclipse treatment planning system (version 15.6). The configuration of the AAA model is based on the physical parameters determined by Monte-Carlo.[11]

Design of Plan

- During the planning of the FIF, two tangential areas were opened to each other, the table angle was not used, the hot dose zones formed in the PTV were drawn automatically in the TPS, and a homogeneous dose distribution was obtained by closing the hot areas with the help of MLC by opening the lower two areas have been done.
- VMAT, while determining the entrance and exit angles of the areas in their planning, was created to be the same as the entrance angles of the two tangential open areas. The fields were opened in a clockwise and counterclockwise direction, with two opposite arcs. A table angle of 30 degrees was not used and the two arcs are coplanar and each of the arcs is given collimator angel of 5 and 355 degrees, respectively.[12]
- IMRT was planned to have five fields. The table and collimator angle was not used. While determining the field angles, the localization of critical organ structures and the shape of the breast structure were taken into account, and patient-specific angles were determined for each patient.

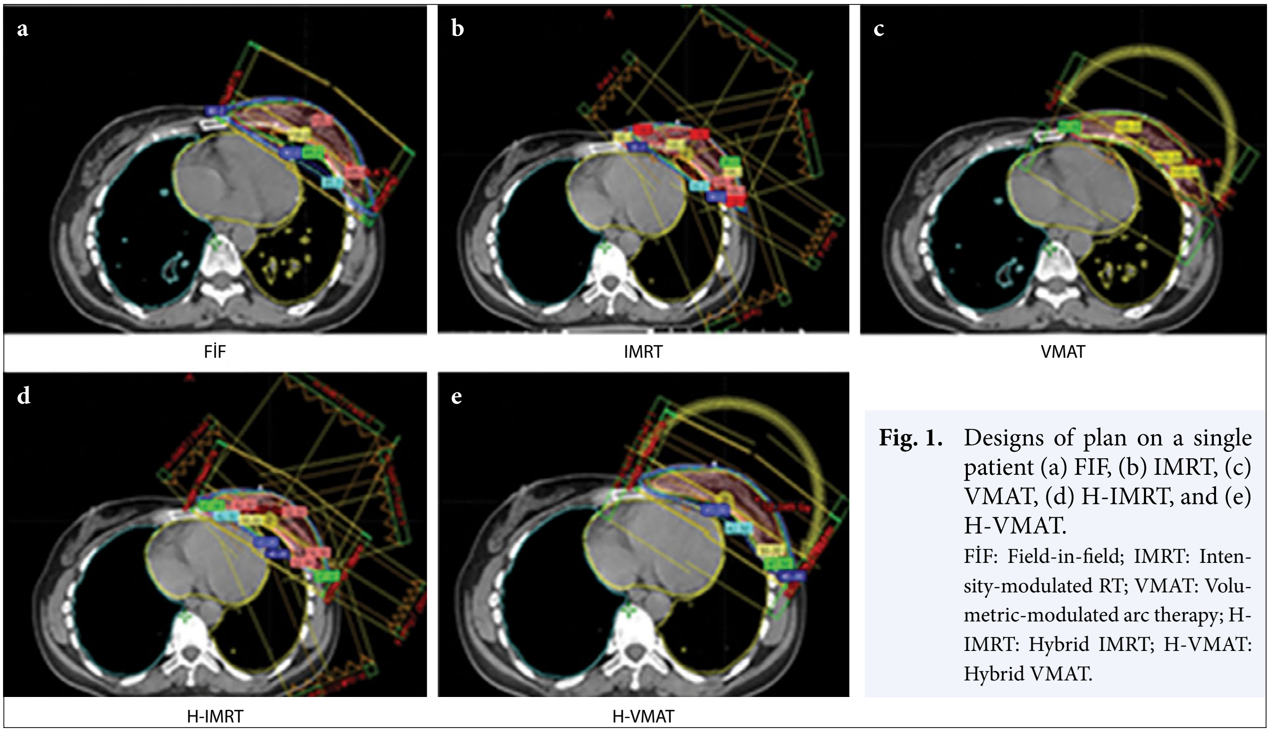

Fig. 1. Designs of plan on a single patient (a) FIF, (b) IMRT, (c) VMAT, (d) H-IMRT, and (e) H-VMAT.
FİF: Field-in-field; IMRT: Intensity-modulated RT; VMAT: Volumetric-modulated arc therapy; H-IMRT: Hybrid IMRT; H-VMAT: Hybrid VMAT.

- In the H-IMRT plan, a mixture of FIF and IMRT techniques was used. FIF technique (26 Gy/13f) was used for the first 13 fractions, and IMRT (24 Gy/12f) for the later 12 times. A total dose of 50 Gy (25 fractions) has been prescribed for H-IMRT plans.
- In the H-VMAT plan, a mixture of FIF and VMAT techniques was used. FIF technique (26 Gy/13f) was used for the first 13 fractions and VMAT (24 Gy/12f) for the later 12 times. A total dose of 50 Gy (25 fractions) has been prescribed for H-IMRT plans.

The plan designs of five different RT plans made in this study on a single patient are given in Figure 1.

Evaluation of Plan

D_{mean}, D_2, and D_{98} parameters were checked for PTV. The formula suggested by ICRU 62 was used while calculating the CI parameter, and the ICRU 83 formula was used for the HI parameter.[13,14] In critical organ structures, D_{40}, D_{10}, $D_{5\%}$, and D_{mean} values for the heart dose, $D_{10\%}$ value for LAD, $D_{60\%}$, $D_{30\%}$, $D_{5\%}$, and D_{mean} values for the lung on the planned side, the parameters were evaluated by looking at the $D_{60\%}$ and D_{mean} values for the lung, and the V_{5Gy} and D_{mean} values for the contralateral breast from the dose-volume histogram. In addition, total MU values were calculated for each plan. The results were transferred to the SPSS (IBM, v17.0) program for statistical analysis and compared with appropriate parameters or non-parametric tests.

RESULTS

Both hybrid plans produced a more homogeneous plan in the target volume compared to the other three techniques (for HI FiF, VMAT, IMRT, H-VMAT, and H-IMRT, 0.14, 0.14, 0.16, 0.12, and 0.13, respectively, p<0.001). Again, both hybrid techniques were able to obtain smaller values for D%2 for 53.25, 53.24, 53.8, 52.41, and 52.47, respectively, p<0.001. There were no significant differences in homogeneity criteria for PTV between FiF, IMRT, and VMAT techniques (p=1, for pairwise comparisons). The mean dose in the ipsilateral lung was decreased by the VMAT and H-VMAT techniques (p=0.024). With the other four techniques, except for the FiF plan, the mean doses of both the contralateral lung and the breast increased significantly (for both, p<0.001). However, with the H-VMAT and H-IMRT planning, both the mean lung dose and breast dose of the contralateral side decreased compared to the VMAT and IMRT techniques. The mean heart dose for the left-sided irradiation was 3.54, 3.40, 4.33, 3.49, and 3.79 for the five techniques, respectively (p=0.029). With FiF, the LAD $D_{10\%}$ value was significantly decreased in the left-sided irradiations with the other four techniques (p<0.001). On the other hand, in the right-sided irradiations, mean heart doses were significantly increased in the other four techniques compared to the FIF technique,

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Table 1 Statistical results of (a) FIF, (b) IMRT, (c) VMAT, (d) H-IMRT, and (e) H-VMAT planning

	FiF	VMAT	IMRT	H-VMAT	H-IMRT	p
PTV $D_{2\%}$	53.25±0.76	53.24±0.64	53.8±1.98	52.41±0.55	52.47±0.85	<0.001
PTV $D_{98\%}$	46.19±0.34	46.22±0.2	45.73 ±0.7	46.35±0.14	46.25±0.29	<0.001
HI	0.14±0.01	0.14±0.02	0.16±0.05	0.12±0.01	0.13±0.02	<0.001
CB V_{5Gy}	0.60±0.27	3.46±0.68	3.74±1.21	2.01±0.36	2.04±0.62	<0.001
CB D_{mean}	0.19±0.094	1.64±0.32	1.52±0.45	0.92±0.17	0.84±0.22	<0.001
IL $D_{60\%}$	1.65±0.44	3.51±0.65	2.99±0.95	2.60±0.50	2.36±0.64	<0.001
IL $D_{30\%}$	6.22±4.01	8.64±1.33	10.22±3.27	7.46±2.40	8.46±2.82	<0.001
IL $D_{5\%}$	45.71±2.30	32.28±1.47	36.47±6.13	38.08±2.19	40.86 ±2.54	<0.001
IL D_{mean}	9.69±2.50	8.79±0.75	9.75 ±1.87	9.17±1.50	9.71±1.56	0.024
CL $D_{10\%}$	0.24±0.12	3.42±0.54	4.28±4.00	1.78±0.3	1.81±0.81	<0.001
CL D_{mean}	0.1±0.06	1.66±0.21	1.84±1.26	0.88±0.13	0.83±0.31	<0.001
H $D_{mean\ R}$	0.63±0.2	2.61±0.53	2.94±0.48	1.56±0.26	1.78±0.23	<0.001
H $D_{mean\ L}$	3.54±1.66	3.40±0.72	4.33±0.92	3.49±1.10	3.79±1.12	0.029
LAD $D_{10\%L}$	39.81±14.29	22.20±8.65	28.41±6.83	31.38±9.68	33.54±9.95	<0.001
MU	235.95±12.57	525.27±45.99	933.59±177.78	381.6±29.18	561.97±61.12	<0.001

FİF: Field-in-field; VMAT: Volumetric-modulated arc therapy; IMRT: Intensity-modulated RT; H-VMAT: Hybrid VMAT; H-IMRT: Hybrid IMRT; PTV: Planned treatment volume; HI: Homogeneity index; CB: Contralateral breast; IL: Ipsilateral lung; CL: Contralateral lung; H: Heart; LAD: Left anterior descending artery; MU: Monitor unit.

while they were found to be lower with H-VMAT and H-IMRT compared to the VMAT and IMRT techniques (0.63, 2.61, 2.94, 1.56, and 1.78, p<0.001, respectively). MU values were found to be the lowest for FiF, while H-VMAT and H-IMRT planning decreased MU values compared to VMAT and IMRT techniques (p<0.001 for 235.95, 525.27, 933.59, 381.6, and 561.97, respectively). The results are shown in Table 1.

DISCUSSION

With the FIF technique, which was developed after the three-dimensional conformal RT (3D-CRT) technique was applied using a mutually wedged area, a more homogeneous dose distribution is achieved, while the doses taken by critical organs can be significantly reduced.[15] However, large differences in breast sizes, geometric shapes, and surface irregularities prevent FIF planning from giving the same accurate results for each patient.[16] With the introduction of IMRT and VMAT techniques, this problem was solved to a large extent, while problems such as prolonged treatment time (increased MU) and increased low-dose area were encountered.[6,7] It has been shown that the hybrid planning idea developed on this basis can reduce the planning time while creating a plan of equivalent quality to IMRT.[17] In our study, protocols were created for planning FIF, VMAT, IMRT, H-VMAT, and H-IMRT, and planning for the right- and left-sided breast cancer patients was done and compared dosimetrically.

The lungs are the organs directly affected during breast irradiation, as they are located just below the breast tissue. Radiation-induced pneumonia is observed in approximately 10% of breast cancer patients, and fibrosis is observed in the lung region where X-rays are transmitted in 90%.[18] In the study of Fragkandrea et al.,[19] lung doses were shown to be directly related to radiation pneumonia and fibrosis. The mean lung dose in patients who did not show signs of pneumonia in computed tomography sections was 11.2 Gy, with a V20 Gy of 16.7%. While the D% value of 25% was reported as 14 Gy, 20.7%, and 23 Gy, respectively, in the group with pneumonia. The 3D-CRT technique was used in the study. In our study, mean ipsilateral lung doses were found to be 9.7 Gy, 8.8 Gy, 9.75 Gy, 9.2 Gy, and 9.7 Gy for FIF, VMAT, IMRT, H-VMAT, and H-IMRT, respectively (p=0.024). $D_{30\%}$ doses were determined as 6.2 Gy, 8.6 Gy, 10.2 Gy, 7.5 Gy, and 8.5 Gy, respectively (p<0.001). These results indicate that all techniques can be applied safely. However, H-VMAT was found to be superior to H-IMRT in terms of ipsilateral lung mean dose (p<0.001). There was no significant difference between VMAT and H-VMAT (p=0.886).

The heart is particularly affected during the left breast irradiation. Although the heart is largely outside the RT area in the right-sided irradiations, it was emphasized that there is no threshold dose for ischemic heart disease in the study of Darby et al.[20] According to this study, every 1 Gy increase in the mean heart dose increases the risk of ischemic heart disease by 7.4%. In our study, LAD and heart doses were evaluated separately for the right (n=15) and left (n=16) breast cancer patients. In the left breast patients, the LAD D 10% value was found to be 39.8 Gy, 22.2 Gy, 28.4 Gy, 31.4 Gy, and 33.5 Gy for FIF, VMAT, IMRT, H-VMAT, and H-IMRT, respectively (p<0.001). VMAT and IMRT provided an advantage in LAD doses compared to the FIF technique (p<0.001 and p 0.005, respectively). In addition, VMAT was found to be more successful in LAD preservation than the H-IMRT technique (p=0.002). The LAD $D_{10\%}$ value in the right-sided patients was seen as zero for all patients. The mean cardiac doses for the left-sided patients were 3.5 Gy, 3.4 Gy, 4.3 Gy, 3.5 Gy, and 3.8 Gy, respectively (p=0.029); for the right-sided patients, it was determined to be 0.6 Gy, 2.6 Gy, 2.9 Gy, 1.6 Gy, and 1.8 Gy, respectively (p<0.001). The lowest mean heart doses were obtained with VMAT and H-VMAT in the left-sided irradiations. In the right breast RT, the FIF technique provides a significant advantage in terms of mean heart dose compared to all other techniques (p<0.001).

It has been reported that the risk of developing secondary cancers is approximately 2 times higher in the IMRT technique compared to 3D-CRT, due to the increase in the low-dose area. It has been emphasized that there will be an increase in the number of secondary cancers in the young population and the patient group with a long survival expectancy, but the risk ratio will remain constant.[21] However, there are also opposing views on this issue. In the study performed by Filippi et al.[22] on patients with mediastinal lymphoma, no difference was found between VMAT and 3D-CRT techniques in terms of secondary cancer risk (breast and thyroid). Despite the contradictory results obtained in studies in the literature, it is known that RT can have a carcinogenic effect in very small doses.[23] Therefore, care should be taken in terms of small dose baths during RT planning. In particular, the doses taken by the contralateral breast and lung must be controlled. Due to the increase in the number of RT fields and entry angles,[17] techniques such as IMRT and VMAT affect more normal tissues until they reach the target. The results obtained with the techniques applied in our study were also found to be compatible with this. The volume of V_{5Gy} for the contralateral breast was 0.6%, 3.5%, 3.7%, 2%, and 2% for the FIF, VMAT, IMRT, H-VMAT, and H-IMRT techniques, respectively (p<0.001). Similarly, the mean contralateral lung doses were 0.1 Gy, 1.7 Gy, 1.8 Gy, 0.9 Gy, and 0.8 Gy, respectively. The FIF technique provides a significant advantage over all other techniques for low-dose volume (p<0.001). Hybrid plans, on the other hand, significantly reduce low-dose volume compared to IMRT and VMAT techniques (p<0.001).

There was a statistically significant difference between the five techniques in terms of D2% for PTV. The dose received by 2% of the PTV for hybrid plans was lowest compared with the other techniques (respectively, 53.25, 53.24, 53.8, 52.41, and 52.47 Gy, p<0.001). A study showed that hybrid plans achieved optimal PTV coverage while avoiding hotspots in PTV volume. These results are in agreement with the results reported by Zheng et al.[24]

Complex techniques such as IMRT and VMAT cause an increase in the MU numbers of the planes.[25] Breast cancer is one of the most common types of cancer and accounts for 30% of patients in radiation oncology clinics.[9] Therefore, prolonged treatment and planning periods become an important workload for clinics. In our study, the mean MU values for FIF, VMAT, IMRT, H-VMAT, and H-IMRT were found to be 235, 525, 933, 381, and 561, respectively. The FIF technique was found to be significantly superior to all other techniques except H-VMAT (p<0.001). Hybrid techniques were found to be statistically significantly effective in shortening the treatment time (p<0.001).

CONCLUSION

All the techniques evaluated in the study can be used safely for breast irradiation. The FIF technique provides significant advantages over IMRT and VMAT in terms of treatment time and low-dose volume. On the other hand, VMAT and IMRT techniques seem to be superior in providing homogeneous dose distribution and protecting neighboring critical organs. It is possible to obtain more balanced and optimal RT plans by combining hybrid techniques with FIF and VMAT-IMRT techniques. For the selection of the appropriate technique, it is necessary to decide on a patient-specific basis according to the patient's anatomical structure, breast volume, and clinical goals during planning. In situations requiring complex planning, hybrid techniques may be preferred to reduce the mean heart dose.

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