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## **Original Article**

# Intensity Modulated Radiation and Volumetric Modulated Arc Therapies in Breast Cancer

May Z. Saddik<sup>1,\*</sup> D, Fatiheea F. Hassan<sup>2</sup>

<sup>1</sup>PhD Student in Department of Basic Sciences, Biophysics Unit, College of Medicine, Hawler Medical University, Erbil, Kurdistan Region, Iraq

<sup>2</sup>Assistant Professor, Biophysics Unit, Department of Basic Science, College of Medicine, Hawler Medical University (HMU), Erbil, Kurdistan Region, Iraq

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## ABSTRACT

**Background:** Breast cancer is the most common malignant neoplasm in women, accounting for 25% of all cancers. Radiotherapy is one of the safest methods compared with other treatments.

**Methods**: In this study, 8 patients with left breast cancer underwent the radiation therapy. After simulating the tomographic data of breast cancer patients, treatment planning was performed in the treatment planning system, and then the clinical target volume and the planned target volume were determined.

**Results**: The mean CI (1.162  $\pm$  0.011) in Intensity Modulated Radiation Therapy (IMRT) was significantly lower than CI (1.173  $\pm$  0.28) in Volumetric Arc Radiation Therapy (VMAT) (P  $\leq$  0.02), indicates that IMRT technique had lower CI which means better dose conformity within the PTV. Also, the mean HI (0.696  $\pm$  0.333) in VMAT was significant compared to IMRT, the mean HI (0.558  $\pm$  0.288) (P  $\leq$  0.04), the results on better PTV dose distribution by using VMAT technique. Planning target volume (PTV) was consistent with indicators and PTV coverage value (97.563  $\pm$  1.471) in IMRT and (96.677  $\pm$  1.018) in VMAT, means that the PTV coverage was better by using IMRT technique rather than VMAT. The mean dose to left breast was (42.118  $\pm$  0464) prescribed dose. Ref. vol. CC, D2%, and D98% were received (736.898  $\pm$  235.140), (4618.931  $\pm$  107.658), and (3765.475  $\pm$  71.195), respectively.

**Conclusion**: IMRT method is one of the new cancer treatment techniques that in comparison with other methods by accurately targeting cancer cells and tumors, it has the least impact on healthy tissues and reduces the side effects as much as possible.

## GRAPHICALABSTRACT



\* Corresponding author: May Z. Saddik

☐ E-mail: Email: may.zeki7@gmail.com

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#### Introduction

Currently, cancer is the leading cause of death in economically developed and developed countries. Due to the aging population, the cancer incidence is increasing, so that it is estimated that 82% of the inhabitants of less developed countries have been diagnosed with cancer in recent years [1]. Breast cancer (BC) is the most common malignant neoplasm in women, accounting for 25% of all cancers diagnosed [2]. It is estimated that 1.67 million cases of breast cancer are diagnosed worldwide each year [1]. In 2018, there were approximately 261,620 cases of breast cancer and 40,920 deaths from breast cancer in the United States [3].

The disease is associated with symptoms such as pain, chest stiffness, decreased range of motion, heaviness, and decreased quality of life [4]. Approximately, 10 to 20% of breast cancers are due to the lack of expression of biomarkers such as human epidermal growth factor receptor 2 (HER2) [5]. Today, various methods of treatment are used, including hormone therapy, radiotherapy, chemotherapy, combinations, and mastectomy [6].

Radiation therapy (RT) is one of the safest methods with less side effects than other treatments used to treat breast cancer [7]. Studies have shown that radiotherapy after mastectomy (PMRT) reduces disease recurrence and mortality from breast cancer [8]. Clinically, in radiotherapy, the cellular response to radiation is affected by factors such as radiation dose, radiation sensitivity, tumor proliferation time, and hypoxia [9]. Therefore, selecting the total radiation dose, the number of rays and the total radiation time is necessary to improve the therapeutic outcome [10]. Increasing the radiation dose and reducing the toxic effects of radiation on the vital tissues and organs near cancerous tissue are the main goals of radiotherapy, which can be controlled due to the emergence of new technologies [11].

Today, two different methods are used for radiation therapy in patients with breast cancer, including Intensified Radiation Therapy (IMRT) and Volumetric Arc Radiotherapy (VMAT) [12]. IMRT optimizes non-uniform radiation beams so that the beams are accurately distributed and a

high dose of beams is focused on the cancerous area [13, 14]. Volumetric Modulated Arc Therapy (VMAT) has also been proposed by Otto et al. which is an emerging treatment model that treats cancerous tissue in a safe manner through shortterm dual-radiation distribution [15]. In VMAT type radiotherapy, the delivery time of the rays is faster and less monitor units are used and it has a higher dose distribution compared with IMRT [16]. IMRT also uses multiple beams with different angles that the intensity of each beam can be adjusted by using multi-leaf collimators (MLCs) to provide consistent doses [17]. In the IMRT method, the radiation dose compliance around the target tissue is improved by 3D-CRT, which minimizes the radiation toxicity to the tissues and organs around the cancerous tissue [18, 19]. VMAT has attracted the attention of therapists as a suitable treatment method due to its improved delivery efficiency compared with IMRT [17]. Although VMAT has been shown to perform better than IMRT, it has not been conclusively proven which method is preferable to the others [20, 21]. The aim of this study was to compare the two methods of IMRT and VMAT radiotherapy to determine which technique has highly conformal and better homogeneity of dose distributions, and thus potentially resulting in better target coverage and an improved cancer control by evaluating clinical and dosimetric outcomes for patients with left breast cancer.

## **Materials and Methods**

Study design

In this comparative study, 8 patients with the left breast cancer underwent the radiation therapy by using IMRT and VMAT techniques. This study performed by using Electa Synergy linac in 2022, which includes 3 photon energies (6, 10, and 18 MV) and 8 electron energies (4, 6, 8, 10, 12, 15, 18, and 22). The LINAC equipped with Multi-Leaf Collimator at Zhinawa Cancer Center. Patients with a mean age of 56 (range, 38-74) years old were selected for the study. All patients were staged according to the American Joint Committee on Cancer report in 2010, 6 of them were in stage III, and 2 patients were in stage II. Participants were immobilized by using chest board

immobilization in supine position with arms above head. The parameters were as follows: the range from 6 cm above the clavicle to 8 cm below the tissue and breast with 3 mm thick slices, intravenous contrast is not necessary and the whole lung must be included as well as the chest wall, supraclavicular, and the lymph nodes were contoured in the CT scan.

## Optima CT scanner

Optima CT 580 RT (general electric Healthcare - USA) 80 cm big bore CT-Scanner special for radiotherapy with flat RT couch. Optima 580 is a 16 slice scanner (it takes 16 slices in one gantry rotation) it can scan with (0.625, 1.25, 2.5, 5, and 10 mm) slice thickness and able to scan 4D-CT images, both helical and axial scan can be done with this scanner.

## Monaco planning system

Monaco is a treatment planning system (TPS) software for radiotherapy produced by Elekta. It has ability to calculate 3D, IMRT, VMAT, SRS, and Brachytherapy plans with a high accuracy by using Monte Carlo algorithm (the most accurate dose calculation available).

The Monaco TPS in (ZCC) is version 5.00.02, works on a network of three main high performance computers (Quad-core Intel xeon 2.93GHz processor, 24GB DDR3 RAM, 4TB Storage) and connected with the center's main network.

VMAT and IMRT plans were generated by using a 6 MV photon beam, with the clinical Monaco Version 5.11.01 TPS. For all patients included in this study, a VMAT plan by using two arcs was calculated through Monte Carlo algorithm.

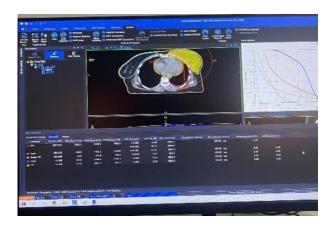


Figure 1: DVH of 211499 ID left breast case (IMRT)

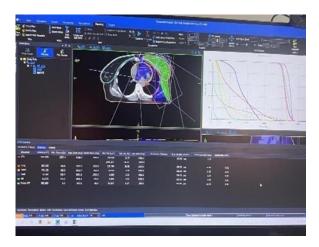


Figure 2: DVH of 211499 ID left breast case (VMAT)

IMRT and VMAT

IMRT radiotherapy is an advanced method used to treat tumors in three dimensions with several intensities of oscillating radiation. In this method, the maximum dose is irradiated to the tumor tissue and the minimum dose of unwanted radiation is applied to the healthy tissues.

In this technique, each fear is divided into smaller parts and the intensity of each proto changes. With the advancement of computer technology, software development for design and delivery in IMRT has been facilitated. Therefore, in addition to the constant dose radiation to tumors, the lower doses are injected to the healthy tissues and they are protected. This method, which is an advanced method of radiotherapy, uses an advanced technology to manipulate photons and protons based on the tumor shape, to treat malignant and benign tumors. In other words, it uses several small photons and protons of different intensities to accurately irradiate the tumor. Therefore, the purpose of using this method is to achieve the desired dose along with maintaining healthy tissue and limiting the side effects of treatment. This method has also the ability to produce nonuniform doses that simultaneously deliver different doses to separate areas in the target tissue volume in each fraction. IMRT is delivered to the target tissue based on "reverse treatment design" and non-uniform irradiation to optimize dose distribution. Several fixed beams that increase treatment delivery time, patient comfort, reproducibility of the treatment position, and movement between wards are required for an IMRT design. With increasing treatment time, there is a concern that complications such as increased repair and the number of malignant cells and radiobiological consequences may occur. VAMT radiotherapy is a type of IMRT which usually involves a beam and sometimes more that focuses the radiation on the cancer cells and reduces the irradiation time. In this method, the device moves in a circle around the patient's axis. This can reduce the risk of side effects by reducing the amount of radiation to the surrounding organs.

#### Intervention

In this study, 5 fields IMRT treatment planning and double arc VMAT treatment planning were used. At the beginning, after simulating the tomographic data of breast cancer patients, treatment planning was performed in the treatment planning system (TPS). TPS is planning software for radiotherapy and treatment of cancer patients, produced by Elekta, and has the ability to calculate threedimensional designs, IMRT, and VMAT. Then, the clinical target volume (CTV) was determined by using the studied tissues and also the planned target volume (PTV). The VMAT and IMRT designs were generated by using the clinical version of Monaco version 5.11.01 TPS. IMRT beams with 7 fields in 7 different angles and VMAT beams were generated as one arc in a clockwise direction and another arc in a counter-clockwise direction. treatment programs Monte algorithms were performed and dosimetric analysis (minimum dose, maximum dose, mean dose, and PTV coverage were calculated by using dose volume histogram (DVH), while conformity index (CI) was evaluated by using the following formula:

$$CI = \frac{volume \ covered \ by \ 95\% \ of \ prescribed \ dose}{volume \ of \ PTV}$$

The D2% represents the maximum dose that will be delivered to 2% of the PTV and D98% is the minimum dose calculated for the 98% of the PTV. Dose homogeneity index (HI) was calculated based on the formula presented in the report of the 83<sup>rd</sup> International Association of Radiation Units (ICRU) for the target tissue according to the following equation:

The values of D2% and D98% for PTVs were obtained from DVH. The D2% represents the maximum dose that will be delivered to 2% of the PTV, Dp is the prescribed dose for PTV, and D98% is the minimum dose calculated for the 98% of the PTV.

## **Data analysis**

All the parameters were calculated from the DVHs. The statistical analyses were carried out by using IBM SPSS Statistics version 23 (SPSS Inc. Armonk, NY.USA). An (independent student t-test) was

performed to analyze the difference between three techniques, and p-value < 0.05 was considered to reveal statistical significance.

#### **Results and Discussion**

In this study, all dosimetric targets of PTV coverage were obtained with both techniques (IMRT and VMAT). Eight patients with the left breast cancer underwent the radiation therapy by using IMRT and VMAT techniques (Figure 1 and 2). Each of the IMRT and VMAT was used for each patient or 16 plans for all patients.

Table 1 summarized the PTV coverage results including Volume CC, Mean dose Gy, Ref. Volume percent, Ref. dose Gy, Ref. volume CC, HI (Homogeneity index), CI (Conformity index), Maximum dose (D2%), and Minimum dose (D98%).

The results demonstrated that the mean CI (1.162  $\pm$  0.011) in IMRT was significantly lower than HI (1.173  $\pm$  0.28) in VMAT (P  $\leq$  0.02), which indicates that IMRT technique is better than VMAT. Likewise, the mean HI (0.696  $\pm$  0.333) in VMAT was significant compared with the mean HI (0.558  $\pm$  0.288) (P $\leq$ 0.04) and investigation of conformity index (CI) and homogeneity index (HI) indices in both techniques showed that IMRT indices relatively improved compared with VMAT in left breast cancer.

Planning target volume (PTV) was consistent with indicators and covered PTV value (97.563 ±

1.471) in IMRT and (96.677  $\pm$  1.018) in VMAT, means that IMRT had a better PTV coverage. Mean dose to left breast was (42.118  $\pm$  0464) prescribed dose. Ref vol CC, D2% and D98% was (736.898  $\pm$  235.140), (4618.931  $\pm$  107.658), and (3765.475  $\pm$  71.195) which received, respectively.

The results showed that there was no significant difference in the mean maximum dose (D2%) between the two diagnostic methods IMRT and VMAT. However, there is a significant difference (P  $\leq$  0.03) between the mean minimum (D98%) IMRT (379.675  $\pm$  72.943) and the mean VMAT (373.275  $\pm$  57.585) which illustrate the mean minimum IMRT is lower.

Dose-volume histograms of all patients by using IMRT and VMAT are depicted in Figure 3. The results revealed that there were better HI and CI by using IMRT technique.

In this study, two methods of IMRT and VMAT were compared to find out which diagnostic method has a higher conformity index (CI), or homogeneity index (HI), as well as the investigation of conformity index (CI) and homogeneity index (HI) indices in both techniques showed that IMRT indices relatively improved compared with VMAT in the left breast cancer. Finally, it is expected that the betterment of these indicators by clinical evaluation and dosimetry of patients with the left breast cancer will lead to better therapeutic coverage and cancer control.

**Table 1:** Comparisons of the PTV dosimetric parameters between IMRT and VMAT techniques for breast cancer patient

PTV	Mean ± SD		P (independent student
	IMRT	VMAT	t-test)
Volume CC	757.453 (244.613)	757.453 (244.613)	1
Mean dose Gy	42.097 (0.525)	42.14 (0.325)	0.431
Ref. volume %	97.563 (1.471)	96.677 (1.018)	0.142
Ref. dose	3808	3808	1
Ref. volume CC	740.681 (245.181)	733.116 (241.525)	0.721
HI	1.162 (0.011)	1.173 (0.28)	0.02
CI	0.696 (0.333)	0.558 (0.288)	0.04
Maximum dose (D2%)	4610.637 (115.34)	4627.225 (106.656)	0.321
Minimum dose (D98%)	3796.675 (72.943)	3734.275 (57.585)	0.03

CI: Conformity index, HI: Homogeneity index, PTV: Planning target volume, VMAT: Volumetric modulated arc therapy, IMRT: Intensity modulated radiotherapy, and SD: Standard deviation

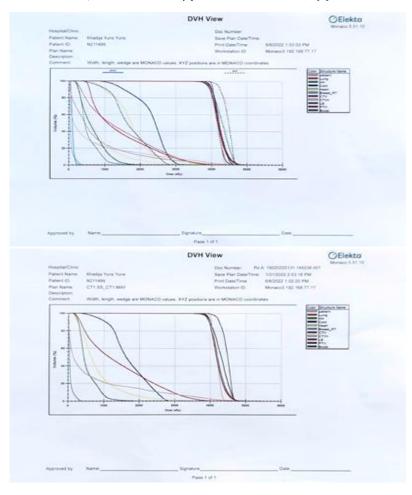


Figure 3: Dose-volume histograms of the planning target volume (breast) in two treatment planning techniques

In radiotherapy, the goal is to deliver a sufficient dose to the tumor and the minimum possible dose to the nearby organs. Radiation therapy, along with the other treatments, can be a useful and effective adjunctive therapy [22]. Various studies have examined the effectiveness of various radiotherapy methods and have presented the positive results of this treatment method. IMRT and VMAT radiation therapy is one of the new methods of treating various types of cancers, which in most cases can prevent the growth of cancer cells. Also, the incidence of side effects is minimized [23].

The results showed that the PTV coverage, conformity index (CI) and homogeneity index (HI) were better in IMRT compared with VMAT which results in better cancer control. These results are consistent with the study of Yazdani *et al.* (2018) which showed that the IMRT compared with VMAT better cancer control [24]. In a study by Muhammad Isa Khan *et al.* (2016), there was no significant difference in IMRT compared with

VMAT to cancer control [25], the results of which are not consistent with the present study. In the study of Rui Wang *et al.* (2022) with the title of dosimetry comparison between IMRT and VMAT in patients with the left breast cancer with modified radical mastectomy, [26]. Planning target volume (PTV) was consistent with indicators and covered, these results are consistent with the study.

The PTV coverage showed the minimum dose (D98%) in different studies. Different results have been obtained according to the working method and the examined organ. In NA Iacovelli *et al.* (2020) study, as the role of IMRT and VMAT parameters in the 5-year survival rate of cancer patients [27], the minimum dose showed a significant difference between IMRT and VMAT and improved the treatment methods in IMRT compared with VMAT revealed that these results are consistent with the present study. In the by study conducted by C Ostheimer *et al.* (2016) [28], no difference in terms of IMRT and VMAT was

observed in the treatment process, which does not agree with the present study, which indicated a significant difference.

Radiotherapy, including IMRT, damages DNA and stops cancer cells from dividing and growing, thus slowing or stopping tumor growth. In many cases, radiotherapy is able to kill all the cancer cells, thereby shrinking or destroying the tumors [29]. Intensity Modulated Radiotherapy (IMRT) is an advanced, high-precision radiotherapy technique that uses computer-controlled linear accelerators to deliver accurate doses of radiation to a malignant tumor or specific areas within the tumor. IMRT allows the radiation dose to be more accurately matched to the three-dimensional shape of the tumor by modulating or controlling the radiation intensity in several small volumes. IMRT also allows the higher doses of radiation to be concentrated on the tumor, while minimizing radiation to surrounding important natural structures [30, 31].

Due to the dose reduction of natural tissues with the IMRT approach, compared with the usual methods of radiotherapy, higher and more effective doses with fewer side effects reach the tumor. In addition, IMRT has the potential to reduce the treatment toxicity even if no dose is increased. Because of the complexity, IMRT requires slightly longer daily treatments, additional programs, and safety tests before starting treatment than with the conventional radiotherapy [32, 33].

The high incidence and long-term survival rate of breast cancer in women, the impact of radiotherapy exposure on the subsequent risk of heart disease and the development of the second primary breast cancer, make it an important issue. Both risks are dose-dependent. Finally, it has been shown that due to the positive effects of IMRT method in reducing the received dose, it can be concluded that it can be used as a suitable treatment method [34].

## Conclusion

The IMRT method is one of the new cancer treatment techniques that, compared with other methods, with the aim of accurately targeting cancer cells and tumors, has the least effect on healthy tissues and reduces side effects as much as possible. Patients can benefit from the new treatment method and follow the cancer treatment process as easily as possible.

#### Limitations

Due to the studied small number of people, while more patients are examined in future through the cohort studies, more attention should be paid to the therapeutic effects and benefits of new treatment methods.

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#### **Authors' contributions**

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

## **Conflict of Interest**

We have no conflicts of interest to disclose.

#### Orcid

May Z. Saddik https://orcid.org/0000-0001-6888-949X

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