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Evaluating Radiation Treatment Modalities for Breast Cancer: A Comparative Dosimetric Analysis of VMAT and 3DCRT under Free-Breathing Conditions"

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Abstract: - This research aims to assess how well Volumetric Modulated Arc Therapy (VMAT), a modern type of external radiation therapy, works in targeting breast cancer while protecting nearby organs from radiation, compared to the traditional Three-Dimensional Conformal Radiotherapy (3DCRT). The study involves breast cancer patients who are treated while breathing normally. A total of 34 patients, all given a standard dose of 40.05 Gy, participated in the study. Half of these patients received treatment planning with 3DCRT, while the other half received VMAT planning.

Keywords: Breast cancer; Hypofractionation; Volumetric modulated arc therapy; 3D conformal radiotherapy; Free-Breathing.

INTRODUCTION:

Breast cancer is a major global health issue, making up a large portion of cancer diagnoses in women. Recent data shows it is the most common cancer among women worldwide, with around 2.3 million new cases diagnosed in 2020 (Bray et al., 2020) [1]. Both developed and developing countries are seeing a rise in breast cancer cases, highlighting the urgent need for effective treatments (Ferlay et al., 2021) [2].

Two key treatments for breast cancer are external beam radiation therapy (EBRT) and surgery. A meta-analysis by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) shows that combining surgery with radiation therapy leads to better outcomes in terms of local control and overall survival (EBCTCG, 2014) [3]. Radiotherapy for breast cancer has evolved significantly to improve precision and protect nearby organs. Traditional methods like two-dimensional (2D) and three-dimensional conformal radiotherapy (3DCRT) have progressed to advanced techniques like intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT). IMRT, for example, precisely targets the tumor while sparing healthy tissue (Jagsi et al., 2018) [4].

The optimal radiotherapy dose for breast cancer has been widely studied. Traditionally, a normofractionation regimen of 50 Gy in 25 sessions is used [5]. However, recent trials have shown that shorter hypofractionated schedules are just as effective and more convenient (Bartelink et al., 2018) [6]. Since breast cancer has low sensitivity to radiation (α/β between 3Gy and 4Gy) [7], several moderate hypofractionated protocols have been developed, including 40.05Gy in 15 sessions [8,9,10]. This approach has become standard in breast cancer radiotherapy, making advanced techniques like VMAT more relevant. VMAT can deliver precise doses to the target area while protecting healthy tissues [11, 12].

This article aims to explore the dosimetric benefits of using VMAT, a modern radiotherapy method, for treating breast cancer compared to the traditional 3DCRT.

METHODS AND MATERIALS:

The study investigates the efficacy of Volumetric Modulated Arc Therapy in the context of breast cancer dosimetry, specifically focusing on safeguarding Organs at Risk while ensuring optimal Planning Target Volume

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coverage under free breathing conditions. A comparative analysis is conducted against the conventional Three-Dimensional Conformal Radiotherapy technique.

A cohort of 34 patients was selected for this study. All participants received a uniform prescribed dose of 40.05 Gy, and the treatment plans were devised utilizing the Monaco 5.1 Treatment Planning System. The cohort was divided into two equal groups, with half of the patients undergoing treatment planning via 3DCRT, while the remaining subjects were planned using VMAT.

In the context of 3DCRT, the technique predominantly relies on employing two or more tangential photon beams with varying energies (typically a mix of 6MV and 18MV). These tangential beams are utilized through direct planning methods. Conversely, VMAT, being a dynamic radiation delivery technique, employs arcs with varied angles customized to the specific target volumes, distinguishing between left and right breast targets (***Figure 1.a***). VMAT's planning process utilizes indirect optimization methods and typically involves employing a finer calculation grid size, often set at 0.3 cm, to enhance precision and dosage distribution within the breast tissue.

Notably, in VMAT calculations for breast cancer treatment, various properties are considered to optimize dosimetry. These properties encompass employing non-uniform beamlet intensities, adjusting multileaf collimator (MLC) positions dynamically during beam delivery, and incorporating modulation of dose rate and gantry speed throughout the arc rotation. Additionally, VMAT optimization algorithms prioritize achieving enhanced dose conformity to the PTV while concurrently limiting radiation exposure to surrounding healthy tissues and OARs, thereby aiming for improved treatment outcomes.

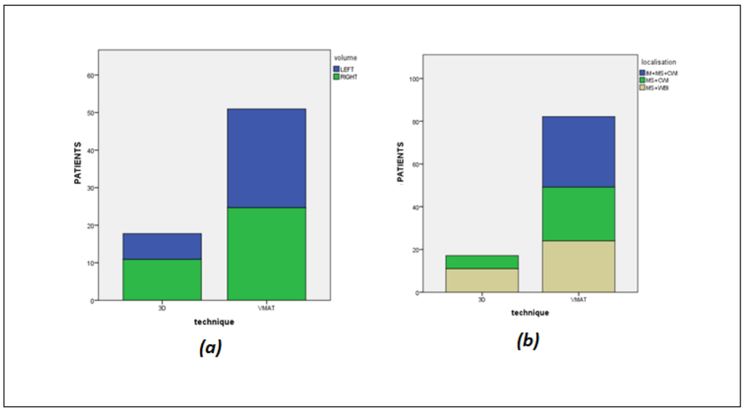

Figure 1: - (a) Patient groups based on breast cancer position (left or right)

-(b) Patient groups based on the cancer volume

For making this study, more inclusive, different target volumes were included (***Figure 1.b***). There were patients with breast plus medial supraclavicular region and axillary apex (MS + WBI) [13], others with the chest-wall plus medial supraclavicular region and axillary apex (MS +CWI) [13], also patients with chest-wall plus medial supraclavicular region and axillary apex plus the internal mammary chain (IM + MS + WBI/CWI) [13].

To reduce the uncertainties related to the contouring in the distribution statistical analysis, an optimal volume was created in both techniques, which includes all targeted volumes (CW/MS/IM).

In this study, a breast board was utilized to ensure patient immobilization during CT scan acquisition, since these treatment plans discussed were used for clinical application.

For PTV distribution and OAR criteria evaluation, the protocol below was considered:

Table 1: a- OAR constraints:

OAR	HEART	IPSILATERAL LUNG	CONTROLATERAL LUNG
	Mean dose < 5 Gy [14]	V17Gy < 35% Mean dose <16 Gy [15]	Mean dose < 4 Gy [15]

b- PTV distribution constraints:

PTV Coverage [16]	D2% < 107% *	D98% > 90%	D95% > 95%	D50% = 100%	Homogeneity Index (HI)** : ($HI = D_{2\%} - D_{98\%}/D_{50}\%$)

- ** Dx% < y% refers to the dose received by a certain percentage (x%) of a specified volume; the dose must be less than a specified percentage of the prescribed dose (y%).*
- *** Homogeneity Index (HI): The ratio of the maximum dose to the prescription dose within the PTV.*

All the statistical measurements mentioned in this article were obtained using Statistical Package for the Social Sciences (SPSS) software version 21.

RESULTS AND DISCUSSION:

To compare the efficacy of VMAT and 3DCRT radiation techniques in ensuring good coverage while minimizing the dose delivered to adjacent organs, a statistical analysis was conducted using SPSS software, represented by the p-value.

Table 2: Statistical analysis:

	Technique	N	Mean	Std. Deviation	P value
$PTV_{2\%}$	3D	17	107.7	1.48	T test (p>0.05)
	VMAT	17	112.4	13.63	
$PTV_{50\%}$	3D	17	100.9	1.69	T test (p>0.05)
	VMAT	17	104.1	9.70	
$PTV_{95\%}$	3D	17	82.2	14.09	T test (p<0.05)
	VMAT	17	90.9	8.48	
$PTV_{98\%}$	3D	17	68.1	21.93	T test (p<0.05)
	VMAT	17	85.6	9.86	
HI	3D	17	.4	.22	T test (p<0.05)
	VMAT	17	.3	.14	

Table 3: Statistical analysis:

	Technique	N	Mean / Median	Std. Deviation	P value
Contralateral lung : mean dose	3D	17	.5	.081	T test (p<0.05)
	VMAT	17	4.5	1.11	
heart	3D	17	1.007 [0.623-3.857]		Mann Whitney test (p<0.05)
	VMAT	17	5.154 [2.458-6.766]		

Ipsilateral lung : 17GY	3D	17	26.7	4.29	T test (p<0.05)
	VMAT	17	30.9	6.82	
Ipsilateral lung : mean dose	3D	17	10.9	1.52	T test (p<0.05)
	VMAT	17	13.5	2.31	

Based on the results from ***Table [2]***, both 3DCRT and VMAT effectively deliver 100% of the prescribed dose to ***50%*** of the Planning Target Volume (PTV). However, VMAT is better than 3DCRT in covering the ***95%*** and ***98%*** isodose lines within the PTV, with statistical significance (***p<0.05***). This means VMAT ensures a larger portion of the target volume receives the intended therapeutic dose. VMAT also has better dose uniformity, as shown by a superior Homogeneity Index (HI). While this improved HI might lead to a slight increase of up to ***2%*** in the maximum dose to the PTV, it should not exceed ***110%*** of the prescribed dose, as stated in reference [17].

The data from ***Table [2]*** strongly suggests that VMAT can improve tumor control through its ability for intensity modulation [18], leading to a more even dose distribution within the PTV. The better HI achieved with VMAT highlights its effectiveness in ensuring the therapeutic dose is well distributed within the target volume [19]. However, this should be considered alongside the slight increase in the maximum dose represented by ***D2%*** [20].

The dosimetric analysis in ***Table [3]*** shows significant differences in OAR doses between VMAT and 3DCRT. Specifically, VMAT results in a higher mean dose to the heart compared to 3DCRT (see ***Figure 2.a***). This is because VMAT plans are more complex, making it harder to protect the heart from radiation, as shown by statistically significant results (***p<0.05***) (***Figure 2.b***) [21]. The same trend is seen in the mean dose to the contralateral lung, where VMAT produces higher doses than 3DCRT, which provides better shielding (***p<0.05***).

Additionally, the dosimetric findings highlight a significant advantage of 3DCRT in reducing ipsilateral lung toxicity (***p<0.05***). This indicates that the conformal nature of 3D planning is more effective in protecting the lung on the same side as the tumor from excessive radiation exposure.

In summary, these findings emphasize the benefits of VMAT in terms of target coverage and dose uniformity. VMAT's ability for intensity modulation provides a better dose distribution within the PTV, which can improve tumor control. However, it is crucial to monitor and manage the slightly higher maximum dose delivered by VMAT. The study also points out the challenge of protecting critical organs, such as the heart and contralateral lung, when using VMAT. This underscores the need to balance the benefits and risks of this advanced radiotherapy technique in clinical practice.

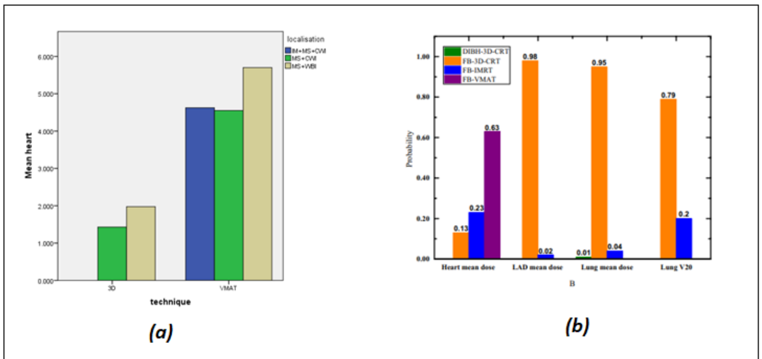

Figure 2: - (a) the variation of the heart mean dose in function of the technique used and breat cancer volume.

- (b) the variation of the heart mean dose in function of the technique used based on Lu Y study [21].

The higher mean dose to the heart seen with Volumetric Modulated Arc Therapy (VMAT) is due to the dynamic and modulated nature of VMAT plans. VMAT uses dynamic arcs and intensity modulation to shape the radiation dose, which requires more complexity compared to the fixed beam arrangements of 3D Conformal Radiotherapy (3DCRT) [22]. Balancing adequate target coverage with minimal heart exposure is challenging in VMAT. This difficulty is highlighted by the study "The new fractionations in breast cancer: a dosimetric study of 3D-CRT versus VMAT" [23], which showed the potential for cardiac toxicity with VMAT. This emphasizes the need for careful planning when using VMAT to treat breast cancer, given the importance of heart health for long-term outcomes.

The increased mean dose to the contralateral lung in VMAT is due to its rotational arc nature. VMAT uses continuous arcs that rotate around the patient, leading to a broader distribution of radiation to the contralateral lung [24]. In contrast, 3D conformal planning allows for more controlled shielding of the contralateral lung, reducing radiation exposure. This highlights a disadvantage of VMAT, as its rotational arc design can increase the risk of radiation-induced lung injury, especially in the contralateral lung.

While VMAT offers advantages in conformal planning and target coverage, its spatial complexity may compromise the sparing of normal tissues, especially the heart and contralateral lung. In contrast, 3D conformal planning, with its simpler and more controlled approach, provides better lung-sparing and a lower risk of ipsilateral lung toxicity compared to VMAT.

Radiotherapy is crucial in the post-operative management of breast cancer, aiming to minimize locoregional recurrence while preserving heart and lung function [25]. The choice between VMAT and 3DCRT should be made carefully, balancing optimal target coverage with the potential exposure of normal tissues. This decision is essential to ensure the best outcomes for breast cancer patients, considering both the therapeutic benefits and potential side effects of each radiotherapy technique.

Despite VMAT's benefits in conformal planning and target coverage, its complexity can compromise the sparing of normal tissues, particularly in the heart and contralateral lung. In contrast, 3D conformal planning offers better lung-sparing and a lower risk of ipsilateral lung toxicity due to its simpler, more controlled approach.

Breast cancer radiotherapy is vital in post-operative care, aiming to reduce locoregional recurrence while preserving cardiac and pulmonary function [25]. Choosing between VMAT and 3DCRT requires careful consideration of the balance between optimal target coverage and potential normal tissue exposure, ensuring the best possible outcome for breast cancer patients with attention to both therapeutic benefits and potential side effects.

CONCLUSION*:*

Volumetric Modulated Arc Therapy (VMAT) has become a valuable tool in modern radiation oncology, offering excellent Planning Target Volume (PTV) coverage and improved dose uniformity [26]. Recent studies show that VMAT delivers highly conformal radiation doses to tumors using dynamic arc therapy [26]. These studies highlight VMAT's ability to reduce dose variations, often measured by the Homogeneity Index (HI). This ensures precise and uniform coverage of the target volume, giving VMAT a significant advantage over 3D Conformal Radiotherapy (3DCRT) ($p<0.05$). VMAT also provides excellent PTV control, which is crucial for effective cancer treatment.

However, despite VMAT's strong dosimetric capabilities, 3DCRT remains a reliable treatment option known for its low risk of radiation-induced toxicity. Choosing between VMAT and 3DCRT requires a careful evaluation that balances optimal target coverage with minimizing potential side effects. Additionally, achieving the best therapeutic outcomes often involves using complementary techniques like deep breath-holding maneuvers [27]. This balanced approach underscores the importance of personalized treatment planning and shared decision-making in clinical practice.

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