Radiotherapy for Breast Cancer: Analysis of the Hybrid Volumetric Arc Therapy Technique

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Radioterapia para Câncer de Mama: Análise da Técnica de Arcoterapia Volumétrica Híbrida

Radioterapia del Cáncer de Mama: Análisis de la Técnica de Arcoterapia Volumétrica Híbrida

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ABSTRACT

Introduction: Radiotherapy is one of the treatment strategies for breast cancer. With advances in radiotherapy treatment modalities, such as intensity modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT), it has become possible to deliver radiation doses while reducing treatment margins and improving radiation conformation to the target volume. **Objective:** To quantitatively analyze a hybrid radiotherapy technique for breast cancer treatment that combines VMAT technology with conventional 3D-CRT, called hybrid volumetric arc therapy (H-VMAT). **Method:** CT images of an anthropomorphic simulator object were acquired to develop the plan. Five hybrid treatment plans were developed: H-VMAT 90% 3D-CRT and 10% VMAT, H-VMAT 80% 3D-CRT and 20% VMAT, H-VMAT 70% 3D-CRT and 30% VMAT, H-VMAT 60% 3D-CRT and 40% VMAT, H-VMAT 50% 3D-CRT and 50% VMAT. **Results:** The hybrid plan with the best dosimetric results was H-VMAT 80% 3D-CRT and 20% VMAT, with excellent coverage of the target volume and doses to organs at risk within the limits, especially the contralateral breast. **Conclusion:** Hybrid techniques can be used to meet the target volume dose conformity and homogeneity indexes established by international protocols, and reduce the dose to organs at risk at the same time.

Key words: Radiotherapy, Conformal; Radiotherapy, Intensity-Modulated; Breast Neoplasms/radiotherapy.

RESUMO

Introdução: A radioterapia é uma das estratégias de tratamento para a neoplasia de mama. Com o avanço das modalidades de tratamentos na radioterapia, como a radioterapia de intensidade modulada (IMRT) e a arcoterapia volumétrica modulada (VMAT), tornou-se possível entregar doses de radiação diminuindo as margens de tratamento e melhorando a conformação da radiação ao volume-alvo. **Objetivo:** Analisar quantitativamente uma técnica híbrida de radioterapia para tratamento de câncer de mama que combina a tecnologia da VMAT com a modalidade convencional de radioterapia conformacional tridimensional (3D-CRT), sendo denominada arcoterapia volumétrica híbrida (H-VMAT). **Método:** Para elaboração do plano, adquiriram-se imagens tomográficas de um objeto simulador antropomórfico. Foram elaborados cinco planos híbridos de tratamento: H-VMAT 90% 3D-CRT e 10% VMAT; H-VMAT 80% 3D-CRT e 20% VMAT; H-VMAT 70% 3D-CRT e 30% VMAT; H-VMAT 60% 3D-CRT e 40% VMAT; e H-VMAT 50% 3D-CRT e 50% VMAT. **Resultados:** O plano híbrido com melhores resultados dosimétricos foi o H-VMAT 80% 3D-CRT e 20% VMAT por apresentar uma excelente cobertura do volume-alvo e doses nos órgãos de risco dentro dos limites, com destaque para a mama contralateral. **Conclusão:** As técnicas híbridas podem ser utilizadas para atender aos índices de conformidade e homogeneidade da dose no volume-alvo estabelecidos pelos protocolos internacionais e, ao mesmo tempo, para que haja redução de dose nos órgãos de risco.

Palavras-chave: Radioterapia Conformacional; Radioterapia de Intensidade Modulada; Neoplasias da Mama/radioterapia.

RESUMEN

Introducción: La radioterapia es una de las estrategias de tratamiento del cáncer de mama. Con los avances en las modalidades de tratamiento radioterápico, como la radioterapia de intensidad modulada (IMRT) y la terapia de arco volumétrico modulado (VMAT), se ha hecho posible administrar dosis de radiación al tiempo que se reducen los márgenes de tratamiento y se mejora la conformación de la radiación en el volumen objetivo. **Objetivo:** Analizar cuantitativamente una técnica de radioterapia híbrida para el tratamiento del cáncer de mama que combina la tecnología VMAT con la 3D-CRT convencional, denominada terapia de arco volumétrico híbrida (H-VMAT). **Método:** Se adquirieron imágenes de TC de un maniquí antropomórfico para elaborar el plan. Se elaboraron cinco planes de tratamiento híbridos: H-VMAT 90% 3D-CRT y 10% VMAT, H-VMAT 80% 3D-CRT y 20% VMAT, H-VMAT 70% 3D-CRT y 30% VMAT, H-VMAT 60% 3D-CRT y 40% VMAT, H-VMAT 50% 3D-CRT y 50% VMAT. **Resultados:** El plan híbrido con mejores resultados dosimétricos fue H-VMAT 80% 3D-CRT y 20% VMAT, con excelente cobertura del volumen objetivo y dosis a los órganos de riesgo dentro de los límites, especialmente la mama contralateral. **Conclusión:** Las técnicas híbridas pueden utilizarse para cumplir con los índices de conformidad y homogeneidad de la dosis en el volumen objetivo establecidos por los protocolos internacionales, reduciendo al mismo tiempo la dosis en los órganos de riesgo.

Palabras clave: Radioterapia Conformacional; Radioterapia de Intensidad Modulada; Neoplasias de la Mama/radioterapia.

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INTRODUCTION

According to the National Cancer Institute (INCA), breast cancer is among the highest incidences of cancers around the world and is the main cause of death among women. About 2.3 million new cases of breast cancer are estimated, adding up to 11.7% of global cases. In Brazil, 73,610 new breast cancer cases are expected for each year of the 2023-2025 period[1]. Radiotherapy is one of the treatment strategies for breast neoplasm. It can be applied to the whole breast or to a part of it (after lumpectomy), to the chest wall (after mastectomy) and to regional lymph nodes[2]. The definition of the radiotherapeutic plan varies according to the patient's anatomy and the laterality of the disease[3], and each dosage technique available demands specific tailoring.

METHOD

Analytical exploratory study with a quantitative approach. To simulate treatment plans regarding hybrid volumetric arc therapy (H-VMAT) techniques, tomographic images were taken from an anthropomorphic phantom (provided by the radiotherapy sector) with an elliptical shape to simulate the anatomy of a human torso of medium height, that is, the structure of the work was developed in such a way that there was no need for analysis by the Research Ethics Committee (CEP), in accordance with Resolution No. 510/2016[4] of the National Health Council (CNS).

Tomographic images were produced in axial cuts with a spacing of 1.25 mm (GE multislice hi-speed device with 64 channels). The DICOM images were inserted in the Eclipse[5] planning system (Varian™ v.15.6, calculated with the analytical anisotropic algorithm – AAA).

Next, the delineations of the organs at risk (OAR) and the planning target volume (PTV) were carried out, according to the recommendations of the anatomy atlas of the Radiation Therapy Oncology Group (RTOG)[6].

Both the clinical target volume (CTV), which encompasses the breast tissue and the chest wall, and the PTV were represented by the left breast in this work. To facilitate the breast outlining and gantry angulations, a medial line was outlined in the sternal region. The following OAR were outlined: ipsilateral lung, contralateral lung, spinal cord, contralateral breast, esophagus, ribs, and cardiac area.

Finally, the determined prescription dose was conventional fractionation regimen of 45 Gy in 25 fractions of 1.8 Gy/day. For volumetric modulated arc therapy (VMAT) plans, an auxiliary delimiting structure was designed for the gantry variations called "ring" (in green) with the purpose of reducing doses in the ipsilateral lung. The plans were calculated for the treatment in the TrueBeam® Stx HD linear accelerator (2.5 mm blades in the isocenter region), with energy of 6MV, dose rate of 600 MU/min.

For the hybrid study proposed for breast treatment, five treatment plans with the following proportions for each technique were evaluated: H-VMAT$_{90/10}$ (90% three-dimensional conformal radiotherapy – 3D-CRT and 10% VMAT), H-VMAT$_{80/20}$ (80% 3D-CRT and 20% VMAT), H-VMAT$_{70/30}$ (70% 3D-CRT and 30% VMAT), H-VMAT$_{60/40}$ (60% 3D-CRT and 40% VMAT), H-VMAT$_{50/50}$ (50% 3D-CRT and 50% VMAT). The best obtained plans were compared in isolation with the 3D-CRT and VMAT techniques. All the plans with VMAT technique were performed with four semi-arcs, configured with the following angulations: 1st arc with clockwise angles from 306° to 45°, 2nd arc with clockwise angles from 45° to 150°, 3rd arc with counterclockwise angles from 150° to 45° and the 4th arc with anticlockwise angulation from 45° to 306°, isocenter positioned between the costal arches, using blocked arches in order to remove the divergence of the radiation beam in the volume of the ipsilateral lung. In all plans with the 3D-CRT technique, compensating filters, parallel and opposing fields with angulations of 306° and 133° were used.

To determine the gantry angulation, the techniques were based on the anatomy of the phantom, mainly assessing the input and output angles in the target breast and its contributions to the ipsilateral lung, contralateral breast, and cardiac area. It is worth noting that the field-in-field technique was not used in the 3D-CRT plan with the objective of maintaining coherence in the use of filters for modulating the hybrid technique.

RESULTS

For the technique combinations proposed in this study, the contribution of the prescribed dose for each technique is presented in Table 1.

In Figure 1, it is possible to observe the distributions and dose conformations in the hybrid plans, that is, the respective partial percentages regarding the 3D-CRT and VMAT plans in each planning, originating the so-called hybrid plan (H-VMAT). By analyzing the plans, it is possible to observe that, in the first one, 90% of the plan used the 3D-CRT plan and 10% of the VMAT plan, in the second one, the percentage was 80% 3D-CRT and 20% VMAT, in the third one, 70% was 3D-CRT and 30% VMAT, in the fourth one, the percentage was 60% 3D-CRT and 40% VMAT, and finally, the fifth plan had a proportion of 50% VMAT and 50% 3D-CRT technique.

Table 1. Proportions of H-VMAT plans along with prescribed doses

Plan proportions	Prescribed dose (cGy)	Technique
$H\text{-}VMAT_{90/10}$	162	3D-CRT
	18	VMAT
$H\text{-}VMAT_{80/20}$	144	3D-CRT
	36	VMAT
$H\text{-}VMAT_{70/30}$	126	3D-CRT
	54	VMAT
$H\text{-}VMAT_{60/40}$	108	3D-CRT
	72	VMAT
$H\text{-}VMAT_{50/50}$	90	3D-CRT
	90	VMAT

Captions: H-VMAT = hybrid volumetric arc therapy; 3D-CRT = three-dimensional conformal radiotherapy; VMAT = volumetric modulated arc therapy.

Among the plans quality assessment criteria are the homogeneity index (HI) of dose distributions, which is recommended to be close to zero[7], and the conformity index (CI) of dose distributions, which should be between 0.95 and 2.0[8,9]. Table 2 shows the HI and CI values obtained. HI values presented a 5% to 6% variation in the target volume, which suggests an acceptable correlation of uniformity[14]. The CI values obtained presented a variation between 1.117 and 1.235, which qualifies all the plans as acceptable according to the ICRU83[7].

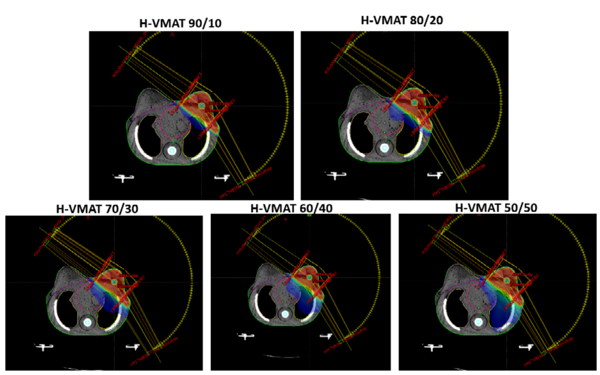

Figure 1. Demonstration of dose distribution in the hybrid plans proportions

Caption: H-VMAT = hybrid volumetric arc therapy.

Based on these findings, it is possible to conclude that hybrid H-VMAT plans presented better results than the isolated techniques such as VMAT, particularly regarding the dose in the OAR. As the VMAT technique percentage increases up to 50%, no significant changes in $D_{95\%}$ and D_{mean} on the target volume[10,11] are observed.

The dosimetric assessment of the treatment plan contains a quantitative analysis of the OAR. The description of dose restrictions among the H-VMAT plan variations is demonstrated in Table 3. The hybrid plans that showed better dose restrictions in the OAR were $H\text{-}VMAT_{90/10}$, followed by the $H\text{-}VMAT_{80/20}$ plan. These plans offer benefits particularly to the contralateral breast, with mean dose lower than 4 Gy, ensuring satisfactory coverage of the target volume, considering $D_{95\%}$ of 46.9 Gy for $H\text{-}VMAT_{90/10}$ and 46.3 Gy for $H\text{-}VMAT_{80/20}$.

Considering the restrictions regarding the ipsilateral lung, the plan showed a contribution in the ipsilateral lung volume of 14.24% above tolerable levels, that is, V_{5Gy} with 57.12%, not in compliance with the RTOG[6,10] recommendation that determines V_{5Gy} in up to 50% of the ipsilateral lung's volume. For the other proportions of the H-VMAT plans, success was achieved in the restrictions pertinent to the preservation of the OAR. Within the acceptable plans regarding OAR, the value of V_{5Gy} for the ipsilateral lung varied from 11.57% ($H\text{-}VMAT_{90/10}$) to 45% ($H\text{-}VMAT_{60/40}$), suggesting that the increase in the VMAT technique contribution to the H-VMAT plan is directly related to the increase in low doses in the ipsilateral lung.

Regarding the dose in the cardiac area, the technique that showed the best benefit was $H\text{-}VMAT_{90/10}$. The partial irradiation of the cardiac area with dose of 25 Gy should be lower than 10% ($V_{25\,Gy}$), ensuring a lower than 1%[12] risk of cardiac mortality. It is noteworthy that all plans presented values significantly lower than the threshold.

Table 2. Dosimetric analysis of the target volume with each proportion

Target volume	H-VMAT 90/10	H-VMAT 80/20	H-VMAT 70/30	H-VMAT 60/40	H-VMAT 50/50	3D-CRT FILTER	VMAT
$D_{95\%}$ (Gy)	46.9	46.3	46.3	46.3	46.3	45	45
D_{mean} (Gy)	48.4	47.5	47.5	47.5	47.6	46.6	46.5
$D_{max.}$ (Gy)	50.2	48.8	48.8	49.2	49.4	48.1	48.3
Prescription curve	100	100	100	100	100	100	100
CI	1.23	1.16	1.17	1.17	1.11	1.03	1.18
HI	0.06	0.06	0.05	0.05	0.05	0.05	0.06

Captions: H-VMAT = hybrid volumetric arc therapy; 3D-CRT = three-dimensional conformal radiotherapy; VMAT = volumetric modulated arc therapy; CI = conformity index; HI = homogeneity index; D = dose.

Based on values shown in Table 3, the H-VMAT$_{50/50}$ plan with a mean dose value of 5.47 Gy for the cardiac area was the only one that did not reach the average dose restriction limit for this organ, which is 4.0 Gy according to the RTOG 1005[6].

The RTOG 1005 determines that the maximum contralateral breast dose does not exceed 3.10 Gy and the $V_{3\ Gy}$ volume does not surpass 5%[6]. The H-VMAT plan in the H-VMAT$_{50/50}$ proportions did not respect the contralateral breast restrictions, and the maximum dose reached 5.8 Gy. The proportions of the H-VMAT$_{90/10}$ and H-VMAT$_{80/20}$ plans presented the best dose reduction in the contralateral breast. The recommended V_{3Gy} dose was observed to be satisfactory for all hybrid plans.

The H-VMAT (H-VMAT$_{90/10}$ and H-VMAT$_{80/20}$) hybrid technique can be used mainly in patients with neoplasms in the left breast, due to the reduction of average dose in the heart and a significant improvement in PTV coverage. The combination of VMAT and 3D-CRT enables a preservation of the average dose in the cardiac area, as well as a reduction in the average dose of the contralateral lung in comparison to isolated techniques. In addition, it offers a dose delivery without increase of low doses in adjacent tissues when compared to isolated techniques[13]. Table 4 shows the OAR doses in the isolated techniques.

It can be verified that the combination of VMAT and 3D-CRT enables a preservation of the average dose in the cardiac area, as well as a reduction in the average dose of the contralateral lung. This fact reduces late toxicities, such as cardiac diseases and pneumonitis, as well as the risks of indirectly and/or consequently developing radiation-induced neoplasms in the contralateral breast and in the lungs[14]. The hybrid VMAT and 3D-CRT plan offers a dose delivery without increase of low doses in adjacent tissues when compared to isolated techniques. The hybrid plan offers the advantage of facilitating modulation and being swifter in removing hot spots.

DISCUSSION

There is a great benefit in using the hybrid technique in other neoplasms, such as the prostate region, bilateral breast, lung, oral cavity, and esophagus[15]. However, in breast treatments, weightings that have a greater contribution to the prescribed dose in three-dimensional treatments and lower percentages in intensity modulated radiotherapy (IMRT) and VMAT treatments are recommended[14].

The obtained results are in line with those published by Ramasubramanian et al.[14], in which the plan configurations that showed a more satisfactory dose delivery were the hybrid plans that have a greater contribution of the prescribed dose in three-dimensional treatments and lower percentages in VMAT treatments.

The H-VMAT hybrid technique can be used mainly in patients with neoplasms in the left breast, due to the reduction of dose in the heart and a significant improvement in PTV coverage. As the other techniques, the treatment using the H-VMAT technique can be controlled by gating and/or deep inspiration breath-hold (DIBH), helping in respiratory control and decreasing exposure of the cardiac

Table 3. Dosimetric assessment of VMAT ratios combined with 3D-CRT

OAR	Parameters	H-VMAT 90/10	H-VMAT 80/20	H-VMAT 70/30	H-VMAT 60/40	H-VMAT 50/50
Contralateral lung	$D_{max.}$ (Gy)	9.9	15.5	2.3	2.5	2.6
	V_{20Gy} (%)	0	0	0	0	0
	V_{10Gy} (%)	0	0	0	0	0
	V_{5Gy} (%)	0	0	0	0	0
Ipsilateral lung	$D_{max.}$ (Gy)	44.5	43.9	44	44.6	44.6
	V_{20Gy} (%)	2.4	2.1	2.6	3.5	4.8
	V_{10Gy} (%)	4.4	5.8	8.5	14.8	19.8
		11.5	18.2	27	45	57.1
Cardiac area	D_{mean} (Gy)	2.7	3.9	4.6	5.3	5.4
	V_{25Gy} (%)	0.03	0.04	0.06	0.11	0.2
	V_{10Gy} (%)	0.15	0.29	0.81	1.4	3.8
Contralateral breast	D_{mean} (Gy)	3.5	3.9	5.5	6.1	5.8
	V_{3Gy} (%)	0	0	0	0	0
	$V_{1,8Gy}$ (%)	0	0	0	0	0

Captions: OAR = organ at risk; H-VMAT = hybrid volumetric arc therapy.; D = dose; V = volume.

Table 4. Dosimetric comparison of the isolated techniques

OAR	Parameters	H-VMAT 90/10	H-VMAT 80/20	3D-CRT FILTRO	VMAT
Contralateral lung	$D_{max.}$ (Gy)	9.9	15.5	11.9	8.4
	V_{5Gy} (%)	0	0	0	3.3
Ipsilateral lung	$D_{max.}$ (Gy)	44.5	43.9	42.3	43.8
	V_{20Gy} (%)	2.4	2.1	2.38	15.7
	V_{10Gy} (%)	4.4	5.8	3.78	43.7
	V_{5Gy} (%)	11.5	18.2	6.95	75.3
Cardiac area	D_{mean} (Gy)	2.7	3.9	1.13	13
	V_{25Gy} (%)	0.03	0.04	0.03	5.7
Contralateral breast	D_{mean} (Gy)	3.5	3.9	3.6	4.5
	V_{3Gy} (%)	0	0	0	3

Captions: OAR = organ at risk; H-VMAT = hybrid volumetric arc therapy; 3D-CRT = three-dimensional conformal radiotherapy; VMAT = volumetric modulated arc therapy.

area[16]. With breathing techniques, it is possible to reduce the dose in the pulmonary cardiac area without compromising the prescribed dose in the target volume. A deep inspiration will elevate the chest wall and expand the volume of lungs, thus pushing the heart to a posterior area and increasing the distance from the target volume[16].

The restriction criteria for evaluating the contralateral breast must consider that there is a probability of radiation causing secondary cancer in the contralateral breast, the so-called stochastic effects[17]. The concern is heightened for young patients diagnosed with breast cancer, as the radiation can cause genetic changes to DNA that might facilitate the occurrence of a second cancer[12]. Therefore, all resources must be employed to minimize late chronic toxicities[13].

Dosimetric results are almost integrally satisfactory for all techniques, isolated or not, they are related to the favorable anatomy of the anthropomorphic phantom. However, it is known that there are implicit difficulties in the daily practice that impair the obtainment of satisfactory results using only the 3D-CRT technique.

CONCLUSION

Considering the dosimetric analysis of H-VMAT proportions, this method of planning can offer an excellent conformity and homogeneity of target volume dose. The H-VMAT proportions that met the requirements for a satisfactory plan were $H\text{-}VMAT_{90/10}$ and $H\text{-}VMAT_{80/20}$ for the phantom used.

Therefore, it is suggested, for future research, the analysis of doses in clinical cases, mainly with their use in patients with unfavorable anatomy or patients who require treatment in the internal mammary lymph node chain.

The combination of VMAT and 3D-CRT enables a preservation of the average dose in the cardiac area, as well as a reduction in the average dose of the contralateral lung. In addition, this technique offers a dose delivery without increase of low doses in adjacent tissues when compared to isolated VMAT technique.

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CONTRIBUTIONS

Tatiane Mayla Domingos Prandi, Herofen Zaias and Patrícia Fernanda Dorow have contributed to the study design, analysis and interpretation of the data, wording, and critical review. Charlene da Silva and Juliana dos Santos Müller have contributed to the analysis of results, wording, and critical review. All the authors approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interest to declare.

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