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A Dosimetric Comparison of Volumetric-Modulated Arc Therapy to Intensity-Modulated Radiation Therapy in the Treatment of Locally Advanced Rectal Carcinoma

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ABSTRACT

Introduction: The study was conducted to compare volumetric-modulated arc therapy (VMAT) with intensity-modulated radiation therapy (IMRT) in patients with locally advanced rectal cancer (LARC).
Material and Methods: Ten computed tomography (CT) scans were selected and for each CT scan, two plans were created (IMRT and VMAT). The average cumulative dose-volume histograms (DVH) of VMAT plans for the planning target volumes (PTVs), organs at risk (OARs), and normal tissues were calculated and compared with those reported for the corresponding IMRT technique.
Results: Target coverage was equivalent for both techniques. For primary PTV, the average homogeneity index (HI) of IMRT was significantly lower than the VMAT plans (0.10±0.04 vs. 0.11±0.03; $P<0.0001$). The average conformity index (CI) values for IMRT and VMAT were 1.21 and 1.12, respectively, with a nonsignificant trend for better results with VMAT ($P=0.1$). For the PTV boost, there was a nonsignificant trend for better results with VMAT in average HI and CI. The VMAT was superior to IMRT in OAR sparing. For monitor units (MUs), VMAT plans required 70% less MUs than IMRT.
Conclusion: For LARC patients, VMAT was able to deliver treatment plans dosimetrically equivalent to IMRT in terms of PTV coverage. The VMAT provided better OAR sparing and significant reduction of MUs in comparison to IMRT.

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Introduction

Colorectal cancer (CRC) is the third most common malignancy diagnosed worldwide. The burden of CRC is predicted to increase to an estimated 2.2 million new cases by the year 2030 [1-2]. The current standard of care for locally advanced rectal cancer (LARC) is preoperative chemoradiotherapy (CRT). Preoperative CRT, as opposed to postoperative CRT, is associated with both a significantly lower rate of local recurrence, as well as a reduction in acute and chronic toxicities as confirmed by previous comparative studies [3-5]. For patients undergoing preoperative CRT, the morbidity associated with the acute and chronic toxicities of the bladder and small bowel remains a concern [5-7].

Modern radiation therapy techniques allow for the reduction in the incidence and severity of treatment-related toxicities, such as the small bowel and bladder toxicities. Two of these techniques are intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT). These techniques allow for a highly conformal dose to be delivered to target volumes while minimizing the dose to surrounding organs at risk (OARs), including the small bowel, bladder, and femoral heads, in comparison to the earlier technique, three-dimensional conformal radiation therapy (3D-CRT) for the treatment of LARC [4-7].

The conformality of dose distribution and associated reduction in dose to OARs are significant due to the dose-volume relationship between these OARs and incidence and severity of acute and chronic toxicities. This relationship has been examined in several studies. The results of these studies revealed that the incidence of acute gastrointestinal (GI)

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toxicity strongly correlates with the amount of the small bowel irradiated with doses as low as 15 Gy. The ability of IMRT and VMAT to reduce the dose to the small bowel provides the benefit of reducing GI toxicity in the case of preoperative CRT [4-8].

Many studies have been performed comparing IMRT to 3D-CRT and VMAT to 3D-CRT. There are few studies that compare IMRT to VMAT for LARC irradiation. Within these studies, there are variations in patient positioning and preparation, as well as equipment and techniques [4-9]. The purpose of the present study was to compare the dosimetric parameters between IMRT and VMAT in terms of target coverage, as well as low and high doses to OARs, such as the small bowel, bladder, femoral heads, and normal tissues, for LARC patients.

Materials and Methods

Simulation and Treatment Planning

Ten patients previously treated with IMRT for LARC (stage T3 or T4) were selected for this noninterventional study. The computed tomography (CT) scans of these patients were used to perform the dosimetry for the VMAT plans and compare the results with the IMRT plans. The CT scans were conducted on the patients in the prone position, immobilized with a carbon-fiber belly board to assist in minimizing the amount of the small bowel in the treatment fields. The patients also adhered to a full bladder protocol for CT and treatment. The CT scan was performed with a slice thickness of 2 mm and extended from the first lumbar vertebral body to 5 cm below the perineum.

The CT scans were imported into a three-dimensional treatment-planning system (Eclipse version 13.6, Varian Medical Systems, USA). The target volumes were contoured according to the recommendation of the International Commission on Radiation Units and Measurements report 62 [10]. A physical examination, colonoscopy, and magnetic resonance imaging (MRI) were utilized to determine the gross tumor volume (GTV). The GTV and areas suspected to be at risk of microscopic disease constituted the clinical target volume (CTV).

For T3 disease, all gross diseases (i.e., rectal and nodal) and mesorectum and internal iliac lymph nodes were included in the primary CTV. For T4 disease, the primary CTV included similar structures as for T3 disease, as well as the external iliac lymph nodes. The GTV with a 2 cm margin to include the presacral space was the volume defined as the CTV boost. A 7 mm expansion of the CTV was performed to generate the planning target volume (PTV). The OARs were also contoured, including the bladder, femoral heads, and small bowel. The small bowel contour was extended 3 cm above and below the PTV.

Treatment Planning Techniques

For each CT dataset, two plans (i.e., IMRT and VMAT) were calculated for the treatment with the Varian Truebeam (Varian Medical Systems, USA) linear accelerator. The plans in the present study consisted of two phases. In phase 1, a dose of 45 Gy in 25 fractions was delivered to the pelvis (i.e., rectum and draining pelvic lymph nodes), and in phase 2, a dose of 5.4 Gy in 3 fractions was delivered to the PTV boost. The IMRT technique comprised of seven coplanar 6 MV photon beams with gantry angles of 207°, 258°, 309°, 0°, 51°, 102°, and 153° for each phase. The VMAT plans consisted of 2 full monoisocentric arcs for each phase.

Evaluation Tools and Statistical Analysis

Dose-volume histograms (DVHs) were used to compare the two different plans for each patient. For the primary PTV and PTV boost, the parameters were reported as $V_{90\%}$, $V_{105\%}$, and $V_{110\%}$ (i.e., the volumes receiving 90%, 105%, and 110% of the prescribed dose, respectively). For the small bowel, the parameters were V_{35}, V_{40}, and V_{45} Gy (i.e., the volumes receiving 35, 40, and 45 Gy, respectively). However, for the bladder and femoral heads, the parameters were V_{40}, V_{45}, and V_{50} Gy (i.e., the volumes receiving 40, 45, and 50 Gy, respectively). For normal tissue, the volume of the body minus the primary PTV and PTV boost receiving low doses in terms of V_2, V_5, V_{10}, V_{20}, and V_{40} Gy (i.e., the volumes receiving 2, 5, 10, 20, and 40 Gy, respectively) were calculated. The number of monitor units (MUs) per fraction required for each plan was reported in this study. The values of the conformity index (CI) and homogeneity index (HI) based on equations 1 and 2 were calculated estimated for comparison.

Equation 1: Conformity index

$$\mathrm{CI} = \frac{\text{Treatment Volume}}{\text{Volume of PTV}} \quad (1)$$

The treatment volume was calculated as the tissue that received 95% of the prescribed dose and totally encompassed the PTV.

Equation 2: Homogeneity index

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}} \quad (2)$$

where $D_{2\%}$, $D_{98\%}$, and $D_{50\%}$ are the doses delivered to 2%, 98%, and 50% of the target volume, respectively. *P*-value was calculated using SPSS software (version 21.0). The average cumulative DVHs of the ten plans for the primary PTV, PTV boost, OARs, small bowel, bladder, femoral heads, and normal tissues were calculated, and the dosimetric analysis was performed in the present study.

Results

Planning Target Volume Coverage, Conformity, and Dose Heterogeneity

All of the dosimetric objectives of PTV coverage were achieved with both techniques. Table 1 tabulates the results of PTV coverage, conformity, and dose homogeneity. For the primary PTV, the average HI was significantly lower in the IMRT plan (0.10±0.04 vs. 0.11±0.03; $P<0.0001$). The average CI values were 1.21

and 1.12 for the IMRT and VMAT plans, respectively. This resulted in a nonsignificant trend for better results with VMAT (P=0.1).

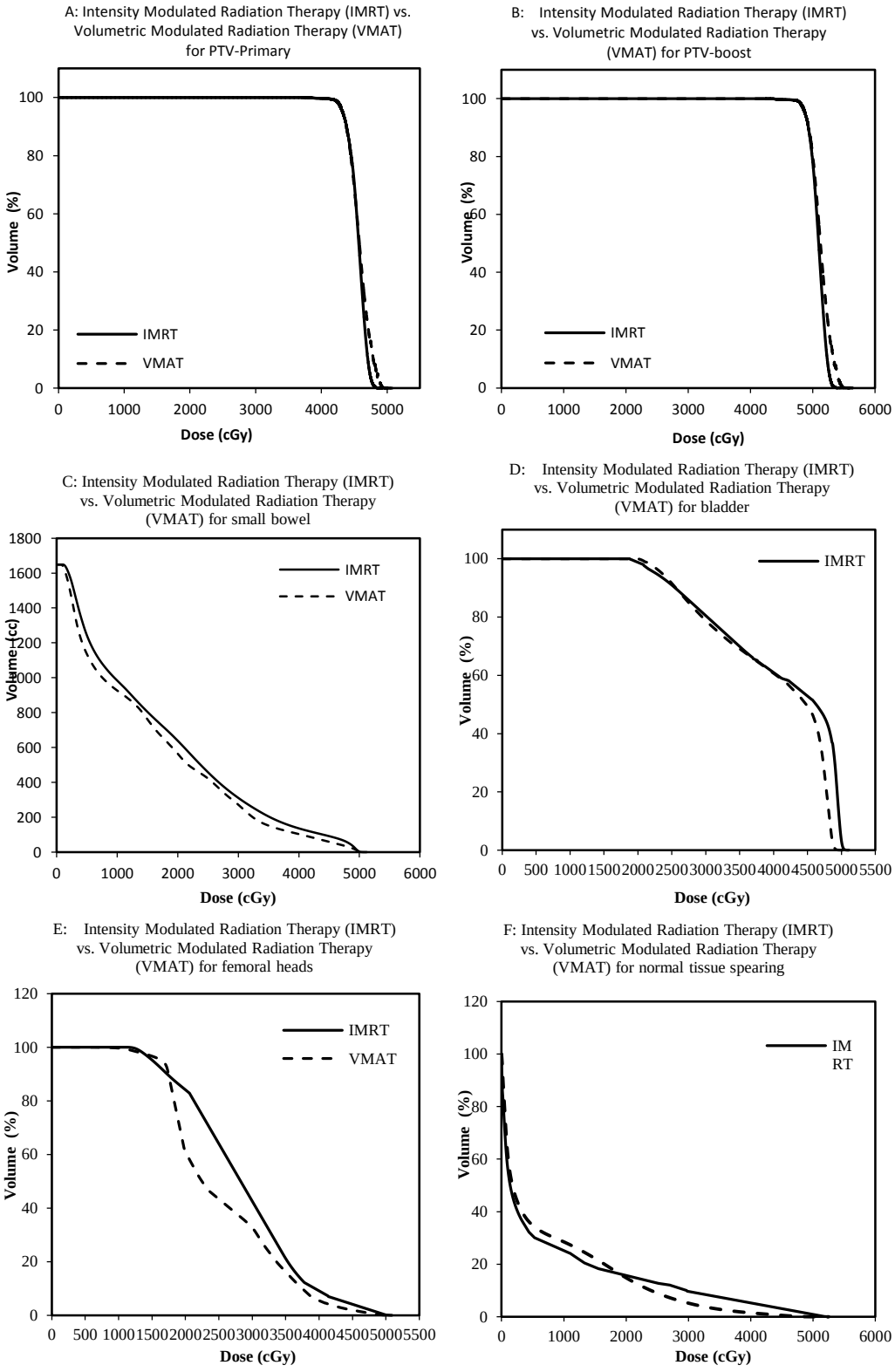

Figure 1. Cumulative dose-volume histograms of target (A: primary planning target volume; B: planning target volume boost), organs at risk (C: small bowel; D: bladder; E: femoral heads), and normal tissue (F: normal tissue) in two treatment planning techniques

Table 1. Comparison of dose parameters between IMRT[a] and VMAT[b] techniques for planning target volumes

Primary PTV[c]:			
Dose parameter	IMRT	VMAT	*P*-value
Homogeneity index	0.10±0.04	0.11±0.03	0.0001
Conformity index	1.21±0.09	1.12±0.1	0.1
V90 Gy (%)	99.9±0.9	99.9±0.7	0.8
V105 Gy (%)	2.3±3	1.1±1.5	0.5
V110 Gy (%)	0	0	-
PTV boost:			
Dose parameter	IMRT	VMAT	*P*-value
Homogeneity index	0.16±0.1	1.12±0.08	0.08
Conformity index	1.08±0.1	1.06±0.09	0.06
V90 Gy (%)	99.9±2.9	99.9±0.5	0.9
V105 Gy (%)	0.4±0.6	1.1±2	0.9
V110 Gy (%)	0	0.03	-

[a] IMRT: Intensity-modulated radiation therapy
[b] VMAT: Volumetric-modulated arc therapy
[c] PTV: Planning target volume

Table 2. Comparison of dose parameters between IMRT[a] and VMAT[b] techniques for OARs[c]

Small bowels:			
Dose parameter	IMRT	VMAT	*P*-value
V_{35} Gy (cc)[d]	76.7±64.5	66.2±63.4	<0.0001
V_{40} Gy (cc)	49.1±45.7	40.4±40.7	<0.0001
V_{45} Gy (cc)	28.9±30.2	18.1±22.7	<0.01
Bladder:			
Dose parameter	IMRT	VMAT	*P*-value
V_{40} Gy (%)	46±9	42.5±15	0.9
V_{45} Gy (%)	31.9±13.7	28.3±11	0.0001
V_{50} Gy (%)	1.9±4	1.2±3.6	0.0001
Femoral heads:			
Dose parameter	IMRT	VMAT	*P*-value
V_{40} Gy (%)	3.9±2.3	2.6±1.9	0.01
V_{45} Gy (%)	0.6±0.6	0.2±1.2	0.003
V_{50} Gy (%)	0	0	-

[a] IMRT: Intensity-modulated radiation therapy
[b] VMAT: Volumetric-modulated arc therapy
[c] OARs: Organs at risk
[d] cc: Cubic centimeter

Table 3. Comparison of dose parameters between IMRT[a] and VMAT[b] techniques for normal tissues and MUs[c]

Normal tissue:			
Dose parameter	IMRT	VMAT	*P*-value
V_2 Gy (cc)[d]	12358±689	12506±637	<0.0001
V_5 Gy (cc)	9524±548	9538±522	<0.0001
V_{10} Gy (cc)	7868±434	8113±400	<0.0001
V_{20} Gy (cc)	5501±310	5061±259	<0.0001
V_{40} Gy (cc)	1776±101	1660±94	<0.0001
MUs:			
Dose parameter	IMRT	VMAT	*P*-value
MUs	2915±299	876±30	<0.01

[a] IMRT: Intensity-modulated radiation therapy
[b] VMAT: Volumetric-modulated arc therapy
[c] MUs: Monitor units
[d] cc: Cubic centimeter

There was also a nonsignificant trend for better results in HI and CI with the VMAT plan for the PTV boost. Figures 1A and 1B show the DVHs for both IMRT and VMAT plans for the target coverage of the PTVs.

Organs at Risk

Table 2 presents the dose parameters and achieved values for the OARs, including the small bowel, bladder, and femoral heads. Figures 1C, 1D, and 1E also depict the differences in DVHs between the two techniques for the OARs. The VMAT plans resulted in significantly better sparing across all dosimetric parameters evaluated for the small bowel (i.e., V_{35}, V_{40}, and V_{45} Gy). The VMAT showed significant sparing with the V_{45} and V_{50} Gy parameters with a nonsignificant trend for better results by VMAT on V_{40} Gy for the bladder. Significantly better sparing was achieved for the femoral heads on V_{40} and V_{45} Gy parameters with VMAT. For the V_{50} Gy parameter, the sparing was similar independent of the utilized technique.

Normal Tissue

For the low dose levels of V_2, V_5, and V_{10} Gy assessed for normal tissue sparing, IMRT was associated with better dose sparing. For the intermediate and high dose levels of V_{20} and V_{40} Gy, VMAT provided better sparing as shown in Table 3 and Figure 1F.

Monitor Units

The IMRT plans resulted in a mean value of 2915±299 MUs per fraction required for treatment delivery. The VMAT plans led to a 70% reduction of required MUs with a mean value of 876±30 MUs (P=0.01) per fraction as detailed in Table 3.

Discussion

The use of modern highly conformal radiation therapy techniques, such as IMRT and VMAT, in the preoperative CRT treatment of LARC has become common practice [11]. Previous studies support the use of these techniques for their demonstrative ability to both improve target volume coverage and reduce dose to the OARs [9, 12-14].

The IMAT (intensity modulated arc therapy) was initially compared with 3D-CRT in the treatment of LARC patients by Duthoy et al. [12]. They showed similar PTV coverage between the techniques with IMAT enabling significantly lower mean doses to the small bowel. The results of the study proved that IMAT is equivalent to 3D-CRT in terms of target coverage with a trend towards increased dose conformity in both primary PTV and PTV boost. The VMAT plans also produced more homogenous dose distributions than IMRT plans.

Cilla et al. [13] reported similar results in their planning study comparing IMRT, 3D-CRT, and VMAT for the treatment of LARC. In the aforementioned study, VMAT had the highest level of conformity although the dose distribution across the PTV was less homogenous than the IMRT and 3D-CRT plans. The VMAT and 3D-CRT plans for a matched group of 25 patients with LARC were calculated in another comparative planning study. Similar PTV coverage for VMAT and 3D-CRT were reported with VMAT achieving better dose conformity and trend to improved homogeneity [14].

For LARC patients receiving preoperative CRT, acute GI toxicity is the most common complication. Many studies demonstrated the presence of a strong dose-volume relationship associated with the severity of diarrhea and volume of the small bowel irradiated at various dose levels [15-18]. According to the results, Baglan et al. [15] confirmed this relationship between the volume of the small bowel irradiated and acute diarrhea at every dose level. Accordingly, they illustrated a predictive model for acute toxicity. Based on the cumulative DVH for small bowel in the present study, VMAT was associated with significantly lower volumes of the small bowel irradiated in comparison to IMRT within a dose range of 35-45 Gy. Cilla et al. [13] also published similar results for the small bowel sparing with VMAT.

The feasibility and efficiency of both IMRT and VMAT techniques for LARC were also evaluated in the present study. The VMAT plans were associated with significantly fewer MUs, which enable faster treatment delivery. The advantages of reduced treatment delivery time are clinically important considering patient comfort, intrafraction movement, and availability of time to employ image-guided radiotherapy, which can further improve the accuracy of the treatment [19-21]. The reduced treatment delivery time is also important since concern has been raised that longer treatment time may have radiobiological implications, including increased tumor cell repair and repopulation during the extra time required for treatment delivery [22-24].

A major concern associated with the use of VMAT is the reported increased potential risk of secondary malignancy. This is due to the increased volume of normal tissue that receives a low dose with VMAT plans and is mostly important for patients with a long life expectancy. The results of this study also revealed that the VMAT plans were associated with an increase in the volume of normal tissue receiving low-dose radiation (V_2, V_5, and V_{10} Gy). This is expected as a result of the spread of dose from the complete 360º utilized VMAT arcs. The VMAT allowed better sparing in the intermediate and high dose levels (i.e., V_{20} and V_{40} Gy). The findings of a study conducted by Zhang et al. [25] support that normal tissue doses in the VMAT plans are lower than those reported in the fixed-field IMRT plans across the intermediate and high dose levels (28-48 Gy) and higher at lower dose levels (i.e., below 22 Gy).

Conclusion

For patients diagnosed with LARC, VMAT was able to deliver treatment plans dosimetrically equivalent to IMRT in terms of achieving highly conformal dose distributions. The VMAT provided better OAR sparing and improved efficiency in treatment delivery as a result of the reduction in treatment delivery time and MUs.

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