TECHNICAL NOTE

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Volumetric-modulated arc therapy versus intensity-modulated radiotherapy for large volume retroperitoneal sarcomas: A comparative analysis of dosimetric and treatment delivery parameters

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Abstract

Purpose: To compare dosimetric and treatment delivery parameter differences between volumetric-modulated arc radiotherapy (VMAT) and intensity-modulated radiotherapy (IMRT) for large volume retroperitoneal sarcomas (RPS).

Materials and Methods: Both VMAT and IMRT planning were performed on CT data-sets of 10 patients with RPS who had been previously treated with preoperative radio-therapy. Plans were optimized to deliver ≥95% dose to the PTV and were evaluated for conformity and homogeneity. Dose to the organs at risk (OARs) (kidney, liver, spinal cord, and bowel space), unspecified tissue, and dose evaluation volumes (DEVs) at 1, 2, and 5 cm from PTV were calculated and compared. Monitor units (MUs) and treatment delivery times were recorded and compared between the two techniques. The deliverability of the large volume RPS VMAT plans was verified by portal dosimetry on a Truebeam™ linac.

Results: VMAT and IMRT plans were equivalent for PTV coverage and homogeneity ($P > 0.05$); however, VMAT plans had slightly better conformity index, CI ($P < 0.001$). Doses to the OARs were not significantly different between VMAT and IMRT plans ($P > 0.05$). Mean doses to the unspecified tissue as well as at 1, 2, and 5 cm DEVs were lower with VMAT compared with IMRT, $P = 0.04$ and $P < 0.01$, respectively. MUs and average beam-on times were both significantly lower in the VMAT vs IMRT plans, $P < 0.001$ and $P = 0.001$, respectively. All VMAT plans passed portal dosimetry delivery verification with an average gamma passing rate of 99.6 ± 0.4%.

Conclusions: VMAT planning for large volume RPS improved CI, and achieved comparable OAR sparing, as compared with IMRT. As treatment delivery time was lower, the use of VMAT for RPS may translate into improved treatment delivery efficiency.

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1 | INTRODUCTION

Retroperitoneal sarcomas (RPS) are rare tumors, comprising approximately 15% of sarcomas. Surgery is the mainstay of treatment for patients with resectable disease; 5-year overall survival is 50%–60%.[1] The predominant pattern of failure after surgery is locoregional.[2–4] Although prospective randomized trials evaluating the role of radiotherapy (RT) for RPS are lacking, multiple retrospective institutional series suggest that RT improves local control and disease-free survival[5–9] vs surgery alone. An expert panel on the treatment of RPS recommended the use of preoperative RT as compared with postoperative RT for several reasons: (a) the dose required preoperatively is lower, (b) reduction in the volume of organs at risk (OARs) receiving RT, and (c) more accurate target volume definition.[10.]

Treatment planning and delivery has vastly improved in the last two decades. Inverse planning systems such as intensity-modulated RT (IMRT) have an advantage of improving target coverage while sparing normal organs over 3D conformal RT.[11–13] RPS are typically large in size and are adjacent to multiple dose-limiting normal organs, making RPS a challenging nonuniform subgroup of tumors where improved treatment planning and treatment delivery would be highly desirable. IMRT is the currently recommended technique for treatment of RPS by expert panel consensus.[10] Unfortunately, delivery of IMRT plans on average can take 20–30 min.[14] Longer treatment times have an impact on the workflow throughput of a treatment unit and uncertainty of target and OAR dose calculations due to intra-fraction motion.[15] One potential solution to overcome these issues is to use volumetric-modulated arc therapy (VMAT).[16] Llacer-Moscardo et al. reported on feasibility of VMAT in seven preoperative and three postoperative RPS cases and implied it is superior than IMRT-based plans.[17] However, a direct comparison study of VMAT versus IMRT treatment planning within the same cohort of patients has not been reported.

The objectives of this study were to directly compare dosimetric and treatment delivery parameter differences between VMAT and sliding window IMRT (swIMRT) in patients treated with preoperative RT for RPS.

2 | METHODS

After receiving study approval for this retrospective planning study from our local institutional research ethics board, 10 patients with RPS who were treated with preoperative RT in 2012–2013 at our institution were identified. Planning CT datasets were retrieved from the Eclipse™ (Varian Medical Systems, Palo Alto, CA, USA) treatment planning system (TPS), and each case was re-planned with both VMAT and swIMRT. In order to ensure consistency over all plans, both the IMRT and VMAT plans were generated by the same planner and the stopping criterion was based on the dosimetric goals listed in the next section.

2.A | Plan generation, dosimetric considerations, and conformity index

The previously defined gross tumor volumes (GTV), clinical target volumes (CTV), and planning target volumes (PTV) were utilized. Organs at risk (OARs) — liver, kidney, spinal cord, and bowel space — were contoured either for actual treatment or for the purposes of this study if they were not done previously. New plans were generated using analytical anisotropic algorithm (AAA) in Varian Eclipse™ v. 11.0.31, using a prescribed dose to the PTV of 45 Gy in 25 fractions. IMRT plans were generated using 4–6 co-planar beams. Beam angles were customized based on size and location of the PTV. Dose volume optimizer (DVO) v. 11.0.31 was used to optimize the IMRT plans. VMAT plans were generated using 2–4 partial arcs. The number of arcs and arc start and stop angles were customized, based on size and location of the PTV. Progressive resolution optimizer (PRO) v. 11.0.31 was used to optimize the plans. All IMRT and VMAT plans were optimized and calculated using 6-MV photons to deliver greater than 95% of the prescription dose to 95% of PTV (D95), while respecting OAR dose constraints based on QUANTEC.[18.]

Conformity was assessed using the van't Reit conformity index (CI).[19] The CI is defined as less than or equal to 1; if CI value is closer to 1, it is considered to be more conformal. Homogeneity was assessed using ICRU83 definition of homogeneity index, defined as $\frac{D2\%-D98\%}{D50\%}$. The dose to the unspecified tissue (all of tissue that is not contoured as a target or an OAR) was also recorded. Dose evaluation volumes (DEVs) at 1, 2, and 5 cm (D1, D2, and D5 cm) expansions from the PTV were created. These structures were trimmed to the body contour in instances where they extended outside the body. Mean doses in DEVs were recorded to estimate dose fall-off. Monitor units (MU) were obtained and treatment delivery times were measured using mock runs of each plan on a treatment unit.

2.B | Plan deliverability and quality assurance (QA)

The deliverability of the VMAT plans was verified using portal dosimetry with an electronic portal imaging device (EPID) mounted on a Varian Truebeam™ linear accelerator (linac) (Varian Medical

Systems, Palo Alto, CA, USA) using a 43 × 43 cm^2 aSi Digital Mega-volt Imager (DMI). This newly developed large area detector allowed for delivery verification of the large field VMAT plans. The plans were assessed based on the gamma criteria[20] of 3%/3 mm with a clinical passing threshold of 95% of points using Varian's Portal Dosimetry software.

2.C | Statistical considerations

All dosimetric comparisons were performed using nonparametric statistical models in Microsoft Excel (Microsoft Corp, Seattle, WA, USA).

TABLE 1 Patient, tumor, and treatment characteristics.

Patient characteristics	
Age, median (range)	62.0 yr (32.2–76.2 yr)
Male, n	4
Female, n	6
Treatment	
Preoperative RT, n	10
Radical surgery, n	9
Palliative surgery, n	1
Histology, n	
Liposarcoma	6
Spindle cell sarcoma	2
Leiomyosarcoma	1
Pleomorphic sarcoma	1
Tumor volume, mean (SD)	2433 cm^3 (3471 cm^3)
PTV, mean (SD)	3311 cm^3 (3287 cm^3)

PTV, planning target volume; RT, radiotherapy; SD, standard deviation.

3 | RESULTS

Table 1 summarizes the patient and tumor characteristics. Mean tumor volume was 2433 cm^3 (standard deviation, SD = 3471 cm^3), and mean PTV was 3311 cm^3 (SD = 3287 cm^3).

Table 2 summarizes dosimetric parameters for all 10 patients. On average, 94.2% of the PTV was covered by 95% of the dose with VMAT plans as compared with 92.5% with swIMRT (P = 0.5). VMAT plans had a better CI, 0.88 (SD = 0.03) compared with swIMRT plans 0.85 (SD = 0.03) (P < 0.0001), but both plans had similar homogeneity within the PTV, 0.068 and 0.066 (P > 0.05), respectively. Doses to the OARs were not significantly different for VMAT and swIMRT plans. Mean doses to the unspecified tissue and DEVs (D1, D2, and D5 cm) were significantly lower for VMAT plans compared with swIMRT plans, P = 0.04 and P < 0.01, respectively. VMAT plans required 490 MUs, 53% lower than swIMRT plans, P < 0.0001.

The measured average beam-on time, as determined by delivering the individual VMAT plans in QA mode on the Truebeam™ linac, was 1.75 min (SD = 0.66 min), which was significantly lower when compared with actual beam-on time for swIMRT plans as delivered during treatment, 7.24 min (SD = 1.18 min) (P < 0.001). All VMAT plans passed the portal dosimetry delivery verification at greater than 98.5% of points passing the gamma criterion of 3%/3 mm. The average gamma passing rate was 99.6 ± 0.4% for all VMAT plans. These large field sarcoma plans are, therefore, indeed deliverable at clinical tolerances. The mean gamma value for all VMAT fields was 0.22 ± 0.04. This is significantly less than the threshold value of 1 and much less than 0.5, which demonstrates that there were no systematic issues in absolute treatment delivery.[21]

TABLE 2 Dosimetric comparisons of target coverage and OARs between VMAT and swIMRT.

	VMAT	swIMRT	P-value
Number of arcs/beam angles, median (range)	2.5 (2–4)	5 (4–6)	<0.001
PTV coverage (D95), mean (range)	94.2% (88.8–97.7)	92.5% (80.0–100.0)	0.5
CI, mean (range)	0.88 (0.83–0.93)	0.85 (0.80–0.91)	<0.001
Uninvolved contralateral kidney mean dose (Gy), (range)	7.0 (2.2–10.1)	7.3 (2.3–12.8)	0.8
Liver mean dose (Gy), mean (range)	14.9 (2.7–23.1)	15.0 (2.8–22.4)	0.6
Spinal cord max dose (Gy), mean (range)	26.9 (12.0–39.7)	29.6 (16.0–45.1)	0.1
Bowel space (D195 cm^3) (Gy) (range)	38.7 (30.2–46.0)	40.5 (33.5–47.4)	0.1
Unspecified tissue mean dose (Gy), mean (range)	15.3 (11.3–21.7)	15.9 (12.3–22.0)	0.04
DEVs (Gy), mean (range)			
1 cm from PTV	39.9 (36.7–41.8)	40.9 (39.0–42.3)	<0.001
2 cm from PTV	33.2 (30.4–36.8)	34.6 (31.7–36.9)	<0.001
5 cm from PTV	21.7 (18.4–26.3)	22.4 (18.8–26.1)	0.009
Monitor units, mean (range)	490 (367–725)	1042 (610–1570)	<0.001
Treatment delivery time (min), mean (SD)	1.75 (0.66)	7.24 (1.18)	<0.001

CI, conformity index; D195 cm^3, dose to 195 cm^3 of bowel space; DEV, dose evaluation volume; Gy, SI unit of dose; OAR, organs at risk; PTV, planning target volume; SD, standard deviation; swIMRT, sliding window intensity-modulated radiotherapy; VMAT, volumetric-modulated arc therapy.

4 | DISCUSSION

Preoperative RT is recommended for RPS to reduce local recurrence.[4,10] Improvement in target dose delivery and reduction of dose to OARs with IMRT compared with 3D-CRT has been established.[22–24] VMAT is an improved and more efficient method of delivering IMRT as demonstrated for other tumor sites.[25–33] A single feasibility study investigating the use of VMAT for treatment of RPS is reported[17]; however, they did not perform a direct comparison of VMAT to IMRT as it has been done for other tumor sites. Therefore, it is important to conduct and report dosimetric comparison studies of VMAT and IMRT in RPS, such that evidence can guide adoption of this technique in clinical practice.

Similar to published literature,[29,34–36] D95 in this study was comparable between VMAT and IMRT plans ($P > 0.5$); however, CI was statistically improved in favor of VMAT ($P < 0.001$). The target volumes in this study, however, were significantly larger than reported by others. Our portal dosimetry measurements demonstrate that the VMAT beams are deliverable for these large volumes (PTV volumes ranging from 415 to 10194 cc). The homogeneity index ($\frac{D2\%-D98\%}{D50\%}$) was 0.068 and 0.066 for VMAT and IMRT, respectively. This is comparable to earlier reported RPS studies (D5%–D95%).[17.]

Reduction of dose to uninvolved critical organs close to the target is an important factor when considering adoption of a new technique. This is especially important in the case of RPS, where large tumors often lie very close to critical structures, such as kidneys. Therefore, any potential dose reduction especially to the uninvolved contralateral kidney may confer therapeutic gain. Jansen et al. have shown the incidence of late kidney injury up to 52% when V20 (volume of kidney receiving 20 Gy) and if mean kidney dose were higher than 66% of prescribed 45 Gy in 25 fractions.[37] The mean doses to uninvolved contralateral kidney with VMAT and IMRT in this study were significantly lower compared with Jansen et al. and are comparable to those reported by Llacer-Moscardo et al.[17] Moreover, we observed a further reduction of mean dose by 4.1% with VMAT compared with swIMRT. Similar reductions in dose were also noticed for other OARs (Table 2); these were not statistically significant, likely due to a small sample size.

Low dose bath of radiation especially from IMRT has been implicated in a potential increase in secondary malignancies.[38,39] Therefore, naturally it is assumed that risk of secondary malignancies would be even higher with arc therapy, where the low dose bath of radiation is splayed over even a larger area. One way to estimate the low dose bath is to measure dose to unspecified tissue outside the PTV and OARs. This is the first study to report mean dose to unspecified tissue outside the target and OARs, and it was significantly lower with VMAT compared with swIMRT ($P = 0.04$). Furthermore, we report dose fall-off from PTV by generating spherical volumes around the PTV. This method allows us to estimate intermediate- to low-dose gradient. This is typically performed in SBRT plans, where dose at 2 cm is used to optimize the plan to generate sharper dose fall-off and decrease intermediate dose.[40] In this study, dose fall-off was measured for three DEVs that we created as dose fall-off estimating structures from the PTV. The mean dose within all three DEVs was significantly lower for VMAT plans compared with swIMRT plans ($P < 0.01$). This indicates a sharper dose fall-off with VMAT, and an overall lower intermediate dose around the PTV for these large volume treatment plans.

The biggest advantage of VMAT over IMRT is shorter treatment time.[33,41–43] In this study, there was 53% reduction in average number of MUs and 76% reduction in measured treatment time with VMAT plans compared with swIMRT plans ($P < 0.001$). This is consistent with other published studies that have compared VMAT and IMRT.[29,31,32,34,35,44,45] The shorter treatment time may translate in improved workflow within a radiation department, as typical IMRT slots are 25–30 min long.[14] Shorter beam-on time may result in decreased intra-fraction motion of the target and OARs during treatment. Zhuang has modeled dose uncertainty in relation to organ motion and field size and concluded that there is higher dose uncertainty with increasing field size and motion amplitude.[15] The treatment of RPS generally requires large field sizes, and previous literature has documented significant motion of these tumors and adjacent organs, particularly in the upper abdomen.[46] IMRT plans that require a higher number of MUs and take longer to deliver, therefore, would be more vulnerable to the increased dose uncertainty from intra-fraction tumor and organ motion. Thus, for RPS patients, VMAT plans that can deliver highly conformal treatment in shorter time may confer a therapeutic advantage, although this hypothesis needs to be assessed in a formal prospective setting. In addition, lower MUs, leading to a shorter beam-on time, reduce the out of field dose due to a reduction in head leakage.

5 | LIMITATIONS

We recognize that this retrospective study has inherent biases of patient and treatment selection. Our results, while intriguing, are hypothesis generating. Formal assessment of patient comfort and toxicity was not done in this study. A prospective study comparing the two treatment techniques may confirm our results and allow for assessment of toxicity and patient comfort with each of these techniques.

6 | CONCLUSIONS

In this study, we compared dosimetry and deliverability of VMAT versus IMRT for large volume targets such as retroperitoneal sarcomas. VMAT is able to generate plans that are comparable in PTV coverage and homogeneity, have a higher conformity, provide comparable or less dose to OARs, but a sharper dose fall-off. These dosimetric advantages are complemented by the decreased delivery time of VMAT plans and reduced monitor units. This could potentially translate into improved comfort for the patient, reduced intra-fraction motion, and improved workflow for a busy radiotherapy department.

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