ORIGINAL ARTICLE

Dosimetric comparison of tomotherapy and volumetric-modulated arc therapy for children with neuroblastoma

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ABSTRACT

Importance: Irradiation treatment for pediatric patients with neuroblastoma represents a major challenge due to the pediatric dose limits for critical structures and the necessity of sufficient dose coverage of the clinical target volume for local control.

Objective: To investigate dosimetric differences between tomotherapy (TOMO) and volumetric-modulated arc therapy (VMAT) as retroperitoneal radiotherapy for children with neuroblastoma.

Methods: Eight patients who received retroperitoneal radiotherapy for neuroblastoma were selected for comparison of TOMO and VMAT treatment plans. The D_{min}, D_{max}, D_{mean}, D_{95}, D_2, and D_{98} of planning target volume (PTV), conformity index (CI), heterogeneity index (HI), and organs at risk (OARs) parameters were compared. Delivery machine unit (MU) and image-guide radiotherapy solution results were also compared.

Results: All patients received a cumulative dose of 19.5 Gy to the PTV. VMAT showed higher CI (0.93 ± 0.02), compared with TOMO (0.87 ± 0.03, $P < 0.001$). Notably, the average PTV HI was significantly better using TOMO (1.05 ± 0.01) than VMAT (1.08 ± 0.02, $P = 0.003$). Compared with VMAT, the D_{min}, D_{95}, and D_{98} all exhibited increases in TOMO; D_{max} variation was less than 1% in TOMO. The $D_{0.1cc}$ for the spinal cord and D_{2cc} for the small intestine were better in TOMO in terms of OARs. However, TOMO had more MUs and required a longer delivery time.

Interpretation: Both planning techniques are capable of producing high-quality treatment plans. TOMO is superior for PTV coverage, but inferior for CI. TOMO requires extra treatment time; its cost is greater than the cost of VMAT.

KEYWORDS
Tomotherapy, Volumetric-modulated arc therapy, Neuroblastoma, Dosimetric comparison, Pediatric

INTRODUCTION

Neuroblastoma is the most common solid extracranial tumor in children. Previous studies have shown a benefit of radiotherapy (RT) to the primary site after chemotherapy and surgical resection in patients with high-risk forms of the disease.[1-3] Radiotherapy constitutes a complex problem because of the shapes of the target volumes and the need to minimize the involvement of organs at risk (OARs).[4] In recent years, new radiotherapy technologies, such as volumetric-modulated arc therapy (VMAT) and helical tomotherapy (TOMO), have been

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widely used in the clinic. Consequently, the application of highly conformal treatment modalities has been of great interest for producing highly conformal dose distributions in the target volumes and minimizing the doses to OARs.[5-7] However, the dose distinction between TOMO and VMAT has not been fully elucidated. To the best of our knowledge, this is the first planning study to compare TOMO and VMAT with regard to retroperitoneal irradiation for neuroblastoma.

METHODS

Ethical approval

The study was approved by Peking Union Medical College Hospital Institutional Review Board. Since this was a retrospective study and the data analysis were performed anonymously, the study was exempt from informed consent from patients' guardians.

Patient population

Between January and April 2020, eight patients with neuroblastoma (three girls and five boys; median age, 3.5 years [range: 2–9 years]) were treated in our Hospital with radical intensity-modulated radiotherapy. All eight patients were diagnosed with stage IV high-risk neuroblastoma and received prescriptions of retroperitoneal irradiation.

Simulation

All patients were immobilized with a children's body thermoplastic mask in the supine position with their arms extended upward (Supplementary Figure S1). All computed tomography (CT) data sets were acquired using a helical CT scanner (Brilliance CT Big Bore; Philips Healthcare, Best, the Netherlands). CT images were obtained at a 5-mm thickness throughout the abdomen and extending to 10 cm beyond the borders of the tumor. The data were transferred to Tomo HD version 2.1.4 (Accuracy, Sunnyvale, California, USA) and Monaco 5.1.2 (Elekta, Stockholm, Sweden) Treatment Planning Systems, in accordance with the Digital Imaging and Communications in Medicine communication protocol.

Structure definition

The planning target volume (PTV) of the retroperitoneum was adopted for this planning study. The PTV was defined as the clinical tumor volume (CTV), as identified by a radiation oncologist, with the addition of a 6.0-mm margin. In addition, the following OARs were delineated for planning dosimetry comparison: body, liver, left kidney, right kidney, spinal cord, small intestine, stomach, and spleen. Security margins of 3 mm were implemented around the spinal cord to allow for patient setup uncertainties (i.e., planning organ at risk volume). A physician checked all contouring results of the PTV and OARs.

Dose prescription and optimization

Both plans were optimized to deliver 1.5 Gy dose per fraction, up to a total of 19.5 Gy, to the PTV. A plan was accepted if 95% of the PTV was covered by 100% of the prescribed dose. Plans were optimized using the treatment planning systems. For TOMO plan optimization, a field width of 2.5 cm, pitch of 0.43, and modulation factor of 3.0 were used for each patient. Each Monaco VMAT plan consisted of 2 arcs per beam; the first arc rotated clockwise and the second arc rotated counterclockwise.[8] The final dose computation was made on a fine grid (convolution superposition) for the Tomo system and a max dose grid voxel size of 3 mm × 3 mm × 3 mm for the Monaco system. TOMO was performed using the collapsed cone convolution/superposition algorithm; VMAT was performed using the Monte Carlo dose calculation algorithm. Plans were optimized, produced, and checked by three dosimetrists and one physicist.

Treatment plan evaluation

For the accumulated dose distribution, the following parameters were analyzed: PTV D_{min}, D_{max}, D_{mean}, D_2, D_{95}, D_{98}, conformity index (CI), heterogeneity index (HI), and OARs (liver, left kidney, right kidney, spinal cord, small intestine, stomach, and spleen).

The CI describes the degree to which the prescribed isodose volume conforms to the shape and size of the target volume(s), using the following formula: $CI = TV_1^2/(TV \times VR_1)$, where TV_1 is the target volume that receives the prescribed dose, TV is the target volume, and VR_1 is the total volume of the prescribed isodose. The HI provides information regarding dose uniformity within the target volume(s), using the following formula: $HI = D_5/D_{95}$, where D_5 is the dose delivered to the hottest 5% of the PTV and D_{95} is the minimum dose received by 95% of the PTV. Delivery machine unit (MU) and image-guide radiotherapy (IGRT) solution results were also compared.

Statistical analysis

The data in this study were analyzed using SPSS 15.0 (SPSS, Inc., Chicago, IL, USA). Paired *t*-tests were used to analyze differences between the two planned dosimetries. A $P < 0.05$ was considered as statistically significant.

RESULTS

Target coverage and dose homogeneity

Figure 1 illustrates the isodose distributions of TOMO and VMAT for three patients in coronal, axial, and sagittal views. Both techniques resulted in similar target coverage; clinically acceptable plans were achieved for both techniques.

The PTV dosimetric parameters and comparisons of the

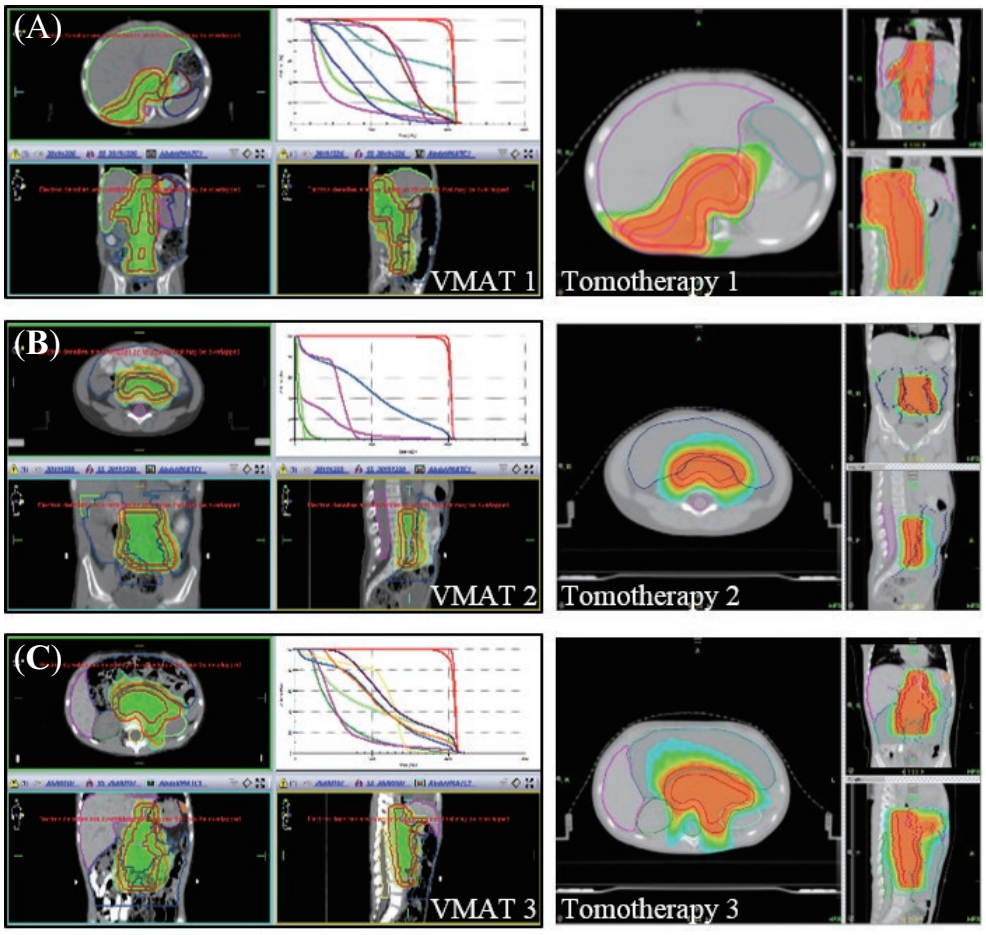

FIGURE 1 Three samples of the isodose distributions of VMAT and tomotherapy. Each row represents the isodose distributions of of axial, sagittal, coronal view, and dose-volume histogram of (A) Patient 2; (B) Patient 4; (C) Patient 3. Both tomotherapy and VMAT were able to produce plans with good coverage of PTV and acceptable sparing of OARs. VMAT, volumetric-modulated arc therapy; OARs, organs at risk; PTV, planning target volume.

eight patients with respect to the two radiotherapy plans are shown in Table 1. TOMO exhibited significantly better mean HI (1.06 ± 0.01), compared with VMAT (1.08 ± 0.02, $P = 0.003$); moreover, VMAT exhibited higher CI, compared with TOMO (0.93 ± 0.02 *vs*. 0.87 ± 0.03, $P < 0.001$). Compared with assessment of VMAT, TOMO exhibited a 25% increase in D_{min} ($P = 0.014$), 2% increase in D_{95} ($P = 0.049$), 5% increase in D_{98} ($P = 0.008$), and less than 1% variation in D_{max} ($P = 0.113$, this difference was not statistically significant). The findings demonstrated that TOMO delivered more optimal target dosimetric parameters, compared with VMAT.

Sparing doses to OARs

The data of dosimetric comparisons of OARs among patients are shown in Table 2. OAR sparing was good and the results were similar for TOMO and VMAT. Notably, TOMO was more advantageous than VMAT in terms of $D_{0.1cc}$ for the spinal cord (the average D_{mean} and $D_{0.1cc}$ was 6.59 Gy, 11.90 Gy in TOMO and 9.09 Gy, 11.31 Gy in VMAT, respectively) and D_{2cc} ($P < 0.05$) for the small intestine.

Machine units

The number of planned machine units was significantly longer for TOMO (3186.13 ± 638.04) than for VMAT (888.60 ± 124.70, $P < 0.001$) by an average of 3.6-fold.

IGRT

In the context of the patients' young age (median, 3.5 years) and corresponding poor compliance, image guidance was able to effectively control the positioning error of radiotherapy and constituted a necessary part of precise radiotherapy. The clinical application of this guidance is shown in Table 3.

DISCUSSION

Dosimetric comparison

Intensity-modulated arc therapy (IMAT) can be planned and delivered by means of several techniques. In this study, we evaluated the potential dosimetric advantages

TABLE 1 Comparison of target PTV dosimetric parameters between TOMO and VMAT for eight patients with neuroblastoma

Patient	Age (years)	Volume (cm^3)	Method	D_{min} (Gy)	D_{max} (Gy)	D_{mean} (Gy)	HI	CI	D_2 (Gy)	D_{95} (Gy)	D_{98} (Gy)
1	2	249.35	TOMO	16.89	20.75	19.88	1.05	0.86	20.82	20.18	19.40
			VMAT	12.18	20.21	19.158	1.11	0.90	20.78	18.67	17.02
2	6	428.72	TOMO	15.95	21.17	20.19	1.05	0.84	20.71	19.60	19.25
			VMAT	14.09	21.45	20.66	1.09	0.92	21.21	19.43	18.33
3	3	283.40	TOMO	14.10	21.13	20.00	1.04	0.83	20.45	19.62	19.30
			VMAT	12.71	21.60	20.64	1.09	0.92	21.25	19.47	18.62
4	4	131.44	TOMO	17.54	20.68	20.07	1.05	0.87	20.54	19.57	19.33
			VMAT	8.41	21.11	20.19	1.06	0.94	20.72	19.49	18.80
5	3	332.30	TOMO	14.51	21.05	20.38	1.05	0.91	20.83	19.83	19.47
			VMAT	11.62	21.39	20.15	1.06	0.95	20.68	19.50	18.93
6	9	620.88	TOMO	14.26	21.25	20.44	1.05	0.88	20.90	19.83	19.50
			VMAT	13.79	21.62	20.51	1.08	0.93	21.09	19.50	18.82
7	7	466.81	TOMO	16.91	20.59	19.82	1.05	0.86	21.16	20.18	19.20
			VMAT	13.16	21.60	20.16	1.08	0.93	21.08	19.50	18.71
8	2	339.78	TOMO	16.15	21.16	20.11	1.05	0.90	20.67	19.54	19.32
			VMAT	14.78	21.09	20.23	1.06	0.95	20.69	19.50	18.87
P				0.014	0.113	0.523	0.003	<0.001	0.166	0.049	0.008

TOMO, tomotherapy; VMAT, volumetric-modulated arc therapy; CI, conformity index; HI, heterogeneity index.

TABLE 2 Comparison of OARs dosimetric parameters between TOMO and VMAT for eight patients with neuroblastoma

Patient	Method	Left kidney		Right kidney		Liver		Spinal cord		Small intestine			Stomach		Spleen	
		D_{mean} (Gy)	D_{33} (Gy)	D_{mean} (Gy)	D_{33} (Gy)	D_{mean} (Gy)	D_{33} (Gy)	D_{mean} (Gy)	$D_{0.1cc}$ (Gy)	D_{mean} (Gy)	D_{50} (Gy)	D_{2cc} (Gy)	D_{mean} (Gy)	D_{50} (Gy)	D_{mean} (Gy)	D_{50} (Gy)
1	TOMO	4.32	3.93	7.63	7.61	6.65	8.65	5.59	13.11	9.14	8.49	20.21	9.32	9.38	5.67	5.81
	VMAT	7.86	9.24	5.18	4.66	6.08	8.15	5.25	10.02	9.48	8.56	20.59	9.06	9.23	8.39	9.14
2	TOMO	4.93	3.86	17.33	19.91	8.97	9.77	10.59	17.92	10.01	9.07	20.21	13.21	12.72	5.95	6.19
	VMAT	4.89	3.99	16.02	20.82	7.63	6.87	14.11	18.23	10.28	9.75	21.04	14.48	14.49	6.74	6.19
3	TOMO	10.93	12.23	6.09	5.12	6.09	5.51	9.87	15.41	10.39	10.02	20.31	13.41	12.73	11.18	9.73
	VMAT	10.07	13.65	5.68	5.94	5.92	5.85	11.21	16.10	10.62	10.54	20.87	13.01	11.61	11.22	10.31
4	TOMO	2.35	1.01	2.43	0.75	1.45	1.32	2.17	4.26	8.91	8.23	20.07	N/A	N/A	N/A	N/A
	VMAT	2.46	2.43	0.56	0.43	0.72	0.96	5.17	8.32	9.46	9.42	20.45	N/A	N/A	N/A	N/A
5	TOMO	12.68	13.29	4.49	3.85	5.68	6.62	3.92	6.24	7.88	5.58	20.75	11.07	9.71	7.25	7.22
	VMAT	14.37	17.81	2.97	2.97	4.95	5.92	7.14	11.31	8.31	7.36	20.52	11.88	11.52	6.21	5.89
6	TOMO	3.81	3.02	14.11	18.53	8.41	7.88	5.06	10.15	7.74	5.39	20.78	11.64	10.82	7.87	7.55
	VMAT	3.05	3.06	12.11	18.03	7.82	7.50	8.65	10.61	8.64	8.77	21.05	11.58	10.84	8.76	8.52
7	TOMO	5.37	4.96	19.84	20.98	11.36	14.46	10.85	19.95	11.67	11.83	19.77	12.97	11.90	7.73	6.95
	VMAT	2.82	2.14	20.46	20.73	10.74	16.24	12.25	19.65	10.80	11.18	19.77	12.76	11.98	8.39	8.21
8	TOMO	8.80	8.67	9.03	8.87	4.65	9.09	4.65	8.14	12.29	12.09	20.53	7.01	6.05	6.99	7.13
	VMAT	6.96	7.30	7.41	7.78	4.34	5.62	8.92	12.26	12.76	13.20	20.68	7.92	8.51	6.52	6.33
P		0.904	0.310	0.007	0.256	0.001	0.238	0.003	0.190	0.334	0.422	0.040	0.352	0.209	0.301	0.351

OARs, organs at risk; TOMO, tomotherapy; VMAT, volumetric-modulated arc therapy; N/A, not applicable.

of TOMO versus VMAT for pediatric neuroblastoma. Previous research has shown that both TOMO and VMAT can produce plans with good coverage of PTV and acceptable sparing of OARs.[9] Although some dosimetric differences were significantly different, they remained only slightly different in terms of the actual dose.[10]

TABLE 3 IGRT solution for patients with neuroblastoma

Method	Frequency	Average time (min)	Scan mode
TOMO	Once a day	1.5–2.0	MVCT
VMAT	Once a day for the first three days of treatment	1.0–1.5	kV CBCT

IGRT, image-guide radiotherapy; TOMO, tomotherapy; VMAT, volumetric-modulated arc therapy; MVCT, megavoltage computed tomography; kV CBCT, kV cone beam computed tomography.

TOMO is the only radiotherapy device that uses the spiral CT scanning mode for tumor treatment.[11] This approach overcomes the limited rotation of traditional accelerators in other radiotherapy devices; thus, 360° focused irradiations can be realized. The multileaf collimator (MLC) and flattening filter free (FFF) energy modes used in TOMO can simultaneously enhance the target dose and reduce the dose to peripheral organs. In recent years, with development of MLC technology, an increasing number of 0.5-cm leaves have been used with accelerators. Compared with the 0.625-cm leaf width used in TOMO, the advantage in dose distribution is gradually reduced. Modern accelerators are high-efficiency radiotherapy devices with integrated image guidance and multiple motion management; they are equipped with 100–160 leaf MLC and FFF energy modes, which can provide efficient and precise treatment. Finally, the dosimetric comparisons of the two planning systems have many variables that may influence the results, especially with respect to target coverage and the sparing of OARs, the importance of nearby OARs, and the experience levels of dosimetrists and oncologists.[11,12]

Simulation and IGRT

External beam radiotherapy is widely used in various manners in the management of neuroblastoma.[7] In this study, the median patient age was 3.5 years; thus, patient compliance was poor during the treatment process, which constituted a challenge for the implementation of precise radiotherapy. The frequent movement of young patients can lead to treatment inaccuracy. All of the patients were immobilized with a children's body thermoplastic mask in the supine position with their arms extended upward. If necessary, sedative drugs should be used during the simulation and treatment process. In this study, half of the patients need sedative drugs in the simulation and treatment process. Image guidance can effectively control positioning errors in radiotherapy and constitutes a necessary component of precise radiotherapy. However, it requires a longer delivery time.

Clinical effectiveness and treatment costs

The length of treatment time is an important consideration. The advantages of reduced treatment time include better patient comfort and compliance, increased patient throughput, and enhanced image guidance. In addition, the treatment room is maintained at a constant temperature, typically between 20°C and 24°C. If the treatment time is excessive in length, patients may develop a chilled. TOMO had significantly more MUs, compared with VMAT, by an average of 3.6-fold; thus, it required longer treatment time. These results indicate that linear accelerators have an advantage in terms of treatment time.[13]

Furthermore, the cost of TOMO treatment is approximately 2–3-fold greater than the cost of VMAT; the extent of this difference varies among medical insurance systems. There is a high probability that the cost of treatment is the main consideration in choosing a treatment method.

In conclusion, both TOMO and VMAT planning techniques can provide high-quality treatment plans that are acceptable for clinical use. TOMO exhibited better D_{min}, D_{95}, D_{98}, and HI, but showed inferior CI. However, TOMO had significantly more MUs, compared with VMAT, and required longer treatment time. Finally, the cost of TOMO treatment is higher than the cost of VMAT. At present, there are not many researches in the field of radiotherapy for children's tumors. It is hoped that more studies will be used to prove the effect of radiotherapy, especially how pediatric neuroblastoma patients can achieve greater benefits.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

1. Castleberry RP, Kun LE, Shuster JJ. Radiotherapy improves the outlook for patients older than 1 year with Pediatric Oncology Group stage C neuroblastoma. J Clin Oncol. 1991;9:789-795.
2. Bradfield SM, Douglas JG, Hawkins DS, Sanders JE, Park JR. Fractionated low-dose radiotherapy after myeloablative stem cell transplantation for local control in patients with high-risk neuroblastoma. Cancer. 2004;100:1268-1275.
3. De Ioris MA, Crocoli A, Contoli B, Garganses MC, Natali G, Toma P, et al. Local control in metastatic neuroblastoma in children over 1 year of age. BMC Cancer. 2015;15:79.
4. Graf R, Wust P, Hildebrandt B, Gögler H, Ullrich R, Herrmann R, et al. Impact of overall treatment time on local control of anal cancer treated with radiochemotherapy. Oncology. 2003;65:14-22.
5. Geurten C, Geurten M, Hoyoux C, Lebrethon MC. Endocrine consequences of neuroblastoma treatment in

children: 20 years' experience of a single center. J Pediatr Endocrinol Metab. 2019;32:347-354.
6. Breneman JC, Donaldson SS, Constine L, Mercharn T, Marcus K, Paulino AC, et al. The Children's Oncology Group radiation oncology discipline: 15 years of contributions to the treatment of childhood cancer. Int J Radiat Oncol Biol Phys. 2018;101:860-874.
7. Arumugam S, Manning-Cork NJ, Gains JE, Boterbergy T, Gaze MN. The evidence for external beam radiotherapy in high-risk neuroblastoma of childhood: A systematic review. Clin Oncol. 2019;31:182-190.
8. Kalet AM, Richardson HL, Nikolaisen DA, Cao N, Lavilla MA, Dempsey C, et al. Dosimetric comparison of single-beam multi-arc and 2-beam multi-arc VMAT optimization in the Monaco treatment planning system. Med Dosim. 2017;42:122-125.
9. Vernat SS, Ali D, Puyraveau M, Viard R, Lisbona A, Fenoglietto P, et al. Is IMAT the ultimate evolution of conformal radiotherapy? Dosimetric comparison of helical tomotherapy and volumetric modulated arc therapy for oropharyngeal cancer in a planning study. Phys Med. 2014;30:280-285.
10. Gleeson I, Rose C, Spurrell J. Dosimetric comparison of helical tomotherapy and VMAT for anal cancer: A single institutional experience. Med Dosim. 2019;44:e32-e38.
11. Mackie TR. History of tomotherapy. Phys Med Biol. 2006;51:R427-R453.
12. Arumugam S, Xing AT, Young T, Thwaites D, Holloway L. Comparison of three commercial dosimetric systems in detecting clinically significant VMAT delivery errors. Phys Med. 2016;32:1238-1244.
13. Gleeson I, Rose C, Spurrell J. Dosimetric comparison of helical tomotherapy and VMAT for anal cancer: A single institutional experience. Med Dosim. 2019;44:e32-e38.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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