https://doi.org/10.5392/IJoC.2017.13.4.012

The Effectiveness of Volumetric Modulated arc Radiotherapy to Treat Patients with Metastatic Spinal Tumors

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ABSTRACT

Among the possible stereotactic body radiation therapy (SBRT) modalities used to treat patients with metastatic spinal tumors, this study compared Cyberknife, tomotherapy, and volumetric modulated arc radiotherapy (VMAT). We established treatment plans for each of them modality and quantitatively analyzed the dose evaluation factors of the dose-volume histogram (DVH) for all spinal bones, focusing on the tumor and spinal cord, in order to examine the usefulness of VMAT. For the treatment planning dose, the mean dose (D_{max}) and $D_{5\%}$ showed statistical differences in the target dose, but no difference was shown in the spinal cord dose. For the DVH indices, tomotherapy showed the best performance was the best in terms of uniformity index, while VMAT showed better performance was better than the other two modalities in terms of the conformity index and the dose gradient index. VMAT had a much shorter treatment time than Cyberknife and tomotherapy. These findings suggest that VMAT FFF is the most effective therapy for SBRT of patients with metastatic spinal tumors for whom a high dose of radiation is prescribed.

***Key words**: Volumetric Modulated Arc Radiotherapy, Cyberknife, Tomotherapy, Spinal Tumors*, S*tereotactic Body Radiation Therapy.*

1. INTRODUCTION

Metastatic tumors are the most common bone tumors and their main primary tumors include breast cancer, prostate cancer, lung cancer, renal cancer, thyroid cancer, and liver cancer. The most frequent site of bone metastasis is the spine [1]. Stereotactic body radiotherapy (SBRT) used to treat metastatic spinal tumors has its downsides because the radiation dose to the spinal cord should be limited owing to the high sensitivity of the spinal cord to radiation. However, radiotherapy is very effective in relieving pain and local control as it delivers a high dose of radiation to the target site. This therapy is also widely used because it reduces occurrences of complications [2], [3]. SBRT delivers a high dose of radiation in 1 to 5 fractions. The high radiation dose per fraction increases the biological effective dose (BED) in tumor cells. However, caution is required because normal tissues are also exposed to high doses of radiation [4]. New radiation therapy technologies, such as intensity modulated radiation therapy (IMRT) and image-guided radiation therapy (IGRT), are necessary to deliver high doses of radiation to the target while minimizing the radiation dose delivered to other major organs surrounding the spine. With the development of various radiation therapy devices and treatment planning systems, SBRT is being performed using various modalities [5]-[7]. The latest trend is the use of volumetric modulated arc therapy (VMAT) that applies a flattening filter-free (FFF) technique [8], [9]. Among possible SBRT modalities, this study compared Cyberknife, tomotherapy, and VMAT. We established treatment plans for each of them and quantitatively analyzed dose evaluation factors of the dose volume histogram (DVH) for all spinal bones, focusing on the tumor and spinal cord, in order to examine the usefulness of VMAT that applies the latest FFF technique in treating patients with metastatic spinal tumors.

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Manuscript received Jun. 08, 2017; revised Dec. 22, 2017; accepted Dec. 22, 2017

2. MATERICL AND METHODS

2.1 Study Subjects

The subjects of this study were 16 patients with metastatic spinal tumors who underwent radiation therapy from 2014 to 2015 in A hospital. The locations where tumors were found were the cervical vertebrae (3 patients), the thoracic vertebrae (7 patients), the lumbar vertebrae (4 patients), and the sacral vertebrae (2 patients). For the simulation, we made a fixation system using the Bodyfix system (Medical Intelligence, Elekta, Germany), Extended Wingboard (CIVICO, MedTec, USA), and S-plate (MedTec, Orange City, IA, USA) to fix the posture of the patients. Using CT-Simulator (SOMATOM Sensation Open 16 MDCT, Siemens AG, Erlangen, Germany), computed tomography (CT) images were acquired, and the acquired CT images were sent to the radiation treatment planning system through the Digital Image Communication in Medicine.

2.2 Treatment Plan

The radiation dose prescription was set at 18 Gy to the gross tumor volume (GTV) so that 90% or more of the target volume was irradiated with the prescription dose. Radiation dose limits for the overall spinal cord and the partial spinal cord were set so that the maximum 0.035 cc received less than 14 Gy (Table 1).

Table 1. GTV & Spinal cord dose constraints used in SBRT

Reference	Goal	Constraints
GTV	$V_{95\%_{pres}}$>95%	18 Gy/ 1 fx
	D_{max}<130%$_{pres}$	$D_{90\%}$ = 18 Gy
		D_{max}= 120%$_{pres}$
Spinal cord	D_{max}<14 Gy	D_{max} = 10 Gy
Others		D_{max} = 12 Gy

The radiation treatment planning system modalities for the SBRT planning are cyberknife (MultiPlan System Ver 5.1.3, Accuray.inc, USA), tomotherapy (TOMO HD version 2.0.4 Licensed, TomoTherapyInc, USA) and VMAT(VERSA HD, RAYSTATION-RTP system Ver4.5.1, Raysearch laboratories AB, SWEDEN). For the Cyberknife treatment planning, 1 or 2 fixed cones were used in the full path mode that does not limit directions; the size of the cone was 10 to 40 mm. For tomotherapy treatment planning, a 2.5 cm dynamic jaw was used; the pitch was set at 0.123–0.143, and 2 fractions were performed per day. For VMAT, an FFF beam with 10 MV of energy was used, 120 segments were set for 1 arc, and its dose rate was variable and up to 2400 monitor unit (MU) per minute.

2.3 Treatment Planning Comparison

For the evaluation of the SBRT planning, doses to the target volume and organs at risk (OAR) were compared and analyzed using the DVH and isodose curves. For the dose comparison factors of the target volume, maximum dose (D_{max}), coverage dose of 5% of the target ($D_{5\%}$), planned volume of prescription dose (V_{Rx}), planned volume of 95% prescription dose ($V_{95\%}$), and planned volume of 98% prescription dose ($D_{98\%}$) were calculated and their averages were calculated as well. For the spinal cord, the dose measured when the volume reached 0.035 cc was defined as the maximum dose, and the means of the D_{max}, volume percentage over 10 Gy (V_{10}) and volume percentage over 7 Gy (V_7) were calculated.

Using DVH indices (uniformity, conformity, and dose gradient), treatment plans were evaluated inside, within the boundaries, and outside of the target structure. The MU and treatment time of each modality were also measured and compared.

2.4 Statistical Analysis

The SPSS 20.0 program (for Windows, NY, IBM Co., USA, Chicago) was used for statistical analysis. For the significance test for treatment planning dose, DVH indices, and treatment time for each modality (Cyberknife, tomotherapy, and VMAT), both parametric and non-parametric tests were conducted. The non-parametric test used was the Kruskal-Wallis test; the parametric test, used was ANOVA. The level of significance was set at 0.05 or less.

3. RESULTS

Using the DVH and isodose curves, treatment plans for the target and the spinal cord were compared. The maximum value of the tumor size was 181.9 cc, the minimum value was 6.5 cc, and the mean was 40.5±46.2 cc.

3.1 Dose Comparison of Treatment Plans

According to the dose analysis of the target volume, the mean D_{max} was 23.9±1.1 Gy for Cyberknife, 22.6 ±1.2 Gy for tomotherapy, and 23.7±1.0 Gy for VMAT. The mean $D_{5\%}$ was 23.2±0.9 Gy for Cyberknife, 21.6±1.0 Gy for tomotherapy, and 22.5±0.6 Gy for VMAT, showing statistically significant differences in both non-parametric and parametric tests. In the means of the target volume's $V_{Rx\%}$ and $V_{95\%}$, tomotherapy showed the highest values at 91.1±3.3% and 96.1±3.3%, respectively, showing significant differences in the non-parametric test only. V_{Rx}, V_{95}, and V_{98} did not show statistically significant differences (Table 2).

Table 2. Target dose

Reference	CYBER	TOMO	VMAT	Non-parametric test		Parametric test	
				x^2	p	F	p
D_{max}(Gy)	23.9±1.1	22.6±1.2	23.7±1.0	7.778	0.020	5.718	0.006
$D_{5\%}$(Gy)	23.2±0.9	21.6±1.0	22.5±0.6	16.239	0.000	13.462	0.000
$D_{98\%}$(Gy)	16.1±0.8	16.4±1.2	16.6±0.4	2.344	0.310	1.454	0.244
$V_{RX\%}$(cc)	89.9±1.7	91.1±3.3	89.1±2.2	7.583	0.023	2.544	0.090
$V_{95\%}$(cc)	95.2±2.1	96.1±3.3	96.0±1.6	1.190	0.552	0.650	0.527

The mean dose (D_{max}) to the spinal code was the highest for Cyberknife (10.9±1.6 Gy) followed by VMAT and tomotherapy. Both V_{10} and V_7 of the spinal code were the highest for VMAT followed by Cyberknife and tomotherapy but they showed no statistically significant differences (Table 3).

Table 3. Spinal cord dose

Reference	CYBER	TOMO	VMAT	Non-parametric test		Parametric test	
				x^2	p	F	p
D_{max}	10.9±1.6	10.3±1.2	10.6±1.9	2.851	0.240	0.701	0.501
V_{10}	0.07±0.2	0.02±0.1	0.19±0.7	3.718	0.156	0.764	0.472
V_7	1.2±1.2	0.6±0.8	1.2±1.5	1.926	0.382	1.270	0.291

3.2 DVH Index Comparison

Modalities were compared with each other using DVH indices. An index value reaching 1 means a stable dose distribution inside the target. In the uniformity index (UI_{eff}) that compares dose distributions inside the target structure, tomotherapy showed the most even distribution at 1.32±0.2, followed by VMAT at 1.35±0.0 and Cyberknife at 1.44±0.1. In the conformity index of prescription (CI_{Rx}) that indicates dose distribution in the boundaries of the target structure, VMAT was the best at 0.81±0.1, followed by Cyberknife at 0.74±0.1 and tomotherapy at 0.72±0.1. In the dose gradient index of prescription ($DGI_{30\%}$) that compares dose distribution outside the target structure, VMAT was the best at 2.15±0.6, followed by Cyberknife and tomotherapy. This indicates there are statistically significant differences in the uniformity index and the conformity index (Table 4).

Table 4. Plan comparison: DVH index

Reference	CYBER	TOMO	VMAT	Non-parametric test		Parametric test	
				x^2	P	F	P
Ui_{eff}	1.44±0.1	1.32±0.2	1.35±0.0	6.285	0.043	4.758	0.013
CI_{Rx}	0.74±0.1	0.72±0.1	0.81±0.1	7.898	0.019	3.402	0.042
$DGI_{30\%}$	2.4±0.9	2.5±0.7	2.1±0.6	2.002	0.367	0.943	0.397

3.3 Treatment Time Comparison

Cyberknife showed the highest MU at 17,103.3±6,820.1 and the longest treatment time at 45.9±17.1 minutes on average. Tomotherapy ranked second in both MU and treatment time. The MU of VMAT was 5,132.9±1,020.4, which is not much different from the MU of tomotherapy. However, the treatment time of VMAT was 3±1.1 minutes, significantly different from that of Cyberknife and tomotherapy (Table5).

Table 5. Plan comparison: Delivery time

Reference	CYBER	TOMO	VMAT	Non-parametric test		Parametric test	
				x^2	p	F	p
Delay-Time(min)	45.9±17.1	15.6±3.2	3.0±1.1	41.850	0.000	77.123	0.000

4. DISCUSSION

SBRT is a treatment method that delivers a high dose of radiation to a small target area in 3~4 fractions. After selecting the location of a small-sized target legion accurately, it delivers a high dose of radiation to this small region. Unlike stereotactic radiosurgery, however, SBRT is delivered in 3~4 fractions to prevent exposure to a high dose of radiation at one time. Therefore, SBRT has been frequently used for the treatment of lesions in the lung and spine [10].

Among the SBRT techniques used for patients with spinal tumors, this study compared the 3 latest radiotherapy planning modalities of Cyberknife, tomotherapy, and VMAT and compared them. In the study by Kang et al. [11] on a dose comparison of Cyberknife and tomotherapy to treat patients with metastatic spinal tumors, tomotherapy had a lower dose of radiation, a shorter treatment time, and a longer MU compared with Cyberknife. The present study had consistent results except for MU; we found that MU is longer for Cyberknife than for tomotherapy. This difference is due to different parameters and target sizes between the two studies. The study by Krzysztof Ślosarek et al. [12] compared radiation doses of Cyberknife, tomotherapy, and VMAT for prostate radiotherapy and found that Cyberknife produced the highest dose of radiation and tomotherapy the lowest dose. This is consistent with the findings of the current study. The limitations of this study are that the number of cases is small and the study using more data is needed.

There has been considerable research on the usefulness of Cyberknife. It has been considered a method that can be applied to SBRT or stereotactic radiosurgery and can replace surgery for all lesions. However, the findings of the present study suggest that other radiotherapy modalities such as tomotherapy or VMAT are also effective candidates for treating metastatic spinal tumors by SBRT.

5. CONCLUSION

The comparison between SBRT modalities for the treatment of patients with metastatic spinal tumors produced the following results. In treatment planning dose, D_{max} and $D_{5\%}$ showed statistical differences in the target dose(< 0.05), but no difference in the spinal cord dose. In DVH indices, tomotherapy performance was the best in terms of the uniformity index, but VMAT performance was better than the other two modalities in in terms of the conformity index and dose gradient index. In treatment time, VMAT(3.0±1.1 min.) showed a much shorter treatment time than Cyberknife(45.9±17.1 min.) and tomotherapy(15.6±3.2 min.). These findings suggest that VMAT FFF is the most effective therapy for SBRT of patients with metastatic spinal tumors for whom a high dose of radiation is prescribed.

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