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Dosimetric Effects of Rotational Setup Error in Volumetric Modulated Arc Radiotherapy on Brain Tumor Patients

Hyo-Kuk Park[1], Jae-Hwan Cho[2], Sungchul Kim[3]*

1. Department of Radiation Oncology, Yonsei Cancer Center, Seoul, South Korea
2. Department of Radiological Technology, Ansan University, Ansan, South Korea
3. Department of Radiological Science, Gachon University Medical campus, Incheo, South Korea

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ABSTRACT

Introduction: This study examined the dosimetric effects based on the rotational setup error to correct patient setup errors occur during volumetric modulated arc radiotherapy (VMAT) for brain tumor patients.

Material and Methods: This study included 1129 cases of cone beam computed tomography (CBCT) images obtained from 46 brain tumor patients, who experienced VMAT and used the 6DoF (degree of freedom) treatment couch. The dosimetric effects regarding the application of the rotational setup error were examined by comparing the treatment plans.

Results: The mean patient setup errors at the lateral (X-axis), longitudinal (Y-axis), and vertical (Z-axis) directions were 0.1±1.4, 0.0±1.1, and -0.4±1.2 mm, respectively. The pitch, roll, and yaw were -0.29±0.61°,-0.42±0.98°, and -0.53±0.69°, respectively. When an absolute value was taken for the setup error, the mean error was 1.06±0.14 mm at the three translation directions, and the error of rotation was 0.82±0.14°, showing a larger error than that of translation. In terms of the mean dose difference by each region of interest (ROI) before and after correcting for the rotational setup error on the treatment plan, Brain_max was 2.17 Gy, and Brain_mean was 0.28 Gy, whereas the maximum and mean of Brain_stem were -3.58 and -4.43 Gy, respectively. These findings suggested a dose difference according to the correction of the rotational setup error.

Conclusion: This study indicated that the dose effect is influenced by the rotational setup error in VMAT of brain tumor patients. Moreover, the 6DoF positional correction could reduce the positional uncertainties and deliver a more accurate dose.

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Introduction

Although a linear accelerator is the most widely used radiation therapy device, more developed devices, such as the CyberKnife and tomotherapy are now available. These developments lead to more advanced methods in treatment (e.g., intensity modulated radiotherapy, stereotactic body radiation therapy, image-guided radiation therapy, and respiration-gated radiation therapy) [1]. The development of radiotherapy techniques has allowed the concentration of high-dose radiation on the tumor site which leads to a higher probability of local control and the prevention of metastatic spread by recurrence. Consequently, the overall treatment rates improve, and the side effects of radiation therapy can be reduced by decreasing the radiation dose to the normal tissues [2].

The problem with the radiation therapy for brain tumor patients is that major normal organs (e.g., brainstem and optic chiasm) are adjacent to the target. Therefore, with regard to the error at treatment, there is a need for higher accuracy and precision during intensity modulated radiotherapy (IMRT) or stereotactic radiation therapy because of the small margin at the planning target volume (PTV) [3,4]. To improve the quality of radiotherapy, the International Commission on Radiation Units and Measurements (ICRU) report No. 62 [5] defined the gross tumor volume as the volume of the tumor, the clinical target volume (CTV), which is expected to be minutely infiltrated, and the internal target volume (ITV), including the internal motion of CTV. The ICRU also suggested the definition of PTV which includes the allowable error of the mechanical accuracy of the equipment and the reproducibility error of the daily patient setup [5].

In general, the patient setup error is corrected using an image guide during radiation therapy. If the error does not exceed the allowable range, the correction is made by moving the couch. The HexaPOD couch (HexaPOD™ evo RT System, Elekta, Stockholm, Sweden) is a table system for radiation therapy that can be adjusted for all six directions,

**Corresponding Author:* Tel: +82-32-820-4361; Email: ksc@gachon.ac.kr

including the front, back, left, right, and slope upon a patient setup correction through an image guide. Similar to the HexaPOD couch, many studies of translational and rotational errors have been conducted using the six degrees of freedom (6DoF) couch to adjust the same patient setup similar to the one in the simulation during radiation therapy [6-,7]. Most studies on the patient setup error in radiation therapy for brain tumor patients have mainly focused on the errors and descriptive statistics [8]. In a study on the dose effect of the patient's postural error, the CT images collected with and without rotational error are obtained and compared with the treatment plan. Or, the images are corrected with a moderate rotational value to re-establish a treatment plan, and then they are compared with the original treatment plan [9]. On the other hand, these methods do not reflect the entire radiotherapy process but are limited to the results at a certain point in time due to the prediction of the specific split treatment time or the mean of total error.

This study examined the patient setup error based on the HexaPOD couch calibration data obtained from the patient setup error and cone beam computed tomography (CBCT) image over the entire treatment process on brain tumor patients. In addition, the dosimetric effects were investigated based on the patient rotational setup error over the entire treatment period with deformable image registration using the atlas-based automatic segmentation (ABAS) of MIM software (MIM Software Inc., Cleveland, OH) and the ART assist function of adaptive radiation therapy (ART).

Materials and Methods

Study subjects

The study population consisted of brain tumor patients referring to the Department of Radiation Oncology at Yonsei hospital from November, 2014 to February, 2016. These patients used the HexaPOD couch and experienced volumetric modulated arc radiotherapy (VMAT) in their treatments. The exclusion criteria were patients who required sedation, pediatric patients aged 10 years or younger, and patients with involuntary movements. First, to analyze the patient setup error, the setup error data were obtained from the CBCT images and the correction values of 1129 cases of 46 patients(1129 CBCT images), who underwent CBCT before each treatment during the entire treatment period. The mean age of the patients (i.e., 28 males and 18 females) was 48 (11~92) years old. The number of treatments was within the range of 10-30, and the mean prescribed dose of radiation therapy was 52.14 Gy. Second, 6 patients were selected randomly from the 46 patients for whom the setup error analysis had been performed to compare the treatment plan according to the rotational setup error. Finally, this study targeted 360 ART plans, which were established based on the deformable image registration with or without a rotational error.

Study Method

Computer simulation

The three-dimensional images of the targeted patients were obtained through a simulation which was performed by computed tomography (CT; Aquilion LB, Toshiba, Tochigi, Japan) based on the treatment plans. Each patient was placed in the supine position, and his head was fixed using a thermoplastic mask for the positional reproducibility of the patient setup. The CT reference line was marked on the outer surface of the thermoplastic mask. The test conditions for CT in the brain tumor patients included the use of a head-brain filter, a 120-kVp tube voltage, and a 250-mAs tube current. The slice thickness was basically 1 mm due to the image quality. The 1-mm or 3-mm image thickness was used through a reconstruction, if necessary, and the image was obtained with a pitch of 0.938. The scan range of CT was sufficient to include the tip of the skull to the distal end of the mandible. A wide field of view of 500-mm was used to grasp the position of the table during treatment planning. The CT scans were performed after injecting 100~150 cc contrast agents to the patient.

Treatment plan

Regarding the setup error, the mean total dose of the patients was 52.14 Gy within 10-30 treatment sessions. On the other hand, patients who experienced 30 treatments with a prescribed dose of 60 Gy were selected randomly to investigate the dosimetric effects by the patient setup error. The treatment plan was established, in which 95% of the prescribed volume of the PTV was greater than 98% of the volume. Due to the fact that the maximum dose was limited, a dose of 70 Gy or less was included in the 2% of the PTV; and the remaining PTV (i.e., 98%) was 60 Gy or less. The dose was prescribed according to the tumor volume and the surrounding organs.

Cone beam computed tomography

According to the established radiation therapy plan, each patient was placed in the supine position, which was similar to that of a simulated CT before radiation therapy, and a thermoplastic mask was placed on the patient to fix the posture. The central point on the mask was marked and aligned with the treatment room laser for the setup. CBCT was conducted for each treatment to confirm the accuracy of the tumor site and patient posture before the treatment. The CBCT images were acquired through XVI (X-ray Volume Imaging v5.0.2 b72. Elekta, Stockholm, Sweden), and the scanning conditions included a 180°/min gantry rotation speed, a 100-kVp tube voltage, and a 36.6-mAs tube current. A total of 366 images (frames) were captured by 200° gantry rotation with a direction range of 70°-230°. As Figure 1 shows, the S20 kV collimator was used, and the kV panel setup was small. Image registration was performed between the CT simulation image and the CBCT image. The clipbox defining the region of interest for image registration was confined to the skull, specifically the treatment area. The bone (T+R) method was selected for image registration centering on the clipbox to allow automatic registration. In terms of the correction of the setup error, the HexaPOD mode was used to correct the three directions of translation and the three directions of rotation. An additional adjustment was performed manually when necessary (Fig. 2).

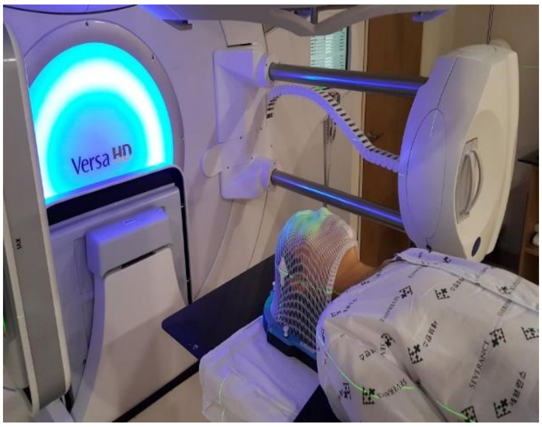

Figure 1. Setup for brain tumor patients using CBCT and Hexapod Couch

Patient setup error analysis

The results of the current study were obtained from the analysis of 1129 CBCT images from brain tumor patients, who experienced HexaPOD couch regarding the corrected values for the translational errors (x, y, and z) and rotational errors (roll, pitch, and yaw) per patient and per treatment. Descriptive statistics (e.g., mean and standard deviation) were measured through the corrected data recorded, whereas the 3D vector values, systematic error (Σ), and random error (σ) were obtained using x, y, and z. The boundary of the PTV was calculated by considering the patient setup error. The vectors of the corrected values for the setup error in the lateral (X-axis), longitudinal (Y-axis), and vertical (Z-axis) directions are as follows:

$$(x^2 + y2 + z^2)^{1/2} \quad (1)$$

According to Remeijer et al. [10], the descriptions on the systematic error (Σ) and random error (σ) were as follows:

$$\mathrm{N} = \sum_{p=1}^{P} Fp \quad (2)$$

Where, p denotes to each patient, and F_p measures fractions for each patient's treatment. Therefore, *N* refers to the total number of measured fractions

The mean value of the total motions of the patient along the coordinate axis can be expressed as:

$$\mathrm{N} = \frac{1}{N}\sum_{p=1}^{P}\sum_{f=1}^{Fp} x_{\mathrm{pf}} \quad (3)$$

Where, x_{pf} signifies the measured patient setup error for each fraction.

For the first component in the change in the mean value, the standard deviation of the random error is as follows:

$$\sigma_p = \sqrt{\frac{1}{F_{\mathrm{p}-1}}\sum_{f=1}^{Fp}(x_{\mathrm{pf}} - m_{\mathrm{p}})^2} \quad (4)$$

Where, m_p is the mean of the patients.

$$m_p = \sum_{f=1}^{Fp}\frac{x_{\mathrm{pf}}}{Fp} \quad (5)$$

Where, σ refers to the mean square root of each standard deviation

$$\sigma = \sqrt{\frac{1}{N-P}\sum_{p=1}^{P}(F_{\mathrm{p}} - 1)\cdot\sigma_p^2} = \sqrt{\frac{1}{N-P}\sum_{p=1}^{P}\sum_{f=1}^{Fp}(x_{\mathrm{pf}} - m_{\mathrm{p}})^2} \quad (6)$$

The second component is the systematic error, which is the mean of the errors that occurred during the entire treatment period, and is as follows:

$$\Sigma = \sqrt{\frac{P}{N(P-1)}\sum_{p=1}^{P}F_p(m_{\mathrm{p}} - M)^2} \quad (7)$$

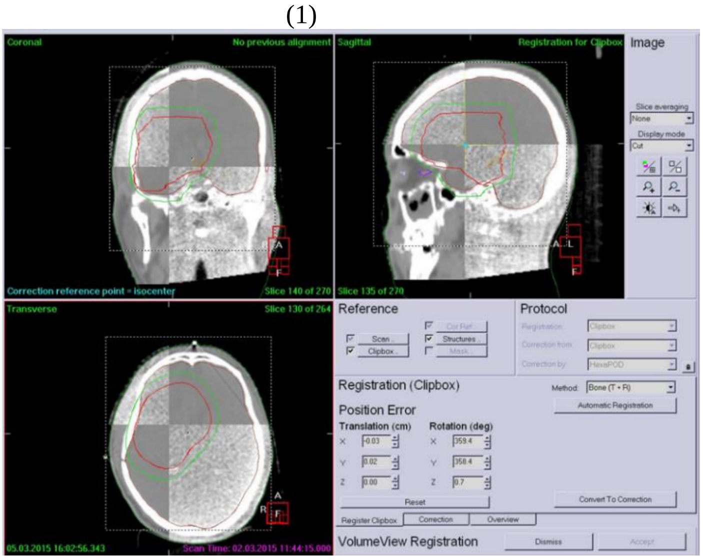

Figure 2. Planning CT to CBCT image registration

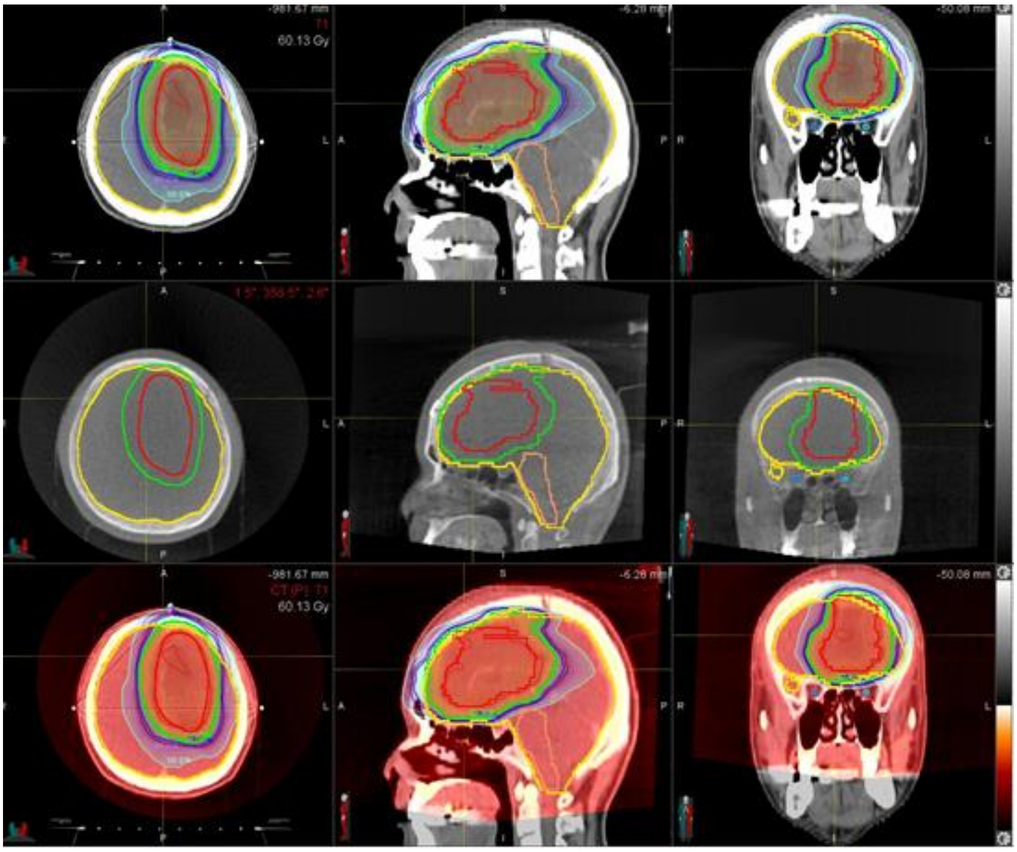

Figure 3. Comparison of the radiation treatment planning of brain tumor patients using MIM software

Comparison of the treatment plan before and after correcting the rotational setup error

Before comparing the dose in the treatment plan for each treatment fraction based on the patient rotational setup error, the ABAS function of the MIM Software was used to draw the ROI under the same conditions. Moreover, the researcher saved the brain CT images of 60 other patients, who were not the subjects of this study, in the MIM in advance. Based on this, 6 of the 46 patients, who were subjects of this study, were selected randomly. For each patient, 180 ROIs for 30 treatment fractions were divided into 2 cases, with and without a rotation error, thereby reproducing 360 CBCT images. The ART Assist™ 6.5 of MIM Software has been upgraded to allow adjustments in three directions of translation and three directions of rotation in the CT images. The dose-volume histogram (DVH) of the corresponding fraction could be obtained by transferring the dose distribution in the original treatment plan to the CBCT image, in which the ROI was reproduced through ABAS. This enables a comparison of the dose distribution of the actual ROI caused by the patient setup error during the entire treatment period. On the other hand, the range of ROI that could be identified was selected because the quality of CBCT image was much lower than that of the CT simulation. There were three steps to compare the treatment plan using the ART Assist™ 6.5. First, DVH and isodose curve were obtained through 180 CBCT images that had been adjusted by reflecting the corrected values of the setup errors for the three directions of translation and three directions of rotation to track the dose for the ROI. Second, DVH and isodose curve were obtained from the 180 CBCT images, for which only the three directions of translation were reflected to track the dose for the ROI (Fig. 3). Third, the treatment plan was compared by obtaining the difference in the dose values of the ROIs before and after applying the corrected values for the patient rotational setup errors.

Statistical Analysis

The data in this study was statistically analyzed by employing SPSS (version, 20). Descriptive statistics were calculated for the six directions of translational errors (x, y, and z) and rotational errors (roll, pitch, and yaw) using 1129 CBCT data. The correlations were tested using the Spearman's rank correlation coefficient from the result of the dose difference in the ROI by comparing the treatment plan before and after correcting the rotational setup errors.

Results

Patient Setup Error Analysis Results

Regarding setup errors, the analysis of the results obtained from comparing 1129 CBCT images of 46 patients with the CT simulation images of each patient, revealed a mean translational error of 0.1±1.4 mm, 0.0±1.1 mm, and -0.4±1.2 mm in the lateral, longitudinal, and vertical directions, respectively (Table

1). The means were recalculated by taking the absolute values for the setup errors, considering that negative values could exist due to the nature of the setup error. The results indicated that the mean translational errors were 1.1 mm, 1.1 mm, and 1.0 mm in the lateral, longitudinal, and vertical directions, respectively, showing an error of approximately 1 mm for each direction. In the case of the rotational error, the mean of the absolute values for the pitch, roll, and yaw were 0.66°, 1.01°, and 0.81°, respectively. This shows that the mean absolute values of the translational and rotational errors were relatively higher than the general mean values. In terms of the absolute value of the largest error, the maximum values of the translational error were 5.3 mm, 3.3 mm, and 4.5 mm in the lateral, longitudinal, and vertical directions, respectively. In the case of the rotational error, the maximum errors for the pitch, roll, and yaw were 1.81°, 2.63°, and 2.16°, respectively. The mean of the vectors of the patients was 0.19 cm, and the 3D vector value for the 50% actual frequency was 0.17 cm. The maximum value of the vector was 4.3 cm, and the minimum value was 0.4 cm (Fig. 4, & 5).

In the systematic error of translation, the maximum was 0.2 mm in the longitudinal direction, and the random error was 0.3 mm for both the lateral and vertical directions. On the other hand, the difference in the values of the three directions was not large (0.1 mm). Regarding all directions of rotation, the largest among the systematic and random errors were 0.98° and 1.05° in the roll direction, respectively (Table 2).

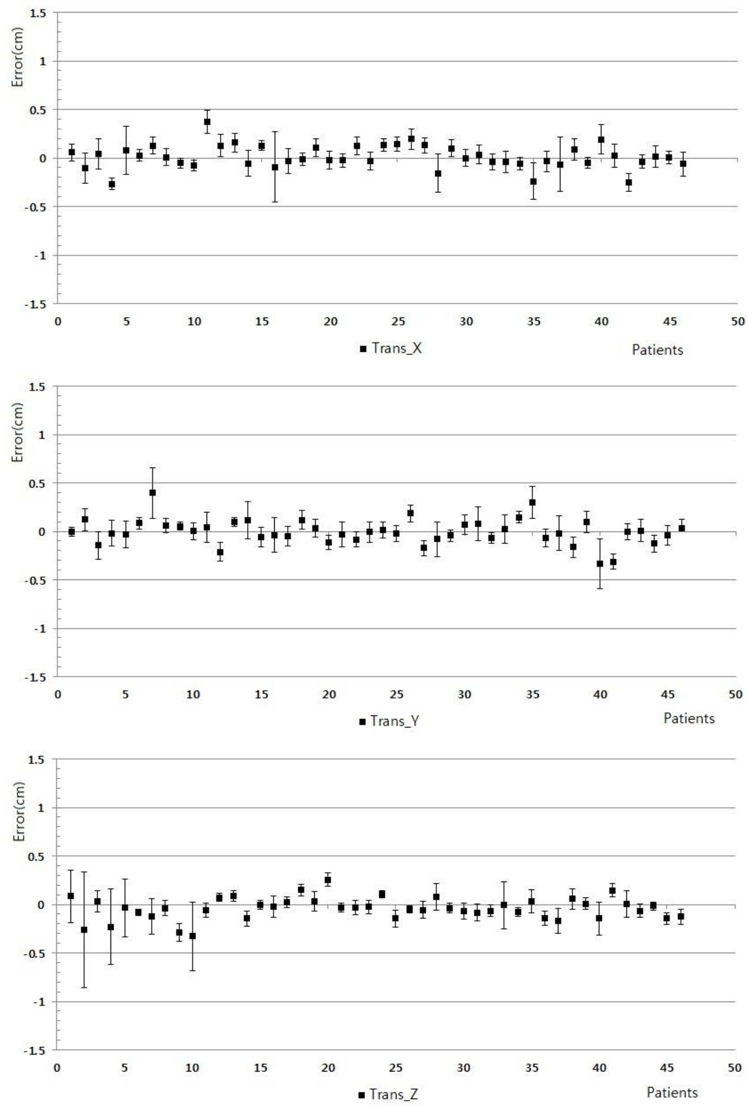

Figure 4. Mean±SD of the individual patient set-up corrections for brain in translation. X-axis: Patients, Y-axis: Error (cm)

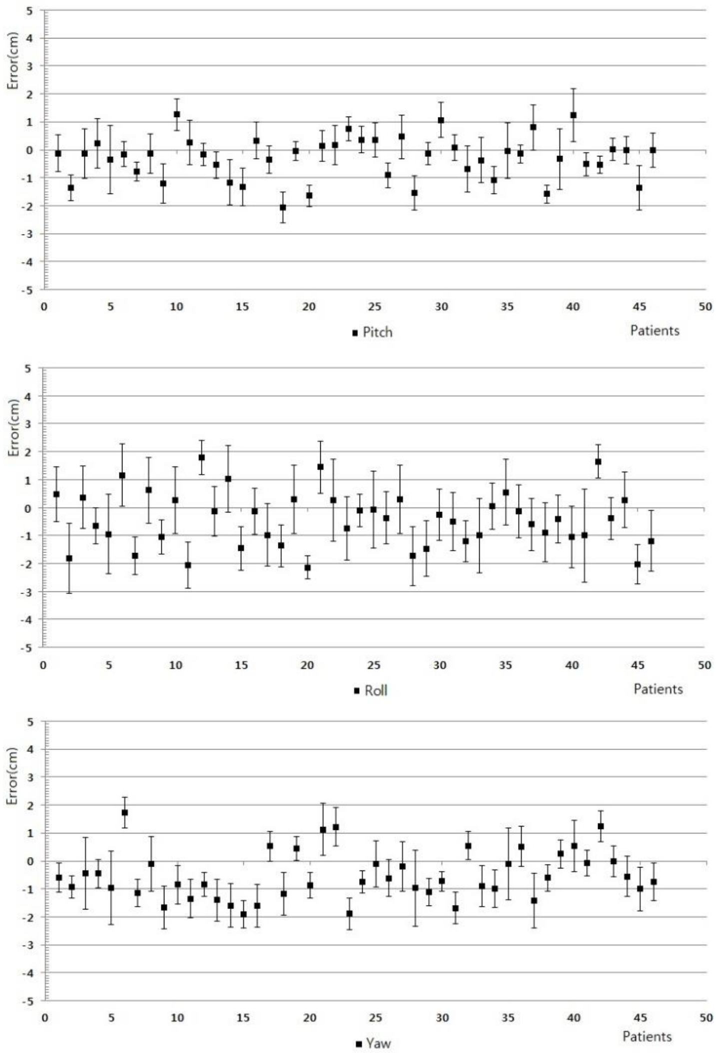

Figure 5. Mean±SD of the individual patient setup corrections for brain in rotation. X-axis: Patients, Y-axis: Error (cm)

Table 1. Descriptive Statistical analysis of the overall translational set-up errors

	Translation(mm)			
	Lateral(x)	Longitudinal(y)	Vertical(z)	3D vector
RMS＊	1.8	1.6	1.6	2.8
SD†	1.4	1.1	1.2	2.1
SE‡	0.3	0.2	0.2	0.5
AVE§	0.1	0	－0.4	0.4
Median	0.2	0.0	－0.4	0.4
Range	6.5	4.5	5.4	9.6
Abs_ave∫	1.1	1.1	1.0	1.8
Abs_max∬	5.3	3.3	4.5	7.7

＊:root mean square †: standard deviation ‡: standard error
§: average ∫: absolute value (Average) ∬: absolute value (Max)

Table 2. Systematic and random errors of all directions

	Translation(mm)		
	Lateral(x)	Longitudinal(y)	Vertical(z)
systematic error	0.1	0.2	0.1
random error	0.3	0.2	0.3
	Rotation(°)		
	Pitch(θ_x)	Roll(θ_y)	Yaw(θ_z)
systematic error	0.6	0.98	0.78
random error	0.43	1.05	0.55

Table 3. Dose difference value before and after applying the Hexapod Couch compared to the original plan

Patients	Contour	Brain(Gy)		Brain_stem(Gy)		Eyes(Gy)	
		max	mean	max	mean	Left	Right
Pt.1	mean	0.00	0.20	1.11	0.56	−1.34	1.10
	95%CI-lower	0.00	0.21	1.06	0.57	−1.72	1.20
	95%CI-upper	0.01	0.20	1.15	0.56	−0.96	0.99
Pt.2	mean	6.84	0.77	−11.77	−14.19	4.47	−3.26
	95%CI-lower	4.47	0.48	−7.58	−9.35	3.47	−2.32
	95%CI-upper	9.21	1.07	−15.95	−19.02	5.47	−4.21
Pt.3	mean	6.17	0.72	−10.69	−12.75	3.66	−2.82
	95%CI-lower	5.12	0.59	−8.86	−10.57	3.02	−2.34
	95%CI-upper	7.22	0.84	−12.52	−14.92	4.29	−3.30
Pt.4	mean	0.01	−0.01	−0.04	−0.06	0.47	0.25
	95%CI-lower	0.01	0.00	−0.02	0.05	0.32	0.09
	95%CI-upper	0.01	−0.01	−0.06	−0.17	0.63	0.41
Pt.5	mean	0.01	−0.01	−0.05	−0.11	0.45	0.29
	95%CI-lower	0.01	−0.01	−0.05	−0.15	0.44	0.32
	95%CI-upper	0.01	−0.01	−0.04	−0.08	0.47	0.26
Pt.6	mean	0.01	−0.01	−0.03	−0.06	0.35	0.20
	95%CI-lower	0.00	0.00	−0.03	−0.03	0.28	0.15
	95%CI-upper	0.01	−0.01	−0.04	−0.09	0.42	0.25

Assessment of dosimetric effects by comparing the treatment plan

Table 3 shows the results of 360 treatment plans as the sum of 180 cases before the correction and 180 cases after correcting the rotational setup errors for 30 treatment fractions after selecting 6 patients randomly. The CBCT images include the ROIs of the brain, brainstem, and both eyes because the quality of the CBCT images for the ROIs was lower than that of the CT simulation images due to the nature of the CBCT image. Based on the comparison of the doses of the treatment plans, the highest dose difference was observed in patient number 2. The variation of the dose difference before and after correcting the rotational setup error of the Brain_max was 4.47-9.21 Gy, while the Brain_mean was 0.48-1.07 Gy. The maximum of the Brain_stem was -7.58 to -15.95 Gy, while the mean of the Brain_stem was -9.35 to -19.02 Gy. There was a large difference between patient number 2 and 3. On the other hand, the dose difference in the rotational setup error was small in the other patients (Table 3). The mean difference for each ROI was 2.17 Gy for the Brain_max and 0.28 Gy for the Brain_mean. In addition, the maximum and mean of the Brain_stem were -3.58 Gy and -4.43 Gy, respectively. The Lt_eye_max and Rt_eye_max were 1.34 Gy and -0.71 Gy, respectively. The analysis of results by Spearman's correlation coefficient showed that there was a significant linear relationship among the mean values of the remaining ROIs after subtracting the difference of the Brain_mean ($P < 0.05$).

Discussion

In radiation therapy, taking the same treatment posture as the one in the simulation is a key variable in delivering the planned prescription dose to the tumor and protecting the adjacent normal tissue.

The most stable posture in radiotherapy is for the head and neck patients because the immobilization devices have been customized to fit the patient's face through a thermoplastic mask. On the other hand, many studies reported that intrafraction and interfraction errors occur during treatment, despite the patients wearing a mask [11]. In this study, the mean error of the three directions of translation was -0.1±1.4 mm, and the mean error of the three directions of rotation was -0.41±0.76°. Considering setup error with a negative value, the absolute values of the mean error were 1.06±0.14°mm and 0.82±0.14° in the three translation directions and the three rotation directions, respectively, which indicated larger errors.

The ABAS function was introduced in various papers, and its efficacy has been emphasized [12, 13]. The comparison of the ROI drawn by ABAS with the ROI drawn directly revealed a 2 mm or slightly lower difference in the left-right (x), craniocaudal (y), and anteroposterior (z) directions. On the other hand, there was a difference of up to 6.5 mm in the optic nerve. Regarding the volumes of the ROIs, the difference was reported to be -36.8%, 50.5%, 32.6%, and 30% in the pituitary gland, optic chiasm, right optic nerve, and left optic nerve, respectively, which showed an approximate difference of 15%-50% [14]. Although there may be a significant difference in the actual ROI, the obtained results are useful in terms of the speed at which the ROI is reproduced. In a study [14] of the ABAS, the ROI was reproduced on the CBCT image, even though there were some cases where there were errors in the ROI, even after performing the smoothing operation several times. In some cases of slice images with an error, the ROI needs to be corrected directly. Therefore, the ROIs of the optic nerve and optic chiasm with extremely large errors were excluded from the comparison of the treatment plans for this study, and the treatment plan doses over the brainstem, both eyes, and brain, which had relatively small errors, were compared.

Peng et al. [15] examined the dosimetry results by the rotational error of IMRT in brain tumor patients. They reported that when the doses of the treatment plans were recalculated with ±1°~ ±7° rotational errors compared to the original treatment plan, the error of the dose increased with increasing rotational error. As a result of identifying the dose distribution of ROI through DVH with MIM Software, the mean difference for each ROI of the target patient was 2.17 Gy for the Brain_max and 0.28 Gy for the Brain_mean, whereas the maximum and mean of the Brain_stem were -3.58 Gy and -4.43 Gy, respectively. The Lt_eye_max and Rt_eye_max were 1.34 Gy and -0.71 Gy, respectively, indicating a difference in the ROI before and after correcting for the rotational setup error. Moreover, the analyzed ROI might not be adjacent to the targets of the patients, and the dosimetric effects might be small because the deformable image registration was not used intentionally to observe the effects of the rotational setup error. Accordingly, dosimetric assessments of the target through dose comparison factors of the treatment plans were excluded.

The findings of the current study revealed the significant effects of dosimetric treatment through the comparison of the treatment plans by considering the rotational setup error each time during the radiation therapy. Therefore, rotational setup error requires more attention in case of VMAT for brain tumor patients whose targets are adjacent to the major normal organs. This means that there is a need of dose limitation for some specific parts of brain, such as brainstem and optic nerve chiasm

Conclusion

Despite the use of the thermoplastic mask and a postural fixation device for brain tumor patients, there was a significant setup error in the rotational as well as translation directions. In addition, it was found that the rotational setup error of each brain tumor patient occurring during every VMAT treatment affected the dose effects. Accordingly, 6DoF positional correction to reduce the positional uncertainties in comparison with 4DoF correction was likely able to be more accurate radiotherapy.

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