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ORIGINAL ARTICLE

Dosimetric comparison of intensity-modulated radiotherapy and three-dimensional conformal radiotherapy for cerebral malignant gliomas

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Summary

Purpose: *To compare the dose distribution characteristics of tumor target area, normal tissues and organs at risk in patients with malignant gliomas treated with intensity-modulated radiotherapy (IMRT) and three-dimensional conformal radiotherapy (3DCRT).*

Methods: *Plans of IMRT and 3DCRT were designed for each of the 96 included patients with malignant gliomas. Tumor dose was 60 Gy, and the dose distribution differences between the target area and normal tissues were compared using dose-volume histogram (DVH).*

Results: *Gross tumor volume (GTV) doses for 95% of the volume in the plans of IMRT and 3DCRT were as follows: 59.82±0.43, 57.68±0.62 Gy (p<0.05); clinical target volume (CTV): 58.16±0.48, 54.47±0.28 Gy (p<0.05); and planning treatment volume (PTV): 57.38±0.74, 54.21±0.48 Gy (p<0.05). The conformal index (CI) values of IMRT and 3DCRT plans were 0.92±0.15 and 0.73±0.12, respectively (p<0.05), whereas the homogeneity index (HI) values variability of IMRT and 3DCRT were 0.78±0.12 and 1.13±0.09 respectively (p<0.05). For normal brain tissues pituitary and optic chiasm, the maximum dose (Dmax) and the mean dose (Dmean) of lens exposure differed significantly between thw two plans (p<0.05).*

Conclusion: *The target dose distribution of IMRT was superior to that of 3DCRT in terms of rationality, uniformity and conformal nature. IMRT may be better in protecting normal tissue and increasing the tumor radiation dose compared with 3DCRT.*

Key words: *cerebral malignant gliomas, dosage, intensity-modulated radiotherapy, three-dimensional conformal radiotherapy*

Introduction

Malignant gliomas are common intracranial tumors, with radiation therapy being the main option for their postoperative primary treatment [1-3]. Postoperative radiotherapy has been reported to significantly prolong patient survival [4-6]. With continuous improvements in radiotherapy technology, techniques such as 3DCRT and IMRT are increasingly used in clinical practice [7-9]. 3DCRT and IMRT are precise radiotherapy techniques, developed on the basis of conventional radiotherapy together with modern imaging techniques and computer technology; these techniques are aimed at improving the radiation dose to the tumor area while reducing the radiation dose to normal tissues [10-12]. To gain a deeper understanding of the advantages and disadvantages of these two radiation therapy techniques for malignant gliomas, we analyzed 96 patients with this disease admitted to and treated at our department between January 2008 and January 2013. The dosimetric characteristics of the 3DCRT and IMRT treatment plans were compared.

Methods

Subjects

This study was conducted in accordance with the

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declaration of Helsinki and after approval from the Ethics Committee of the Armed Police Corps Hospital of Henan. Written informed consent was obtained from all participants.

Ninety-six patients (51 males and 45 females) with pathologically confirmed malignant glioma who received postoperative radiation therapy with either IMRT or 3CDRT at our department between January 2008 and January 2013 were selected and studied. Patient age ranged from 22 to 78 years (median 41). The surgical procedures comprised partial or near-complete resection. The lesion was located in the temporal lobe in 23 (23.96%) cases, in the frontal lobe in 21 (21.88%) cases, in the occipital lobe in 19 (19.79%) cases, in the parietal lobe in 17 (17.71%) cases, and in the cerebellum in 16 (16.67%) cases. Pathological classification was performed according to the 2007 World Health Organization (WHO) classification criteria: 52 (54.17%) cases were classified as grade III and 44 (45.83%) cases as grade IV. The GTV ranged from 5.66 to 21.45 cm^3, with a median of 12.52 cm^3. The period between surgery and radiotherapy ranged from 13 to 46 days (median 26).

Computed tomography (CT) scans of the head

The patients were placed in the supine position. The Topslane-Venus head spacer (Topslane Co., US) was used, and patients were immobilized using appropriate neck pillows and a thermoplastic mask to fix the head and neck. Contrast-enhanced scans were obtained using a spiral CT scanner (Philips, Holland), from the second cervical vertebra to the top of the skull, with layer spacing and a thickness of 2–3 mm. Scanned images were uploaded to the Topslane-Venus radiotherapy treatment planning system (Topslane Co., US). The PrimusE (Siemens Corporation, Germany) linear accelerator equipped with an electric multi-leaf collimator system was used.

Determination of the tumor target area and critical organs and tissues

Target coverage: The GTV was determined according to No. 50, 62, and other requirements of the International Commission of Radiation Units and Measurements (ICRU). The CTV was determined to be the GTV with a 2–3 cm added margin on all sides, based on the postoperative residual lesions and the residual cavity observed on magnetic resonance imaging scans. The PTV included the CTV with a 5–10 mm added margin.

Dose to the vital organs: The brainstem, pituitary gland, optic chiasm, optic nerve, eye, and lens were determined to be the vital organs that required protection according to the risk for side effects determined in the radiotherapy treatment plan.

Radiation treatment plans

Radiation was delivered using a 6MV-X linear accelerator. The IMRT and 3DCRT plans were designed using the Topslane-Venus radiotherapy planning system. The tumor dose was 60 Gy, with 30 fractions at 2 Gy per fraction, 5 times a week. The IMRT plan involved static IMRT (step and shoot) technology and inverse planning, with 4–8 coplanar radiation fields, each having several sub-fields. The 3DCRT plan involved 6 non-coplanar fixed radiation fields, designed to avoid important and sensitive organs such that the target dose distribution was conformal to the shape of the tumor.

Evaluation of the radiation treatment plans

The IMRT and 3DCRT plans were comprehensively evaluated according to the dose-volume histogram and two-dimensional isodose distribution figures: the 95% isodose line of the GTV, CTV, and PTV and the highest dose (Dmax) and average dose (Dmean) to the GTV, CTV, and PTV. The conformal index (CI) was defined as the ratio of the volume included in the isodose line for 95% of the prescribed dose and the PTV volume. CI values ranged from 0 to 1, with an ideal score of 1 representing complete inclusion of the target area within the isodose line. The homogeneity index (HI) for the volume dose in the planned target areas was defined as HI = (Dmax - Dmin) / Dmin, with Dmin representing the minimum dose. HI represents dose distribution uniformity in the target area, with an ideal value of 0. The maximum dose to important tissues and organs was set as follows: brainstem: <45 Gy, pituitary gland: <50 Gy, optic chiasm: <50 Gy, lens: <5 Gy, and eye: <35 Gy.

Table 1. Index value comparisons of 95% volume of GTV, CTV and PTV in IMRT and 3DCRT plans (mean±SD). The volume receiving 95% of the prescribed dose was within the range of the GTV, CTV and PTV with both treatment plans, although the results of IMRT were superior compared with 3DCRT in all cases (p<0.05)

	GTV (Gy)	*CTV (Gy)*	*PTV (Gy)*
IMRT	59.82 ± 0.43	58.16 ± 0.48	57.38 ± 0.74
3DCRT	57.68 ± 0.62	54.47 ± 0.28	54.21 ± 0.48
p value	<0.05	<0.05	<0.05

IMRT: intensity-modulated radiotherapy, 3DCRT: three-dimensional conformal radiotherapy, GTV: gross tumor volume, CTV: clinical target volume, PTV: planning treatment volume

Statistics

Statistical analyses were performed using the SPSS 13.0 statistical software (SPSS Inc, Chicago, Ill). Multiple comparisons between different groups were assessed by one-way analysis of variance (ANOVA). Mean values between two independent groups were compared by Student's t-test. A p value <0.05 was considered to be statistically significant.

Results

Comparison of target dose distribution between IMRT and 3DCRT

The volume receiving 95% of the prescribed dose was within the range of the GTV, CTV, and PTV with both treatment plans, although the results of IMRT were superior to that of 3DCRT in all cases (p<0.05) (Table 1).

Comparison of the planned CI and HI of the target area between IMRT and 3DCRT

The planned CI and HI of the target region were superior with the IMRT plan compared with the 3DCRT plan, and the difference was statistically significant (p<0.05; Table 2).

Comparison of radiation doses to important tissues and organs between IMRT and 3DCRT

Radiation doses to the brain, optic chiasm, and lens were lower with the IMRT plan than with the 3DCRT plan (p<0.05), suggesting that IMRT could better protect vital organs and tissues compared with 3DCRT. The radiation doses to the two eyeballs and to the brainstem did not differ between the two plans (p>0.05) (Table 3).

Table 2. Comparison of CI value and HI value in IMRT and 3DCRT plans (mean±SD). The planned CI and HI of the target region were superior with the IMRT plan compared with the 3DCRT plan (p<0.05)

	CI value	*HI value*
IMRT	0.92 ± 0.15	0.78 ± 0.12
3DCRT	0.73 ± 0.12	1.13 ± 0.09
p value	<0.05	<0.05

CI value: conformal index value, HI value: homogeneity index value, IMRT: intensity-modulated radiotherapy, 3DCRT: three-dimensional conformal radiotherapy

Discussion

Patients with cerebral malignant gliomas classified as grade III or IV according to the WHO grading system (2007 edition) [1,2], which account for three-fourths of all glioma cases [1-3], were included in this study. Surgery is the first choice of treatment, but because of infiltrative growth and no obvious boundaries with the surrounding normal tissue in higher grade malignant gliomas, coupled with the peculiarity of the anatomical location, complete surgical resection is often difficult if not impossible [13-15]. Postoperative radiation therapy has been used as conventional treatment for malignant gliomas since the 1980s [13,14], with the radiation dose generally being 60 Gy, at 1.8–2.0 Gy per fraction. Due to the limited tolerance to radiation doses of normal tissues and vital organs surrounding the tumors, tumor area coverage with conventional radiotherapy techniques is suboptimal and the rate of complications is high. In recent years, with the advances in radiotherapy techniques, the use of precision radiotherapy techniques such as 3DCRT and IMRT has gradually increased in clinical practice [14-16]. In 3DCRT, the tumor target is exposed to high doses of radiation, while the surrounding normal tissues and organs are better protected due to the forward designed treatment plan and non-coplanar multiple field conformal radiotherapy technology. Theoretically, IMRT is considered to be an advancement of 3DCRT [14,15]. Based on reverse engineering, IMRT has more advantages than 3DCRT in terms of dose distribution in the tumor target area and protection of the surrounding normal tissues, especially for tumors with a large and irregular shape as well as a functional area location [13,15,17]. However, there are few reports on the dosimetric comparison of IMRT and 3DCRT for intracranial tumors in the clinical setting. The results of this clinical study supported the theory of IMRT being superior to 3DCRT.

On comparing 3DCRT and IMRT in 96 patients with malignant gliomas, we found that conformity was better with IMRT than with 3DCRT, with the CI being 0.92±0.15 for IMRT, which was significantly higher than 0.73±0.12 for 3DCRT. The higher CI value for IMRT indicates better protection of the normal tissues surrounding the tumor target areas [17,18]. The radiation dose to the normal tissues surrounding the target areas was significantly lower with IMRT than with 3DCRT (p<0.05). The HI for dose distribution within the target area is an index for dose uniformity in the tumor target [19]. According to the principles of radiation oncology, the plan with a uniform radiation dose distribution within the tumor target

Table 3. Comparison of Dmax and Dmean for important tissues and organs in IMRT and 3DCRT plans (mean±SD). Radiation doses to the brain, optic chiasm, and lens were significantly lower with the IMRT compared with 3DCRT plan (p<0.05), suggesting that IMRT could protect better vital organs and tissues. The radiation doses to the two eyeballs and to the brainstem did not differ between the two plans (p>0.05)

Organs/tissues		*IMRT*	*3DCRT*	*p value*
Pituitary (Gy)	Dmax	32.2 ± 1.2	38.6 ± 3.1	<0.05
	Dmean	25.6 ± 3.6	33.1 ± 2.6	<0.05
Optic chiasm (Gy)	Dmax	42.2 ± 3.2	47.6 ± 1.2	<0.05
	Dmean	31.4 ± 2.2	38.8 ± 4.1	<0.05
Left lens (Gy)	Dmax	16.4 ± 1.6	22.1 ± 2.2	<0.05
	Dmean	3.8 ± 2.4	8.5 ± 2.6	<0.05
Right lens (Gy)	Dmax	13.1 ± 2.2	21.8 ± 2.1	<0.05
	Dmean	1.9 ± 1.2	7.4 ± 1.3	<0.05
Left eyeball (Gy)	Dmax	34.2 ± 2.6	33.9 ± 2.7	>0.05
	Dmean	24.3 ± 3.2	24.6 ± 4.1	>0.05
Right eyeball (Gy)	Dmax	33.7 ± 3.3	33.3 ± 3.9	>0.05
	Dmean	26.6 ± 2.1	26.8 ± 1.9	>0.05
Brainstem (Gy)	Dmax	33.3 ± 2.2	33.6 ± 2.6	>0.05
	Dmean	23.8 ± 2.2	23.6 ± 2.8	>0.05
Normal brain tissues (Gy)	Dmax	38.8 ± 3.8	46.5 ± 4.2	<0.05
	Dmean	20.1 ± 2.2	38.6 ± 2.8	<0.05

IMRT: intensity-modulated radiotherapy , 3DCRT: three dimensional conformal radiotherapy

area is an ideal radiotherapy plan [12]. In this study, the HI values reflecting target dose uniformity were better with IMRT (0.78±0.12) than with 3DCRT (1.23±0.08).

With regard to the 95% dose distribution, the GTV, CTV, and PTV doses were significantly higher with IMRT than with 3DCRT (59.82±0.43 vs 57.68±0.62, 58.16±0.48 vs 54.47±0.28, and 57.38±0.74 vs 54.21±0.48, respectively) (p<0.05). Thus, the radiation dose to the tumor was higher with IMRT than with 3DCRT, and therefore, tumor control was better with IMRT than with 3DCRT.

The level of protection of vital organs surrounding the target is also a measure of the merit of a radiotherapy plan [4,5,20]. The radiation dose to the vital organs surrounding the target is an important factor to consider when determining the rate of radiotherapy complications. The radiotherapy dose to the vital organs directly affects dose distribution within the target, thereby affecting tumor control. In this study, the radiation doses to normal brain tissue, the pituitary gland, optic nerve, and lens were significantly lower with in IMRT than with 3DCRT, indicating that protection of vital tissues and the organs surrounding the target area is better with IMRT than with 3DCRT, reducing the damage to key organs.

In conclusion, IMRT is associated with higher radiation doses to the tumor target area and better tumor control compared to 3DCRT. IMRT also afforded better protection of normal tissues and vital organs surrounding the target area compared with 3DCRT, thereby reducing concurrent radiotherapy complications to achieve a higher gain ratio for the treatment of tumors and improve efficacy. Further studies are warranted to compare the long-term survival outcomes and dose efficiency between IMRT and 3DCRT.

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