Comparison of linac-based fractionated stereotactic radiotherapy and tomotherapy treatment plans for intra-cranial tumors*

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Abstract This study compares and analyzes stereotactic radiotherapy using tomotherapy and linac-based fractionated stereotactic radiotherapy in the treatment of intra-cranial tumors, according to some cases. In this study, linac-based fractionated stereotactic radiotherapy and tomotherapy treatment were administered to five patients diagnosed with intra-cranial cancer in which the dose of 18–20 Gy was applied on 3–5 separate occasions. The tumor dosing was decided by evaluating the inhomogeneous index (II) and conformity index (CI). Also, the radiation-sensitive tissue was evaluated using low dose factors V_1, V_2, V_3, V_4, V_5, and V_{10}, as well as the non-irradiation ratio volume (NIV). The values of the II for each prescription dose in the linac-based non-coplanar radiotherapy plan and tomotherapy treatment plan were (0.125±0.113) and (0.090±0.180), respectively, and the values of the CI were (0.899±0.149) and (0.917±0.114), respectively. The low dose areas, V_1, V_2, V_3, V_4, V_5, and V_{10}, in radiation-sensitive tissues in the linac-based non-coplanar radiotherapy plan fell into the ranges 0.3%–95.6%, 0.1%–87.6%, 0.1%–78.8%, 38.8%–69.9%, 26.6%–65.2%, and 4.2%–39.7%, respectively, and the tomotherapy treatment plan had ranges of 13.6%–100%, 3.5%–100%, 0.4%–94.9%, 0.2%–82.2%, 0.1%–78.5%, and 0.3%–46.3%, respectively. Regarding the NIV for each organ, it is possible to obtain similar values except for the irradiation area of the brain stem. The percentages of $\mathrm{NIV}_{10\%}$, $\mathrm{NIV}_{20\%}$, and $\mathrm{NIV}_{30\%}$for the brain stem in each patient were 15%–99.8%, 33.4%–100%, and 39.8%–100%, respectively, in the fractionated stereotactic treatment plan and 44.2%–96.5%, 77.7%–99.8%, and 87.8%–100%, respectively, in the tomotherapy treatment plan. In order to achieve higher-quality treatment of intra-cranial tumors, treatment plans should be tailored according to the isodose target volume, inhomogeneous index, conformity index, position of the tumor upon fractionated stereotactic radiosurgery, and radiation dosage for radiation-sensitive tissues.

Key words fractionated stereotactic radiotherapy, tomotherapy, treatment plan, virtual organ delineation

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1 Introduction

In general, perfect resection of intra-cranial tumors is not possible via surgery. Therefore, radiotherapy has been used as either an independent method of surgery or an auxiliary treatment approach. Radiotherapy involves a dosage limit for radiation-sensitive tissues and a maximum dosage directed at the tumor.

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However, delivering the maximum dose to the tumor without exceeding the limit for the surrounding radiation-sensitive tissue is quite difficult. Thus, a special radiotherapy method is required [1].

Fractionated stereotactic radiotherapy (FSRT) and tomotherapy have been used as special radiotherapy methods. Non-coplanar fractionated stereotactic radiotherapy can irradiate a higher dose than regular radiotherapy using stereotactic devices and shows excellent success in protecting radiation-sensitive tissues around tumors [2]. Tomotherapy can be applied to spiral intensity modulated radiotherapy (IMRT) with energy of 6 MV and has been used as a representative treatment method for complex targets because it enables radiologists to compare the sections that are to be treated by obtaining megavoltage computed tomography (MVCT) before applying radiotherapy.

Several studies on the comparison and analysis of linac-based fractionated stereotactic radiotherapy and tomotherapy plans have been reported. However, there are few studies of a more detailed dose limitation method in the tomotherapy and case analyses. In addition, although tomotherapy cannot be applied in combination with non-coplanar irradiation, it can be used as part of a treatment plan similar to the linac-based fractionated stereotactic radiotherapy plan if virtual organ delineation (VOD) or beam limitation is configured to coplanar irradiation.

Emilie et al. [1] reported that linac-based non-coplanar irradiation fractionated stereotactic radiotherapy achieved better results in terms of the prescription isodose of tumor volume, 54%, and inhomogeneous index, 2%, than that of the tomotherapy. Yartzev et al. [3] reported that tomotherapy represented an increase in dose homogeneity of 1.3%, as compared with that of the methods of 3D conformal radiotherapy, IMRT, and stereotactic arc therapy in the treatment of a small intra-cranial tumors. Chunhui et al. [4] reported that the non-coplanar intensity modulated radiosurgery treatment plan shows an increase in dose conformity to (1.53±0.38) and (1.26±0.10), as compared with that of tomotherapy, but that the dose homogeneity shows almost similar levels of (1.15±0.05) and (1.18±0.09) in both plans.

Based on the results of other researchers, it is difficult to determine which is a better treatment modality: FSRT or tomotherapy. Thus, this study established linac-based FSRT and tomotherapy treatment plans based on the same tumor volume and radiation-sensitive tissue for the same patients and obtained the prescription isodose to target volume (PITV), inhomogeneity index (II), and conformity index (CI) [5]. Then, this study attempted to find an effective treatment plan for each case by obtaining and analyzing low dose area and non-irradiation volume (NIV) data for radiation-sensitive tissue.

2 Materials and methods

This study established a stereotactic radiotherapy plan for a total of five patients. The equipment used in the treatment plan was a linac-based FSRT system (Clinac iX, Varian, USA) and a tomotherapy system (Hi-Art, Tomotherapy, USA), and the treatment plan systems used in the plan were the iPlan system (iPlan RT Dose 3.0.2, BrainLab, Germany) and the tomotherapy treatment plan system (Tomotherapy Planning Station version 3.2.1.6, Tomotherapy, USA).

2.1 Patients

The treatment plan was applied to five intra-cranial cancer patients in which each patient demonstrated that the arteriovenous malformation (AVM), pituitary adenoma, intraventicular tumor, and meningioma represented a single tumor, and the brain metastasis of the lung showed two tumors. The size of tumors, eyeballs, lens, brain stems, optic chiasms, optic nerves, and pituitaries were determined to be 0.1–13.1 cc, 7.9–10.8 cc, 0.1–0.3 cc, 19.6–23.8 cc, 0.2–0.3 cc, 0.5–1.2 cc, and 0.4–1.3 cc, respectively. In addition, the dose of 20 Gy was applied to the arteriovenous malformation, pituitary adenoma, and intraventicular tumor at five separate times, and the dose of 18 Gy was applied to the brain metastasis of the lung at three separate times. Also, the dose of 25 Gy was applied to the meningioma at five separate times (Table 1).

2.2 Radiotherapy plan

The linac-based fractionated stereotactic radiotherapy plan was performed by combining CT images and MRIs, and included the prescription dose in the range of 95% by configuring the planning target volume with the margin of irradiation space by 2–3 mm in the gross tumor volume. Then, an inverse treatment plan was established for irradiating the minimum dose to the radiation-sensitive tissue around the tumor. Next, a tomotherapy plan was established by comparing it with the linac-based FSRT plan.

Table 1. Patient characteristic.

Pt.(No.)	diagnosis	*P/Gy	†F	volume/cc							
				PTV	OAR						
					orbit (Rt/Lt)	lens (Rt/Lt)	brain stem	optic chiasm	optic nerve	pituitary
1	AVM	20	5	8.3	9.9/9.8	0.2/0.2	22.3	0.3	0.5	0.4
2	pituitary adenoma	20	5	0.7	9.7/10.8	0.2/0.2	19.6	0.3	1	N/A
3	bram mets of lung	18	3	0.1 ‡(1.4)	10.1/10.1	0.2/0.1	21.4	0.2	1.2	0.8
4	intraventricular	20	5	5.5	9.5/1.7	0.2/0	23.5	0.3	0.5	0.5
5	meningioma	25	5	13.1	8.0/7.9	0.3/0.3	23.8	0.3	1	1.3

*Abbreviation; *P: prescription; †F: Fraction; ‡(): another target

2.3 Configuration of the direction of the beam

The linac-based FSRT plan was established for 6–7 beam directions in a non-coplanar space, and the tomotherapy plan was performed using virtual organs for the rotational irradiation in a coplanar space or by limiting the beam directions (complete, directional). In the analysis methods, the complete method limits all beams which pass through the predetermined radiation-sensitive tissue, and the directional method cannot produce beams that can arrive at the target after passing through the predetermined radiation-sensitive tissue, even though this method can produce beams that can pass through the predetermined radiation-sensitive tissue after passing the target. The tomotherapy cannot control the direction of beams one by one. To obtain results in tomotherapy, which irradiates the radiation in a spiral way, that are similar to those of the fractionated stereotactic radiotherapy, this study applied the complete method that fully intercepts all beams that are irradiated to the neighboring radiation-sensitive tissue, and the directional method that limits the direction of beams that are irradiated to the target and passed through the neighboring organs. Also, this study used both complete and directional methods to an area, which is to be specifically limited, by configuring virtual organ delineations (Table 2).

2.4 Dose limitation

Linac-based fractionated stereotactic radiotherapy generates a treatment plan that performs 50% of volume for the target and prescription dose of 100% and can be divided into three different types for each radiation-sensitive tissue, such as OAR Type 1 (100% guardian), OAR Type 2 (66% guardian), and OAR Type 3 (33% guardian). Also, a detailed dose limitation can be applied. The tomotherapy performs the dose limitations using the field width (1, 2.5, and 5 cm), pitch, calculation grid (coarse, normal, and fine), modulation factor, maximum dose, maximum dose penalty, Dose volume histogram (DVH) volume, DVH dose, minimum dose, minimum dose penalty, and DVH Patient penalty. In the fractionated stereotactic radiotherapy plan, the OAR type was determined for the radiation-sensitive tissue in which the dose and volume were selectively controlled. In the tomotherapy treatment plan, the field width, pitch, calculation grid, and modulation factor were determined to be 1 cm, 0.287, normal, and 3–5, respectively. Also, the maximum dose and minimum dose were determined to be the same value as the prescription dose. The DVH volume, DVH dose, and each penalty were selectively determined in the treatment plan.

Table 2. Beam direction of the radiation treatment plan.

*Pt.(No.)	target(No.)	beam direction			
		iPlan	tomotherapy		
			blocking		‖VOD(No.)
			complete(No.)	directional(No.)	
1	1	†Non-7	7	1	1
2	1	†Non-7	0	0	1
3	2	†Non-7‡(7)	5	3	1
4	1	†Non-7	1	1	1
5	1	†Non-6	1	1	1

*abbreviation; *Pt: Patient; †Non: non-coplanar beam; ‡(): beam number for the other location tumor; ‖VOD: virtual organ delineation

2.5 Dose analysis

The dose analysis for a tumor was evaluated using the inhomogeneity index (II) and conformity index (CI). The in-homogeneity index was determined by the rate of the average dose of the planning target volume (PTV) and the difference between the maximum and the minimum doses of the PTV, with a value that is closer to 0 being better (see Eq. (1)). The conformity index represented the degree of conformity to the PTV for the isodose volume prescribed in the treatment plan, as was first proposed in the ICRU 62 [6]. It can be determined by the rate of the treated volume (V_{PTV}) surrounded by the prescribed isodose surface (V_{TV}) and PTV (see Eq. (2)).

$$\text{Inhomogeneity index } (II) = (PTV \text{ max. dose} - PTV \text{ min. dose})/(PTV \text{ max. dose}) \quad (II \fallingdotseq 0, \text{ good}) \quad (1)$$

$$CI = V_{\mathrm{TV}}/V_{\mathrm{PTV}} \quad (CI \fallingdotseq 1, \text{ good}) \quad (2)$$

(V_{TV}: treated volume enclosed by the prescription isodose surface; V_{PTV}: planning target volume).

The dose analysis for the radiation-sensitive tissue was evaluated using the low dose areas of V_1, V_2, V_3, V_4, V_5, and V_{10} (V_i: irradiated volume enclosed by the i Gy) and non-irradiated volume (NIV), and the non-irradiated volume can be determined by the ratio of the difference between the irradiation area ($Or_{n\%}$) and the entire volume (Or_{TV}) of the radiation-sensitive tissue and the entire volume. The closer the value is to 1, the better (see Eq. (3)).

$$NIV_{n\%} = (Or_{\mathrm{TV}} \text{-} Or_{n\%})/Or_{\mathrm{TV}} \quad (NIV \fallingdotseq 1, \text{ good}) \quad (3)$$

(Or_{TV}: total volume of organ at risk, $Or_{n\%}$: irradiated volume of organ at risk).

3 Results

The values of the II and CI for the doses accepted by tumors in both the linac-based fractionated stereotactic radiotherapy and the tomotherapy plans were calculated to be (0.125±0.113) and (0.090±0.180), respectively, for the FSRT, and (0.899±0.149) and (0.917±0.114), respectively, for the tomotherapy (Table 3). Table 4 and Table 5 represent the low dose area and NIV for the radiation-sensitive tissue, respectively. The dose investigated in the eyeballs and lens was almost zero because the beam direction was limited in the linac-based FSRT, and the beam direction was also limited in the tomotherapy using virtual organ delineations. Because the position of the tumor was adjacent to the brain stem and optic chiasms, the results of the values in the low dose areas and non-irradiate volume for the two organs were compared (Figs. 1 and 2). In the case of the pituitary adenoma that showed the largest difference in the low dose areas at the optic chiasm, the value of V_1 was 95.6% in the fractionated stereotactic radiotherapy plan and 100% in the tomotherapy plan. Also, the values of V_2, V_3, V_4, V_5, and V_{10} in both the fractionated stereotactic radiotherapy and tomotherapy plans were 87.6% and 100%, 78.8% and 94.9%, 69.9% and 82.2%, 65.2% and 78.5%, and 39.7% and 46.3%, respectively. In the case of the brain stem, the maximum values of V_1, V_2, V_3, V_4, V_5, and V_{10} in both fractionated stereotactic radiotherapy and tomotherapy plans were 94.3% and 67.5%, 83.6 and 59.7%, 73.6% and 53.8%, 59% and 48.8%, 48.9% and 43.9%, and 20.6% and 21%, respectively. In addition, in the case of the non-irradiated volume for the brain stem, the values of $\mathrm{NIV}_{10\%}$, $\mathrm{NIV}_{20\%}$, and $\mathrm{NIV}_{30\%}$ were 15%–99.8% and 44.2%–96.5%, 33.4%–100% and 77.7%–99%, and 56.1%–100% and 87.8%–100%, respectively (Fig. 3).

Table 3. Inhomogeneity index (II), conformity index (CI) and mean values for each patient.

Pt.(No.)	inhomogeneity index(II)		conformity index(CI)	
	tomotherapy	i-plan	tomotherapy	i-plan
1	0.212	0.226	0.954	0.952
2	0.049	0.106	0.971	0.840
3	0.032	0.092	0.900	0.833
	0.052	0.110	0.857	0.826
4	0.121	0.108	0.925	0.970
5	0.075	0.107	0.893	0.975
mean	0.090±0.180	0.125±0.133	0.917±0.114	0.899±0.149

Table 4. Plan evaluation including the comparison of a low dose volume to selected organs at risk (OAR).

Pt.(No.)	OAR	V_1(%)		V_2(%)		V_3(%)		V_4(%)		V_5(%)		V_{10}(%)	
		*A	†B	*A	†B	*A	†B	*A	†B	*A	†B	*A	†B
1	brainstem	90.7	39.2	83.3	24.9	58.8	14.4	38.8	8.7	28.9	5.2	4.2	0.3
	chiasm	1.7	68.3	–	17.6	–	–	–	–	–	–	–	–
	pituitary	24.4	25.8	–	–	–	–	–	–	–	–	–	–
	nerve	–	13.6	–	–	–	–	–	–	–	–	–	–
2	brainstem	1.8	52.8	0.6	20.6	–	5.9	–	1.2	–	–	–	–
	chiasm	95.6	100.0	87.6	100.0	78.8	94.9	69.9	82.2	65.2	78.5	39.7	46.3
	nerve	0.3	20.0	–	8.3	–	5.4	–	4.5	–	3.1	–	–
3	brainstem	92.3	67.5	83.6	59.7	73.6	53.8	59.0	48.8	48.9	43.9	20.6	21.0
4	brainstem	1.3	24.5	0.2	3.5	0.1	0.4	–	0.2	–	0.1	–	–
	chiasm	12.8	83.7	0.1	11.0	–	–	–	–	–	–	–	–
	pituitary	28.1	56.0	10.7	16.4	–	2.5	–	–	–	–	–	–
	nerve	26.0	37.5	1.8	16.6	–	–	–	–	–	–	–	–
5	brainstem	94.3	20.3	76.5	12.2	59.3	8.9	41.1	6.9	26.6	5.3	5.4	1.5

*abbreviation; *A: iPlan; †B: tomotherapy

Table 5. Plan evaluation including the comparison of NIV to selected organs at risk (OAR).

Pt.(No.)	OAR	$NIV_{10\%}$		$NIV_{20\%}$		$NIV_{30\%}$	
		*A	†B	*A	†B	*A	†B
1	brainstem	0.166	0.751	0.610	0.913	0.798	0.969
	chiasm	–	0.833	–	–	–	–
2	brainstem	0.994	0.794	1.000	0.990	1.000	1.000
	chiasm	0.124	0.000	0.301	0.167	0.398	0.267
3	brainstem	0.150	0.442	0.334	0.962	0.561	0.969
4	brainstem	0.998	0.965	1.000	0.998	1.000	1.000
	chiasm	0.999	–	–	–	–	–
	pituitary	0.900	0.836	–	–	–	–
	nerve	0.980	0.834	–	–	–	–
5	brainstem	0.262	0.563	0.732	0.777	0.906	0.878

*abbreviation; *A: iPlan; †B: tomotherapy

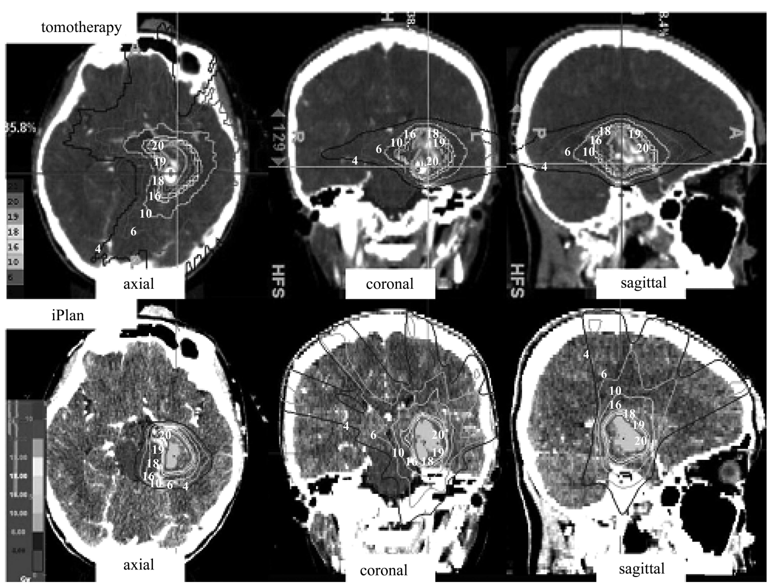

Fig. 1. Comparison of a linac based FSRT plan with a tomotherapy plan for the AVM patient. This figure demonstrates the relative sized of the isodose volumes. 4, 6, 16, 18, 21 Gy and so on are shown; upper: tomotherapy, lower: iPlan.

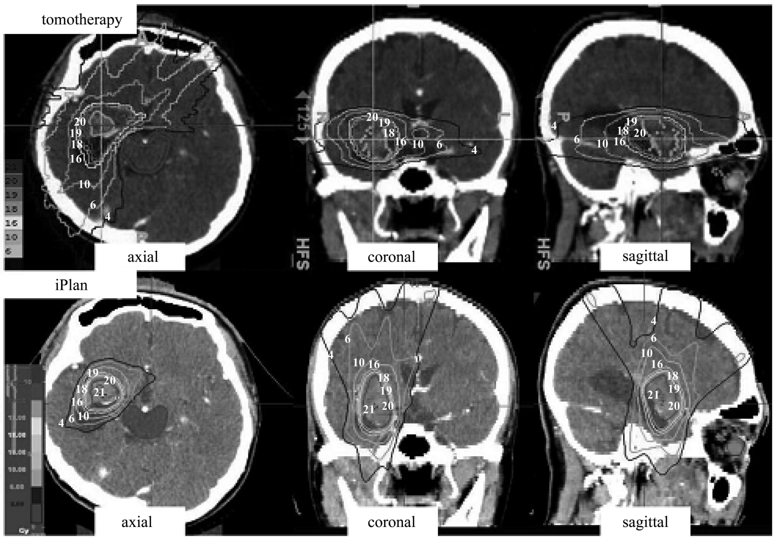

Fig. 2. Comparison of linac based FSRT plan with a tomotherapy plan for the Intraventricular patient. This figure demonstrates the relative size of the isodose volumes. 4, 10, 16, 18, 21 Gy and so on are shown; upper: tomotherapy, lower: iPlan.

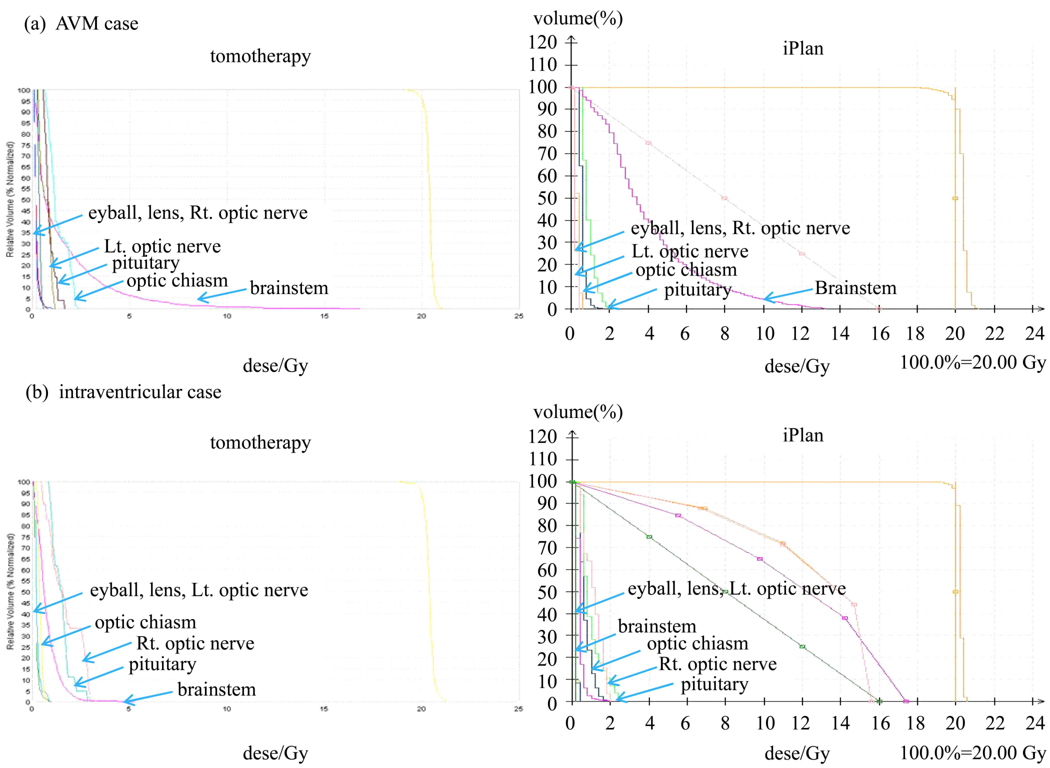

Fig. 3. (color online) Dose volume histogram (DVH) for iPlan, tomotherapy radiation treatment planning (left: tomotherapy, right: iPlan); (a) AVM case; (b) Intraventricular case.

4 Discussion and conclusion

Despite the disadvantage that tomotherapy is not able to be performed in combination with non-coplanar irradiation, it can be incorporated into a plan similar to the linac-based FSRT if the coplanar irradiation of the VOD and beam direction is limited. Because the references and methods for limiting the dose differ between the linac-based FSRT and tomotherapy, establishing a specific standard according to certain case characteristics is important. As each organ has its own tolerance dose, considering the NIV values within the tolerance dose of the neighboring radiation-sensitive tissue in selecting an effective treatment plan is important, even while the range of prescription doses that includes the target is wide. The treatment range and the values of the II in both linac-based FSRT and tomotherapy can be influenced by the margin of the irradiation space. Also, in the case of the linac-based FSRT, there were some differences in the treatment range and the values of the II because the treatment plans were established by determining the PTV with a margin of 2–3 mm in the irradiation space for the gross tumor volume in the iPlan. In the case where the position of the tumor is close to the radiation-sensitive tissue, tomotherapy showed increases in the value of the II of 6.7%–190.7%, respectively. Also, the increases in V_1, V_2, V_3, V_4, V_5, and V_{10} for the radiation-sensitive tissues were 56.8%–78.5%, 28.6%–84.1%, 26.9%–85%, 17.3%–83.2%, 10.2%–82%, and 72.2%–92.9%, respectively. The increases in the values of $\mathrm{NIV}_{10\%}$, $\mathrm{NIV}_{20\%}$, and $\mathrm{NIV}_{30\%}$ were 114.9%–352.4%, 6.1%–188%, and 21.4%–72.7%, respectively. In the case of the distance between the position of the tumor and the radiation-sensitive tissue that shows a distance, the linac-based FSRT plan showed increases in the value of II of 11%. Also, the increases in the values of V_1, V_2, V_3, V_4, V_5, and V_{10} for the radiation-sensitive tissue were 4.6%–3917.6%, 14.2%–3333.3%, 20.4%–300%, 17.6%, 20.4%, and 16.6%, respectively, and the increases in the values of $\mathrm{NIV}_{10\%}$, $\mathrm{NIV}_{20\%}$, and $\mathrm{NIV}_{30\%}$ were 3.3%–100%, 0.2%–44.6%, and 33%, respectively. In this study, therefore, the quality of radiation therapy can be increased by selecting either the iPlan or tomotherapy, depending on the position of the tumors.

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