Dosimetric Comparison of Gamma Knife® Icon™ and linear accelerator-based FSRT plans for the re-irradiation of large (> 14 cm³) recurrent glioblastomas

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MOTIVATION

Prognosis for glioblastomas (GBM) remains generally poor as 90% of patients experience recurrences, which are then treated palliatively with re-irradiation in the form of linac-based FSRT. Unfortunately, a large percentage of these re-irradiation patients experience CNS toxicity effects, primarily radionecrosis, due to the recurrence usually being within 2 cm of the high dose tumor volume previously irradiated [1, 2]. The Gamma Knife® Icon™ allows for clinically deliverable GK FSRT treatments as an alternative to standard linac-based FSRT for larger tumors. In a prior study, Han *et al.* created GK FSRT plans for large brain metastases which reduced normal brain V12Gy and V20Gy by ~20% compared to linac-based plans, with an average treatment time of 64 minutes [3]. In this work, we aim to develop GK FSRT treatment plans for large and irregularly shaped recurrent GBM targets. We aim to achieve similar reduction in normal brain dose while keeping clinical feasibility in mind by limiting the GK treatment time to ideally less than 20 minutes, with an absolute maximum of 40 minutes.

PURPOSE

To investigate dosimetric differences between clinically deliverable Leksell Gamma Knife® (GK) Icon™ and linear accelerator-based FSRT plans on the basis of normal brain sparing for re-irradiation of large (> 14cm³) recurrent glioblastomas (GBM).

MATERIALS AND METHODS

Sixteen patients with large, recurrent GBM (PTV mean = 35.2 cm³, range 15.0 – 74.8 cm³) were treated using re-irradiation via linac-based FSRT with a dose of 35 Gy in 10 fractions. For each patient, a new GK FSRT plan was created in Leksell GammaPlan® V11 (LGP) with identical treatment volumes and prescription dose to the linac-based plans. GK FSRT planning goals included: target coverage PTV V100% ≥ 95%, conformity index ≥ 0.8, gradient index < 3, treatment time ≤ 20 minutes (< 40 minutes maximum), and OAR constraints (brainstem, optic nerves, and optic chiasm maximum doses (0.03 cm³)) < 15 Gy. GK treatment times were allowed to exceed 20 minutes, with an absolute maximum treatment time of 40 minutes, only in cases where the 20 minute treatment time constraint caused all other GK treatment planning goals to degrade. GK treatment times, as obtained from GammaPlan®, were scaled from the initial planned value to reflect a nominal dose rate of 2.5 Gy/min.

Dosimetric comparisons of the GK and linac-based FSRT plans were performed in MIM Software V6.7 with a 1 mm dose grid. For both plan types, target coverage, conformity index (CI), gradient index (GI), normal brain V4Gy, V12Gy, V20Gy, mean brain dose and treatment time were recorded. Two-tailed paired t-tests were conducted to evaluate the statistical significance of the difference between the two treatment modalities for all plan comparison parameters ($p < 0.05$). The difference in normal brain V12 and mean brain dose values between GK Icon™ and linac-based FSRT plans were investigated for dependence on PTV size, target location (via GammaPlan® target coordinates), and target irregularity. Target irregularity was measured by the ratio of the largest axial dimension of the target and the equivalent diameter of the PTV. The equivalent diameter is equal to the diameter of a sphere that has a volume identical to that of the PTV. As the irregularity ratio increases from unity, the tumor shape is thought to be more irregular.

TABLE 1: Plan comparison parameters for both treatment modalities

	Linac-based	GK	P-value (* 0.05)
TC*	96.3% (76.6% - 100%)	92.9% (76.0% - 95.2%)	**0.0006**
CI	0.79 (0.64 - 0.94)	0.84 (0.69 - 0.89)	0.0572
GI	3.05 (2.32 - 5.85)	2.70 (2.46 - 3.08)	0.0827
V4 (cm³)	470.4 (219.3 - 637.1)	420.5 (199.3 - 702.2)	0.0726
V12 (cm³)*	123.9 (52.8 - 206.9)	90.8 (45.2 - 162.8)	**0.0001**
V20 (cm³)*	51.2 (22.9 - 87.2)	34.7 (17.8 - 69.9)	**0.0000**
Mean Brain Dose (Gy)*	4.4 (2.41 - 6.0)	4.0 (2.07 - 6.27)	**0.0194**
Treatment Time (minutes)*	5.6 (4 - 8)	20.6 (12.6 - 31.3)	**0.0000**

RESULTS

The plan comparison results are listed in Table 1 for the two different modalities. There was a significant decrease in target coverage (mean = -3.35%, max = -5.92%) for the GK plans due to differences in plan normalization based on our clinical practice. There was an increase in CI (mean = 7.65%, max = 33.8%) and a decrease in GI (mean = -7.49%, max = -47.3%) with the GK plans compared to the linac-based plans, but neither of these differences were significant. The GK FSRT plans resulted in a significant ($p < 0.05$) decrease in mean normal brain V20Gy, normal brain V12Gy and mean brain dose values by 32.4%, 25.9% and 8.85%, and an average decrease in V4Gy values by 10.0% compared to the linac-based plans. The mean GK treatment time was 20.6 minutes (max = 31.3 minutes), significantly increased compared to the linac-based plans (mean = 5.63 minutes, max = 8 minutes). Figure 1 shows a side-by-side comparison for an example patient.

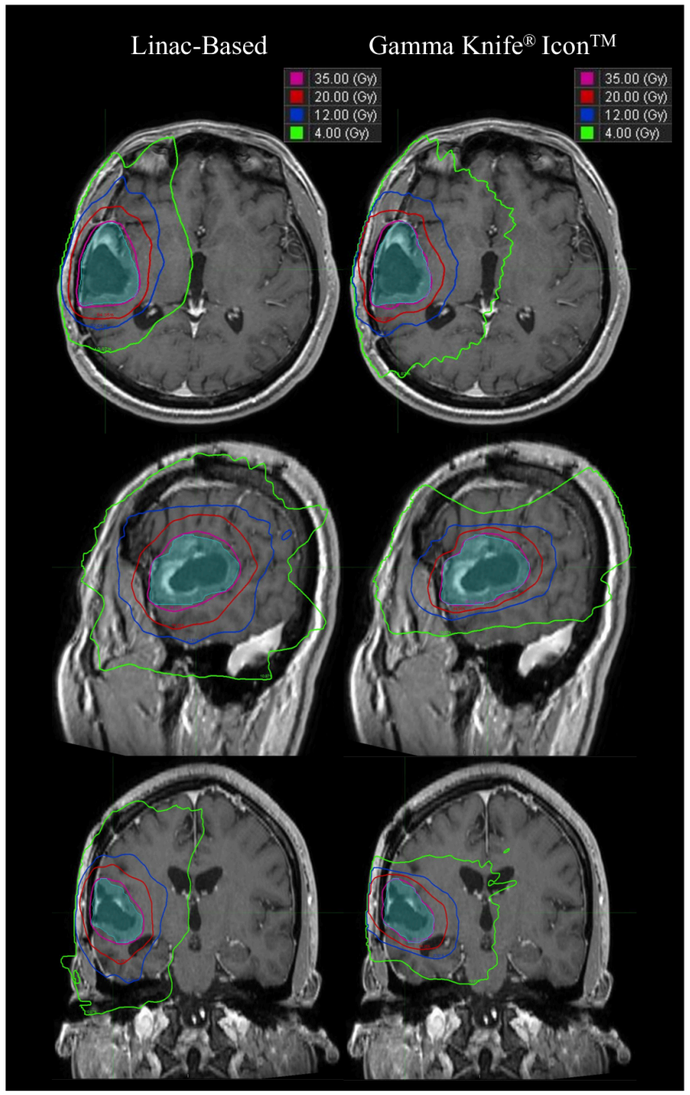

Figure 1. Dose distributions of linac-based (left) and GK (right) plans for patient 15 in axial, sagittal, and coronal views (top to bottom). For this patient, the GK FSRT plan produced a change in normal brain V4Gy = -31%, V12Gy = -46%, V20Gy = -51%, and mean brain dose = -20%.

RESULTS

The normal brain dose sparing benefits (reduction in V4Gy, V12Gy, V20Gy, and mean brain dose values) of GK compared to linac-based plans were inversely correlated with PTV size ($p < 0.05$), as shown in Figure 2. Regression analysis predicted that PTVs between 14 – 47 cm³ will receive the most benefit from GK planning, resulting in a 36.2 – 20.1% decrease in V12Gy and a 18.7% - 3.2% decrease in mean brain dose with GK FSRT plans compared to linac-based plans. Normal brain dose sparing differences between modalities was found to have a significant relationship ($p < 0.05$) with target volume location in the AP direction, with the largest reduction in normal brain dose predicted to occur in the anterior region of the brain near the optic structures. The reduction in V12Gy and mean brain dose values in GK compared to linac-based plans was found to significantly ($p < 0.05$) increase as the irregularity ratio increased from unity.

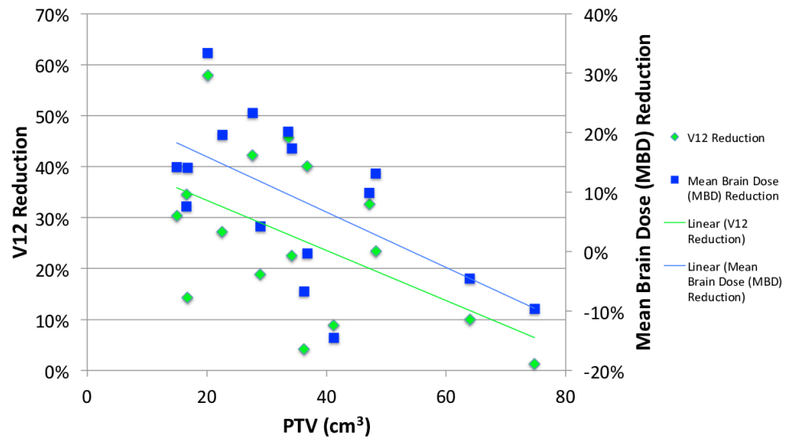

Figure 2. PTV size dependent reduction of V12 and mean brain dose values due to GK plans compared to standard linac-based plans, with linear regression analysis.

DISCUSSION

The decrease in target coverage in GK compared to linac-based plans resulting from differences in our clinical practice could contribute to some of the normal brain dose sparing benefits seen here, but future work will directly compare plans with similar normalization to quantify this effect. In this study, we limited our population to targets > 14 cm³ and were limited by the LGP software to targets with a maximum axial extent < 7.5 cm. In future work we intend to investigate normal brain sparing for PTV < 14 cm³.

CONCLUSION

Clinically deliverable GK FSRT treatment plans significantly decrease normal brain dose compared to standard linac-based FSRT for the re-irradiation of large (> 14 cm³) recurrent glioblastomas. Patients with targets in close proximity to OARs or an irregular shape will most benefit from GK compared to linac-based treatments. GK FSRT has the potential to improve patient outcomes for this patient population by reducing the risk of CNS toxicities.

REFERENCES

[1] Korytko T, Radivoyevitch T, Colussi V, et al. 12 Gy gamma knife radiosurgical volume is a predictor for radiation necrosis in non-AVM intracranial tumors. *Int J Radiat Oncol Biol Phys*. 2006. doi:10.1016/j.ijrobp.2005.07.980

[2] Lawrence YR, Li XA, el Naqa I, et al. Radiation Dose-Volume Effects in the Brain. *Int J Radiat Oncol Biol Phys*. 2010. doi:10.1016/j.ijrobp.2009.02.091

[3] Han EY, Wang H, Luo D, Li J, Wang X. Dosimetric comparison of fractionated radiosurgery plans using frameless Gamma Knife ICON and CyberKnife systems with linear accelerator–based radiosurgery plans for multiple large brain metastases. *J Neurosurg*. April 2019:1-7. doi: 10.3171/2019.1.jns182769