



# Radiobiological comparison of pencil beam- and shot-based treatment delivery techniques in stereotactic radiosurgery of intracranial benign lesions: Preliminary results of a bicentric study



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**Background and Purpose:** Stereotactic radiosurgery (SRS) utilizes “step-and-shoot” irradiation techniques, delivering the planned dose sequentially through either isocentric radiation shots (e.g., Gamma Knife™) or non-isocentric pencil beams (e.g., CyberKnife™). These methods create complex spatial and temporal dose variations, influencing radiation-induced DNA damage repair and ultimately affecting treatment outcomes. This study aims to compare the radiobiological effects of the two most widely used “step-and-shoot” SRS techniques—those implemented in the Gamma Knife (GK) and CyberKnife (CK) systems—for treating intracranial benign tumors.

**Materials and Methods:** Vestibular Schwannoma (VS) cases – with Koos grading scale score of 1 to 3 – treated with GK-SRS in a single fraction were retrospectively analyzed. A therapeutic dose of 12 Gy was prescribed in all cases. The VS cases were replanned in a CK (model VSI, Linac output rate: 800 MU/min) system employing the fixed collimators. Computed Tomography (CT) images, HU-to-density calibration data, and contoured structures utilized in GK treatment planning were used for CK planning. CK plan optimization strategy resulted in clinically deliverable plans, with a sole obligation to keep the VS target coverage (by the prescription dose iso-surface) higher than 95% to match the corresponding property of GK plans.

For each case, the plan data were extracted from both GK and CK systems and used to independently calculate the dose and dose rate distributions for each radiation shot (for the GK system) or irradiating beam (for the CK system) on a voxel-by-voxel basis. The resulting dosimetry data were then used to obtain corresponding BED distributions accounting for sublethal repair effects, using the Millan and Canney formula [1], as revised by Pop *et al* [2] and employing an a/b ratio of 2.47 Gy.

**Table 1.** Statistical analysis of the studied CK and GK plans

Characteristic	CK N = 15 <sup>1</sup>	GK N = 15 <sup>1</sup>	p-value <sup>2</sup>
Isodose (%)	64.00, (60.00 - 76.00)	50.00, (50.00 - 65.00)	<0.001
Treatment Time (min)	35.00, (17.00 - 56.00)	36.00, (19.00 - 74.00)	0.34
BOT (min)	13.70, (6.96 - 28.13)	33.50, (17.30 - 70.50)	<0.001
V12Gy (cc)	0.42, (0.10 - 5.24)	0.41, (0.12 - 5.35)	0.68
Idx Coverage	0.97, (0.95 - 0.99)	0.99, (0.97 - 1.00)	<0.001
Idx Conformality	1.18, (1.08 - 1.54)	1.19, (1.07 - 1.85)	0.62
Idx Selectivity	0.84, (0.77 - 0.98)	0.84, (0.53 - 0.94)	0.16
Idx Gradient	3.77, (2.84 - 5.61)	2.89, (2.59 - 3.67)	0.002
Idx Paddick	0.83, (0.75 - 0.95)	0.83, (0.53 - 0.94)	0.25
R50	4.43, (2.99 - 8.80)	3.52, (2.77 - 6.84)	0.15
Dmin (Gy)	10.72, (8.81 - 11.75)	9.70, (7.70 - 11.50)	0.051
Dmax (Gy)	18.75, (15.79 - 20.00)	24.00, (18.60 - 24.30)	<0.001
Dmean (Gy)	15.01, (13.80 - 15.70)	16.80, (15.60 - 18.20)	<0.001
D98 (Gy)	11.90, (11.44 - 12.15)	12.20, (11.50 - 12.90)	<0.001
BEDmin (Gy)	43.59, (15.85 - 62.86)	40.68, (26.35 - 55.17)	0.15
BEDmean (Gy)	90.06, (79.35 - 111.37)	99.46, (83.33 - 123.87)	0.002
BEDmax (Gy)	139.88, (108.23 - 296.00)	192.16, (123.02 - 207.71)	<0.001
BED98	51.81, (22.45 - 64.40)	54.28, (46.89 - 66.21)	0.51
Integral Dose (mJ)	5.37, (1.02 - 73.56)	6.00, (1.20 - 81.80)	0.65
Integral BED	39.95, (6.50 - 426.27)	35.05, (6.38 - 434.33)	0.90

<sup>1</sup> Median, (Min - Max)

<sup>2</sup> Wilcoxon rank sum test; Wilcoxon rank sum exact test

**Results:** Fifteen cases were retrospectively analyzed, with clinical and planning details summarized in Table 1. Key findings include:

1. Different isodose lines are used to prescribed the therapeutic dose, with GK dose distributions being more inhomogeneous than CK distributions.
2. Treatment times were similar, but beam on time (BOT) was significantly shorter in CK.
3. Plan quality indices were comparable, except from coverage and gradient index, where GK plans showed higher coverage and lower gradient indices than CK plans. These findings should be interpreted with caution due to the retrospective nature of the study and the small VS tumors analyzed (median volume: 0.36 cm<sup>3</sup>)
4. GK plans exhibited higher Dmax, Dmean and marginal dose (D98) than CK plans, attributed to the higher inhomogeneity of the GK dose distributions and the small tumor volumes studied
5. BEDmin and marginal BED (BED98) were similar between the plans from the two systems, whereas BEDmax, and BEDmean were higher in GK plans due to the higher inhomogeneity of the GK dose distributions and the relatively small volume of the studied tumors.

**Conclusion:** Robot trajectory time significantly contributes to the total CK treatment time, whereas in GK, treatment time depends on the number of radiation shots and the activity of Co-60 sources. No statistically significant difference was observed in BED98 delivered to the VS targets. Differences in mean and max dose and BED levels reflect the different dose prescription policy in the two SRS platforms.

## References

- [1] W.T. Millar, P.A. Canney, *Int. J. Radiat. Biol.* 64 (1993) 275–291.
- [2] L.A.. Pop, W.T. Millar, M. van der Plas, A.J. van der Kogel, *Radiother. Oncol.* 55 (2000) 301–315.