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Exploring the Feasibility and Potential of Spatially Fractionated Radiotherapy (SFRT) for Treating Recurrent Glioblastoma Multiforme (GBM)

Yuwei Zhou*, Sean Tanny, Michael Milano, Brian Marples, Hyunuk Jung, and Dandan Zheng

University of Rochester, Rochester, NY

UR MEDICINE — WILMOT CANCER INSTITUTE

PURPOSE / OBJECTIVES

- Recent experience with multi-metastasis stereotactic radiotherapy and the rise of SFRT suggest that a highly-heterogenous dose distribution may be more effective and tolerable for larger cranial targets than conventional radiotherapy.
- Recurrent GBM patients suffer from high rates of toxicity and often are not able to tolerate a tumoricidal dose using conventional RT alone.
- A more effective dose could be delivered and better tolerated using an SFRT technique as an upfront boost for conventional RT.
- This study explores the feasibility of planning SFRT for recurrent GBM patients, leveraging its strengths of selective killing and sparing, immune response stimulation, and selective vascular disruption.

MATERIAL & METHODS

- We have performed a retrospective dosimetric study simulating the feasibility of performing SFRT in the context of five recurrent GBM patients.
- For each patient, a single-fraction SFRT treatment was replanned based on recurrent course (2nd course) planning CT and contours. SFRT vertices were generated in the PTV using a published script, along with a manual vertex design to target ~10% of GTV and avoid critical OARs.
- SFRT vertices size are 1-2 cm diameter and spacing between vertices is 2-4 cm.
- A peak dose of 15Gy was prescribed to the vertices, while the valley dose was constrained below 5Gy.
- All SFRT plans were planned with 4-7 non-coplanar semi-arcs (6MV flattening-filter-free beam) in Eclipse on Varian Edge® equipped with HD-MLC.
- In SFRT 2nd course, SFRT plan replaced the first fraction of the original conventional recurrent treatment plan . Compared to the conventional RT 2nd course, prescription of SFRT course was escalated. SFRT sum plan is the composite plan of 1st course and SFRT 2nd course treatment plans.
- Accumulative EQD2 of the sum plans to the targets and OARs (such as normal brain, brainstem and chiasm etc.) were analyzed and compared using the original sum plan (1st course +2nd course) vs. SFRT sum plan.

SUMMARY / CONCLUSION

- **Preliminary planning results have demonstrated that clinically-acceptable SFRT plans can be achieved with a vertex size of 1-2 cm diameter and spacing between vertices of 2-4 cm. Peak-to-valley ratios >3 were consistently achieved. If SFRT vertices were completed inside GTV, nearby OARs and normal brain sparing was reduced or similar with SFRT compared with original RT.**

Contact Information

*Yuwei Zhou. PhD, DABR. Yuwei_Zhou@URMC.Rochester.edu

RESULTS

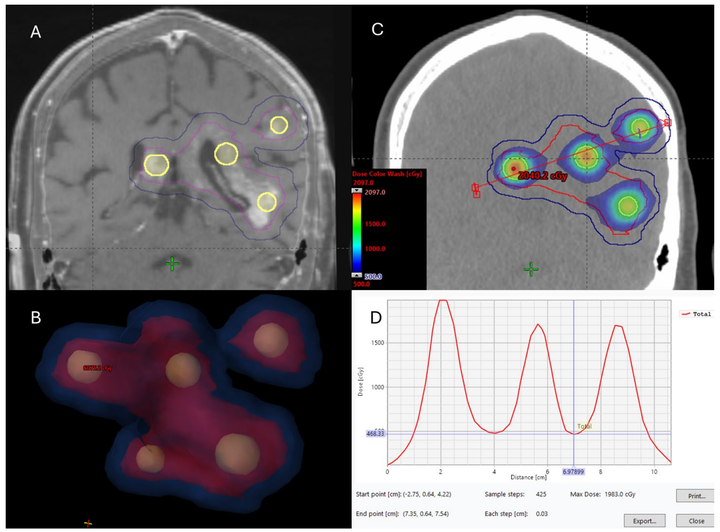

Figure 1. A) Manually modified vertices (yellow) GTV (red) and PTV (dark blue) on fused coronal T1 contrast MR of P5. B) 3 sets of vertices contours in 3D: dark blue segment is PTV; red segment GTV; yellow segment is vertices. C) Dose distribution of one-fraction SFRT plan (Peak dose: 15Gy, Valley dose <5Gy). D) Dose profile along the red arrow in Figure 1C.

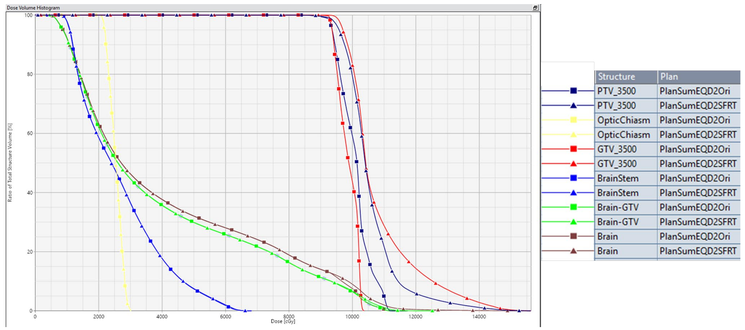

Figure 2. Original and SFRT sum plans DVH plots of P5

Table 1. EQD2 and DVH gamma analysis of OARs in sum plans

	Brain-GTV				Brainstem				Chiasm*			
	EQD2 D0.1cc (Gy)			DVH Gamma analysis (1%/1%)	EQD2 D0.1cc (Gy)			DVH Gamma analysis (1%/1%)	EQD2 D0.035cc (Gy)			DVH Gamma analysis (1%/1%)
	Original	SFRT	Diff %		Original	SFRT	Diff %		Original	SFRT	Diff %	
P1	114.19	168.74	48%	87%	68.69	69.39	1.0%	99%	61.28	61.75	0.8%	86%
P2	110.52	194.25	76%	85%	26.01	26.31	1.2%	89%	13.42	13.50	0.6%	80%
P3	127.06	158.26	25%	80%	68.69	69.42	1.1%	96%	61.56	62.09	0.9%	86%
P4	121.05	123.99	2%	66%	52.40	52.06	-0.7%	95%	11.86	11.64	-1.8%	63%
P5	111.88	120.44	8%	91%	63.33	63.69	0.6%	100%	27.71	27.65	-0.2%	98%

Table 2. EQD2, V95% and DVH gamma analysis of targets in sum plans

	PTV						GTV			
	EQD2 D0.1cc			V95%		DVH Gamma analysis (1%/1%)	EQD2 D0.1cc			DVH Gamma analysis (1%/1%)
	Original	SFRT	Diff %	Original	SFRT		Original	SFRT	Diff %	
P1	120.42	168.75	40.1%	100.0%	100.0%	56%	108.17	158.30	46.3%	62%
P2	111.37	194.26	74.4%	94.9%	96.6%	53%	105.29	153.79	46.1%	57%
P3	126.25	170.29	34.9%	98.1%	98.6%	65%	123.13	170.27	38.3%	64%
P4	121.63	153.77	26.4%	100.0%	99.9%	55%	121.13	153.78	27.0%	46%
P5	111.87	151.16	35.1%	91.8%	88.9%	62%	103.37	151.16	46.2%	66%

Table 3. V120Gy evaluation of EQD2 SFRT sum plan

	V120Gy (cc)			
	Brain	Brain-GTV	PTV	GTV
P1	16.4	8.9	17	7.8
P2	12.3	7.3	12.3	5
P3	122.2	121.7	131.7	38.7
P4	7	0.3	6.9	6.8
P5	7.1	0.1	7.1	7

- Plan quality of all SFRT plans met our study design goal.
- Compared to original plan, accumulative EQD2 of brainstem and chiasm in SFRT sum plan was reduced or similar as original plan. None of the accumulative EQD2 exceed 70Gy.
- Compared to original 2nd course, the prescription of SFRT course was escalated. Thus, the increase of accumulative EQD2 in brain and targets is inevitable. However, if we limited the SFRT vertices completely inside GTV (for example, P4 and P5), the V120Gy of normal brain can be controlled (0.3 and 0.2 cc for P4 and P5 respectively). That may be one planning instruction for recurrent SFRT plan.
- The coverage of V95% of SFRT sum plan was generally identical with original sum plan.