Protons offer reduced normal-tissue exposure for patients receiving stereotactic body radiation therapy (SBRT) for liver tumors: A comparative study based on RTOG 1112

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**Background:** Increasing interest in proton stereotactic body radiation therapy (SBRT) due to its inherent physical properties led the investigators of RTOG 1112, randomized phase III study of sorafenib versus SBRT followed by sorafenib in hepatocellular carcinoma, to include protons as a treatment modality. While many prior dosimetric investigations have been done evaluating different proton versus intensity modulated radiation therapy (IMRT) plans, to our knowledge no evaluation of passively scattered proton SBRT vs IMRT has been completed. Evaluating passively scattered proton planning is important as passively scattered proton beam treatments remain a large portion of all proton treatments and have advantages over other proton techniques. The purpose of this study is a rigorous dosimetric comparison of passively scattered proton vs photon SBRT.

**Methods:** Fourteen metastatic liver lesions in nine patients were evaluated. Proton and IMRT plans were developed per RTOG 1112 specifications for each of the lesions independently with a prescription dose of 50Gy in 5 fractions. Dose volume histograms (DVH) were then analyzed and that data presented. A non-parametric substitute for the t-test in a paired sample, the signed-rank test of Wilcoxon, with a significance level of  $\alpha$ =0.05 was performed.

**Results:** Both proton and IMRT plans were able to achieve 95% coverage of the planning treatment volume (PTV) with 100% of the dose, while meeting the normal tissue constraints. The lesions ranged in size from 1-3.1cm, with PTV volumes of 11.4-73.4cm3. Proton plans significantly reduced the V5 (volume of liver receiving at least 5 Gy), V10, and V15 (p=0.001), with absolute reductions of 20.8%, 15.6%, 5.7% respectively. The mean liver dose was reduced from 7.61 Gy for the IMRT plan to 4.62Gy for the proton plan (p = 0.002). The volume of normal liver spared doses greater than 15 Gy was also reduced, where protons spared a median of 83 cm3 more than IMRT (range 21-198 cm3). The stomach V10 was also reduced (0.7% vs 10.7%, p= 0.003) (see table).

## **Conclusions**

This study represents the first data for passively scattered proton beam SBRT demonstrating significant sparing of normal liver when compared to IMRT. The improved treatment plan forms a solid basis for proton inclusion in RTOG 1112, where the clinical outcomes will validate the dosimetric findings in this study.

Table

Organ At Risk	DVH Parameter	Proton Plan	IMRT Plan	p-value
V10 (%)	14.1 ±8.5	29.7 ±8.3	0.001	
V15 (%)	10.7 ±4.8	16.4 ±5.4	0.001	
V20 (%)	9.0 ±4.1	10.8 ±4.2	0.003	
V30 (%)	6.8 ±3.4	6.2 ±2.8	0.026	
V40 (%)	4.8 ±2.7	4.1 ±2.0	0.002	
Mean(Gy)	4.62 ±2.5	7.61 ± 2.2	0.001	
Stomach	V10 (%)	0.7 ± 0.7	10.7 ±2.6	0.003
	Max (Gy)	2.1± 2.0	13.7 ±2.0	0.001
Biliary Duct	V10 (%)	4.5 ±3.4	10.6 ±5.1	0.285
	V20 (%)	2.8 ±2.8	2.2 ±2.2	0.317