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Objectives

This study is a preliminary analysis of prospective registry (PRO-LIT) of primary and metastatic liver malignancy cases treated with proton beam therapy (PBT) at a high-volume tertiary center. We aimed to record clinical outcomes, toxicity, and biochemical responses in our PBT cases and assess the feasibility of hypofractionated PBT in complex liver malignancies.

Methods

Data was prospectively collected from patients treated with PBT for primary or secondary liver malignancies between 2020 and 2025. Patient demographics, liver disease etiology (hepatitis, NASH, cirrhosis), Child-Pugh score, tumor characteristics (segmental location, PVTT), prior therapies, radiation details (dose, fractionation, volumes), and response parameters (AFP, PIVKA-II, radiologic imaging) were analyzed. Patients were treated with image-guided pencil beam scanning PBT using hypofractionated regimens tailored to disease extent and location.

Results

A total of 29 patients (23 HCC, 4 cholangiocarcinoma, 2 metastatic) were analyzed; 25 were male, with a median age of 67 years (range 45-85). Most patients had Child-Pugh A, six classified as B7 and no CP-C. Ten patients had PVTT (Vp2–Vp4). Of primary HCC, 16 cases were treated with 15–20 fraction (45–67.5 GyE) (mean GTV – 280.1 cc) and 5 fraction SBRT (40-50 GyE) in selected 7 cases (mean GTV 43cc). All proton plans met Liver-GTV > 700 cc dose constraints and had superior dosimetry over photon in comparative plans (Figure 1). The median CTV and GTV volumes were 1000 cc and 292.4 cc, respectively. Biochemical response showed a median AFP reduction of 73.4% (range -26% -99.3%), with parallel declines in PIVKA-II (median 82.5%). Among 25 evaluable patients, 72% showed complete or partial radiological response at 3–6 months. PVTT cases demonstrated favorable local control and biochemical stabilization. No grade III/IV liver toxicities were reported. Two cases developed transient immune-related adverse events post-combination therapy, managed conservatively.

Conclusions

This institutional registry demonstrates that proton therapy is a safe and effective modality for managing liver malignancies in a real-world setting. PBT offers excellent liver sparing, making it particularly valuable in patients with cirrhosis, large tumor or limited normal liver volumes, PVTT, or prior treatments. Hypofractionated regimens (especially 15–20 fractions) show promising efficacy in bulky and vascular-involved tumors. We also demonstrated safety and feasibility of 5 fraction PBT in liver cases with better dosimetry as compared to photon. Continued prospective follow-up will define survival outcomes and support the integration of PBT into multi-modality liver cancer care.

