

Auditory Outcomes in Patients Who Received Proton Radiotherapy for Craniopharyngioma

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Background

- Pediatric craniopharyngioma is a rare, benign neuroepithelial brain tumor that arises near the pituitary gland and hypothalamus during embryonic development. The current therapeutic approach for managing craniopharyngioma includes a maximal tumor resection or partial tumor resection followed by radiotherapy.
- Conventional 3-dimensional methods of photon-based radiotherapy have historically been used to treat a variety of pediatric brain tumors, including craniopharyngioma; however, photon radiotherapy is associated with late effects such as sensorineural hearing loss (SNHL). Incidence of SNHL has been reported in 14% to 27% of children treated with photon radiotherapy and no ototoxic chemotherapy¹⁻³.
- Methods of irradiation have evolved over the past four decades with advances in radiation physics and computer technology leading to greater precision of radiation delivery, dose reduction to normal tissues, and less adverse effects.
- Proton radiotherapy (PRT) is an advanced method of irradiation currently being investigated in a limited number of institutions for the management of childhood cancer. While photon- and proton-based radiation techniques offer similar tumor control,⁴ protons enable a reduction in doses delivered to surrounding normal tissues, potentially decreasing acute and late toxicities when compared to photons⁵. We report early auditory outcomes in children treated with proton radiotherapy (PRT) for craniopharyngioma.

Objectives

- Describe early auditory outcomes in children and adolescents treated with PRT for craniopharyngioma by reporting the incidence, onset, and severity of ototoxicity based on comparisons of conventional frequency (CF: 0.25 to 8.0 kHz) and extended high-frequency (EHF: 9.0 to 16.0 kHz) pure-tone audiometric thresholds over time, examining changes in distortion-product otoacoustic emission (DPOAE) levels over time; exploring the potential impact PRT has on speech-in-noise (SIN) perception over time.

Methods

- CF audiometry, EHF audiometry, DPOAE testing, and SIN assessments were prospectively and longitudinally conducted on 74 children with a median of two post-PRT evaluations (range, 1 to 5) per patient.
- Ototoxicity was classified using the Chang Ototoxicity Grading Scale and the American Speech-Language-Hearing Association (ASHA) criteria.
- Comparisons were made between baseline and most recent DPOAE levels with evidence of ototoxicity based on criterion reductions ≥ 6 dB.
- The critical difference values for comparing SIN scores between two conditions (i.e., pre- and post-PRT) were used to determine a significant change between test scores.

Results

- At last evaluation, no patients had SNHL in the CF range, and two patients had SNHL (Chang 1a) in the EHF range. Based on the ASHA criteria, a decrease in hearing was observed in zero patients in the CF range alone; in nine patients in the EHF range alone; and in 15 patients in both the CF and EHF ranges. Patients who met the ASHA criteria for decreased hearing were more likely to experience a decline in the EHF range compared to the CF range (McNemar's test exact $P = 0.0039$) (Figure 1).
- The median time to onset of decreased hearing was 24.6 months (range: 11.1 to 63.4 months), and the estimated probability of not having decreased hearing sensitivity at the end of 3 years post-PRT was $70\% \pm 7.4\%$ and $38\% \pm 15\%$ at 5 years (Figure 2).
- DPOAE levels decreased at a faster rate at higher versus lower frequencies (Table 1). For 41 evaluable patients, SIN perception did not decline over time ($P = 0.6463$).

Figure 1. Decreased hearing by ASHA criteria.

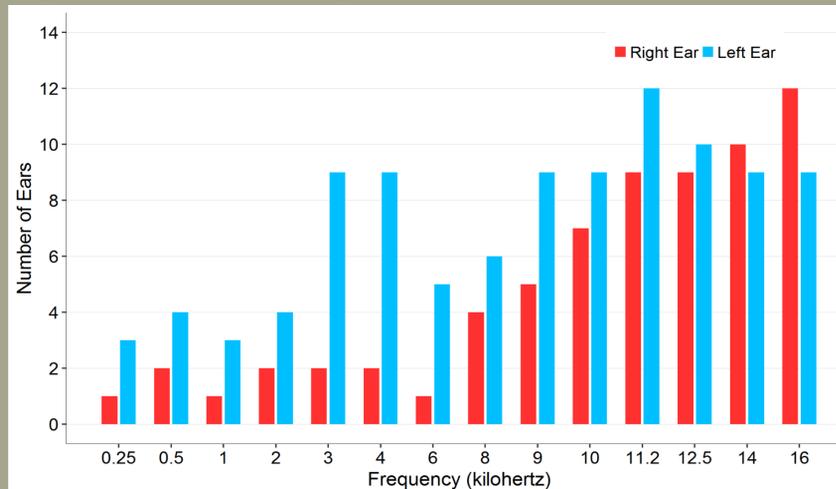


Figure 2. Onset of decreased hearing by ASHA criteria

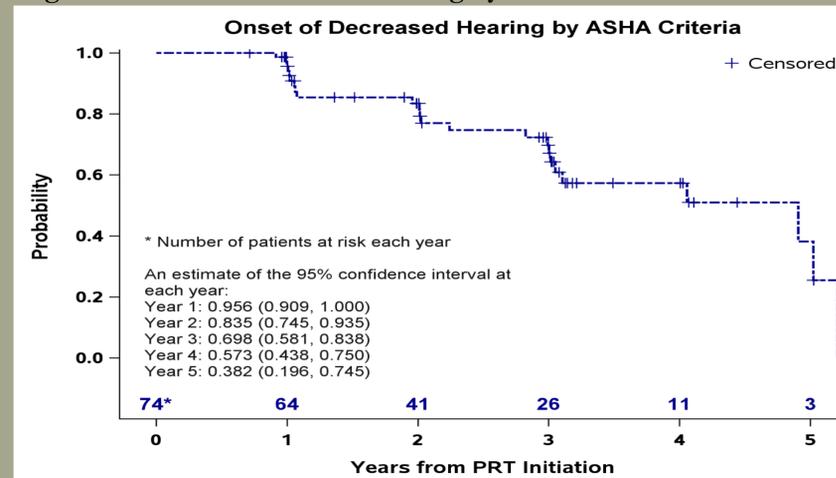


Table 1. Mixed model analyses of DPOAE level over time

Freq (kHz)	No (%) patients*	Effect	Estimate	95% CI of the Estimate	P
1.5	67 (91)	Time (years)	-0.7009	-1.1636, -0.2382	0.0035
2	69 (93)	Time (years)	-0.8760	-1.2476, -0.5044	<.0001
3	66 (89)	Time (years)	-0.7789	-1.1568, -0.4010	0.0001
		Age at PRT initiation (years)	-0.4053	-0.7208, -0.0898	0.0127
4	63 (85)	Time (years)	-0.5843	-1.1220, -0.0466	0.0346
		Age at PRT initiation (years)	-0.4080	-0.7712, -0.0448	0.0283
6	59 (80)	Time (years)	-2.0530	-2.7659, -1.3401	<.0001
		Age at PRT initiation (years)	-0.7223	-1.0931, -0.3515	0.0002
8	40 (54)	Time (years)	-1.6543	-2.6367, -0.6719	0.0017

Conclusions

At a median follow-up time of two years post-PRT, normal hearing was maintained within the CF range. However, sub-clinical decreases in hearing were observed, particularly in the EHF range and in DPOAE level; thus, long-term follow-up is recommended to monitor for potential auditory late effects from PRT.

References

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