Acoustic Neuroma Today

Hypofractionated Stereotactic Radiosurgery for Acoustic Neuroma: The CyberKnife

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Traditional radiation therapy (RT) typically delivers radiation to a wide target field within the body resulting in the treatment of both the tumor and a significant volume of surrounding healthy tissue. This technology is ideal for tumors that invade the surrounding tissue and when tumor margins are not well defined. In an effort to protect the healthy tissue, traditional RT is delivered in small daily doses or fractions divided into 30-40 sessions. This dosing strategy is commonly referred to as *hyperfractionation*. The sub-lethal daily doses allow healthy tissue to repair itself; a capability not present in tumor cells. However, the total dosage delivered to the patient is limited by the tolerance of healthy tissue in close proximity to the target. In some cases, this limitation may result in the inability to adequately control tumor growth. Regardless, once a patient has received his or her limit, radiation treatment must stop in an effort to prevent healthy tissue damage.

Stereotactic radiosurgery (SRS) devices such as Gamma Knife and CyberKnife are designed to deliver high dose radiation with extreme accuracy, targeting the tumor with minimal damage to the surrounding healthy tissue. Using extreme precision in targeting rather than hyperfractionation for protecting healthy tissue enables higher more effective dosing to stubborn tumor cells. Traditionally, radiosurgery was delivered in a single session or fraction. The ablation of the target tissue within a single fraction was compared to the definitive cut using a surgeon's scalpel, hence the term *radiosurgery*. However, even with the extreme precision, in some cases such as with tumors located within the brain or spinal cord, *hypofractionation* (i.e., dose delivery in 2-5 fractions) becomes necessary when protection of even a very small amount of healthy tissue is critical.

The CyberKnife system was one of the first radiosurgery devices to use hypofractionation as an added measure of safety. It allows for less damage to surrounding healthy tissue and for clinicians to complete treatment in 1 to 5 days compared to several weeks required for traditional RT. Hypofractionated SRS using CyberKnife has been performed successfully in cases when single-session SRS treatments are considered too risky, such as with tumors within the brainstem, spinal cord, or optic nerves. The combination of high dose precision and hypofractionation has enabled successful treatment of lesions previously considered untreatable with surgery, radiation therapy, or single-session radiosurgery.

Excellent tumor control rates of 95% or more have been reported with single-session SRS (e.g., Gamma Knife), conventionally fractionated stereotactic radiotherapy and proton beam irradiation. Given the impressive rates of tumor control with these modalities, more attention is being paid to functional outcome such as hearing preservation, as well as trigeminal nerve and facial nerve function. The radiobiological rationale behind fractionation is to minimize radiation-induced normal tissue complications. However, conventionally fractionated treatment schedules typically require multiple sessions over 5 to 6 weeks, which may be in-convenient for those living distant from the radiation facility. Furthermore, when the target tissue's radiation sensitivity approaches that of the surrounding critical tissues, as it does with benign (e.g., acoustic neuroma) compared to most metastatic tumors, stricter treatment limitations using conventional fractionation do not provide much room for improvement.

The treatment strategy for acoustic neuromas at Stanford University has focused on using CyberKnife for hypofractionated SRS in 3 fractions in an effort to maintain high tumor control rates while reducing treatment toxicity. Initial data from Stanford (1999) for 33 patients using 21 Gy in 3 fractions was encouraging. The tumor control rate was 97%. Preservation of useful hearing was 77%,[1] compared to 51% overall hearing preservation in compiled single-session SRS data.[2] However, dosages used for single-session SRS have been reduced to 12-13 Gy over the past decade, and this has maintained tumor control rates of 95% or more while improving hearing preservation in single-session SRS to 60.5%, according to the analysis by Yang et al, and up to 68-77% in some single-institution reports.[3] The reduction of dose also resulted in a decreased risk of trigeminal (0.7-5%) and facial nerve injury (0-4.5%) in single session SRS.[4]

How do more recent CyberKnife hypofractionated SRS results compare to the single-session SRS data? A 2011 Stanford report has looked at 383 cases, 90% of which were treated with 18 Gy in 3 fractions (about equivalent to 12 Gy for single-session SRS). The 3 and 5 year tumor control rates were shown to be 99% and 96%, respectively.[5] The serviceable hearing preservation rate was 76%. There was no case of facial weakness; eight patients (2%) developed trigeminal nerve dysfunction, half of which was transient.

Although these results are promising, the retrospective nature of this study, along with variables such as tumor size, degree of hearing loss, presence of neurofibromatosis-type 2 and the range of complication rates, make direct comparisons with single-session SRS difficult. However, an interesting observation of the Stanford report is that low risk of complications was seen with larger-volume tumors, perhaps indicating a benefit of hypofractionated SRS compared to single-session SRS in this subset of cases.

The current Stanford protocol for treatment of acoustic neuroma using CyberKnife is 18Gy in 3 daily sessions. Each session lasts approximately 50 minutes. CyberKnife patients do not require the application of a rigid stereotactic head frame. Instead, the patient's face and head are held steady to the CyberKnife table using a soft customized see-through and breathable aquaplast mask. CyberKnife treatment for acoustic neuroma results in excellent tumor control with promising hearing preservation and non-auditory complication rates. Despite these successes, more research is needed to continue optimizing the functional outcomes in these patients and to better distinguish between the various treatment options. Until then, with comparable results across all non-invasive modalities, certain considerations such as number of sessions and frame-based vs. frameless technology may be reasonable when choosing a particular treatment option.

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[1] J.C.Poen et al, "Fractionated Stereotactic Radiosurgery and Preservation of Hearing in Patients with Vestibular Schwannoma: A Preliminary Report," *Neurosurgery*, 1999;45(6), 1299-1305.

[2] I.Yang et al, "A Comprehensive Analysis of Hearing Preservation after Radiosurgery for Vestibular Schwannoma," *Jour of Neurosurgery*, 2010;112(4), 851-859.

[3] For example: R.Chopra et al, "Long-term Follow-up of Acoustic Schwannoma Radiosurgery with Marginal Doses of 12 to 13 Gy," *Int J Radiat Oncol Biol Phys*, 2004;68(3),845-851; T.Hasegawa et al, "Stereotactic Radiosurgery for Vestibular Schwannomas: Analysis of 317 Patients Followed More than 5 Years," *Neurosurgery*, 2005;57(2),257-65.

[4] For example: L.D.Lunsford et al, "Radiosurgery of Vestibular Schwannomas: Summary of Experience in 829 Cases," *Jour Neurosurgery*, 2005;102 (Suppl), 195-99: J.M.Hempel et al, "Functional Outcome after Gamma Knife Treatment in Vestibular Schwannomas, *Eur Arch Otorhinolaryngol*, 2006;263(8), 714-18.

[5] A.Hansasuta et al, "Multisession Stereotactic Radiosurgery for Vestibular Schwannomas: Single-institution Experience with 383 Cases," *Neurosurgery*, 2011;69(6),1200-1209.