



Multisession Radiosurgery for Hearing Preservation

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Clinically relevant dose-tolerance limits with reliable estimates of risk in 1-5 fractions for cochlea are still unknown. Timmerman's limits from the October 2008 issue of *Seminars in Radiation Oncology* have served as the basis for clinical practice, augmented by updated constraints in TG-101 and QUANTEC, but the corresponding estimates of risk have not yet been well-reported. A total of 37 acoustic neuroma CyberKnife cases from MedStar Georgetown University Hospital treated in 3 or 5 fractions were combined with single-fraction Gamma Knife data from the 69 cases in Timmer 2009 to form an aggregate dataset of 106 cochlea cases treated in 1-5 fractions. Probit dose-response modeling was performed in the DVH Evaluator software to estimate normal tissue complication probability. QUANTEC recommends keeping single-fraction maximum dose to the cochlea less than 14 Gy to maintain less than 25% risk of serviceable hearing loss, and our 17.9% risk estimate for 14 Gy in 1 fraction is within their predicted range. In 5 fractions, our estimate of the Timmerman 27.5 Gy maximum cochlea dose limit was 17.4%. For cases in which lower risk is required, the Timmerman 12 Gy in 1 fraction and the TG-101 limit of 25 Gy in 5 fractions had an estimated risk level of 11.8% and 13.8%, respectively. High-risk and low-risk dose tolerance with risk estimates in 1-5 fractions are all presented.

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Radiosurgery or hypofractionated radiotherapy (stereotactic body radiotherapy [SBRT]) is a well-established modality for the management of acoustic neuromas (AN) that are slow-growing benign tumors. These tumors arise from the cochlea-vestibular nerve complex within the internal auditory canal and can expand into the cerebellopontine angle. A “wait-and-

see” approach is an option but these tumors can grow causing compression of the seventh and eighth cranial nerves and brainstem, as well as hearing loss, and many patients inevitably require treatment.¹⁻⁴ Régis et al³ found that only 78%, 43%, and 14% of patients in the wait-and-see group maintained tumor control and functional hearing at 1, 2, and 5 years, respectively, whereas the Gamma Knife group had 88%, 79%, and 60% of patients for the same endpoints and time periods. Although AN usually grow slowly, Kondziolka et al⁴ observed that more than 95% of their patients in the “wait-and-scan” group had measurable growth by the 10-year follow-up. Common treatments of these tumors are microsurgical resection, radiation therapy, or conservative management with radiologic surveillance.^{5,6} Potential complications following SBRT for AN include trigeminal neuropathy, facial nerve dysfunction, ataxia, and hearing loss.

Leksell⁷ and Norén et al⁸ were the first to treat AN with Gamma Knife (Elekta Inc, Stockholm, Sweden) beginning in the 1960s, with reports of very favorable results.⁷⁻⁹ In the mid-1980s, with the worldwide availability of the Gamma Knife and with the development of linear accelerators adapted for

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stereotactic irradiation, this noninvasive radiation treatment became more popular. By the year 2000, several authors had claimed excellent local control rates with radiosurgery, comparable with surgery, but with a high rate of preservation of hearing and facial and trigeminal nerve function.⁹⁻¹² Seeking a potential fractionation benefit, several groups began fractionated regimens on a stereotactic linac^{9,13-15} or CyberKnife (Accuray Inc, Palo Alto, CA).¹⁶⁻¹⁹ However, despite more than 40 years of clinical use and numerous publications, quantitative estimates of complication risks as a function of cochlea dose remain elusive.

As SBRT is increasingly being applied for the treatment of AN, it is important to determine reliable dose-tolerance limits for the cochlea to guide clinical practice. The goal of this study was to determine clinically relevant SBRT dose-tolerance limits for hearing preservation, when treatments are given in 1-5 fractions, based on statistical analysis of clinical outcomes data.

Single-Fraction Cochlea Dose Tolerance

A PubMed search for cochlea AND ((stereotactic AND radiation) OR radiosurgery) found 96 articles in June 2015, but among them we found no dose-response models, and could only find a single publication with cochlea doses and hearing preservation outcomes for each patient, Timmer et al²⁰. The cochlea $D_{\max}$ data from this Gamma Knife series of 69 patients treated from June 2003–November 2007 at the Radboud University Nijmegen Medical Center in The Netherlands are reproduced in Figure 1(A). Patient and treatment characteristics are already described,²⁰ so only the details most important for interpreting our dose-response model are summarized in Table 1. The Gardner-Robertson scale,²¹ shown in Table 2, includes 3 frequency pure tone average

Table 1 Summary of Patient and Treatment Characteristics

Characteristic	Present Study	Timmer et al ²⁰
Number of cases	37	69
Median age, y	58 (31-85)	53 (24-76)
Median follow-up, mo	51 (15-108)	14.2 (3-56)
Median tumor volume, cc	1.03 (0.14-7.60)	2.28 (0.02-10.20)
Number of cases per fraction		
1 Fraction	0	69
3 Fractions	2	0
5 Fractions	35	0
Delivery method		
CyberKnife		Gamma Knife
< 50 dB hearing preservation	4	6

(PTA) as well as speech discrimination scores. The Timmer et al²⁰ study did measure speech discrimination scores for each patient but unfortunately they were not published as a function of dose for each patient like the PTA was in Figure 1(A), so our probit dose-response model could only be based on PTA alone. The selected end point was 50 dB of hearing loss in 1 ear, which is part of the Gardner-Robertson scale for serviceable hearing.

Statistical modeling

The probit model^{22,23} was used to estimate the normal tissue complication probability (NTCP) dose-response for cochlea $D_{\max}$ in terms of the normalized slope m and the $TD_{50}(V)$ 50% tolerance dose (TD) for a given partial volume (V) by

$$NTCP = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^t e^{-x^2/2} dx \quad (1)$$

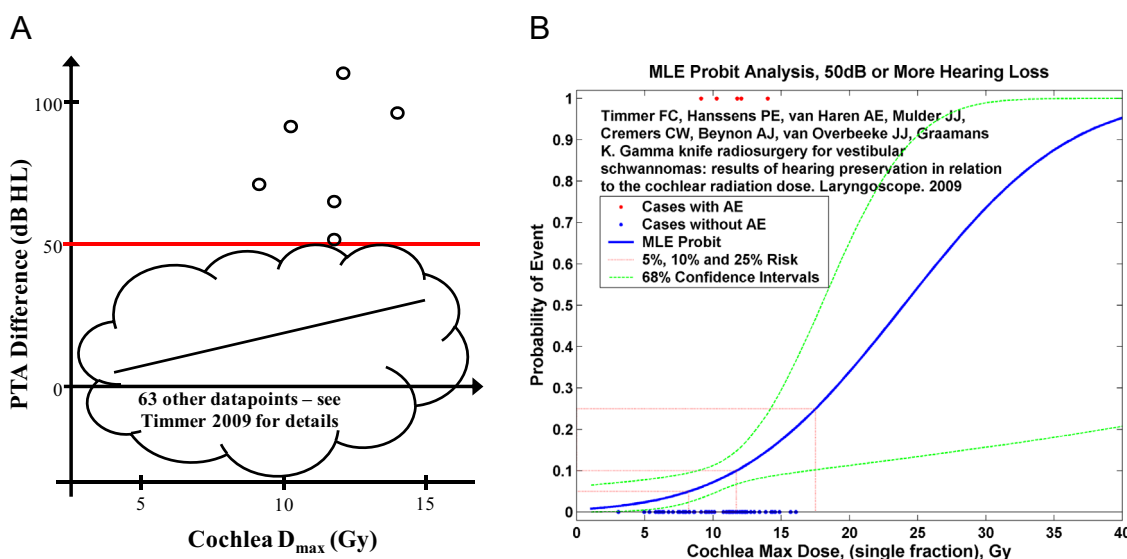


Figure 1 Single-fraction cochlea tolerance. (A) Change in pure tone average (PTA) from study by Timmer et al as a function of cochlea $D_{\max}$; the 6 data points shown are the ones exceeding 50 dB of hearing loss and the rest may be found in the article by Timmer et al.²⁰ (B) Corresponding dose-tolerance model for the end point of 50 dB hearing loss. AE, adverse event; dB, decibel; MLE, maximum likelihood estimate. (Color version of figure is available online.)

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