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CLINICAL INVESTIGATION **Brain**

TOWARD DOSE OPTIMIZATION FOR FRACTIONATED STEREOTACTIC RADIOTHERAPY FOR ACOUSTIC NEUROMAS: COMPARISON OF TWO DOSE COHORTS

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Purpose: To describe our initial experience of fractionated stereotactic radiotherapy dose reduction comparing two dose cohorts with examination of tumor control rates and serviceable hearing preservation rates.
Methods and Materials: After institutional review board approval, we initiated a retrospective chart review to study the hearing outcomes and tumor control rates. All data were entered into a JMP, version 7.01, statistical spreadsheet for analysis.
Results: A total of 89 patients with serviceable hearing had complete serial audiometric data available for analysis. The higher dose cohort included 43 patients treated to 50.4 Gy with a median follow-up (latest audiogram) of 53 weeks and the lower dose cohort included 46 patients treated to 46.8 Gy with a median follow-up of 65 weeks. The tumor control rate was 100% in both cohorts, and the pure tone average was significantly improved in the low-dose cohort (33 dB vs. 40 dB, $p = 0.023$, chi-square). When the patient data were analyzed at comparable follow-up points, the actuarial hearing preservation rate was significantly longer for the low-dose cohort than for the high-dose cohort (165 weeks vs. 79 weeks, $p = .0318$, log–rank). Multivariate analysis revealed the dose cohort ($p = 0.0282$) and pretreatment Gardner-Robertson class ($p = 0.0215$) to be highly significant variables affecting the hearing outcome.
Conclusion: A lower total dose at 46.8 Gy was associated with a 100% local control tumor rate and a greater hearing preservation rate. An additional dose reduction is justified to achieve the optimal dose that will yield the greatest hearing preservation rate without compromising tumor control for these patients.

Acoustic neuroma, Fractionated stereotactic radiotherapy.

INTRODUCTION

Acoustic schwannomas are intracranial extra-axial tumors that arise from Schwann cells surrounding the vestibular or cochlear nerves. They represent 8% of all intracranial tumors and have an overall incidence of 1 in 100,000 person-years. These tumors can result in diminished hearing, as well as tinnitus, headache, facial numbness or weakness, and balance disturbances. The management of acoustic schwannomas has changed during the past 30 years.

Surgery was initially the mainstay of treatment and recent published surgical data have shown local control rates as great as 97%; however, even to the present, an unavoidable incidence of postoperative morbidity has remained, such as a loss of serviceable hearing, facial neuropathy, aseptic meningitis, and cerebrospinal fluid leak. Stereotactic single-fraction radiosurgery (SRS) became an important noninvasive treatment alternative to the surgical resection of acoustic neuromas. A growing body of published data supports the use of single-fraction SRS as the standard of care for these patients. As the median age of diagnosis of this disease is 50 years, comorbidities from treatment play an important role in the patient's quality of life. As such, although initial SRS has maintained local control with a low incidence of recurrence, the toxicity profile was again high with doses of 18–25 Gy. This led to a dose reduction to the common standard of 12 Gy, which reduced treatment morbidity while maintaining tumor control.

More recent data have revealed that fractionated stereotactic radiotherapy (FSRT) may provide a comparably high rate of tumor control while also achieving a greater rate of hearing

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preservation in a serviceable hearing range. As in the SRS paradigm, we sought to improve hearing preservation by dose reduction. This study was designed to compare the rate of hearing preservation in the serviceable range in two FSRT dose cohorts. Furthermore, additional outcomes, such as the rates of tumor control and other cranial neuropathy rates, were analyzed.

METHODS AND MATERIALS

Patient enrollment

Before treatment, the cases of all patients were discussed at a multidisciplinary tumor board and found to be suitable for FSRT. All patients treated met the following criteria: (*1*) a newly diagnosed tumor with interval growth on serial magnetic resonance imaging (MRI), (*2*) serviceable hearing on the involved side as documented by audiogram, and (*3*) Karnofsky performance scale score of ≥70. Also, neurofibromatosis type 2 patients were excluded from the analysis. We identified 101 patients for review with serviceable, Gardner-Robertson 1 or 2 hearing levels treated with FSRT. Of those, 89 patients had serial audiometric data available for analysis.

Radiation technique

The entire cohort was treated on a dedicated Varian 600SR Clinac 6-MV stereotactic linear accelerator (1), later modified to a Novalis unit with a mini-multileaf collimator. Treatment planning was done with computed tomography-MRI fusion on either the Radionics X-Knife or the Novalis Brain Lab treatment planning software. The lesions were identified and contoured by the neurosurgeon. The patients were treated with conventional 1.8-Gy fractions delivered daily 5 d/wk for 4–6 weeks to a cumulative dose of either 50.4 Gy or 46.8 Gy. Because the dose reductions for single-fraction SRS were widely associated with uncompromised tumor control but greater hearing preservation rates, we decided to decrease our uniform total dose prescription by roughly 10% in 2002. The dose reduction to 46.8 Gy was applied to all patients as a treatment policy subsequent to November 2002 and represented our first dose iteration toward FSRT dose optimization. With the Radionics system, few isocenters were used, and conformality was attained with noncoplanar arc beam shaping and differential beam weighting. The Brain Lab system used a single isocenter and conformal dynamic arcs with mini-multileaf collimation.

Post-treatment assessment

All patients were followed serially with MRI scans, audiograms, and neurologic examinations, which included assessment of cranial nerve function. Tumor diameters and volumes were calculated using the MRI data obtained at routine intervals after treatment. The cochlea dose was analyzed by contouring the cochlea from the computed tomography-based data, adjusted to a bone window, and analyzing the cochlear dose from the automated dose–volume histograms provided by the treatment planning software. The homogeneity index was calculated by dividing the maximal target dose to the prescribed isosurface dose, and the conformality index was calculated by dividing the prescribed isosurface volume by the target volume (2). We reviewed the pre- and post-treatment MRI scans to assess the tumor control rates. Audiograms were considered reliable if the pure tone average (PTA) approximated the speech reception threshold, and hearing was graded according to the Gardner-Robertson scale. The date of the latest audiogram served as the date of the most recent follow-up, not the date of the actual follow-up encounters. Because many patients were not compliant with long-term follow-up audiometry, the median follow-up for the high-dose cohort (HDC) was actually comparable to that of the low-dose cohort (LDC), and the overall median follow-up for both dose cohorts was not reflective of the study period. The PTA was calculated from the audiometric masked bone conduction response at 500, 1,000, and 2,000 Hz, and a speech discrimination score was documented. Facial nerve function was assessed using the House-Brackman grading scale, and trigeminal nerve function was documented by the patient's pain perception, as well as the corneal reflex.

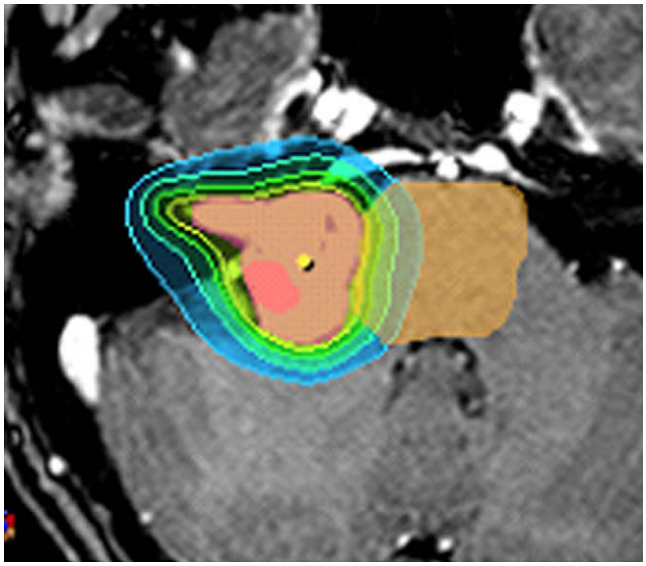

Fig. 1. Typical treatment plan for acoustic neuroma with single isocenter plan and dynamic arc conformal technique. Yellow line indicates 90% isodose prescription line.

Statistical analysis

All data were entered into and analyzed using a JMP, version 7.01, statistical spreadsheet. Tumor control was defined as either tumor shrinkage, no further growth, or one interval of documented growth after treatment with no additional growth on subsequent imaging intervals requiring no further intervention. The tumor control rates and cranial nerve preservation rates were established using the Kaplan-Meier product limit method, and differences were assessed by the log–rank test with statistical significance at $p < 0.05$. The audiometric data were judged not to fit a normalized distribution; therefore, the nonparametric Wilcoxon rank sum test was to assess

Table 1. Radiosurgery indexes by dose cohort

Index	HDC	LDC
Isosurface prescription	0.87	0.88
Isocenters (*n*)	1.14	1.18
MDPD	1.16	1.16
PITV	2.95	2.36*

Abbreviations: HDC = high-dose cohort; LDC = low-dose cohort; MDPD = maximal target dose to prescribed isosurface dose; PITV = prescribed isosurface volume by target volume.

* $p < 0.033$, Wilcoxon test.

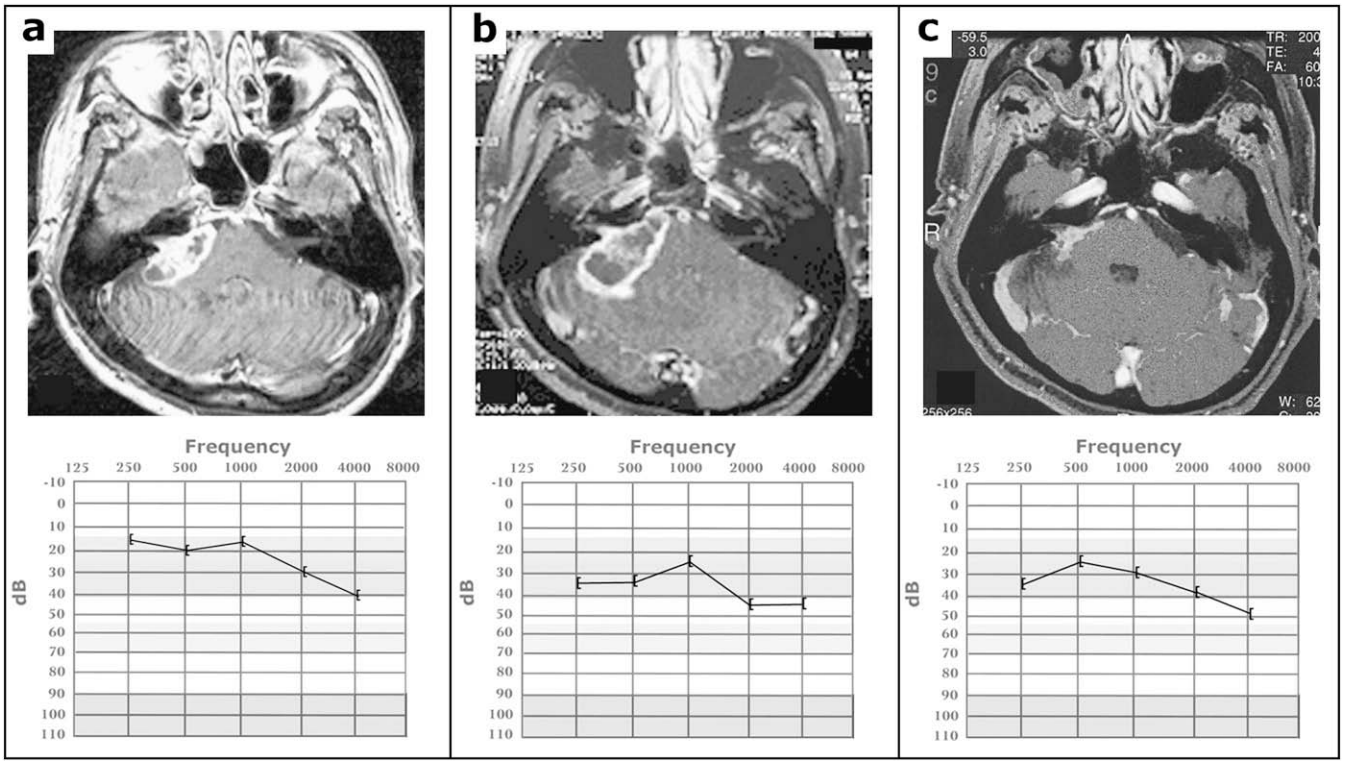

Fig. 2. Serial magnetic resonance imaging scans (Upper) with associated audiograms obtained at same time (Lower) in patient treated with fractionated stereotactic radiotherapy to 46.8 Gy. (a) Pretreatment T_1-weighted gadolinium-enhanced axial image featuring right acoustic neuroma. Audiogram reflects pure tone average of 22 and speech discrimination score of 95%, representing Gardner-Robertson level 1 pretreatment serviceable hearing. (b) Post-treatment T_1-weighted gadolinium-enhanced axial image at 6 months featuring some enlargement and extensive central necrosis of tumor. Audiogram at 6 months after treatment reflects some audiometric decay with pure tone average of 35 and speech discrimination score of 100%, representing a decrease to Gardner-Robertson level 2 serviceable hearing. (c) Post-treatment T_1-weighted gadolinium-enhanced axial image at 42 months featuring marked diminution in tumor size. Audiogram at 42 months after treatment reflects stable audiogram with pure tone average of 30 and speech discrimination score of 92%, back to lowest range of Gardner-Robertson level 1 serviceable hearing.

the pre- and post-treatment PTA and speech discrimination score. Kaplan-Meier analysis of hearing preservation was performed for both cohorts and corrected for comparable follow-up. The LDC was treated initially with circular collimators (Radionics and the Varian 600SR) and subsequently with the micro-minileaf collimator (Novalis, BrainLAB), so we performed a subanalysis of these groups in this cohort to note any differences.

Table 2. Analysis of mean cochlear dose measurements for both cohorts

Cochlear dose	HDC	LDC
Maximum (Gy)	47	41*
Minimum (Gy)	31	22†
V_{90}	36	24‡
V_{80}	39	28§
V_{50}	41	30¶

Abbreviations: V_{90}, V_{80}, V_{50} = 90%, 80%, and 50% cochlear volume dose, respectively; other abbreviations as in Table 1.

* $p = 0.001$ vs. HDC.
† $p = 0.001$ vs. HDC.
‡ $p = 0.002$ vs. HDC.
§ $p = 0.002$ vs. HDC.
¶ $p = 0.003$ vs. HDC.

RESULTS

Patient demographics

A total of 101 patients with serviceable hearing, Gardner-Robertson class 1 and 2 were treated with FSRT between 1994 and 2007. Of this initial cohort, 89 patients had complete data for analysis. Of the 89 patients, 43 (18 men and 25 women) were treated to a total dose of 50.4 Gy, designated the HDC. The remaining 46 patients (22 men and 24 women) were treated to a total dose of 46.8 Gy, designated the LDC. The median age was 52 years and was not significantly different between the HDC and LDC. Of the 89 patients, 61 (31 in the HDC and 30 in the LDC) had Gardner-Robertson class 1 hearing and 28 (12 in the HDC and 16 in the LDC) had class 2 hearing before treatment.

Analysis of radiosurgery quality indexes between dose cohorts

A typical single isocenter Novalis treatment plan for an acoustic tumor is featured in Fig. 1. No significant difference was found in the mean isosurface prescription between the two dose cohorts. We assessed the conformality and homogeneity indexes between the dose cohorts and found no

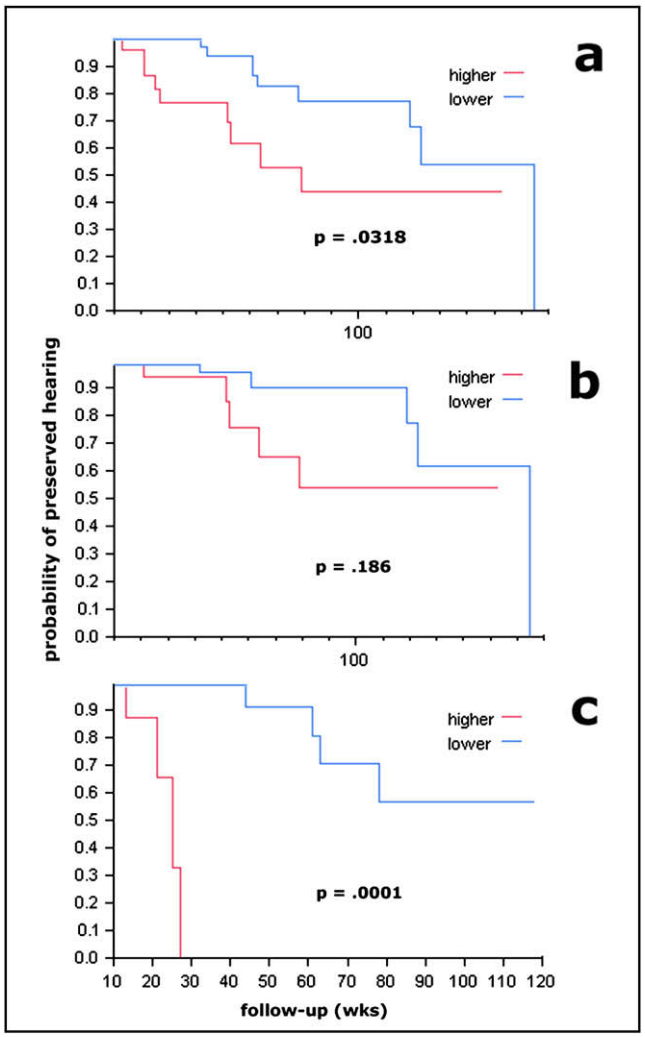

Fig. 3. (a) Kaplan-Meier analysis of hearing outcomes in patients with pretreatment serviceable hearing, corrected for follow-up (≤165 weeks) with significant improvement in low-dose cohort (LDC) (p = 0.0318, log–rank test). Blue indicates LDC (n = 42); red, high-dose cohort (HDC) (n = 31). (b) Kaplan-Meier analysis of hearing outcomes in patients with pretreatment Gardner-Robertson level 1 hearing, corrected for follow-up (≤165 weeks), with trend favoring LDC (p = 0.186, log–rank test). Blue indicates LDC (n = 28); red, HDC (n = 20). (c) Kaplan-Meier analysis of hearing outcomes in patients with pretreatment Gardner-Robertson level 2 hearing, corrected for follow-up (≤165 weeks), with significant improvement in LDC (p < 0.0001, log–rank test). Blue indicates LDC (n = 14); red, HDC (n = 11).

difference in dose homogeneity, but a significant difference in dose conformality (Table 1). The former observation was most likely because the isosurface prescriptions were comparable and thus the dose gradients were comparably shallow. The latter observation was most likely because most of the LDC were treated using the Novalis unit, and the single isocenter dynamic arc technique with mini-multileaf collimation yielded greater dose conformality.

Tumor control rates

The mean tumor volumes were not significantly different at 1.54 cm^3 and 1.57 cm^3 for the HDC and LDC, respectively, excluding one outlier representing 1 patient in the HDC with a 14.4-cm^3 tumor. The actuarial tumor control rate was 100% for both cohorts. Two patients in the LDC had one interval of tumor growth with stabilization on subsequent MRI scans. An example of a radiographic response after treatment at 46.8 Gy (lower dose) is shown in Fig. 2. The corresponding audiometry for each follow-up examination is also given.

Table 3. Multivariate analysis of factors for hearing preservation

Variable	Risk ratio	95% CI	p (χ^2)
Pretreatment Gardner-Robertson Grade 2	0.422	1.139–4.831	0.0215
Lower dose cohort	2.04	0.2580–.9264	0.0282
Tumor volume	0.908	0.7559–1.069	0.2572
Age	1.01	0.9785–1.038	0.5788
Maximal dose to cochlea (Gy)	1.01	0.9734–1.029	0.9856

Abbreviation: CI = confidence interval.

Cranial neuropathy

No incidence of trigeminal neuropathies for either dose cohort was recorded. One instance of a House Brackman Grade 2 facial neuropathy occurred in the LDC cohort that subsequently resolved.

Dose to cochlea

From recently published data, we retrospectively analyzed the dose to the cochlea for both dose cohorts (3, 4). Although we found statistically significant differences in all dose measurements to the cochlea between the dose cohorts (Table 2), we found no statistically significant relationship between the cochlear dose (assessed as the maximal dose [Table 2], minimal dose, or incremental doses between the minimal and maximal dose) and serviceable hearing preservation (data not shown).

Hearing preservation rates

A total of 89 patients had serial audiometric data available for analysis. The HDC included 43 patients treated to 50.4 Gy, with an overall median follow-up of 404 weeks (range, 295–630) and a median hearing (latest audiogram) follow-up of 53 weeks (mean, 114; range, 10–544). The LDC included 46 patients treated to 46.8 Gy, with an overall median follow-up of 194 weeks (range, 73–286) and a median hearing (latest audiogram) follow-up of 65 weeks (mean, 78; range, 11–233). Both groups were treated using daily fractions with a 1.8-Gy isosurface prescription. The PTA was significantly improved in the LDC compared with the HDC (33 dB vs. 40 dB, p = 0.023, chi-square test), and the difference in the PTA after treatment was smaller in the LDC, although this was of borderline statistical significance (10 dB vs. 15 dB change after FSRT, p = 0.0577).

Table 4. Hearing outcomes for two FSRT dose cohorts

Audiometric data	Before FSRT		After FSRT			
	PTA (dB)	SDS (%)	PTA (dB)	ΔPTA	SDS (%)	ΔSDS
50.4 Gy						
Serviceable (n = 43)	25	89	40	−15	67	−22
Serviceable G-R 1 (n = 31)	19	93	36	−17	72	−21
Serviceable G-R 2 (n = 12)	40	80	50	−10	54	−26
Corrected for follow-up (≤165 wk) (n = 30)	26	90	40	−14	70	−20
G-R 1, ≤165 wk (n = 20)	20	95	35	−15	80	−15
G-R 2, ≤165 wk (n = 10)	40	80	50	10	51	−29
46.8 Gy						
Serviceable (n = 46)	23	90	33*	−10†	75	−13
Serviceable G-R 1 (n = 30)	17	94	27‡	−10§	82	−12
Serviceable G-R 2 (n = 16)	34	81	43	−9	62	−19
Corrected for follow-up (≤165 wk) (n = 44)	23	90	33	−10	74	−16
G-R 1, ≤165 wk (n = 29)	16	94	30	−14	82	−12
G-R 2, ≤165 wk (n = 15)	35	82	44	−9	60	−16

Abbreviations: FSRT = fractionated stereotactic radiotherapy; PTA = pure tone average; SDS = speech discrimination score; G-R = Gardner-Robertson.

* p = 0.023 vs. 50.4-Gy dose cohort, Wilcoxon, one-way chi-square test.

† p = 0.0582 vs. 50.4-Gy dose cohort, Wilcoxon, one-way chi-square test.

‡ p = 0.0286 vs. 50.4-Gy dose cohort, Wilcoxon, one-way chi-square test.

§ p = 0.0448 vs. 50.4-Gy dose cohort, Wilcoxon, one-way chi-square test.

The PTA remained significantly improved in the LDC after treatment compared with the PTA in HDC (32 dB vs. 40 dB, p = 0.0238, Wilcoxon test). This was also observed in the Gardner-Robertson level 1 pretreatment hearing cohort (27 dB vs. 37 dB, p = 0.028), and the difference in PTA after treatment was significantly smaller in the LDC (10 dB vs. 18 dB change after FSRT, p = 0.044). The trend toward an improved PTA in the LDC cohort was also noted in the Gardner-Robertson level 2 cohort, but this was not significant (43 dB vs. 50 dB, p = 0.149). When patients with serviceable hearing were analyzed at a comparable 3-year follow-up, the raw hearing preservation rate was better in the LDC group (79% vs. 68% in the HDC), and the actuarial hearing preservation rate was significantly longer for the LDC than for the HDC (165 vs. 79 weeks, p = 0.0318, log–rank test; and p = 0.0054, Wilcoxon test, Fig. 3a). When analyzing the outcomes for patients within each serviceable hearing cohort, a greater likelihood of maintaining Gardner-Robertson level 1 hearing was noted in the LDC, with a trend that was not significant (p = 0.186, log–rank test; and p = 0.1000, Wilcoxon test, Fig. 3b). A significantly greater likelihood of maintaining Gardner-Robertson level 2 hearing was noted in the LDC (p < 0.0001, log–rank test; and p = 0.0006, Wilcoxon test, Fig. 3c).

Multivariate analysis revealed the dose cohort and pretreatment Gardner-Robertson grade to be highly significant factors contributing to the likelihood of hearing preservation. However, patient age, tumor size, and maximal dose to the cochlea did not have any significance (Table 3).

We noted no differences in outcomes according to whether the patients were treated using the Varian 600SR or the Novalis unit. All audiometric outcomes are summarized in Table 4.

DISCUSSION

In a prospective, nonrandomized comparison of Gamma knife single-fraction SRS and FSRT for the treatment of acoustic neuromas, we noted a distinct benefit with FSRT when assessing hearing (5). We initially designed a treatment paradigm using conventional 1.8-Gy fractions, recognizing the importance of a low daily dose treatment, particularly for targets involving or near special sensory cranial nerves such as the optic nerve or cochlear nerve. The hearing outcomes favored FSRT in this analysis. We have postulated that FSRT yields a greater rate of hearing preservation compared with an optimal SRS treatment based on arguments of dose conformality and dose homogeneity (6). It remains unknown whether the predictive factors for hearing deterioration are different or the same when assessing single and fractionated dosing schedules.

In the present study, we systematically explored a dose reduction in an attempt to optimize FSRT for acoustic neuromas. Our rationale was based on a review of the current literature that reflect improved hearing outcomes and diminished rates of facial and trigeminal neuropathies when the single-fraction isosurface dose prescription was lowered (7). Reports of hearing preservation were nonuniform, ranging from subjective hearing outcomes to standard audiometric scales. The most widely cited scale was the Gardner-Robertson scale (9). However, despite this scale, disparities still existed in the reported outcomes because of differences, for example, in the derivation of the PTA. We selected only those studies that featured audiometric outcomes using the Gardner-Robertson scale confirmed by audiometric data and excluded analyses that included patients with neurofibromatosis type 2. As an exception, the earliest studies available reported all treated patients, including neurofibromatosis

Table 5. SRS and FSRT reported series for treatment of acoustic neuroma

Investigator	*n*	Isodose prescription (Gy)	Tumor control rate (%)	Rate of cranial neuropathy (%)		
				V	VII	VIII (m/s/y)
GKRS 1988–1998						
Flickinger *et al.* (8), 1993	85	12–20 (median 17)	89*	33*	29*	35 (s, 2)†
Pollock *et al.* (21), 1995	36	16–20	100	59	67	42 (s, 2)†
Kondziolka *et al.* (22), 1998	162	12–20 (16.6 mean)	98	27	21	47 (s, 5–10)‡
Results		Median 18	96*	29*	26*	41
GKRS 1999–2005						
Andrews *et al.* (5), 2001	69	12	100	2	1	33 (s, 0.8)‡
Karpinos *et al.* (23), 2002	96	10–24 (mean 14.5)	91	11	4	44 (s, 4)‡
Regis *et al.* (24), 2002	104	12–14	100	4	2	50 (s, >3)‡
Iwai *et al.* (25), 2003	51	8–12 (median 12)	96	4	0	56 (s, 5)‡
Flickinger (26), 2004	313	12–13	99	4	0	79 (s, 6)†
van Eck *et al.* (27), 2005	78	13	98	2.5	1.2	83
Hasegawa *et al.* (28), 2005	74	≤13	NS	NS	NS	68 (s, 7)
Results		Median 13	97	5§	1§	59§
Standard-dose FSRT 1999–2007						
Shirato *et al.* (13), 1999	39	36–44; 2 Gy/Fx + 4-Gy boost	97	16	8	78 (s, 2)†,¶
Paek *et al.* (29), 2004	72	45; 1.8 Gy/Fx	100	7	4	85 (s, 1)†
						57 (s, 2)†
Koh *et al.* (30), 2007	60	50	96	2	2	77 (s, 2.7)‡
Thomas *et al.* (4), 2007	34	45	100	9	0	59 (s, 3)‡
Present study						
HDC	43	50.4	100	0	0	68
LDC	46	46.8	100	0	2	79
Results		Median 45.9	99	6§	3§	70§
Hypo-FSRT 1999–2005						
Poen *et al.* (31), 1999	33	21 @ 3 × 7	97	16	3	77
Williams (14), 2002	111	25 @ 5 × 5	100	2	0	83
Chang *et al.* (32), 2005	61	18–21 @ 3 × 7	98	0	3	74
Results		Median 21	98	6§	2§	78§

Abbreviations: SRS = stereotactic radiosurgery; FSRT = fractionated stereotactic radiotherapy; m/s/y = measurable or serviceable hearing preservation rates at years of follow-up; GKRS = gamma knife radiosurgery; Fx = fraction; HDC = high-dose cohort; LDC = low-dose cohort.

* Included neurofibromatosis type 2 patients.

† Actuarial hearing preservation rate.

§ $p < 0.05$ vs. gamma knife cohort, 1988–1998, Dunnett's comparison of means.

‡ Raw hearing preservation rate.

¶ Unclear effect of 4-Gy boost on hearing preservation.

type 2 patients (8). Other scales or outcomes that used subjective hearing results were excluded. The most informative reports included the actual audiometric data, but most reports did not.

By 2002, a dose of 12–13 Gy was generally considered to be the optimal dose for the treatment of acoustic neuromas. Any dose greater than this isodose prescription resulted in a greater rate of hearing loss (9). Also by 2002, a dose less than this isodose prescription resulted in greater tumor recurrence rates (10). Table 5 reflects the Gamma knife downward dose iterations over time to improve the rates of cranial neuropathy. Favorable results were also reported for the treatment of acoustic neuromas with FSRT (11), but no systematic attempt was made at dose optimization (12–15) for FSRT (16) or conventional RT (17) for hearing preservation. We feel clear indications for one or the other technique have emerged (18) based on our parallel analysis of hearing preservation adapting Goldsmith's previous model of vision tolerance to radiation (19). In Goldsmith's model, the authors derived a new unit of nominal standard dose that incorporates total dose and number of fractions into a single quantitative term, the optic RET (19). With data derived from published literature (Table 5), we constructed a hearing RET model for acoustic neuromas (6). Using this model, and given the close relationship of the cochlear nerve to the acoustic tumor, we concluded that a radiosurgical dose should be both highly conformal and homogeneous and should not exceed the hearing RET limits to obtain high rates of hearing preservation (6).

In November 2002, we reduced the total dose from 50.4 Gy to 46.8 Gy and followed this cohort for 5 years to assess the hearing preservation rates and tumor control rates. This dose fractionation scheme also was less than the hearing RET limit for hearing preservation. With quantitative audiometric data, the results from the present study support total dose reduction as a means of improving serviceable hearing outcomes without compromising tumor control. These data have shown that the most important variables affecting serviceable hearing outcomes include the total dose prescription and the initial Gardner-Robertson hearing grade. The former

observation, borne out for SRS, was also borne out in the present downward dose iteration for FSRT. Given the widely acknowledged hearing loss associated with RT, the latter observation supports early intervention in patients with Gardner-Robertson level 1 hearing to maximize the likelihood of a plateau at above the threshold for serviceable hearing. The importance of both of these variables is most evident in the Gardner-Robertson Grade 2 cohort in which a greater dose and marginal pretreatment serviceable hearing led to a significant probability of serviceable hearing loss (Fig. 3c).

Although we analyzed the cochlear dose (maximal dose, minimal dose, and dose to 90%, 80%, and 50% of the cochlear volume), we found no correlation between any of these data and the hearing outcomes. Whether the cochlea has a different α/β ratio than the cochlear nerve or a cochlear dose threshold represents an important variable in RT outcomes (3, 4) will remain unclear until more prospective data are available. Similar ambiguity applies to other factors, because neither patient age (3) nor tumor volume (20) were important variables related to serviceable hearing preservation in the present analysis.

From the promising results of the present data, two issues are unresolved. First, is whether the present dose is ideal for the management of acoustic neuromas in patients with serviceable hearing or whether an additional dose reduction is warranted. This question merits future investigations to explore whether additional FSRT dose reductions achieve better outcomes for acoustic neuromas patients. An optimal FSRT dose would simultaneously achieve the greatest tumor control and hearing preservation. Second, given the promising trend in hearing preservation and low rates of facial and trigeminal neuropathies with FSRT, should these patients be treated with FSRT or SRS? The optimal FSRT dose should be compared with the established optimal SRS dose in a Phase III randomized trial, with the tumor control rates and hearing preservation rates as endpoints. A standard audiometric scale should be used, and hearing should be assessed immediately before, and at regular intervals after, treatment.

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