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CLINICAL-PATIENT STUDIES

Safety and efficacy of fractionated stereotactic radiotherapy for acoustic neuromas

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Abstract *Background*: The treatment of acoustic neuromas (AN) has historically involved surgical excision or stereotactic radiosurgery, with a relatively limited number of reports available describing the use of fractionated stereotactic radiotherapy (FSRT). To enhance the existing knowledge regarding the safety and efficacy of this treatment modality, we describe our initial experience with FSRT for AN. *Methods*: From 1999–2005, 20 patients (12F, 8M) with AN underwent FSRT. All patients were treated using the Radionics X-Knife 4.0 3D planning system, receiving 54 Gy in 1.8 Gy daily fractions with a prescription isodose line of 90%. Treatments were delivered stereotactically using a dedicated Varian 6/100 linear accelerator, with immobilization achieved via the Gill-Thomas-Cosman relocatable frame. Median tumor size (maximum diameter) was 2.1 cm (range, 1.1–3.4 cm). Median patient age was 49.5 years, with median follow-up of 22 months (range, 1–66 months). All patients were evaluated with pre- and post-gadolinium-enhanced magnetic resonance imaging. *Results*: Following FSRT, local tumor control was achieved in every patient, with the treatment well-tolerated by all patients. No patient experienced acute complications or facial nerve weakness. Two patients experienced permanent trigeminal nerve morbidity manifesting as facial numbness. All nine patients with preserved hearing before treatment had hearing preservation at last follow-up, although four of these patients experienced hearing decline following FSRT. *Conclusion*: In our series of 20 patients with AN, all had local tumor control following FSRT, with minimal morbidity. These results support the growing body of literature demonstrating the safety and efficacy of FSRT in achieving local control for AN, further validating the viability of FSRT as a treatment modality for this patient population.

Keywords Fractionated stereotactic radiotherapy · Acoustic neuroma · Tumor control · Morbidity

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Introduction

Arising from the Schwann cells of the vestibular portion of the eighth cranial nerve, acoustic neuromas typically present clinically with tinnitus, imbalance and/or unilateral sensorineural hearing loss. Approximately 2,500 new cases are diagnosed per year in the United States, yielding a relative incidence of 1/100,000 per year [1]. With the advent of modern imaging, tumors of previously undetectable size can be identified via gadolinium-enhanced magnetic resonance (MR) imaging, identifying an even larger number of patients with tumors than previously estimated [2]. The majority of acoustic neuromas enlarge within 1–2 years of diagnosis, which can result in severe consequences due to the important structures in the vicinity of these lesions, namely the brainstem and adjacent cranial nerves [3, 4].

The two major goals of acoustic neuroma treatment are prevention of tumor growth and avoidance of injury to the adjacent trigeminal, facial and cochlear nerves [5–10]. To accomplish these goals, the predominant treatment modality has traditionally been microsurgical excision [6,

8, 10]. However, within the past two decades, stereotactic radiosurgery has emerged as an attractive alternative with similar efficacy and less morbidity for tumors with an average diameter of less than three centimeters [11–16].

Fractionated stereotactic radiotherapy (FSRT) refers to closed-skull multi-session irradiation of an intracranial target where the focusing accuracy has a precision of 1 mm. Similar to single-fraction stereotactic radiosurgery, the goal of FSRT is the control of tumor growth in contrast to microsurgical excision. Because of its multi-session nature, FSRT can be used to treat acoustic neuromas with potentially less morbidity than stereotactic radiosurgery, and has emerged as a potential alternative to microsurgical excision as a treatment modality for acoustic neuromas [15, 17–21]. To enhance the existing knowledge regarding the safety and efficacy of FSRT in this patient population, we describe our initial experience using FSRT to treat acoustic neuromas.

Clinical materials and methods

From January 1999 to September 2005, 20 patients (12 women, eight men) with acoustic neuromas who underwent FSRT at the University of Minnesota Medical Center were retrospectively reviewed. Ten tumors were located in the left cerebellopontine angle, and 10 were on the right, with six patients having undergone acoustic neuroma resection prior to FSRT. All patients had treatment planning using the Radionics X-Knife 3D planning system (Integra Radionics, Burlington, MA) as previously described [22]; however, planning was performed strictly based on following contrast-enhanced computerized tomography (CT) scanning alone (magnetic resonance imaging was not utilized). The median total dose received was 54 Gy, delivered in daily 1.8 Gy daily fractions. Treatments were delivered using a dedicated Varian 6/100 linear accelerator (Varian Medical Systems, Inc., Palo Alto, CA), with head immobilization accomplished via the Gill-Thomas-Cosman relocatable stereotactic frame (Integra Radionics, Burlington, MA).

Mean tumor size was 2.1 cm (median, 2.0 cm; range, 1.1–3.4 cm) in maximum diameter, and the median prescription isodose line was 90% of the maximum dose. The maximum dose was delivered within the tumor in all cases. Median patient age was 49.5 years (mean, 49.4 years; range, 26–75 years), with median follow-up of 22 months (mean, 21.8 months; range, 1–66 months), and mean dosage to the brainstem of 0.060 Gy per fraction (range, 0.013–0.191 Gy). Nine patients (45%) had useful hearing at the time of FSRT, and two patients (10%) had neurofibromatosis type 2. All patients were evaluated with pre- and post-gadolinium-enhanced MR imaging and the Gardner-Robertson hearing classification system [8].

Results

Following FSRT, local control (defined as absence of tumor progression) was achieved in all 20 patients (100%), with the treatment well tolerated by each patient. All nine patients with preserved hearing before treatment had hearing preservation at last follow-up. Only four patients suffered reduced hearing after treatment. Neither patient with NF-2 had useful hearing prior to or following FSRT. Permanent trigeminal nerve morbidity occurred in two patients (10%), manifesting as facial numbness and or V2 dysesthesia. No patient experienced facial nerve morbidity (facial weakness). Neither of the patients who suffered morbidity had undergone resection prior to FSRT. No patient experienced acute complications or other signs of radiation toxicity following FSRT, and there was no mortality.

Discussion

The use of fractionated stereotactic radiotherapy for the treatment of acoustic neuromas is a relatively recent development, with the vast majority of the literature comprising patients treated within the past 10 years [17–21, 23–28]. Previous studies have demonstrated that FSRT treatment of acoustic neuroma prevents tumor growth and hearing loss compared with observation alone [23–24], with comparable rates of tumor control to single-fraction stereotactic radiosurgery [17–19, 25–27] and less morbidity associated with the trigeminal nerve [24, 25, 28–30]. To expand the knowledge regarding the safety and efficacy of FSRT in the treatment of acoustic neuromas, we reviewed our initial experience over a 7-year period.

The findings of this report support the growing body of literature asserting the safety and efficacy of FSRT for acoustic neuromas. Of particular interest is our finding of 10% permanent trigeminal nerve morbidity, which is comparable to the 1–12% reported previously for FSRT [17–19, 23, 25, 26, 28] and superior to the majority of reports for single-fraction stereotactic radiosurgery, where trigeminal nerve morbidity has been reported as high as 56% [13, 15, 29, 30], although more recent reports using median doses less than 14 Gy have reported morbidity of up to 11% [31–34]. Our findings of complete tumor control and no facial nerve morbidity after treatment are comparable or superior to previously reported series examining FSRT for acoustic neuroma [17–19, 21, 25, 26, 28] (Table 1) and recent SRS series reporting 0–9% facial nerve morbidity [31–34], further underscoring the importance of FSRT as an attractive alternative treatment for acoustic neuromas. Although some may question the convenience of a 30-day course of treatment (FSRT) as opposed to a single day

Table 1 Recent literature regarding the safety and efficacy of FSRT for acoustic neuromas

Authors (ref. no.)	Number of patients	Median follow-up (months)	Local tumor control	Facial nerve morbidity
Combs et al. [17]	106	48.5	93%	2.3%
Chan et al. [18]	70	45.3	98%	1%
Williams [19]	150	23 (1.9 years)	100%	None
Lederman et al. [21]	38	27.1	100%	2.6%
Fuss et al. [25]	51	42 (mean only)	95%	None
Andrews et al. [26]	56	29.8 (mean only)	97%	1%
Meijer et al. [28]	80	33 (mean only)	94%	3%
Present study	20	22	100%	None

(SRS), the lower incidence of permanent trigeminal nerve and facial nerve morbidity associated with FSRT compared with SRS demonstrated in the literature [13, 15, 17–19, 25, 26, 28–34] may more than compensate for the relative short-term inconvenience of FSRT.

Conclusion

In our series of 20 patients with acoustic neuromas, all had local tumor control following FSRT, with minimal morbidity to the trigeminal nerve, and no morbidity to the facial nerve. There were no acute complications. These results support the growing evidence demonstrating the safety and efficacy of FSRT in achieving local control for acoustic neuromas, further validating this treatment modality for this patient population. Future studies are needed to evaluate the efficacy of FSRT in achieving local control of other tumors of the skull base.

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References

1. Acoustic Neuroma (1991) NIH Conseus Dev Conf Consens Statement 9:1–24
2. Wayman JW, Dutcher PO, Manzione JV, Nelson CN, Kido DK (1989) Gadolinium-DPTA-enhanced magnetic resonance imaging in cerebellopontine angle tumors. Laryngoscope 99:1167–1170
3. Bederson JB, Von Ammon K, Wichmann WW, Yasargil MG (1991) Conservative treatment of patients with acoustic tumors. Neurosurgery 28:646–651
4. Laasonen EM, Troupp H (1986) Volume growth rate of acoustic neurinomas. Neuroradiology 28:203–207
5. Cerullo CJ, Grutsch JF, Heiferman K, Osterdock R (1993) The preservation of hearing and facial nerve function in a consecutive series of unilateral vestibular nerve schwannoma surgical patients (Acoustic neuroma). Surg Neurol 39:485–493
6. Ebersold MJ, Harner SG, Beatty CW, Harper CM, Quast LM (1992) Current results of the retrosigmoid approach to acoustic neurinoma. J Neurosurg 76:901–909
7. Fischer G, Fischer C, Remond J (1992) Hearing preservation in acoustic neurinoma surgery. J Neurosurg 76:910–917
8. Gardner G, Robertson JH (1988) Hearing preservation in unilateral acoustic neuroma surgery. Ann Otol Rhinol Laryngol 97:55–66
9. Haines SJ, Levine SC (1993) Intracanalicular acoustic neuroma: early surgery for preservation of hearing. J Neurosurg 79:515–520
10. Jannetta PJ, Møller AR, Møller MB (1984) Technique of hearing preservation in small acoustic neuromas. Ann Surg 200:513–523
11. Combs SE, Thilmann C, Debus J, Schulz-Ertner D (2006) Long-term outcome of stereotactic radiosurgery (SRS) in patients with acoustic neuromas. Int J Radiat Oncol Biol Phys 64:1341–1347
12. Hasegawa T, Fujitani S, Katsumata S, Kida Y, Yoshimoto M, Koike J (2005) Stereotactic radiosurgery for vestibular schwannomas: analysis of 317 patients followed more than 5 years. Neurosurgery 57:257–265
13. Myrseth E, Moller P, Pedersen PH, Vassbotn FS, Wentzel-Larsen T, Lund-Johansen M (2005) Vestibular schwannomas: clinical results and quality of life after microsurgery or gamma knife radiosurgery. Neurosurgery 56:927–935
14. Lunsford LD, Niranjan A, Flickinger JC, Maitz A, Kondziolka D (2005) Radiosurgery of vestibular schwannomas: summary of experience in 829 cases. J Neurosurg 102(Suppl):195–199
15. Pollock BE, Lunsford LD, Kondziolka D, Flickinger JC, Bissonette DJ, Kelsey SF, Jannetta PJ (1995) Outcome analysis of acoustic neuroma management: a comparison of microsurgery and stereotactic radiosurgery. Neurosurgery 36:215–229
16. Kondziolka D, Lunsford LD, McLaughlin MR, Flickinger JC (1998) Long-term outcomes after radiosurgery for acoustic neuromas. N Engl J Med 339:1426–1433
17. Combs SE, Volk S, Schulz-Ertner D, Huber PE, Thilmann C, Debus J (2005) Management of acoustic neuromas with fractionated stereotactic radiotherapy (FSRT): long-term results in 106 patients treated in a single institution. Int J Radiat Oncol Biol Phys 63:75–81
18. Chan AW, Black P, Ojemann RG, Barker FG 2nd, Kooy HM, Lopes VV, McKenna MJ, Shrieve DC, Martuza RL, Loeffler JS (2005) Stereotactic radiotherapy for vestibular schwannomas: favorable outcome with minimal toxicity. Neurosurgery 57:60–70
19. Williams JA (2002) Fractionated stereotactic radiotherapy for acoustic neuromas. Acta Neurochir (Wien) 144:1249–1254
20. Andrews DW, Silverman CL, Glass J, Downes B, Riley RJ, Corn BW, Werner-Wasik M, Curran WJ Jr, McCune CE, Rosenwasser RH et al (1995) Preservation of cranial nerve function after treatment of acoustic neurinomas with fractionated stereotactic radiotherapy. Preliminary observations in 26 patients. Stereotact Funct Neurosurg 64:165–182
21. Lederman G, Lowry J, Wertheim S, Fine M, Lombardi E, Wronski M, Arbit E (1997) Acoustic neuroma: potential benefits

of fractionated stereotactic radiosurgery. Stereotact Funct Neurosurg 69(1–4 Pt 2):175–182
22. McClelland S III, Higgins PD, Gerbi BJ, Orner JB, Hall WA (2007) Fractionated stereotactic radiotherapy for pituitary adenomas following microsurgical resection: safety and efficacy. Technol Cancer Res Treat 6:177–180
23. Shirato H, Sakamoto T, Sawamura Y, Kagei K, Isu T, Kato T, Fukuda S, Suzuki K, Soma S, Inuyama Y, Miyasaka K (1999) Comparison between observation policy and fractionated stereotactic radiotherapy (SRT) as an initial management for vestibular schwannoma. Int J Radiat Oncol Biol Phys 44:545–550
24. Sakamoto T, Shirato H, Takeichi N, Aoyama H, Fukuda S, Miyasaka K (2001) Annual rate of hearing loss falls after fractionated stereotactic irradiation for vestibular schwannoma. Radiother Oncol 60(1):45–48
25. Fuss M, Debus J, Lohr F, Huber P, Rhein B, Engenhart-Cabillic R, Wannenmacher M (2000) Conventionally fractionated stereotactic radiotherapy (FSRT) for acoustic neuromas. Int J Radiat Oncol Biol Phys 48:1381–1387
26. Andrews DW, Suarez O, Goldman HW, Downes MB, Bednarz G, Corn BW, Werner-Wasik M, Rosenstock J, Curran WJ Jr (2001) Stereotactic radiosurgery and fractionated radiotherapy for the treatment of acoustic schwannomas: comparative observations of 125 patients treated at one institution. Int J Radiat Oncol Biol Phys 50:1265–1278
27. Sakamoto T, Shirato H, Sato N, Kagei K, Sawamura Y, Suzuki K, Takizawa H, Hokunan K, Isu T, Fukuda S, Inuyama Y, Miyasaka K (1998) Audiological assessment before and after fractionated stereotactic irradiation for vestibular schwannoma. Radiother Oncol 49(2):185–190
28. Meijer OW, Vandertop WP, Baayen JC, Slotman BJ (2003) Single-fraction vs. fractionated linac-based stereotactic radiosurgery for vestibular schwannoma: a single-institution study. Int J Radiat Oncol Biol Phys 56:1390–1396
29. Noren G (1996) The Gamma knife and acoustic tumors. Med Health R I 79:232–235
30. Foote RL, Coffey RJ, Swanson JW, Harner SG, Beatty CW, Kline RW, Stevens LN, Hu TC (1995) Stereotactic radiosurgery using the gamma knife for acoustic neuromas. Int J Radiat Oncol Biol Phys 32:1153–1160
31. Weber DC, Chan AW, Bussiere MR, Harsh GR IV, Ancukiewicz M, Barker FG II, Thornton AT, Martuza RL, Nadol JB Jr, Chapman PH, Loeffler JS (2003) Proton beam radiosurgery for vestibular schwannoma: tumor control and cranial nerve toxicity. Neurosurgery 53:577–588
32. Rutten I, Baumert BG, Seidel L, Kotolenko S, Collignon J, Kaschten B, Albert A, Martin D, Deneufbourg JM, Demanez JP, Stevenaert A (2007) Long-term follow-up reveals low toxicity of radiosurgery for vestibular schwannoma. Radiother Oncol 82:83–89
33. Chopra R, Kondziolka D, Niranjan A, Lunsford LD, Flickinger JC (2007) Long-term follow-up of acoustic schwannoma radiosurgery with marginal tumor doses of 12 to 13 Gy. Int J Radiat Oncol Biol Phys 68:845–851
34. Friedman WA, Bradshaw P, Myers A, Bova FJ (2006) Linear accelerator radiosurgery for vestibular schwannomas. J Neurosurg 105:657–661