Advances in Radiation Oncology (2019) **4**, 43-49

advances
in radiation oncology

www.advancesradonc.org

Scientific Article

Analysis of MRI Volumetric Changes After Hypofractionated Stereotactic Radiation Therapy for Benign Intracranial Neoplasms

Kathryn R. Fega MD, PhD [a], Geoffrey P. Fletcher MD [b], Mark R. Waddle MD [c], Jennifer L. Peterson MD [c], Jonathan B. Ashman MD, PhD [a], David M. Barrs MD [d], Bernard R. Bendok MD [e], Naresh P. Patel MD [e], Alyx B. Porter MD [f], Sujay A. Vora MD [a,*]

[a]Department of Radiation Oncology, Mayo Clinic Hospital, Phoenix, Arizona; [b]Department of Radiology, Mayo Clinic Hospital, Phoenix, Arizona; [c]Department of Radiation Oncology, Mayo Clinic, Jacksonville, Florida; [d]Department of Otolaryngology, Head and Neck Surgery, Mayo Clinic Hospital, Phoenix, Arizona; [e]Department of Neurologic Surgery, Mayo Clinic Hospital, Phoenix, Arizona; and [f]Department of Neurology, Mayo Clinic Hospital, Phoenix, Arizona

Received 8 December 2017; revised 2 August 2018; accepted 10 August 2018

Abstract

Purpose: To quantitatively assess volumetric changes after hypofractionated stereotactic radiation therapy (HFSRT) in patients treated for vestibular schwannomas and meningiomas.

Methods and materials: We retrospectively reviewed records of patients treated with HFSRT at our institution from 2002 to 2014. Patients received a median dose of 25 Gy in 5 fractions. After treatment, they underwent clinical and radiologic follow-up with magnetic resonance imaging (MRI) at 3- to 12-month intervals. Gross tumor volume was outlined on each thin slice of contrast-enhanced T1 series before and on each scan after HFSRT. Volumetric changes were calculated and compared with neuroradiologist interpretations.

Results: Forty-three patients underwent 182 MRI scans. Tumor types included vestibular schwannoma (n = 34) and meningioma (n = 9). Median follow-up time was 29 months. Median gross tumor volume was 3.1 cm^3. Local control was 81.4% for the entire cohort at the time of last follow-up. Transient volume expansion was noted in 17 patients (50%) with vestibular schwannoma and 2 (22%) with meningioma. For all patients, transient volume expansion and subsequent regression occurred at a median time of 5.5 and 12 months, respectively. Neuroradiologist agreement with regard to tumor regression, progression, or stability occurred in 155 of 182 total reports (85%). The largest discordance identified was a stable finding on the MRI interpretation when the measured volumetric change exceeded 20% (n = 24 [13%]).

Presented at the American Society for Radiation Oncology (ASTRO) annual meeting, Boston, Massachusetts, September 25-28, 2016.
Sources of support: This work had no specific funding.
Conflicts of interest: The authors have no conflicts of interest to disclose.

* Corresponding author. Department of Radiation Oncology, Mayo Clinic Hospital, 5777 E Mayo Blvd, Phoenix, AZ 85054.
E-mail address: vora.sujay@mayo.edu (S.A. Vora).

https://doi.org/10.1016/j.adro.2018.08.013

Conclusions: HFSRT is associated with excellent local control and a low incidence of toxicity. With volumetric MRI measurement, transient volume expansion was a common finding and was associated with temporary adverse effects. Although the neuroradiologist's interpretation generally agreed with the volumetric MRI measurement, the overall 15% discordance rate emphasizes the potential benefit of considering volumetric measurements, which may help clinicians correlate posttreatment symptoms with MRI findings.

Introduction

The management of benign meningiomas and vestibular schwannomas can be associated with unique challenges. Because these lesions are rarely life threatening, the decision to treat is often determined by current symptoms or the potential for worsening symptoms and the associated changes in quality of life. Potential treatments include surgical resection, radiation therapy, and close observation. The optimal treatment depends on tumor- and patient-related factors plus clinician and patient preferences.

Surgical management remains the first-line treatment for select patients when tumor resection would improve symptoms from mass effect[1,2] or when surgery is potentially curative with gross total resection.[3,4] However, surgery may pose challenges, depending on the intracranial location of the tumor, and includes risk of complications such as infection, bleeding, and neurologic loss. Radiation therapy is an alternative to surgery, especially for patients with benign tumors that are not amenable to surgical resection or recur after surgery.[5–8]

Radiation therapy options include conventionally fractionated radiation therapy, stereotactic single-fraction radiosurgery, and hypofractionated stereotactic radiation therapy (HFSRT). Prior studies of conventional radiation therapy for benign central nervous system neoplasms have reported excellent local control (>80%), but patients must undergo 5 to 6 weeks of radiation therapy.[9–11] Single-fraction stereotactic radiosurgery also has excellent local control for smaller benign intracranial neoplasms, but depending on tumor-related factors (eg, location, size), they can be associated with increased risk of complications such as tumor-related swelling, hearing loss, and cranial neuropathies.[10,12–16] HFSRT has the ability to balance the therapeutic ratio through fractionation and a short treatment course.[17–20] However, the posttreatment changes of these tumors have not been well characterized radiographically, particularly after HFSRT.

Magnetic resonance imaging (MRI) is the most common method of assessing response to radiation therapy. Nevertheless, differentiating between tumor progression and radiation therapy effects can be difficult.[21] Often the clinician relies on the radiologist's interpretation of post–radiation therapy changes, but changes such as tumor-related swelling, transient volume expansion (TVE), and central necrosis can challenge the radiologist.[22] These radiation therapy effects may be more pronounced in shorter, high-dose treatments.[23–25] Historically, MRI-based measurements of tumor expansion or shrinkage have been interpolated by using the maximal tumor dimensions for height, width, and anteroposterior diameter. When assessing tumor growth or shrinkage, 1- or 2-dimensional analysis may be insufficient for tumors that are irregularly shaped or multilobulated and may be subject to interobserver differences. Therefore volumetric measurements potentially are advantageous for analyzing tumor response to radiation therapy over time. The aim of our study was to quantitatively assess volumetric changes, toxicities, and clinical outcomes after HFSRT in patients with vestibular schwannomas or meningiomas.

Methods and materials

Study design and patient population

This study was approved by the Mayo Clinic Institutional Review Board. The reporting of this study is in compliance with the Strengthening the Reporting of Observational Studies in Epidemiology statement.[26] We retrospectively identified all patients with vestibular schwannomas or meningiomas who were treated at Mayo Clinic (Phoenix, Arizona) (an academic tertiary medical center) with linear accelerator–based HFSRT from January 1, 2002, through December 31, 2014. To meet the inclusion criteria, patients had to be at least 18 years old, had to have received a radiographic diagnosis of a vestibular schwannoma or meningioma, and could not have received prior radiation therapy to the tumor site. Patients were required to have received HFSRT (ie, 3-5 treatments). Patients were excluded from analysis if they did not receive follow-up clinical evaluation at our institution or if they had only computed tomography imaging.

HFSRT technique

All patients were treated with a linear accelerator (Varian Medical Systems). Patient immobilization was achieved with a commercial head mask fixation system. Patients underwent a planning computed tomography scan of the brain, and image fusion was performed with dedicated pretreatment MRI thin-cut sequences. The gross tumor volume (GTV) was delineated as a contrast-enhancing tumor demonstrated on T1 postgadolinium MRI imaging. The clinical target volume was equal to the GTV. The planning target volume was generated by the geometric expansion of GTV plus a margin (median, 2 mm; range, 0-3 mm). Patients were treated daily with image guidance. The median radiation dose was 25 Gy in 5 fractions (range, 18 Gy [3 fractions] to 35 Gy [5 fractions]). The prescribed dose was delivered to the 77% to 100% isodose line (mean, 89%) and normalized to the maximum dose to ensure coverage of at least 95% of the planning target volume with the prescription dose.

Clinical and radiologic follow-up

After treatment, patients underwent clinical and radiologic MRI follow-up at 3- to 12-month intervals. All patients included in this study had pretreatment MRI imaging with at least 2 posttreatment MRI scans. A comprehensive clinical evaluation and neurologic examination were performed before treatment and at each clinical follow-up visit.

MRI volumetric assessment and response criteria

All posttreatment MRI scans was imported into the radiation planning system and contoured by 1 individual (K.R.F.). Volumetric measurements were generated retrospectively by outlining the GTV, including cystic changes, on each thin-cut slice of contrast-enhanced T1 series before and on each scan after HFSRT. The thinnest cuts available (slice thickness, 1-2.5 mm) were used for contouring. Volumetric changes were calculated for each available MRI scan and compared with the baseline tumor volume before radiation therapy. Percentage changes in size were reported as an increase, decrease, or no change compared with the original tumor volume.

Modified Response Evaluation Criteria in Solid Tumors (RECIST) criteria[27] were used to define disease progression and stability. Although RECIST criteria defined progression as an increase of 20% in the sum of the linear measurements, we used a volumetric approach in which $\geq$20% change in volume was considered progressive disease. Stable disease was defined as no change or a volume change $<$30%. Partial response to treatment was defined as at least a 30% decrease in volume. Local control was defined as either stable disease or a partial response to treatment. TVE was defined as an increase of more than 20% from baseline with a subsequent decrease to within 20% of baseline. TVE patients were not defined as those with progression but were categorized based on their final volume size relative to baseline.

All diagnostic MRI scans were read and interpreted by a member of the neuroradiology department (G.P.F.). Tumor size was characterized as increased, decreased, or no change based on the diameter change of the tumor measured from the coronal, sagittal, and axial cross-sections. If the neuroradiologist's interpretation of a linear change agreed with our interpretation of a volumetric change (increase, decrease, or stable disease), this was considered concordant. If the report specified a change in size but the volumetric change was stable (within 20% of baseline), this was considered discordant. If a report specified no change when a volumetric change exceeding 20% was measured, this was also considered discordant.

Results

We identified 43 patients with 182 MRI scans who were treated with HFSRT during the study period. Baseline characteristics are shown in Table 1. The median (range) duration of follow-up was 29 (6-142) months.

Figure 1 shows the final change in volume for patients with vestibular schwannoma; compared with baseline, 12 patients (35%) had a partial response to treatment, 14 (41%) remained stable, and 8 (24%) had more than 20% volumetric growth. The largest expansion was observed in patient 34, who had a very small acoustic neuroma at presentation. This lesion progressed to a volumetric change of 800%. The lesion ultimately was resected. Post-HFSRT changes in vestibular schwannoma volume over time are shown in Figure 2.

Figure 3 shows the final change in volume for patients with meningioma; compared with baseline, 6 patients (67%) had a partial response to treatment, 3 (33%) remained stable, and no patients had a progressive expansion. Post-HFSRT changes in volume over time are shown in Figure 4.

TVE was identified in 17 patients with vestibular schwannoma (50%). Median time of TVE was 6 months (range, 3-13 months), with a return to pretreatment size or decrease in size identified within a median time of 13 months (range, 6-59 months). Two patients with meningioma (22%) had TVE at a median time of 2.5 months (range, 2-3 months), with a return to pretreatment size or a decrease in size within a median time of 9.5 months (range, 7-12 months).

TVE was associated with increased toxicity in 11 patients (65%) with vestibular schwannoma. Symptoms included hearing loss (n = 5), imbalance (n = 3),

Table 1 Baseline characteristics (N = 43)

Characteristic	Value
Male sex, n (%)	20 (47)
Age, median (range), y	68 (33-87)
Primary intracranial tumor, n (%)	
Vestibular schwannoma	34 (79)
Meningioma	9 (21)
Gross tumor volume, median, cm^3	3.1
Radiation dose and fractionation, n (%)	
35 Gy, 5 treatments	2 (5)
27.5 Gy, 5 treatments	1 (2)
25 Gy, 5 treatments	23 (53)
21 Gy, 3 treatments	2 (5)
20 Gy, 5 treatments	12 (28)
20 Gy, 4 treatments	1 (2)
18 Gy, 3 treatments	2 (5)
MRI scans per patient after radiation therapy, median (range)	
Vestibular schwannoma	3 (2-11)
Meningioma	4 (2-7)

Abbreviation: MRI = magnetic resonance imaging.

dizziness (n = 3), facial paresthesias (n = 2), tinnitus (n = 2), headache (n = 2), and vertigo (n = 2), with some patients experiencing multiple symptoms. Hearing loss persisted in all patients, and the other symptoms resolved for 6 patients (55%) within a median time of 6.5 months (range, 1-15 months). A total of 6 patients (30%), 5 with vestibular schwannoma and 1 with meningioma, had grade 2 toxicity requiring corticosteroids. Toxicity that included speech difficulty and weakness was seen in 1 of the 2 patients with meningioma, with symptoms resolving within 12 months after radiation.

Tumor volumetric assessment for each follow-up MRI scan was compared with the neuroradiologist's interpretation of size change for each report. The assessment was concordant with the volumetric change (in terms of tumor regression, stability, or progression) for 155 reports (85%). For 24 reports (13%), the report specified no change in size, but the volumetric change (increase or decrease) exceeded 20%. Furthermore, for 3 reports (2%), a report specified a change in size, but no volumetric change was noted.

Local control was observed in 35 patients (81.4%) at the time of last follow-up. Progression or TVE was found in 8 patients (18.6%). Progression did not occur in any patients with meningioma. A weak correlation was identified between the changes in volume as a function of time after completion of radiation therapy (Fig 5).

Discussion

Our findings indicate that subtle posttreatment MRI changes after HFSRT are common and difficult to interpret. This study provides more accurate 3-dimensional MRI volumetric data, with changes observed over time. We believe that this information supplements the neuroradiologist's report and helps the clinician appropriately counsel patients. Although we generally found good correlation between volumetric measurements and the neuroradiologist's interpretation using RECIST criteria, we noted a 15% discordance rate.

Overall, HFSRT delivered high local control rates with low reported toxicity. TVE was fairly common, although generally self-limited. Several cases were associated with short-term toxicity. Our study adds evidence to the literature reporting that this fractionation regimen is a reasonable option.

The natural disease course of vestibular schwannomas and grade 1 meningiomas is a relatively slow potential doubling time, growth rate, and mitotic rate. Because treatment response rates differ based on the activity of the cells in question, slow-growing cells will likely also respond more slowly to radiation therapy. Furthermore, reabsorption of killed tumor cell populations may not necessarily occur, leaving the lesion size unchanged. The opposite effect can occur as well, with lesions first increasing in size as a secondary effect of radiation and then regressing; TVE potentially causes symptoms and can be a therapeutic complication.[22,28,29] Thus, one of the main challenges for the clinician is interpreting post–radiation therapy MRI scans and reports. Differentiating among partial response, stable change, TVE, and clear tumor progression from a single scan is difficult. In general, multiple scans over months to years are needed to draw a more accurate conclusion.

The purpose of this study was to provide more objective data on how these tumors behave after treatment by using more accurate MRI volumetric measurements. Although RECIST criteria are useful for the interpretation of these radiologic changes after radiation therapy for malignant disease,[27] they are not ideal for benign intracranial neoplasms because of the small changes typically found after treatment. The RECIST criteria require a relative change of more than 20% and an absolute change of more than 5 mm from baseline. They also considered lesions smaller than 10 mm to be nonmeasurable.

In our series, the volumetric measurement was concordant with the neuroradiologist's interpretation for 155 reports (85%). For 24 reports (13%), discordance was attributed to a volumetric change exceeding 20% and the neuroradiologist reporting no change. Interestingly, many of these patients had reported toxicities, which added to the clinical dilemma when the MRI scan was interpreted as showing no change. By using MRI volumes to define progression, small differences in linear measurements would be mitigated because each change on a thin-slice MRI scan would have a smaller effect on the overall volume.

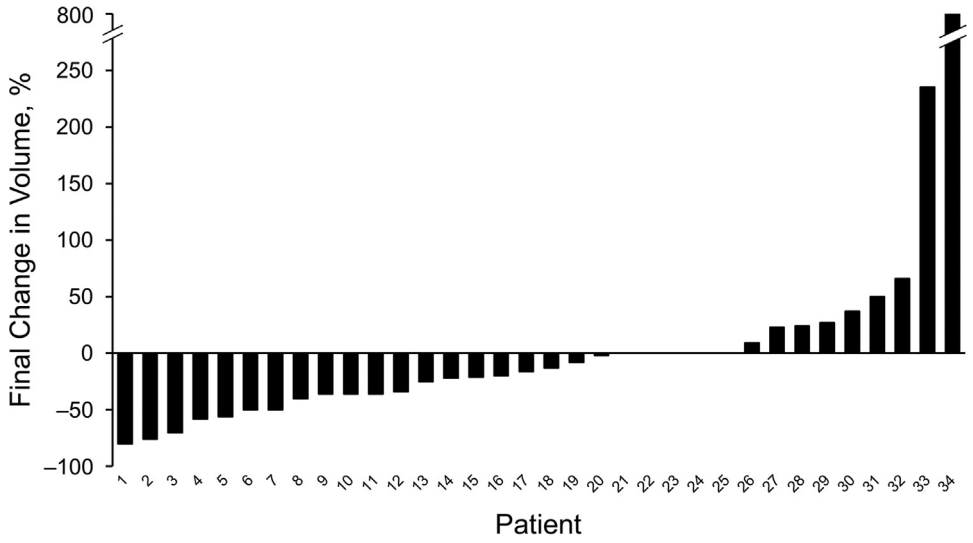

Figure 1 Final change in volume for patients with vestibular schwannoma. Numbers represent individual patients.

In our study, we were able to achieve a high local control rate of 83% with the use of HFSRT; this rate is likely an underestimation as a result of TVE changes and date of last follow-up. TVE occurred in 19 of 43 lesions (44%). This high rate was mostly attributed to treatment-related central necrosis, which caused a temporary increase in overall volume. For patients with vestibular schwannoma, the temporary size increase caused symptoms in 61%; at last follow-up, symptoms had resolved in 55% of patients. However, hearing loss persisted in all affected patients with vestibular schwannoma.

Few studies have investigated the role of volumetric MRI measurements in patients with benign central nervous system neoplasms who have been treated with single-fraction radiosurgery, conventional fractionated stereotactic radiation therapy, or HFSRT.[17,19,20] All report good local control rates with low toxicity. However, the differences in definitions for local control and progression makes direct comparisons difficult. Matsuo et al[30] evaluated patients with vestibular schwannoma treated with single-fraction radiosurgery and used a volume change of 20% to define shrinkage or growth. They noted a transient enlargement pattern in 54.5%, with a 27% shrinkage rate and an 11% progression rate. van de Langenberg et al[31] examined patients with vestibular schwannoma treated with single-fraction radiosurgery or conventional fractionated stereotactic radiation therapy and used a volume change of 19.7% to define shrinkage or growth. They noted that 65% of patients had shrinkage, 13% had progression, and 54% had transient enlargement. Harrison et al[32] examined patients receiving single-fraction radiosurgery for meningiomas, defining progression as >15% volume change and regression as ≤15% volume change. They found regression in 67% and progression in 7%. Allowing for differences in definition, these results are similar to our findings.

In terms of HFSRT, Gorman et al[20] evaluated the role of HFSRT in skull-based meningiomas and defined a partial response as a ≥50% decrease in maximum tumor diameter and stable disease as being between a <25%

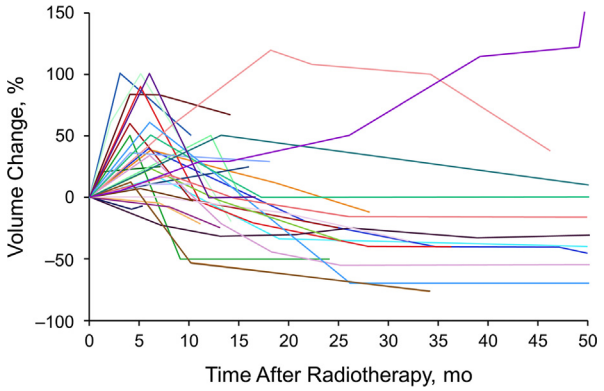

Figure 2 Changes in vestibular schwannoma volume after hypofractionated stereotactic radiation therapy (n = 34). One patient had a maximum volume change of 800% (change at last follow-up).

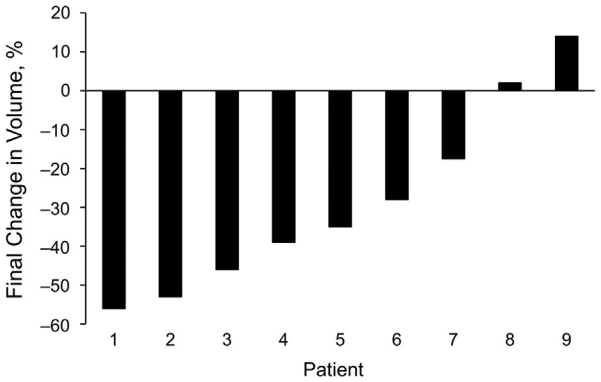

Figure 3 Final change in volume for patients with meningioma. Numbers represent individual patients.

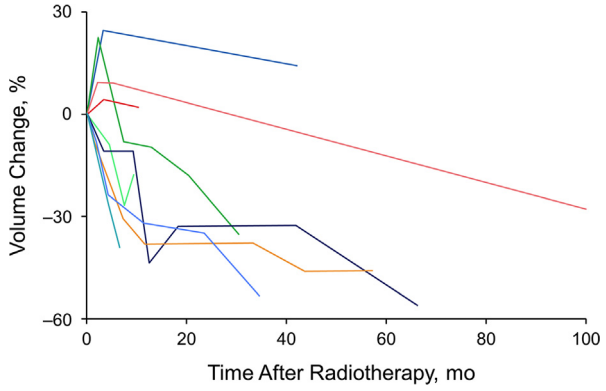

Figure 4 Changes in meningioma volume after hypofractionated stereotactic radiation therapy (n = 9).

increase and <50% decrease in maximum tumor diameter. Mahadevan et al[17] evaluated clinical outcomes after HFSRT for benign skull-based tumors and reported local control as size stability and nonprogression in the MRI scan. Kapoor et al[33] defined radiographic progression for any tumor greater than the baseline volume and significant radiographic progression when the tumor volume was more than double the treatment volume. They found that patients with tumor volumes <1 cm^3 were more likely to have significant radiologic progression compared with patients with larger-volume tumors. Our study is the first to compare volumetric measurements and a neuroradiologist's interpretation.

Limitations of this study include the differences in slice thickness obtained during the MRI scan, which can markedly affect volumetric measurements (particularly for very small lesions), intraobserver differences in volumetric measurements and radiologist interpretation, and the impact of TVE on final volume calculations.

Conclusions

Volumetric MRI measurements provide additional information that may be used to correlate changes in tumor volume with symptoms or toxicities, if they arise. Clinicians should be aware of the possible discordance between radiologic reports and volume measurements, particularly in managing patients with symptoms. Continued follow-up and medical management of symptoms is important before determining true disease progression. HFSRT remains a good option for excellent local control and minimal toxicity in patients with vestibular schwannomas and meningiomas.

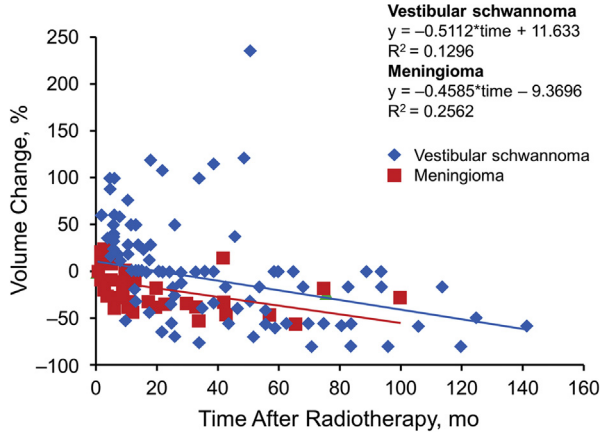

Figure 5 Volume change in tumor size from baseline over time, stratified by tumor type.

References

1. Kallio M, Sankila R, Hakulinen T, Jaaskelainen J. Factors affecting operative and excess long-term mortality in 935 patients with intracranial meningioma. *Neurosurgery*. 1992;31:2-12.
2. Samii M, Matthies C. Management of 1000 vestibular schwannomas (acoustic neuromas): the facial nerve—preservation and restitution of function. *Neurosurgery*. 1997;40:684-694. discussion 694-685.
3. Mendenhall WM, Friedman WA, Amdur RJ, Foote KD. Management of benign skull base meningiomas: a review. *Skull Base*. 2004; 14:53-60. discussion 61.
4. Piepmeier J, Baehring JM. Surgical resection for patients with benign primary brain tumors and low grade gliomas. *J Neurooncol*. 2004;69:55-65.
5. Kollova A, Liscak R, Novotny J, Jr, Vladyka V, Simonova G, Janouskova L. Gamma Knife surgery for benign meningioma. *J Neurosurg*. 2007;107:325-336.
6. Kondziolka D, Lunsford LD, McLaughlin MR, Flickinger JC. Long-term outcomes after radiosurgery for acoustic neuromas. *N Engl J Med*. 1998;339:1426-1433.
7. Kondziolka D, Mousavi SH, Kano H, Flickinger JC, Lunsford LD. The newly diagnosed vestibular schwannoma: Radiosurgery, resection, or observation? *Neurosurg Focus*. 2012;33:E8.
8. Pollock BE, Stafford SL, Utter A, Giannini C, Schreiner SA. Stereotactic radiosurgery provides equivalent tumor control to Simpson grade 1 resection for patients with small- to medium-size meningiomas. *Int J Radiat Oncol Biol Phys*. 2003;55:1000-1005.
9. Combs SE, Adeberg S, Dittmar JO, et al. Skull base meningiomas: Long-term results and patient self-reported outcome in 507 patients treated with fractionated stereotactic radiotherapy (FSRT) or intensity modulated radiotherapy (IMRT). *Radiother Oncol*. 2013; 106:186-191.
10. Minniti G, Amichetti M, Enrici RM. Radiotherapy and radiosurgery for benign skull base meningiomas. *Radiat Oncol*. 2009;4:4-42.
11. Aoyama H, Onodera S, Takeichi N, et al. Symptomatic outcomes in relation to tumor expansion after fractionated stereotactic radiation therapy for vestibular schwannomas: Single-institutional long-term experience. *Int J Radiat Oncol Biol Phys*. 2013;85:329-334.
12. Chihara Y, Ito K, Sugasawa K, Shin M. Neurological complications after acoustic neurinoma radiosurgery: revised risk factors based on long-term follow-up. *Acta Otolaryngol Suppl*. 2007;559:65-70.
13. Ebinu JO, Lwu S, Monsalves E, et al. Gamma Knife radiosurgery for the treatment of cystic cerebral metastases. *Int J Radiat Oncol Biol Phys*. 2013;85:667-671.
14. Kim YH, Kim DG, Han JH, et al. Hearing outcomes after stereotactic radiosurgery for unilateral intracanalicular vestibular schwannomas: Implication of transient volume expansion. *Int J Radiat Oncol Biol Phys*. 2013;85:61-67.
15. Kondziolka D, Mathieu D, Lunsford LD, et al. Radiosurgery as definitive management of intracranial meningiomas. *Neurosurgery*. 2008;62:53-58.
16. Sheehan JP, Lee CC, Xu Z, Przybylowski CJ, Melmer PD, Schlesinger D. Edema following Gamma Knife radiosurgery for

parasagittal and parafalcine meningiomas. *J Neurosurg*. 2015;26:1-7.
17. Mahadevan A, Floyd S, Wong E, Chen C, Kasper E. Clinical outcome after hypofractionated stereotactic radiotherapy (HSRT) for benign skull base tumors. *Comput Aided Surg*. 2011;16:112-120.
18. Sakanaka K, Mizowaki T, Arakawa Y, et al. Hypofractionated stereotactic radiotherapy for acoustic neuromas: Safety and effectiveness over 8 years of experience. *Int J Clin Oncol*. 2011;16:27-32.
19. Haghighi N, Seely A, Paul E, Dally M. Hypofractionated stereotactic radiotherapy for benign intracranial tumours of the cavernous sinus. *J Clin Neurosci*. 2015;22:1450-1455.
20. Gorman L, Ruben J, Myers R, Dally M. Role of hypofractionated stereotactic radiotherapy in treatment of skull base meningiomas. *J Clin Neurosci*. 2008;15:856-862.
21. Walker AJ, Ruzevick J, Malayeri AA, et al. Postradiation imaging changes in the CNS: how can we differentiate between treatment effect and disease progression? *Future Oncol*. 2014;10:1277-1297.
22. Tran DK, Jensen RL. Treatment-related brain tumor imaging changes: So-called "pseudoprogression" vs. tumor progression: Review and future research opportunities. *Surg Neurol Int*. 2013;4(Suppl 3):S129-135.
23. Alomari A, Rauch PJ, Orsaria M, Minja FJ, Chiang VL, Vortmeyer AO. Radiologic and histologic consequences of radiosurgery for brain tumors. *J Neurooncol*. 2014;117:33-42.
24. Hayhurst C, Zadeh G. Tumor pseudoprogression following radiosurgery for vestibular schwannoma. *Neuro Oncol*. 2012;14:87-92.
25. Pollock BE. Management of vestibular schwannomas that enlarge after stereotactic radiosurgery: Treatment recommendations based on a 15 year experience. *Neurosurgery*. 2006;58:241-248. discussion 241-248.
26. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61:344-349.
27. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). *Eur J Cancer*. 2009;45:228-247.
28. Brandes AA, Franceschi E, Tosoni A, et al. MGMT promoter methylation status can predict the incidence and outcome of pseudoprogression after concomitant radiochemotherapy in newly diagnosed glioblastoma patients. *J Clin Oncol*. 2008;26:2192-2197.
29. Ruzevick J, Kleinberg L, Rigamonti D. Imaging changes following stereotactic radiosurgery for metastatic intracranial tumors: Differentiating pseudoprogression from tumor progression and its effect on clinical practice. *Neurosurg Rev*. 2014;37:193-201.
30. Matsuo T, Okunaga T, Kamada K, Izumo T, Hayashi N, Nagata I. Long-term follow-up results of linear accelerator-based radiosurgery for vestibular schwannoma using serial three-dimensional spoiled gradient-echo MRI. *J Clin Neurosci*. 2015;22:320-325.
31. van de Langenberg R, Dohmen AJC, de Bondt BJ, Nelemans PJ, Baumert BG, Stokroos RJ. Volume changes after stereotactic LINAC radiotherapy in vestibular schwannoma: Control rate and growth patterns. *Int J Radiat Oncol Biol Phys*. 2012;84:343-349.
32. Harrison G, Kano H, Lunsford LD, Flickinger JC, Kondziolka D. Quantitative tumor volumetric responses after Gamma Knife radiosurgery for meningiomas. *J Neurosurg*. 2016;124:146-154.
33. Kapoor S, Batra S, Carson K, et al. Long-term outcomes of vestibular schwannomas treated with fractionated stereotactic radiotherapy: an institutional experience. *Int J Radiat Oncol Biol Phys*. 2011;81:647-653.