



Clinical Study

Long-term follow-up results of linear accelerator-based radiosurgery for vestibular schwannoma using serial three-dimensional spoiled gradient-echo MRI



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ABSTRACT

We examined the characteristic changes in vestibular schwannoma (VS) volume after treatment with linear accelerator-based radiosurgery (LBRS) and the long-term therapeutic effects, by performing three-dimensional (3D) MRI evaluations of tumor volumes. We included 44 patients in whom tumor volume changes could be observed using 3D-spoiled gradient-echo MRI for at least 5 years. Examinations were performed every 3–4 months for the first 2 years after treatment and every 6–12 months thereafter. Enlargement or shrinkage was determined as a change of at least 20% from the volume at the time of treatment. The median observation period was 13.8 years (range, 5.5–19.5 years). The tumor control rates at 5 and 10 years after treatment and at the final MRI were 90.9%, 90.0%, and 88.6%, respectively. Tumor volume changes were categorized into the following four patterns: enlargement, five patients (11.4%); stable, three patients (6.8%); transient enlargement, 24 patients (54.5%); and direct shrinkage, 12 patients (27.3%). Bimodal peaks were observed in three of the 24 patients with transient enlargement. Tumor volume changes from 5 and 10 years post-LBRS to the final observation point were observed in 27 (64.2%) and 10 patients (33.3%), respectively. The long-term tumor volume changes observed after LBRS suggest that radiation exerts long-term effects on tumors. Furthermore, while transient enlargements in tumor volume were characteristic, true tumor enlargements should be characterized by increased volumes of more than two-fold and continued growth for at least 2 years.

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1. Introduction

The traditional treatment for vestibular schwannoma (VS) is microsurgery. However, since 1951, when Leksell et al. [1,2] reported a therapeutic method involving the use of gamma knife radiosurgery, many studies have reported the usefulness of this method as an additional treatment for remnant tumors after microsurgical removal or as a primary treatment for relatively small tumors [3–6]. Moreover, linear accelerator-based radiosurgery (LBRS) for VS treatment has been reported to result in similar tumor control rates as gamma knife methods [7,8].

This study measured and evaluated changes in tumor volumes based on three-dimensional (3D) spoiled gradient-echo (SPGR) MRI to examine the long-term therapeutic effects of stereotactic radiosurgery (SRS). Transient tumor enlargement is a characteristic

post-SRS reaction of VS, as is a decline in central enhancement on gadolinium (Gd)-contrast MRI [9–15]. In 2005, we suggested [16] a two-fold increase in tumor volume or a continuous increase in tumor volume for at least 2 years as a key criterion for determining that the tumor volume would continue to increase.

2. Materials and methods

2.1. Patient and tumor characteristics

From January 1994 to September 2002, LBRS was performed on 56 patients with VS at our institution. Of these cases, continuous tumor volume measurements via 3D-SPGR MRI for a period of at least 5 years were available for 44 patients (15 men, 29 women), who were subsequently included in the study. Twelve patients were excluded to avoid the possible influence of prior surgery on post-SRS volume changes. All 44 patients in this report had received LBRS as initial treatment. The median age was 58 years

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Table 1

Treatment characteristics and central enhancement according to pattern of tumor volume change for vestibular schwannoma treated with linear accelerator-based radiosurgery

Parameter	Total	Enlargement	Stable	Shrinkage	
				Transient enlargement	Direct shrinkage
Patients, n	44	5	3	24	12
Median age, years (range)	58 (21–76)	52 (44–75)	68 (29–78)	55 (21–74)	60 (40–76)
Median tumor volume, ml (range)	2.38 (0.4–8.99)	1.99 (0.4–6.9)	2.28 (2.27–2.36)	1.75 (0.76–8.99)	2.85 (1.46–6.56)
Median dose to tumor margin, Gy (range)	–	14 (12–14)	14 (12–14)	14 (13–15)	14 (12–16)
Median isocenters, n (range)	–	2 (1–3)	2 (1–2)	2 (1–4)	2 (1–4)
Loss of central enhancement, n	–	2	1	20	7
Median interval to loss, months (range)	–	8.5 (7–10)	3	4 (3–8)	4 (3–6)

(range, 21–76 years). All tumors were unilateral, and the median tumor volume was 2.38 ml (range, 0.4–8.99 ml; [Table 1](#)).

2.2. Radiosurgical procedure

Radiosurgery was performed using the 10-MeV X-ray beam of a linear accelerator (Clinac 2100C, Varian Medical Systems, Milpitas, CA, USA). A convergent beam irradiation system (F.L. Fischer, Freiburg, Germany) was used as the SRS system. Radiosurgery planning was performed using the STP 3D-planning system (F.L. Fischer). Target definition was based on CT scan and MRI T1-weighted post-contrast planning images. Depending on the tumor size and configuration, one to four isocenters (median, two isocenters) were targeted. The collimators used were 6–29 mm in diameter (80% of the field size, 8.7–49.9 mm). More than two collimators were used to treat irregularly shaped lesions. The median radiation dose directed to the tumor margin was 14 Gy (range, 10–16 Gy), and the median maximum dose was 23.2 Gy (range, 17–36.13 Gy). When applied to the brainstem, the radiation dose was limited to 10 Gy.

2.3. Follow-up evaluations

MRI evaluations were performed every 3–4 months for 2 years after treatment and every 6–12 months thereafter in all patients. To measure tumor volumes, we obtained 3D-SPGR MRI sequences using the following settings: repetition time, 45 ms; echo time, 3.1 ms; field of view, 180 × 180 mm; slice thickness, 1 mm; and matrix, 256 × 160. Computer-assisted measurements were used to calculate the tumor area in each Gd-enhanced MRI. The volume was determined by multiplying the area by the section thickness. Tumor shrinkage or growth was defined as a volume change of more than 20%.

To examine changes in tumor volume after 5 and 10 years post-LBRS, analyses were performed with the tumor volumes at 5 and 10 years, respectively, reset to 100%.

3. Results

3.1. Tumor volume control

Changes in tumor volume were continuously monitored in 44 patients using 3D-SPGR MRI for at least 5 years. The mean observation period was 13.8 years (range, 5.5–19.5 years). Of these 44 patients, volume measurements at 5 years post-treatment showed shrinkage in 28 (63.6%), stability in 12 (27.2%), and enlargement in four (9.1%). Of the 30 patients with measurements at 10 years post-treatment, shrinkage was observed in 17 (56.7%), stability in 10 (33.3%), and enlargement in three (10.0%). The tumor control rates at 5 and 10 years were 90.9% and 90.0%, respectively. The measurements at the time of final MRI showed shrinkage in 36 patients

(81.8%), stability in three patients (6.8%), and enlargement in five patients (11.4%), resulting in a tumor control rate of 88.6%.

Although re-irradiation was performed in two patients in whom the tumors enlarged continuously for at least 2 years and the tumor volume increased more than two-fold from the time of treatment, in both patients the tumors were controlled during a follow-up period of at least 15 years. No patients required surgical removal due to tumor enlargement ([Fig. 1](#)).

3.2. Tumor volume change patterns

Tumor volume changes were categorized into four patterns. (1) Enlargement pattern ([Fig. 1A](#)), seen in three patients where the tumor volume had increased at the final MRI and in two patients where additional irradiation with LBRS was performed due to tumor volume increase, for a total of five patients (11.4%). (2) Stable pattern ([Fig. 1B](#)), seen in three patients (6.8%) in whom there was no change in tumor volume at the final MRI. (3) Transient enlargement pattern ([Fig. 1C](#)), seen in 24 patients (54.5%) where tumor volume increase occurred during follow-up but shrinkage was observed at the final MRI. (4) Direct shrinkage pattern ([Fig. 1D](#)), seen in 12 patients (27.3%) where tumor volumes did not increase during follow-up and shrinkage was observed at the final MRI.

[Table 1](#) shows the treatment characteristics for each tumor volume change pattern. There were no significant differences in age, tumor volume, radiation treatment dose, or the number of targeted isocenters between the four volume change pattern groups.

3.3. Timing of peak volume after LBRS and tumor growth rate

A peak was defined as an increase in tumor volume of at least 20% since the time of treatment (that is, the same definition as for enlargement), after which there was a decline. Peak formation was found in 25 patients (24 patients with a transient enlargement pattern, and one of five patients with an enlargement growth pattern), including three patients with a bimodal peak, bringing the total number of peaks to 28. [Figure 2](#) shows the growth rates of the tumors and the time until peak formation.

The first peak occurred at a median time of 0.75 years (range, 0.3–4.1 years) after treatment, while the second peak occurred at a median time of 3.3 years (range, 3.2–6.7 years). The median enlargement factors were 1.35-fold (range 1.2–3.02-fold) for the first peak and 1.29-fold (range 1.27–1.4-fold) for the second peak.

The first peak occurred within 2 years, and the increase was two-fold or less in 22 patients (88%). When we examined only patients with a transient enlargement pattern, we found no enlargement that continued for 2 years or longer, and no enlargement to more than twice the original size.

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