Effect of treatment plan quality on outcomes after radiosurgery for vestibular schwannoma

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Object. The goal in this study was to review the effects of treatment plan quality on outcomes after radiosurgery for vestibular schwannoma (VS).

Methods. Between July 1988 and August 2005, 390 patients were treated. The results of this experience have been published recently. In this study the authors looked at dosimetry variables: conformity of treatment plan and steepness of dose gradient, in the same group of patients. Over the duration of this study, dosimetry evolved from a single isocenter with marginal conformity to multiple isocenters with high conformity. Multivariate statistics were used to determine the effects of these variables on tumor control and on two types of complication, facial weakness and facial numbness.

Results. The 5-year actuarial tumor control was 91%. Dosimetry had no effect on tumor control. Eighteen patients (4.6%) reported new-onset facial weakness and 14 (3.6%) reported new-onset facial numbness. Since 1994, when peripheral treatment doses were lowered to 1250 cGy, only three (1%) of 298 patients have experienced facial weakness and two (0.7%) of 298 have experienced facial numbness. Statistical analysis confirms, as in the prior study, that treatment volume and treatment dose are significant predictors of both facial weakness and facial numbness. In this model, prior tumor growth was also significant. Dosimetry, however, is definitely not a significant predictor of either complication.

Conclusions. Treatment dose appears to be much more important than treatment plan quality in the prevention of facial numbness or weakness after radiosurgery for VS. (DOI: 10.3171/JNS-07/11/0913)

KEY WORDS • dosimetry • radiosurgery • vestibular schwannoma

The optimum treatment of VSs is controversial. Options include observation, surgery (several different approaches), radiotherapy, and radiosurgery.12,17 Radiosurgery has become a popular alternative to open surgery for smaller tumors.1,5,7 High tumor control rates and low complication rates have been reported in multiple series.8,10,11,13,14,16,19–24,26,27 Our experience with radiosurgery for treatment of VSs at the University of Florida has recently been published.8,9 In that study of 390 patients, tumor volume and treatment dose were found to have a statistically significant effect on subsequent new-onset facial numbness and on new-onset facial weakness. That study spanned more than a decade, during which time many improvements occurred in radiosurgical treatment planning, leading to significantly more conformal radiation shapes.

In this study we examine two measures of treatment dosimetry quality: conformity of the radiation treatment isodose to the tumor shape and steepness of the radiation dose gradient. We attempt to answer this question: does the quality of treatment plan affect tumor control or complications after radiosurgery?

Clinical Material and Methods

Treatment Plan Variables

Variables associated with treatment plan quality were determined by first contouring the tumors in 1-mm slices on the original targeting images, using software developed at our institution. Resulting tumor volumes were coupled with the original radiosurgical dosimetry plans to generate dose-volume histograms. Using the method described by Wagner et al.,28 a conformity index, a dose gradient index, and a conformity/gradient index were calculated for each patient by using point measurements from the target and total volume, dose-volume histogram curves (Fig. 1).

The conformity index is the ratio of target volume to prescription isodose volume, scaled to 100, such that a “perfect score” is 100. The gradient index measures the effective radius of the isodose volume and the effective radius of the half isodose volume to determine the number of millimeters needed to move from a full peripheral treatment dose to half of that dose. An “ideal” gradient is assumed to be 3 mm, which yields an index of 100. The conformity/gradient index is simply the average of the conformity and gradient values.

Outcomes Definition

The following outcomes were identified and analyzed:
local control, new-onset facial weakness, and new-onset facial numbness. Local control was defined as lost if the last imaging follow-up study demonstrated any tumor enlargement. Facial weakness and facial numbness were defined as new-onset deficit any time after radiosurgery, regardless of degree or permanence. Hearing was not evaluated in this study.

As in our prior study, follow-up review included both clinical evaluation and imaging studies. All films were reviewed by the senior author (W.A.F.) and visually compared with the radiosurgery treatment films. Phone interviews with patients or referring physicians were used to confirm clinical status when such information was not available from clinic visits at the University of Florida.

Statistical Analysis

The Cox proportional hazards model was used to explore the relationship between the new treatment quality variables (conformity index, gradient index, and conformity/gradient index) and tumor control. The variables shown in the previous study to correlate with complications (treatment volume and treatment dose) were tested first, and then the conformity index, gradient index, and conformity/gradient index were added to the model.

The “PROC PHREG” and “PROC LOGISTIC” procedures in the statistical software (Version 9.1; SAS Institute, Inc.) were used. Parameters were determined to be statistically significant at a probability level of 0.05.

Results

Actuarial local control was 91% at 5 years. The conformity index, gradient index, and conformity/gradient index had no effect on local control (Table 1). The mean follow-up duration was 40 months, with 61 patients continuing in follow-up for 5 years.

Facial Weakness. Eighteen patients (4.6%) experienced new-onset facial weakness after treatment. Only three (1%) of 298 patients treated at the 1250-cGy dose used since 1994 have experienced facial weakness. Logistic regression analysis again confirmed that, in this model, prior tumor growth, treatment volume, and treatment dose were significantly associated with facial weakness (Table 2), whereas conformity index, gradient index, and conformity/gradient index were not.

Facial Numbness. Fourteen patients (3.6%) experienced new-onset facial numbness after treatment. Only two (0.7%) of 298 patients treated at the 1250-cGy dose experienced facial numbness. Logistic regression analysis confirmed that prior growth, tumor volume, and treatment dose were significantly associated with facial numbness (Table 2), whereas conformity index, gradient index, and conformity/gradient index were not.

Discussion

Foote et al. performed an analysis of risk factors associated with radiosurgery for VS at the University of Florida and showed that maximum dose to the brainstem was the best predictor of subsequent cranial neuropathies. A prescription dose of 1250 cGy to the tumor margin yielded the best combination of maximum tumor control and minimum treatment complications. Prior resection was shown to cor-
Radiosurgery for vestibular schwannoma

TABLE 1

<table>
<thead>
<tr>
<th>Time (yrs)</th>
<th>Total No. of Patients</th>
<th>Fail†</th>
<th>Survivor Function</th>
<th>SEM</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>251</td>
<td>4</td>
<td>0.99</td>
<td>0.01</td>
</tr>
<tr>
<td>2</td>
<td>196</td>
<td>4</td>
<td>0.97</td>
<td>0.01</td>
</tr>
<tr>
<td>5</td>
<td>61</td>
<td>0</td>
<td>0.91</td>
<td>0.02</td>
</tr>
<tr>
<td>10</td>
<td>9</td>
<td>0</td>
<td>0.91</td>
<td>0.02</td>
</tr>
</tbody>
</table>

* SEM = standard error of the mean. † The tumor grew.

TABLE 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>SEM</th>
<th>p Value*</th>
</tr>
</thead>
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<tr>
<td>facial weakness</td>
<td>8.93</td>
<td>0.71</td>
<td>0.002</td>
</tr>
<tr>
<td>prior tumor growth</td>
<td>1.23</td>
<td>0.09</td>
<td>0.019</td>
</tr>
<tr>
<td>treatment vol</td>
<td>5.80</td>
<td>0.42</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>conformity index</td>
<td>1.01</td>
<td>0.02</td>
<td>0.759</td>
</tr>
<tr>
<td>gradient index</td>
<td>1.04</td>
<td>0.04</td>
<td>0.360</td>
</tr>
<tr>
<td>facial numbness</td>
<td>9.94</td>
<td>0.87</td>
<td>0.008</td>
</tr>
<tr>
<td>treatment vol</td>
<td>1.33</td>
<td>0.09</td>
<td>0.003</td>
</tr>
<tr>
<td>treatment dose</td>
<td>6.35</td>
<td>0.49</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>conformity index</td>
<td>1.01</td>
<td>0.02</td>
<td>0.647</td>
</tr>
<tr>
<td>gradient index</td>
<td>1.02</td>
<td>0.05</td>
<td>0.676</td>
</tr>
</tbody>
</table>

* Prior tumor growth, treatment volume, and treatment dose are statistically significant, whereas gradient index and conformity index are not.

relate with subsequent cranial nerve complications. This study did not demonstrate a relationship between number of isocenters (and, presumably, conformity) and complications.

Other authors have qualitatively addressed the issue of conformity versus subsequent complications. Spiegelmann et al.25 have reported their experience. They reviewed the methods and results of linear accelerator radiosurgery in 44 patients with VSs who were treated between 1993 and 1997. Computed tomography scanning was selected as the stereotactic imaging modality for target definition. A single, conformally shaped isocenter was used in the treatment of 40 patients; two or three isocenters were used in four patients who harbored very irregular tumors. The radiation dose directed to the tumor border was the only parameter that changed during the study period: in the first 24 patients who were treated, the dose was 15 to 20 Gy, whereas in the last 20 patients the dose was reduced to 11 to 14 Gy. After a mean follow-up period of 32 months (range 12–60 months), 98% of the tumors were controlled. The actuarial hearing preservation rate was 71%. New transient facial neuropathy developed in 24% of the patients and persisted to a mild degree in 8%. Radiation dose correlated significantly with the incidence of cranial neuropathy, particularly in large tumors (≥ 4 cm³).

Karpinos et al.15 compared radiosurgery and microsurgery in 96 patients with VSs. Facial neuropathy was seen in 6.1% of the patients treated with radiosurgery. Trigeminal neuropathy was seen in 12.2% of the radiosurgery group. A mean dose of 14.5 Gy was used. In this study there was no correlation between dose, tumor size, or number of isocenters used and the outcome.

Flickinger et al.4 reported on 131 patients treated with radiosurgery. The incidence of trigeminal and facial neuropathy was quite high: 29 and 33%. In this early study, increasing the number of isocenters correlated with reduced complications, but the conclusion may have been biased by the consistent use of treatment doses that are much higher than those used today. In a more recent study of 190 patients treated with “current methods,” Flickinger and colleagues2 found that only marginal dose correlated with the development of facial weakness. In yet another study of 313 patients treated with 12- to 13-Gy doses,3 they found that trigeminal neuropathy correlated with increasing tumor volume. Other authors have suggested that the length of cranial nerve irradiated correlated with complications.16

Friedman et al.5 recently updated the University of Florida experience. They demonstrated that treatment volume and treatment dose correlated with subsequent cranial neuropathies. With each cubic centimeter increase in volume, the odds of facial weakness increased by 17% and the odds of facial numbness increased by 28%. With each 250-cGy increase in dose, the odds of facial weakness increased eight times and the odds of facial numbness increased seven times.

This study was the first in which the effect of conformity is quantitatively explored, and it is the first in which the effect of dose gradient on treatment outcomes after radiosurgery for VS is explored. In this analysis, no significant effect of those treatment variables was found in relation to tumor control, facial weakness, or facial numbness. Our study confirms the significance of tumor volume and treatment dose. In this model, prior tumor growth was also a significant predictor, possibly because other variables analyzed in the previous study were not part of this multivariate analysis. Prior tumor growth may very well correlate with prior tumor resection, which was found to be significant in the earlier study by Foote et al.6

Conclusions

Conformity and dose gradient, within the bounds of radiosurgery as practiced from 1988 to 2005 at the University of Florida, have no significant effect on outcomes after radiosurgery for VS. We found that dose is the most important treatment factor. Each 250-cGy dose increase over the “optimum” dose of 1250 cGy increases the risk of facial numbness or facial weakness by a factor of 6.

Acknowledgments

We gratefully acknowledge the support from the Lawrence M. Goodman Trust. Many thanks as well to Dr. Keith Muller and Qin Li for statistical analysis of the tumor outcomes.

References


Manuscript submitted October 16, 2006. Accepted March 1, 2007. This study was supported by the Lawrence M. Goodman Trust.

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