

The behavior of residual tumors and facial nerve outcomes after incomplete excision of vestibular schwannomas

Clinical article

ZHENGNONG CHEN, M.D., PH.D.,¹ SAMPATH CHANDRA PRASAD, M.S., D.N.B.,²
FILIPPO DI LELLA, M.D., PH.D.,² MARIMAR MEDINA, M.D.,² ENRICO PICCIRILLO, M.D.,²
ABDELKADER TAIBAH, M.D.,² ALESSANDRA RUSSO, M.D.,² SHANKAI YIN, M.D., PH.D.,¹
AND MARIO SANNA, M.D.^{2,3}

¹Department of Otolaryngology, Affiliated Sixth People's Hospital to Shanghai Jiao Tong University, and Otolaryngology Institute, Shanghai Jiao Tong University, Shanghai, China; ²Department of Otology & Skull Base Surgery, Gruppo Otologico, Piacenza-Rome; and ³Department of Otolaryngology, University of Cheiti, Italy

Object. The authors evaluated the behavior of residual tumors and facial nerve outcomes after incomplete excision of vestibular schwannomas (VSs).

Methods. The case records of all patients who underwent surgical treatment of VSs were analyzed. All patients in whom an incomplete excision had been performed were analyzed. Incomplete excision was defined as near-total resection (NTR), subtotal resection (STR), and partial resection (PR). Tumors in the NTR and STR categories were followed up with a wait-and-rescan approach, whereas the tumors in the PR category were subjected to a second-stage surgery and were excluded from this series. All patients included in the study underwent baseline MRI at the 3rd and 12th postoperative months, and repeat imaging was subsequently performed every year for 7–10 years postoperatively or as indicated clinically. Preoperative and postoperative facial function was noted.

Results. Of the 2368 patients who underwent surgery for VS, 111 patients who had incomplete excisions of VSs were included in the study. Of these patients, 73 (65.77%) had undergone NTR and 38 (34.23%) had undergone STR. Of the VSs, 62 (55.86%) were cystic and 44 (70.97%) of these cystic VSs underwent NTR. The residual tumor was left behind on the facial nerve alone in 62 patients (55.86%), on the facial nerve and vessels in 2 patients (1.80%), on the facial nerve and brainstem in 15 patients (13.51%), and on the brainstem alone in 25 patients (22.52%). In the 105 patients with normal preoperative facial nerve function, postoperative facial nerve function was House-Brackmann (HB) Grades I and II in 51 patients (48.57%), HB Grade III in 34 patients (32.38%), and HB Grades IV–VI in 20 patients (19.05%). Seven patients (6.3%) showed evidence of tumor regrowth on follow-up MRI. All 7 patients (100%) who showed evidence of tumor regrowth had undergone STR. No patient in the NTR group exhibited regrowth. The Kaplan-Meier plot demonstrated a 5-year tumor regrowth-free survival of 92%, with a mean disease-free interval of 140 months (95% CI 127–151 months). The follow-up period ranged from 12 to 156 months (mean 45.4 months).

Conclusions. The authors' report and review of the literature show that there is undoubtedly merit for NTR and STR for preservation of the facial nerve. On the basis of this they propose an algorithm for the management of incomplete VS excisions. Patients who undergo incomplete excisions must be subjected to follow-up MRI for a period of at least 7–10 years. When compared with STR, NTR via an enlarged translabyrinthine approach has shown to have a lower rate of regrowth of residual tumor, while having almost the same result in terms of facial nerve function. (<http://thejns.org/doi/abs/10.3171/2014.2.JNS131497>)

KEY WORDS • vestibular schwannoma • surgery • incomplete excision • regrowth • near-total resection • subtotal resection • facial nerve • oncology

VESTIBULAR schwannoma (VS) is the most common tumor of the cerebellopontine angle, and microsurgical removal remains central to its management.³⁴ The goal of surgical removal must be to achieve complete tumor eradication with preservation of facial and cochlear nerve function. However, in certain instances it becomes

Abbreviations used in this paper: GKS = Gamma Knife surgery; GTR = gross-total resection; HB = House-Brackmann; NTR = near-total resection; PR = partial resection; SRS = stereotactic radiosurgery; STR = subtotal resection; VS = vestibular schwannoma.

impossible to achieve complete tumor eradication due to the tumor's intimate relationship with important structures, such as the facial nerve, brainstem, vessels, and other nerves in the cerebellopontine angle, without compromising such structures. This is especially true in patients with large tumors or in those with associated severe comorbidities, where the aim of surgery may be to perform a primary debulking followed by a second-stage excision. Intraoperative vital sign changes or excessive bleeding may also force the procedure to be abandoned before total tumor excision has been achieved.

In case of involvement of the facial nerve, the dilemma that the surgeon is faced with is that of whether to preserve the nerve at the cost of leaving behind a small remnant of tumor or achieve total eradication by sacrificing the nerve. The decision to leave behind tumor in an attempt to save the nerve can be justified if the following 2 factors can be proved: 1) that the incidence and the rate of tumor regrowth is acceptably low, and 2) that there is a significant benefit in terms of postoperative preservation of facial nerve function. In an attempt to rationalize this decision-making process we evaluated the behavior of all residual tumors, in terms of regrowth and facial nerve function, after incomplete excisions of VSs.

Methods

This was a retrospective study of patients surgically treated for VS between January 1987 and December 2010 at the Gruppo Otologico, Piacenza-Rome, Italy, a quaternary referral center for otology and skull base surgery. The case records of all patients who underwent surgical treatment of VSs were analyzed. All patients in whom an incomplete excision was performed were analyzed. Excisions of VSs were defined as in Table 1. Tumors in the NTR (near-total resection) and STR (subtotal resection) categories were followed up with a wait-and-rescan approach, whereas the tumors in the PR (partial resection) category were subjected to a second-stage surgery. The clinical features, investigations, surgical procedure, indications for incomplete excision, sites of residual tumor, and postoperative follow-up of the patients included in the series were noted and analyzed.

After surgery, all patients included in the study underwent follow-up at the outpatient clinic and baseline MRI at the 3rd and 12th postoperative months and subsequently every year for 7–10 years postoperatively or as indicated clinically. Preoperative and postoperative facial nerve function was noted and was classified according to the House-Brackmann (HB) grading of facial nerve function. The preoperative tumor size and postoperative residual tumor size were evaluated using MRI (1.5 T) by measuring their diameters in 2 perpendicular directions (in mm). Growth of the residual tumor was determined by the increase in its greatest dimension on follow-up MRI studies.

Results

A total of 2368 patients underwent surgery for VS between 1987 and 2010 at the Gruppo Otologico. Of these, 88 patients underwent a retrosigmoid approach and 90 underwent a middle cranial fossa approach for small tumors, and total excision was achieved in all cases. Of the remaining 2190 patients who underwent an extended transabyrinthine approach, 155 patients (7.1%) had incomplete excisions (Fig. 1). Patients in the PR category were excluded from this series. Patients with neurofibromatosis, those with a history of radiotherapy or radiosurgery, those in whom the facial nerve was sacrificed during surgery, and those with less than 1 year of follow-up were also excluded. Therefore, 111 patients who had undergone incomplete excisions of their VS were included in the study. The male/female ratio was 41:70. Patient age ranged from 25 to 82

TABLE 1: Definitions of VS resections

Extent of resection	Definition
GTR	total (100%) tumor clearance as evident from the surgeon's subjective observation & on 1-yr postop MRI
NTR	<2% of the tumor or tumor capsule is left behind during surgery as evident from the surgeon's subjective observation & if 1) it is manifest or 2) absent on 1-yr postop MRI
STR	2–5% of the tumor left behind during surgery as noted by the surgeon & evident on 1-yr postop MRI
PR	>5% of the tumor left behind during surgery as noted by the surgeon & evident on 1-yr postop MRI

years (mean 62 years). The follow-up period ranged from 12 to 156 months (mean 45.4 months); 42 (38%) of our patients were followed up for more than 5 years. On Kaplan-Meier analysis (Fig. 2), the 5-year tumor regrowth-free survival was 92%, with a mean tumor regrowth-free period of 140 months (95% CI 127–151 months).

Near-Total Versus Subtotal Resection

Of the 111 patients, 73 (65.77%) underwent an NTR, while the remaining 38 (34.23%) underwent an STR. The tumor sizes undergoing NTR ranged from 10 to 50 mm (mean 29 mm), while those treated with STR ranged from 20 to 50 mm (mean 32.2 mm).

Cystic Versus Solid Tumors

Of the 111 tumors, 62 (55.86%) were cystic VSs and the remaining 49 (44.14%) were solid VSs (Table 2); 44 (70.97%) of the cystic VSs underwent NTR and 18 (29.03%) underwent STR. Of the solid tumors 29 (59.18%) underwent NTR and 20 (40.82%) underwent STR. The percentage of cystic VSs in the NTR group (44 [60.27%] of 73) was higher than that in the STR group (18 [47.37%] of 38); however, the difference was not statistically significant (chi-square test, $p > 0.05$).

Sites of Residual Tumors

Of the 111 patients who underwent incomplete tumor excision, the residual tumor was left behind on the facial nerve alone in 62 patients (55.86%), on the facial nerve and vessels in 2 patients (1.80%), on the facial nerve and brainstem in 15 patients (13.51%), on the brainstem alone in 25 patients (22.52%), on the brainstem and vessels in 4 patients (3.60%), and on a vessel alone in 3 patients (2.70%) (Table 3).

Overall, the facial nerve was involved in 51 (69.86%) of 73 tumors that underwent NTR and 28 (73.68%) of 38 tumors that underwent STR. Similarly, the brainstem was involved in 28 (38.36%) of 73 tumors that underwent NTR and 16 (42.1%) of 38 tumors that underwent STR. The vessels were involved in 8 (11.0%) of 73 tumors that underwent NTR and 1 (2.63%) of 38 tumors that underwent STR.

The behavior of residual tumors after incomplete excision of VS

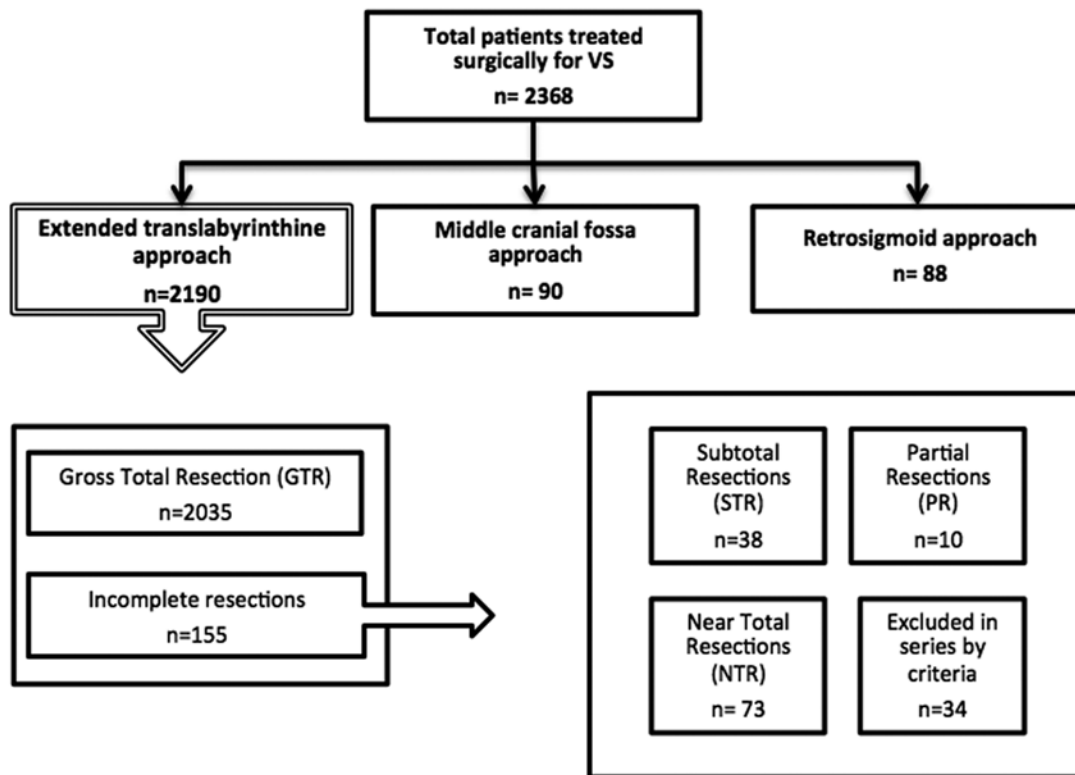


Fig. 1. Flowchart showing the study population.

Facial Nerve Status

Facial nerve status was evaluated immediately postoperatively and during follow-up. Of the 111 patients, 6 patients had preoperative facial nerve paralysis and were excluded from analysis. In the remaining 105 cases with normal preoperative facial nerve function, anatomical integrity of the facial nerve was preserved in all cases. Postoperative facial nerve function was HB Grades I and II in 51 patients (48.57%), HB Grade III in 34 patients (32.38%), and HB Grades IV–VI in 20 patients (19.05%).

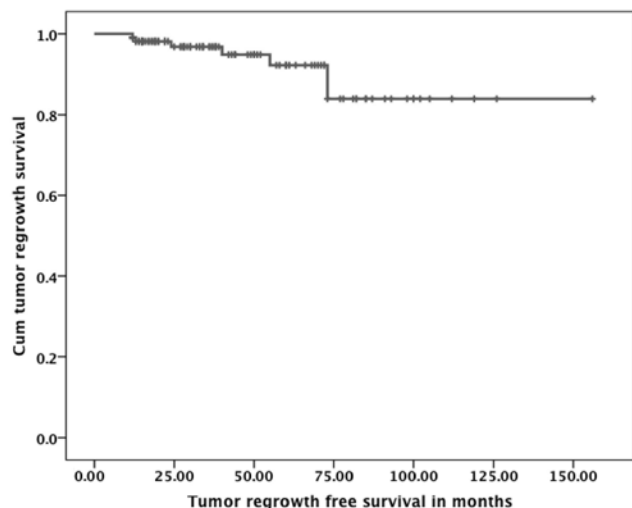


Fig. 2. Kaplan-Meier survival analysis for tumor regrowth outcome period. Cum = cumulative.

Postoperatively at 1 year (Tables 4 and 5), 33 patients in the NTR group (49.25%) had good facial nerve function (HB Grades I and II), 24 (35.82%) had intermediate facial nerve function (HB Grade III), and 10 (14.93%) had poor facial nerve function (HB Grades IV–VI). In the STR group, 18 patients (47.37%) had good facial nerve function (HB Grades I and II), 10 (26.32%) had intermediate facial nerve function (HB Grade III), and 10 patients (26.32%) had poor facial nerve function (HB Grades IV–VI). There was no significant difference in good, intermediate, and unsatisfactory facial nerve function between the groups (chi-square test, $p > 0.05$). Of the 6 patients with preoperative facial nerve paralysis, 3 had HB Grade VI paralysis after undergoing previous surgery at other centers and presented with large residual tumors, which were treated with revision surgery at our center. One patient had preoperative HB Grade III function, and 2 patients had preoperative HB Grade II facial nerve function. There was no deterioration in facial nerve function in any of our patients during long-term follow-up. More than 50% of patients with tumors smaller than 3 cm had good facial nerve function after they underwent NTR or STR,

TABLE 2: Cystic and solid tumors treated with NTR or STR

VS Type	No. of Tumors (%)		
	NTR	STR	Total
cystic	44	18	62 (55.86)
solid	29	20	49 (44.14)
total	73 (65.8)	38 (34.2)	111 (100)

TABLE 3: Site of residual tumors in NTR and STR*

Resection	No. of Residual Tumors (%)						Total
	FN	FN+V	FN+BS	BS	BS+V	V	
NTR	41	1	9	15	4	3	73
STR	21	1	6	10	0	0	38
total	62 (55.86)	2 (1.80)	15 (13.51)	25 (22.52)	4 (3.60)	3 (2.70)	111 (100)

* BS = brainstem; FN = facial nerve; V = vessels.

while about 30% patients with tumor size larger than 3 cm had good facial nerve function.

Details of Patients With Tumor Regrowth and Management

Seven patients (6.3%) showed evidence of tumor regrowth on follow-up with MRI (Table 6). All 7 patients who showed evidence of tumor regrowth were in the STR group. No patient in the NTR group exhibited regrowth. The incidence of regrowth in the STR group was 7 (18.4%) of 38. Six (30%) of the 20 patients with solid VSs and 1 (5.56%) of the 18 patients with cystic VSs exhibited regrowth. The difference was not statistically significant (Fisher exact test, $p > 0.05$). Of the 7 patients, 1 had a minimal and slow increase in size on follow-up but with no clinical impact and hence underwent a wait-and-rescan follow-up. Six other patients showed sizable and rapid regrowth of the residual tumors and needed further treatment. Three of the patients underwent a second surgery with total excision in 1 case and near-total excision in 2 cases, and 3 other patients were treated with stereotactic radiosurgery (SRS).

Discussion

Considering that VSs are benign slow-growing tumors, partial removal can be used as a strategy to reduce postoperative morbidity, and therefore it is important to know the behavior of the residual tumor in incomplete resections. While some authors believe that small fragments of residual tumor are effectively devitalized and do not grow,^{23,28,33} others have proved that the proliferative activity of the tumor itself, as measured by monoclonal antibody MIB-1, may contribute to regrowth.^{1,5,20} The factors that need to be addressed are the pattern of regrowth of the residual tumors and the postoperative function of the facial nerve because these have the potential to influence decision making. If the incidence of regrowth in incomplete excisions is acceptably low and a good postoperative facial nerve function is established, a sound policy would be to leave behind tumor in cases in which it is closely adherent to the facial nerve and other important neurovasculature. This could be especially important in elderly patients and patients with comorbid conditions.

Terminology of Incomplete Resections and Algorithm

A variety of terms have been used to describe incomplete resections of VSs and those commonly used are near-total resection, subtotal resection, and partial resection.²¹ There is considerable ambiguity among reports regarding the definitions of NTR and STR (Table 7).^{8,10,12,14,17,25,35}

While most authors describe NTR and STR as percentages of initial tumor volume as evaluated intraoperatively, others specifically calculate it as the diameter or volume of tumor detected on postoperative MRI.^{15,35} Both descriptions have drawbacks. The drawback of the first description is that the percentage remnant of total tumor volume is itself a relative indicator. For example, a 5% residual of a 2-cm tumor is less than a 5% residual of a 4-cm tumor.¹⁸ A drawback in the second description is that not all tumors left behind in the NTR group are visualized by postoperative MRI, and minimal residual tumor can be missed or lost due to regression of the tumor itself. Also, in early postoperative MRI, leptomeningeal, perineural, dural, or nodular enhancement within the internal auditory canal mimicking the residual tumor can be frequently seen and can often be difficult to distinguish from the tumor remnants.^{15,35} When it comes to volumetric versus diametric measurements of tumor, while some authors have stressed that volumetric determination is a reliable measure of tumor size and minimizes the risk of error due to partial volume effects,^{19,35} other investigators have found no differences in growth results between measurements of tumor volume and tumor diameter.¹¹ Volumetric determination also requires expertise and an imaging technique that may not be available at all centers.

For comparability in reporting outcomes, a standard norm should be universally adopted that clearly differen-

TABLE 4: Facial nerve function in patients with residual tumor*

FN Function†	No. of Patients (%)		
	NTR	STR	Total
good			
I	24	14	38
II	9	4	13
total	33 (49.25)	18 (47.37)	51 (48.57)
intermediate			
III	24 (35.82)	10 (26.32)	34 (32.38)
poor			
IV	4	3	7
V	1	3	4
VI	5	4	9
total	10 (14.93)	10 (26.32)	20 (19.05)
overall total	67 (100)	38 (100)	105 (100)

* Six patients with preoperative facial nerve paralysis were excluded from facial nerve function analysis.

† Roman numerals correspond to HB grades.

The behavior of residual tumors after incomplete excision of VS

TABLE 5: Facial nerve function in the patients with residual tumor according to size

Residual Tumor Size (cm)	No. of Patients (%)									
	HB I–II			HB III			HB IV–VI			Total
	NTR	STR	Subtotal	NTR	STR	Subtotal	NTR	STR	Subtotal	
1.0–2.0	7	1	8 (50.0)	4	2	6 (37.5)	2	0	2 (12.5)	16
2.1–3.0	19	12	31 (57.4)	14	4	18 (33.3)	2	3	5 (9.3)	54
3.1–4.0	6	3	9 (33.3)	4	2	6 (22.2)	6	6	12 (44.4)	27
>4.1	1	2	3 (37.5)	2	2	4 (50.0)	0	1	1 (12.5)	8

tiates between STR and NTR.¹⁸ We are of the opinion that VS resections must be classified in a way that includes the surgeon's observation and the postoperative detection of tumor on MRI. The resections can be categorized as gross total resection (GTR), NTR, STR, and PR as shown in Table 1.

Indications for NTR and STR

From the time when Dandy in 1925 advocated total excision of all VSs in the initial surgery there has been a shift in surgical practice, a willingness to leave a tumor remnant in situ if there was any concern that a more aggressive resection would cause trauma to the facial nerve and other neurovascular structures.¹² Most authors agree that the current indications for NTR and STR are 1) involvement of the facial nerve, the brainstem, or the vasculature of the cerebellopontine angle and brainstem; 2) unexpected bleeding during surgery; 3) older age; and 4) comorbidities. We have encountered a few other specific situations that required NTR or STR such as blindness in the eye on the side contralateral to tumor (where a special effort was made to preserve the ipsilateral facial nerve), intraoperative change in vital parameters, or cerebellar edema in large VSs. However, such cases were not included in the present series as they did not fit into the present inclusion criteria.

Extent of Resection and Regrowth

Although many factors have been reported to contribute to regrowth in patients with tumor remnants, including the extent of resection,^{12,32} postoperative imaging findings,⁷ and the proliferative activity of the tumor itself,^{1,5,20} little is known about the clinicopathological characteristics of VSs that recur during long-term follow-up after incomplete

resection.¹⁵ In Table 7 we compare our results with other studies regarding the incidence of regrowth in incomplete VS resections. The reported incidence of regrowth in the subset of NTR ranged from 0% to 3.5% and in the subset of STR from 18.4% to 73.9%. In both groups our series represented the lowest rate of recurrences when compared with all other studies. It is evident from other studies and ours that the degree of resection correlates with recurrence rate. The study by Vakilian et al.³⁵ showed that patients who had tumor regrowth had mean postoperative tumor volumes that were significantly larger ($p = 0.041$) than those patients with stable residual tumors. All patients with residual tumor volumes in excess of 2.5 cm³ exhibited further tumor growth. In their study, univariate analysis demonstrated that only postoperative tumor volume ($p < 0.05$) was significantly associated with growth. Sex, age, preoperative and postoperative planimetric dimensions, and preoperative volume had no significant association with tumor growth. In their study Carlson et al.¹⁰ reported that among those patients with nodular enhancement on baseline postoperative MRI, a maximum linear diameter of at least 15 mm or a volume of at least 0.4 cm³ was associated with an approximately 5-fold increased risk for future growth ($p < 0.02$).

Tumor Consistency and Regrowth

Cystic VSs are widely described as being more aggressive and having shorter symptomatic periods before presentation, poorer responses to radiosurgery, and worse outcomes from surgical intervention.²⁹ Factors that lead to unfavorable surgical outcomes include engulfment of and adherence to neurovascular structures, hypervascular solid portions of the tumor, and absence of an adequate subarachnoid dissection plane. Proliferative activities of cystic tumors are also reportedly higher than average.¹

TABLE 6: Characteristics of patients with residual tumor regrowth

Case No.	Age (yrs)	Cyst	Extent of Resection	Site of Residual Tumor	Interval for Regrowth (mos)	Treatment	HB Grade
1	65	no	STR	BS	13	surgery	III
2	69	no	STR	FN	12	SRS	III
3	74	no	STR	FN	24	GKS	I
4	46	no	STR	BS	40	GKS	IV
5	77	no	STR	FN	55	surgery	IV
6	78	no	STR	FN	73	wait & scan	II
7	47	yes	STR	FN+BS	72	surgery	VI

TABLE 7: Comparison of the present study with others*

Authors & Year	No. of IRs in Study/Total No. of VSs Undergoing Op	No. of Approaches & Type	Follow-Up (in mos)†	Type of Resection; No. (%)	Average Tumor Size (cm)	Definition/Description of Terminology	No. of Regrowths (%)		Intervention for Regrowth‡	
							w/in NTR or STR Subset	Op	Wait & Rescan	SRS
Martin et al., 2012	65/229	54 TL, 11 RS	66	NTR; 54 (81.8) STR; 11 (16.7)	NA	"small fragment," "microscopic fragment," & "small nubbins," <5% of tumor remnant >5% of tumor remnant	1 (1.9)	1 (9.1)	1 (1.9)	1 (1.9)
Vakilian et al., 2012	40/NA	NA	75.6 81.6	NTR; 10 (25) IR; 30 (75)	2.92	postop residual vol on MRI <0.01 cm ³ postop residual vol on MRI >0.01 cm ³	0 (0)	3 (10)	5 (16.7)	2 (18.2)
Carlson et al., 2012	59/350	19 TL, 40 RS	42	NTR; 32 (54.2) STR; 27 (45.8)	NA	small tumor remnant <5 x 5 x 2 mm >5 x 5 x 2 mm	1 (3.1) 6 (22.2)	NA	NA	NA
Godefroy et al., 2009	37/51 large VSs	37 TL	49	NTR/IPR; 29 (78.4) STR; 8 (21.6)	1.46 2.08	<5% of tumor left in situ >5% of tumor left in situ	1 (3.5) 2 (25)	NA	2	NA
Freeman et al., 2007	171/1083	132 TL, 36 RS, 3 MCF	96 156	NTR; 128 (74.9) STR; 43 (25.1)	NA	tiny fragment of the tumor capsule left behind, usually on the FN tumor remnant more than a few mm in size left behind	2 (1.6) 8 (18.6)	4 (9.3)	4 (9.3)	2 (1.6)
Bloch et al., 2004	79/NA	57 TL, 17 RS, 5 MCF	60	NTR; 50 (63.3) STR; 29 (36.7)	2.40 3.10	tumor remnants <25mm ² & 2 mm thick anything larger than NTR	1 (3) 6 (31.6)	2 (10.5)	4 (21.1)	1 (3)
El-Kashlan et al., 2000	39/128	27 TL, 12 SO	74.4	NTR; 16 (41) STR; 23 (59)	2.61	>95% of tumor removed <95% of tumor removed	0 (0) 17 (73.9)	NA	8 (34.8)	2 (8.7)
present series	111/2190	111 TL	45.4	NTR; 73 (65.76) STR; 38 (34.23)	2.90 3.22	<2% of the tumor or tumor capsule is left behind during surgery as evident from the surgeon's subjective observation & if 1) it is manifest or 2) absent on 6-mo postop MRI 2-5% of the tumor left behind during surgery as noted by the surgeon & evident on 6 mos postop MRI	0 (0) 7 (18.4)	1 (2.6)	3 (7.9)	3 (7.9)

* IR = incomplete resection; MCF = middle cranial fossa; NA = not available; RS = retrosigmoid; SO = suboccipital; TL = translabrynthine.
 † In the studies by Vakilian et al. and Freeman et al., follow-up is reported as the median. In all other studies, follow-up is reported as the mean.
 ‡ Reported as the number of patients (%).

The behavior of residual tumors after incomplete excision of VS

Although it is more likely that cystic tumors may only undergo incomplete excision, there is no evidence in the literature to indicate that cystic tumors are more prone to regrowth than solid VSs. In our study, 62 incomplete resections (55.86%) included cystic VSs. However, only 1 (1.6%) of them showed regrowth that was a cystic VS.

Other Factors Influencing Regrowth

There could be other factors influencing tumor regrowth. In general, tumor regrowth after surgery is influenced by the cellularity and vascularity of the tumor itself.¹⁵ It has been shown that vascularization is derived from tumor angiogenesis when the VS is larger than 20 mm.²² Another factor that may influence regrowth is the fact that VS growth is slower in elderly patients.^{1,26,33} One research group studied the growth behavior of 50 untreated VSs in elderly patients and found measurable tumor growth (0.005–1.24 cm/year) in 50% of those cases and significant tumor growth (> 0.2 cm/year) in 20%. The authors stressed that conservative management should be continued in elderly patients with asymptomatic tumors.²⁶ In contrast, a recent study of patients with VSs managed conservatively demonstrated no significant association between tumor growth rate and age.⁴

Interval for Tumor Recurrence and Implications

It has been reported that after initial surgery, most residual tumors appear to have a quiescent period with no evidence of growth on follow-up imaging studies.¹²

Previous studies have reported a mean interval between surgery and regrowth of 32–43 months with a range between 7.2 and 108 months.^{8,10,12,17} Our study is consistent with other studies with a mean interval between surgery and regrowth of 41 months (range 12–73 months). This implies that patients with incomplete resections must be subjected to follow-up MRI for a period of at least 7–10 years with a peak index of suspicion at around 3 years for regrowth. In incomplete resections, it is our policy to obtain a baseline MRI study at the 3rd postoperative month and repeat imaging every year for 7–10 years postoperatively or as indicated clinically.

Facial Nerve Outcome After Incomplete Excisions

The facial nerve outcome of various studies of incomplete VS excisions is compared in Table 8. In NTR, good facial nerve outcomes (HB Grades I and II) have been reported to be between 51% and 84% and in STR, in the range of 55% and 100%. We have had good facial nerve outcomes in 47.4% of patients undergoing NTR and in 49.3% of the patients undergoing STR. The lower percentages of good facial nerve function postoperatively in our series could be attributed to the fact that, as in all our earlier reports,^{6,13,30} we prefer to err on the side of the worse grade in cases in which the HB grades were between II and III. Table 7 also points to the fact that the tumors in our series were larger than those in all other series as measured by the mean tumor diameter, which could also be a factor affecting facial nerve outcome. In

TABLE 8: Summary of facial outcomes after NTR and STR

Authors & Year	No. of IRs in Study/Total No. of VSs Undergoing Op	No. of Approaches & Type	Follow-Up (in mos) [*]	Extent of Resection; No. (%)	Average Tumor Size (cm)	Patients w/ Residuals at 1 Yr		
						HB I–II	HB III	HB IV–VI
Martin et al., 2012	65/229	54 TL, 11 RS	66	NTR; 54 (81.8) STR; 11 (16.7)	NA	~55%	~28% (III–IV)	
Vakilian et al., 2012	40/NA	NA	75.6 81.6	NTR; 10 (25) IR; 30 (75)	2.92	NA		
Carlson et al., 2012	59/350	19 TL, 40 RS	42	NTR; 32 (54.2) STR; 27 (45.8)	NA	NA		
Bloch et al., 2011	169/624	NA: TL, RS, MCF	37	NTR; 76 (45) STR; 93 (55)	NA	39 (51.3%) 51 (54.8%)	37 (48.7%) 42 (45.2%)	
Godefroy et al., 2009	37/51 large VSs	37 TL	49	NTR/PR; 29 (78.4) STR; 8 (21.6)	1.46 2.08	22 (75.9%) 8 (100%)	7 (24.1%, III–IV)	0 (V–VI) 0
Freeman et al., 2007	171/1083	132 TL, 36 RS, 3 MCF	96 156	NTR; 128 (74.9) STR; 43 (25.1)	NA	NA		
Bloch et al., 2004	79/NA	57 TL, 17 RS, 5 MCF	60	50 (63.35) STR; 29 (36.7)	2.40 3.10	NA NA	NA NA	NA NA
El-Kashlan et al., 2000	39/128	27 TL, 12 SO	74.4	NTR; 16 (41) STR; 23 (59)	2.61	34	0	5
present series [†]	105/2190	105 TL (105)	45.4	NTR; 67 (63.8) STR; 38 (36.2)	2.90 3.22	33 (49.3%) 18 (47.4%)	24 (35.8%) 10 (26.3%)	10 (14.9%) 10 (26.3%)

* In the studies by Vakilian et al. and Freeman et al., follow-up is reported as the median. In all other studies, follow-up is reported as the mean.

† Six patients with preoperative facial nerve paralysis were excluded from facial nerve function analysis.

their study, Bloch et al.⁹ proved that tumor size is one of the main predictors of facial nerve outcomes in VS. As the tumor grows, the facial nerve is under tension, which increases the likelihood of stretch injury and poor vascularization may explain the high rate of facial palsy seen in patients with large tumors. Falcioni et al.¹³ pointed out that the results of the facial nerve for VSs larger than 3 cm were not satisfactory in a high percentage of their cases; in fact, in this group of patients, 20.6% had HB Grades IV–VI 1 year after surgery, even in cases in which there was anatomical preservation of the nerve.

Management Algorithm

Treatment options for residual tumor regrowth are wait-and-rescan, SRS, or revision surgery. The enlarged translabyrinthine approach in VS surgery has the advantages of a low rate of morbidity and a short hospital stay, and in our opinion this is the best approach for the removal of large VSs.^{3,31} Our policy for incomplete resections is to try to achieve NTR in as many cases as possible and proceed to an STR only in the remaining cases. All patients undergo follow-up for 7–10 years. In partial resections, we prefer to perform a staged surgery and achieve a GTR if possible or at least an NTR or STR. Based on this we propose the algorithm shown in Fig. 3. The mean age of the patients who underwent NTR or STR in our series is 62 years. Eight patients (7.2%) were younger than 40 years, 29 (26.1%) were between 40 and 60 years, and 74 (66.67%) of the patients were older than 60 years of age. Of the 8 patients younger than 40 years, 6 had involvement of the

brainstem or important vessels and 2 had involvement of the facial nerve. Seven patients (87.5%) underwent NTR and 1 (12.5%) underwent STR. This reflects our policy to try to achieve GTR in all young patients whenever possible and if not, at least an NTR. Our experience shows that GTR also can lead to recurrences in a very small percentage of cases.² The algorithm incorporates our management policy in such a scenario. In elderly patients, despite the fact that complete removal is the main target of the surgery, adoption of NTR or STR in selected cases can decrease neurovascular injury, improve postoperative facial nerve results, and reduce the duration of surgery.²⁷ In case of a regrowth following such a scenario, SRS or Gamma Knife surgery (GKS) is preferable.

Stereotactic radiosurgery is a useful tool in the management of residual tumors. There have been encouraging reports wherein large VSs have been managed by planned STR followed by SRS.³⁶ Preservation of facial nerve function is reportedly good following SRS.³⁶ Indications and protocols for SRS are still evolving, and more reports are likely to emerge in the future that will increase the role for SRS. However, a drawback is that of malignant transformation after SRS and although this has not been proven in a large study, this could lie between 1 in 1000 and 3 in 200,000 treated patients.^{16,24} We prefer to apply SRS in specific situations such as in elderly patients with residual tumors, patients with comorbid conditions, or in patients with slow-growing residual tumors after NTR or STR. A comparison between surgery and SRS for residual tumors is beyond the scope of this article.

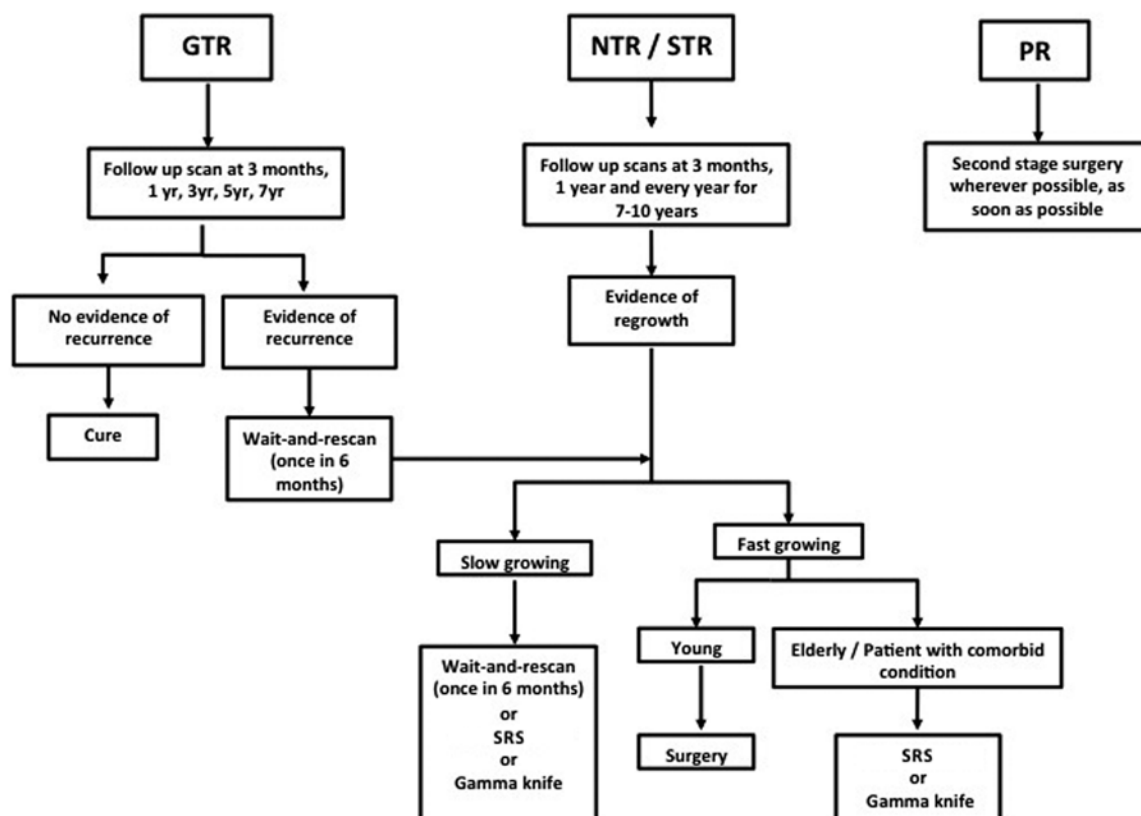


Fig. 3. Algorithm for management of VS in complete and incomplete resections.

Conclusions

The decision to leave behind tumor attached to the facial nerve in an attempt to save the nerve can be justified if the following 2 factors can be proved: 1) that the incidence and the rate of tumor regrowth is acceptably low and 2) if there is a significant benefit in terms of postoperative facial nerve function preservation. Our report and a review of literature have shown that this is indeed the case and hence there is undoubtedly merit in the concept of NTR and STR for preservation of important neurovasculature, especially the facial nerve. On the basis of this we propose an algorithm for the management of patients with incomplete excisions of VSs. Patients with incomplete excisions must be subjected to follow-up MRI for a period of at least 7–10 years. Tumor regrowth is likely in solid tumors. When compared with STR, NTR through an enlarged translabyrinthine approach has shown to have a lower rate of regrowth of residual tumor, while having almost the same result in terms of facial nerve function.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Yin. Acquisition of data: Chen, Di Lella, Piccirillo. Drafting the article: Chen, Prasad, Medina. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Yin. Study supervision: Yin, Sanna.

References

1. Aguiar PH, Tatagiba M, Dankoweit-Timpe E, Matthies C, Samii M, Ostertag H: Proliferative activity of acoustic neuromas without neurofibromatosis determined by monoclonal antibody MIB 1. *Acta Neurochir (Wien)* **134**:35–39, 1995
2. Ahmad RA, Sivalingam S, Topsakal V, Russo A, Taibah A, Sanna M: Rate of recurrent vestibular schwannoma after total removal via different surgical approaches. *Ann Otol Rhinol Laryngol* **121**:156–161, 2012
3. Angeli RD, Piccirillo E, Di Trapani G, Sequino G, Taibah A, Sanna M: Enlarged translabyrinthine approach with transapical extension in the management of giant vestibular schwannomas: personal experience and review of literature. *Otol Neurotol* **32**:125–131, 2011
4. Bakkouri WE, Kania RE, Guichard JP, Lot G, Herman P, Huy PT: Conservative management of 386 cases of unilateral vestibular schwannoma: tumor growth and consequences for treatment. Clinical article. *J Neurosurg* **110**:662–669, 2009
5. Bedavanija A, Brieger J, Lehr HA, Maurer J, Mann WJ: Association of proliferative activity and size in acoustic neuroma: implications for timing of surgery. *J Neurosurg* **98**:807–811, 2003
6. Ben Ammar M, Piccirillo E, Topsakal V, Taibah A, Sanna M: Surgical results and technical refinements in translabyrinthine excision of vestibular schwannomas: the Gruppo Otológico experience. *Neurosurgery* **70**:1481–1491, 2012
7. Bennett ML, Jackson CG, Kaufmann R, Warren F: Postoperative imaging of vestibular schwannomas. *Otolaryngol Head Neck Surg* **138**:667–671, 2008
8. Bloch DC, Oghalai JS, Jackler RK, Osofsky M, Pitts LH: The fate of the tumor remnant after less-than-complete acoustic neuroma resection. *Otolaryngol Head Neck Surg* **130**:104–112, 2004
9. Bloch O, Sughrue ME, Kaur R, Kane AJ, Rutkowski MJ, Kaur G, et al: Factors associated with preservation of facial nerve function after surgical resection of vestibular schwannoma. *J Neurooncol* **102**:281–286, 2011
10. Carlson ML, Van Abel KM, Driscoll CL, Neff BA, Beatty CW, Lane JJ, et al: Magnetic resonance imaging surveillance following vestibular schwannoma resection. *Laryngoscope* **122**:378–388, 2012
11. Charabi S, Tos M, Thomsen J, Charabi B, Mantoni M: Vestibular schwannoma growth: the continuing controversy. *Laryngoscope* **110**:1720–1725, 2000
12. El-Kashlan HK, Zeitoun H, Arts HA, Hoff JT, Telian SA: Recurrence of acoustic neuroma after incomplete resection. *Am J Otol* **21**:389–392, 2000
13. Falcioni M, Fois P, Taibah A, Sanna M: Facial nerve function after vestibular schwannoma surgery. Clinical article. *J Neurosurg* **115**:820–826, 2011
14. Freeman SR, Ramsden RT, Saeed SR, Alzoubi FQ, Simo R, Rutherford SA, et al: Revision surgery for residual or recurrent vestibular schwannoma. *Otol Neurotol* **28**:1076–1082, 2007
15. Fukuda M, Oishi M, Hiraishi T, Natsumeda M, Fujii Y: Clinicopathological factors related to regrowth of vestibular schwannoma after incomplete resection. Clinical article. *J Neurosurg* **114**:1224–1231, 2011
16. Ganz JC: Gamma knife radiosurgery and its possible relationship to malignancy: a review. *J Neurosurg* **97** (5 Suppl): 644–652, 2002
17. Godefroy WP, van der Mey AG, de Bruine FT, Hoekstra ER, Malessy MJ: Surgery for large vestibular schwannoma: residual tumor and outcome. *Otol Neurotol* **30**:629–634, 2009
18. Gurgel RK, Theodosopoulos PV, Jackler RK: Subtotal/near-total treatment of vestibular schwannomas. *Curr Opin Otolaryngol Head Neck Surg* **20**:380–384, 2012
19. Herwadker A, Vokurka EA, Evans DG, Ramsden RT, Jackson A: Size and growth rate of sporadic vestibular schwannoma: predictive value of information available at presentation. *Otol Neurotol* **26**:86–92, 2005
20. Hwang SK, Kim DG, Paek SH, Kim CY, Kim MK, Chi JG, et al: Aggressive vestibular schwannomas with postoperative rapid growth: clinicopathological analysis of 15 cases. *Neurosurgery* **51**:1381–1391, 2002
21. Kanzaki J, Tos M, Sanna M, Moffat DA, Monsell EM, Berliner KI: New and modified reporting systems from the consensus meeting on systems for reporting results in vestibular schwannoma. *Otol Neurotol* **24**:642–649, 2003
22. Kasantikul V, Netsky MG, Glasscock ME III, Hays JW: Acoustic neurilemmoma. Clinicopathological study of 103 patients. *J Neurosurg* **52**:28–35, 1980
23. Kemink JL, Langman AW, Niparko JK, Graham MD: Operative management of acoustic neuromas: the priority of neurologic function over complete resection. *Otolaryngol Head Neck Surg* **104**:96–99, 1991
24. Liscak R, Vladyka V, Urgosik D, Simonova G, Vymazal J: Repeated treatment of vestibular schwannomas after gamma knife radiosurgery. *Acta Neurochir (Wien)* **151**:317–324, 2009
25. Martin TP, Fox H, Ho EC, Holder R, Walsh R, Irving RM: Facial nerve outcomes in functional vestibular schwannoma surgery: less than total tumour excision significantly improves results. *J Laryngol Otol* **126**:120–124, 2012
26. Nedzelski JM, Canter RJ, Kassel EE, Rowed DW, Tator CH: Is no treatment good treatment in the management of acoustic neuromas in the elderly? *Laryngoscope* **96**:825–829, 1986
27. Nuseir A, Sequino G, De Donato G, Taibah A, Sanna M: Surgical management of vestibular schwannoma in elderly patients. *Eur Arch Otorhinolaryngol* **269**:17–23, 2012

28. Patni AH, Kartush JM: Staged resection of large acoustic neuromas. **Otolaryngol Head Neck Surg** **132**:11–19, 2005
29. Piccirillo E, Wiet MR, Flanagan S, Dispenza F, Giannuzzi A, Mancini F, et al: Cystic vestibular schwannoma: classification, management, and facial nerve outcomes. **Otol Neurotol** **30**:826–834, 2009
30. Rabelo de Freitas M, Russo A, Sequino G, Piccirillo E, Sanna M: Analysis of hearing preservation and facial nerve function for patients undergoing vestibular schwannoma surgery: the middle cranial fossa approach versus the retrosigmoid approach—personal experience and literature review. **Audiol Neurootol** **17**:71–81, 2012
31. Sanna M, Russo A, Taibah A, Falcioni M, Agarwal M: Enlarged translabyrinthine approach for the management of large and giant acoustic neuromas: a report of 175 consecutive cases. **Ann Otol Rhinol Laryngol** **113**:319–328, 2004
32. Seol HJ, Kim CH, Park CK, Kim CH, Kim DG, Chung YS, et al: Optimal extent of resection in vestibular schwannoma surgery: relationship to recurrence and facial nerve preservation. **Neurol Med Chir (Tokyo)** **46**:176–181, 2006
33. Silverstein H, McDaniel A, Norrell H, Wazen J: Conservative management of acoustic neuroma in the elderly patient. **Laryngoscope** **95**:766–770, 1985
34. Spielmann PM, Sillars H: Assessing the threshold for vestibular schwannoma resection and the behavior of residual tumor. **Otol Neurotol** **34**:935–938, 2013
35. Vakilian S, Souhami L, Melançon D, Zeitouni A: Volumetric measurement of vestibular schwannoma tumour growth following partial resection: predictors for recurrence. **J Neurol Surg B Skull Base** **73**:117–120, 2012
36. van de Langenberg R, Hanssens PE, van Overbeeke JJ, Verheul JB, Nelemans PJ, de Bondt BJ, et al: Management of large vestibular schwannoma. Part I. Planned subtotal resection followed by Gamma Knife surgery: radiological and clinical aspects. Clinical article. **J Neurosurg** **115**:875–884, 2011

Manuscript submitted July 18, 2013.

Accepted February 18, 2014.

Please include this information when citing this paper: published online April 11, 2014; DOI: 10.3171/2014.2.JNS131497.

Address correspondence to: Shankai Yin, M.D., Ph.D., Department of Otolaryngology, Affiliated Sixth People's Hospital, Shanghai Jiao Tong University, 600 Yishan Rd., Shanghai 200233, China. email: yinshankai@china.com.