Residual tumour after vestibular schwannoma surgery

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Abstract

Objective: To evaluate residual tumour occurrence after vestibular schwannoma surgery, based on intra-operative registration and magnetic resonance imaging one year post-operatively.

Methods: Patients undergoing translabyrinthine surgery for vestibular schwannoma in Denmark between 1976 and 2008 were registered in a national database covering 5.5 million inhabitants.

Results: Translabyrinthine surgery was undertaken on 1143 patients. Of these, 978 had total, 140 near-total and 25 subtotal tumour excision, as assessed intra-operatively by the surgeon. One year after surgery, 65 per cent of small tumour remnants and 11 per cent of large tumour remnants were not visible on magnetic resonance imaging. The mean pre-operative size was significantly smaller for totally excised tumours, compared with near-totally and subtotally excised tumours. Revision surgery was performed for 14 patients (1.2 per cent), of whom 2 had received total, 5 near-total and 6 subtotal excisions initially.

Conclusion: Most residual tumours disappear spontaneously, probably due to devascularisation. Few patients with a small residual vestibular schwannoma will require revision surgery or secondary radiotherapy.

Key words: Neuroma, Acoustic; Facial Palsy; Surgical Procedures, Operative; Outcomes Research; Complications

Introduction

Vestibular schwannoma has an incidence which approaches 20 per million per year,[1] and accounts for approximately 8 per cent of intracranial tumours.[2] In Denmark, sporadic unilateral vestibular schwannomas smaller than approximately 20 mm (extrameatally) are followed by yearly magnetic resonance imaging (MRI). If the tumour is cystic, larger than approximately 20 mm or expanding, surgery or radiotherapy is recommended. Patient age, psychology and co-morbidity may influence this management strategy. The aim of surgery is total tumour removal and minimal post-operative morbidity. However, complete tumour removal may increase the risk of facial nerve paresis.[3–6] Consequently, the surgeon may intentionally leave residual tumour tissue behind in order to preserve facial nerve function. Furthermore, fragments of tumour are sometimes left behind due to adherence to the brainstem, cerebellum, blood vessels or other cranial nerves. Based on the surgeon's assessment, the extent of tumour removal may be divided into three groups: total, near-total and subtotal excision.[7–10] 'Subtotal excision' is defined as excision of less than 95 per cent of the original tumour. 'Near-total excision' is defined as excision of more than 95 per cent of the original tumour, while the term 'total excision' is used when the surgeon estimates that the entire tumour has been excised.

The aim of this study was to assess the occurrence of residual vestibular schwannoma intra-operatively and at MRI one year after surgery, as well as the need for revision surgery and the facial nerve function in relation to the extent of tumour removal. In addition, patient age, gender and primary treatment strategy were related to the occurrence of residual tumour.

Materials and methods

Since 1975, all patients with a unilateral cerebellopontine angle tumour resembling a vestibular schwannoma had been registered prospectively in a database at one centre in Denmark (a country of 5.5 million inhabitants). Of the 2008 patients registered between January 1976 and January 2008, 1143 were operated upon via the translabyrinthine approach. Parameters in the vestibular schwannoma database included: age; sex; tumour size; facial nerve function (according to House–Brackmann staging); MRI before and one year after surgery; treatment strategy; and extent of tumour removal, assigned by the surgeon as either total excision, near-total excision (i.e. tiny fragments of tumour capsule, less than a few millimetres, left

behind) or subtotal excision (i.e. remnant larger than a few millimetres).

Residual tumour was retained in 165 patients operated upon using the translabyrinthine approach (14 per cent). Of these 165 patients, 25 (15 per cent) died of causes unrelated to their vestibular schwannoma, before the first follow-up MRI could be performed. Patients treated in the 1970s and 1980s did not receive MRI scanning, even if residual tumour was present, as this imaging modality was not available at that time; these patients underwent MRI scanning when it became available. In 12 patients (7 per cent), MRI was not performed because of emmigration, claustrophobia, or patients declining a follow-up MRI scan performed to exclude tumour growth. Thus, MRI scans taken at least one year after surgery were available for 128 patients (78 per cent of patients with residual tumours) (Figure 1).

The occurrence and amount of residual tumour one year post-operatively were evaluated on 1.5-tesla

FIG. 1

Flow diagram showing the study population. MRI = magnetic resonance imaging

MRI scans using T1-weighted sequences with a slice thickness of 1 mm, with gadolinium enhancement and fat suppression. Subsequently, yearly MRIs were performed in all tumour remnant patients to check for tumour remnant growth.

The indication for revision surgery or radiotherapy depended on tumour remnant growth, subsequent size and patient symptoms. Choice of management strategy was further influenced by age, comorbidity and psychological factors. Until 2002, patients with total tumour excision only received post-operative MRI scanning if they had unexpected symptoms ($n = 891$ patients). After 2002, a routine MRI scan was performed on all patients one year after surgery ($n = 252$ patients).

Fisher's exact test was used to compare subgroups regarding the presence of residual tumour on the follow-up MRI. The chi-square test was used to compare the occurrence and extent of incomplete tumour resection between groups. One-way analysis of variance, with Bonferroni correction for multiple comparisons, was used to compare pre-operative tumour size and age. A p value of less than 0.05 was chosen to indicate statistical significance. All calculations were made using the SPSS version 17.0 software program. The reported tumour sizes represent the largest extrameatal diameter, and do not include the intrameatal part of the tumour.
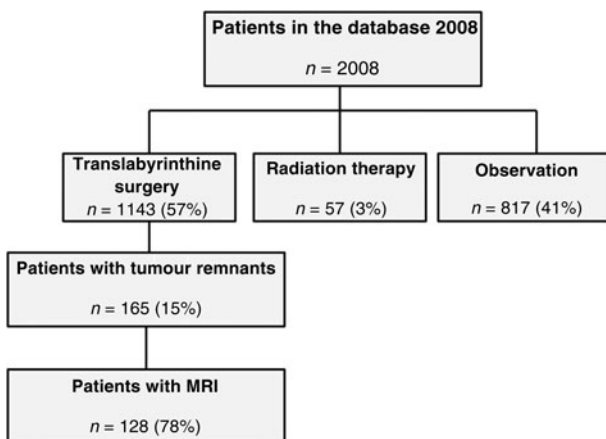
Results

Details of the surgical outcome of the 1143 translabyrinthine cases are provided in Table I.

Total excision was achieved in 978 patients (86 per cent), following a median follow-up period of 19 years for revision surgery (range, 3–34 years). Three of these 978 patients (0.3 per cent) required revision surgery, following the unexpected finding of a tumour remnant at routine MRI scanning one year

TABLE I
TRANSLABYRINTHINE SURGERY FOR VESTIBULAR SCHWANNOMA: PATIENT DATA AND OUTCOMES

Parameter	Tumour excision type			Total	p
	Total	Near-total	Subtotal		
Cases (*n* (%))	978 (86)	140 (12)	25 (2)	1143 (100)	
Pre-op tumour size* (mean (SD); mm)	23 (14)	28 (13)	34 (12)	24 (14)	0.001
Follow-up (med (range); yr)	19 (3–34)	9 (3–31)	10 (3–32)	17 (3–34)	
Revision surgery (*n* (%))	3 (0.3)	5 (3.6)	6 (24)	14 (1.2)	0.001
Radiotherapy (*n* (%))	1 (0.1)	4 (3)	2 (8)	7 (0.6)	
Treatment strategy[†]					0.07
– Immediate surgery (*n* (%))	849 (86)	112 (11)	23 (2)	984 (100)	
– Observation then surgery (*n* (%))	128 (82)	27 (17)	2 (1)	157 (100)	
Sex					0.8
– Female (*n* (%))	550 (86)	76 (12)	13 (2)	639 (100)	
– Male (*n* (%))	428 (85)	64 (13)	12 (2)	504 (100)	
Facial nerve function[‡]					0.13
– HB grade I–II (*n* (%))	687 (71)	83 (62)	15 (65)	785 (69)	
– HB grade III–VI (*n* (%))	284 (29)	50 (38)	8 (35)	342 (31)	
Age (mean (SD); yr)	52 (13)	56 (13)	55 (16)	53 (13)	0.01

*Largest extrameatal diameter. [†]Two patients had primary radiosurgery and subsequent surgery, and are not included in the analysis of treatment stategy. [‡]Data were missing for 16 patients. Pre-op = pre-operative; SD = standard deviation; med = median; yr = years; Revn = revision; HB = House–Brackmann

post-operatively and subsequently growth of that tumour remnant.

Near-total excision was achieved in 140 patients (12 per cent), following a median follow-up period of 9 years for revision surgery (range, 3–31 years), of whom 5 (3.6 per cent) required revision surgery.

Twenty-five patients (2 per cent) had subtotal excision, of whom 6 (24 per cent) required revision surgery (median follow-up time, 10 years; range, 3–32 years). In four cases of subtotal excision, debulking was the primary surgical goal.

There was a significant correlation between the need for revision surgery and the tumour remnant size ($p = 0.001$). The pre-operative tumour size was significantly smaller in patients undergoing total excisions than in those receiving near-total or subtotal excisions (23 mm versus 28 and 34 mm, respectively; $p < 0.001$).

Seven patients (0.6 per cent) received stereotactic radiotherapy because of a growing tumour remnant (Table I). One patient underwent radiotherapy and subsequent revision surgery. One of the 978 total excision patients (0.1 per cent) received radiotherapy for an unexpected, growing remnant. Radiotherapy was received by four patients (3 per cent) with near-total excisions and two patients (8 per cent) with sub-total excisions.

The results of MRI scans taken one year after surgery are given in Table II. Tumours which had undergone near-total excision were not visible in 65 per cent of cases. More surprisingly, 11 per cent of subtotally excised tumours were not visible one year after surgery (for an example, see Figure 2). The proportion of tumour remnants which were between 1 and 10 mm was 20 per cent in the near-total excision group and 17 per cent in the subtotal excision group. One patient (1 per cent) had a tumour remnant larger than 30 mm.

Patients undergoing near-total tumour excision were significantly older than those receiving total tumour excision (mean ages of 56 and 52 years, respectively; $p = 0.01$). The mean age of patients receiving subtotal tumour excision was 55 years. Age had no influence on the occurrence of residual tumour at MRI one year after surgery. Patients requiring revision surgery had a mean age of 43 years, and were significant younger than patients not needing revision surgery ($p = 0.04$).

Gender had no impact on the initial operation result or the occurrence of residual tumour (Table I and III). Six women and eight men required revision surgery.

Of the 1143 patients who underwent surgery, 157 had initially been observed for tumour growth. These 'wait and scan' patients had significantly smaller tumours than the 984 patients who had undergone immediate surgery (mean largest extrameatal diameters of 10 and 27 mm, respectively). Two patients received radiotherapy prior to surgery, and were for that reason

TABLE II
PATIENTS WITH NON-TOTAL TUMOUR EXCISION: RESIDUAL TUMOUR SIZE ONE YEAR POST-OPERATIVELY*

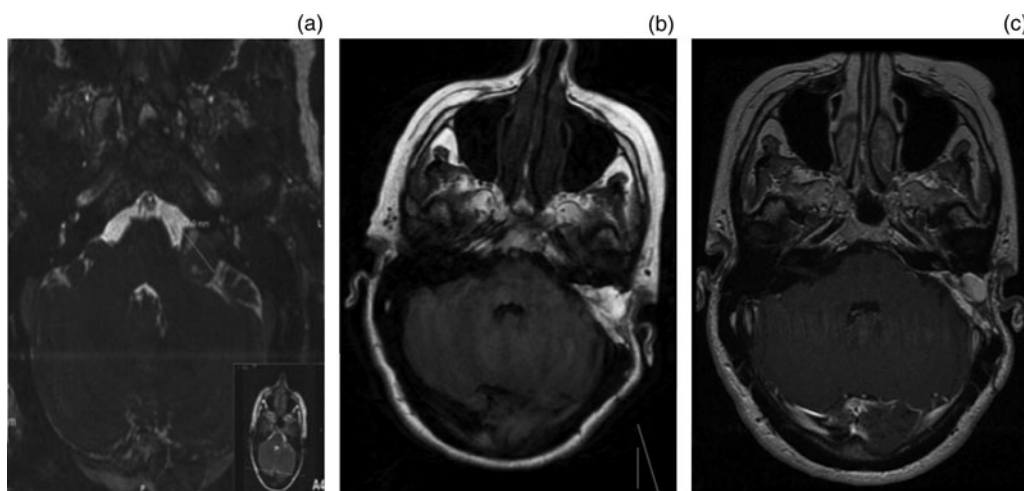| Excision type	Tumour size (pts; n (%))					Total (pts; n (%))
	0 mm	1–10 mm	11–20 mm	21–30 mm	31–40 mm	
Near-total	72 (65)	22 (20)	12 (11)	4 (4)	0 (0)	110 (100)
Subtotal	2 (11)	3 (17)	9 (50)	3 (17)	1 (6)	18 (100)
Sum	74 (58)	25 (20)	21 (16)	7 (6)	1 (1)	128 (100)

*On magnetic resonance imaging scan. Pts = patients

FIG. 2

Magnetic resonance imaging (MRI) scans of a patient with a subtotally excised tumour not visible either one or two years post-operatively. (a) Pre-operative axial MRI scan; (b) axial, T1-weighted, contrast-enhanced MRI scan taken one year post-operatively; (c) axial, T1-weighted, contrast-enhanced MRI taken two years post-operatively.

TABLE III
PATIENTS WITH NON-TOTAL TUMOUR EXCISION: DATA BY ONE-YEAR POST-OPERATIVE RESIDUAL TUMOUR STATUS*

Parameter	Residual tumour?		Total	p
	Yes	No		
Cases (n (%))	54 (42)	74 (58)	128 (100)	
Pre-op tumour size† (mean (SD); mm)	30 (10)	24 (12)	27 (12)	0.006
Age (mean (SD); yr)	55 (15)	53 (12)	54 (13)	0.28
Sex				>0.99
– Female (n (%))	28 (41)	40 (59)	68 (100)	
– Male (n (%))	26 (43)	34 (57)	60 (100)	
Facial nerve function‡				0.4
– HB grade I–II (n (%))	38 (70)	46 (63)	84 (66)	
– HB grade III–VI (n (%))	16 (30)	27 (37)	43 (34)	
Treatment strategy**				0.03
– Immediate surgery (n (%))	48 (48)	53 (52)	101 (100)	
– Observation then surgery (n (%))	5 (19)	21 (81)	26 (100)	

*From magnetic resonance imaging scan. †Largest extrameatal diameter. ‡Facial nerve function data were missing for one patient. **One patient had primary radiotherapy and subsequent surgery and was thus excluded. Pre-op = pre-operative; SD = standard deviation; yr = years; HB = House–Brackmann

excluded from the analysis of treatment strategy. In the 'wait and scan' group, subtotal excision was seldom performed, but near-total excision was more frequent than in the immediate surgery group. Compared with the immediate surgery group, a significantly smaller proportion of the 'wait and scan' group had tumour remnants identified on follow-up MRI scans (48 versus 19 per cent, respectively; p = 0.03).

Facial nerve function one year after surgery, according to the House–Brackmann grading system, is given in Table IV. For statistical purposes, facial nerve function outcome was divided into good (i.e. House–Brackmann grade I–II) or poor (House–Brackmann grade III–VI). There were no statistically significant differences in facial nerve function between patients undergoing total, near-total or subtotal tumour excision (good facial nerve outcomes were seen in 71, 62 and 65 per cent, respectively) (p = 0.13). There was also no statistically significant difference in facial nerve function between patients with and without residual tumour on follow-up MRI (p = 0.17).

As described above, revision surgery was performed when growth of a tumour remnant was observed at the yearly follow-up MRIs performed in the patients with

TABLE IV
FACIAL NERVE FUNCTION ONE YEAR POST-OPERATIVELY, BY TUMOUR EXCISION TYPE*

HB grade	Excision type (pts; n (%))			Total (pts; n (%))
	Total	Near-total	Subtotal	
I	548 (56)	57 (43)	9 (39)	614 (55)
II	139 (14)	26 (20)	6 (26)	171 (15)
III	83 (9)	21 (16)	2 (9)	106 (9)
IV	51 (5)	10 (8)	3 (13)	64 (6)
V	36 (4)	9 (7)	1 (4)	46 (4)
VI	114 (12)	10 (8)	2 (9)	126 (11)
Total	971 (100)	133 (100)	23 (100)	1127 (100)

*Data were missing for 16 patients. HB = House–Brackmann; pts = patients

incomplete tumour removal. As a case example, magnetic resonance images from a patient requiring revision surgery are shown in Figure 3.

Discussion

To date, the present study is the largest case series investigating residual tumour after translabyrinthine resection of vestibular schwannoma.

The study found that 58 per cent of all tumour remnants were not visible on follow-up MRI one year after surgery. Surprisingly, 11 per cent of subtotally excised tumours were likewise not visible on the follow-up MRI. Other studies have found similar regression in near-totally excised tumours[8,11] but not in sub-totally excised tumours. A possible explanation for the observed tumour disappearance may be post-operative tumour necrosis due to devascularisation, as a result of disruption of tumour feeding vessels during surgery. Studies of staged tumour resections have found that residual tumour remnants are relatively avascular.[12] Vascular endothelial growth factor is a potent mediator of angiogenesis; since this factor is related to vestibular schwannoma growth,[13] it may help explain why some tumour remnants grow and others do not. Another possible explanation is detection limitations on MRI scans with contrast enhancement, even when employing 1-mm slices. Persistent, non-specific radiological enhancement within the post-operative field is common and this makes the diagnosis of tumour recurrence challenging. Nodular enhancement on the initial post-operative MRI increases the risk of future recurrence, compared with linear enhancement.[14]

The outcome of tumour remnants is controversial. The reported proportion of cases with regrowth requiring revision surgery varies between 15 and 56 per cent,[4–6,10,15–19] considerably larger percentages than in the present series, in which the need for revision surgery was very small (1.2 per cent). A study by Carlson et al.[14] of MRI surveillance following
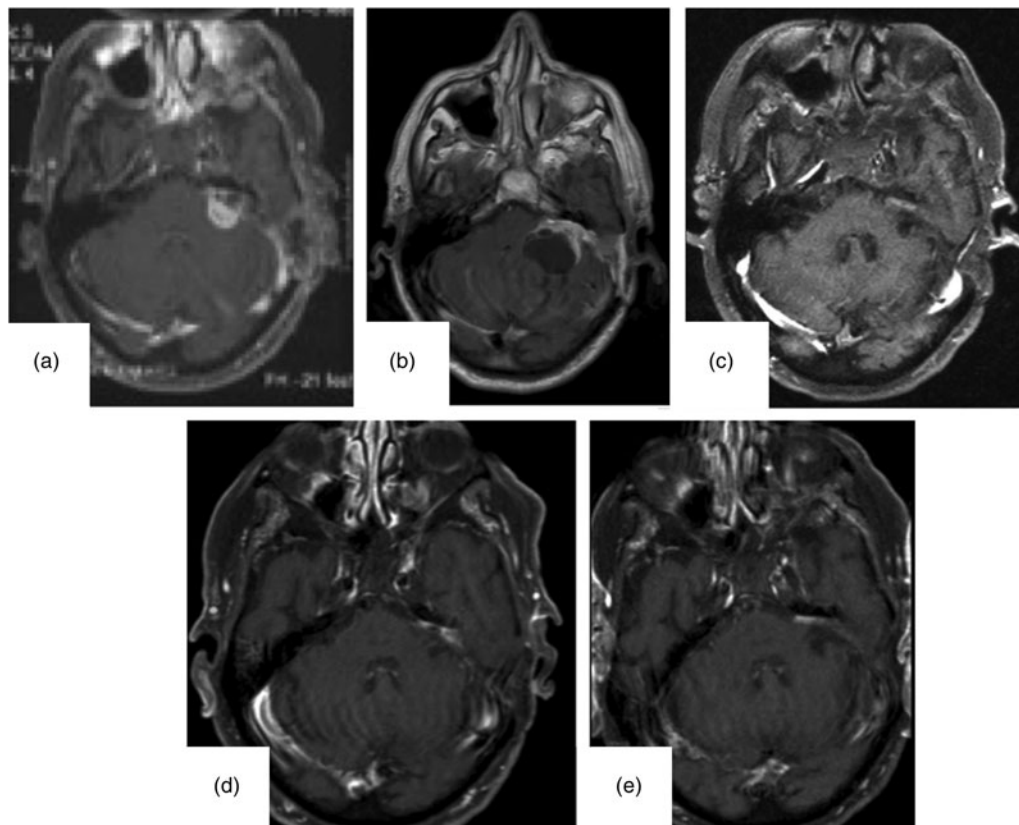
FIG. 3

Magnetic resonance imaging (MRI) scans for a 74-year-old patient with a 38 mm vestibular schwannoma operated upon without complications, achieving near-total excision (according to the surgeon). (a) Axial MRI taken one year post-operatively showing an 18-mm remnant. (b) Axial MRI taken two years post-operatively showing cystic tumour growth to 36 mm; the patient had gait disturbance and left hemi-paresis, and underwent repeated surgery. (c) Axial MRI taken one year after re-operation; subsequently, the patient was observed for growth of the tumour remnant. (d) Axial MRI taken two years after re-operation, showing no change. (e) Axial MRI taken three years after re-operation, showing no change.

vestibular schwannoma resection found that 12 of 203 patients experienced recurrence at a mean of 3.0 years following surgery. Patients receiving subtotal excision recurred earlier than those receiving total or near-total excision. The present study had a median follow up of 19 years (considering need for revision surgery).

In the current study, the size of the tumour remnant was the most important predictor of the need for revision surgery. We found that 0.3 per cent of patients with total excision, 3.6 per cent with near-total excision and 24 per cent with subtotal excision required revision surgery. Freeman et al.[7] reported revision surgery frequencies of the same order, with revision surgery required in 0.5 per cent of total excision, 1.6 per cent of near-total excision and 26 per cent of subtotal excision patients. El-Kashlan et al.[17] reported a need for revision surgery in 39 per cent of subtotally excised and 6 per cent of near-totally excised vestibular schwannomas.

It has been suggested that female patients have a more aggressive course.[7] Most studies of revision surgery find a higher female to male ratio (1.5 women to 1 man).[7,10] In our study, however, we found a higher proportion of male revision surgery patients. There was no difference between men and women regarding intra-operative and MRI assessment

of tumour removal. A previous study found no correlation with progesterone and oestrogen receptors.[20]

Patients receiving initial observation and subsequent surgery had smaller tumours pre-operatively than patients undergoing immediate surgery without observation. Surprisingly, there were more near-total excisions in the observation plus surgery group, compared with the immediate surgery group, although the pre-operative tumour size was smaller in the former group. One possible explanation is that most patients in the observation plus surgery group were operated upon after approximately 1990, when the strategy of initial observation for smaller tumours was introduced, and when there was increasing awareness of the feasibility of retaining residual tumour tissue.

There was a non-statistically significant trend towards better facial nerve function in patients undergoing total tumour excision compared with those undergoing near-total or subtotal excision. This was probably because, in patients for whom near-total or subtotal excisions were chosen, tumours were more adherent to a relatively thinner or more distended facial nerve. This hypothesis is supported by the fact that the pre-operative tumour size was larger in near-total and subtotal excision patients, compared with

total excision patients (27 and 37 mm versus 23 mm, respectively; $p < 0.001$).

- **At surgery, residual vestibular schwannoma may intentionally be left to preserve facial nerve function or prevent complications**
- **Most residual tumour remnants disappear spontaneously, probably due to devascularisation**
- **Few patients with a small tumour remnant will require revision surgery**
- **Tumour remnant size is the most important predictor of revision surgery**

On the whole, our study's facial nerve function results were comparable to those of other authors. Falcioni et al.[21] found a lower prevalence of good facial nerve function (i.e. House–Brackmann grade of I–II): 65 per cent of total resection patients and 50 per cent of partial resection patients.[21] On the other hand, Arriaga and Chen[22] and Gjuric et al.[23] found a somewhat higher prevalence of good facial nerve function; however, the tumour sizes in their study population were smaller.

Conclusion

Based on follow-up MRI scans one year after translabyrinthine surgery for vestibular schwannoma, we conclude that a large number of residual tumours disappear spontaneously, probably due to devascularisation. In this study, very few patients with residual tumour required revision surgery. The size of the tumour remnant is the most important predictor of the need for revision surgery.

References

1 Stangerup SE, Tos M, Thomsen J, Caye-Thomasen P. True incidence of vestibular schwannoma? *Neurosurgery* 2010;**67**: 1335–40
2 Lalwani AK. *Current Diagnosis and Treatment in Otolaryngology Head and Neck Surgery*, 2nd edn. New York: McGraw Hill, 2008;765–772
3 Arriaga MA, Luxford WM, Atkins JS, Kwartler JA. Predicting long-term facial nerve outcome after acoustic neuroma surgery. *Otolaryngol Head Neck Surg* 1993;**108**:220–4
4 Lownie SP, Drake CG. Radical intracapsular removal of acoustic neurinomas. Long-term follow-up review of 11 patients. *J Neurosurg* 1991;**74**:422–5
5 Arlt F, Trantakis C, Seifert V, Bootz F, Strauss G, Meixensberger J. Recurrence rate, time to progression and facial nerve function in microsurgery of vestibular schwannoma. *Neurol Res* 2011;**33**:1032–7
6 Martin TPC, Fox H, Ho E-C, 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* 2012;**126**:120–4
7 Freeman SRM, Ramsden RT, Saeed SR, Alzoubi FQ, Simo R, Rutherford SA et al. Revision surgery for residual or recurrent vestibular schwannoma. *Otol Neurotol* 2007;**28**:1076–82
8 Godefroy WP, van der Mey AG, de Bruine FT, Hoekstra ER, Malessy JA. Surgery for large vestibular schwannoma: residual tumor and outcome. *Otol Neurotol* 2009;**30**:629–34
9 Kanzaki J, Tos M, Sanna M, Moffat D. New and modified reporting systems from the consensus meeting on systems for reporting results in vestibular schwannoma. *Otol Neurotol* 2003;**24**:642–8
10 Sanna M, Falcioni M, Taibah A, Donato GD, Russo A, Piccirillo E. Treatment of residual vestibular schwannoma. *Otol Neurotol* 2002;**23**:980–7
11 Lye RH, Pace-Balzan A, Ramsden RT, Gillespie JE, Dutton JM. The fate of tumour rests following removal of acoustic neuromas: an MRI Gd-DTPA study. *Br J Neurosurg* 1992;**6**:195–201
12 Donzelli R, Motta G, Cavallo LM, Maiuri F, De Divitiis E. One-stage removal of residual intracanalicular acoustic neuroma and hemihypoglossal-intratemporal facial nerve anastomosis: technical note. *Neurosurgery* 2003;**53**:1444–7
13 Cayé-Thomasen P, Werther K, Nalla A, Bøg-Hansen TC, Nielsen HJ, Stangerup S-E et al. VEGF and VEGF receptor-1 concentration in vestibular schwannoma homogenates correlates to tumor growth rate. *Otol Neurotol* 2005;**26**:98–101
14 Carlson ML, Van Abel KM, Driscoll CL, Neff BA, Beatty CW, Lane JI et al. Magnetic resonance imaging surveillance following vestibular schwannoma resection. *Laryngoscope* 2012;**122**: 378–88
15 Beatty CW, Ebersold MJ, Harner SG. Residual and recurrent acoustic neuromas. *Laryngoscope* 1987;**97**:1168–71
16 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* 2004;**130**: 104–12
17 El-Kashlan HK, Zeitoun H, Arts HA, Hoff JT, Telian SA. Recurrence of acoustic neuroma after incomplete resection. *Am J Otol* 2000;**21**:389–92
18 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* 1991;**104**:96–9
19 Silverstein H, Rosenberg SI, Flanzer JM, Wannamaker HH, Seidman MD. An algorithm for the management of acoustic neuromas regarding age, hearing, tumor size, and symptoms. *Otolaryngol Head Neck Surg* 1993;**108**:1–10
20 Curley JW, Ramsden RT, Howell A, Healy K, Lye RH. Oestrogen and progesterone receptors in acoustic neuroma. *J Laryngol Otol* 1990;**104**:865–7
21 Falcioni M, Fois P, Taibah A, Sanna M. Facial nerve function after vestibular schwannoma surgery. *J Neurosurg* 2011;**115**: 820–6
22 Arriaga MA, Chen DA. Facial function in hearing preservation acoustic neuroma surgery. *Arch Otolaryngol Head Neck Surg* 2001;**127**:543–6
23 Gjuric M, Wigand ME, Wolf SR. Enlarged middle fossa vestibular schwannoma surgery: experience with 735 cases. *Otol Neurotol* 2001;**22**:223–30

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