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Treatment options for acoustic neuroma

Wendy L. Schneider and David Hailey

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This Health Technology Assessment Report has been prepared on the basis of available information of which the Foundation is aware from public literature and expert opinion and attempts to be current to the date of publication. It has been externally reviewed. Additional information and comments relative to the report are welcome and should be sent to:

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Contents

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Summary

- Available treatment options for persons with acoustic neuroma are microsurgery, stereotactic radiosurgery (SRS) and watchful waiting.
- Microsurgery is the primary treatment option for acoustic neuroma. Surgical techniques continue to evolve.
- Surgical removal of these tumours requires considerable expertise to maintain low morbidity and mortality rates.
- There is evidence, from methodologically weak studies, that SRS is efficacious in treatment of acoustic neuroma in suitably selected individuals.
- Evidence on the comparative effectiveness of SRS and microsurgery remains limited.
- Both SRS and microsurgery have associated short-term and long-term complications. Unlike SRS, microsurgery will require post-operative hospital stay and subsequent convalescence.
- There is no evidence of any difference in effectiveness between the LINAC and Gamma Knife approaches to SRS.
- The overall performance of SRS will depend on the expertise of the patient management team and the quality of imaging and treatment planning, rather than the method used to deliver radiation.
- Watchful waiting is preferred for older persons with slow growing tumours.
- Regardless of the modality of treatment, it is imperative that patients be referred to centres of excellence. These would be centres that treat large numbers of patients with acoustic neuroma.

Background

In 1998, the AHFMR issued a report on stereotactic radiosurgery (SRS) which drew together available information on this technology, including cost implications for the province (34). The present health technology assessment report has been prepared following a request by Alberta Health and Wellness for additional information on the use of SRS in the treatment of acoustic neuroma, one of the applications which was considered in the earlier publication.

Two main issues are considered here. The first is the place and role of SRS in management of acoustic neuroma, in comparison with neurosurgical techniques. The second is the comparative performance of the two most commonly available forms of SRS, the modified linear accelerator (LINAC) and the Gamma Knife® (GK), a device that makes use of radiation from cobalt-60 sources. Matters related to cost have not been addressed in detail.

Stereotactic radiosurgery has been considered by several health technology assessment agencies. The earlier AHFMR report drew on these previous analyses, included additional information from the recent literature and considered cost and other details that were applicable to Alberta. In this report, the earlier HTA literature has again been used as the base source and more recent information related to treatment of acoustic neuroma with SRS has been obtained from the literature. Details of the search methodology are shown in Appendix A.

Given the importance of the first issue identified above, further attention has been given to recent literature on microsurgery for acoustic neuroma. A comprehensive survey of neurosurgical techniques has not been attempted. The more significant publications from the last three years have been reviewed to provide some further background and context for the radiosurgical approach.

Definition and treatment of acoustic neuroma

An acoustic neuroma (also known as a vestibular schwannoma) is a benign tumour that typically arises from the inferior vestibular nerve in the internal auditory meatus and cerebellopontine angle. Symptoms include hearing loss, balance disturbances, pain, headache and tinnitus (5, 29, 38, 40).

Neurofibromatosis (NF) is a genetic disorder that affects cell growth of neural tissues. In NF-Type 2 (NF-2), most of the tumour forms in the 8th cranial nerve (acoustic neuroma) but may be present in other intracranial and intraspinal locations. These are treated by use of microsurgical techniques in an attempt to remove the tumour(s) and preserve hearing. This disorder affects about 1 in 50,000 people (37, 38).

An acoustic neuroma is composed of two distinct types of tissue, Antoni A and Antoni B, depending on cellular morphology and spatial distribution. Understanding the histology of acoustic neuroma tissue is very important in determining tumour regression or progression in CT and MRI studies (42).

Acoustic neuroma usually presents with a progressive unilateral loss of hearing. With microsurgical treatment, complete tumour removal is achieved in more than 95% of cases. Some clinicians use SRS in the treatment of patients with bilateral tumours (NF-2) because of the possibility of preserving residual hearing (11). However, an NF-2 patient who undergoes radiation treatment risks scarring and damage to the cochlear nucleus, so that implantation of an auditory brainstem implant is not feasible. Surgical removal of the tumour with subsequent implantation may retain or restore hearing (House, personal communication).

Description and role of stereotactic radiosurgery

Stereotactic radiosurgery is a type of radiotherapy. Ionizing radiation is precisely targeted using computer-aided imaging such as computerized tomography (CT) and magnetic resonance imaging (MRI), and applied to an intracranial lesion (3, 11, 34). The alternative management options are microsurgery and watchful waiting.

The two most frequently used types of devices for radiosurgery are units with multiple cobalt-60 sources and those based on a linear accelerator. In the former, highly collimated beams of radiation from the cobalt sources intersect at the target. In the latter, the source of a highly collimated beam of high-energy photons directed at the target turns through an arc or set of arcs. The accuracy of target localization, the steepness of fall-off of the radiation dose outside the target and the ability to irradiate an irregularly shaped target are all comparable for these two types of devices (35).

Earlier assessments of SRS

There have been several earlier health technology assessments of stereotactic radiosurgery. Table 1 outlines conclusions from several assessments which have considered the effectiveness of LINAC and GK approaches in the treatment of acoustic neuroma (6, 11, 12, 41).

The previous assessment of SRS by AHFMR (34) noted that points made in several of the reports included:

- The quality of the available evidence on SRS effectiveness is limited.
- There is insufficient information to compare the effectiveness of the GK and LINAC approaches.
- Comparison of SRS with other approaches is also limited.

- The GK approach is more expensive than the LINAC.
- Excellent quality assurance is necessary.
- Placement of SRS in specialized centres is essential as to ensure skills maintenance of the radiosurgery team.

Points made on treatment of acoustic neuroma in the summaries in Table 1 include the importance of microsurgery as a treatment option and the need for appropriate selection of patients.

The previous AHFMR report gave some consideration to the treatment of acoustic neuroma. It concluded, on the basis of information from other HTA reports and data from more recent literature, that the role of SRS still does not seem well defined in relation to treatment of this tumour. Microsurgery will remain a major option for patients with this condition (34).

Watchful waiting is the treatment of choice in older patients. Treatment of any kind in this population should only commence upon confirmation of tumour growth on MRI follow-up studies ((4,9), (House, personal communication)).

Table 1: Conclusions on treatment of acoustic neuroma from earlier SRS assessments

Agency	Conclusions
Health Council of the Netherlands (11) October 1994	• SRS should, in general, be viewed at present as an emerging technology that has gone beyond the experimental stage. It is often used as an adjunct to a neurosurgical intervention. • Surgery and microsurgery, as well as conventional external radiotherapy, remain the principal forms of treatment for intracranial disorders. SRS for acoustic neuroma would primarily seem to be useful when microsurgical intervention involves large risks. This may be the case with older patients, patients with bilateral tumours or patients with recurrent tumours after surgery. • There is a preference for SRS in the treatment of patients with bilateral tumours (NF-Type 2) because of the possibility of preserving residual hearing. • For the application of SRS in a routine clinical setting, both the GK and the LINAC can be considered suitable, when looking at the quality and financial aspects. • It is still too early to decide whether SRS is more effective than 'standard' treatment modalities.
Minnesota Health Care Commission, Health Technology Advisory Committee (12) June 1995	• There is insufficient evidence regarding the clinical superiority of GK versus LINAC SRS. • Conventional surgery still indicated in young, healthy patients with acoustic neuroma.
University Health Consortium Technology Assessment Program of the Clinical Practice Advancement Center (41) September 1995	• Surgical resection is the standard therapy for acoustic neuroma. • SRS with a GK or LINAC is a safe alternative treatment for selected patients. Eligible SRS patients include those who are elderly, who have a tumour in a high-risk or inoperable location, those with residual tumour after resection, those with medical comorbidities, and patients who refuse open surgical resection. • Experience with SRS in the treatment of acoustic neuroma suggest that this approach is relatively safe and effective in comparison with surgical resection in selected patients. Additional data from RCTs in larger numbers of cases are required to establish the role of SRS, especially in regard to the use of LINAC versus GK procedures as well as selection criteria for using this approach rather than microsurgery. • GK and LINAC can be used to treat the same indications. Current patterns of practice indicate that the GK is currently used to treat mainly small benign brain tumours and AVMs, whereas the LINAC is used mostly for larger malignant brain tumours. There are no clinically proven differences in outcomes in studies treating similar indications. • Available clinical literature contains no evidence that conclusively shows a difference in the safety and efficacy of SRS performed with a GK versus a LINAC.
ECRI (6) February 1996	• There is no evidence that one SRS method is superior to the other. • SRS for acoustic neuroma provides high rates of short-term tumour control. There are no long-term studies. It is not possible to determine whether SRS prevents tumour recurrence. • Poor study methodology makes it impossible to prove that SRS preserves hearing in the affected ear more often than conventional surgery.

Recent evidence of efficacy and effectiveness of SRS in treatment of acoustic neuroma

Table 2 summarizes 15 recent papers on treatment of acoustic neuroma with SRS that include patient outcomes (7, 8, 14, 16, 19, 21, 24, 25, 27, 29, 32, 39, 42-44). The first six of these were also included in the earlier AHFMR assessment. Outcomes were reported on 1,006 patients who had been treated with SRS, 871 with the GK and 135 with the LINAC.

None of these studies compared the GK and LINAC approaches. Ten of them were observational studies with consecutive clinical series, five were retrospective and the remaining one probably so.

Two papers retrospectively compared SRS with microsurgery (27, 29). That by Roijen et al. used a case control approach with surgical cases from the Netherlands being compared to SRS – treated patients in Sweden. This was primarily an economic study. Clinical and quality of life outcomes from this paper are included in the Table.

Some general points that emerge from these studies include:

- Comparison with alternative treatment (surgery) is made in only two studies.
- The methodological quality of the studies, in terms of the classification of Jovell and Navarro-Rubio (17), is Poor or Poor-Fair.
- While some patients have been followed for a number of years post -SRS, overall follow-up is quite short. This limits the significance of the data on clinical outcomes.
- Nine studies report on tumour control. Control is typically 95% or more, though poorer results were obtained in some series. Control is taken to include tumours that do not increase in size.
- Hearing preservation is discussed in ten papers. The limited information available suggests a steady decrease in hearing preservation over two years following SRS treatment.

It is difficult to make a judgement on the efficacy of SRS in relation to microsurgery (or watchful waiting) because of the absence of comparative studies and variations in the patient populations.

Table 2: SRS in the treatment of acoustic neuroma (vestibular schwannoma)

Authors	Number of patients	Treatment modality	Outcomes	Comments
Pollock et al. Retrospective study ('90-'91) (27) 1995	87 Follow-up: patients in both treatment groups were contacted a minimum of two years after surgery.	Surgery: 40 GK SRS: 47 25-36 Gy contingent upon tumour size and location	Long term results: 31 (78%) patients had Facial Grade** I or II Return to Functional Independence: < 1 month = 12 (30%) ≤ 6 months = 21 (53%) Long term results: 43 (92%) patients had Facial Grade I or II Return to Functional Independence: < 1 month = 35 (75%) ≤ 6 months = 6 (13%)	Fair to poor level of scientific evidence*. "Careful" selection criteria. Outcomes are "facial nerve function (patient's perspective of therapeutic success)" "useful hearing", and "functional independence". As well, there is a "patient's subjective rating of tumour management". Authors question whether hearing preservation should be a goal of acoustic neuroma surgery. Avg acoustic neuroma < 3 cm in size
Hirato et al. (14) 1995	28 3 patients bilateral tumour 6 already deaf when treated Mean follow-up was 16 mo, longest 24 mo.	GK SRS: 25.2 Gy (0) at the centre	69% had lowering of the MRI signal intensity in tumour centre 59% had tumour shrinkage 3 cases of enlarged tumour 2 cases of hydrocephalus Hearing preservation (22 patients evaluated): 85% at 3 mo 80% at 6 mo 75% at 12 mo 60% at 18 mo 50% at 24 mo	Abstract only Authors conclude that low dose GK SRS is effective in suppressing growth of acoustic schwannoma with preservation of hearing. Maximum tumour diameter was 35 mm.
Mendenhall et al. Retrospective study ('88-'94) (24) 1996	56 Follow-up: minimum of one year	LINAC SRS: 10-22.5 Gy, contingent on lesion size and location.	55 patients (98%) achieved local control 13 patients (23%) developed complications 5-year actuarial local control rate was 95% Risk of complication was related to the dose and treatment volume	Abstract only "Local control" is the endpoint defined, therefore, LINAC SRS results cannot be compared to surgical outcomes. Tumour sizes not mentioned.

Table 2: SRS in the treatment of acoustic neuroma (con't)

Authors	Number of patients	Treatment modality	Outcomes	Comments
Forster et al. Clinical series ('86-'89) (8) 1996	27 (29) in 2 series Follow-up: median of 6 y 7 mo,	GK SRS: 25 Gy to periphery (Group 1, 15 patients) 17.5 Gy to periphery (Group 2, 12 patients)	Success endpoint was control of tumour size or shrinkage lack of growth = tumour control 10% decrease in tumour diameter = shrinkage Group 1: tumour control in 12/17 tumours, failure in 5. Group 2: tumour control in 11/12 tumours, failure in 1. Group 1 patients had higher incidence of cranial neuropathy; complete facial palsy in 1 patient, partial weakness in 2 patients and transient in 2 patients. Trigeminal neuropathy developed in 4/14 patients with normal facial sensation. Group 2 showed 1/9 patients had partial loss of facial nerve function and 1/11 patients had transient facial sensory loss. Preservation of useful hearing in 4/11 patients in Group 1 and 5/7 patients in Group 2.	Poor level of scientific evidence. Good patient follow-up. Authors conclude that SRS is an effective alternative treatment for patients with tumours $<$ 3 cm in diameter with negligible mortality and morbidity compared with surgery. Advantages are short hospitalization and maintenance of functional level and employment status after the procedure. However, SRS does not replace microsurgery but should be considered as an alternative. Tumour $\leq$ 3cm.
Varlotto et al. Clinical series (43) 1996	12 4 patients prior surgery Follow-up: 16-44 mo, median of 26.5 mo	LINAC SRS: Fractionated regime – 54 Gy total dose in 27-30 fractions of 1.8 Gy/day.	Endpoint: tumour regression/stabilization. After a median follow-up of 26.5 mo, local control was found in 12 out of 12 lesions; 3 showed tumour regression, the remaining 9 tumour stabilization. One patient developed worsening of pre-existing 5th cranial neuropathy, 1 experienced a decrease in hearing.	Abstract only. Authors concluded that SRS provided excellent local control without new cranial nerve deficits. Results, however, are tentative in nature because of small sample size and short median follow-up.
Ito et al., Retrospective study ('90-'94) (16) 1996	46 consecutive patients Follow-up: $>$3 mo	GK: number of Gy not mentioned in abstract	Endpoints: pure tone audiometry, auditory brain stem response and caloric test. Tumour growth occurred in 2 patients; 7 of 38 patients with preserved hearing of any extent became deaf within 1 y with deterioration rate of 8dB/y. Preserved caloric response was present in 13 patients before treatment and disappeared in 9 patients 4-13 mo after treatment, however their hearing was preserved. Delayed facial palsy and persistent trigeminal neuropathy occurred in 10 and 7 of the 46 patients respectively. Severe facial palsy tended to persist.	Abstract only. Authors conclude that because of the serious facial nerve complications that occurred in some patients, further study to disclose the risk factors for neurological dysfunction would be needed for SRS to become a true, safe alternative to microsurgery.

Table 2: SRS in the treatment of acoustic neuroma (con't)

Authors	Number of patients	Treatment modality	Outcomes	Comments
Flickinger, et al. Retrospective clinical series ('87 to '94) (7) 1996	n=273 (unilateral tumours) Group 1: n=118, CT-guided SRS ('87 to '91) Follow-up: median 47 mo Group 2: n=155, MRI-guided SRS ('91 to '94) Follow-up: median 13 mo Tumour sizes not mentioned. Thirteen patients had complete ipsilateral facial paralysis prior to SRS therefore were excluded in the outcomes analyses for facial neuropathy.	GK Grp 1: median 34 Gy (range: 22 – 50 Gy) maximum tumour dose Grp 2: median 28 Gy (range: 24 – 38 Gy) maximum tumour dose	[Tumour control rate defined as no requirement for surgical intervention; Gardner-Robertson scale used to classify hearing function] Actuarial 7-y clinical tumour control rate for the entire series was 96.4± 2.3%; 7-y radiographic tumour control rate was 91.0± 3.4%. Tumour progression requiring surgery: 3 patients (2 from CT-, 1 from MRI- group) Small amount of growth in 6; 4 had no subsequent growth, 2 showed shrinkage during further follow-up. Tumour shrinkage was documented in 38% (81 out of 211 patients) with follow-up >1 y. Facial neuropathy (temporary or permanent) developed in 36/260; actuarial incidence of 17.2± 2.7% at 3 y (and 7 y). Significantly less neuropathy developed in the MRI-group (7.6%) compared with the CT-group (27.1%). Trigeminal neuropathy in 49/273 patients for a 3-y (and 7-y) actuarial incidence of 22.6%. Incidence significantly less in the MRI- (7.6%) than in the CT- (35.6%) guided group at 3 y. Pain rather than numbness in 4/49 patients. 53/146 patients with pre-operative hearing Class I-IV developed a drop in hearing Class. 38/146 patients deteriorated to Class V. 25/63 patients with pre-operative Class I-II hearing developed loss of serviceable hearing (Class I-II to Class III-V). Deterioration in hearing Class occurred significantly less in the MRI- (32.3%) compared with the CT-group (60.6%) at 3 y. Deterioration to Class V hearing developed significantly less often in the MRI group (14.1%) compared to the CT group (50.9%) at 3 y.	Authors state that MRI-based treatment planning provided greater tumour resolution leading to the use of more isocentres to keep the plan conformal but also appears to have decreased treatment toxicity. However, outcomes in the MRI group require further follow-up before stating definitively that there are no differences in outcomes using CT- or MRI-guided imaging for treatment planning. Many aspects of treatment planning have changed over time, therefore only randomized clinical trials could show with certainty that MRI-planning and lower treatment doses were the most important factors leading to lower toxicity. Poor level of scientific rigour.

Table 2: SRS in the treatment of acoustic neuroma (con't)

Authors	Number of patients	Treatment modality	Outcomes	Comments
Tomasevic et al. Clinical series ('91 to '96) (39) 1998	31 patients with 34 acoustic neuroma Previous microsurgery: 12 of the 34 acoustic neuroma Follow-up: 3 month intervals the 1st y, 6 mo for the 2nd y, and yearly thereafter, for a (0) follow-up of 32.0 mo (range 0 to 65 mo). (0) size: 23.1 mm, (range 10-43 mm)	LINAC SRS: 4 to 20.5 Gy, (0) 20.29 Gy. Dose was reduced to 16 to 18 Gy.	One in 34 acoustic neuroma increased in size on subsequent imaging following SRS. Two patients died unrelated to their acoustic neuroma or SRS. Two patients were lost to follow-up. Three patients had just been treated, therefore follow-up data was not available. At 6 mo following SRS, 26 of 27 displayed non-progression of disease. Twenty two of these 27 patients showed <50% reduction in size following SRS, 3 showed >50% reduction in size and 1 acoustic neuroma was found to disappear upon subsequent neuro-imaging post-SRS. Complications: Following SRS there were complications in 14 of 34 AN cases. They included hearing (9), facial nerve (8), trigeminal nerve (6), disequilibirum (5), tinnitus (1) and hydrocephalus (1). Eight of the treated AN had 1 complication, 5 had 2, and 1 had 4 complications. Complication rate was found to be independent of whether or not the patients had previous microsurgery.	Authors state that the goal of SRS is not eradication of the tumour but control of tumour growth. SRS does not attempt to replace microsurgery as a treatment modality for acoustic neuroma. It should be considered as an alternative treatment option in certain patients. A multi-disciplinary team involving otologists, neurosurgeons and radiation oncologists in order to determine which patients are best suited for SRS, should assess patients. Poor level of scientific evidence.

Table 2: SRS in the treatment of acoustic neuroma (con't)

Authors	Number of patients	Treatment modality	Outcomes	Comments
Sakamoto et al. Clinical series ('91 to '97) (32) 1998	n=24 SRS was the initial treatment in these 24 patients. NF-2: 1 patient Audiological follow-up: 5 to 69 mo, median-22 mo. Tumour size range: 5 to 30 mm, (0) = 15.7 mm	LINAC SRS fractionated therapy: Between '91 and '93, 44 Gy in 22 fractions in 5.5 wks followed by a 4 Gy single boost at tumour centre. Irradiation schedule reduced to 36 Gy, 20 fractions over 5 wks.	Pure tone average (PTA) was measured before and after fractionated SRS. Hearing was judged to be preserved if PTA did not decrease by more than 10 dB at the last follow-up compared to the pre-treatment PTA. Measurements performed on the non-tumour side were used for comparison. Pretreatment: Normal hearing: 3 patients Slight hearing impairment: 9 Moderate hearing impairment: 7 Severe hearing impairment: 5 Post-SRS treatment: 50% of patients showed a change in PTA of less than 10 dB and 79.2% showed a change in PTA of less than 20 dB. One patient who showed gradual impairment in hearing before SRS experienced deafness after SRS treatment. Mean hearing loss at 1, 2, and 3 y after SRS was 8, 11, and 15 dB, respectively. Hearing preservation rate (HPR) for males and females was 62.5% and 43.8%, respectively. Hearing preservation was more likely to occur in cases of sudden hearing loss than for those with gradual hearing loss. HPR was 66.7% and 25.0% for patients with sudden hearing loss and for those with progressive hearing loss, respectively.	Authors state that fractionated therapy resulted in a 96% preservation of PTA of less than 90 dB with a median follow-up of 22 mo for all patients with measurable pretreatment hearing in this study. Results of this study showed that the pretreatment hearing level was predictive of the audiological outcome after fractionated SRS. This study is weak in that the number of patients was too small and the follow-up time was too short. Further study is required to confirm results of fractionated SRS. Poor level of scientific evidence.

Table 2: SRS in the treatment of acoustic neuroma (con't)

Authors	Number of patients	Treatment modality	Outcomes	Comments
Valentino et al. Clinical series ('84 to '93) (42) 1998	24 acoustic neuroma (23 patients) Prior surgery in 7 patients, SRS was the primary treatment in 16 patients. Two patients were operated on after SRS. Treated acoustic neuroma volumes ranged from 1.9 cm^3 to 18.80 cm^3 0 = 6.68 cm^3 Follow-up: 2 to 8 y (0 = 3 y 4 mo)	LINAC: 12 to 45 Gy given in 1 to 5 sessions Pre- and post-SRS imaging included CT/MRI studies	Tumours were classified as solid (15), mixed (7) and cystic (2). From 9 to 12 mo post-SRS, 5 of the 15 solid acoustic neuroma showed a reduced volume ranging from 39% to 100% of the original size. One of these patients underwent surgery. Nine acoustic neuroma of the same type remained stable, while 1 patient with NF-2 presented slightly increased tumour volume 2 years post-SRS and underwent surgery. Both patients with cystic acoustic neuroma showed a reduction in tumour volume of 94% and 58%, 24 and 12 mo post-SRS, respectively. Of the 7 mixed acoustic neuroma, 2 showed a reduction in tumour volume of 82% and 44 % 12 and 3 mo post-SRS, and tumour volume in the other 5 patients remained stable at a CT/MRI follow-up of 24-30 mo. Sixteen of the 22 solid or mixed acoustic neuroma showed early or delayed attenuation changes at CT/MRI enhanced studies, which were associated with a reduction of the tumour volume in 12 patients.	Authors believe that SRS is a most attractive technique for acoustic neuroma but the question of 'if and when' it may be an alternative to microsurgery is debatable. Poor level of scientific rigour. The strength of this study was the long clinical follow-up.

Table 2: SRS in the treatment of acoustic neuroma (con't)

Authors	Number of patients	Treatment modality	Outcomes	Comments
Vermeulen et al. Clinical series ('93 to '97) (44) 1998	n=52 patients (54 acoustic neuroma) Intracanalicular (IC) tumours: 14 Follow-up: 0.1 to 2.7 y (0 1.4 y) One patient treated for residual tumour after a craniotomy. Tumour volume range: 0.2-1.4 cm^3 0 = 0.4 cm^3 Extracanalicular (EC) tumours: 40 Follow-up: 0.1 to 3.3 y (0 1.6 y) Four patients treated for residual tumour after a craniotomy Tumour volume range: 0.3-20.6 cm^3 0 = 4.4 cm^3 Bilateral tumours: 4 patients	GK: 15 or 16 Gy minimum dose, depending on tumour diameter/volume. Pre- and post-SRS imaging included contrast-enhanced MRI	[Local control was defined as no growth or tumour regression on subsequent MRI scan at 6-mo intervals after SRS.] Imaging was available for 12 of the 14 IC and 30 of the 38 EC patients. Two IC and 7 EC patients were treated ≤ 6 mo from the time of this evaluation. One EC patient was lost to follow-up. Decrease or no change in tumour size: 26 EC patients at six mo follow-up. Seventeen of these patients at follow-up ≥ 1 y revealing 14/17 tumour control. 12 IC patients at six mo follow-up, 8/8 at ≥ 1 y. Neurological side effects: (more common in IC patients) Acute and new facial neuropathy symptoms developed in 6/14 IC patients, and 2/40 (acute) and 5/40 (new) EC patients. New and acute symptoms of vertigo were observed in 4/14 IC and 0/40 EC patients Subjective post-SRS diminished hearing was observed in 9/40 EC and 2/14 IC patients.	Authors have recently begun a protocol that reduces the dose for IC tumours to 12 Gy in an attempt to reduce the toxicity even further. Most side effects with treatment of the IC tumours as with the EC version, have resolved over time. The IC patient group requires special dose considerations until further toxicity studies have been obtained and reviewed. Poor level of scientific rigour (very small number of IC patients).

Table 2: SRS in the treatment of acoustic neuroma (con't)

Authors	Number of patients	Treatment modality	Outcomes	Comments
Kwon et al. Clinical series ('90 to '96) (21) 1998	n=88 Follow-up MRI available for 63 patients. - Nine NF-2 tumours in 7 patients GK SRS was used as a secondary treatment in 37 tumours, 51 patients were treated with GK SRS as the primary treatment. Follow-up: 7 to 84 mo, 0 = 52 mo	GK SRS: 0 marginal dose 12.6 Gy. Used the KULA system and usually used MRI in dose planning.	MRI was obtained in 63 patients. Tumour unchanged: in 27 (42.8%) Tumour reduced: in 33 (52.4%) Tumour increased: in 3 (4.8%) Combined tumour control rate: 95% Central necrosis: in 21 (33%) of patients Postoperative shunt required: in 3 (3.5%) Craniotomy with tumour removal required in 2 patients after GK SRS. Postoperative facial neuropathy noted in 7 (8%) patients, developed after 4 mo in 1 patient, 6 mo in 3, 7 mo in 1, 12 mo in 2. In 4 patients the facial palsy improved from grade III to grade I, over a period between 4 and 51 mo. Trigeminal neuralgia was noted in 3 (3.4%) patients, it recovered in all at 13, 22, and 24 mo after SRS. Preserved hearing: 3 patients had preserved hearing prior to GK SRS, 2 of them still have preserved hearing at 11 and 19 mo after GK SRS.	Authors state that the recovery period from GK SRS is 10 to 57 mo. In order to decrease the complication rates, the marginal dose from an initial 16 Gy was reduced to 12-13 Gy. However, the number of patients treated at each dose was not mentioned. Study concludes stating GK SRS for acoustic tumour is an excellent treatment modality for small- to medium-sized tumours with or without prior microsurgical tumour removal. Poor level of scientific evidence.

Table 2: SRS in the treatment of acoustic neuroma (con't)

Authors	Number of patients	Treatment modality	Outcomes	Comments
Miller et al. Prospective study ('90 to '95) (25) 1999	n=82 Series 1: 42 patients, 5 with NF-2, 9 with previous surgery Series 2: 40 patients, 3 with NF-2, 12 with previous surgery. Follow-up: 0.1 to 6 y, median 2.3 y	GK SRS, dose dependent on tumour diameter (standard-dose protocol) or tumour volume (reduced-dose protocol) Standard-dose protocol (Series 1): 16 to 20 Gy minimal tumour dose Reduced-dose protocol (Series 2): 12 to 16 Gy minimal tumour dose	[Any measurable increase in tumour diameter was considered to constitute progression] 75/78 (96%) patients showed stable or partial regression of the tumour, progression in 3 (4%). These 3 were in the standard-dose protocol, 2/3 required salvage microsurgery. Patients with smaller tumours ($\leq$ 2.0 cm or 4.2 cm^3) showed no significant association observed between dose level and risk of facial neuropathy. However, patients with larger tumours ($\geq$ 2.1 cm or 4.2 cm^3) showed a significant association observed between dose level ($<$ 18 Gy vs. $\geq$ 18 Gy) and risk of facial neuropathy. No significant associations were observed between risk of trigeminal neuropathy and tumour dose in any diameter or volume category. Thirteen of 79 patients had useful hearing before SRS. Actuarial incidence of useful hearing post-SRS was 92% at 1 y and 39% at 2 y.	Authors state that no patient in Series 2 has experienced clinical or radiographic tumour progression, however the follow-up time is too short to make definitive conclusions about the lower dose protocol. It appears that refinements in treatment planning and neuroimaging in combination with reduced radiosurgical doses appear to have reduced significantly the risk of post-SRS cranial neuropathy. Fair to poor level of scientific evidence. The strength of the study was the high percentage of patients available for follow-up.

Table 2: SRS in the treatment of acoustic neuroma (con't)

Authors	Number of patients	Treatment modality	Outcomes	Comments
Kondziolka et al. (19) Retrospective study, consecutive patients ('87 to '92) Survey was conducted 5 to 10 y after SRS (response rate 77% [115/149]).	n=162 Follow-up on 149 (Unilateral tumours) Prior resection had been performed on 42 patients (26%) (2 prior resections in 8 patients, 3 prior resections in 2 patients and 4 prior resections in 1 patient) Patients with NF-2 were excluded from the analysis. Follow-up: MRI or CT scans were requested every 6 mo for the 1st 2 y, annually for next 2 y, then once every 2 y. Hearing patients had serial audiograms at 6-12 mo intervals.	GK SRS: initially 18 – 20 Gy, decreased to 16 - 18 Gy in the first 2 y, then in '92 further reduced to 14 – 16 Gy single session radiation of tumour ('87 to '90 SRS was guided by CT imaging) ('91 to '92 SRS was guided by MRI) Doses for individual patients selected according to: tumour volume, surgical history, hearing status, facial motor function and the patient's wishes.	[Gardner-Robertson scale was used to classify hearing function. Tumour enlargement or regression was defined as a change of ± 2 mm.] At 1 y evaluation, tumours were: unchanged – 73.8% smaller – 25.5% larger – 0.7% At 2 y tumours were: unchanged – 48.4% smaller – 46.9% larger – 4.7% At 3 y tumours were: unchanged – 38.1% smaller – 58.8% larger – 3.1% Of 97 patients who had a minimum of 5 y follow-up, 72% (70 cases) had a decrease in tumour volume and 28% (27 cases) had no change in the size of their tumours. Facial nerve function: Normal facial nerve function was preserved in 122 (79%) of 155 evaluated patients. Of 32 patients who had useful hearing before SRS, 15 (47%) maintained useful hearing and some degree of hearing and sound recognition was preserved in 52 of 85 patients (61%).	Authors determined with multivariate analysis that several factors were related to the onset of facial neuropathy: a higher dose of radiation to the tumour margin and a tumour that was larger in transverse diameter that the other tumours. Planning radiation doses on the basis of CT scans, as compared with MRI, was a significant risk factor for hearing loss. Poor level of scientific evidence. Conflicting results are shown in paper, i.e. 'normal' facial function on the HB scale is Grade I, yet this paper reports 'normal' as HB Grades I, II & III. In Figure 2, the "N" does not match up with number of patients in study.

Table 2: SRS in the treatment of acoustic neuroma (con't)

Authors	Number of patients	Treatment modality	Outcomes	Comments
Roijen et al. Retrospective (Case control) ('90 - '95)	53 Surgery (Netherlands) Medium follow-up 24 mo. (1-53) 92 SRS (Sweden) Medium follow-up 24 mo. (0.5-75)	Surgery 53 GK SRS 92	Short term infection etc. in 2-7% of surgical cases, none in SRS series. VII nerve complications 10% surgery, 2% SRS were affected <u>Health-related quality of life</u> General health rating better for SRS than surgery (good – excellent 81% vs 69%) SF36 SRS > surgery in 3 of 8 domains, moderate differences EuroQol SRS 0.89 vs surgery 0.77	Primarily an economic study, clinical outcomes not considered in detail. For short term follow-up in these groups, differences in clinical outcomes were small. Health-related QOL better for SRS-treated patients than surgical cases.

AN = Acoustic neuroma
* Levels of scientific evidence – see Appendix A

** Facial grade based on the scale of House JW, Brackmann DE: Facial nerve grading system Otolaryngol Head Nec Surg 93:146-147, 1985

Microsurgery for removal of acoustic neuroma

In the last 25 years, microsurgical techniques have been combined with CT and MRI and intraoperative neurophysiological monitoring, leading to further improvements in the surgical results of patients with acoustic neuroma (10, 13, 18, 20, 31, 33). Surgical objectives include the total removal of the tumour without major morbidity, excellent preservation of facial function, and preservation of serviceable hearing. More recently, cost-effectiveness has emerged as a consideration (10, 36). In general, tumour characteristics that give the best chance for hearing preservation with a microsurgical approach include:

- small size
- radical in presentation (near brainstem)
- involving superior vestibular nerve on pre-operative electronystagmogram testing
- not extending into the CPA by more than one cm
- having favourable ABR recordings (13).

The surgical approach used depends on the judgement of the surgeon and the location and size of the tumour. In addition the members of the surgery team contribute to the evaluation. Acoustic neuroma surgery overlaps several specialty fields including neurosurgery, neurotology, and otolaryngology.

Incomplete surgical removal of the acoustic neuroma is chosen by some patients, after consulting their surgeons, in order to reduce the risks of complications. The patient is informed as to the chances of further surgery, which is assessed by follow-up imaging studies and are increased by the onset and subsequent worsening of symptoms. Partial tumour removal has been suggested for patients who have a tumour in their only hearing ear; this occurs primarily in NF-2 patients.

Description of microsurgical approaches

The website of the U.S. Acoustic Neuroma Society describes the three most common surgical approaches for the removal of an acoustic neuroma (1). Total removal of an acoustic neuroma has been greatly refined as a result of the introduction of microsurgical instruments, the operating microscope, and intraoperative monitoring of the facial and cochlear nerves. The three most common surgical approaches to the removal of an acoustic neuroma are the middle fossa (MF), retrosigmoid (RS) and translabyrinthine (TL).

The MF approach opens the bone above the ear and the bone overlying the tumour is removed. This method is used in patients with good hearing and small tumours that extend out of the internal auditory canal no further than one centimeter towards the brainstem.

In the RS approach the bone is opened behind the mastoid and inner ear and the tumour is approached from behind. This allows the possibility of hearing preservation and may be used for both small and large tumours. Surgeons in support of this approach state that hearing may be preserved in tumours up to 2.5 cm (1).

In the TL approach the incision is made behind the ear with the mastoid bone being removed. This approach involves removing the inner ear structures, and thus destroys hearing. Therefore, it is only used for cases where hearing loss is severe or the tumour is so large that hearing conservation is not a realistic goal.

In centres of excellence where microsurgery for acoustic neuroma is done frequently, the average operating time is anywhere from two to six hours. In centres where the surgery is rarely performed it may take several more hours to remove an acoustic neuroma. The hospital stays are averaging around five days. In the vast majority of cases the patient requires no further therapy or follow-up. However, in the case of SRS, the goal is tumour control rather than removal and consequently the total number of follow-up imaging studies are not known (House, personal communication).

The purported treatment of choice for acoustic neuroma is microsurgery. An experienced surgeon, operating on tumours in the same size range as that appropriate for SRS, can produce results comparable to those from radiosurgery and the long-term tumour cure or control rate appears more certain with microsurgery (1).

Outcomes of acoustic neuroma microsurgery

Table 3 outlines the outcomes of various approaches to acoustic neuroma surgery. There are ten reports providing examples of recent studies of microsurgical techniques (2, 10, 13, 15, 18, 20, 28, 31, 33, 36). The general consensus is that the type of surgery used is dependent on tumour size and whether or not the patient has pre-operative hearing. The studies have several inconsistencies such as methodological design, and different outcome definitions for facial nerve function and preserved hearing. Refinements continue to be made to surgical techniques and there have been some good results reported on both facial nerve function and hearing preservation.

Table 3: Microsurgery in the treatment of acoustic neuroma (vestibular schwannoma)

Authors	Number of patients (n) Selection criteria Follow-up	Surgical procedure	Outcomes	Comments
Rowed et al. (31) Consecutive surgeries ('85 - '96)	n=26 intracanalicular tumours (this study is part of a larger series) Patient selection: serviceable hearing, maximum tumour diameter of 1.5 cm Follow-up: audiol - min. 1 y imaging - 1, 3, & 5 y	RS approach to preserve hearing with intraoperative monitoring of ipsilateral cochlear and cochlear nerve function.	[Serviceable hearing is defined by an SRT of $\leq$ 50 dB, SDS of $\geq$60%] Hearing was preserved in 13 of 26 (50%) of patients. Facial function: 25 of 26 (96%) of patients demonstrated normal or near-normal facial function, Grade I or II according to the House and Brackmann classification. One patient had Grade III facial nerve function.	Authors state that early detection and operation of acoustic neuroma would appear to be the best way to preserve serviceable binaural (both ears) hearing and normal facial nerve function until a reliable method of predicting growth of intracanalicular acoustic neuroma is found. The RS approach is familiar to neurosurgeons, yields results for hearing preservation comparable to those of the MF approach and, possibly, superior results for facial nerve function. Poor level of scientific evidence. Good length of follow-up.

Table 3: Microsurgery in the treatment of acoustic neuroma (con't)

Authors	Number of patients (n) Selection criteria Follow-up	Surgical procedure	Outcomes	Comments
Ramina et al. (28) Retrospective case review ('88 to '96)	n=83 Previous surgery in 10 patients. Tumour size was >3.0 cm in 65 patients (78%) and smaller in 18 (22%). Some hearing in 12 patients NF-2 in 6 patients (in addition these patients had other tumours) Follow-up: 4.5 ± 3 y	RS: 80 patients, in 1 case (NF-2) bilateral surgical removal was performed. One patient with a 40 mm cystic acoustic neuroma and in poor clinical condition underwent stereotactic biopsy and aspiration of the cyst. Intraoperative monitoring of the facial nerve performed in 40 patients, cochlear nerve monitored in 10 cases.	["Serviceable" hearing defined as better than 50 dB and 50% discrimination] Total removal of the acoustic neuroma was achieved in 77 out of 80 patients. Two patients had subtotal removal due to one having extremely high tumour vascularization and the other due to adhesion to the brainstem (55 mm tumour). No size increase of tumour remnant during a 20 and 28 mo follow-up, respectively. One NF-2 patient had a subtotal removal of a 45 mm tumour because he presented a facial palsy of the opposite side. Facial nerve function (HB grades I to III) could be preserved in 69 patients (90%) of 76 patients with normal pre-op facial function. Hearing preservation was possible in 7 cases; 5 retained serviceable hearing, one developed post-op non-serviceable hearing and the last case had pre- and post-op non-serviceable hearing. No late deterioration of hearing was observed in the follow-up of these patients.	Authors comment that SRS results should be analyzed carefully, especially since newer protocols have reduced the dosage of radiation to the tumour. When comparing microsurgery with SRS a short follow-up of 2 to 3 y is a concept for malignant tumours and not applicable to slow growing lesions. The natural history of acoustic neuroma lesion growth is not known. Poor level of scientific evidence. Hearing preservation outcomes were based on a very small patient population.

Table 3: Microsurgery in the treatment of acoustic neuroma (con't)

Authors	Number of patients (n) Selection criteria Follow-up	Surgical procedure	Outcomes	Comments
Arriaga et al. (2) Retrospective study ('89 to '96)	n=59 (This study is part of a larger series). Hearing preservation surgery performed in 60 procedures in 59 patients, as 1 had NF-2 with a bilateral tumour. Patients were considered as candidates if hearing in the affected ear retained 50dB SRT and 50% SDS, if they had NF-2, or if they had less than a 30dB SRT difference between the two ears.	The anatomic location of the tumour and patient age directed the surgical approach. MF: used when tumours of the internal auditory canal were less than 1 cm into the CPA (57% of patients). RS: used when tumours exceeded the limits for MF surgery (43%). Continuous facial nerve monitoring, ABR monitoring and occasional direct 8th nerve monitoring.	[Hearing data is presented according to the recommendations of the Hearing and Equilibrium Subcommittee of the AAO-HNS] Good post-op facial nerve function (HB grades I & II) was present in 54 (90%) patients. The 0 diameter of tumours in the MF approach was significantly smaller (0.72 ±0.34 cm) than that of the RS tumours (1.66 ±0.76 cm). Measurable hearing was preserved in 77% of cases (MF-85%, RS-65%). Useful hearing (Class A, B or C) was preserved in 67% of cases (MF-74%, RS-58%). Hearing was preserved at the same or better Class in 57% of patients overall (MF-68%, RS-42%). Despite an obvious trend for better hearing preservation with the MF approach there was not a significant difference between the two approaches for success of hearing preservation surgery. Hearing improvement occurred in 8 of 59 cases, in this series (MF-18%, RS-8%).	A point made by the authors is that hearing preservation is not the primary objective of acoustic neuroma surgery, rather it is safe, complete removal of the neoplasm before it causes serious neurologic morbidity from brainstem compression. And, because of social and psychological implications facial function preservation is the second priority. Generally, hearing preservation is the third priority for patients and it was only attempted in 20% of the total acoustic neuroma patients during the time of this review. Poor level of scientific evidence.

Table 3: Microsurgery in the treatment of acoustic neuroma (con't)

Authors	Number of patients (n) Selection criteria Follow-up	Surgical procedure	Outcomes	Comments
Kanzaki et al. (18) Retrospective case review ('91 – '96)	n=94 unilateral acoustic neuroma (this study is part of a larger series) Patient selection: serviceable hearing, 36 small intracanalicular tumours (0 size=6.0mm), 58 cases in which tumour extended 4-20 mm into the posterior fossa (0 size=7.8 mm). Overall 0 tumour size was 6.9 mm. Follow-up: (post-operative hearing patients) 2 y or longer (2-15 y)	Extended middle cranial fossa (62 cases), or middle cranial fossa (32 cases) approach, depending on size of tumour. Intraoperative hearing monitored by ECochG, auditory brainstem response, and direct compound action potential. Facial nerve function monitored using needle electromyography in combination with stimulus microinstruments.	[Serviceable hearing was defined as a PTA ≤50dB, SDS ≥50% before surgery] There were 47 (50%) cases where measurable hearing was preserved. Hearing was preserved in 25 (69.4%) of the 36 patients with an IC tumour and in 22 (37.9%) of the 58 patients with a tumour of 4-20 mm in size. However, there was no significant difference in hearing preservation rate between variations of the MF approach.	Authors state that quality of preserved hearing may be more important than the hearing preservation rate. Pathologic changes in the cochlear nerve may be a factor affecting the possibility of hearing preservation. Poor level of scientific evidence. Although not listed as an outcome measure, the facial nerve was monitored during surgery. The follow-up findings are only reported for the preserved hearing group.

Table 3: Microsurgery in the treatment of acoustic neuroma (con't)

Authors	Number of patients (n) Selection criteria Follow-up	Surgical procedure	Outcomes	Comments
Koos et al. (20) Retrospective case review using intraoperative photographs, videotapes and case records ('80 – '96)	n=115 part of a larger series of consecutive patients Patient selection criteria: Tumours of Grade I or II according to the Koos grading system Grade I: purely intracanalicular (14 patients), all with preserved hearing Grade II: tumours that extend into the CPA (101 patients), 87 of 101 patients had preserved hearing Documented exam of facial nerve function 12 and 18 mo post-operatively	Retromastoid approach was used with patient in the sitting position. (The suboccipital approach with emphasis on preservation of facial nerve and cochlear nerve function.) There was no facial nerve nor brainstem auditory evoked potential monitoring during surgery.	[A PTA of less than 50 dB and an SDS of greater than 50% were defined as preserved hearing] No topographic relationships could be determined for Grade I tumours. The Grade II tumours were observed either to indent the nerve complex without splitting the nerve bundles and/or be interposed between nerve bundles of the 8th and 7th cranial nerves. Patients with Grade I tumours had preserved hearing before and after surgery (100% hearing preservation rate). Overall, 76/87 patients with Grade II lesions had preserved hearing post-operatively. Combining the patients' results of Grades I and II tumours this represents a 78% hearing preservation rate (90 of 115 patients). Facial nerve was anatomically preserved in 113 of 115 cases (98%), in 2 patients the nerve was partially destroyed. Of the 113, 99 had full function and the remaining 14 had partial function.	Authors conclude that neurotopographic relationships exist between the tumour and the nerve bundles of the vestibulo-cochlear nerve complex in small acoustic neuroma. The study reaffirms the notion that tumour size and the patient's preoperative hearing level should be considered the primary determinants of the success of hearing preservation surgery attempts. Poor level of scientific evidence. Authors remark about the ongoing debate regarding the appropriate audiometric minimum for good hearing; there is no standard consensus.

Table 3: Microsurgery in the treatment of acoustic neuroma (con't)

Authors	Number of patients (n) Selection criteria Follow-up	Surgical procedure	Outcomes	Comments
Sampath et al. (33) Retrospective case review ('73 – '94)	n=611 Patient selection: those with pre-op facial nerve dysfunction, schwannoma of other cranial nerves, previous acoustic neuroma surgery, other pathology, or indefinite follow-up findings were excluded from the study. Follow-up: Immediate post-op period, 6 mo and 1 y. For patients who did not have a direct 1 y follow-up exam facial nerve outcome was assessed at the 6 mo follow-up visit. Imaging follow-up: annually for 5 y.	TL approach used for patients with absent hearing and small-to-moderate sized tumours (25.5%). RS (or suboccipital) approach for patients with preserved hearing or moderate-to-large sized tumours (72.7%). MF approach was used for selected patients with small intracanalicular tumours and intact hearing (1.8%). All but one patient had a gross total resection of tumour. Not mentioned whether any nerves were monitored during surgery.	[Goal of the study was to determine the rate of facial nerve transection, the incidence of postoperative palsy, and to correlate facial nerve outcome with tumour size, surgical approach, and intraoperative facial nerve injury.] In 596 patients (97.6%) facial nerve was anatomically preserved. Fifteen patients (2.45%) had facial nerve transection after the tumour was removed; 8 of these underwent immediate repair. One y after surgery, 5 of these patients had Grade III or IV (HB-scale), 3 continued to have a poor facial functional outcome (Grade V or VI). Of 75 patients evaluated for facial nerve function at 6 mo, 85.3%had HB Grade I or II, 9.3% Grade 3 or 4, 1.3% Grade V or VI. Remaining 536 patients were evaluated for facial nerve function at 1 y, 89.7% had Grade I or II, 8.9% Grade III or IV, 1.3% Grade V or VI. Tumour size had more of an effect immediately post-surgery; effects of tumour size become less apparent with time.	Authors point out that although the integrity of the facial nerve may be preserved the functional outcome may differ significantly. Results of this study indicate that equivalent outcomes can be achieved with each surgical approach and therefore, the size and location of the tumour, the patients' preoperative hearing function, the nerve of origin and the experience of the surgeon should dictate the operative approach. Poor level of scientific evidence. Outcomes of facial nerve function as they correlate with tumour size were reported on a very small subset of patients (75 of 611).

Table 3: Microsurgery in the treatment of acoustic neuroma (con't)

Authors	Number of patients (n) Selection criteria Follow-up	Surgical procedure	Outcomes	Comments
Gormley et al. (10) Retrospective case review, consecutive patients ('85 – '96)	n=179 Previous treatment included 9 patients having undergone microsurgery, 2 had both microsurgery and radiosurgery. Four patients had NF-Type 2. Follow-up: 0 70 mo, median: 65 mo range 3 – 171 mo (Two patients died during the follow-up period due to unrelated tumours.)	RS, transmeatal approach: 157 patients (84%) Transpetrosal, RS approach in 18 patients (10%) TL approach: 8 patients (4%) Transmastoid, transpetrosal, partial labyrinthectomy approach: 4 patients (2%) Seven patients were treated in planned two-stage operations, thus 187 surgeries were performed.	Total tumour resection: 178 patients (99%) (determined by imaging studies). Facial nerve function: Of 67 patients with small-sized AN, 64 recovered to a post-op Grade I or II (on HB scale) function within 3 mo, and 3 to a Grade III or IV. Of 80 patients with medium-sized AN 59 recovered to a Grade I or II and 21 to Grade III or IV. (Results of 4 patients are not included here because of pre-op facial paralysis after radio/microsurgery performed elsewhere) Of 26 patients with large-sized acoustic neuroma, 10 recovered to Grade I or II, 15 to Grade III or IV and 1 to Grade V or VI. (Results of 2 patients were excluded because of pre-op facial paralysis after microsurgery performed elsewhere). Hearing preservation: (Functional hearing is defined as SRT ≤50 dB combined with SDS ≥50%) Only 69 of the 179 patients had pre-op hearing; 42 with small tumours, 24 with medium and 3 with large. Post-op preserved hearing: 20 from small tumour group, 6 from medium and 0 from large tumour group.	Authors comment that the management strategy for AN must be based on uniform criteria for measuring tumour size and pre-op hearing function. Tumour size, the most important determination of results, has not been uniformly reported, making a comparison of different surgical approaches difficult. A comparison of long term results must consider these differences as well as cranial nerve morbidity, which includes facial nerve function, hearing preservation, complications from treatment and long-term tumour control. Poor level of scientific evidence. The strength of the study was the length of follow-up.

Table 3: Microsurgery in the treatment of acoustic neuroma (con't)

Authors	Number of patients (n) Selection criteria Follow-up	Surgical procedure	Outcomes	Comments
Slattery et al. (36) Prospective case review, consecutive surgeries ('93 – '95)	n=151 (part of a larger series of consecutive surgeries) NF-Type 2: 11 patients, 1 with bilateral acoustic neuroma, each tumour is reported separately. All but one patient had normal facial nerve function pre-op. Follow-up: one y available for 147 patients.	MF approach with 100% total tumour excision. Intraoperative facial nerve monitoring used in all cases; auditory brainstem response was performed in 130 cases (86%), and direct 8th nerve intraoperative monitoring was performed in 40 cases (26%).	Facial nerve function: 95% of patients had an excellent recovery graded as HB I or II, 5% had grade III or IV. [Criterion for hearing preservation was that of the AAO-HNS Committee on Hearing and Equilibrium Categories for the Reporting of Hearing Preservation in acoustic neuroma.] Post-op hearing results available for 143 patients. Measurable hearing was preserved in 98 (68%) of patients. There were 45 (32%) patients in whom a dead ear developed as a result of surgery. Long-term follow-up for recurrent tumours is not yet available, however, no recurrent tumours have been identified.	A team approach is used for treating acoustic neuroma patients, the neurosurgeon and otologist work together to remove the tumours. Authors found no relation between tumour size or origin of the tumour and final facial nerve function. [The current recommendation to patients is to have an MRI 5 y after the procedure. Yearly audiograms are recommended for those patients in whom hearing has been preserved.] The MF approach is reliable and offers the potential for full tumour removal with hearing preservation. Fair level of scientific evidence.

Table 3: Microsurgery in the treatment of acoustic neuroma (con't)

Authors	Number of patients (n) Selection criteria Follow-up	Surgical procedure	Outcomes	Comments
Irving et al. (15) Retrospective study Consecutively treated patients, groups matched by tumour size in order to compare surgical approaches. MF group: ('89 – '96) RS group: ('87 – '95)	n=98 (100 tumours) NF-2: 3 patients, 2 underwent bilateral tumour removal; each tumour is reported separately. Patients had tumours with a CPA component ≤ 2 cm as determined by chart review. Patients with a PTA of > 50 dB and an SDS > 50% were chosen for hearing preservation surgery. MF group follow-up: 10 mo (1 mo to 3 y) RS group follow-up: 19 mo (1 mo to 8 y)	MF approach in 48 patients RS approach in 50 patients Neuromonitoring included electromyographic, intraoperative facial nerve, and intraoperative auditory brainstem response.	Hearing preservation in 26 MF patients (52%) showed Class B or better results. Seven RS patients had Class B or better results. Some post-op hearing was recordable in 32 (64%) of the patients in the MF group and in 17 (34%) of those in the RS group. The results obtained with the MF approach were superior (and statistically significant) for intracanalicular tumours and for tumour with a CPA component measuring 0.1 to 1.0 cm. [Hearing was classified according to the AAO-HNS system] Pre-op there was 100% facial function in all 98 patients. At 1 y 40 MF patients were available for assessment and all 40 had HB Grade I or II facial function, 49 RS patients were available and 47 had HB Grade I or II facial function.	This study demonstrated significantly better hearing preservation with the MF approach when compared with the RS for size-matched groups of intracanalicular tumours and tumours extending 1 cm or less into the CPA. Poor level of scientific evidence. The strength of the study was the length of follow-up.

Table 3: Microsurgery in the treatment of acoustic neuroma (con't)

Authors	Number of patients (n) Selection criteria Follow-up	Surgical procedure	Outcomes	Comments
Hecht et al. (13) Retrospective case review ('81 to '95)	n=60 (part of a larger series of consecutive surgeries) Patients with pre-op serviceable hearing were considered for hearing preservation surgery. Follow-up: audiograms were performed in all patients 2 days before surgery and 6 to 8 weeks after surgery.	MF: 18 patients (used for laterally based intracanalicular tumours) RS: 42 patients (used for medially based tumours that had extended into the CPA.	[Hearing preservation was defined using both the Gardner and Shelton systems for classification] Overall hearing was preserved in 22 (36.7%) of the 60 patients; 8 of 18 MF patients and 14 of 42 RS patients. The average tumour size was 1.4 cm for the 60 patients evaluated. Tumour size was determined by either pre-operative CT or MRI scans. The 0 tumour size for MF patients who had preserved hearing was 0.74 cm, those unsuccessful had an 0 tumour size of 1.5 cm. The 0 tumour size for RS patients who had preserved hearing was 1.4 cm; those unsuccessful had a 0 tumour size of 1.9 cm.	Better interspecialty definitions of hearing preservation are needed. Good hearing versus serviceable hearing should include the middle ear. This requires an understanding by physicians of dynamic range and the ability to fit the patient with a hearing aid. Poor level of scientific evidence. A weakness in this study is the very short follow-up period.

SDS = speech discrimination score
CPA = cerebellopontine angle
RS = retrosigmoid
SRT = speech reception threshold
TL = translabyrinthine
AAO-HNS= American Academy of Otolaryngology-Head and Neck Surgery
ECochG = electrocochleography
MF = middle fossa
HB – House Brackmann

Treatment complications

Complications after SRS

Significant proportions of patients experienced complications in some series, including neuropathy (Table 2). In the study by Kondziolka et al. (19) complications were described by 36 patients and resolved in 20 (56%). The complications included balance problems (7 patients), facial twitching (6), facial weakness (4), tinnitus (3), hydrocephalus (3), numbness (2) and headache (2). The three patients who reported signs and symptoms of hydrocephalus required placement of a ventriculoperitoneal shunt. Other complications that were reported in approximately 1% of cases included: facial pain, watery eyes, low blood pressure, bleeding from tumour, dizziness, and dry eyes.

Complications after microsurgery

Details of complications were not included in some of the literature reviewed for this report. Reviews such as that by Sampath et al.(33) summarize typical results at centres with experience in this type of surgery. Mortality is low, at 0.2 – 0.3%. There are higher mortality rates reported in some series, though a number of deaths appear to have been unrelated to the acoustic neuroma surgery. Surgical morbidity will occur in 1% to 2% and infection in 3% to 4%. CSF leaks have been reported as a post-surgical complication in as many as 25% of all cases, although with newer surgical techniques this percentage is falling.

For longer-term events, Sampath et al. refer to tumour recurrence in 0.82% of cases. Tumour recurrence was detected during follow-up imaging studies (0 = 8.7 y, range 1 to 21 y). Perhaps 10% to 20% of cases will have non-acceptable facial nerve function at more than six months after surgery (33). Driscoll et al. (5), reported on 210 patients who had acoustic neuroma removal using the RS approach. They noted that 31% had dysequilibrium which lasted more than three months after surgery. Age of more than 55.5 years, female gender, consistent pre-operative dysequilibrium and central findings on electronystagmography were associated with worse outcomes.

Complications in 179 patients reported by Gormley et al. (10) included: CSF fistula in 14.5%, aseptic meningitis in 3%, VP shunt/hydrocephalus in 3%, wound infection in 2%, and lower cranial nerve palsy in 2%.

There were two deaths (1%) reported. One patient died of a myocardial infarction and the other had chronic obstructive lung disease, and died as a result of pulmonary complications and systemic sepsis. Each of these patients had undergone uncomplicated tumour resections. Cerebellar and brain stem injury/ataxia occurred in one patient (1%).

Ramina et al. (28) mention complications in their series of 83 patients that include CSF rhinorrea in seven cases (9%), meningitis in four (5%), CSF leak through the wound in two, hematoma in tumour bed in three (surgically evacuated). Two patients died after surgery due to intracerebellar hematomas and brainstem infarction. Another patient died 12 days after surgery due to a pulmonary infection.

Complications in the Slattery et al. (36) study included: nine cases (7%) of post-operative CSF leak. Hospital stay was prolonged by one day for each patient. Six of these patients required lumbar drainage for resolution of the CSF leak. There were three cases of meningitis. There were no wound hematomas or infections that required additional surgical treatment, no deaths or brain injury secondary to retraction of the temporal lobe or injury to other cranial nerves.

Irving et al. (15) retrospectively compared the MF and RS approaches for hearing preservation surgery. The results were equal at one year with respect to facial nerve outcome. However, there was an increased incidence of transient facial palsy in patients who underwent surgery via the MF route

Complications for SRS and microsurgery mentioned in the literature reviewed for this report are outlined in Table 4. This provides a general indication of most common adverse effects associated with the different approaches.

Some of the complications of SRS treatment are long term and in some cases become apparent months or years after the radiosurgery procedure.

Complications of microsurgery will often be apparent shortly after the operation and lengthen post-operative hospital stay.

There is also a risk of death from microsurgery. However, this will be very low in centres of excellence.

Table 4: SRS and microsurgery complications

Complication	Proportion of patients in series	
	SRS	Microsurgery
Balance problems / dysequilibrium (5, 19, 39, 44)	16.1%, 7.7%, 19.4%	31%
Facial twitching / weakness / lower cranial nerve palsy (10, 16, 19, 21, 39, 44)	21.7%, 25.8%, 25%, 8%, 27.8%	2%
Trigeminal neuropathy (16, 21, 39)	15.2%, 19.3%, 3.4%	
Tinnitus (19, 39)	3.2%, 8.3%	
Hydrocephalus (10, 19, 21, 39)	3.2%, 8.3%, 3.5%	3%
CSF leak (10, 28, 36)		14.5%, 9%, 7%
Meningitis (10, 28, 36)		3%, 5%, 2%
Numbness (19)	5.6%	
Headache (19)	5.6%	
Tumour recurrence/enlargement (16, 21, 25, 33)	4.8%, 4%, 4.3%	0.82%

Note: Only complications mentioned in the cited reports are included.

Discussion

The present assessment has similar findings to those in earlier HTA reports that have considered treatment of acoustic neuroma by SRS. In summary:

- There is evidence that SRS is efficacious in the treatment of acoustic neuroma in suitably selected individuals. However, all studies have methodological weaknesses. There are no RCTs of SRS in comparison with other forms of treatment.
- There is also evidence that SRS has adverse effects in a proportion of patients who are treated for this condition. Comparative data with surgical outcomes have some limitations.
- Microsurgery will remain the primary option for many individuals with acoustic neuroma.
- There is no convincing evidence that either the Gamma Knife or the LINAC versions of SRS is superior to the other in terms of patient outcomes.

A further point is that there are continuing, significant developments in surgical procedures for acoustic neuroma.

Stereotactic radiosurgery is a technology that has aroused strong feelings and much polemic in the literature. There is no shortage of opinion on the pros and cons of this approach. Unfortunately, much of this seems uninformed by reasonable quality evidence. Some assertions seem to have been driven by hopes for less invasive treatment of patients, commercial pressures and availability of resources at particular institutions.

Some recent commentaries give an indication of the arguments and issues that have been raised. Ross and Tator (30) reviewed literature on treatment of acoustic neuroma using SRS. They note that the majority of patients have been treated with the Gamma Knife. LINAC-SRS is regarded as promising, but lacking long-term follow-up. These authors take the view that it is not practical to pool LINAC data because of the variation in equipment and protocols, and suggest that each LINAC-SRS unit must be evaluated separately.

They acknowledge the potential of the LINAC approach to provide fractionated SRS, but state that a biological advantage of fractionation for benign lesions has never been established. Young (personal communication) also considers that the efficacy of fractionated treatment is unproven.

In Canada, most patients and many referring physicians have chosen the Gamma Knife treatment as the preferred method of SRS (30) (this is available in the USA but not in Canada).

A different view of the Canadian situation is given by Schwartz (35). He provides a short comparison of the Gamma Knife and LINAC approaches and suggests that essentially their effectiveness is equivalent. He draws attention to the fact that the place of SRS in treatment of acoustic neuroma is less well defined than for arteriovenous malformations (AVMs) and that claims of high response rates are over-stated. He strongly defends the standards of quality of Canadian SRS facilities and suggests that, while SRS treatment outside the country should remain an option for the individual, this should not be at public expense.

A response to Schwartz (23) noted the promise of fractionated SRS and also made the point that the quality of SRS at a given centre has more to do with the expertise of the team as a whole than with the particular irradiation technology employed.

Brada and Cruikshank (3) suggest that some media reports on SRS are misleading and offer false hope. They cite the data from Flickinger et al. (7) that tumour control of acoustic neuroma is 91% with a 17% risk of VIIth and a 65% risk of VIIIth neuropathy at five years. They suggest that, on present evidence, single fraction SRS for brain tumours is associated with higher toxicity than is seen with fractionated irradiation. Also, they comment that a statement in a newspaper article that "about

80,000 people have been treated with the Gamma Knife world wide" reflects uncontrolled spread of an unproved technique and the power of marketing.

Responses to the recent article by Kondziolka et al. (19) include comment from the University of Alberta Skull Base Centre that both the age of the patient and the size of the tumour are important in decisions on whether or not to use SRS in treatment of acoustic neuroma (4). For patients over 65 with acoustic neuromas that are not causing distortion of the brainstem, observation rather than surgery is recommended. Other comments draw attention to issues related to use of fractionation, outcome measures used and numbers of patients available for long-term follow-up (22, 26).

Direct comparison between SRS and microsurgery has been uncommon. The useful study by Roijen et al. (29) considered costs and clinical outcomes of microsurgery compared to SRS in treatment of acoustic neuroma patients. This drew on retrospective data in a case control design, with a consecutive series of 53 patients treated surgically in the Netherlands being compared with a similar group in Sweden treated with SRS. Data on production losses and qualify of life were obtained by questionnaires.

Differences in clinical outcomes from the two patient groups were small. The general health rating was better for patients treated with SRS than for those who had microsurgery. Direct and indirect costs of microsurgery were higher than for SRS, so that for the short-term SRS was more cost-effective than microsurgery for these patient groups. Longer-term more rigorous studies would be needed to further establish efficacy in terms of tumour control, quality of life and adverse effects. Further comparative studies of this sort are required, taking into account conditions in other health care systems and developments in health technology. For example, the length of hospital stay appears to have been considerably longer in the Dutch series than would currently be the case at Canadian centres.

Some important themes emerge from the primary data, reviews and commentaries considered in this report:

- The quality of evidence on the comparative effectiveness and safety of SRS over microsurgery for acoustic neuroma remains limited.
- Technical developments in both surgery and SRS need to be considered. Use of fractionation in SRS is a potentially important development though its efficacy is unproven.
- The overall performance of SRS will depend on the expertise of the patient management team and the quality of imaging and treatment planning, as well as the method used to deliver radiation.

The latter point suggests that the views of Ross and Tator (30) regarding comparison of data from different sites will apply to Gamma Knife SRS as well as to LINAC SRS. Given the variation in expertise, patient selection and protocols across sites,

combining data from different centres will be problematical for either version of SRS. Combining data will be necessary to get some indication of overall efficacy and effectiveness, but the limitations in reliability need to be recognized.

From the perspective of health policy in Alberta, two general areas to consider are approaches to treatment of the individual with acoustic neuroma and availability of SRS facilities in the province.

In regard to the first issue:

- There is evidence, from low quality studies, that SRS is efficacious in the treatment of acoustic neuroma in appropriately selected individuals.
- Microsurgery will remain a major option for many patients, and techniques will continue to evolve.
- Both SRS and microsurgery are associated with complications. Unlike SRS, microsurgery will require post-operative hospital stay and subsequent convalescence. There is also a risk of death, though this will be very small in centres of excellence.
- The choice between SRS and microsurgery may be complex and will be a matter for individual patients and their physicians.
- There is no evidence of any difference in outcomes between the Gamma Knife and LINAC forms of SRS in the treatment of acoustic neuroma.
- The effectiveness of either SRS approach will be related to the overall expertise of the patient management teams. Good results can be expected with either the Gamma Knife or the LINAC at centres of excellence.
- Availability of fractionated radiation through the LINAC approach may be an advantage, but good evidence of benefit from fractionation in treatment of acoustic neuroma has yet to emerge.

With regard to the second health policy issue identified here, any SRS facility in Alberta should be based on use of the LINAC, for reasons discussed in detail in the previous report by the AHFMR (34). LINAC SRS offers cost advantages and appears to have greater scope for further technical development than the Gamma Knife.

Appendix A: Methodology

A search was undertaken for articles pertaining to treatment options for acoustic neuroma/vestibular schwannoma. The databases searched with corresponding search terms are listed in the following table. Earlier technology assessments of SRS supplemented information contained in the literature.

The following subject headings and textwords were used alone or in combination:

	Subject Headings	Textwords
MEDLINE	Neurofibromatosis 2/ Microsurgery/ Radiosurgery/ exp Neuroma, acoustic/ Neurilemmoma/	NF2.mp. NF-2.mp. (neurofibromatosis adj4 (2 or II)).mp acoustic neuroma$.mp. microsurg$.mp. retrosigmoid.mp. translabyrinthin$.mp. middle fossa.mp. gamma knife.mp. GK$.mp. linac.mp linear accelerat$.mp. vestibular schwannoma$.mp. acoustic schwannoma$. acoustic nerve cancer.mp. acoustic Neurofibroma.mp. radiosurg$.mp.
EMBASE	Neurofibromatosis/ exp Acoustic neurinoma/ exp Microsurgery Stereotaxic surgery/ exp Radiosurgery/ exp Linear accelerator/	
CURRENT CONTENTS	STEREOTAXIC-RADIOSURGERY VESTIBULAR-SCHWANNOMA; MICROSURGERY-; ACOUSTIC-NEUROMA; SURGICAL-MANAGEMENT ACOUSTIC-NEUROMA-SURGERY GAMMA-KNIFE GAMMA-KNIFE-RADIOSURGERY NEURINOMA- LINEAR-ACCELERATOR LINEAR-ACCELERATOR- RADIOSURGERY LINAC-RADIOSURGERY	

Date Limits: 1996-1999

Publication Type limits:

- Clinical Trials
- Controlled Clinical Trials
- Randomized Controlled Clinical Trials
- Multicenter Studies
- Comparative Studies
- Prospective Studies
- Retrospective studies

Case reports were excluded

Jovell and Navarro-Rubio (17) have published a classification scheme that comments on quality of evidence. Assignment to categories is dependent on conditions of scientific rigour. Tables 2 and 3 in this report classify the level of scientific evidence from each of the studies with:

Good:	Meta-analysis of randomized controlled trials (RCTs) or from large sample RCTs;
Good to Fair:	Small sample RCTs and non-randomized controlled prospective trials;
Fair:	Non-randomized controlled retrospective trials, cohort studies and case-control studies;
Poor:	Non-controlled clinical series and various other approaches.

In this health technology assessment:

Efficacy refers to the performance of a technology under 'ideal' conditions or conditions of best practice; and

Effectiveness refers to the performance of a technology under 'routine' conditions. For example when it has become widely distributed in a health care system.

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