Neurosurgical Review (2020) 43:941–949
https://doi.org/10.1007/s10143-019-01103-6

REVIEW

Stereotactic radiosurgery and radiotherapy for acoustic neuromas

Maria-Aggeliki Kalogeridi[1] · Andromachi Kougioumtzopoulou[2] · Anna Zygogianni[3] · Vassilis Kouloulias[2]

Received: 5 December 2018 / Revised: 6 February 2019 / Accepted: 5 April 2019 / Published online: 13 April 2019

Abstract

Neuromas are benign intracranial tumors with indolent natural history. Surgery is the mainstay of treatment and only after the introduction of single-fraction stereotactic radiosurgery (SRS), radiotherapy emerged as an alternative viable option. In this review, we focused on SRS or conventionally fractionated stereotactic radiotherapeutic (FSRT) approaches. We described the results of different doses used for SRS and FSRT, the current status, and a comparison between the two radiotherapy approaches. Stereotactic radiotherapy techniques aim to control tumor growth with minimal toxicity. SRS using either a cobalt unit or a linear accelerator has given high rates of tumor control and of cranial nerve function preservation with marginal doses range of 12–14 Gy. Fractionated stereotactic radiotherapy (FSRT) is optimal for tumors larger than 3 cm. Doses as low as 50.4 Gy provide excellent control rates and low morbidity. Overall, both SRS and FSRT are equally effective and safe options for neuroma patients who do not need immediate surgical decompression.

Keywords Neuroma · Stereotactic radiosurgery · Stereotactic radiotherapy · SRS · FSRT

Introduction

Acoustic neuromas are benign intracranial nerve sheath tumors arising from the vestibular branch of the eighth cranial nerve (acoustic nerve). They represent 6–10% of all intracranial tumors. Incidence is in the range of 0.6–1.2 per 100,000 population per year for sporadic cases [1]. The only identified risk factor for development of acoustic neuroma is neurofibromatosis-2 (NF-2). The majority of patients present a progressive and unilateral hearing loss or unilateral tinnitus, ataxia, vertigo, change in facial sensation, and headache. However, current imaging modalities are able to detect a potential acoustic neuroma before it becomes symptomatic [2]. In a prospective cohort study which included 945 patients who underwent contrast-enhanced magnetic resonance imaging (MRI) scans, the diagnosis of acoustic neuroma was an incidental finding in 2.1% of the patients [3]. Based on MRI scan findings, most acoustic neuromas have an intracanalicular component [4, 5].

Current treatment management of acoustic neuromas includes observation, microsurgical resection, stereotactic radiosurgery (SRS), or fractionated stereotactic radiotherapy (FSRT) [6]. The choice of treatment depends on various factors including size, location, previous treatment, and tumor progression [7]. Observation is considered an option for small lesions with minimal annual growth rate in asymptomatic patients [8, 9]. A therapeutic intervention is appropriate for growing tumors with deteriorating symptoms. Increasing tumor size is associated with the increased use of surgery and older age is associated with an increased likelihood conservative management [10].

Methods

For literature review, we searched Pubmed database using the keywords neuroma, schwannoma, stereotactic, radiosurgery, and radiotherapy. We included articles published in English after 2005. We also evaluated references cited in selected papers and included earlier historical and valuable articles. Paper selection was based on the number of patients and follow-up length. Those with analysis of results on local control and toxicity were included in this review. For SRS, we included studies using both cobalt units or linear accelerators. For

✉ Vassilis Kouloulias
vkouloul@ece.ntua.gr

[1] Radiotherapy Department, Alexandras General Hospital, Athens, Greece

[2] Medical School, 2nd Dpt Radiology, Radiotherapy Unit, National and Kapodistrian University of Athens, Athens, Greece

[3] Medical School, 1st Dpt Radiology, Radiotherapy Unit, National and Kapodistrian University of Athens, Athens, Greece

FSRT, we included studies with conventional fractionation or hypofractionated schedules. Reviews and meta-analysis were included, but case reports were excluded in this review.

Results

Stereotactic radiosurgery

SRS was introduced in 1969 by the neurosurgeon Lars Leksell in Karolinska Hospital, as an alternative option to surgical resection for acoustic neuromas [11]. Local control rates were over 80% in a median follow-up of 3.7 years, while trigeminal and facial nerve impairment rates were 18% and 14%, respectively. Initially, the use of SRS for neuromas was considered for elderly or medically inoperable patients, bilateral tumors, and in postsurgical recurrence. Despite the lack of randomized studies comparing the two modalities, SRS and surgery for the treatment of acoustic neuromas, recent meta-analysis reported similar long-term tumor outcome for both modalities and significant favorable long-term hearing preservation outcome for patients treated with SRS compared with surgery [12].

Nowadays, several studies evaluating the efficacy and toxicity of radiosurgery have established the role of SRS as a viable non-surgical treatment option for properly selected neuroma patients (Table 1).

Stereotactic radiosurgery can be offered using either a Cobalt unit (Gamma Knife) or a Linear Accelerator (X-knife) with comparable results.

In older series, dose range of 10–25 Gy was used in SRS achieving high local control rates, with the expense of high rates of hearing loss and nerve toxicity [13, 14]. A reference study of this early period of SRS is performed by Flickinger et al. where 134 patients with acoustic neuroma were treated with gamma knife SRS, and the dose delivered range was 12–20 Gy (median 17 Gy) prescribed to the 40–70% isodose [14]. The authors reported, 4-year actuarial tumor control rate 89.2 ± 6.0%, the rate of preservation of useful hearing was only 35% and the incidence rate of post-treatment rate of facial and trigeminal neuropathy was 29.0% and 32.9%, respectively. The first cohort study performed with LINAC-based SRS for acoustic neuromas in 56 patients reported a 5-year control rate of 95% and the prescribed dose range was 10–22.5 Gy [15]. Reference isodoses depended on the number of isocenters used. For 36 patients treated with one isocenter, the dose was specified at the 80% isodose line, and for the remaining two patients at the 88% and 90% isodose lines. For patients treated with 2–3 isocenters, the dose was specified at the 68% line (one patient), the 70% line (13 patients), and the 80% line (four patients). The incidence of trigeminal or facial neuropathy was 73% and useful hearing preservation was 51%.

Kondziolka et al. evaluated 162 consecutive patients who underwent radiosurgery for acoustic neuromas between 1987 and 1992 and reported long-term outcome results [16]. Factors such as tumor volume, surgical history, hearing status, and facial motor function were considered to determine the specific doses for individual patients. The mean dose delivered to the tumor margin in this series of patients was 16.6 Gy (range 12–20) prescribed to the 50% isodose line for the majority of patients (78%). At 1-year evaluation, 73.8% of tumors was unchanged and 25.5% was smaller. Three years after the intervention, the respective rates were 38.1% and 58.8% while 3.1% of patients had radiological tumor enlargement. This change was related to either tumor growth or necrosis-related tumor margin expansion. Further imaging follow-up identifies patients with progressive tumor growth. Seventy-two percent of patients evaluated for at least 5 years had a decrease in tumor volume and 28% had stable disease. At 5-year evaluation, 79% of the patients preserved normal facial nerve function and 73% normal trigeminal nerve function. Fifty-one percent of the patients had no change in hearing ability. No new neurologic deficits appeared more than 28 months after radiosurgery.

In addition to the tumor volume, the dose of radiation to the margin was identified as significantly associated with the risk of trigeminal neuropathy and the onset of facial neuropathy in

Table 1 Selected studies of stereotactic radiosurgery (SRS) and fractionated stereotactic radiotherapy (FRST)

Author, year	RT	No. of pts	FU median (months)	Dose/dose per fr (median)	Volume median (cc)	PFS (%)	Hearing preservation (%)	Facial preservation (%)	Trigeminal preservation (%)
Murphy, 2010 [21]	SRS	103	43.2	13	1.95	91.5–5 y	NA	99	95
Chopra, 2007 [19]	SRS	216	68	13	1.3	98.3–10 y	44	94.9	100
Friedman, 2006 [22]	SRS	295	40		2.2	12.5	NA	99.3	99.3
Myrseth, 2005 [20]	SRS	103	36	12.2	NA	93	32	NA	94.8
Combs, 2005 [29]	FSRT	106	48.5	57.6/1.8	3.9	LC 96.6	94	96.6	97.7
Koh, 2007 [34]	FSRT	60	31.9	50/2	4.9	LC 100	77.3	100	100

RT radiotherapy, *No.* number, *pts* patients, *FU* follow-up, *fr* fraction, *PFS* progression-free survival, *SRS* stereotactic radiosurgery, *NA* not available, *FSRT* fractionated stereotactic radiotherapy, *LC* local control

multivariate analysis. These results are in line with other series using higher doses [17, 18].

Although SRS provides high local control rates, the cranial nerve toxicity and hearing preservation need improvement and dose de-escalation emerged as possible option.

Numerous series examine SRS using marginal tumor doses of 12–13 Gy for acoustic neuromas report long-term outcomes regarding the effectiveness and safety of this approach [19–22].

In a small series of 25 patients with intracanalicular acoustic neuromas treated with 12 Gy prescribed to the 50–60% isodose line, excellent results are reported after long-term follow-up (mean 7.4 years) [23]. The 5- and 10-year tumor control rates were 96% and hearing preservation was achieved in 64% of the patients. No post-radiosurgery cranial nerve toxicity was reported.

A retrospective study of patients treated with SRS for intracanalicular neuromas reported that all patients who received a marginal tumor dose of 14 Gy or less had serviceable hearing preservation and only one out of five patients that received a higher dose of 14 Gy [24]. In a following retrospective study, 216 acoustic neuromas patients underwent Gamma Knife SRS with marginal tumor doses of 12–13 Gy [19]. The marginal tumor dose was prescribed to the 50% isodose volume in 199 patients, 55% in 12 patients, 60% in 4 patients, and 65% in 1 patient. The 10-year actuarial resection-free control rate was 98.3% while the 10-year preservation rates for facial and trigeminal nerve were 100% and 94.9%, respectively. Preservation of hearing level and serviceable hearing at 10 years were 44.0% and 44.5%, respectively. A cohort study of 46 patients with acoustic neuromas treated with LINAC SRS using a median marginal dose of 14 Gy (range 10–16 Gy) reported tumor control in 73.8% of patients [25]. In addition, 66.7% of patients retained useful hearing and new trigeminal and facial neuropathy occurred only in 2.4 and 4.8% of the patients, respectively. Recently, Hasegawa et al. reported their long-term results on tumor control and adverse events after Gamma Knife SRS for acoustic neuromas [26]. Between 1991 and 2000, 440 patients were treated and evaluated. SRS received 79% of patients as primary treatment while the rest had undergone prior resection the median follow-up was 12.5 years. The actuarial 5- and ≥ 10-year progression-free survival was 93% and 92%, respectively. No patient developed treatment failure > 10 years after treatment. The actuarial 10-year facial nerve preservation rate was 97% in the high marginal dose group (> 13 Gy) and 100% in the low marginal dose group (≤ 13 Gy). The isodose line for the tumor margin varied from 40 to 95% (median 50%). Ten patients (2.3%) developed delayed cyst formation.

In a prospective study, neuroma patients were treated with SRS 12 Gy prescribed to the periphery of the tumor with minimum 95% coverage (113 patients) or observation (124 patients) [27]. After a median follow-up of 55 months, useful hearing loss was comparable between the two groups (74% vs 64%). Moreover, there was a significant reduction in tumor volume over time in the SRS group, while the development of symptoms and QoL were not significantly different between the groups.

Our previously published experience with LINAC-based SRS for the treatment of acoustic neuroma patients revealed excellent local control in the long-term follow-up period [28]. Furthermore, 58% of the lesions decreased in size and 42% were stable after a median follow-up period of 55 months. Hearing preservations were not assessed due to the absence of useful hearing in the study patients. Post-SRS-related facial or trigeminal neuropathy was not developed in none of the patients.

Overall, in the case of SRS, contemporary series using 12–14 Gy report tumor control rates > 90% [7]. Hearing preservation in the modern era of lower doses (12–14 Gy) used for SRS is in the range of 41–79% [7]. Furthermore, the high rates of 5-year trigeminal (79–99%) and facial nerve preservation (95–100%) can be achieved with marginal doses of 12–14 Gy and cranial nerve toxicity should not exclude SRS as a treatment option [7].

Fractionated stereotactic radiotherapy

Conventionally fractionated stereotactic radiotherapy at higher doses (dose > 54 Gy; 1.8Gy/fraction) has been used for neuroma patients [29, 30].

Combs et al. reported the long-term results in 106 acoustic neuroma patients treated in a single institution [29]. Patients received 57.6 Gy given in 1.8 Gy per fraction on a median tumor volume of 3.9 mL (range, 2.7–30.7 mL). The 90% isodose line encompassed the PTV. After a follow-up time of 48.5 months, 5-year local control rate was 93% and hearing preservation for non-NF-2 cases was 98%. Cranial nerve toxicity other than hearing impairment was rare. The rate of radiation-induced toxicity to the trigeminal and facial nerve was 3.4% and 2.3%, respectively.

In a study published by Selch et al., in 48 acoustic neuroma patients treated with FSRT, the 5-year actuarial local tumor control rate was 100% and the 5-year actuarial rate of preservation of facial and trigeminal nerve function was 97.2 and 96.2%, respectively, and the delivered dose was 54 Gy in 1.8 Gy daily fractions [31].

Lower doses (50.4–52.5Gy; 1.8Gy/fraction) have also shown excellent results for tumor control and toxicity profile [32–34]. A single-institution experience using a mean dose of 50 Gy in 25 fractions over 5 weeks to treat 60 neuroma patients were effective and safe in median tumor volumes of 4.9 cm^3 (range, 0.3–49.0 cm^3) [34]. The 5-year actuarial local control rate was 96.2% and the estimated 5-year progression-free survival (PFS) was 92.8%. The overall hearing preservation rate was 77.3%. There were no cases of new cranial nerve toxicity post-FSRT.

Conventional FSRT was used to treat 158 neuroma patients with 50.4 Gy [33]. After a median follow-up period of

60 months, trigeminal and facial impairment rates were 3.2% and 2.5%, respectively. The preservation of useful hearing was possible in 54% of the cases. Local control was 99.3% at 3 years and 95.2% after more than 7 years of follow-up.

Further dose de-escalation (46.8Gy; 1.8 Gy/fractions) is associated with excellent preservation of functional hearing status and limited cranial nerve toxicity without compromising tumor local control [35].

Hypofractionated schedules have also been used for FSRT. In a retrospective series of 383 neuroma patients, 90% were treated with 18 Gy over 3 fractions. Local control rate was 99% and 96% at 3 and 5 years, respectively, and larger sized tumors and NF-2-related tumors were associated with lower control rates. Serviceable hearing was maintained in 70% of the patents after treatment and smaller sized tumors were associated with better hearing preservation. No cases of facial weakness were reported while trigeminal dysfunction was as low as 2% [36].

Excellent tumor control (99.1%) is reported in 117 patients treated with CyberKnife (18 Gy given in 3 fractions) related to normalization of 72–90% isodose line (mean 79.4%) and an average of 97.1% tumor coverage and follow-up to 61.1 months while 80% of patients preserved their hearing [37]. Larger tumor volume, smaller cochlea size, and higher prescribed cochlear doses were associated with hearing degradation.

Hypofractionated schedules of stereotactic radiotherapy delivering 4 Gy in 5 fractions or 5 Gy in 5 fractions have also given high tumor control rates (> 97%) with acceptable hearing preservation and facial or trigeminal toxicity ≤ 3%. Meijer treated 12 initial patients with 20 Gy over 5 fractions and 68 following patients with 25 Gy over 5 fractions at the 80% isodose line [38]. After 33 months of follow-up, tumor control rate was 94%, while facial and trigeminal nerve preservation was 97% and 98%, respectively. These results are in line with Anderson et al., who treated 37 patients with 20 Gy and reported tumor control rate approximately 91%, and limited facial nerve toxicity [39]. Recently, Patel reported the results of 383 neuroma patients treated with 25 Gy in 5 fractions prescribed to the 80% isodose line after a median follow-up of 72 months [40]. Treatment failure requiring salvage microsurgery was 2.3%. More than 50% of patients maintained serviceable hearing, while cranial nerve toxicity was acceptable.

Proton beam stereotactic radiosurgery has also been shown to be an effective technique by means of tumor control [41, 42]. Eighty-eight patients treated at the Harvard Cyclotron Laboratory with proton beam stereotactic radiosurgery and followed up for a median 38.7 months were reported by Weber et al. [41]. A median dose of 12 cobalt Gray equivalents (range, 10–18 cobalt Gray equivalents) was prescribed to the 70 to 108% isodose lines (median, 70%). The 2- and 5-year tumor control rates were 95.3% and 93.6%. Three patients (3.4%) underwent shunting for hydrocephalus. Of the 21 patients with functional hearing, 7 (33.3%) retained serviceable hearing ability. Actuarial 5-year normal facial and trigeminal nerve function preservation rates were 91.1% and 89.4%.

As proton radiotherapy has the advantage of superior conformality of dose distribution in comparison to photon RT, protons were used to minimize normal tissue toxicity rather than achieving higher tumor control. However, definitive conclusions regarding the superiority of proton beam SRT cannot be safely drown due to the small patient series and the short-term follow-up time. Larger series and longer follow-up periods are necessary before strong recommendations are made.

Overall, both conventional FSRT and hypofractionated achieve high control rates 81–98% and 96–100%, respectively [7, 43]. Cranial nerve toxicity outcomes were also satisfactory with both approaches conventional or hypofractionation. Conventional regimens provided 91–98% 5-year facial nerve preservation rate and 89–97% 5-year trigeminal nerve preservation rate, while hypofractionation schedules were 100% and 99–100%, respectively. Hearing preservation rates were in the range of 50–54% for conventional regimens versus 70–76% for hypofractionation.

Nowadays, modern technology allows comparable dose conformality for both radiosurgery and fractionated stereotactic radiotherapy. However, both radiotherapy approaches are likely to produce higher morbidity rates if optimal conformality index is not achieved.

Stereotactic radiosurgery vs fractionated stereotactic radiotherapy

There are no randomized trials comparing SRS with FSRT for the treatment of acoustic neuroma patients. However, useful conclusions are based on five non-randomized studies reporting on efficacy and toxicity (Table 2).

Recently, Combs et al. reported the outcome of 451 acoustic neuroma patients treated with SRS or FSRT [44]. Median dose delivered was 13 Gy in SRS group or 57.6 Gy given in 1.8 Gy daily fractions in the FSRT group. After a median follow-up of 67 months, both SRS and FSRT were equally effective in tumor control with a 3-year and 10-year local control rate of 97% and 94%, respectively. Similarly, there was no significant difference between the two groups in terms of toxicity. Furthermore, facial and trigeminal nerve toxicity were comparable between SRS and FSRT. Loss of useful hearing was observed in 14% of the patients in the FSRT group and in 16% of the patients in the SRS group.

A retrospective series of 100 acoustic neuroma patients from a single institution compared SRS with FSRT in terms of clinical outcome and toxicity [39]. In SRS arm, the prescribed median dose was 12.5 Gy (range 9.7–16 Gy) and in FSRT arm, the prescribed dose was either 45–50.4 Gy given in 1.8 Gy per fraction or a hypofractionated schedule of 20 Gy delivered in 5 fractions.

Table 2 Selected studies of comparing stereotactic radiosurgery (SRS) and fractionated stereotactic radiotherapy (FRST)

Author, year	No. of pts	FU median (months)	Dose (median)	Volume median (cc)	Local control (%)	Hearing preservation (%)	Facial neuropathy (%)	Trigeminal neuropathy (%)
Kopp, 2011 [46]	115	30.1	SRS 12 Gy	NA	98.5	85	None	13
		32.1	FSRT 54 Gy/30 fr	NA	97.9	79	None	None
Collen, 2011 [45]	119	56	SRS 12.5 Gy	1.7	95	4 years: 82	16	6
		73	FSRT 50 Gy/25 fr 30–40 gy/10 fr	6.3		4 years: 59	3	3
Puataweepong, 2014 [47]	139	61	SRS 12 Gy	NA	5 years: 95	5 years: 75	1 patient	None
			FSRT 50 Gy/25 fr	NA	5 years: 95	5 years: 63		None
			HSRT 25 Gy/5 fr	NA	100	5 years: 87	2 patients	None
Anderson, 2014 [39]	48	83.6	SRS 12.5 Gy	NA	5 years: 97	60	2.1	10.5
		53.6	FSRT 45–50.4 Gy/25–28 fr	NA	5 years: 100	44.4	0	5.3
		47.1	20 Gy/5 fr	NA	5 years: 90.5	63.2	2.1	20.5
Combs, 2015 [44]	441	67	SRS 13 Gy	NA	5 years: 95	86	< 1	1.8
		67	FSRT 57.6 Gy/32 fr	NA	5 years: 95	84	1	14

No. number, *pts* patients, *FU* follow-up, *SRS* stereotactic radiosurgery, *NA* not available, *FSRT* fractionated stereotactic radiotherapy, *NA* not available, *fr* fraction *HSRT* hypofractionated stereotactic radiotherapy

The 5-year local control rate was 97% for SRS, 90.5% for hypofractionated FSRT, and 100.0% for FSRT. Serviceable hearing preservation rates were 60%, 63.2%, and 44.4% for SRS, hypofractionated FSRT, and FSRT patients. No differences in 5-year cranial nerves toxicity was reported between the different stereotactic radiotherapy techniques.

A prospective cohort study compared SRS with FSRT for the treatment of acoustic neuroma patients [45]. The SRS group received a median single dose of 12.5 Gy and the FSRT group received either 50 Gy given in 25 fractions or a hypofractionated schedule of 30–40 Gy given in 10 fractions. The authors reported no difference regarding local control, hearing preservation, or trigeminal neuropathy. However, facial nerve toxicity was significantly increased in the SRS compared to FSRT group. In a similar prospective cohort study of 115 patients with acoustic neuroma who underwent either SRS or FSRT, the clinical outcome was comparable for the two radiotherapy techniques [46]. The authors reported 98.5% local control rate for the SRS group and 97.9% for the FSRT group. The hearing preservation was 85% for the SRS group and 79% for the FSRT group. Radiotherapy-related neuropathy regarding trigeminal nerve was 13% in the SRS group. The retrospective study performed by Puataweepong et al. compared SRS with FSRT and reported no difference regarding 5-year local control rate between the two radiotherapy techniques. In addition, there was no difference regarding hearing preservation [47].

Overall, none of the five non-randomized studies comparing SRS to FSRT reported a significant difference in 5-year local control rate between single fraction or radiosurgery of fractionated stereotactic radiotherapy [39, 44–47]. Moreover, pooled analysis of hearing preservation rates as well as facial and trigeminal dysfunction confirmed that there was no significant difference between the two radiotherapy approaches [7].

Discussion

Current management options for acoustic neuromas include observation, microsurgery, SRS, and FSRT.

For asymptomatic or minimally symptomatic patients, observation through serial imaging studies is a viable option since slow growth is considered characteristic of these tumors [48]. “Wait and see” avoids the complications of therapeutic approaches such as surgery or radiotherapy at the cost of increased risk of tumor progression and neurologic deterioration. A disadvantage of active surveillance is the high percentage of patients who lose useful hearing. Smoutha et al. reported that hearing impairment occurred in 51% of patients in a retrospective review of studies with an average follow-up time of 3.2 years [49]. Moreover, higher incidence of hearing loss, tinnitus or vertigo associated with wait and see policy give a lower quality score compared to microsurgery or radiosurgery

after 5 and 10 years of follow-up [50]. Since up to 24% of patients will eventually require treatment during follow-up, delaying the therapeutic intervention may have a negative impact on treatment success and complications.

Intervention required when hearing is threatened, symptoms begin to impair quality of life or tumor grows quickly, the choice of treatment depends on several tumor-related factors as well as patients' preference. While surgery is mandatory for large neuromas necessitating immediate decompression, radiotherapy is effective and safe for slow growing tumors with non-threatening symptoms.

Surgical resection, that has traditionally been the standard of care for acoustic neuromas, can achieve local control rates of up to 90–95% though this is at the cost of treatment-related toxicity and morbidity [51, 52]. After the introduction of SRS by Lars Leksell, radiosurgery has been used to treat smaller acoustic neuromas (< 3.5 maximum diameter) not requiring immediate intervention for decompression. Although there are no randomized trials comparing microsurgery to SRS, prospective and retrospective comparison demonstrated that radiosurgical treatment for acoustic neuroma is an alternative to microsurgery [53, 54]. SRS yields equivalent tumor control and serviceable hearing preservation rates while is associated with lower rates of acute and long-term development of facial and trigeminal neuropathy, postoperative complications, and hospital stay.

The results of a matched cohort analysis conducted to evaluate clinical outcomes in neuroma patients treated with microsurgery or SRS were recently published [55]. Three hundred ninety-nine patients with small- to medium-sized neuromas (less than 2.8 cm in diameter) were matched for age at surgery, lesion size, hearing status, and House-Brackmann score. There was a statistically significant difference of serviceable hearing preservation in favor of SRS (42.8% vs 85.7%, $p < 0.01$) after an average follow-up interval of 43.7 months and 30.3 months for microsurgery and SRS, respectively. Morbidity was low for both groups, but facial dysfunction was higher in the microsurgery group (11% vs 0%, $p < 0.01$). The need for subsequent intervention was similar between the two groups.

The recent meta-analysis by Maniakas et al. confirmed that SRS and microsurgery are equally effective in terms of local control [12]. However, SRS demonstrates a more favorable long-term hearing preservation outcome as compared with microsurgery.

Moreover, a recent systematic review of controlled studies comparing microsurgery and radiosurgery showed that SRS can be considered the best practice for solitary acoustic neuromas of less than 3 cm [56].

On top of that, neuroma patients enjoy similar QoL throughout the follow-up period after undergoing observation, radiation therapy, or surgery [57].

An international multicenter cross-sectional study comparing microsurgery, stereotactic radiosurgery, observation, and non-tumor controls recently reported small differences in long-term quality of life outcomes in patients with vestibular schwannoma [58].

Radiotherapy has been established as a viable option for carefully selected acoustic neuroma patients due to technological advances and the excellent results after long-term follow-up. Both single fraction SRS and FSRT can achieve optimal coverage and highly conformal dose distribution to the target, minimizing toxicity of surrounding normal tissue. SRS is appropriate for small tumors (< 3 cm in diameter) while size is not a contraindication for FSRT. However, despite the encouraging reports of fractionated stereotactic radiotherapy for larger neuromas (> 3 cm) [59], there is a concern of increased morbidity of radiotherapeutic approaches for this population [59]. A retrospective study of 25 patients with neuromas ≥ 3 cm showed increased morbidity rates and cranial and complication rates for either SRT or SRS in comparison to results for smaller lesions [60].

Early SRS series used higher doses in the range of 16–22 Gy. High local control rates were achieved at the cost of high toxicity rates. In order to maintain a low toxicity profile, a marginal dose of 12–13 Gy was used in modern series. Long-term follow-up confirmed that lower doses are associated with a more favorable toxicity profile without compromising local control (> 90%).

Similarly, older series of FSRT used median doses of 57.6 Gy. Although they gave high tumor control rates, toxicity was of concern. Deescalated doses of up to 50.4 in 1.8 Gy fractions of FSRT have been proven both safe and effective after long-term follow-up. This long course of RT may not be convenient for patients or busy radiotherapy departments but is suitable for tumors > 3 cm that are not amenable to SRS or those with irregular shape. In these cases, hypofractionated SRT with daily doses > 2.5 Gy is also an attracting option. Hypofractionated SRT, usually given in 3–5 fractions, has a short overall treatment time in comparison to protracted conventionally fractionated schemes of 6 weeks. It allows a more conformal dose distribution in comparison to single fraction SRS and a more homogenous dose distribution in the target volume. Excellent results are reported with 18 Gy in 3 fractions after long-term follow-up.

Although single-fraction SRS may be more convenient as a 1-day outpatient procedure, it has no advantage over FSRT in terms of local control of overall toxicity. Although there are no randomized studies directly comparing SRS to FSRT, pooled results from six non-randomized studies find no significant difference in local control, hearing preservation or facial and trigeminal nerve toxicity between the two modalities.

Moreover, fractionated radiotherapy may have a radiobiological disadvantage in case of protracted treatment interruptions (> 3 days).

After SRS or FSRT, a transient tumor expansion termed pseudoprogression may become evident during follow-up

with imaging studies [61]. Pseudoprogression is induced by high doses of irradiation and is a phenomenon that causes confusion whether further treatment is needed. Observation is an alternative option to surgery if the expansion does not cause mass effect symptoms; a regression to original size of the tumor is feasible after the observed expansion [62].

Conclusions

Three therapeutic options are available for acoustic neuromas observation radiotherapy and surgery. Treatment decision should be based on tumor characteristics and clinical symptoms and patient preference. Both SRS and FSRT offer high local control rates with minimal toxicity and low overall morbidity. Radiotherapy is a viable option for properly selected neuroma patient.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Not applicable due to the review type of the paper.

Informed consent Not applicable due to the review type of the paper.

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