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Hypofractionated stereotactic radiotherapy of acoustic neuroma

Volume changes and hearing results after 89-month median follow-up

In the course of the last decade, the reported incidence of acoustic neuroma has increased, reaching 15 to 20/million per year [49], mainly because of the more frequent use of magnetic resonance imaging (MRI). In addition to traditional microsurgery, alternative approaches like “wait and scan” or stereotactic radiotherapy are used [3, 5, 35, 36]. The goal of hypofractionated stereotactic radiotherapy is to reach a high tumor control rate and a low rate of cranial nerve toxicity with a comfortable technique in a short treatment time. Here, we report a series of hypofractionated radiotherapy for acoustic neuroma and provide long term follow-up details regarding the dynamics of tumor volumes and hearing preservation.

Patients and methods

Between July 2001 and December 2007, 29 consecutive patients (11 men, 18 women) with unilateral acoustic neuroma were treated within a prospective radiation protocol. Mean and median patient age was 57 years (range 32–75 years). Eight patients had surgery prior to radiotherapy. All patients had a growing tumor and/or increasing clinical symptoms before ad-

mission. Patients with neurofibromatosis type II were excluded. The mean maximal extrameatal tumor diameter was 13.9 mm (range 8–29 mm). The median tumor volume amounted to 0.9 ml (range 0.2–8.8 ml) and the median planning target volume (PTV) was 1.7 ml (range 0.4–12.7 ml). The stereotactic system originally described by Leibinger–Fischer (Freiburg, Germany) was applied. The patient’s head was immobilized by using an individual mask made of scotch cast (Heidelberg mask). Images for planning were generated with multiplanar T1-weighted contrast-enhanced MRI sequences (Harmony, Siemens), reconstructed with a slice thickness of 2 mm. A contrast-enhanced planning CT (XVision, Toshiba) with a slice thickness of 2 mm was obtained with the patient’s head fixed in the stereotactic mask system. CT and MR images were merged on the stereotactic planning workstation. The PTV was defined as gross tumor volume as visible on the T1-weighted MR images plus a 1–1.5 mm margin. A manually driven micro-multi-leaf collimator with a leaf width of 1 mm was used for field shaping. We created 4–6 fixed beams to apply 4 Gy to the ICRU reference point for 3–5 fractions per week,

encompassing the PTV within the 90 % isodose volume (90 % = 3.6 Gy).

A total of 21 of 23 patients with any hearing capacity before treatment had audiological examination before radiotherapy with pure tone audiogram and evaluation of speech discrimination and were therefore eligible for the assessment of hearing preservation. All 29 patients had clinical and neurological examination before irradiation and were evaluable regarding changes of tumor volume.

Follow-up

MRI, clinical, and audiological follow-up started 6 months after irradiation and was repeated annually. Grading of the cranial nerve VII function was described according to the House–Brackmann score [18]. In addition, synkinesis—if present—was scored. Function of the cranial nerve V was noted descriptively as numbness and/or trigeminal neuropathy.

Hearing was scored according to the guidelines of the American Academy of Otolaryngology–Head and Neck Surgery Foundation (AAO-HNSF) [9]. As recommended, the pure tone average (PTA) was defined as the mean of the measured 0.5,

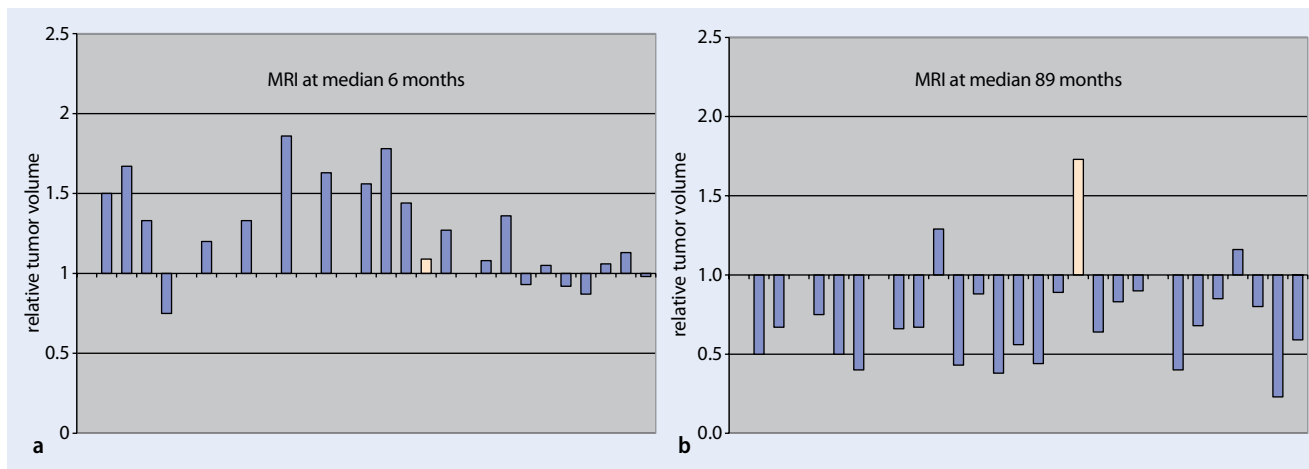


Fig. 1 ▲ Tumor volumes relative to the volumes at irradiation in individual patients at a median imaging follow-up time of 6 months (a) or 89 months (b). One out of 29 patients developed a late progression (light bar)

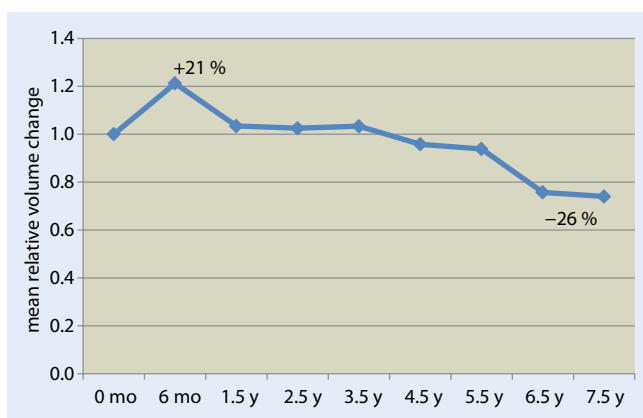


Fig. 2 ◀ Mean relative tumor volume change over time

1.0, 2.0, and 3.0 kHz values in decibel. The speech discrimination score (SDS) was measured as the fraction of standardized words that could be understood at a sound intensity of 30–40 dB louder than the individual PTA value. The median audiological follow-up time was 71.3 months (mean 80.5 months; range 43.0–129.7 months).

Sequential MRI examinations were done with the same technique as for radiotherapy planning and the 3D tumor volume was generated from the 2 mm axial T1 contrast-enhanced images in the same manner as for the initial dose planning. All 29 patients had sequential MRI examinations with a median follow-up time of 89.5 months (mean 85.8 months; range 30.5–128.7 months). In the literature, an increase in the largest tumor diameter of >2 mm is often taken as a criterion for progression [5]. We tried to compare this one dimensional increase of 2 mm with our measured 3D volumes

by transforming these volumes to spheres with the same volume and increasing their radius by 1 mm, to make a 3D volumetric increase comparable to a one dimensional increase of 2 mm or more.

Statistics

Actuarial hearing preservation rates were calculated using the Kaplan–Meier method [23]. The differences between groups were assessed with the Fisher exact test and a 2-tailed t-test for categorical and continuous data sets, respectively. Statistical analyses were performed using IBM SPSS Statistics version 20.

Results

At last follow-up, 28 of the 29 patients were alive. One woman died 61 months after radiation treatment from metastat-

ic extracerebral cancer; her neuroma was locally controlled.

Tumor control

No patient required salvage treatment; the intervention-free tumor control rate is 100%. The treatment for 1 of the 29 patients was recorded as a failure according to the definition described above with increasing tumor volume at 100.9 months after treatment without neurological symptoms except for further hearing deterioration (crude tumor control rate 96.6%).

Tumor volume

We observed transient volume enlargement in 17 of 29 patients (58.6%) after a median MRI follow-up time of 6 months ($p = 0.019$), but permanent volume reduction in 22 out of 29 patients (75.9%) after a median MRI follow-up time of 89.5 months ($p < 0.001$). At this late time point, only 3 out of 29 patients (10.3%) had a larger volume compared to the volume at treatment, the volume in 4 patients was unchanged (■ Fig. 1). Mean volume reduction per patient was 0.41 ml, while the mean maximal volume enlargement in relation to initial volume was +21% (■ Fig. 2).

Hearing evaluation

Of 23 patients with hearing capacity before radiotherapy, 21 had serial pure tone and speech audiometry and were, there-

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Hypofractionated stereotactic radiotherapy of acoustic neuroma. Volume changes and hearing results after 89-month median follow-up**Abstract**

Purpose. The goal of this work was to evaluate toxicity and local control following hypofractionated stereotactic radiation treatment with special focus on changes in tumor volume and hearing capacity.

Patients and methods. In all, 29 patients with unilateral acoustic neuroma were treated between 2001 and 2007 within a prospective radiation protocol (7 × 4 Gy ICRU dose). Median tumor volume was 0.9 ml. Follow-up started at 6 months and was repeated annually with MRI volumetry and audiometry. Hearing preservation was defined as preservation of Class A/B hearing according to the guidelines of the American Academy of Otolaryngology (1995).

Results. No patient had any intervention after a median imaging follow-up of 89.5 months, one patient showed radiological progression. Transient increase of tumor volume developed in 17/29 patients, whereas 22/29 patients (75.9%) presented with a volume reduction at last follow-up. A total of 21 patients were eligible for hearing evaluation. Mean pure tone average (PTA) deteriorated from 39.3 to 65.9 dB and mean speech discrimination score (SDS) dropped from 74.3 to 38.1%. The 5-year actuarial Class A/B hearing preservation rate was 50.0 ± 14.4%.

Conclusion. Radiation increases only minimally, if at all, the hearing deterioration which emerges by observation alone. Presbycusis is not responsible for this deterior-

ation. Transient tumor enlargement is common. Today radiation of small- and medium-sized acoustic neuroma can be performed with different highly conformal techniques as fractionated treatment or single low-dose radiosurgery with equal results regarding tumor control, hearing preservation, and side effects. Hypofractionation is more comfortable for the patient than conventional regimens and represents a serious alternative to frameless radiosurgery.

Keywords

Stereotactic radiotherapy · Acoustic neuroma · Hearing preservation · Hearing impairment · Local control

Hypofractionierte stereotaktische Bestrahlung des Akustikusneurinoms. Volumenänderungen und Hörergebnisse nach einer medianen Nachbeobachtungszeit von 89 Monaten**Zusammenfassung**

Ziel. Ziel der Studie war die Evaluierung der Toxizität und der lokalen Tumorkontrolle einer hypofraktionierten stereotaktischen Bestrahlung mit besonderem Augenmerk auf Veränderungen von Tumolvolumen und Hörvermögen.

Patienten und Methoden. Insgesamt wurden zwischen 2001 und 2007 29 Patienten mit unilateralem Akustikusneurinom innerhalb eines prospektiven Bestrahlungsprotokolls behandelt (7 mal 4 Gy ICRU-Dosis). Das mediane Tumolvolumen betrug 0,9 ml. Die Nachsorge startete nach 6 Monaten und wurde jährlich wiederholt mit MRI-Volumetrie und Audiometrie. Der Hörerhalt wurde definiert als Erhalt eines Class-A/B-Hörvermögens nach den Richtlinien der American Academy of Otolaryngology (1995).

Ergebnisse. Kein Patient benötigte eine Intervention nach einer medianen Nachbe-

obachtungszeit von 89,5 Monaten, ein Patient entwickelte eine radiologische Progression. Eine vorübergehende Volumenzunahme zeigte sich bei 17/29 Patienten nach 6 Monaten, eine Volumenreduktion wiesen 22/29 Patienten (75,9%) bei der jüngsten Nachsorgeuntersuchung auf. Insgesamt waren 21 Patienten bezüglich des Hörerhalts auswertbar. Der Mittelwert im Tonaudiogramm (PTA) verschlechterte sich von 39,3 dB auf 65,9 dB, das durchschnittliche Sprachverständnis (SDS) fiel von 74,3% auf 38,1%. Der aktuarische 5-Jahres-Class-A/B-Hörerhalt betrug 50,0 ± 14,4%.

Schlussfolgerung. Der Grad der Hörminderung nach Bestrahlung ist, wenn überhaupt, nur minimal deutlicher als nach alleiniger Beobachtung. Presbycusis ist nicht verantwortlich für diese zunehmende Hypakusis. Eine vorübergehende Volumenzunahme ist häu-

fig. Heute ist eine Bestrahlung von kleinen bis mittelgroßen Akustikusneurinomen mit jeder hochkonformalen Technik als fraktionierter oder niedrigdosierte singuläre Behandlung mit gleichwertigem Ergebnis bezüglich Tumorkontrolle, Hörerhalt und Nebenwirkungen durchführbar. Die hypofraktionierte Bestrahlung ist für den Patienten komfortabler als konventionelle Schemata und eine ernsthafte Alternative zur nichtinvasiven Radiochirurgie.

Schlüsselwörter

Stereotaktische Strahlentherapie · Akustikusneurinom · Hörerhalt · Hörbeeinträchtigung · Lokale Kontrolle

fore, evaluable for hearing preservation. In all, 2 of the 23 patients refused repeated audiometry. Only 1 of 8 patients with prior excisional surgery were included in the hearing evaluation. Between 5 and 11 sequential audiograms per patient (mean 7.3 audiograms per patient) were recorded. A total of 109 of 153 audiograms (71.2%) were generated at our hospital.

The mean PTA level before radiotherapy was 39.3 dB (range 9–71 dB). This level dropped to a mean of 48.3 dB (range 6–83 dB) at a median follow-up time of 7 months and to 53.6 dB (range 6–94 dB) at 20 months ($p < 0.001$) with further deterioration thereafter to 65.9 dB (range 15–120 dB) at 71.3 months ($p < 0.001$). The dynamics of the mean pure tone val-

ues for different frequencies at different time points are depicted in **Fig. 3a, b**. The mean PTA level before radiotherapy on the contralateral ear was 19.3 dB and changed minimally to 22.3 dB at a median of 71.3 months (**Fig. 3c**; $p < 0.001$ for comparison with the ipsilateral ear). Only 3 patients were initially admitted with presbycusis.

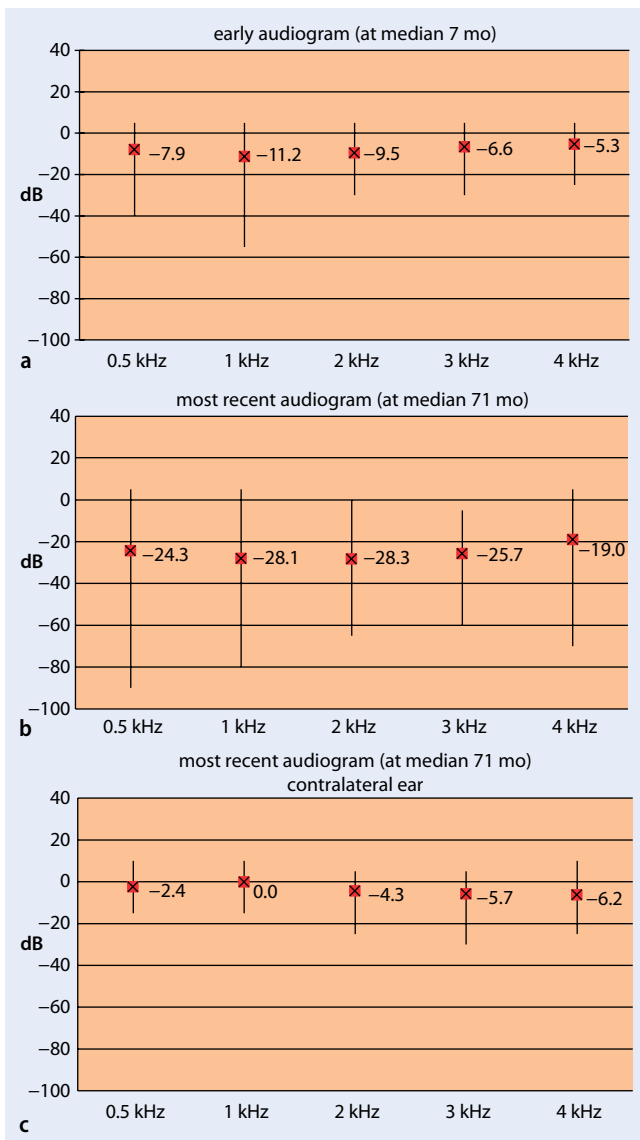


Fig. 3 ◀ Mean pure tone deterioration at different frequencies including individual spans at a median audiological follow-up time of 7 months (a) or 71 months (b). No relevant deterioration in the contralateral ear after long-term follow-up (c). Abbreviations: dB decibel, kHz kilo-Hertz, mo months

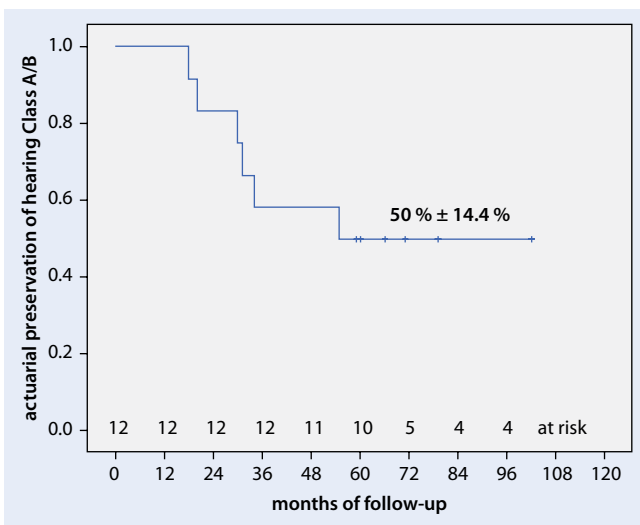


Fig. 4 ◀ Actuarial rate for the preservation of serviceable hearing (n = 12)

The speech discrimination score (SDS) was available for all 21 evaluated patients before and after radiotherapy. The mean SDS value before radiotherapy was 74.3% (range 25–100%). This value dropped at last follow-up to a mean of 38.1% (range 0–100%; $p < 0.001$). The actuarial 5-year rate of preserving Class A/B hearing (n = 12) was $50.0 \pm 14.4\%$ (Fig. 4). All 6 patients with an initial SDS of 90–100% had their Class A/B hearing preserved, but no patient with an initial SDS of $< 90\%$ ($p = 0.002$ Fisher exact test).

Cranial nerve toxicities

One of 29 patients at risk developed a new minimal facial nerve deficit grade 3 at 30 months which resumed to grade 1 after 4 years. This patient also presented with facial synkinesis between 30 and 40 months. Electromyography revealed a pathological signal for the ipsilateral nasal muscle. One other patient developed facial synkinesis between 7 and 12 months after radiotherapy. One 65-year-old woman developed severe ipsilateral facial nerve paresis grade 6 at 80 months after irradiation as a side effect of influenza vaccination [54].

Two patients developed mild partial numbness which persisted in one. One other patient reported discrete temporary symptoms of trigeminal neuropathy at 70 months after treatment and received anticonvulsive drug treatment. Cranial nerve lesions related to surgery (8 patients at risk) did not deteriorate after radiotherapy.

Other toxicities

Two patients have ongoing postoperative sicca syndrome of the ipsilateral eye. Dizziness and tinnitus were present in almost all patients at the time of admission and changed marginally after radiotherapy. Small field alopecia occurred regularly in 1 or 2 areas at the entrance site of the beam and was temporary in almost all patients. Thus far, no radiation related secondary tumor was found, but the observation time with respect to possible tumor induction is rather short.

Discussion

This study has the longest imaging and audiological follow-up of all reported hypofractionation series for acoustic neuroma. We measured a volume reduction in 76% and a transient volume increase in 59% with only 1/29 patients presenting with a late progression. With a median audiological follow-up time of 71 months, we found a 7-year actuarial rate for preserving a serviceable hearing (i.e., class A/B hearing) of $50 \pm 14.4\%$. Mean PTA level dropped from 39.2 to 65.9 dB, mean SDS from 67.1 to 38.1%. We did not find a conspicuous hearing deterioration in the contralateral ear and presbycusis was already present in 3 patients before irradiation. Hasegawa et al. [16] also did not observe a marked hearing deterioration in the contralateral ear in their long-term follow-up study after radiosurgery.

Several other authors reported about hypofractionated regimens in patients with acoustic neuroma [1, 4, 7, 11, 15, 19–22, 24, 25, 27, 30–34, 38–41, 46, 53]. The definition of tumor size, local control, and hearing preservation were quite different between the studies. Some initial papers had follow-up reports in abstract form only; mean or median follow-up times were less than 5 years in most studies. A crude tumor control rate of 80–100% and actuarial 5-year rates of 88–100% were reported. Tumor size reduction varied greatly from 10 to 81% (Table 1 and 2). A transient increase in tumor diameter was reported by Sakanaka et al. [46] in 48% of their cases. Henzel et al. [17] compared three-dimensional volume shrinkage between radiosurgery and conventional fractionated stereotactic radiotherapy and found significantly more shrinkage in the fractionated group. Kapoor et al. [24] updated results from the John Hopkins Hospital and used the term radiological progression for any enlargement of tumors after at least 18 months of follow-up. However, a transient increase of tumor volume is common after the 18 months period. Therefore, this study could indeed not differentiate exactly between transient increase of volume and real progression. The development of tumor volume was also examined in some radiosurgery studies. Naganou et al. [37] reported on the development

of the relative tumor volume over time in their study with a mean follow-up time of 7.5 years and found a transient increase of 28% at 6 months after treatment with a final decrease of 31% at 5 years, values quite similar to the findings in our study.

Hearing preservation was reported in some hypofractionation studies without objective data, in most studies as crude rate and in only one study [33] as actuarial rate. The period of audiological follow-up was mostly shorter than imaging follow-up or was not separately stated. Only a few studies presented specific data for PTA and SDS.

It has been postulated that conventional fractionation may preserve hearing to a greater extent than single fraction radiosurgery [12]. There are studies with actuarial 4- to 5-year hearing preservation rates of 82–94%. These studies had objective audiological data only for a minority of patients; the final definition of hearing preservation was mainly based on a subjective questionnaire. Sequential follow-up audiometry was performed in one of such study [26] for 68/115 patients, but the final hearing outcome was again defined subjectively after a median follow-up time of 32.1 months. However, studies with subjective hearing evaluation are not able to evaluate the hearing ability of each ear separately. Studies with objective audiological evaluation and more than 3 years of follow-up [2, 28, 29, 42, 47, 51] resulted in a crude hearing preservation rate of 54% (129/239 patients) and actuarial 3- to 5-year rates of 54.5–72%.

Rasmussen et al. [42] stated that fractionated stereotactic radiotherapy accelerates hearing loss compared to observation alone, but their conclusion was based on their very low 2-year hearing preservation rate of 38% in the irradiated patients.

Most authors did not find a relation between tumor volume and hearing preservation. Hearing capacity deters even in untreated patients without tumor growth [50, 52]. The question of a threshold dose to the cochlea was mainly studied in radiosurgery series, but each study found a different cut off value between 3 and 6 Gy. It is well known that there are conditions independent of radiation dose, which influence hearing ability: Goddard et al. [13] found that fluid between the neuroma and

lateral end of the internal acoustic canal results in better hearing preservation in operated patients. Higher levels of fibroblast growth factor 2 were measured by Dilwali et al. [10] in patients with a better hearing capacity. Other factors for hearing deterioration are compression of the stato-acoustic nerve or of the surrounding vasculature from the tumor itself, loss of inner ear fluid or a hypointense signal on T2 MR images. Even dysfunction of the cochlea itself may contribute to hearing deterioration [45]. Long-term follow-up in radiosurgery studies revealed continuous hearing loss beyond 5 years after treatment [8, 44].

In some prospective long-term observational studies with exact audiological evaluation [14, 43, 48], a continuous hearing deterioration dependent on follow-up time was found, which is not very different to the deterioration after radiotherapy (Table 3). Breivik et al. [6] did not find a difference in hearing deterioration between observation and radiosurgery.

Conclusion

Hypofractionated stereotactic radiotherapy of acoustic neuroma leads to a very small—if any—increase in hearing deterioration compared to observation alone. Presbycusis is not responsible for this deterioration. Transient tumor enlargement is common and mostly without symptoms.

To date, considering variations and shortcomings in reporting of volumes, dose specifications and standardized recording of late sequelae, there is no strong evidence regarding superiority of any treatment schedule. Radiation of small- and medium-sized acoustic neuroma can be successfully performed by different highly conformal radiation techniques and doses as fractionated treatment or single low dose radiosurgery (both frame-based or frameless) with equal results regarding tumor control, hearing preservation, and side effects. Hypofractionation is more comfortable for the patient than time-consuming conservative fractionation regimens. It also serves as a serious alternative to frameless single dose radiosurgery.

Table 1 Literature summary of hypofractionation regimens for acoustic neuroma with respect to tumor volume and tumor control

| Authors | Year | Institute/ town | n | Regimen | Tumor volume | Follow- up (mo) | Local control | Size↓ | Transient size ↑ |
|--|------|---|-----------|--|--|------------------------------------|---|------------|---------------------|
| Lederman et al. [27] | 1997 | Staten Island Univ., NY | 23 16 | < 3 cm: 4x5 Gy (1 fx/wk) > 3 cm: 5x4 Gy (1 fx/wk) | 1.8 ml ⁱ 4.4 ml ⁱ | 16 ^h 21 ^h | 100% ^b | 61% 81% | |
| Makara et al. (abstract) [31] ^a | 2003 | Staten Island Univ., NY | 257 66 | < 3 cm: 4x5 Gy > 3 cm: 5x4 Gy | 1.6 cm ⁱ 3.6 cm ⁱ | 33 ⁱ | < 3 cm: 98% ^b > 3 cm: 100% ^b | | |
| Kalapurakal et al. [22] | 1999 | Temple Univ., Philadelphia, PA | 6 13 | 6x6 Gy (1 fx/wk) 6x5 Gy (1 fx/wk) | 3.5 cm ⁱ | 54 ^h | 100% | 53% | |
| Dziuba et al. (abstract) [11] | 2000 | Th. Jefferson Univ., Phila- delphia, PA | 59 | 9x4 Gy (2 fx/wk) 25x2 Gy | 1.8 cm ⁱ | 34 ⁵ | | | |
| Williams et al. [53] | 2003 | John Hopkins Univ., Balti- more, MD | 70 10 | < 3 cm: 5x5 Gy > 3 cm: 10x3 Gy | 1.4 cm ⁱ 2.8 cm ⁱ | 19 ^h | 100% ^b | 36% 60% | |
| Qiu et al. (abstract) [41] ^a | 2010 | John Hopkins Univ., Balti- more, MD | 385 | 5x5 Gy | 0.8 ml ^h | 41 ^h | | | |
| Meijer et al. [33] | 2003 | Amsterdam | 12 68 | < 1995: 5x4 Gy > 1995: 5x5 Gy | 2.5 cm ⁱ | 35 ⁱ | Act. 5 years 94% ^c | | |
| Ishihara et al. [19] | 2004 | Yamaguchi Univ., Japan | 14 24 | 15–20.5 Gy in 1–3 fx ^e 11.9–20.1 Gy in 1–3 fx ^f | 4.7 ml ⁱ 8.2 ml ⁱ | 27 ^h | 94% ^b | 18% | |
| Chang et al. [7] | 2005 | Stanford Univ., CA | 61 | 3x6–7 Gy | 1.9 cm ⁱ | 48 ^h | 98% | 48% | |
| Hansasuta et al. [15] ^a | 2011 | “ | 383 | 3x6 Gy (n=346) | 1.1 ml ^h | 43 ^h | Act. 5 years 96% ^d | | |
| Anderson et al. (abstract) [1] | 2007 | Madison, WI | 31 20 | 5x4 Gy (1 fx/wk) 25–28x1.8 Gy | 2.6 ml ⁱ | 13 ^h 16 ^h | Act. 5 years 88% Act. 5 years 100% | | |
| Ju et al. [21] | 2008 | Taipei | 21 | 18–20 Gy in 3 fx | 5.4 ml ⁱ | 15 ⁱ | 100% | 43% | |
| Sakanaka et al. [46] | 2011 | Kyoto | 13 12 | < 2003: 10–13x3 Gy > 2003: 5–6x4 Gy | 1.3 cm ^h 1.9 cm ^h | 87 ^h 40 ^h | 100% ^b 92% ^b | 58% 64% | 48% |
| Norén et al. (ISRS Paris) [38] | 2011 | Providence, RI | 37 | γ knife: 5x3 Gy | | | 86% ^d | 43% | |
| Badakhshi et al. (e-poster) [4] | 2011 | Berlin | 60 | 7x5 Gy 30x1.8 Gy | | 29 ^h | 98% | | |
| McWilliams et al. [32] | 2011 | Pittsburgh, PA | 10 | 5x5 Gy | 1.4 cm ^h | 13 ^h | 80% ^c | 20% | |
| Mahadevan et al. [30] | 2011 | Boston, MA | 10 | 5x5 Gy | | 22 ^h | 100% | 20% | |
| Ogino et al. (abstract) [39] | 2011 | Nagoya | 30 | 5x4.5–5.5 Gy | 0.8–5.5 ml ^h | 18–36 ^h | 3 years 80–100% | | 37% |
| Johnson et al. (abstract) [20] | 2012 | Atlanta, GA | 29 | 10x3 Gy | | 37 ⁱ | Act. 5 years 89% | 10% | |
| Polovnikov et al. [40] | 2013 | Novosibirsk | 12 | 5–6x4.5–5 Gy | | | | | |
| Karam SD et al. [25] | 2013 | Washington, DC | 37 | 5x5 Gy (n=35) 3x7 Gy (n=2) | 1.0 ml ^h | 51 ^h | 100% ^d Act. 5 years 91% | | |
| Morimoto et al. [34] | 2013 | Osaka | 25 | 18–25 Gy in 3–5 fx | | 80 ^h | 7 years 95% ^c | | |
| Current study | 2013 | Salzburg | 29 | 7x4 Gy ^g | 0.9 ml ^h | 89 ^h | 100% ^d 96.6% ^c | 76% | 59% |

Act. actuarial, fx fractions, fx/wk fractions per week, GR Gardner Robertson Grade, mo months, n number of treated patients

^aUpdate of a prior study, ^bIncrease in size, ^cIncrease ≥ 2 mm, ^dNo further intervention, ^eGR 1–2, ^fGR 3–5, ^gICRU dose, ^hMedian, ⁱMean

Table 2 Literature summary of hypofractionation regimens for acoustic neuroma with respect to hearing preservation

| Authors | Year | n | Regimen | n (audiol.) | Audiol. follow-up (mo) | A/B preservation | PTA difference | SDS difference |
|-------------------------------|------|-----|------------------------|-------------|------------------------|-------------------------------|-------------------------|----------------|
| Lederman et al. [27] | 1997 | 23 | < 3 cm: 4 × 5 Gy | 21 | | 20/21 ^a | | |
| | | 16 | > 3 cm: 5 × 4 Gy | 11 | | 1/11 ^a | | |
| Makara et al. (abstract) [31] | 2003 | 257 | < 3 cm: 4 × 5 Gy | 141 | | 105/141 ^a | | |
| | | 66 | > 3 cm: 5 × 4 Gy | 23 | | 15/23 ^a | | |
| Kalapurakal et al. [22] | 1999 | 6 | 6 × 6 Gy (1 fx/wk) | 9 | | 9/9 ^a | | |
| | | 13 | 6 × 5 Gy (1 fx/wk) | | | | | |
| Dziuba et al. (abstract) [11] | 2000 | 59 | 9 × 4 Gy (2 fx/wk) | | | 83% ^b | | |
| | | | 25 × 2 Gy | | | | | |
| Williams et al. [53] | 2003 | 70 | < 3 cm: 5 × 5 Gy | 32 | 19 ^d | 18/19 | 41 → 38 dB ^c | 68 → 67.5% |
| | | 10 | > 3 cm: 10 × 3 Gy | | | | | |
| Qiu et al. (abstract) [41] | 2010 | 385 | 5 × 5 Gy | 79 | 27 ^d | 29% | | |
| Meijer et al. [33] | 2003 | 12 | < 1995: 5 × 4 Gy | 55 | | Act. 5 years 61% ^f | | |
| | | 68 | > 1995: 5 × 5 Gy | | | | | |
| Ishihara et al. [19] | 2004 | 14 | 15–20.5 Gy in 1–3 fx | | | 13/14 | | |
| | | 24 | 11.9–20.1 Gy in 1–3 fx | | | | | |
| Chang et al. [7] | 2005 | 61 | 3 × 6–7 Gy | 48 | 48 ^e | 74% (26/35) | 35 → 49 dB | 72 → 61% |
| Hansasuta et al. [15] | 2011 | 383 | 3 × 6 Gy (n = 346) | 200 | 36 ^d | 76% (151/200) | | |
| Ju et al. [21] | 2008 | 21 | 18–20 Gy in 3 fx | 18 | | 72% ^g | | |
| Sakanaka et al. [46] | 2011 | 13 | < 2003: 10–13 × 3 Gy | 2 | 37 ^d | 0/2 | 32 → 60 dB | |
| | | 12 | > 2003: 5–6 × 4 Gy | 5 | 43 ^d | 4/5 | 18 → 40 dB | |
| Norén (ISRS Paris) [38] | 2011 | 37 | γ knife: 5 × 3 Gy | 37 | | 22/33 | | |
| McWilliams et al. [32] | 2011 | 10 | 5 × 5 Gy | 10 | 13 ^d | 1/4 | 57 → 65 dB | 49 → 32% |
| Ogino et al. (abstract) [39] | 2011 | 30 | 5 × 4.5–5.5 Gy | 17 | | 16/17 | | |
| Karam SD et al. [25] | 2013 | 37 | 5 × 5 Gy (n = 35) | 19 | 18 ^d | 11/14 | | |
| | | | 3 × 7 Gy (n = 2) | | | | | |
| Morimoto et al. [34] | 2013 | 25 | 18–25 Gy in 3–5 fx | 12 | | 6/12 | 30 → 57 dB | |
| Current study | 2013 | 29 | 7 × 4 Gy ICRU | 21 | 71 ^d | 6/12 | 39 → 64 dB | 74 → 38% |
| | | | | | | Act. 7 years 50% | | |

n number of treated patients, n (audiol.) number of patients with audiological follow-up, mo months, A/B Hearing class A or B, fx fractions, fx/wk fractions per week, Act. actuarial, PTA pure tone average, SDS speech discrimination score.

^aNo worsening, ^bPreserved functional hearing, ^cSpeech reception threshold, ^dMedian, ^eMean, ^fPhone use, ^gPreserved hearing class,

Table 3 Development of audiological data over time in patients with observation only (prospective studies) and its relation to the data from our own study

| | Stangerup [48] | Salzburg | Raut [43] | Hajioff [14] |
|-------------------------|-------------------|-------------------|-------------------|-------------------|
| Patients (n) | 573 | 21 | 55 | 40 |
| Follow-up time (months) | 47 ^a | 71 ^b | 80 ^a | 121 ^b |
| PTA ↑ (dB) | 13.6 ^a | 26.6 ^a | 28.4 ^a | 35.6 ^b |
| SDS ↓ (%) | 15.7 ^a | 36.2 ^a | 38.3 ^a | 40.3 ^b |

PTA pure tone average, SDS speech discrimination score, dB decibel

^aMean, ^bMedian

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Compliance with ethical guidelines

Conflict of interest. M. Kranzinger, F. Zehentmayr, G. Fastner, G. Oberascher, F. Merz, O. Nairz, H. Rahim, and F. Sedlmayer state that there are no conflicts of interest.

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