ORIGINAL ARTICLE

Fractionated stereotactic radiosurgery for vestibular schwannomas using cyberknife: A single institution experience

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Abstract

Objective: To assess tumour control, hearing preservation status, and complication ratio after fractionated stereotactic radiosurgery/radiotherapy by using CyberKnife device in patients with vestibular schwannomas.

Methods: This retrospective study was conducted at Izmir Ataturk Research and Tranining Hospital, Turkey, and comprised data of vestibular schwannomas patients treated with stereotactic radiosurgery/radiotherapy from March 2010 to December 2013. The patients were subjected to a dose ranging from 12 to 30Gy using CyberKnife system with an average of three fractions. SPSS 17 was used for data analysis. Paired t-test and Pearson's chi-square test were used to compare clinical parameters between groups. P<0.05 was considered significant.

Results: Of the 41 patients, 26(63.4%) were women and 15(36.6%) were men. The median follow-up duration after stereotactic radiosurgery/radiotherapy was 25 months (interquartile range: 9-44 months). Radiographic control evaluation ratio was 95.7% with a median follow-up of 3 years (IQR: 18.5 months). Results of 23(56%) patients showed stabile response, 17(42%) regression response and 1(2%) progression response. There were no statistically significant changes between pre- and post-stereotactic radiosurgery/radiotherapy symptoms (p>0.05). One (2.4%) patient reported new onset facial paresis.

Conclusion: Stereotactic radiosurgery/radiotherapy treatment of vestibular schwannomas resulted in a good ratio of tumour control. Hearing preservation status and ratios of toxicity were comparable to published literature.

Keywords: Vestibular schwannoma, Cyberknife, Stereotactic radiosurgery, Stereotactic radiotherapy. (JPMA 66: 1089; 2016)

Introduction

Vestibular schwannomas (VS) are benign tumours originating from vestibular constituent of the vestibulocochlear nerve. They make up about 6% of all brain tumours with an incidence of 9-13 per million people per year. When the tumours grow, they affect cranial nerves VII, VIII, and V, as well as the brainstem, causing tinnitus, hearing loss, dizziness, vertigo, and gait instability. The unilateral or sporadic tumours, making up 95% of VS, are the most common.[1-3] Hearing loss is the most common preliminary which presents symptoms and is generally followed by tinnitus, disequilibrium, trigeminal nerve dysfunction, vertigo, headache, facial nerve dysfunction, and diplopia. Symptoms generally result from tumour progression as it grows in the internal auditory canal through the cerebellopontine angle and finally leading to compression of neighbouring cranial nerves and the brainstem.[4,5]

Treatment options for VS involve observation, microsurgery, and radiation therapy. The optimal indication for each individual should be determined on the basis of the size and location of the tumour, as well as the hearing level and patient age. Most radiation therapy techniques by using alternative approaches to tumour targeting have been performed for the treatment of VS. These contain stereotactic radiosurgery (SRS) by using GammaKnife (GK) and CyberKnife (CK) or stereotactic radiotherapy (SRT) using CK or a linear accelerator (LINAC).[1,6,7] Even though surgery presents both instancy and low rates of recurrence, the potential morbidity of surgical resection of acoustic neuromas (ANs) can be meaningful. SRS or SRT supplies a non-invasive, single-session treatment sparing operative morbidity. The outcomes of SRS for ANs demonstrate high ratios of control, but may also end up being a risk to the neighbouring normal cranial nerves.[8,9] The present study was planned to assess tumour control, hearing preservation status and complication ratio after fractionated SRS/SRT by using CK device in patients with VS.

Patients and Methods

This retrospective study was conducted at Izmir Ataturk Research and Tranining Hospital, Turkey, and comprised VS patients treated with SRS/SRT between March 2010 and December 2013. Eligibility for the treatment included radiographic evidence of ANs with documented increase in the size or deterioration in the hearing that was shown by magnetic resonance imaging (MRI) or audiogram within the

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12 months prior to SRS/SRT. Patients with neurofibromatosis were excluded. Medical records were examined for age at diagnosis, gender, volume of tumours, dosage of total radiotherapy, fraction dose, fraction numbers, pre-treatment of hearing status, vertigo, tinnitus, headache and facial nerve status. All patients had had unilateral tumours.

Patients were treated by using CK (Accuray, Sunnyvale, California) system and immobilised by using termoplastic head and neck masks. Simulation computed tomography (CT) (Toshiba, Aquilion, Japan) was performed using 1.25mm thick slices by administering intravenous contrast material. CT and magnetic resonance (MR) T1-weighted images with contrast were obtained and transferred to the planning system of the CK computer. An individualised treatment plan was created for each patient. To better identify the target volume, CT and MR images were used by superimposing. Fusion of MR images was performed using gadolinium-dependent, T1-weighted slices, which showed better contrast absorption in tumour and also better imaging quality. Using MRI and CT scan images, the gross tumour volume (GTV) and critical organs were sketched. Planning tumour volume (PTV) was determined as GTV + 2 mm margin (Figure-1). Inverse planning was used to determine the dose to normal tissue, specifically the cochlea and vestibular organ. In evaluating the selected treatment plan, factors such as the homogeneity index and conformity index were considered.[10]

Patients underwent a post-treatment monitoring with an MRI scan, audiogram, and clinic visits six months after the completion of SRS/SRT for the first two years, then annually thereafter. Patients undergoing neurological examination and tumour volume responses were evaluated with MRI. Tumour volume with $\geq$2 mm reduction was called as regression response, unchanged volume called as stabile response and $\geq$2 mm increase was called progression response. Patients were asked the cause for selecting this type of treatment, advances of symptoms, development of any new symptoms since treatment. They were asked if their hearing had changed since the treatment, and if worsening noted, whether that condition has affected their daily life. Hearing loss was evaluated with Gardner Robertson scale.[11]

SPSS 17 was used for statistical analyses. Radiographic tumour control was defined as progression on the follow-up MRI according to a neuroradiologist interpretation. Kaplan-Meier product-limit method was used to calculate tumour control rate and patients were censored at the time of their last follow-up. Hearing preservation was defined as maintenance of Gardner- Robertson Grade 1- 2 hearing after SRS. The paired t-test and Pearson's chi-square test were used to compare clinical parameters between groups. P<0.05 was considered statistically significant.

Results

Of the 41 patients, 26(63.4%) were women and 15(36.6%) were men. The overall median age was 53 years (interquartile range [IQR]: 21-80 years) (Table-1). Mean tumour size was 20 $\pm$ 7.9 mm (range: 3.5-36mm). Nine (22%) patients underwent surgery prior to SRS/SRT. In the other 32(78%) patients, SRS/SRT was administered as the

Table-1: Characteristics of patients.

Age (median, range, years)	53, 21-80
Gender	**n (%)**
Male	26 (63)
Female	15 (37)
Location	**n (%)**
Right	19 (46)
Left	22 (54)
Prior surgery rate	**n (%)**
Yes	9 (22)
No	28 (78)
Hearing loss rate	**%**
Pre-FSR	61
Partial	34
Complete	
Post-FSR	
Partial	56
Complete	41

FSR: Fractionated stereotactic radiotherapy.

Table-2: Treatment characteristics of patients.

Characteristics	Range	Median
Fraction number	1-7	3
Fraction dose (Gy)	4.25 - 13	6
Tumour volume (mm)	3.5 - 36	20
HI	1.08 - 1.32	1.16
CI	1.14 - 1.69	1.28
nCI	1.09 - 1.47	1.20
Dose Prescription isodose line (%)	75 - 92	85
Coverage (%)	96.23 - 99.88	98.80

HI: Homogeneity index
CI: Conformity index
nCI: new Conformity index.

Table-3: Treatment complications of non-auditory.

	Pre-treatment [n (%)]	Post-treatment [n (%)]	p
Disequilibrium	22 (54)	14 (34)	0.478
Tinnitus	26 (63)	18 (44)	0.377
Headache	21 (51)	15 (37)	0.565
Facial paresis	8 (20)	9 (22)	0.853

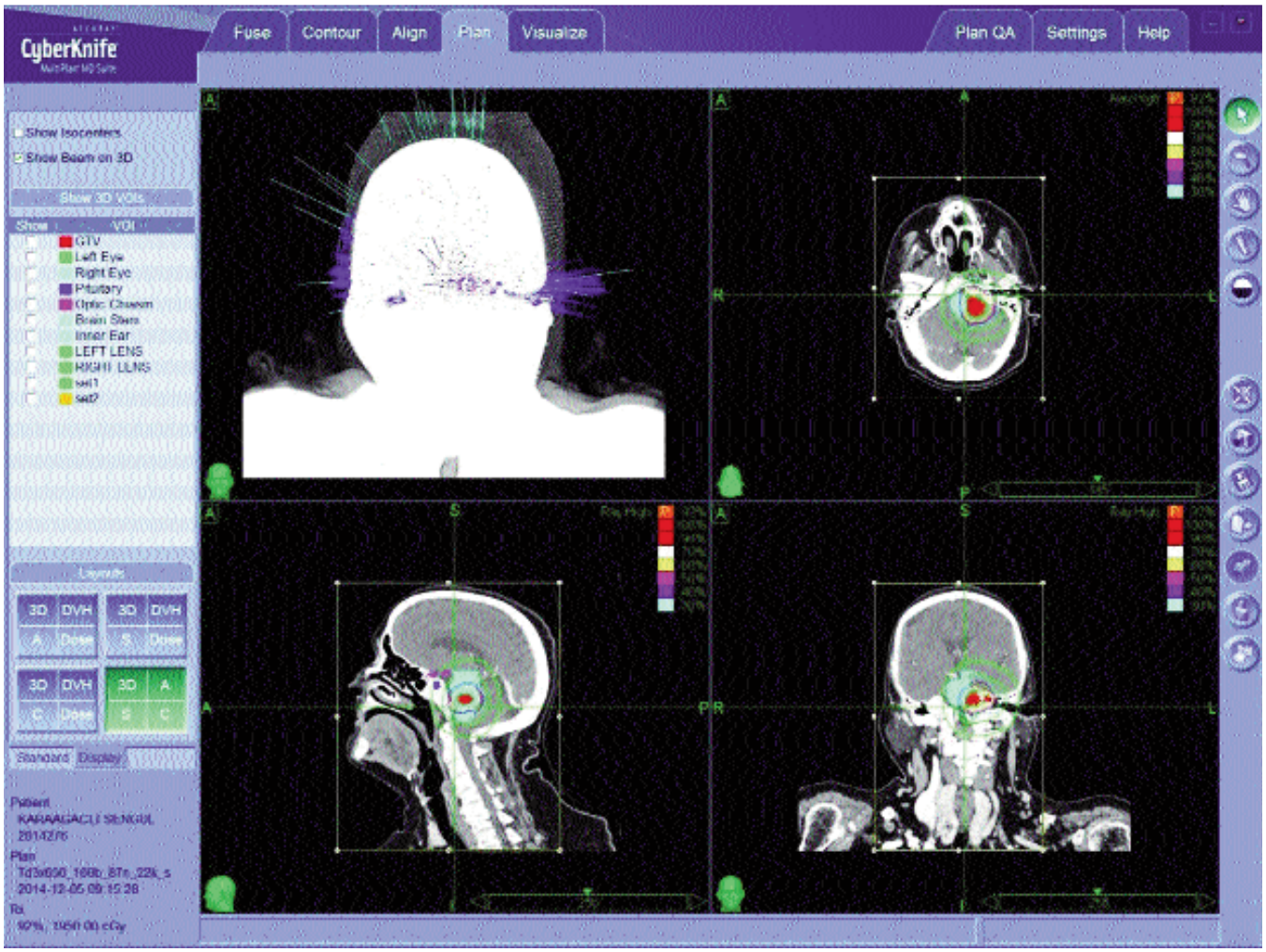

Figure-1: SRT treatment planning in a single patient.

SRT: Stereotactic radiotherapy

initial therapy. Prior to SRS/SRT Gardner-Robinson score for patients was 1 in 14(34%) patients. The median follow-up time was 25 months (IQR: 9-44 months). Results of 23(56%) showed stabile response, 17(42%) regression response and 1(2%) progression response. Radiological tumour control ratio was 95.7% at a median follow-up of three years [(IQR: 18.5 months), (Figures-2,3)].

Tumours were administered a median dose of 18 Gy (IQR: 12-30Gy) and median fraction of 3 (IQR: 1-7) (Table-2). Overall, 30(73%) patients were administered 3 fractions and total 18Gy dose.

It was found that 2(5%) patients had good hearing, 22(54%) had non-serviceable hearing and 17(42%) had poor hearing after SRS/SRT. Moreover, 3(7.3%) patients who had poor hearing before SRS/SRT presented worsening hearing. Patients who had good and non-serviceable hearing before SRS/SRT reported no changes in hearing. Hearing preservation rate was 81.7% with follow-up of three years (IQR: 18.5 months).

In 1(2.4%) patient there was hydrocephali duo to tumour progression. Ventriculoperitoneal (VP) shunt was performed on that patient. There were no statistically significant changes between pre- and post-SRS/SRT symptoms of patients. But 1(2.4%) patient presented a new onset facial paresis. Some of the patients who reported tinnitus, facial paresis, disequilibrium and headache presented resolution of symptoms. There were no reports of trigeminal neuralgia (TGN) (Table-3).

Discussion

The alternatives for treatment of the ANs involve surgery, radiosurgery and fractionated SRT. Various modern surgical

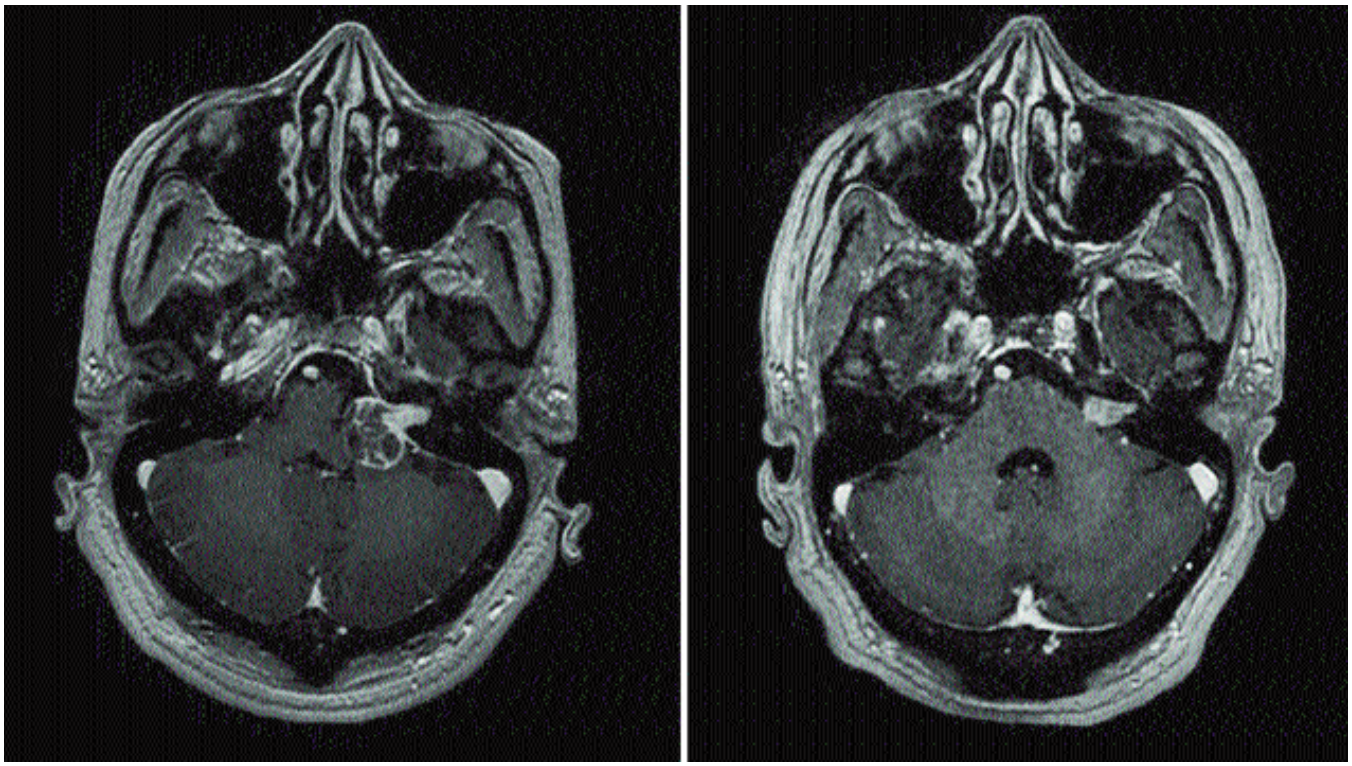

Figure-2, 3: A patient's pre and post SRS MR images.

SRS: Stereotactic radiosurgery. MR: Magnetic resonance

options offer whole tumour removal with both anatomic and functional preservation of the facial nerve in nearly 90% of patients.

For surgery, the capacity for preservation of the facial nerve might change inversely with size of the ANs. Gormley et al. presented the preservation of postoperative facial nerve function and demonstrated preserved function (House Brackman grade I or II) in 96% of minor tumours (<2 centimetres diameter), 74% of medium tumours (2.0-3.9cm), and 38% of large tumours (4.0cm and greater). Sterkers et al. presented that the ratio of preserved facial function (grade I or II) increased from 20% to 52% for large tumours (larger than 3cm), from 42% to 81% for medium tumours (2-3cm in diameter) and from 70% to 92% for minor tumours (up to and involving 2cm in diameter).[12-14]

Surgical resection was once the traditional indication for VS. Today, however, continuous advancement in imaging technology and increased awareness of VS favour the early diagnosis of small- and medium-sized intracranial VS tumours. Therefore, the current management strategy for VS has shifted to observation, microsurgery, and radiation therapy, with an emphasis on the preservation of facial nerve function and hearing.[15]

Ever further progress in radiosurgery for VS has been achieved in the past few years, and the requirements essential to performing a successful radiosurgical treatment have become available with several platforms (GK, various LINACs and, most recently, CK). Gamma radiosurgery, representing the gold standard in the SRS system, has been clinically proven to be effective in VS tumour control, but its hearing preservation rate, ranging from 55-79%, is not satisfactory as a functional preservation-oriented treatment option.[16] Recently, the CK system has emerged as a revolutionary treatment not only for VS but also for the whole body, owing to its robotic arm and computerised image processing, enabling real-time image guidance, and its dynamic tracking software, allowing for precise irradiation of the target volume. However, to our knowledge, published articles discussing the treatment of VS with CK are limited. Therefore, our study aimed to evaluate the clinical outcomes, including tumour control and hearing retention, and possible prognostic factors of hearing loss in VS patients treated with CK.[1,17,18]

Tumour control has been achieved in VS patients treated with SRS, including those with the CK system. It was reported in recent studies that high ratios of tumour control with various radiation treatment techniques involving GK-based SRS, LINAC-based SRS, conventionally fractionated SRT, proton-

beam radiation therapy. Outcomes from publications with the frameless CK-based fractionated stereotactic radiotherapy (FSR) by using the CK system have also been identical.[11,19,20] Ishihara et al. presented a 94% radiographic tumour control ratio at a median follow-up of 27 months by using the same system while the Stanford series presented a radiographic control ratio of 98% at a mean follow-up of 48 months.[19] In their late update, the Stanford group presented an interventional tumour control ratio of 99 and 96% at three and five years, respectively, with the use of multisession SRS outcomes. In our study, 23(56%) had had stabile response, 17(42%) regression response and 1(2%) progression response with a median follow-up 25 months. Our patients had 95.7% radiographic tumour control rate at three years. SRS has been developed to reduce the toxicity in VS radiotherapy. It is generally reported that after SRS in VS, several adverse effects can be encountered, such as hearing loss, facial nerve damage, radiation induced trigeminal neuropathy, headache, tinnitus, imbalance.[1] In this study, condition of three patients worsened from poor hearing before SRS to none hearing after SRS. There were no change in hearing status of patients who had good or non-serviceable before SRS. In one patient there was hydrocephali duo to tumour progression. Some symptoms like imbalance, tinnitus, headache and facial paresis were decreased before SRS treatment.

Two major treatment options are available for patients with VS, namely microsurgery and radiosurgery. Radiosurgical treatment for VS is an alternative to microsurgery. Two modalities in VS for tumour control showed no statistical significance in tumour growth control between the two groups. It is associated with a lower rate of immediate and long-term development of facial and trigeminal neuropathy, postoperative complications and hospital stay. Radiosurgery yields better measurable hearing preservation than microsurgery and equivalent serviceable hearing preservation rate and tumour growth control.[21]

Conclusion

VS patients receiving SRS treatment achieved an excellent tumour control rate of 95.7% and good hearing preservation with minimal toxicity on the cranial nerves. Also, FSR can be indicated for residual or re-growing tumours in patients who had previous surgical resections. SRS/SRT using CK is a preferable treatment choice with a tolerable side effects and favourable local tumour control.

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Conflict of Interest: No.

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