



Review Article

Single Fraction Stereotactic Radiosurgery (SRS) versus Fractionated Stereotactic Radiotherapy (FSRT) for Vestibular Schwannoma (VS)

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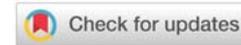
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Abstract

Vestibular schwannoma (VS), also referred to as acoustic neuroma, is one of the common benign intracranial tumors with rising incidence due to improved and more frequent neuroimaging. These common tumors of the cerebellopontine angle arise from the Schwann cells of vestibulocochlear nerve, and management with main therapeutic modalities of surgery and radiation therapy (RT) may be considered while observation is also an option for selected patients. Intervention may be required for VS although these slow growing tumors may follow an indolent disease course. Decision for management with a given modality should take into account several factors including lesion location, size, and closeness to critical structures, age, symptomatology, patient preferences, and logistical issues. RT has traditionally served as a viable treatment modality for VS management and radiosurgical applications in the forms of single fraction Stereotactic Radiosurgery (SRS) or Fractionated Stereotactic Radiotherapy (FSRT) have been utilized for treatment of patients. Selection of dose and fractionation is critical for safe and effective radiosurgical treatment of VS. Studies of SRS and FSRT for VS management consistently reported high tumor control rates with both modalities. It appears that smaller VS lesions are well suited for single dose SRS while FSRT may serve as an excellent treatment alternative for management of larger VS lesions particularly for improving the toxicity profile of treatment. Herein, we assess the use of single fraction SRS versus FSRT for management of VS in light of the literature with focus on recent trends and future perspectives.

Introduction

Vestibular schwannoma (VS), formerly referred to as acoustic neuroma, is one of the common benign intracranial tumors with rising incidence due to improved and more frequent neuroimaging [1-3]. These common tumors of the cerebellopontine angle arise from the Schwann cells of vestibulocochlear nerve, and management with main therapeutic modalities of surgery and radiation therapy (RT) may be considered while observation is also an option for selected patients [4-8]. Several studies have also addressed multimodality management of VS to improve the toxicity profile of treatment [9-11]. Intervention may be required

for VS although these slow growing tumors may follow an indolent disease course. Affected patients may suffer from a plethora of symptoms including headache, dizziness, tinnitus, vertigo, hearing loss, incoordination or instability with gait disturbances, cranial nerve symptoms as a result of facial or trigeminal nerve involvement, facial dysesthesia or spasms, dysphagia, dysarthria, cerebellar seizures, symptoms of increased intracranial pressure and respiratory distress [11,12]. Typical location for VS is the internal auricular canal or cerebellopontine angle. Tumors may be in intricate association with critical neurovascular structures, and symptomatology may occur due to compression with the mass effect which may result in substantial quality of life deterioration [12].



Decision for management with a given modality should take into account several factors including lesion location, size, and closeness to critical structures, age, symptomatology, patient preferences, and logistical issues [12]. RT has traditionally served as a viable treatment modality for VS management and radiosurgical applications in the forms of single fraction Stereotactic Radiosurgery (SRS) or Fractionated Stereotactic Radiotherapy (FSRT) have been utilized for treatment of patients. Selection of dose and fractionation is critical for safe and effective radiosurgical treatment of VS. Surgery has been a major management modality for VS either with the translabyrinthine approach, middle cranial fossa approach, or the retrosigmoid approach also referred to as the retromastoid approach or suboccipital approach. Surgical modalities have their unique advantages and drawbacks for VS management. Hearing preservation may be provided with the middle cranial fossa approach particularly for smaller VS lesions. Retrosigmoid approach may offer the advantage of superior facial nerve preservation albeit with the risk of cerebrospinal fluid fistula and pain in the postoperative period. While the translabyrinthine approach may typically lead to complete loss of hearing, it may serve as a therapeutic option for management of patients who suffer from larger tumors leading to poorer hearing at the preoperative period. Toxicity profile of surgery has clearly been improved by incorporation of modernized microsurgical techniques and equipment, however, patients undergoing surgery for VS may suffer from several complications including hearing loss, dysfunction of facial nerve or other cranial nerves, postoperative headache, and cerebrospinal fluid leakage which may lead to deterioration in quality of life. Combined modality management with less extensive surgical resection followed by irradiation may offer a viable therapeutic option for selected patients with VS to achieve reduced toxicity while maintaining local control. In the context of irradiation for VS, a continuing debate is about the optimal selection of radiotherapeutic modality as conventionally fractionated RT or radiosurgical strategies in the form of SRS and FSRT. Herein, we assess the use of single fraction SRS versus FSRT for management of VS in light of the literature with focus on recent trends and future perspectives.

SRS versus FSRT for VS management

Since its inception, radiosurgery has been judiciously utilized for precisely focused irradiation of various central nervous system disorders and tumors throughout the human body with promising treatment results [12-49]. Radiosurgery exerts its effects of focused and ablative treatment by several mechanisms such as vascular endothelial damage. Extreme hypofractionation by radiosurgery induces unique effects for successful management of several tumors. A high dose per fraction is required for achieving ablative treatment, however, delivery of very high doses in a single fraction should be performed under robust immobilization and image guidance to avoid untoward toxicity. Fractionation of treatment may be used to exploit the advantage of reoxygenation between fractions which may render the tumors more radiosensitive to subsequent treatment fractions. Also, repair of normal tissues between treatment fractions may result in reduced risk

of adverse effects and an improvement in the toxicity profile of treatment. In the context of VS radiosurgery, encouraging outcomes have been achieved by both SRS and FSRT [49-57].

In the study by Meijer et al. assessing single fraction versus fractionated linear accelerator based radiosurgery for VS, 49 patients were treated with single fraction SRS and 80 patients were treated with FSRT [51]. Mean tumor diameter was 2.6 cm in the single fraction SRS group and 2.5 cm for the fractionated group with no statistical difference, and mean follow up duration was 33 months for both groups. Fractionated treatment group received either 5 x 4 Gy or 5 x 5 Gy at the 80% isodose by use of a relocatable stereotactic head frame. Single fraction SRS dose was either 10 Gy or 12.5 Gy at the 80% isodose by use of an invasive stereotactic head frame [51]. Both fractionation schemes were comparable in terms of 5-year local control probability, 5-year facial nerve preservation probability, and 5-year hearing preservation probability without statistically significant difference [51]. However, 5-year trigeminal nerve preservation rate was higher with the fractionated scheme, which was statistically significant ($p = 0.048$) [51]. The authors concluded that single fraction treatment appeared to be as good as fractionated treatment except for the small difference in trigeminal nerve preservation rate in favor of fractionated schedule [51].

In the study by Combs et al. evaluating outcomes with SRS versus FSRT for linear accelerator based VS management, both treatment schemes were well tolerated [52]. For the 202 VS lesions in 200 patients, median total FSRT dose was 57.6 Gy for 172 patients receiving FSRT and median SRS dose was 13 Gy single dose for 30 patients receiving single fraction SRS with the linear accelerator [52]. Tumor size was ≤ 1 cm for 37 lesions (18%), ≤ 2 cm for 101 lesions (50%), ≤ 3 cm for 48 lesions (24%), ≤ 4 cm for 15 lesions (7%), and ≥ 4 cm for 1 lesion (1%) [52]. Local control rates were found to be comparable with both treatment schemes, and SRS with a single dose of ≤ 13 Gy was found to be a safe alternative to FSRT [52]. The authors concluded that FSRT could be safely administered for management of VS of all sizes while SRS should be reserved for smaller VS lesions [52].

In the study by Collen et al. comparatively evaluating outcomes of SRS and FSRT for linear accelerator based VS management, overall 5-year local control rate was 95% at a median follow-up of 62 months [53]. Mean largest tumor diameter was 16.6 mm in the single fraction SRS group and 24.6 mm for the FSRT group [53]. Median single dose for single fraction SRS was 12.5 Gy prescribed to the 80% isodose line encompassing the target volume [53]. FSRT group received either 10 x 3-4 Gy or 25 x 2 Gy prescribed to the 100% isodose line and 95% isodose line encompassed the planning target volumes for these patients [53]. Four year probability of preservation of useful hearing was 59% with SRS and 82% with FSRT [53]. The authors concluded that linac-based RT resulted in good local control and acceptable clinical outcome for small to medium sized VS, however, radiosurgery remained to be a challenge for large VS with Koos grade of 3 or more given the increased risk of facial nerve neuropathy [53].



In the study by Anderson et al. assessing long term outcomes of SRS and FSRT for linear accelerator based VS, median tumor maximum dimension was 1.5 cm for the SRS group and 1.7 cm for the FSRT group [54]. Median tumor volume was 0.66 cc for SRS group and 1.35 cc for FSRT group [54]. Single fraction SRS median peripheral dose was 12.5 Gy. FSRT group received either 45 to 50.4 Gy in 25 to 28 fractions with conventional fractionation or 5 x 4 Gy with a once weekly hypofractionated schedule [54]. Five year progression free rates were equivalent with no differences in 5-year rates of trigeminal and facial nerve toxicity, vestibular dysfunction, or tinnitus [54].

In the systematic review by Persson et al. evaluating SRS versus FSRT for tumor control in VS patients, progression free survival rates were on the order of 92% to 100% for both treatment options [55].

In the study by Udawatta et al. assessing outcomes of SRS, FSRT and hypoFSRT for VS, mean largest dimension of preoperative tumor volume was 1.8 cm in FSRT cohort, 1.3 cm in SRS cohort, and 1.4 cm in hypoFSRT cohort [55]. Median dose for single fraction SRS was 12 Gy, and patients in the FSRT and hypoFSRT cohorts received 50.4 Gy in 28 fractions and 25 Gy in 5 fractions, respectively [55]. Excellent tumor control rates were achieved by all modalities [56]. However, relatively increased incidence and shorter time to hearing deterioration was reported in the SRS cohort compared to the FSRT and hypoFSRT cohorts [56].

A recent study comparatively evaluating linear accelerator based SRS versus hypoFSRT delivered in 3 or 5 fractions for VS reported high rate of local control with no significant differences between treatment schedules [57]. Median tumor volume was 1 cc for the whole patient group. Single session SRS dose was 12 Gy while patients in hypoFSRT group received either 18–21 Gy in 3 fractions or 25 Gy in 5 fractions. Overall local control rate was 93.4% for the whole group while local control rates for SRS and hypoFSRT groups were 89.2% and 94.7% – 97.4% respectively [57].

Overall, studies of SRS and FSRT for VS management consistently reported high tumor control rates with both modalities [49–57]. It appears that smaller VS lesions are well suited for single dose SRS while FSRT may serve as an excellent treatment alternative for management of larger VS lesions particularly for improving the toxicity profile of treatment. Future randomized trials are needed to shed light on optimal management of patients with VS.

Conclusion and future perspectives

There have been unprecedented advances and substantial improvements in the radiation oncology discipline such as contemporary irradiation technologies such as Intensity Modulated Radiation Therapy (IMRT), Image Guided Radiation Therapy (IGRT), Breathing Adapted Radiation Therapy (BART), Adaptive Radiation Therapy (ART) as well as radiosurgical applications along with automatic segmentation techniques and incorporation of molecular imaging for improved staging and target definition of several cancers [12–70]. State of the art

radiosurgical applications along with improved neuroimaging technologies have paved the way for widespread adoption of radiosurgery to serve as the primary therapeutic modality for several intracranial disorders and tumors. In the context of VS radiosurgery, studies of SRS and FSRT consistently reported high tumor control rates with both modalities. It appears that smaller VS lesions are well suited for single dose SRS while FSRT may serve as an excellent treatment alternative for management of larger VS lesions particularly for improving the toxicity profile of treatment. Future randomized trials are needed to shed light on optimal management of patients with VS.

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