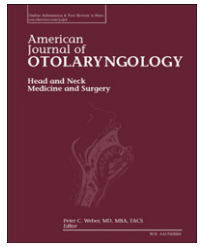
Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/amjoto



Initial radiographic tumor control is similar following single or multi-fractionated stereotactic radiosurgery for jugular paragangliomas☆,☆☆

Daniel Schuster, MD[a], *Alex D. Sweeney, MD*[b], *Mark J. Stavas, MD*[c], *Kyrollos Y. Tawfik, BS*[d], *Albert Attia, MD*[c], *Anthony J. Cmelak, MD*[c,1], *George B. Wanna, MD*[a,*]

[a] *Department of Otolaryngology–Head and Neck Surgery, Vanderbilt University Medical Center, Nashville, TN*
[b] *Bobby R. Alford Department of Otolaryngology–Head and Neck Surgery, Baylor College of Medicine, Houston, TX*
[c] *Department of Radiation Oncology, Vanderbilt University Medical Center, Nashville, TN*
[d] *College of Medicine, Meharry Medical College, Nashville, TN*

ARTICLE INFO

Article history:
Received 29 October 2015

ABSTRACT

Objective: To evaluate radiographic tumor control and treatment-related toxicity in glomus jugulare tumors treated with stereotactic radiosurgery (SRS).
Study design: Retrospective chart review.
Setting: Tertiary academic referral center.
Patients: Glomus jugulare tumors treated with SRS between 1998 and 2014 were identified. The data analysis only included patients with at least 18 months of post-treatment follow up (FU).
Intervention: Patients were treated with either single fraction or fractionated SRS.
Main outcome measure: Patient demographics and tumor characteristics were assessed. Radiographic control was determined by comparing pre and post treatment MRI, and was categorized as no change, regression, or progression.
Results: Eighteen patients were treated with SRS, and 14 met inclusion criteria. Median age at treatment was 55 years (range 35–79), and 71.4% of patients were female. 5 patients (35.7%) received single fraction SRS (dose range 15–18 Gy), and 9 (64.3%) fractionated therapy (dose 3–7 Gy × 3–15 fractions). Median tumor volume was 3.78 cm^3 (range 1.15–30.6). Median FU was 28.8 months (range 18.6–56.1), with a mean of 31.7 months. At their last recorded MRI, 7 patients (50%) had tumor stability, 6 (42.9%) had improvement, and 1 (7.1%) had progression. Disease improvement and progression rates in the single fraction group were 40% and 0%, and in the multiple-fraction group, 44.4% and 11.1%, respectively. There was no statistically significant difference in disease improvement ($p = 0.88$) or progression ($p = 0.48$) rates between groups (unpaired t-test).
Conclusions: At a median follow up of 28 months, both single fraction and fractionated SRS appear to have comparable radiographic tumor control outcomes and toxicity profiles.

☆ Financial material and support: Internal departmental funding was utilized without commercial sponsorship or support.
☆☆ Conflict(s) of interest to declare: There are no relevant conflicts of interest to disclose.
* *Corresponding author at:* Division of Otology/Neurotology, Bill Wilkerson Center for Otolaryngology & Communication Sciences 7209 Medical Center East, South Tower 1215 21st Avenue South Nashville, TN 37232-8605. Tel.: +1 615 322 6180; fax: +1 615 343 9556.
E-mail address: george.wanna@vanderbilt.edu (G.B. Wanna).
[1] Co-senior author.

http://dx.doi.org/10.1016/j.amjoto.2016.01.002
0196-0709/

1. Introduction

Jugular paragangliomas (JPs) are rare, typically benign, tumors of neuroendocrine origin arising from the autonomic ganglia around the jugular bulb. Their underlying pathogenesis is an area of ongoing research [1]. Expansion in the confined space of the jugular foramen can compromise neurologic and vascular structures [2–4]. Tumors that grow on serial imaging or that present with lower cranial neuropathies (IX, X, XI, XII) [5] often require treatment to mitigate the risks of continued growth.

The pathophysiology, epidemiology, diagnosis, and treatment for JPs have been recently described [6,7]. Management options include observation, surgical resection, fractionated external beam radiation therapy (EBRT), and stereotactic radiosurgery (SRS). The most appropriate therapy for a given tumor accounts for the location and extent of the tumor, patient age and health, the anticipated morbidity of treatment and patient preferences [8]. Historically, gross total resection was the preferred treatment, offering an excellent chance of cure at the expense of lower cranial nerve function. However, newer evidence has suggested that less invasive techniques may offer similar tumor control rates and/or improved overall quality of life. In particular, analyses of a "wait-and-scan" approach and cranial nerve-sparing subtotal resection have been explored by our center [9,10].

Radiosurgery has emerged as a promising consideration in the management of JPs [11–19]. A recent meta-analysis showed 97% radiographic tumor control across all studies [20]. However, the outcome differences between single fraction and fractionated SRS remain unexplored. In the present study, we aim to evaluate radiographic JP control in a series of patients treated with LINAC SRS at a single tertiary care referral center and compare radiographic control rates between patients receiving single and fractionated treatment.

2. Subjects and methods

Institutional review board approval was obtained, and a database query of patients treated for JP between 1998 and 2014 at Vanderbilt University Medical Center was performed. Patients who were treated with SRS were identified. Patients undergoing SRS chose to do so after being counseled about all treatment modalities and the associated risks and benefits of each. Patients with less than 18 months of follow up were excluded. Patient demographic data, tumor characteristics, radiation dose, and fractionation scheme were recorded. Patients were divided into two subcategories for data analysis: single and multiple fraction SRS.

Radiographic control was the primary outcome, and was assessed by comparing the most recent post-treatment MRI with the pre-treatment MRI. A staff neuroradiologist reviewed each MRI. Disease progression was defined as an increase of ≥2 mm in any axial dimension of the tumor, whereas improvement was defined as a decrease of ≥2 mm. Means, medians, and ranges were used to summarize continuous features, and categorical data were displayed as frequency counts and percentages. Rates of radiographic control were compared using the unpaired t-test, and p-values < 0.05 were considered to be statistically significant.

Table 1 – Tumor characteristics and dosimetric variables.

Pretreatment tumor volume (cm^3)	
Mean	7.65
Median	3.78
Range	1.15–30.60
Prescription isodose line (%)	
Mean	76.5
Median	81
Range	39-90
Dose constraints (Gy)	
Cochlea maximum dose	12.5 (single fraction), 22 (5 fractions)
Brainstem maximum dose	12.5 (single fraction), 25 (5 fractions)
Parotid	<20

All patients underwent a pretreatment contrast enhanced thin-sliced MRI, which was fused to a high-resolution CT obtained at the time of simulation to assist in treatment volume design. Dosimetric planning was performed using BrainLab iPlan® RT software. Early patients in the series were treated with frame-based immobilization using a Clinac 4 (Varian, Palo Alto, CA) and Radionics treatment planning systems, and more recent patients were treated with the Novalis TX™ and ExacTrac® treatment systems. An aquaplast mask with bite block was used for non-invasive immobilization in these patients. Tumor characteristics, and dosimetric variables are listed in Table 1.

3. Results

Fourteen patients met inclusion criteria. Patient demographic details are summarized in Table 2. The average age at treatment was 55 years (range, 35–79 years; median, 55 years), and 10 patients (71.4%) were female. Five patients (35.7%) received single fraction SRS, and 9 (64.3%) underwent fractionated treatment. In the single fraction group, the radiation dose ranged from 15–18 Gy. Patients undergoing fractionated SRS underwent 3–15 fractions ranging from 3 to 7 Gy per fraction with a median dose of 25 Gy. Median tumor volume was 3.78 cm^3 (range 1.15–30.6). There was no statistical difference in tumor volume between patients in each group ($p = 0.99$).

Mean clinical follow-up length was 31.7 months (median 28.8, range 18.6–56.1). Three patients (21.4%) had previously undergone at least one surgery for resection of their JP. The other 11 patients (78.6%) had SRS without prior surgical intervention.

Radiographic control, defined as either stability or decrease in tumor size on MRI at the last recorded follow-up, was 92.9%. Seven patients (50%) had no change in tumor size, while decreased tumor size was noted in 6 patients (42.9%). Only 1 patient (7.1%) had radiographic progression. In the single fraction group, disease improvement was noted in 40% of the patients, and the disease progression rate was 0%. In the multiple fraction group, these rates were 44.4% and 11.1%, respectively. There was no statistically significant difference between groups in disease improvement rate ($p = 0.88$) or disease progression rate ($p = 0.48$). There were no acute radiation toxicities noted. One patient developed a cranial nerve XII palsy following fractionated SRS, presenting as tongue deviation. However, there was no statistically significant