Gamma Knife radiosurgery of vestibular schwannoma case series

2022

In a study, 51 planning scenarios of 17 patients with VS were planned for GKSRS using forward plan (FP), inverse plan (IP), and hybrid plan (HP) in Leksell GammaPlan (LGP10.1) using the TMR10 algorithm. The planning images were obtained using the following MRI (GE, USA) scan parameters: T1W images-MPRAGE sequence, FOV-256mmx256mm, matrix size-512mmx512mm, and the slice thickness 1 mm. The total dose was prescribed 12Gy and normalized at 50% isodose level.

The plan parameters were compared dosimetrically by maintaining FP as a base plan. The statistical analysis, including one-factor, repeated measures ANOVA and Bonferroni correction tests, were performed. The p-value for planning parameters such as brainstem dose, beam ON time, and gradient index significantly favored HP.

Overall, results show that HP is an efficient method for GKSRS of VS. The p-value was less than 0.001 and statistically significant for various plan indices $^{1)}$

2019

A study included 307 patients who had serviceable hearing (Gardner Robertson Scale [GR] grade 1 or 2, speech discrimination score \geq 50%, pure tone audiometry average \leq 50 dB) at the time of SRS. Johnson et al. evaluated parameters that included age, tumor volume, hearing status, disequilibrium, tinnitus, Koos grading scale, sex, and tumor margin dose. The Pittsburgh Hearing Prediction Score (PHPS) was evaluated as a method to predict long-term hearing outcomes in these cases.

At a median of 7.6 years after SRS (range 1-23 years), tumor control was achieved in 95% of patients. The overall serviceable hearing preservation rate was 77.8% at 3 years, 68.8% at 5 years, and 51.8% at 10 years. The PHPS assigns a total of 5 points based on patient age (1 point if < 45 years, 2 points if 45-59 years, and 3 points if \geq 60 years), tumor volume (0 points if < 1.2 cm3, 1 point if \geq 1.2 cm3), and GR grade (0 points if grade 1 hearing, 1 point if grade 2 hearing) The serviceable hearing preservation rate was 92.3% at 10 years in patients whose score total was 1. In contrast, none of the patients whose PHPS was 5 maintained serviceable hearing at 10 years (p < 0.001).

SRS resulted in a high rate of long-term tumor control and cranial nerve preservation. The Pittsburgh Hearing Prediction Score (PHPS) helped to predict long-term hearing preservation rates in patients who underwent SRS when they still had a serviceable hearing. The best long-term hearing preservation rates were found in younger patients with smaller tumor volumes ²⁾.

2016

The records of 420 patients treated with GKRS for VS with a median marginal dose of 11 Gy were retrospectively analyzed. Patients with neurofibromatosis Type 2 or who had undergone treatment for

VS previously were excluded.

Klijn et al assessed tumor control and complication rates with chart review and used the Cox proportional hazards model to identify predictors of tumor control. Preservation of serviceable hearing, defined as Gardner-Robertson Class I-II, was evaluated in a subgroup of 71 patients with serviceable hearing at baseline and with available follow-up audiograms.

The median VS tumor volume was 1.4 cm(3), and the median length of follow-up was 5.1 years. Actuarial 5-and 10-year tumor control rates were 91.3% and 84.8%, respectively. Only tumor volume was a statistically significant predictor of tumor control rate. The tumor control rate decreased from 94.1% for tumors smaller than 0.5 cm(3) to 80.7% for tumors larger than 6 cm(3). Thirteen patients (3.1%) had new or increased permanent trigeminal nerve neuropathy, 4 (1.0%) had new or increased permanent facial weakness, and 5 (1.2%) exhibited new or increased hydrocephalus requiring a shunting procedure. Actuarial 3-year and 5-year hearing preservation rates were 65% and 42%, respectively.

The 5-year actuarial tumor control rate of 91.3% in this cohort of patients with VS compared slightly unfavorably with the rates reported in other large studies, but the complication and hearing preservation rates in this study were similar to those reported previously. Various factors may contribute to the observed differences in reported outcomes. These factors include variations in treatment indication and in the definition of treatment failure, as well as a lack of standardization of terminology and of evaluation of complications. Last, differences in dosimetric variables may also be an explanatory factor ³⁾.

2015

lorio-Morin et al. conducted a single-center, retrospective evaluation of patient undergoing GKRS for Koos grade 4 vestibular schwannomas. We evaluated clinical, imaging, and treatment characteristics and assessed treatment outcome. Inclusion criteria were tumor size of \geq 4 cm and follow-up of at least 6 months. Patients with neurofibromatosis type 2 were excluded. Primary outcomes measured were tumor control rate, hearing and facial function preservation rate, and complications. All possible factors were analyzed to assess clinical significance.

Sixty-eight patients met inclusion criteria. Median follow-up was 47 months (range, 6-125 months). Baseline hearing was serviceable in 60%. Median tumor volume at radiosurgery was 7.4 cm (range, 4-19 cm). The median marginal dose used was 12 Gy at the 50% isodose line. Actuarial tumor control rates were 95% and 92% at 2 and 10 years, respectively. Actuarial serviceable hearing preservation rates were 89% and 49% at 2 and 5 years, respectively. Facial nerve preservation was 100%. Clinical complications included balance disturbance (11%), facial pain (10%), facial numbness (5%), and tinnitus (10%). Most complications were mild and transient. Hydrocephalus occurred in 3 patients, requiring ventriculoperitoneal shunt insertion. Larger tumor size was significantly associated with persisting symptoms post-treatment.

Patients with Koos grade 4 vestibular schwannomas and minimal symptoms can be treated safely and effectively with GKRS $^{4)}$.

The records of 420 patients treated with GKRS for VS with a median marginal dose of 11 Gy were

retrospectively analyzed. Patients with neurofibromatosis Type 2 or who had undergone treatment for VS previously were excluded. The authors assessed tumor control and complication rates with chart review and used the Cox proportional hazards model to identify predictors of tumor control. Preservation of serviceable hearing, defined as Gardner-Robertson Class I-II, was evaluated in a subgroup of 71 patients with serviceable hearing at baseline and with available follow-up audiograms. RESULTS The median VS tumor volume was 1.4 cm3, and the median length of follow-up was 5.1 years. Actuarial 5-and 10-year tumor control rates were 91.3% and 84.8%, respectively. Only tumor volume was a statistically significant predictor of tumor control rate. The tumor control rate decreased from 94.1% for tumors smaller than 0.5 cm3 to 80.7% for tumors larger than 6 cm3. Thirteen patients (3.1%) had new or increased permanent trigeminal nerve neuropathy, 4 (1.0%) had new or increased permanent facial weakness, and 5 (1.2%) exhibited new or increased hydrocephalus requiring a shunting procedure. Actuarial 3-year and 5-year hearing preservation rates were 65% and 42%, respectively. CONCLUSIONS The 5-year actuarial tumor control rate of 91.3% in this cohort of patients with VS compared slightly unfavorably with the rates reported in other large studies, but the complication and hearing preservation rates in this study were similar to those reported previously. Various factors may contribute to the observed differences in reported outcomes. These factors include variations in treatment indication and in the definition of treatment failure, as well as a lack of standardization of terminology and of evaluation of complications. Last, differences in dosimetric variables may also be an explanatory factor ⁵⁾.

A series of 33 VSs larger than 8 cm3 (range 8-24 cm3, mean 11 cm3, median 9.4 cm3) were treated using the CyberKnife from 2003 to 2011 with the multisession SRS technique in 2-5 fractions (14-19.5 Gy). Five patients had undergone surgical removal and 5 had ventriculoperitoneal shunts. Nine patients were eligible for but refused surgery. Twelve patients were older than 70 years and 5 were younger than 40 years. Two female patients had neurofibromatosis.

The follow-up period ranged from 12 to 111 months (median 48 months); radiological growth control was achieved in 94% of cases: 19 tumors (58%) displayed no size variation or reduction in tumor diameter; 12 (36%), after a transient enlargement, presented with arrested growth or shrinkage. Seven patients had a volume reduction of more than 50%. Two patients (6%) needed debulking and 2 were treated with ventriculoperitoneal shunts. Actuarial progressionfree survival rates at 1 year and 5 years were 97% and 83%, respectively. Hearing was retained in 7 of the 8 patients with serviceable baseline hearing. Adverse events were limited to 1 case each of vertigo, tongue paresthesia, and trigeminal neuralgia.

The good control rate obtained with multisession SRS deepens the controversy of the radiobiology of VSs and may extend the indication of radiation therapy (fractionated or SRS) for large VSs to include patients without symptoms of mass effect. The limited number of cases and short follow-up period do not provide sufficient support for widespread application of multisession SRS in young patients. Further studies with multisession SRS are warranted ⁶.

Sixty-eight patients with Gardener Robertson scale I hearing were identified between 2006 and 2009. Twenty-five patients had no subjective hearing loss (group A) and 43 patients reported subjective hearing loss (group B) before GKRS. The median tumor volume (1 cm) and tumor margin dose (12.5 Gy) were the same in both groups.

Serviceable hearing retention rates (GR grade I or II) were 100% for group A compared with 81% at 1

year, 60% at 2 years, and 57% at 3 years after GKRS for group B patients. Group A patients had significantly higher rates of hearing preservation in either GR class I (P < .001) or GR class II (P < .001). Patients with a pure tone average (PTA) <15 dB before GKRS had significantly higher rates of preservation of GR class I or II hearing.

At 2 to 3 years after GKRS, patients without subjective hearing loss or a PTA <15 dB had higher rates of grade I or II hearing preservation. Modification of the GR hearing classification into 2 groups of grade I hearing (group A, those with no subjective hearing loss and a PTA <15 dB; and group B, those with subjective hearing loss and a PTA >15 dB) may be useful to help predict hearing preservation rates at 2 to 3 years after GKRS ⁷⁾.

245 patients were male (55%), and 204 were female (45%). Median age was 60years (range 17-88years). Median tumor diameter was 15mm. For fractionated stereotactic radiotherapy FSRT, a median dose of 57.6Gy in median single doses of 1.8Gy was applied. For SRS, median dose was 13Gy. The median follow-up time was 67 months.

Local control was 97% at 36months, 95% at 60months, and 94% at 120months with no difference between FSRT and SRS (p=0.39). "Useful hearing" was present 46%. After RT, "useful hearing" was preserved in 85% of the patients. Loss of useful hearing was observed in the FSRT group in 14%, and in the SRS group in 16% of the patients. For patients treated with SRS \leq 13Gy, useful hearing deterioration was 13%. For trigeminal and facial nerve toxicity, there was no difference between FSRT and SRS.

Supported by this large multicentric series, both SRS and FSRT can be recommended for the treatment of VS. SRS application is limited by tumor size, and is associated with a steep dose-response-curve. When chosen diligently based on tumor volume, pre-treatment characteristics and volume-dependent dose-prescription in SRS (\leq 13Gy), both treatments may be considered equally effective⁸⁾.

2014

From 1994-2009, 235 patients underwent GKRS in Zurich for unilateral sporadic VS. Tumor progression with a volume increase of \geq 20 % occurred in 21/235 (8.9 %) patients at 3.4 ± 0.9 years following GKRS. Seventeen out of 235 (7 %) patients had a clinically relevant tumor progression requiring microsurgery or repeat radiosurgery.

According to this data, time may be a good parameter distinguishing tumor progression due to tumor growth from TTE due to tumor swelling in VS following GKRS. Tumor growth seems to occur at about 3-4 years following GKRS for VS as opposed to TTE, which seems to be present at about 6-18 months following GKRS for VS ⁹.

From October 2003 to September 2007, 133 consecutive patients with vestibular schwannomas were treated according to the concept of robotic Gamma Knife microradiosurgery, which is based on precise irradiation of the lesion, sparing adjacent structures, and delivery of the high radiation energy to the target. Multiple small-sized isocenters located within the border of the neoplasm were applied.

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The mean marginal dose was 11.5 Gy (range, 11-12 Gy). In total, 126 cases with a minimum posttreatment follow-up of 2 years (range, 2-7 years; median, 4 years) were analyzed. Temporary enlargement was noted in 25 % of tumors at 6 months after radiosurgery. At 3 years of follow-up, tumor shrinkage, stabilization, and increase in volume were marked in 73 %, 23 %, and 4 % of cases, respectively. All progressing lesions spontaneously stabilized later on and did not require additional management. In 3 % of patients, transitory impairment of the facial nerve function was marked; however, neither its permanent dysfunction nor trigeminal neuropathy attributed to radiosurgery was noted. Impairment of hearing compared to its pretreatment level was revealed in 4 %, 12 %, 13 %, and 16 % of patients at 6 months, 1 year, 2 years, and 3 years after radiosurgery, respectively, and this trend was statistically significant (P = 0.0042). Overall, 77 % of patients with serviceable hearing before treatment preserved it 3 years thereafter. In conclusion, modern Gamma Knife radiosurgery provides effective and safe management of vestibular schwannomas. Nevertheless, possible temporary tumor enlargement, delay of its growth arrest, transient dysfunction of the cranial nerves, and gradual deterioration of hearing after irradiation should be always taken into consideration ¹⁰.

2013

Between 1994 and 2008, 65 patients with vestibular schwannomas between 3 and 4 cm in one extracanalicular maximum diameter (median tumor volume 9 ml) underwent Gamma Knife surgery. Seventeen patients (26%) had previously undergone resection.

The median follow-up duration was 36 months (range 1-146 months). At the first planned imaging follow-up at 6 months, 5 tumors (8%) were slightly expanded, 53 (82%) were stable in size, and 7 (11%) were smaller. Two patients (3%) underwent resection within 6 months due to progressive symptoms. Two years later, with 63 tumors overall after the 2 post-SRS resections, 16 tumors (25%) had a volume reduction of more than 50%, 22 (35%) tumors had a volume reduction of 10–50%, 18 (29%) were stable in volume (volume change < 10%), and 7 (11%) had larger volumes (5 of the 7 patients underwent resection and 1 of the 7 underwent repeat SRS). Eighteen (82%) of 22 patients with serviceable hearing before SRS still had serviceable hearing after SRS more than 2 years later. Three patients (5%) developed symptomatic hydrocephalus and underwent placement of a ventriculoperitoneal shunt. In 4 patients (6%) trigeminal sensory dysfunction developed, and in 1 patient (2%) mild facial weakness (House-Brackmann Grade II) developed after SRS. In univariate analysis, patients who had a previous resection (p = 0.010), those with a tumor volume exceeding 10 ml (p = 0.05), and those with Koos Grade 4 tumors (p = 0.02) had less likelihood of tumor control after SRS.

Although microsurgical resection remains the primary management choice in patients with low comorbidities, most vestibular schwannomas with a maximum diameter less than 4 cm and without significant mass effect can be managed satisfactorily with Gamma Knife radiosurgery ¹¹.

A study compared 24 patients with large VSs (> 3 cm in maximum diameter) treated with GKS with 49 small VSs (\leq 3 cm) matched for age, sex, radiosurgical margin and maximal doses, length of follow-up, and indication.

Actuarial tumor progression-free survival (PFS) for the large VS cohort was 95.2% and 81.8% at 3 and 5 years, respectively, compared with 97% and 90% for small VSs (p = 0.009). Overall clinical outcome was better in small VSs compared with large VSs (p < 0.001). Patients with small VSs presenting with House-Brackmann Grade I (good facial function) had better neurological outcomes compared with

patients with large VSs (p = 0.003). Treatment failure occurred in 6 patients with large VSs; 3 each were treated with resection or repeat GKS. Treatment failure did not occur in the small VS group. Two patients in the large VS group required ventriculoperitoneal shunt placement. Univariate analysis did not identify any predictors of treatment failure among the large VS cohort.

Patients with large VSs treated using GKS had shorter PFS and worse clinical outcomes compared with age-, sex-, and indication-matched patients with small VSs. Nevertheless, GKS has efficacy for some patients with large VSs and represents a reasonable treatment option for selected patients¹²⁾.

2012

In 386 patients treated with single-fraction radiosurgery, tumor volume was the only predictor of trigeminal neuropathy ¹³⁾.

New facial numbress occurred in one patient (2.2%) with normal fifth cranial nerve function prior to stereotactic radiotherapy in 50 patients $^{14)}$

2011

Between 1994 and 2008, 65 patients with vestibular schwannomas between 3 and 4 cm in one extracanalicular maximum diameter (median tumor volume 9 ml) underwent Gamma Knife surgery. Seventeen patients (26%) had previously undergone resection. RESULTS:

The median follow-up duration was 36 months (range 1-146 months). At the first planned imaging follow-up at 6 months, 5 tumors (8%) were slightly expanded, 53 (82%) were stable in size, and 7 (11%) were smaller. Two patients (3%) underwent resection within 6 months due to progressive symptoms. Two years later, with 63 tumors overall after the 2 post-SRS resections, 16 tumors (25%) had a volume reduction of more than 50%, 22 (35%) tumors had a volume reduction of 10-50%, 18 (29%) were stable in volume (volume change < 10%), and 7 (11%) had larger volumes (5 of the 7 patients underwent resection and 1 of the 7 underwent repeat SRS). Eighteen (82%) of 22 patients with serviceable hearing before SRS still had serviceable hearing after SRS more than 2 years later. Three patients (5%) developed symptomatic hydrocephalus and underwent placement of a ventriculoperitoneal shunt. In 4 patients (6%) trigeminal sensory dysfunction developed, and in 1 patient (2%) mild facial weakness (House-Brackmann Grade II) developed after SRS. In univariate analysis, patients who had a previous resection (p = 0.010), those with a tumor volume exceeding 10 ml (p = 0.05), and those with Koos Grade 4 tumors (p = 0.02) had less likelihood of tumor control after SRS. CONCLUSIONS:

Although microsurgical resection remains the primary management choice in patients with low comorbidities, most vestibular schwannomas with a maximum diameter less than 4 cm and without significant mass effect can be managed satisfactorily with Gamma Knife radiosurgery ¹⁵.

1995

Twenty-seven of the 1560 patients treated by radiosurgery during the period 1984-1993 had acoustic neurinomas. Four cases were excluded from this study because they had a follow-up of less than 2

years. There were 24 neurinomas treated in 23 patients as one patient had a bilateral tumour. Seven patients underwent radiosurgery for a recurrent tumour (already operated on once or twice), while it was the first treatment for 16 patients. The tumour volume ranged from 1.99 cm3 to 18.30 cm3, and the patient follow-up was from 2 to 8 years. To determine the target on CT/NMR for linear accelerator stereotactic irradiation, the Greitz-Bergström non-invasive head fixation device was used. It was again adopted for subsequent serial imaging, and for repeat radiosurgery when necessary. The total peripheral tumour dose ranged from 12 to 45 Gy. In 9 patients there was a reduction in tumour volume varying from 39 to 100%, while 14 of the neurinomas appeared stable after an average follow-up of 3 years. In one patient there was an increase in size of the tumour. Variable morphological changes were present in 66% of the neurinomas treated. Radiosurgery is indicated as an alternative to microsurgery for inoperable patients and for those who refuse surgery, for recurrent tumours, and as a post-operative complementary treatment for partially removed tumours. A gradual approach to radiosurgery, depending on tumour response, allows a greater efficacy with minimal risk. In the present series no complications were observed. Hearing was preserved at almost the same level as that prior to radiosurgery in all patients ¹⁶

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Last update: 2024/06/07 02:55

