



Medical Physics Contribution

Feasibility Study of Stereotactic Radiosurgery Treatment of Glomus Jugulare Tumors via HyperArc VMAT



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ABSTRACT

This study aims to report on the clinical validation and feasibility of utilizing a novel fully automated treatment planning and delivery system, HyperArc VMAT stereotactic radiosurgery (SRS) for glomus jugulare tumors (GJT). Independent dose verification of the HyperArc module via the MD Anderson's SRS head phantom irradiation and credentialing results showed compliance with the SRS treatment requirements per IROC MD Anderson's standard. Following the Alliance clinical trial, AAPM, RTOG protocols, and QUANTEC requirements, utilizing selected three-partial arc geometry of HyperArc module on TrueBeam Linac with 6MV-FFF beam, GJT SRS plans were generated for nine previously treated Gamma Knife (GK) radiosurgery patients using advanced Acuros-based algorithm to account for tissue inhomogeneity corrections and frameless immobilization with Q-fix mask and Encompass device insert. HyperArc VMAT produced highly conformal SRS dose distributions to GJT, a steep dose gradient around the GJT, and spared adjacent critical organs including the spinal cord (< 3.0 Gy). Due to faster patient setup and less MLC modulation through the target (average beam-on time, 6.2 minutes), the HyperArc VMAT plan can deliver a single high-dose of 18 Gy to the GJT in less than 15 minutes overall treatment time, significantly improving patient comfort and clinic workflow. Pretreatment portal dosimetry quality assurance results and independent dose verification via Monte Carlo-based physics second check met our clinical SRS protocol's requirements for treatment. Due to the highly conformal dose distribution, rapid dose fall-off, excellent sparing of adjacent critical organs, and highly precise and accurate treatment, clinical implementation of frameless HyperArc VMAT for GJT patients who may not have access to nor tolerate frame-based GK SRS treatment are underway.

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Introduction

Gamma Knife (GK) stereotactic radiosurgery (SRS) is an effective treatment option for rare, slow-growing but destructive glomus jugulare tumors (GJT).^{1–3} However, GK-SRS is not readily available for all patient populations. Additionally, GK faces many challenges such as machine clearance issues, longer treatment times, painful headframe placement, inability to access the entire tumor coverage (in some cases) in the inferior direction (GK can access down to C2 vertebral level only), and difficulty arranging anesthesia time for claustrophobic patients or who may not tolerate headframe fixation. Though alternative treatment modalities for GJT such as robotic CyberKnife (CK)^{4–7} and traditional frame-based Linac-based

SRS have been used,^{8–13} longer treatment times with CK can be problematic for some patients.^{4–7} Traditional Linac-based, particularly cone-based SRS suffers from patient collision issues but offers an effective treatment option for GJT by providing excellent tumor control (LC) rate (100%, LC for 49 months median follow up) with a lower risk of radiation-induced toxicity.¹³

For faster SRS treatment of intracranial lesions, and to increase treatment delivery accuracy, improve clinic workflow, and patient tolerability, Varian recently introduced a Truebeam™ Linac-based (or superior) fully-automated noncoplanar frameless treatment delivery platform, HyperArc™ module, in the Eclipse™ treatment planning system (TPS; Varian Medical Systems, Version 15.6) which has generated global clinical interest.^{14–20} While coupling with the high dose rate flattening filter-free (FFF) beams,²¹ HyperArc VMAT can rapidly deliver a single high dose treatment to multiple intracranial lesions and improve treatment delivery accuracy, patient compliance, and comfort. The aim of this retrospec-

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tive study was to independently validate the HyperArc module via MD Anderson's SRS head phantom and evaluate the plan quality and treatment delivery efficiency of an innovative fully-automated therapeutic approach as a novel application of HyperArc VMAT in the SRS treatment of patients with GJT to potentially mitigate all of these challenges mentioned above.

Methods and Materials

HyperArc VMAT SRS credentialing

For the clinical implementation of the HyperArc VMAT for SRS treatment of GJT, an independent dose verification of the HyperArc VMAT treatments on the TrueBeam Linac (Varian Medical Systems, Palo Alto, CA) was performed using IROC MD Anderson's SRS credentialing anthropomorphic head phantom containing a 1.9 cm diameter spherical target and dosimetry systems (two orthogonal films and two TLD capsules) inserted. This phantom was imaged using the HyperArc setup with Q-fix mask, headrest, and the Encompass support device planned (Eclipse, Version 15.6, Varian Medical Systems, Palo Alto, CA) and irradiated with an SRS single dose of 25.0 Gy to the target for credentialing based upon the Alliance A071801 skull-based brain SRS/SRT trial²² following the AAPM and RTOG protocols requirements for the single fraction schemata.^{23,24} A full noncoplanar HyperArc VMAT geometry with one full coplanar arc and three-partial arcs with 6MV-FFF beam on TrueBeam Linac equipped with 120Millenium MLC and a perfect pitch couch was used. Advanced Acuros-based dose calculation with 1.0 mm calculation grid sizes (CGS) was validated in the Varian Eclipse treatment planning system (TPS, Version 15.6, Palo Alto, CA).^{25,26} The credentialing results of IROC MD Anderson's SRS head phantom incorporating dosimetry inserts in the tumor satisfied both the TLD and film dosimetric requirements established by the IROC for the SRS/SRT treatment on TrueBeam Linac. In this independent measurement, the average absolute TLD dose and film measurement results were within $\pm 2.0\%$ and 97% gamma index overall three planes, respectively. The phantom irradiation results met MD Anderson's credentialing requirement for SRS treatment using HyperArc module in Eclipse TPS.

Glomus HyperArc VMAT SRS plans

Nine (five right-sided and four left-sided) patients with GJT were included in this retrospective planning study approved by our institutional review board. These patients were previously treated via single-fraction GK radiosurgery in our center. High resolution gadolinium single contrast MPRAGE MRI images (Siemens MAGNETOM, 1.5T MRI System, Ferndale, MI) were used for tumor and organs at risk (OAR) delineation and were coregistered to planning CT images in the Varian Eclipse TPS. The MPRAGE MRI images were 512×512 pixels with 1 mm slice thickness and no gap in between the slices. The target volume was delineated by an experienced radiation oncologist on the MRI with the gross tumor volume (GTV) defined by the visible tumor with no additional margin; therefore, the planning target volume (PTV) equals the GTV using our departmental SRS protocol. The organ at risk (OAR) contours for dose reporting included: skin, brain, brainstem, optic apparatus, cochlea, and spinal cord. Average tumor volume was 6.2 ± 2.4 cc (4.05 to 14.44 cc) corresponding to an average of 2.21 cm tumor diameter and a maximum up to 3.05 cm. For full scatter simulation, the body contour was expanded (in Eclipse TPS) to include the Q-fix mask, SRS headrest, integrated shim system, and integraBite mouthpiece. Additionally, beam attenuation through the Encompass base and Encompass support device was accounted for.

Each patient was planned retrospectively by an experienced clinical SRS physicist using the fully-automated non-coplanar HyperArc VMAT Module in Varian's Eclipse TPS with 6MV-FFF beam (1400 MU/min). Single-dose of 18 Gy in one fraction was prescribed to 95% of the PTV receiving 100% of the prescription dose. Highly heterogeneous target dose distributions were allowed, with the hotspot (125 to 140%) in the center of the target, and on average was 136% of the prescription dose. For all HyperArc SRS plans, the isocenter was automatically chosen in the center of the target and still allowed isocenter locations that were within a specific Patient Protection Zone as defined by the HyperArc module to reduce the risk of gantry collision with the patient. All HyperArc VMAT plans utilized select three-partial noncoplanar arcs (each 180° arc length), which were automatically selected based on left-sided (couch: 0° , 315° , 270°) vs right-sided (couch: 0° , 45° , 90°) glomus tumor location and to avoid the gantry collision as well as minimize the beam entrance through the opposite side of the brain. The collimator angle for each arc was also automatically optimized based on the target shape, size, and location to further minimize the leakage dose and potentially improve the target dose conformity.¹⁹ All treatment plans were optimized with the Photon Optimizer (PO) MLC algorithm and the final dose calculation was performed with a more accurate advanced Acuros-based dose calculation algorithm^{25,26} on the planning CT images with a 1.0 mm CGS and automatic SRS normal tissue objectives. For HyperArc VMAT SRS planning, the goal was to maintain highly conformal dose distribution to the glomus target and minimize dose to adjacent OAR, including the spinal cord, to be as low as possible. Dose tolerances to the OAR were followed according to the AAPM, RTOG protocols, and QUANTEC requirements for the single dose of SRS treatment schemata.^{23,24,27}

Treatment plan evaluation

The isodose distributions, dose volume histograms (DVHs), and target dose metrics of the HyperArc VMAT SRS plans were evaluated. Additionally, these plans were evaluated for target conformity, tumor dose heterogeneity, and maximal dose 2 cm away in any direction from the target (D2cm). Using the percentage prescribed isodose volume and target size, the RTOG conformity index (CI), the Paddick conformation number (PCN), and the gradient index were documented.²⁸⁻³⁰ The maximal dose to immediately adjacent OAR was recorded for the optic apparatus, brainstem, spinal cord, and skin. Mean dose to normal brain and cochlea were recorded. Furthermore, treatment delivery efficiency and accuracy were documented by recording the total number of monitor units (MU) and the beam modulation factor (MF), which is defined as the ratio of the total number of MU to the prescription dose in cGy. The beam-on time (BOT) was recorded during portal dosimetry (PD) quality assurance (QA) measurement on the Truebeam Linac for each glomus SRS plans. Dosimetric verification of HyperArc plans was performed using the PD measurement QA procedure with a gamma evaluation criterion of 2%/2mm and a low dose threshold set to 10%.³¹ The delivered dose rate was also confirmed by further reviewing each HyperArc VMAT (control points) for all patients under the MLC properties in the Eclipse TPS at Truebeam Linac. For each patient, BOT was added to patiently setup and verification time, including conebeam CT imaging and image registration time and dry-run time, and estimated overall treatment time. Moreover, for independent dose verification, the second MU check of these HyperArc VMAT SRS plans were performed by using an in-house Monte Carlo (MC) code³² that was based on the PENELOPE MC algorithm.³³ The mean and standard deviation (range) for each plan quality metric was recorded for all dosimetric parameters, target coverage, OAR doses, and treatment delivery parameters including the PD QA pass rates.

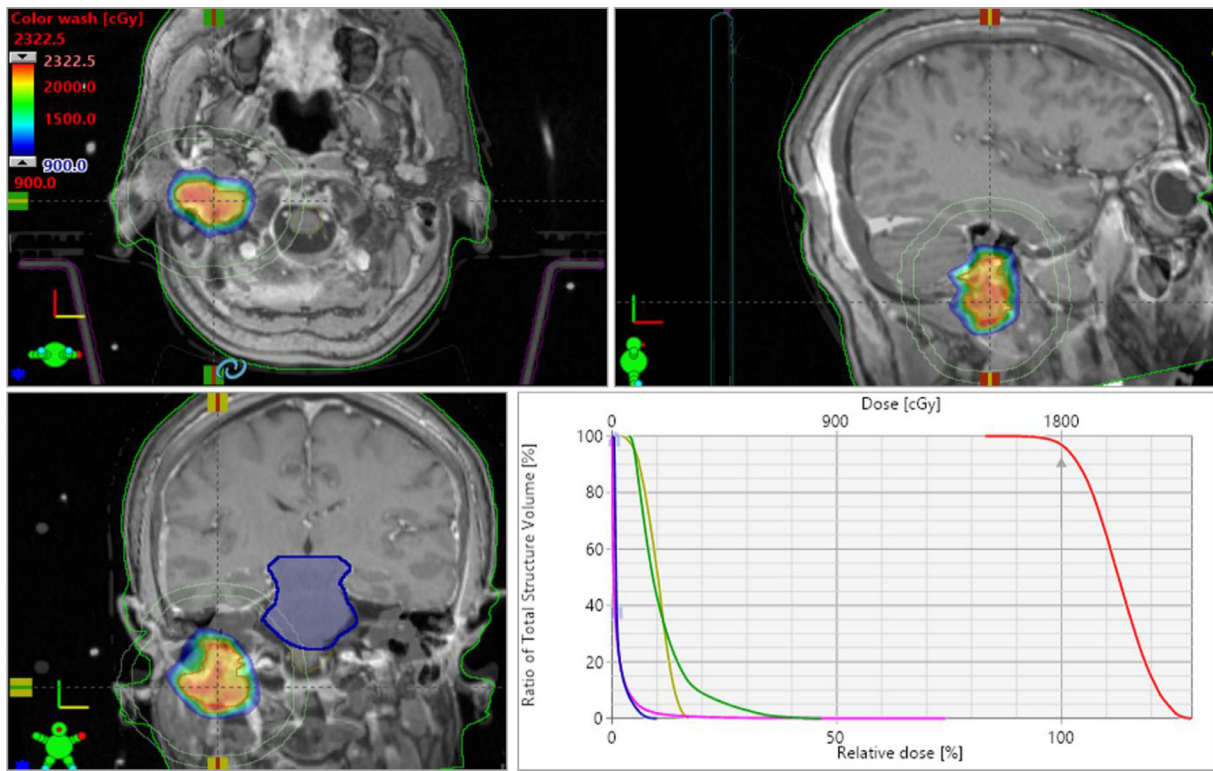


Fig. 1. This is a radiosurgical dose distribution showed in the blended planning CT and MRI in all three views (axial-, coronal- and sagittal) and the corresponding DVH for the right glomus target (red) of 8.5 cc planned for a single dose of 18 Gy using a HyperArc VMAT module (patient #9). This plan was normalized to deliver PTVD95 full dose (see, gray arrow), and the 50% isodose color wash (blue, intermediate dose spillage) with a very steep dose gradient (see D2cm, light green ring) around the target volume. The cross-hair shows the isocenter location. The proximity of the OAR sparing and DVH for skin (pink), brainstem (blue), spinal cord (yellow), and right cochlea (green) is shown. (Color version of figure is available online.)

Results

Target coverage and conformity

All HyperArc VMAT GJT plans demonstrated highly conformal target coverage with adequate dose to PTV and rapid intermediate dose fall-off with lower values of gradient index and D2cm as shown in Table 1. Overall, the minimum, mean, and maximum doses to the PTV were 16 Gy, 21 Gy, and 24.5 Gy on average, respectively. The HyperArc VMAT plans exhibited RTOG conformity index and PCN values closer to unity, suggesting that the HyperArc SRS plans to GJT can provide highly conformal dose distributions to the target. Smaller values of GI (< 3.5) and D2cm (< 22.6%) suggests a steep dose gradient of intermediate dose-spillage beyond the target with HyperArc VMAT plans – greatly desirable for the GJT SRS treatment.

Table 1

Summary of the PTV coverage and intermediate dose spill for all 9 glomus SRS patients planned via HyperArc VMAT. Dose was 18 Gy in one fraction. Mean ± SD (range) was reported. CI, Conformity index; D2cm, Maximal dose at 2 cm away from the target; GI, Gradient index; HI, Heterogeneity index; PCN; Paddick conformation number; SD, standard deviation.

PTV	Volume covered by Rx dose (%)	96.8 ± 0.4 (95.9–97.2)
	PCN	0.81 ± 0.03 (0.77–0.85)
	CI	1.08 ± 0.04 (1.02–1.12)
	HI	1.36 ± 0.06 (1.28–1.47)
Intermediate dose fall-off	D2cm (%)	18.73 ± 2.25 (15.5–22.6)
	GI	3.04 ± 0.27 (2.63–3.47)
Absolute dose to PTV	Minimum (Gy)	16.23 ± 0.56 (15.49–16.97)
	Mean (Gy)	21.02 ± 0.65 (20.27–22.54)
	Maximum (Gy)	24.57 ± 1.05 (23.23–26.39)

The example patient case (patient # 9) shown in Fig. 1 had a GJT with 8.5 cc (2.5 cm diameter) and located in the right neck. The HyperArc VMAT SRS plan consisted of three right-sided non-coplanar partial arcs of 180° arc-length (couch: 0°, 45°, 90°) of the fully-automated HyperArc module. For single dose of 18 Gy treatment, the total 5631 MU was delivered with a beam MF of 3.13. Beam on time was 5.63 minutes with a total estimated treatment time (including patient setup, conebeam CT imaging, image registration time and dry run time) within 15 minutes. In this case, the HyperArc VMAT SRS plan provided a highly conformal target dose distribution with a CI, PCN, D_{2cm}, and GI of 1.11, 0.82, 19.8%, and 3.07, respectively. All parameters were deemed highly desirable for SRS treatment of GJT following high single-dose schemata.^{22–24, 27} In this case, maximal dose to OAR including optic apparatus, brainstem, skin, and spinal cord were 1.11 Gy, 3.04 Gy, 9.6 Gy, and 3.13 Gy, respectively. Mean doses to cochlea and brain tissue were less than 2.0 Gy and 1.0 Gy, respectively.

Dose to adjacent critical organs

For all HyperArc GJT SRS plans, clinically relevant dose to immediately adjacent OAR was achieved. In this cohort, for each patient, the HyperArc VMAT SRS plan provided a significantly lower maximal dose to adjacent OAR: optic apparatus (average 1.6 Gy, maximum 2.1 Gy), brainstem (average 3.04 Gy, maximum 4.8 Gy), skin (average 6.6 Gy, maximum 10.0 Gy), spinal cord (average 2.3 Gy, maximum 3.1 Gy), respectively. Mean doses to cochlea (average 4.6 Gy, maximum 6.9 Gy) and normal brain (average 0.53 Gy, maximum 1.03 Gy), respectively; all dosimetric parameters to the OAR were highly desirable for SRS treatment of GJT and deemed within AAPM, RTOG protocols, and QUANTEC guidelines.^{22–24,27}

Table 2

Summary of treatment delivery parameters (mean, SD and range) of HyperArc VMAT for all nine GJT SRS plans. MC, Monte Carlo; SD, standard deviation.

Treatment delivery parameters	
Total monitor units (MU)	6203 ± 665 (5137–7133)
Modulation factor (MF)	3.45 ± 0.66 (2.85–3.96)
Beam-on time, BOT (min)	6.25 ± 0.66 (5.16–7.13)
Overall treatment time (min)	14.20 ± 0.68 (13.15–15.19)
Pre-treatment QA pass rate [2%/2mm] (%)	97.7 ± 1.8 (96.6–100.0)
Eclipse TPS vs MC calculation agreement (%)	2.45 ± 0.6 (1.36–2.89)

Treatment delivery efficiency and accuracy

Treatment delivery efficiency was documented by recording the total number of MU, beam modulation factors, and BOT. The estimated overall treatment time was recorded during portal-dosimetry quality assurance procedure. For the single dose of 18 Gy, the HyperArc VMAT plans provided 6203 MU on average, corresponding to a relatively lower MF of 3.45 (Table 2).

The major advantage of the HyperArc plans was the faster treatment delivery with shorter BOT and overall treatment time of 6.25 minutes and 14.2 minutes, on average respectively. The pretreatment patient-specific PD-QA results and independent dose verification with inhouse MC calculation (both within 3% of the planned dose distribution) suggested that accurate delivery of HyperArc VMAT SRS treatment to GJT is anticipated (Table 2).

Discussion

In this report, we have presented the clinical validation and implementation of HyperArc VMAT by evaluating plan quality, treatment delivery efficiency, and accuracy of SRS treatments of GJT using a fully-automated HyperArc module with 6MV-FFF beam (1400MU/min) on Truebeam Linac. Following the independent dose verification by IROC MD Anderson's phantom irradiation and credentialing results, we found that all GJT generated HyperArc VMAT module plans had a high target conformity, tumor dose heterogeneity, and rapid intermediate dose fall-off around the target, which was in compliance with the OAR dose tolerances per SRS protocols and QUANTEC requirements. It should be noted that the steep dose gradient around the target with HyperArc plans along with a GI of < 3.0 and D2cm of < 23% were highly desirable for SRS treatment for the GJT. Moreover, the main advantage of the HyperArc VMAT SRS plan was low MLC modulation with a significantly short BOT suggesting less plan complexity and hence significantly affecting the overall treatment time, which can be delivered in less than 15 minutes. The average gamma passing rates of 97.7% (2%/2mm clinical gamma passing criteria) and independent MC dose verification within 3% demonstrate an excellent potential for fast, reliable, and accurate delivery of HyperArc VMAT SRS in the treatment of GJT on a Truebeam Linac.

Multiple treatment options have been shown in the management of GJT. Surgical resection has been the mainstay of the treatment and provides an excellent local control for GJT. However, some patients have inoperable tumors or large lesions that have a high morbidity risk with surgery, including cranial nerve injury.^{34,35} As mentioned above, most of the SRS series for the treatment of GJT include patients treated with frame-based GK radiosurgery^{1–4} and/or a robotic CyberKnife SRS.^{5–7} Although the clinical outcomes of these treatments were excellent tumor local-control and lower treatment-related morbidity, the major challenges were long treatment times and patient discomfort. Utilizing Brainlab (Feldkirchen, Germany) system with 4 to 10 noncoplanar dynamic conformal arcs and pencil beam algorithm, 16 patients were treated to a median dose of 25 Gy in five fractions.⁸ In this

fractionated-SRT series, 5-year local control rate of 88% was reported with a median follow-up interval of 44 months with only one patient developing grade 2 vertigo and another patient developing grade 3 headache from hydrocephalus requiring ventriculoperitoneal shunt. Moreover, BOT and overall treatment time were not reported. In contrast, our single dose of 18 Gy HyperArc VMAT SRS plan used a more accurate advanced Acuros-based dose calculation engine, more accurate patient setup, and verification via Q-fix mask and Encompass support device, that can be delivered within 15 minutes door-to-door treatment time—significantly improving patient comfort, compliance, and clinic workflow.

Limitations of this study include its retrospective nature of the single arm treatment planning and clinical validation study. Moreover, frameless Linac-based SRS treatments present unique challenges of accurate and precise treatment delivery compared to frame-based SRS such as GK radiosurgery. However, due to the advancement of conebeam CT-guided patient setup and verification with perfect pitch couch and much tighter Q-fix mask and Encompass device insert with pre-defined Patient Protection Zone that avoids patient collision issues in the HyperArc VMAT SRS, more accurate treatment is anticipated. Therefore, in the treatment of GJT, it would be an ideal treatment option for those patients who deny or do not qualify for the frame-based SRS treatment. Furthermore, in the traditional Linac-based treatment, the potential for patient movement during beam-on time increases with increasing overall treatment time leading to potential degradation of positional accuracy and increasing the risk of a geographic miss or exposing adjacent critical organs to a higher dose of radiation.^{36,37} However, our shorter overall treatment time of < 15 minutes mitigates that risk and is an attractive treatment option in the effective management of GJT. Future research includes analyzing intra-fraction movement errors in the stereotactic treatment of GJT via HyperArc VMAT and reporting clinical outcomes.

Conclusion

Independent dose verification of the HyperArc module via irradiation of IROC MD Anderson's SRS head phantom met the SRS treatment requirement credentialing. HyperArc VMAT SRS provided highly conformal dose distribution, rapid dose fall-off, adequate sparing of adjacent critical organs, and a highly precise and accurate treatment that could be delivered to GJT within 15 minutes door-to-door treatment time – providing an attractive treatment option to glomus jugulare tumors to those patients who may not tolerate or do not qualify for frame-based SRS treatment. Due to the steep dose gradient, acceptable plan quality, and fast and accurate treatment, clinical implementation of stereotactic treatment of GJT patients in our center using HyperArc VMAT is ongoing.

Conflict of Interest

None.

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References

- 1 Sheehan, J.; Tanaka, S.; Link, M.; et al. Gamma knife surgery for the management of glomus tumors: A multicenter study. *J Neurosurg* **117**(2):246–54; 2012.
- 2 Winford, T.; Dorton, L.; Browne, J.; et al. Stereotactic radiosurgical treatment of glomus jugulare tumors. *Otol. Neurotol* **38**:555–62; 2017.
- 3 Dobberpuhl, M.; Maxwell, S.; Feddock, J.; et al. Treatment outcomes for single modality management of glomus jugulare tumors with stereotactic radiosurgery. *Otol. Neurotol* **37**:1406–10; 2016.

- 4 Guss, Z.; Batra, S.; Limb, C.; et al. Radiosurgery of glomus jugulare tumors: A meta-analysis. *Int. J. Radiat. Oncol. Biol. Phys* **81**(4):e497–502; 2011.
- 5 Wegner, R.; Rodriguez, K.; Heron, D.; et al. Linac-based stereotactic body radiation therapy for treatment of glomus jugulare tumors. *Radiother. Oncol* **97**(3):395–8; 2010.
- 6 Tse, V.; Sillanpaa, J.; Minn, A.; et al. Glomus tumors treated with stereotactic radiosurgery: A retrospective study. *J. Radiosurg. SBRT* **5**(1):73; 2017.
- 7 Patel, A.; Rodriguze-Lopez, J.; Hirsch, B.; et al. Long-term outcomes with linear accelerator stereotactic radiosurgery for treatment of jugulotympanic paragangliomas. *Head & Neck* **43**:449–55; 2021.
- 8 Gigliotti, M.; Hasan, S.; Liang, Y.; et al. A 10-year experience of linear accelerator-based stereotactic radiosurgery/radiotherapy (SRS/SRT) for paraganglioma: A single institution experience and review of the literature. *J. Radiosurg. SBRT* **5**(3):183–90; 2018.
- 9 Maarouf, M.; Voges, J.; Landwehr, P.; et al. Stereotactic linear accelerator-based radiosurgery for the treatment of patients with glomus jugulare tumors. *Cancer* **97**(4):1093–8; 2003.
- 10 Martín, I.; Avila, R.; Herrera, M.; et al. Role of radiosurgery in the management of glomus tumors. *Head Neck* **38**:798–804; 2016.
- 11 Poznanovic, S.; Cass, S.; Kavanagh, B. Short-term tumor control and acute toxicity after stereotactic radiosurgery for glomus jugulare tumors. *Otolaryngol. Head Neck Surg* **134**(3):437–42; 2006.
- 12 Magno, E.; Brito, J.; Mario, S.; et al. Stereotactic radiosurgery for the treatment of glomus jugulare tumors. *Surg. Neurol. Int* **4**(SUPPL6):429; 2013.
- 13 Sager, O.; Beyzadeoglu, M.; Dincoglan, F.; et al. Evaluation of linear accelerator-based stereotactic radiosurgery in the management of glomus jugulare tumors. *Tumori* **100**(2):184–8; 2014.
- 14 Ohira, S.; Ueda, Y.; Akino, Y.; et al. HyperArc VMAT planning for single and multiple brain metastases stereotactic radiosurgery: A new treatment planning approach. *Radiat. Oncol* **13**(1):13; 2018.
- 15 Ruggieri, R.; Naccarato, R.; Mazzola, M.; et al. Linac-based VMAT radiosurgery for multiple brain lesions: Comparison between a conventional multi-isocenter approach and a new dedicated mono-isocenter technique. *Radiat. Oncol.* **13**:38; 2018.
- 16 Kadoya, N.; Abe, Y.; Kajikawa, T.; et al. Automated noncoplanar treatment planning strategy in stereotactic radiosurgery of multiple cranial metastases: HyperArc and CyberKnife dose distributions. *Med. Dosim* **44**:394–400; 2019.
- 17 Liu, H.; Thomas, E.; Li, J.; et al. Interinstitutional plan quality assessment of 2 Linac-based, single-isocenter multiple metastasis radiosurgery techniques. *Adv. Radiat. Oncol.*:1–10 2019.
- 18 Vergalasova, I.; Liu, H.; Alonso-Basanta, M.; et al. Multi-institutional dosimetric evaluation of modern-day stereotactic radiosurgery (SRS) treatment options for multiple brain metastases. *Front. Oncol* **9**:483; 2019.
- 19 Ohira, S.; Sagawa, T.; Ueda, Y.; et al. Effect of collimator angle on HyperArc stereotactic radiosurgery planning for single and multiple brain metastases. *Med. Dosim.* **45**:85–91; 2020.
- 20 Alongi, F.; Fiorentino, A.; Gregucci, F.; et al. First experience and clinical results using a new non-coplanar mono-isocenter technique (HyperArc™) for Linac-based VMAT radiosurgery in brain metastases. *J. Cancer Res. Clin. Oncol.* **145**:193–200; 2019.
- 21 Xiao, Y.; Kry, S.; Popple, R.; et al. Flattening filter-free accelerators: A report from the AAPM therapy emerging technology assessment work group. *J. Appl. Clin. Med. Phys* **16**:12–29; 2015.
- 22 <number>22.</number>Alliance A071801 clinical trial, Version 2.0 (2020); 1–10
- 23 Benedict, S.; Yenice, K.; Followill, D.; et al. Stereotactic body radiation therapy: The report of AAPM Task Group 101. *Med. Phys* **37**:4078–100; 2010.
- 24 A randomized phase II study comparing 2 stereotactic body radiation therapy (SBRT) schedules for medically inoperable patients with stage I peripheral non-small cell lung cancer: RTOG 0915 protocol. (2014) 1–67
- 25 Eclipse algorithms reference guide and HyperArc VMAT planning manual (Version 15.6), Varian Medical Systems, (2019)
- 26 Vassiliev, O.; Wareing, T.; et al. Validation of a new grid-based Boltzmann equation solver for dose calculation in radiotherapy with photon beams. *Phys. Med. Biol* **55**:581–98; 2010.
- 27 Marks, L.; Yorke, E.; Jackson, A.; et al. Use of normal tissue complication probability models in the clinic. *Int. J. Radiat. Oncol. Biol. Phys* **76**(3):S10–19; 2010 Supplement.
- 28 International Commission on Radiation Units and Measurements (ICRU). Prescribing, recording and reporting photon beam therapy. *ICRU Report 62. (Supplement to ICRU Report 50)*. Bethesda, MD: ICRU Publications; 1999.
- 29 Paddick, I. A simple scoring ratio to index the conformity of radiosurgical treatment plans. *J Neurosurg* **93**(Suppl 3):219–22; 2000.
- 30 Paddick, I.; Lippitz, B. A simple dose gradient measurement tool to complement the conformity index. *J. Neurosurg.* **105**:194–201; 2006.
- 31 Miften, M.; Olch, A.; Mihaildis, D.; et al. Tolerance limits and methodologies for IMRT measurement-based verification QA: Recommendations of AAPM Task Group No. 218. *Med. Phys.* **45**:e53–83; 2018.
- 32 Chen, Q.; Oldland, T.; Sanford, L.; et al. Cloud Based Monte Carlo independent dose calculation tool for Varian Linac: Implementation and validation. *Med. Phys.* **46**; 2019 E278–E278.
- 33 Salvat, F.; José, F.; Sempau, J. PENELOPE-2008: A code system for Monte Carlo simulation of electron and photon transport. In: *Workshop Proceedings*, 4; 2006. p. 7.
- 34 Liebermann, R.; Adler, J.; Soltys, S.; et al. Stereotactic radiosurgery as a primary treatment for new and recurrent paragangliomas: Is open surgical resection still the treatment of choice? *World Neurosurg* **77**(5–6):745–61; 2012.
- 35 Fayad, J.; Keles, B.; Brackmann, D. Jugular foramen tumors: Clinical characteristics and treatment outcomes. *Otol Neurotol* **31**(2):299–305; 2010.
- 36 Mangesius, J.; Seppi, T.; Weigel, R.; et al. Intrafractional 6D head movement increases with time of mask fixation during stereotactic intracranial RT-sessions. *Radiat Oncol* **14**(1):231; 2019.
- 37 Wang, C.; Lin, Y.; Tseng, H.; et al. Prolonged treatment time deteriorates positioning accuracy for stereotactic radiosurgery. *PLoS One* **10**(4):e0123359; 2015.