Impact of ^{68}Ga -DOTATOC PET/MRI on robotic radiosurgery treatment planning in meningioma patients: first experiences in a single institution

*Güliz Acker, MD,¹⁻³ Anne Kluge, PhD,^{3,4} Mathias Lukas, MSc,⁵ Alfredo Conti, MD, PhD, FEBNS,^{1,3,6} Diana Pasemann, MSc,^{3,4} Franziska Meinert,^{1,3} Phuong Thuy Anh Nguyen,^{1,3} Claudius Jelgersma,^{1,3} Franziska Loebel, MD,^{1,3} Volker Budach, MD,^{3,4} Peter Vajkoczy, MD,^{1,3} Christian Furth, MD,⁵ Alexander D. J. Baur, MD,⁵ and Carolin Senger, MD^{3,4}

¹Department of Neurosurgery and Center for Stroke Research Berlin (CSB), ³Charité CyberKnife Center, ⁴Department of Radiation Oncology, and ⁵Department of Nuclear Medicine, Charité—Universitätsmedizin Berlin, Germany; ²Berlin Institute of Health (BIH), Berlin, Germany; and ⁶Department of Neurosurgery, University of Messina, Messina, Italy

OBJECTIVE For stereotactic radiosurgery (SRS) planning, precise contouring of tumor boundaries and organs at risk is of utmost importance. Correct interpretation of standard neuroimaging (i.e., CT and MRI) can be challenging after previous surgeries or in cases of skull base lesions with complex shapes. The aim of this study was to evaluate the impact of ^{68}Ga -DOTATOC PET/MRI on treatment planning for image-guided SRS by CyberKnife.

METHODS The authors retrospectively identified 11 meningioma treatments in 10 patients who received a ^{68}Ga -DOTATOC PET/MRI prior to SRS. The planning target volume (PTV) used for the patients' treatment was defined as the reference standard. This was contoured by a treating radiosurgeon (RS0) using fused planning CT and PET/MRI data sets. The same tumors were then contoured by another experienced radiosurgeon (RS1) and by a less-experienced radiosurgeon (RS2), both blinded to PET data sets. A comparison of target volumes with focus on volume-based metrics and distance to critical structures was performed. RS1 and RS2 also filled in a questionnaire analyzing the confidence level and the subjective need for the implementation of PET data sets for contouring.

RESULTS Analysis showed a subjective personal preference for PET/MRI in all cases for both radiosurgeons, particularly in proximity to critical structures. The analysis of the planning volumes per physician showed significantly smaller RS2-PTV in comparison to RS1-PTV and to RS0-PTV, whereas the median volumes were comparable between RS1-PTV and RS2-PTV (median: RS0: 4.3 cm³ [IQR 3.4–6.5 cm³] and RS1: 4.5 cm³ [IQR 2.7–6 cm³] vs RS2: 2.6 cm³ [IQR 2–5 cm³]; $p = 0.003$). This was also reflected in the best spatial congruency between the 2 experienced physicians (RS0 and RS1). The percentage of the left-out volume contoured by RS1 and RS2 compared to RS0 with PET/MRI demonstrated a relevant left-out-volume portion in both cases with greater extent for the less-experienced radiosurgeon (RS2) (RS1: 19.1% [IQR 8.5%–22%] vs RS2: 40.2% [IQR 34.2%–53%]). No significant differences were detected regarding investigated critical structures.

CONCLUSIONS This study demonstrated a relevant impact of PET/MRI on target volume delineation of meningiomas. The extent was highly dependent on the experience of the treating physician. This preliminary study supports the relevance of ^{68}Ga -DOTATOC PET/MRI as a tool for radiosurgical treatment planning of meningiomas.

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KEYWORDS meningioma; stereotactic radiosurgery; CyberKnife; ^{68}Ga -DOTATOC PET/MRI

MENINGIOMAS are the most common benign primary central nervous system tumors,⁸ and treatment is often required due to neurological deficits or seizures.¹² Surgery represents the first treatment option,¹⁶ but patients with benign meningiomas as well as those

with higher-grade lesions (WHO grades II and III) located at the skull base with proximity to critical neurovascular structures may benefit from upfront or adjuvant radiation therapy.^{4-6,16} Stereotactic radiosurgery (SRS) has been increasingly applied during the last decade for residual

ABBREVIATIONS FSRT = fractionated stereotactic radiation therapy; ^{68}Ga -DOTATOC = gallium-68-labeled [DOTA⁰-Phe¹-Tyr³]octreotide; GTV = gross tumor volume; IMRT = intensity-modulated radiotherapy; IQR = interquartile range; MP-RAGE = magnetization-prepared rapid acquisition with gradient echo; OAR = organ at risk; PET = positron emission tomography; PTV = planning target volume; RS = radiosurgeon; SRS = stereotactic radiosurgery; SSTR = somatostatin receptor.

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* A.D.J.B. and C.S. contributed equally to this work.

or recurrent intracranial meningiomas and for high-risk patients and those who refuse surgery. The most critical step of SRS treatment planning is the precise definition of tumor boundaries together with boundaries of the organs at risk (OARs). It is a matter of fact, also from a revised Leksell concept, that accuracy of targeting depends strongly on the quality of cross-sectional imaging.¹³ In selected cases, especially for skull base tumors or tumors that have recurred after previous skull base surgeries, the standard diagnostic tools, namely contrast-enhanced CT and MRI, have several limits with respect to the precise depiction of tumor borders.⁹ Positron emission tomography (PET) has increasingly been applied in such cases for better tumor visualization, and in particular somatostatin receptor (SSTR) subtype 2–based PET has been shown to provide valuable diagnostic information in cases of meningioma.¹ The most common SSTR ligands for PET imaging are ⁶⁸Ga-DOTATOC, ⁶⁸Ga-DOTATATE, and ⁶⁸Ga-DOTANOC.⁹ The recent report of the RANO/PET group supplied level 2 evidence for the valuable input of ⁶⁸Ga-DOTATOC PET in tumor contouring for radiotherapy planning.⁹ However, the currently published studies analyzing the role of ⁶⁸Ga-DOTATOC PET in radiation therapy planning used only PET/CT, with the exception of 1 case report in which PET/MRI was used.^{11,14,15,17,18} The PET/MRI system may have a substantial advantage over PET/CT because of the precise co-registration of the PET data with MRI used to define tumor boundaries. Therefore, the aim of our study was to analyze the impact of ⁶⁸Ga-DOTATOC PET/MRI in the process of treatment planning of the image-guided SRS with CyberKnife (Accuray Inc.) with comparison of different experience levels in tumor contouring.

Methods

Study Design

We retrospectively identified 11 meningioma treatments in 10 patients who had received ⁶⁸Ga-DOTATOC PET/MRI within 4 weeks prior to CyberKnife radiosurgery in our center. All patients had undergone PET/MRI as a part of their routine work-up. This study was approved by the Charité ethics committee.

Data regarding disease grade, location, and previously performed treatment modalities were gathered from the electronic patient charts. We defined the true treatment plan volume that was contoured by a single experienced radiosurgeon (RS0; > 1000 SRS cases personally managed) using the fused planning CT and PET/MRI data sets as the reference standard. The same tumors were then contoured by another experienced radiosurgeon (RS1; > 1000 SRS cases) and by a less-experienced radiosurgeon in training (RS2; < 100 SRS cases), both blinded to PET data sets. We compared planning target volumes (PTVs) of the 2 radiosurgeons participating in the study (RS1 and RS2) and also compared their PTVs to the reference standard (RS0-PTV). We focused on volume- and dose-based metrics. In addition, the shortest distances of the target volumes from critical structures such as the optic tract and brainstem were investigated. Therefore, all lesions with a distance ≤ 10 mm from these critical struc-

tures were analyzed. Acute complications and short-term clinical follow-up data were recorded.

⁶⁸Ga-DOTATOC PET/MRI

PET/MRI was performed using the tracer ⁶⁸Ga-DOTATOC (gallium-68–labeled [DOTA⁰-Phe¹-Tyr³] octreotide) and a dedicated, commercially available 3-T PET/MRI scanner (Biograph mMR, Siemens Healthcare GmbH). The tracer was administered intravenously (median 165 MBq; interquartile range [IQR] 154–180 MBq). The PET scan was performed a median time of 59 minutes (IQR 54–82 minutes) after administration of ⁶⁸Ga-DOTATOC, with the patient in a supine position; the PET scan covered the whole skull (20 minutes' duration, single bed position, 3D list mode acquisition). PET raw data were reconstructed using an ordered subset expectation maximization (OSEM) algorithm (iterations 3, subsets 3, image matrix 344 × 344 × 127, voxel size 1.04 × 1.04 × 2.03 mm³), and images were filtered using a 3-mm 3D Gaussian filter. The attenuation and scatter correction were based on an ultra-short echo time (UTE) sequence.

MRI scans were performed simultaneously with PET scans using a standardized imaging protocol. Acquired sequences included 2D T1- and T2-weighted sequences of the whole skull in different orthogonal image planes. In addition, 2D T1- and T2-weighted sequences of the optic tract were acquired in selected patients. For contrast-enhanced T1-weighted imaging a body-weight–adjusted dose of a gadolinium-based contrast agent (Gadovist, Bayer Healthcare) was injected intravenously, followed by a saline flush. Contrast-enhanced isotropic 3D high-resolution T1-weighted sequences were acquired in all patients (MP-RAGE [magnetization-prepared rapid acquisition with gradient echo] sequence).

Robotic Radiosurgery Planning and Treatment

All patients were referred to SRS either immediately after surgery or when local or distant disease progression was identified. The decision to perform SRS was made in consensus between patient, referring neurosurgeon, and radiation oncologist in charge. All cases were discussed at the multidisciplinary neuro-oncology tumor conference prior to treatment. In recording tumor characteristics, we used the latest available histological diagnosis.

For treatment planning, high-resolution thin-slice (0.75-mm) CT scans were acquired. A body-weight–adjusted dose of an iodine-based contrast agent (Ultravist 370, Bayer Healthcare) was injected intravenously, followed by a saline flush. Treatment planning was based on planning CT and co-registered PET/MRI data sets (contrast-enhanced T1-weighted MP-RAGE, attenuation-corrected PET). The gross tumor volume (GTV) was defined as the tumor volume based on CT and PET/MRI data sets.

Windowing of PET images was individually performed by a single radiosurgeon. This was accomplished by adjusting the PET window in such a way that the PET-based volume matched the edges of the volume obtained from the simultaneously acquired MR images (PET/MRI), where MR images clearly showed a sharp demarcation of the tumor (e.g., in areas where the tumor was adjacent to

CSF). Once the PET window was set, it was used to contour the tumor in areas where MR images were insufficient to delineate tumor margins (e.g., adjacent to surgical beds or skull base or venous sinuses).

Three different dose concepts were used with respect to the tumor size and proximity to organs at risk. The SRS radiation dose was applied either as single fraction within a range of 14 to 16 Gy, as 3 fractions of 7 Gy (21 Gy total), or as 5 fractions within a range of 4.5 to 6.5 Gy (22.5–32.5 Gy total). The prescription isodose was 70% in 10 cases and 85% in 1 case, depending on the tumor grade planning target volume (PTV), which was either equal to the GTV (no additional margins were added) or with a 1-mm additional margin. Treatment planning and dose calculations were performed with the MultiPlan 4.6 (Accuray Inc.).

Treatment was delivered by a CyberKnife Radiosurgery System VSI (Accuray Inc.), which combines a lightweight linear accelerator with 6-MV photon energy mounted on a 6-axis robotic arm. The image guidance system consists of 2 orthogonally positioned x-ray cameras continually acquiring stereoscopic x-ray images during radiosurgery treatment. Using the 6D skull tracking, the robotic arm aims each radiation beam taking into account any rotational and translational changes of the patient. All measured displacements are automatically corrected, maintaining less than 0.95-mm accuracy and preserving conformal dose distribution. Patients were placed on the robotic couch covering the head with a thermoplastic mask for immobilization.

In addition, for each treatment, RS1 and RS2 filled out a questionnaire that evaluated their confidence level as well as their subjective need for using PET data sets for contouring (5-point Likert scale: Supplementary Fig. 1).

Data Analysis

Planning target volumes and dose statistics such as normalized conformity index (nCI) and volume covered with the prescription isodose could be extracted directly from the treatment planning system. Bland-Altman plots were generated to visualize the difference between the volumes contoured by different radiosurgeons.² To analyze the shape difference between these individual target volumes, the Dice coefficient (as a measure of spatial congruency [1: perfect overlap, 0: no overlap]) and the distance to critical structures were calculated.⁷ Additionally, the percentage of the reference volume that would not have been treated if RS1 or RS2 had contoured with MRI and planning CT only was extracted using customized Python programs (Python 3.6). All metrics were compared using the Wilcoxon signed-rank test for paired samples. A *p* value < 0.05 was considered significant. Cohen's weighted κ was calculated to determine the agreement between the sufficiency of tumor border identifications and the confidence levels of the 2 PET-blinded radiosurgeons (RS1 and RS2) as specified in the questionnaire.³ For statistical analysis, IBM SPSS Statistics (version 25; IBM Corp.) software was used.

Results

Patient Characteristics

Eleven lesions could be included in the analysis. The

total number of patients was 10 because 1 patient was treated twice for different lesions (Supplementary Table 1). With the exception of 1 parasagittal meningioma, all tumors were located at the skull base; 72.7% of the patients had undergone prior surgery, with a median time interval of 4.5 ± 7.5 years (range 0.1–22.4 years) between surgery and radiosurgery (Supplementary Table 1). The tumor histology was unknown or not documented in 5 cases; 36% of the tumors were grade II meningiomas. We observed no acute toxicity related to the treatment within the 1st month after the therapy. The mean follow-up time was 4.5 ± 3.8 months. Within the follow-up period, 1 patient with a sphenoorbital lesion reported suffering from a mild temporary trigeminal neuralgia, although her vision improved after therapy. No further complications were recorded that might be related to a planning error.

Comparison of Planned Target Volumes

The RS0-PTV and RS1-PTV did not differ significantly (mean difference 0.31 ± 1.31 cm³; Fig. 1A). The RS1-PTV was smaller than the RS0-PTV in 60% of the cases and larger in 30% (Supplementary Table 2). The volumes contoured by the less-experienced physician (RS2-PTV) were smaller than the RS0-PTV based on PET/MRI and also smaller than the RS1-PTV, while the median RS0-PTV and RS1-PTV were similar (RS0: 4.3 cm³ [IQR 3.4–6.5 cm³], RS1: 4.5 cm³ [IQR 2.7–6 cm³], RS2: 2.6 cm³ [IQR 2–5 cm³]; RS0 vs RS1, *p* = 0.657; RS0 vs RS2, *p* = 0.003; RS1 vs RS2, *p* = 0.003; Fig. 1B).

The calculation of the spatial overlap of each RS1-PTV and RS2-PTV with the reference standard (RS0-PTV) demonstrated the best overlap between the experienced physicians, RS0 and RS1, whereas we recorded a smaller overlap between RS2-PTV and both RS0-PTV and RS1-PTV (median Dice coefficients—RS0 to RS1: 0.83 [IQR 0.8–0.9], RS0 to RS2: 0.7 [IQR 0.62–0.78], RS1 to RS2: 0.7 [0.67–0.83]; RS0-PTV to RS1-PTV vs RS0 to RS2-PTV: *p* = 0.003; RS0-PTV to RS1-PTV vs RS1-PTV to RS2-PTV: *p* = 0.046; Fig. 1C). The percentage of the RS0-PTV (based on PET/MRI data) that would not have been treated if RS1 or RS2 had contoured based on CT and MRI data sets only, namely the left-out volume, was greater for RS2-PTV than for RS1-PTV (left-out RS1-PTV: 19.1% [IQR 8.5%–22%] vs left-out RS2-PTV: 40.2% [IQR 34.2%–53%]; *p* = 0.003; Figs. 2 and 3).

Distance to Critical Structures

By trend, RS2 was more restrictive and kept a larger distance between the PTV and OARs by reducing the PTV borders. We did not detect any significant differences regarding either of the critical structures of interest (Table 1).

Evaluation of Radiosurgeon Confidence

The questionnaire results demonstrated a high level of uncertainty about tumor borders where contouring was based on CT and MRI especially in close proximity to critical structures. Overall, levels of confidence about identification of the tumor borders based on CT and MRI data sets were comparable between RS1 and RS2 (median values for RS1 and RS2, respectively—CT: 4/5 and 3/5, κ

FIG. 1. Comparison of the contoured tumor volumes per physician. **A:** Bland-Altman plots of the target volumes for each patient demonstrating the smallest differences between the volumes of the experienced physicians RS0 and RS1. Major differences were seen between RS0 and RS2. **B:** Comparison of the median volumes of 11 tumors per physician showed significantly smaller tumor volumes contoured by the RS2 in comparison to RS0 and RS1 (Wilcoxon signed-rank test, **p < 0.01; RS0 vs RS2, p = 0.003; RS1 vs RS2, p = 0.003). **C:** The box plots of the Dice coefficient (1: perfect overlap, 0: no overlap) demonstrate the best overlap between the experienced physicians. There was little overlap between RS2 and either RS0 or RS1 (Wilcoxon signed-rank test, *p < 0.05, **p < 0.01; RS0/RS1 vs RS0/RS2: p = 0.003; RS0/RS1 vs RS1/RS2: p = 0.046). In panels B and C, the white circles represent outliers and the boxes present the IQRs, with the medians indicated by the thick black lines.

= -0.014; MRI: 3/5 and 3/5, κ = -0.082). However, when the results were analyzed on a per lesion basis, the confidence level differed between both radiosurgeons. The overall confidence level was higher for the experienced

radiosurgeon, RS1, while the less-experienced radiosurgeon, RS2, felt unconfident in all of the skull base cases (median values for RS1 and RS2, respectively: 3/5 and 1/5, κ = 0.016; Table 2).

FIG. 2. Comparison of contoured lesion coverage. A representative case demonstrating each contour per physician: the reference standard (RS0-PTV) in red, the experienced radiosurgeon (RS1-PTV) in yellow, and the less-experienced radiosurgeon 2 (RS2-PTV) in dark blue shown on the CT scan (left), on the MRI (center), and on the co-registered CT and PET (right) with the addition of the green line for the 70% isodose line and bright blue line outside for the 20% isodose line. This example highlights the importance of PET/MRI for the identification of the full tumor extension, here in particular the intraorbital tumor portion. In addition, physiological uptake of the tracer in the pituitary gland in proximity to the contoured lesion is seen.

FIG. 3. The quantification of the median left-out volume contoured by radiosurgeon 1 (RS1) or radiosurgeon 2 (RS2) with CT and MRI only in comparison to the treated volume contoured based on the PET/MRI (reference standard [RS0]), demonstrating a significantly higher left-out-volume portion for RS2 compared to RS1 (Wilcoxon signed-rank test, $**p < 0.01$; RS1 vs RS2: $p = 0.003$). The white circle represents an outlier and the boxes present the IQR, with the medians indicated by the thick black lines.

The responses about the potential impact of adding PET for PTV definition were overall similar for both RS1 and RS2. Both responded that this would be desirable to improve PTV definition close to critical structures such as the optic tract and brainstem. The less-experienced radiosurgeon also assessed PET as desirable in 2 cases for identification of the overall borders and in 2 cases for identification of vessel regions. For detailed results of the questionnaire see Table 2.

Discussion

Our preliminary data suggest a significant impact of PET/MRI in the contouring of meningiomas, especially at the beginning of the learning curve. The detailed analysis of results revealed also that there was a difference for the experienced radiosurgeon when the PTV was contoured with or without PET, which highlights the potential clinical impact of this imaging modality in meningioma SRS.

Compared to CT, MRI offers improved soft tissue contrast and allows accurate visualization of intracranial tissues, including critical structures for radiosurgery planning, such as the optic tract. Furthermore, the simultaneous acquisition of PET and MRI data sets results in more accurate co-registration. A case report published in 2012 compared PET/MRI with PET/CT for intensity-modulated radiotherapy (IMRT), showing that PET/MRI provided more detailed visualization of meningioma especially in small infiltrative regions.¹⁸ However, to our best knowledge, no further studies evaluating PET/MRI have been performed since then. Other studies have shown significant tumor volume differences with the use of PET/CT for planning compared to the use of CT and MRI.^{10,11,14,17} Another advantage of PET/MRI over PET/CT is the avoidance of additional radiation exposure due to CT performed for attenuation correction.

Gehler et al. reported that the use of ⁶⁸Ga-DOTATOC-

TABLE 1. Minimum distance of contoured volumes from optic tract and/or brainstem ≤ 10 mm

Tumor Location	Distance From Optic Tract			Distance From Brainstem		
	RS0	RS1	RS2	RS0	RS1	RS2
Sphenopetrosal	3.4	6.2	6.9	0.8	0.0	0.0
Optic nerve sheath	0.6	0.0	0.8			
Sphenoorbital	0.0	0.0	2.8	6.5	4.8	8.9
Sinus cavernosus	2.7	2.7	3.9	5.2	5.2	5.3
Optic nerve sheath bilateral	0.0	0.0	0.0			
Anterior clinoid	0.6	0.8	1.2			
Petroclival	0.6	0.0	0.0	3.8	2.4	2.4
Tuberculum sellae	0.0	0.0	0.0	5.4	4.6	6.8
Tuberculum sellae/chiasm	0.0	0.0	0.0			
Median	0.6	0.0	0.8	5.2	4.6	5.3
25th percentile	0.0	0.0	0.0	2.3	1.2	1.2
75th percentile	0.6	0.0	0.8	6.0	5.0	7.8

RS = radiosurgeon.

Distances are in millimeters; 0 denotes no distance or the presence of overlap.

PET in IMRT planning led to additional information about tumor extension in 17 (65%) of 26 cases; overall GTV with PET was smaller than with MRI/CT in 10 patients (38%), larger in 13 patients (50%), and almost the same in 3 patients (12%).¹⁰ Graf et al. analyzed the role of PET/CT in fractionated stereotactic radiation therapy (FSRT) planning in 48 patients and showed that the addition of ⁶⁸Ga-DOTATOC-PET resulted in more than 10% modification of the tumor size, mostly a reduction of the tumor volume.¹¹ Milker-Zabel et al. investigated the role of PET/CT for FSRT planning in 26 patients and reported a significant alteration in target definition in 73%, where in 38% of the cases the volume was smaller.¹⁴ Stade et al. recently published the impact of ⁶⁸Ga-DOTATOC-PET on treatment planning of advanced photons and protons in a small cohort of 10 patients and reported significant reductions of the target volumes in most cases.¹⁷ We observed in our study also a relevant impact of PET/MRI on the target volumes in both directions, especially in regions close to OARs, where it is difficult to find the best compromise between tumor coverage and protection of critical structures. Consequently, if the planning had not been based on the additional information provided by PET, a significant part of the tumor would have not been treated (experienced RS1-PTV compared to the reference PTV: in 6 cases, 54.5%). Importantly, due the fact that PTV is equal to GTV in the majority of the cases, a precise tumor definition is much more important in SRS than in FSRT because of the missing generous safety margins. Thus the impact of PET/MRI may be even more relevant in SRS.

Furthermore, our study not only highlights the impact of PET/MRI in contouring of selected cases but also compared different experience levels. Overall, our results underscore a potentially higher relevance of the PET/MRI modality for physicians in training as increased experience in contouring may at least partially compensate for the additional information value provided by PET. How-

TABLE 2. Results of the questionnaire analyzing the identification of the tumor borders and the confidence level of the 2 participating radiosurgeons

Lesion No.	Location	RS 1				RS 2			
		Lesion Borders by MRI	Lesion Borders by CT	Confidence Level	PET Required Regions*	Lesion Borders by MRI	Lesion Borders by CT	Confidence Level	PET Required Regions*
1	Sinus cavernosus	1	4	2	Intrasellar, optic canal	3	2	1	Intrasellar, optic canal, borders
2	Tuberculum sellae	3	4	3	Intraorbital, intrasellar	2	3	1	Optic chiasm
3	Sphenopetrosal	3	3	3	Meckel's cave	4	2	1	Dural origin, Meckel's cave
4	Optic nerve sheath	3	4	3	Intraorbital	1	3	1	Intraorbital
5	Sphenoorbital	2	4	2	Intraorbital	3	2	1	Intraorbital, sinus cavernosus
6	Sphenoorbital	1	4	3	Intraorbital, clivus	3	3	1	Intrasellar
7	Petroclival	4	1	4	Temporal base	3	3	1	Temporal base, bone infiltration
8	Optic nerve sheath	4	4	4	Intraorbital, jugum sphenoidale	3	3	1	Optic chiasm
9	Anterior clinoid	4	4	4	Optic canal	3	3	1	Sinus cavernosus, MCA, borders
10	Tuberculum sellae	3	4	3	Intrasellar, optic canal	3	3	1	Intrasellar, sinus cavernosus, carotid artery
11	Falx	4	4	4	Right side	4	4	3	Sinus cavernosus
Median		3	4	3		3	3	1	

MCA = middle cerebral artery.

A 5-point Likert scale was used for the scoring, with 1 indicating the lowest and 5 indicating the highest level for identification of the borders and confidence.

* Regions for which PET provided essential information.

ever, we also detected a high relevance for the experienced physician. Clinically, one of the most relevant analyses was the percentage of the RS0-PTV that would not have been treated if RS1 or RS2 had contoured without the help of PET/MRI. It could be demonstrated that a less-experienced physician would have left out 40.2% of the target volume, while even an experienced radiosurgeon would have left out 19% of the target volume.

A technical issue is the visualization of PET uptake values or the windowing of PET images that influences the tumor size and delineation in visual assessment. This seems to be especially true for volume definitions using PET/CT data. However, this issue may be at least in part resolved by simultaneous PET/MRI acquisitions, with the improved soft tissue contrast of MRI compared to CT. The improved sensitivity of PET for meningiomas, in comparison to MRI,¹ allows an improved visualization of tumor boundaries, especially in areas where MRI is of limited value to delineate true tumor extension (e.g., in areas where tumor is adjacent to scar tissue from previous surgery or close to the skull base and venous sinuses). In our study, the same radiosurgeon used PET/MRI for PTV definition in all cases, using a predefined and reproducible approach, so that adjustment of the windowing of PET images was somewhat standardized. Nonetheless, fully standardized windowing protocols for PET data would be desirable (e.g., standard uptake value [SUV]–based or SUV-independent automatic thresholding or threshold-

ing by standardized windowing based on reproducible measurements in reference tissues), and to the best of our knowledge these are still lacking. In addition, the accuracy of target volume planning for meningiomas based on PET data might be limited by the fact that the pituitary gland usually has strong tracer uptake and therefore differentiation from tumor might be complicated.¹⁴ This was evident in 3 cases in our study with tumors being located in proximity to the pituitary gland.

Based on our analysis showing relevant left-out tumor volume without PET and high demand in challenging cases for more imaging support to improve the radiosurgeon's confidence, we are convinced that PET/MRI may provide a substantial therapeutic benefit. This technique should be applied especially in cases of skull base meningiomas, e.g., after optic decompression or in locations where demarcation of tumor margins by MRI is complicated, such as near the optic nerve sheath, at the skull base, or near the venous sinuses. The possible effects on tumor progression and overall patient outcome still need to be demonstrated. Nonetheless, our results warrant future studies, including follow-up investigations.

Conclusions

Even considering the limitations of our study represented by the low number of cases and operators with the lack of standardization for interpretation of PET data sets, our

study supports the integration of ^{68}Ga -DOTATOC-PET/MRI in the contouring of skull base meningiomas. The impact appears to be higher for less-experienced physician, but not negligible for those with a long experience of SRS. To our knowledge this is the first case series highlighting the impact of PET/MRI in CyberKnife radiosurgery treatment planning. Further studies to establish technical standards are warranted.

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Disclosures

Mathias Lukas reports an employee relationship with Siemens Healthcare GmbH. Alexander Baur reports having received payments as a speaker for Bayer Pharmaceuticals and Bender.

Author Contributions

Conception and design: Acker, Senger. Acquisition of data: Conti, Acker, Meinert, Nguyen, Jelgersma. Analysis and interpretation of data: Acker, Kluge, Lukas. Drafting the article: Acker, Baur, Senger. Critically revising the article: Conti, Kluge, Lukas, Pasemann, Budach, Vajkoczy, Furth, Baur, Senger. Reviewed submitted version of manuscript: Acker, Budach, Vajkoczy, Furth, Baur, Senger. Approved the final version of the manuscript on behalf of all authors: Conti. Statistical analysis: Kluge, Lukas. Administrative/technical/material support: Kluge, Pasemann, Jelgersma, Loebel, Baur. Study supervision: Conti, Acker, Senger.

Supplemental Information

Online-Only Content

Supplemental material is available online.

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Correspondence

Alfredo Conti: Charité–Universitätsmedizin Berlin, Germany. alfredo.conti@charite.de.