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Original article

# Clinical outcome after high-precision radiotherapy for skull base meningiomas: Pooled data from three large German centers for radiation oncology

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*Purpose:* To evaluate outcome in patients with base of skull meningiomas treated with modern high precision radiation therapy (RT) techniques.
*Patients and methods:* 927 patients from three centers were treated with either radiosurgery or fractionated high-precision RT for meningiomas. Treatment planning was based on CT and MRI following institutional guidelines. For radiosurgery, a median dose of 13 Gy was applied, for fractionated treatments, a median dose of 54 Gy in 1.8 Gy single fractions was prescribed. Follow-up included a clinical examination as well as contrast-enhanced imaging. All patients were followed up prospectively after radiotherapy in the three departments within a strict follow-up regimen. The median follow-up time was 81 months (range 1–348 months).
*Results:* Median local control was 79 months (range 1–348 months). Local control (LC) was 98% at 1 year, 94% at 3 years, 92% at 5 years and 86% at 10 years. There was no difference between radiosurgery and fractionated RT. We analyzed the influence of higher doses on LC and could show that dose did not impact LC. Moreover, there was no difference between 54 Gy and 57.6 Gy in the fractionated group. Side effects were below 5% in both groups without any severe treatment-related complications.
*Discussion:* Based on the pooled data analysis this manuscript provides a large series of meningiomas of the skull base treated with modern high precision RT demonstrating excellent local control and low rates of side effects. Such data support the recommendation of RT for skull base meningiomas in the interdisciplinary tumor board discussions. The strong role of RT must influence treatment recommendations keeping in mind the individual risk–benefit profile of treatment alternatives.


Skull base meningioma is a challenging entity: Most cases are low-grade meningiomas characterized by slow growth patterns which are rather expansive than invasive. Due to the intricate anatomy in the skull base region meningiomas are generally in very close vicinity to sensitive normal tissue structures. For all treatment alternatives, the small spaces and narrow anatomical boundaries must be kept in mind when deciding on the treatment method and when counseling patients.

For a long time, surgical removal was the standard of care, independently of the size, location or histology. However, due to the anatomical limitations, neurosurgical intervention may bear the risk of significant side effects. Over the last decade radiation therapy (RT) has become a valid treatment alternative for the treatment of meningiomas. Especially with the advent of high precision techniques, such as stereotactic radiotherapy or intensity modulated radiotherapy (IMRT). Local dose deposition became possible, while normal tissue could be spared and acute as well as long-term treatment-related side effects could be kept very low. Several institutions have treated skull base meningiomas successfully: long-term local control is associated with a beneficial toxicity profile with very low rates of side effects; moreover, quality of life (QoL) is preserved in the majority of patients, or even improved [1–12]. Previously, a detailed questionnaire has been developed which has shown that long-term local control is

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**Table 1**
Patients' characteristics.

| | Single Dose | Fractionated Treatment |
|---|---|---|
| Patients per Center, *n* | | |
| HD | 0 | 507 |
| MUC | 16 | 197 |
| FB | 103 | 104 |
| Age, years (median, range) | 59 (14–83) | 59 (21–86) |
| Total Dose, Gy (median, range) | 13 (8–20) | 54 (47,4–66.2) |
| Single Dose, Gy (median, range) | 13 (8–20) | 1,8 (1,6–2.5) |
| Follow-up, months (median, range) | 59 (3–186) | 81 (7–349) |
| GTV, ml (median, range) | 3.72 (1.37–8,17) | 30.25 (1.2–753.97) |

excellent and can be associated with an improvement in symptoms and QoL over time [1]; this patient-reported outcome has been validated by an independent cohort confirming the convincing data for meningioma RT [13]. This results in the context of several other reports having led to much controversy as to when surgery, which previously was the treatment of choice, still remains necessary; consensus statements, however, often still underestimate the real value of RT in this clinical situation: Radiation oncologists report an excellent long-term outcome for smaller as well as larger lesions, thus arguing that resection could be potentially limited to large lesions leading to extensive normal tissue compression. However, surgery still remains the treatment of choice in the majority of cases and depending on the surgical team even complex lesions can be resected successfully.

To generate a large-scale database to evaluate the value of RT for skull base meningiomas several institutions have reported their outcome after fractionated stereotactic radiation therapy (FSRT) or intensity modulated radiotherapy (IMRT), including various sizes of patient populations [1,2,14–31]; the three largest centers have pooled their data in the present manuscript bringing together experiences and treatment concepts to evaluate the best-available radiotherapy concept and to prove the efficacy independently of departmental boundaries.

The present analysis reports on the pooled data of three large radiation oncology centers for radiosurgery and high-precision RT (FSRT or IMRT) for skull base meningiomas to evaluate long-term outcome as well as treatment-related side effects in a very large group of patients.

## Materials and methods

The inclusion criteria were low grade (WHO Grade I) skull base meningioma, either histologically or imaging confirmed with clear imaging criteria for low grade meningiomas (e.g. dural-based mass, isointense to gray matter on both T1 and T2 weighted imaging, contrast-enhancing on both MRI and CT), with an indication for RT. A total of 927 patients were included into the database. Ethics approval was obtained from all three institutions. Munich/TUM included 213 (23%) patients, Freiburg 207 patients (22%), and Heidelberg 507 patients (55%). The median age was 58 years (range 14–86 years). Detailed information on treatment characteristics are summarized in Table 1. 808 patients (87%) were treated with fractionated radiotherapy and 119 patients (13%) with radiosurgery. Typical treatment plans for both approaches are shown in Fig. 1.

### *Heidelberg treatment planning*

507 patients (55%) were included from Heidelberg in the present analysis. Patients were fixed in an individual mask fixation either made of Scotch Cast or thermoplast as published previously [1]. Based on CT as well as MR-imaging, the Gross Tumor Volume (GTV) was delineated, including the macroscopically visible lesions including any bony infiltrations. A Clinical Target Volume (CTV) was added of 1–2 mm accounting for a potential microscopic spread. The Planning Target Volume (PTV) depended on the technique and was 1–3 mm. (68)Ga-DOTATOC PET was added for target volume definition when available [28]. Treatment was delivered using a 6 MV linear accelerator (Siemens, Erlangen, Germany) or a tomotherapy system (Tomotherapy, Madison, Wisconsin). FSRT was applied using 3–5 non-coplanar fields individually shaped by an add-on micro-multileaf collimator with a resolution of 1.5 or 5 mm at isocenter. IMRT was delivered using the step-and-shoot technique or with 5–9 fields or as helical IMRT. All patients were treated with a fractionated regimen and a median dose of 57.6 Gy in 1.8 Gy single fractions.

### *Munich/TUM treatment planning*

Munich/TUM contributed 213 patients (23%), of which 16 patients (8%) were treated with radiosurgery [32]. Treatment planning was performed using Brainlab mask fixation as well as Exac Trac© for positioning and positioning verification. The GTV was contoured on CT and MR-imaging with and without contrast enhancement, including information from (68)Ga-DOTATOC- or Methionine-PET when available, including the macroscopic lesion and bony infiltration. For FSRT, the CTV of 1–2 mm to the brain and 3–4 to dura/tentorium was added as well as the PTV between 1 and 2 mm depending on the RT technique. For radiosurgery, the CTV was 1 mm to GTV in all directions; the PTV 1 mm to CTV.

Radiosurgery was delivered with a median dose of 16 Gy/100% isodose (range 13–17 Gy). All other patients (92%) were treated with fractionated regimens with a median total dose of 54 Gy in 1.8 Gy single fractions.

### *Freiburg treatment planning*

207 patients (22%) were treated with FSRT ($n = 104$; 50%) or radiosurgery ($n = 103$; 50%). The head was fixed using a self-made individual mask or a Brainlab mask fixation as well as Exac Trac© for positioning and positioning verification. The GTV was delineated based on (68)Ga-DOTATOC- or Methionine-PET. The GTV, CTV, and PTV were delineated similar to the Munich/TUM concept, using the same total dose and fractionation (see Munich/TUM treatment planning). The treatment was delivered using a True-Beam Novalis Radiosurgery 6 MeV LINAC.

### *Follow up, data collection and analysis*

All patients were followed up prospectively after RT in the three departments within a strict follow-up regimen. A first follow-up visit was scheduled 6 weeks after completion of RT, thereafter in 3 months intervals for the first year. From the second year on, follow-up intervals were extended to 6–12 months, or as required clinically. All visits included contrast-enhanced imaging and thorough clinical assessment. Additional examinations were scheduled as needed, including ophthalmologic examination, neurological treatment or endocrinological evaluations. Progression-free survival (determined as local control) was determined based on the RECIST criteria evaluating two orthogonal diameters of the lesion.

After RT, the median follow-up time was 81 months (range 1–348 months).

The data from all three centers were collected in a common database. Local control (LC) as defined as the interval from the first day of RT to local tumor progression or death (also any cause). Events were censored at last follow-up. Analysis of prognostic factors on local control was performed using the Kaplan–Meier

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