J Neurooncol (2013) 113:135–141
DOI 10.1007/s11060-013-1099-1

CLINICAL STUDY

# Quality of life after stereotactic radiotherapy for meningioma: a prospective non-randomized study

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Received: 6 December 2012 / Accepted: 22 February 2013 / Published online: 28 February 2013


**Abstract** Stereotactic radiotherapy (SRT) is well-established in the treatment of meningiomas offering high local control with low toxicity. However, the impact of SRT on quality of life (QoL) of patients remains largely unknown. This work aimed to prospectively evaluate QoL (longitudinal analysis) during and after SRT of meningiomas. We performed a single center, one-armed, prospective non-randomized study to assess QoL before and at the end of SRT (median fraction dose: 1.8 Gy; median cumulative dose: 54.0 Gy) and furthermore biannually until 24 months after SRT with the "medical outcome study short form 36". This questionnaire evaluates 8 health parameters summarized in "physical component scale" (PCS) and "mental component scale" (MCS). Between 2005 and 2007, 67 patients were enrolled and treated with SRT. 42/52 patients underwent previous operations and 10/52 primary SRT. Complete follow-up data were available from 44 patients. Compared to the german normal population (GNP) a general decrease in the mean values of all parameters was observed. After SRT mean values still declined and 12 months after SRT all parameters normalized towards their initial values. The cohort (previous operations) had better values for MCS ($p = 0.004$). The cohort (primary SRT) had worse values for PCS that increased asymptotically 6 months after SRT to values of cohort (previous operations) ($p = 0.054$). Gender, age and tumor related symptoms did not affect QoL according to MCS and PCS ($p > 0.05$). Local control was 98 %. Treatment was well tolerated and no severe side effects were observed. Patients with meningiomas have an impaired QoL compared to GNP. The QoL assessment after SRT revealed three phases: "depressive phase", "recovery phase" and "normalization phase". Patients treated with primary SRT developed a stable increase of the mean values for PCS. Gender, age, applied dose, symptomatology did not affect QoL.

**Keywords** Quality of life · Meningioma · Stereotactic radiotherapy · Prospective study

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## Introduction

Stereotactic radiotherapy (SRT) of meningiomas results in high local tumor control rates of [1–4] with low risk of clinically significant (CTC III–IV) early and late toxicity [3, 4].

Despite such high local tumor control rate and a modest risk of severe treatment-related side effects, important QoL parameters such as emotional, physical, cognitive functioning and mental health are often affected in this group of patients, especially in young individuals [5]. However, the impact of SRT on the quality of life (QoL) of patients with meningiomas remains largely unknown. Different groups have reported on the QoL after microsurgical resection, with or without radiotherapy [6–8]. However, these studies have several limitations such as retrospective nature, small patient cohorts, poorly-defined time of QoL assessments

and lack of clear distinction between microsurgical and radio-therapeutical effects on QoL [6–8]. Notably, patients were treated using 3D-conventional radiotherapy instead of modern, high precision techniques such as SRT [6–8].

To our best knowledge, to date no prospective study reports on the QoL of patients treated with SRT. Thus, this work aimed to prospectively evaluate the QoL in terms of a longitudinal analysis during and after SRT of meningiomas.

## Methods

### Study design and eligibility criteria

The present QoL study constitutes a single center, one-armed, prospective non-randomized study. Eligibility criteria included patients aged 18 years or older, good ECOG performance score (0–2) and Karnofsky performance status ($\geq$70 %), life expectancy longer than 2 years and compliance in filling the study questionnaire. Where feasible, meningioma (WHO I–III°) was histopathologically confirmed. Patients were eligible without histopathological confirmation in cases of complex skull base meningioma, optic nerve sheath meningioma or cavernous sinus-invading meningioma were biopsy was avoided to prevent potential damage of organs at risk. In these cases diagnosis was based on the contrast-enhanced T1 weighted MRI-scans.

SRT constitutes the standard radiotherapy technique for the treatment of patients with meningioma in our center. Primary SRT was performed in patients with small tumors causing minor symptoms, in patients favoring SRT instead of surgery, in patients with tumors where gross total resection was not possible or associated with a high risk for postoperative deficits, and in elderly patients with high medical operation risk. After incomplete microsurgical resection of scull base meningeomas patients underwent additive SRT.

### Assessment of the quality of life (QoL) and statistical analysis

QoL was assessed before initiation of SRT (baseline assessment), at the last day of SRT and thereafter biannually. Primary endpoint was the QoL throughout SRT and during the follow-up period of 2 years. QoL was assessed with the "medical outcome study short form 36" (SF36) [9]. This questionnaire comprises of 36 items assessing 8 major health parameters: physical functioning (pf), physical role functioning (rolph), bodily pain (pain), general health (ghp), vitality (vital), social functioning (social), emotional role functioning (rolem) and mental health (mh) summarized in "physical component scale" (PCS) and "mental component scale" (MCS). The values for PCS and MCS were compared according to age, gender, irradiation dose, changes in symptoms and previous operations and were tested using the Kruskal–Wallis test with a significance threshold of 0.05. Local control was calculated with the Kaplan–Maier method. Secondary endpoints were local tumor control, acute and late side effects, and symptom control.

### 3D-treatment planning

SRT was performed as previously described [10]. Patients were immobilized with an individually-formed mask attached to a stereotactic frame. Patients underwent CT- and MRI scans with 1–3 mm slice thickness without gap for treatment planning. After stereotactic registration and image fusion, the planning target volume (PTV) and the critical structures such as eyes, optic nerves, optic chiasm, and brainstem were contoured. 3D-dose distribution was calculated by "Voxelplan" [10]. PTV was encompassed by 90–95 % of the prescribed dose at the reference point, usually at the isocenter and the dose to organs at risk was taken into consideration [10].

### Irradiation technique

Treatment was delivered by a linear-accelerator with 6 MV photons (Siemens KD2) using a micro-multileaf collimator with 1 mm leaf thickness. The gross target volume (GTV) was defined as the area of contrast-enhancement on T1-weighted MRI. The planning treatment volume (PTV) included the GTV plus 2 mm safety-margin. We used 4–5 isocentric, irregularly shaped, non-coplanar static beams with a single isocenter. Fraction dose was 1.8 Gy and the cumulative median dose was 50.4 and 59.4 Gy for Grade I and Grade II–III meningiomas, respectively.

### Clinical examinations and follow-up

Patients underwent weekly clinical examinations throughout the course of radiotherapy. They were followed at 6, 12, 18 and 24 months after SRT and thereafter yearly including clinical examination (evaluation of symptoms and neurological status) and MRI scans. Acute toxicity was evaluated using the common toxicity criteria (CTC; version 3) [11] and late toxicity using the LENT-SOMA score [12].

## Results

### Patient characteristics

Between 2005 and 2007, 67 patients were enrolled in this study, were treated with SRT in the Department of Radiation Oncology, Philipps University Marburg, Germany. Fifteen patients were excluded because of non-compliance

with filling the questionnaire form during follow-up. Of note, these 15 patients only completed the QoL questionnaire before initiation of SRT but not after that and hence no QoL data were available for this patient subgroup after the beginning of SRT. Therefore, the analysis of QoL was based on the questionnaires of 52 patients (39 females; 13 males). Median age was 57 years (range: 40–81 years). From these, 42/52 patients underwent previous surgery (single time) and 10/52 underwent primary SRT. From the patient cohort that had previously been operated ($n = 42$), 33 patients suffered from WHO Grade I, 7 from WHO Grade II and 2 from WHO Grade III meningioma.

From the 52 patients, 8 patients failed to fill all the questionnaire forms up to 2 years after radiotherapy. Three patients died from progressive senile decay and one patient died from a newly diagnosed, metastasized breast cancer. Two patients did not fill in further questionnaires because of dementia and further 2 patients because of non-compliance. Hence follow-up data reaching the endpoint at 2 years post-radiotherapy were available from 44 patients.

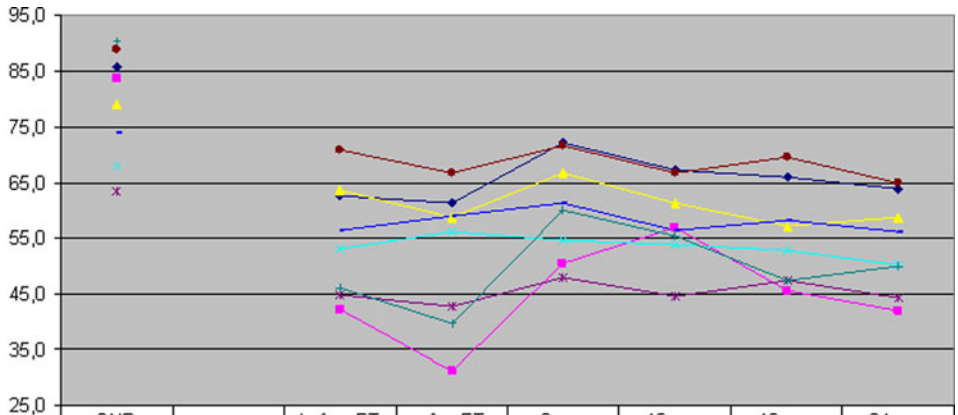
Regarding the localization of meningioma in the patients included in the final analysis ($n = 52$), 29 were located in the medial wing of sphenoid, 8 were petroclival, 3 were tentorial, 4 were at the falx cerebri, 1 directly invaded the optic nerve, 1 invaded the olfactory nerve and 6 were extending from petroclival bone up to the sphenoid bone.

Clinical symptoms before the beginning of SRT included ptosis and diplopia ($n = 15$), visual impairment ($n = 30$; one patient had complete amaurosis), diplopia ($n = 6$), anosmia ($n = 1$), trigeminal neuralgia ($n = 12$), facial paralysis ($n = 2$), dizziness and hearing impairment ($n = 9$; one patient with complete hearing loss), unilateral exophtalmus ($n = 12$) and motor-sensory symptoms due to brainstem compression ($n = 7$).

## Quality of life

Prior start of radiotherapy, we observed a general decrease in the mean values of all 8 health parameters, as compared to the mean values for the "German normal population" (GNP) i.e. to population without meningioma (Fig. 1; Table 1). At the end of the RT the mean values in 6 health parameters had further declined. The most prominent decline of the mean values was noticed for rolph (−11.0), rolem (−6.5) and for pain (−5.0). The values of social (−3.9), vital (−2.0) and pf (−1.3) as well decreased during radiotherapy to a lower extent. On the contrary, mean values for mh (+2.5) and for ghp (+3.0) improved until the end of radiotherapy.

All health parameters increased after the completion of radiotherapy. Except rolph, all health parameters reached their maximum value 6 months after SRT. The mean values for rolem (+20.2) and rolph (+25.6) showed the biggest increase after SRT. Twelve months after SRT all




| | GNP | | before RT | after RT | 6 mo | 12 mo | 18 mo | 24 mo |
|---|---|---|---|---|---|---|---|---|
| pf | 85,7 | | 62,7 | 61,4 | 72,0 | 67,1 | 65,8 | 63,9 |
| rolph | 83,7 | | 42,3 | 31,3 | 50,5 | 56,9 | 45,6 | 42,0 |
| pain | 79,1 | | 63,7 | 58,7 | 66,6 | 61,2 | 57,2 | 58,7 |
| ghp | 68,1 | | 53,0 | 56,2 | 54,5 | 53,8 | 52,8 | 50,2 |
| vital | 63,3 | | 44,7 | 42,7 | 48,0 | 44,6 | 47,4 | 44,3 |
| social | 88,8 | | 70,7 | 66,8 | 71,6 | 66,8 | 69,4 | 64,8 |
| rolem | 90,4 | | 46,2 | 39,7 | 59,9 | 55,3 | 47,4 | 50,0 |
| mh | 73,9 | | 56,5 | 59,0 | 61,3 | 56,5 | 58,2 | 56,1 |

**Fig. 1** Summary of the mean values of the "medical outcome study short form 36" for the 8 health parameters prior start of stereotactic radiotherapy until 24 months after completion of radiotherapy. *GNP* German normal population, *RT* radiotherapy, *Mo* months, *pf* physical functioning, *rolph* physical role functioning, *pain* bodily pain, *ghp* general health, *vital* vitality, *social* social functioning, *rolem* emotional role functioning, *mh* mental health

**Table 1** Comparison of the mean values of the "medical outcome study short form 36" for the German normal population and the patients before stereotactic radiotherapy with regard to all health parameters

| Health Domains | Before start of RT | GNP | *p* |
|---|---|---|---|
| pf | 62.7 | 85.7 | <0.001 |
| rolph | 42.3 | 83.7 | <0.001 |
| Pain | 63.7 | 79.1 | 0.005 |
| Ghp | 53.0 | 68.1 | <0.001 |
| Vital | 44.7 | 63.3 | 0.004 |
| Social | 70.7 | 88.8 | <0.001 |
| rolem | 46.2 | 90.4 | <0.001 |
| mh | 56.5 | 73.9 | 0.203 |

*GNP* german normal population, *RT* radiotherapy, *p* probability, *pf* physical functioning, *rolph* physical role functioning, *pain* bodily pain, *ghp* general health, *vital* vitality, *social* social functioning, *rolem* emotional role functioning, *mh* mental health

parameters began to normalize towards their initial values (follow-up interval: "24 months after-RT").

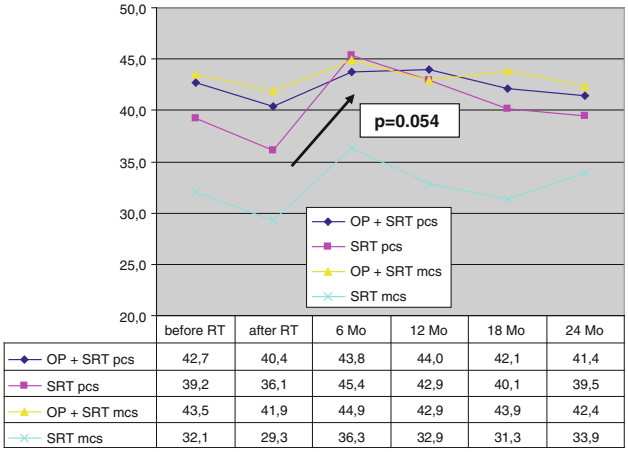
### Determinant factors

Patients who had undergone previous operations had significantly higher MCS values already before SRT ("before RT", $p = 0.004$) as compared to patients who received primary SRT. At the end of RT ($p = 0.014$) and in each follow-up interval after SRT ($p = 0.006$) the values for MCS were also significantly higher in the group of patients who received previous surgery plus radiotherapy as compared to the group of patients who received SRT alone. This significance did exist until the end of SRT and during all follow up investigations. The two groups of patients who received either surgery plus stereotactic irradiation or stereotactic irradiation alone are referred to in the remainder of the text as suffix "OP + SRT" and "primary SRT", respectively.

Comparing the mean values between PCS $_{\text{OP + SRT}}$ and PCS $_{\text{primary SRT}}$ there were no statistically significant differences seen at any interval. Between the intervals "after RT" i.e. immediately upon completion of radiotherapy, and "6 months after SRT" the mean values for PCS $_{\text{primary SRT}}$ increased (+9.3) and reached similar mean values as PCS $_{\text{OP + SRT}}$ but did not reach significance ($p = 0.054$).

At the follow-up interval "12 months after RT" all mean values for PCS and MCS began to normalize towards their initial values (follow-up interval "24 months after RT"). Details are shown in Fig. 2.

The values for MCS and PCS were not significantly affected by sex (male vs. female), age (≤57 vs. >57 years), radiation dose (≤54 vs. >54 Gy) or change in tumor related symptoms (improvement vs. no change) ($p > 0.05$). For details see Fig. 3a–c.




| | before RT | after RT | 6 Mo | 12 Mo | 18 Mo | 24 Mo |
|---|---|---|---|---|---|---|
| OP + SRT pcs | 42,7 | 40,4 | 43,8 | 44,0 | 42,1 | 41,4 |
| SRT pcs | 39,2 | 36,1 | 45,4 | 42,9 | 40,1 | 39,5 |
| OP + SRT mcs | 43,5 | 41,9 | 44,9 | 42,9 | 43,9 | 42,4 |
| SRT mcs | 32,1 | 29,3 | 36,3 | 32,9 | 31,3 | 33,9 |

**Fig. 2** Summary of the mean values for physical component summary and mental component summary of the "medical outcome study short form 36" according to the determinant factors operation(s) plus stereotactic radiotherapy or stereotactic radiotherapy. The *black arrow* indicates the trend towards significance ($p = 0.054$). *RT* radiotherapy, *SRT* stereotactic radiotherapy, *Mo* months, *OP* operation(s), *pcs* physical component summary, *mcs*: mental component summary

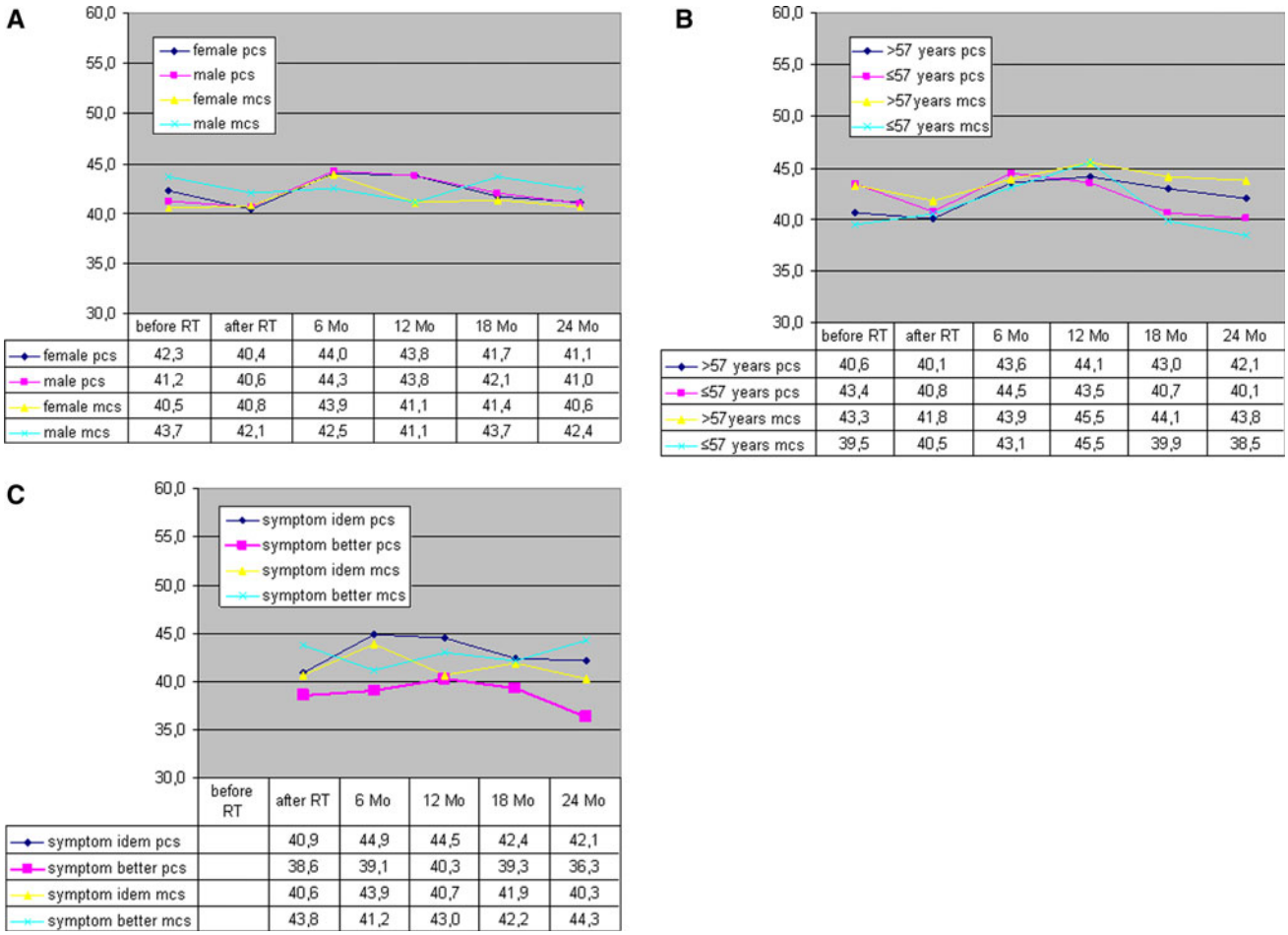
### Local control and side effects

Local control was 98 %. One patient suffering from a WHO III meningioma developed a relapse 18 months after SRT. No clinically severe acute (CTC III–IV°) or late toxicity was observed. Low-grade toxicity (I°) occurred in 5/52 cases. Three patients developed conjunctivitis and increased lacrimation and two patients developed diminution of visual field (I–II°). From the 52 patients, nine showed improvement of their leading tumor related symptoms and 43 remained stable. No patient developed any worsening of symptoms.

## Discussion

SRT is effective in the treatment of meningiomas, especially of the skull base. The actuarial 5 and 10 year progression-free survival after SRS is 78–95.4 and 55–86 %, respectively [13–15]. Similarly, local control rates after SRT range between 94 and 95 % with a median follow-up of 30–33 months [16, 17]. The 3 and 5 year progression-free rate has been 96 and 93 %, respectively [18].

After SRT, acute toxicity CTC III° (usually caused by temporary brain edema), only occurred in 2.5 % of the cases [19] while CTC I–II° (transient low-grade headache, vertigo or nausea) was observed more frequently [19], similarly to the findings of the present study. Importantly, no severe late toxicity III–IV° has been reported so far [16, 17, 19, 20]. However, the impact of SRT in the QoL of patients with meningiomas assessed under prospective conditions remains unknown.




| | before RT | after RT | 6 Mo | 12 Mo | 18 Mo | 24 Mo |
|---|---|---|---|---|---|---|
| female pcs | 42,3 | 40,4 | 44,0 | 43,8 | 41,7 | 41,1 |
| male pcs | 41,2 | 40,6 | 44,3 | 43,8 | 42,1 | 41,0 |
| female mcs | 40,5 | 40,8 | 43,9 | 41,1 | 41,4 | 40,6 |
| male mcs | 43,7 | 42,1 | 42,5 | 41,1 | 43,7 | 42,4 |

| | before RT | after RT | 6 Mo | 12 Mo | 18 Mo | 24 Mo |
|---|---|---|---|---|---|---|
| >57 years pcs | 40,6 | 40,1 | 43,6 | 44,1 | 43,0 | 42,1 |
| ≤57 years pcs | 43,4 | 40,8 | 44,5 | 43,5 | 40,7 | 40,1 |
| >57years mcs | 43,3 | 41,8 | 43,9 | 45,5 | 44,1 | 43,8 |
| ≤57 years mcs | 39,5 | 40,5 | 43,1 | 45,5 | 39,9 | 38,5 |

| | before RT | after RT | 6 Mo | 12 Mo | 18 Mo | 24 Mo |
|---|---|---|---|---|---|---|
| symptom idem pcs | | 40,9 | 44,9 | 44,5 | 42,4 | 42,1 |
| symptom better pcs | | 38,6 | 39,1 | 40,3 | 39,3 | 36,3 |
| symptom idem mcs | | 40,6 | 43,9 | 40,7 | 41,9 | 40,3 |
| symptom better mcs | | 43,8 | 41,2 | 43,0 | 42,2 | 44,3 |

**Fig. 3** Comparison of the mean values for physical component summary and mental component summary of the "medical outcome study short form 36" according to **a** gender (female vs. male); **b** age (≤57 vs. >57 years); **c** changes in tumor related symptoms (improvement vs. no change)

This is the first prospective study to investigate the QoL in patients with meningioma during and after stereotactic radiotherapy. In our cohort, patients with meningiomas were characterized by a high psychological strain before application of radiotherapy, possibly due to the primary diagnosis. Indeed, the values of all 8 health parameters were lower (25–50 %) in comparison to the GNP already before the beginning of SRT. The biggest difference between our patients and the GNP before initiating SRT were noticed for rolem (−44.2–48.9 %) and rolph (−41.4–49.5 %). Similarly, the physical and the emotional role functioning were substantially affected due to the tumor diagnosis while pain (−15.7, 19.5 %) and ghp (−15.1, 22.2 %) were less affected. The relatively high non-compliance in filling the QoL assessment questionnaire of our patients could be attributed to the high psychological strain, at least in part, that led to loss of interest in our study.

Upon completion of SRT, the mean values in 6 of the 8 health parameters were declined even more and reached their lowest point. The biggest decline was noticed for rolph and rolem but also for pain. Patients receiving radiotherapy often report fatigue. Relevant to fatigue, the decline of nearly all health parameters after SRT describes the first phase of QoL, the "depressive phase". Following this, at the follow-up interval "6 months after RT" all parameters except rolph reached their peaks. The biggest increase after SRT was noticed for rolem (+20.2) and for rolph (+25.6). During this time, patients obviously recover from the acute toxicity of radiotherapy. This increase of the mean values describes the second phase of QoL, the "recovery phase". Finally, during the third phase, all health parameters began to normalize towards their initial mean values, the "normalization phase", at follow-up interval "24 months after RT".

Dijkstra et al. [6] reported late neurocognitive sequelae in patients with WHO grade I meningioma undergoing surgery, with or without adjuvant radiotherapy. Neurocognitive functioning of the patients was assessed at least 1 year after treatment or later. They found significant impairments in executive functioning, verbal memory, information-processing capacity, psychomotor speed and working memory. However, this study ($n = 89$) evaluated retrospectively the

influence of age, gender and educational level, as assessed by the Dutch scoring system, and not the impact of the applied radiotherapy. Furthermore, radiotherapy was applied using 3D-CRT and not as SRT [6]. In a similar work, Van Nieuwenhuizen et al. [7] reported the differential effects of surgery and radiotherapy on neurocognitive functioning and health-related quality of life in WHO I meningioma patients. In this retrospective study the authors evaluated QoL in patients treated with surgery only ($n = 18$) versus surgery plus adjuvant external beam radiation ($n = 18$). To assess the QoL, the SF36 questionnaire was used, similar to our study. No differences between the two cohorts were observed in regards to neurocognitive functioning and QoL. Patients treated with surgery plus radiotherapy had significantly lower QoL scores than patients treated with surgery alone, but these differences lost significance after correction for the duration of disease [7].

Retrospectively, Krupp et al. [5] reported significant negative correlation between patient age and cognitive performance after surgically treated supratentorial meningiomas. Despite normal cognitive performance, 73 % of patients <55 years and 20 % of patients >55 years were not satisfied with their life. In this study, 68 % of the younger patients described an inability to accept having this severe disease as a young person. Furthermore, patients living as singles had higher frequency of depressive coping and less satisfaction of life [5].

In regards to MCS in our cohort, patients undergoing previous operation had higher mean parameter values already before SRT and during all follow-up intervals until 24 month after completion of SRT. This phenomenon might be caused by a bias. In the cohort $_{\text{primary SRT}}$ ($n = 10$) 2 patients died because of metastasized breast cancer and senile decay. A further patient developed dementia and did not reach the endpoint of the study. Patients' age, dose or gender were distributed equally in both cohorts (primary SRT vs. previous operations). Mental health and general health improved until the end of SRT, in contrast to the other health parameters. This could be attributed to the improved local tumor control after radiotherapy, at least in part.

Van Nieuwenhuizen et al. [7] reported lower values for PCS in patients undergoing surgery plus RT. Furthermore, they had significantly impaired physical functioning, more role limitations by physical health problems and vitality. In contrast to van Nieuwenhuizen et al. [7] we found no statistically significant differences for PCS between patients who had undergone previous operations or primary SRT at any interval. However, the mean values of patients who had undergone primary SRT approached the mean value level of patients undergoing previous operations during the intervals "after RT" i.e. immediately after completion of SRT, and "6 months after RT". This improvement in PCS values after primary SRT was constant until "24 months after RT" and showed a trend towards significance ($p = 0.054$). This would indicate that SRT could improve PCS, even though the number of patients in this cohort was small ($n = 10$).

The QoL was not affected by sex, age or the applied dose. This was comparable to Waagemans et al. [8] reporting long-term impact of cognitive deficits and epilepsy on QoL in patients with low-grade meningiomas treated with surgery ±RT. However, in this retrospective study the authors found a significantly impaired QoL in 5 out of 8 SF36 scales in patients that received antiepileptic drugs [8].

Meningioma patients often suffer from neurological deficits. Although an improvement of the symptomatology was observed after SRT, surprisingly this improvement did not lead to better QoL in our study. This could be attributed to the long disease history and the inability to accept having this severe disease [8].

We would like to acknowledge the limitations of our study. Although QoL was assessed with the SF36 questionnaire, different methods such as the EORTCBN20 questionaire [21] or the functional assessment of cancer therapy-meningioma (FACT-MNG) that constitutes a modified combination of the functional assessment of cancer therapy-brain (FACT-BR) and SF36 outcome instruments [22], could also be used to evaluate the outcome of our patients. In addition, despite the prospective nature of the present work, our findings should be validated in a larger patient cohort.

## Conclusion

This is the first prospective study to investigate the QoL in patients with meningioma after treatment with SRT. Patients with meningiomas have an impaired QoL compared to GNP. The QoL assessment after SRT revealed three phases: 1. "Depressive Phase", 2. "Recovery Phase", and 3. "Normalization Phase". Patients treated with primary SRT developed a stable increase of the mean values for PCS. Other parameters (gender, age, applied dose, changes in symptomatology) did not affect QoL.

**Acknowledgments** Conflict of interest The authors indicate no potential conflicts of interest or financial interests.

## References

1. Pollock BE, Stafford SL (2005) Results of stereotactic radiosurgery for patients with imaging defined cavernous sinus meningiomas. Int J Radiat Oncol Biol Phys 62:1427–1431
2. Hasegawa T, Kida Y, Yoshimoto M et al (2007) Long-term outcomes of Gamma Knife surgery for cavernous sinus meningioma. J Neurosurg 107:745–751

3. Hamm K, Henzel M, Gross MW et al (2006) Stereotactic radiotherapy of meningiomas compressing optical pathways. Int J Radiat Oncol Biol Phys 66(Suppl):7–13
4. Milker-Zabel S, Zabel-du Bois A, Huber P et al (2006) Fractionated stereotactic radiation therapy in the management of benign cavernous sinus meningiomas: long-term experience and review of the literature. Strahlenther Onkol 182:65–640
5. Krupp W, Klein C, Koschny R et al (2009) Assessment of neuropsychological parameters and quality of life to evaluate outcome in patients with surgically treated supratentorial meningiomas. Neurosurgery 64:40–47
6. Dijkstra M, van Nieuwenhuizen D, Stalpers LJ et al (2009) Late neurocognitive sequelae in patients with WHO grade I meningioma. J Neurol Neurosurg Psychiatry 80:910–915
7. van Nieuwenhuizen D, Klein M, Stalpers LJ et al (2007) Differential effect of surgery and radiotherapy on neurocognitive functioning and health-related quality of life in WHO grade I meningioma patients. J Neurooncol 84:271–278
8. Waagemans ML, van Nieuwenhuizen D, Dijkstra M et al (2011) Long-term impact of cognitive deficits and epilepsy on quality of life in patients with low-grade meningiomas. Neurosurgery 69:72–79
9. King JT Jr, McGinnis KA, Roberts MS (2003) Quality of life assessment with the medical outcomes study short form-36 among patients with cervical spondylotic myelopathy. Neurosurgery 52:113–121
10. Henzel M, Hamm K, Sitter H et al (2009) Comparison of stereotactic radiosurgery and fractionated stereotactic radiotherapy of acoustic neurinomas according to 3D tumor volume shrinkage and quality of life. Strahlenther Onkol 185:567–573
11. Trotti A, Byhardt R, Stetz J et al (2000) Common toxicity criteria: version 2.0. An improved reference for grading the acute effects of cancer treatment: impact on radiotherapy. Int J Radiat Oncol Biol Phys 47:13–47
12. Bruner DW, Wasserman T (2009) The impact on quality of life by radiation late effects. Int J Radiat Oncol Biol Phys 31:1353–1355
13. Hasegawa T, Kida Y, Yoshimoto M et al (2011) Gamma Knife surgery for convexity, parasagittal, and falcine meningiomas. J Neurosurg 114:1392–1398
14. Williams BJ, Yen CP, Starke RM et al (2011) Gamma Knife surgery for parasellar meningiomas: long-term results including complications, predictive factors, and progression-free survival. J Neurosurg 114:1571–1577
15. Flannery TJ, Kano H, Lunsford LD et al (2010) Long-term control of petroclival meningiomas through radiosurgery. J Neurosurg 112:957–964
16. Litré CF, Colin P, Noudel R et al (2009) Fractionated stereotactic radiotherapy treatment of cavernous sinus meningiomas: a study of 100 cases. Int J Radiat Oncol Biol Phys 74:1012–1017
17. Arvold ND, Lessell S, Bussiere M et al (2009) Visual outcome and tumor control after conformal radiotherapy for patients with optic nerve sheath meningioma. Int J Radiat Oncol Biol Phys 75:1166–1172
18. Minniti G, Clarke E, Cavallo L et al (2011) Fractionated stereotactic conformal radiotherapy for large benign skull base meningiomas. Radiat Oncol 6:36–42
19. Henzel M, Gross MW, Hamm K et al (2006) Stereotactic radiotherapy of meningiomas: symptomatology, acute and late toxicity. Strahlenther Onkol 182:382–388
20. Milker-Zabel S, Zabel A, Schulz-Ertner D et al (2005) Fractionated stereotactic radiotherapy in patients with benign or atypical intracranial meningioma: long-term experience and prognostic factors. Int J Radiat Oncol Biol Phys 61:809–816
21. Taphoorn MJ, Claassens L, Aaronson NK et al (2010) An international validation study of the EORTC brain cancer module (EORTC QLQ-BN20) for assessing health-related quality of life and symptoms in brain cancer patients. Eur J Cancer 46:1033–1040
22. Zlotnick D, Kalkanis SN, Quinones-Hinojosa A et al (2010) FACT-MNG: tumor site specific web-based outcome instrument for meningioma patients. J Neurooncol 99:423–431