

Research Article**Radiosurgery for meningioma: Evaluation of radiological outcome and contributing factors of recurrence**

**Morteza Tabatabaeefar¹, Shaghayegh Hasas Yeganeh^{1*}, Reza Zarghampour¹,
Alireza Zali², Sohrab shahzadi², Sohrab Sadeghi², Mohamad Ali Bitaraf³,
Mazdak Alikhani⁴, Ghazale Geraieli⁴, Maziyar Azar⁵, Farid Kazemi⁵,
Soraya Salmanian⁶ and Elham Saied Zadeh⁷**

¹Department of radiation oncology, shaheed beheshti university of medical sciences, Tehran, Iran

²Department of neurosurgery, shaheed beheshti university of medical sciences, Tehran, Iran

³Department of neurosurgery, Tehran university of medical sciences, Tehran, Iran

⁴Gamma knife center, Tehran, Iran

⁵Department of neurosurgery, Iran university of medical sciences, Tehran, Iran

⁶Department of radiation oncology, Iran university of medical sciences, Tehran, Iran

⁷Department of medical physics, Azad university of medical sciences, Tehran, Iran

*: corresponding Author: Shaghayegh Hassas Yeganeh

Shaheed Madani Street, Imam hosein Hospital, Tehran, Iran

Tel: +98 21 73432600 Fax: +98 21 73432625

E-mail: Dr.shaghayegh.yeganeh@gmail.com

ABSTRACTS

Background: Meningioma is one of the most common benign brain tumors with various clinical manifestations. Since the most common prevalence age of meningioma is forth to fifth decades which are the active population, the attention to optimal treatment and contributing factors for recurrence would result in health improvement by reduction in mortality. In this study the therapeutic outcomes and contributing factors for recurrence were evaluated among patients with treated meningioma by radiosurgery.

Materials and methods: In this retrospective study 1082 consecutive meningioma patients treated in Gamma-Knife Center since 2003 to 2011 were enrolled and the required data were collected from existing medical documents including the therapeutic outcomes.

Results: Totally 1082 cases including 1164 lesions were included. The mean age was 52 years (7 to 88 years). 293 patients (27.1%) were male and 789 subjects (72.9%) were female. The mean follow-up time was 39.4 ± 24.9 months. In 403 cases, the follow-up was not complete and in remaining cases, the size of lesion was reduced in 338 lesions (44%), not changed in 377 cases (49%), and was increased in 46 lesions (7%). Hence, totally 93% of cases were controlled by treatment. Also 80 patients (6.8%) had recurrence.

Conclusions: Totally according to the obtained results it may be concluded that Gamma-knife surgery is effective in more than ninety percent of cases with cranial meningioma leading to low recurrence rate. However further studies should be carried out to determine the other contributing factors for recurrence and also comparison of the results of Gamma-knife therapy with other conventional methods.

Keywords: Meningioma, Gamma-Knife Surgery, Outcome

INTRODUCTION

Meningioma is one of the most common benign brain tumors with various clinical manifestations including seizure, headache, limb weakness, and cranial nerve disorders depending to the location of tumor. Extensive surgical removal is the only

definite treatment which sometimes may be performed accompanying with some additional treatments such as radiotherapy. Some patients may experience recurrence months or years after tumor removal (1). Meningioma may arise from

each part of brain or spinal cord. Ninety percent of meningioma tumors are intracranial or are at skull base (30-40%) or in the medulla oblongata (2, 12). Access to intracranial meningioma is difficult and complete resection is not possible. Conventional radiotherapy after incomplete tumor resection would result in five-year recurrence-free survival of 95%. However 10.5 to 32 percent of cases would have recurrence. In new radiotherapy techniques such as stereotactic radiosurgery, stereotactic radiotherapy in multiple sessions, and IMRT the accuracy in treatment, less tissue injury, and better tumor control has been achieved. Five-year control with stereotactic radiosurgery has been reported in different studies to be 85 to 100 percent. Regarding the slow course of benign meningioma and life expectancy in patients, the long-term follow-up for results and adverse effects is necessary (8). Gamma-knife is a type of radiosurgery for treatment of deep brain lesions by high-energy x-ray without open surgery. It would result in access to deepest brain parts which may not be operated with conventional surgeries. In gamma-knife method which is effective on majority of brain tumors depending on tumor type and growth rate include many gamma beams radiated to the tumor from a cobalt source with high-dose in one session. No harm is seen in normal or critical tissues (5, 11). Since the most common prevalence age of meningioma is forth to fifth decades which are the active population, the attention to optimal treatment and contributing factors for recurrence would result in health improvement by reduction in mortality (1). In this study the therapeutic outcomes and contributing factors for recurrence were evaluated among patients with treated meningioma by radiosurgery.

MATERIALS AND METHODS

In this retrospective study 1082 consecutive meningioma patients treated in Gamma-Knife Center since 2003 to 2011 were enrolled and the required data were collected from existing medical documents. The survival was assessed by phone. Sampling was performed in a census manner. The checklist included age, gender, location, volume, and count of lesions, primary

or adjuvant treatment with gamma-knife, history of radiotherapy, characteristics of plan including maximal dose, tumor dose, mean marginal dose, and accepted isodose, and the treatment outcomes according to lesion size in MRI. The incomplete data were excluded. After data collection was completed, the data analysis was performed by SPSS software (Chicago, IL, Version 21.0, IBM Co). Univariate and multiple Cox regression tests were used to determine the effects of different variables on recurrence regarding different follow-up times.

RESULTS

Totally 1082 cases including 1164 lesions were included. The mean age was 52 years (7 to 88 years). 293 patients (27.1%) were male and 789 subjects (72.9%) were female. The mean follow-up time was 39.4 ± 24.9 months (ranging from 1 to 12 months). In 403 cases, the follow-up was not complete and in remaining cases, the size of lesion was reduced in 338 lesions (44%), not changed in 377 cases (49%), and was increased in 46 lesions (7%). Hence, totally 93% of cases were controlled by treatment. Also 80 patients (6.8%) had recurrence. In both univariate and multivariate analysis the age had significant effect on recurrence ($P=0.017$) with 2% increase in the risk per increased year of age. The mean age was 55.2 ± 13.1 and 52.1 ± 13.1 years, in those with and without recurrence, respectively. The lesions were multiple in 104 patients (9.6%); among them 14 cases (13.46%) had recurrence versus 6.21% in patients with single lesions. The difference was only significant in univariate analysis ($P=0.011$) and the multivariate analysis showed no significance. The treatment was primary in 589 patients (50.6%). Among primary cases, 28.8% versus 68% in those with positive surgical history had recurrence ($P=0.0001$). However there was no significant effect in multivariate analysis. Previous radiotherapy was not seen in 1102 patients (94.3%) which among them 80% versus 20% among those with radiotherapy history had recurrence showing significant difference in both univariate and multivariate analysis with 3.48 times more risk of recurrence. The mean volume of lesions was 10.7 cm which was 19 cm (ranging from 1.7 to 98 cm) in recurrent

cases. It had significant effect in both univariate and multivariate analysis; with 4% increase per 1 cm³ increase in tumor volume. The mean total dose was 13.5 ± 1.3 (ranging from 8 to 18 gray) without significant effect in univariate and multivariate analysis. Also the mean marginal dose was 53.1 ± 13.7 (49.8 ± 8.4 gray in recurrent cases) with significant effect only in univariate but not multivariate analysis. The location of lesions has been shown in Figure 1.

The recurrence rate was significantly lower in CPA and higher in tentorial and orbital regions that may be due to restricted drug administration in these regions. There were 343 non-skull base lesions (Table 1) with 13.1% rate of recurrence and 782 skull base lesions with 4.47% rate of recurrence showing 3 times more risk of recurrence in non-skull base tumors. However it was not significant in multivariate analysis (P=0.378).

Figure 1- Location of lesions in understudy patients

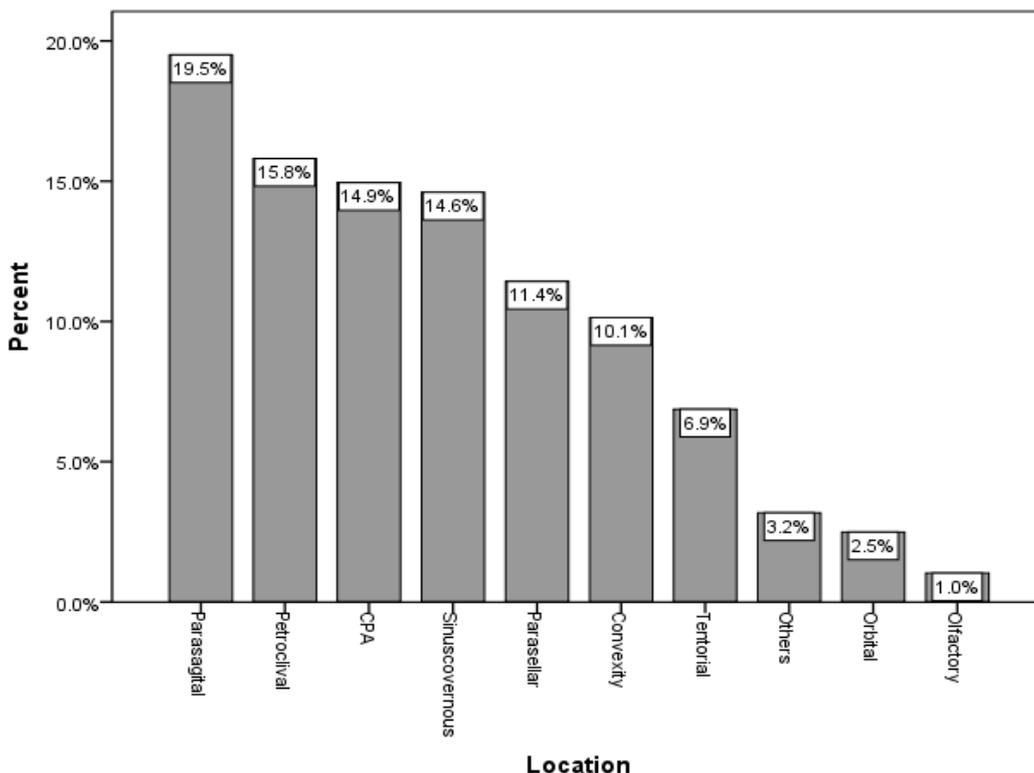


Table 1- Comparison of finding among skull base and non-skull base lesions

	Skull Base	Non Skull Base
Lesion Count	782 (67.29%)	343 (29.46%)
Recurrence Rate	35 (43.75%)	45 (56.25%)
Coverage	97.97	98.53
Maximal Dose	25.56	28.48
Tumor Dose	13.48	13.69
Marginal Coverage	55.01	48.98

DISCUSSION

The study by Chang et al demonstrated a male to female ratio of 1 to 5.3 but it was 1 to 2.6 in our study. In a systematic review by Minniti et al about skull-base meningioma it was seen that there is no significant difference between recurrence rate in those with previous surgery and those with primary treatment. However in our study the risk rate was three percent more among those with primary treatment with P value less than 0.001. It may be due to more

invasions of operated tumors. However the difference was not significant in multivariate analysis. The review study by Minniti and colleagues in 2009 demonstrated that the lesion size was decreased in 3 percent of cases, and increased in 6 percent of patients but without change in 60 percent. We also similarly had 7 percent of lesions with increased volume as non-controlled cases. In the study by Bitaraf et al in Iran with mean follow-up time of seventeen months, the diameter of lesion was decreased in

65 patients (20 percent) and increased in seven patients and remained without change in 77 percent. Accordingly the control rate in their study is more than our control rate in current study. We had 44 percent reduction and 7 percent increase and 49 percent without change lesions. Totally according to the obtained results it may be concluded that Gamma-knife surgery is effective in more than ninety percent of cases with cranial meningioma leading to low recurrence rate. However further studies should be carried out to determine the other contributing factors for recurrence and also comparison of the results of Gamma-knife therapy with other conventional methods.

REFERENCES

1. Farokhi M, Ansari Z. Evaluation of cases with recurrence and contributing factors in brain meningioma during 20-year period. *J Tehran Univ Med Sci.* 2006; 64(12):91-6.
2. Bupa Cromwell Hospital, Gamma knife stereotactic radiosurgery for a meningioma, Patient Information. www.bupacromwellhospital.com
3. Bitaraf MA, Azar M, Miri M, et al. Treatment outcomes in 230 cases of skull base meningioma with Gamma-Knife radiosurgery in Iran. *J Tehran Univ Med Sci.* 1980; 68(3):162-7.
4. Schmieder K, Engelhardt M, Wawrzyniak S, et al. The impact of microsurgery, stereotactic radiosurgery and radiotherapy in the treatment of meningiomas depending on different localizations. *GMS Health Technology Assessment.* 2010; 6:1861-3.
5. Koga T, Shin M, et al. Role of Gamma Knife Radiosurgery in Neurosurgery: Past and Future Perspectives. *Neurol Med Chir (Tokyo)* 2010; 50: 737-48.
6. Igaki H, Maruyama K, et al. Stereotactic Radiosurgery for Skull Base Meningioma. *Neurol Med Chir (Tokyo)* 2009; 49: 456-61.
7. Mendenhall WM, Friedman WA, Amdur RJ, et al. Management of Benign Skull Base Meningiomas: A Review. *Skull Base,* 2004; 14: 1.
8. Minniti G, Amichetti M, et al. Radiotherapy and radiosurgery for benign skull base meningiomas. *Radiation Oncology.* 2009; 4:42.
9. Kondziolka D, Mathieu D, Lunsford L. Radiosurgery as definitive management of intracranial meningiomas. *Neurosurgery.* 2008; 62(1): 53-60.
10. Chang JH, Chang JW, Choi JY, et al. Complications after gamma knife radiosurgery for benign meningiomas. *J Neurol Neurosurg Psychiatry.* 2003; 74:226-30.
11. Han JH, Kim DG, Chung HT, et al. Gamma Knife Radiosurgery for Skull Base Meningiomas: Long-Term Radiologic and Clinical Outcome. 14 October 2008; www.pubmed.com
12. Iwai Y, Yamanaka K, et al. Gamma Knife radiosurgery for skull base meningioma: long-term results of low-dose treatment. *J Neurosurg.* 2008; 109(5):804-10.
13. Onodera S, Aoyama H, Katoh N, et al. Long-term Outcomes of Fractionated Stereotactic Radiotherapy for Intracranial Skull Base Benign Meningiomas in Single Institution. *Jpn J Clin Oncol;* 2011; 41(4): 462-8.