

Experience of CyberKnife Robotic Radiosurgery in treating intra and extra-cranial tumours: A review of outcomes

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Abstract

Objective: To determine the success rate and complication of CyberKnife Robotic Radiosurgery for treating intracranial and extra cranial tumours.

Methods: The cross-sectional observational study was carried out at the Department of CyberKnife Robotic Radiosurgery at the Jinnah Postgraduate Medical Centre, Karachi, and reviewed data related to a year from December 2012 to December 2013. Patients referred from different hospitals within and outside Pakistan for stereotactic radiosurgery were included. The patients had benign tumours less than 7cm size, post-operative residual tumour and recurrent tumour with post-radiotherapy. Patients were followed up every three months with contrast magnetic resonance imaging. Radiosurgery was considered successful if patients improved clinically with radiologically stable disease or if there was interval reduction in the size of tumour. SPSS 17 was used for data analysis.

Results: Initially, 260 patients were selected, but 9(3.5%) were lost, and the final sample size was 251(96.5%). Clinically successful outcome results were seen in 225(90%) patients, while 8(3%) showed no change in symptoms and 18(7%) patients' follow-up is awaited. Radiological improvement was noted in 218(87%); stable disease in 138(55%) and 80(32%) cases showed more than 30% reduction in size after 6-12 months of follow-up. Only 5(2%) cases showed subtle increase in size within 3-month interval due to post-radiation oedema. Acute transient post-radiation changes were seen in 25(10%) patients, sub-acute changes in 4(1.59%) and 1(0.3%) patient showed radionecrosis after 9-month interval.

Conclusion: Cyberknife was an effective, safe and successful treatment alternative to surgery in benign and malignant tumours with low risk of post-radiotherapy complication compared to conventional radiation.

Keywords: CyberKnife Robotic Radiosurgery, tumours, Karachi. (JPMA 65: 374; 2015)

Introduction

The CyberKnife is a frameless robotic radiosurgery system used for treating benign tumours, malignant tumours and other medical conditions. It is a method of delivering radiotherapy, with the intention of targeting treatment more accurately than standard radiotherapy.¹ The two main elements of the CyberKnife are the radiation produced from a small linear particle accelerator and a robotic arm which allows the energy to be directed at any part of the body from any direction.²

The CyberKnife Robotic Radiosurgery System improves on other radiosurgery techniques by eliminating the need for stereotactic frames. As a result, the CyberKnife enables doctors to achieve a high level of accuracy in a non-invasive manner and allows patients to be treated on an outpatient basis.^{3,4} It has a strong record of proven clinical effectiveness.⁵ It is used either on a stand-alone basis or in combination with other brain cancer

treatments, such as chemotherapy, surgery or whole-brain radiation therapy.

CyberKnife brain cancer treatments involve a team approach in which several specialists participate. The team may include a neurosurgeon, a radiation oncologist, radiologist, a medical physicist, a radiation therapist and other medical support staff.

Once the team is in place, preparations begin for the treatment. Generally there are three steps involved: set-up and imaging; treatment planning; and CyberKnife treatment

Side effects vary from patient to patient. Generally some patients experience minimal side effects and these often go away within a week or two. Prior to the treatment, the doctor discusses with the patient all possible side effects they may experience. The doctor may also prescribe medication designed to control any side effects should they occur.

The current study was planned to determine the success rate and complication of CyberKnife Robotic Radiosurgery in a tertiary care setting.

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Material and Methods

The cross-sectional observational study was carried out at the Department of CyberKnife Robotic Radiosurgery at the Jinnah Postgraduate Medical Centre (JPMC), Karachi, which is the only place in the country where it is offered free of cost. Data was reviewed for a period of 12 months from December 2012 to December 2013. Tumours that were less than 7cm in size, primary intracranial, intra-spinal and head and neck biopsy proven, post-operative residual, post-operative and post-radiotherapy recurrent in nature were included. Large-sized tumours greater than 7cm, tumours involving a critical structure, recent history of conventional radiation and extracranial metastatic disease were excluded.

Patients had been referred from all over Pakistan and also from outside the country, including those from Afghanistan, Bahrain, Saudi Arabia, Yemen, United Arab Emirates, Kenya, Malaysia and Russia. Data regarding demographics, indications, success rate and complications were obtained from medical records. Clinical outcomes were obtained on telephonic follow-up from patients who had come from other cities.

Since computed tomography (CT) scans and magnetic resonance imaging (MRI) reports along with investigations requested by the consultant were used to collect data, informed consent from the patients was not needed.

Before the start of the procedure, all patients had a meeting with the radiation oncologist. Patients were free to discuss their fears and complications of procedure. In various tumours, hormone levels are assessed before the treatment, while in some cases tumour perimetry/audiometry were also done prior to the initiation of the procedure. In some patients, conscious sedation was used, while some others required general anaesthesia. After the treatment, patients were kept in the recovery room for any immediate complication.

Radiation surgery was performed by trained radiation technologist. Procedure was carried out in CyberKnife suite equipped with CyberKnife Accuray G4 system with ordinary treatment couch. Selected patients underwent CT scan with contrast (Toshiba Asteion 16 slices CT scanner) and MRI 3D contrast (Phillips 1.5 tesla MRI unit), except for trigeminal neuralgia in which Balanced Turbo Field Echo (BTFE) was preferred for cranial nerve definition according to our protocol depending upon the diagnosed case. It was followed by tumour planning and dose planning on Treatment planning system (TPS) (). Radiation was given in either single fraction, three fractions or five fractions (hypo-fractionated

radiosurgery) depending upon the case. After the procedure, the radiation oncologist prescribed symptomatic medicines and steroids for a week in order to reduce post-procedural oedema.

The patients were followed up every three months with contrast MRI. The success rate and complications in relation to underlying pathology were analysed. Radiosurgery was considered successful in clinically improved patients with or without radiological improvement (Stable disease). Treatment response was weighted on the basis of Response Evaluation Criteria In Solid Tumours (RECIST).⁶

SPSS 17 was used statistical analysis. Data variables included age, gender, number of cases, radiation dose, size of tumour, number of fractions and nature of complications after radiosurgery.

Results

Initially, 260 patients were selected, but 9(3.5%) were lost, and the final sample size was 251(96.5%). There were 128(50.9%) adult males and 108(43%) adult females in addition to 15(5.9%) children (Figure-1). The overall mean age was 47 ± 14.5 years (range: 3.5-84 years).

There were 39(15.5%) cases of meningioma, 32(12.7%) of Arteriovenous malformation (AVM), 30(11.9%) pituitary adenomas, 29(11.5%) Acoustic neuroma, 20(7.9%) Glioblastoma multiforme (GBM)/high-grade Astrocytoma, 10(3.9%) Glomusjugulare, 12(4.7%) trigeminal neuralgia, 10(3.9%) brain metastases, 9(3.5%) trigeminalschwannoma, 9(3.5%) Glioma, 6(2.3%) Haemangioblastoma, 5(1.9%) Oligodendroglioma, 5(1.9%) Ependymoma, 3(1.1%) Neurofibroma, 2(0.79%) Craniopharyngioma and 18(7.1%) other tumours (Figure-2).

Clinically successful outcome results were seen in 225(90%) patients, while 8(3%) showed no change in

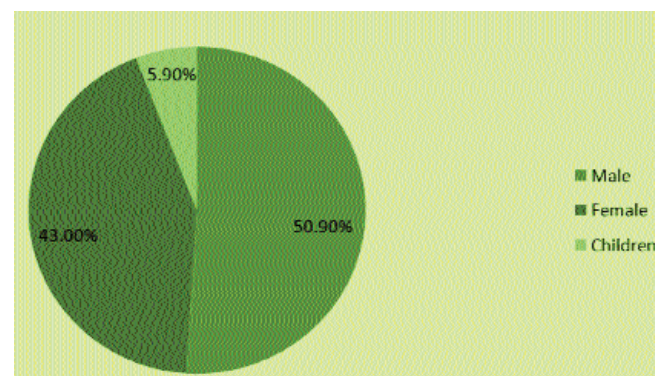


Figure-1: Gender distribution.

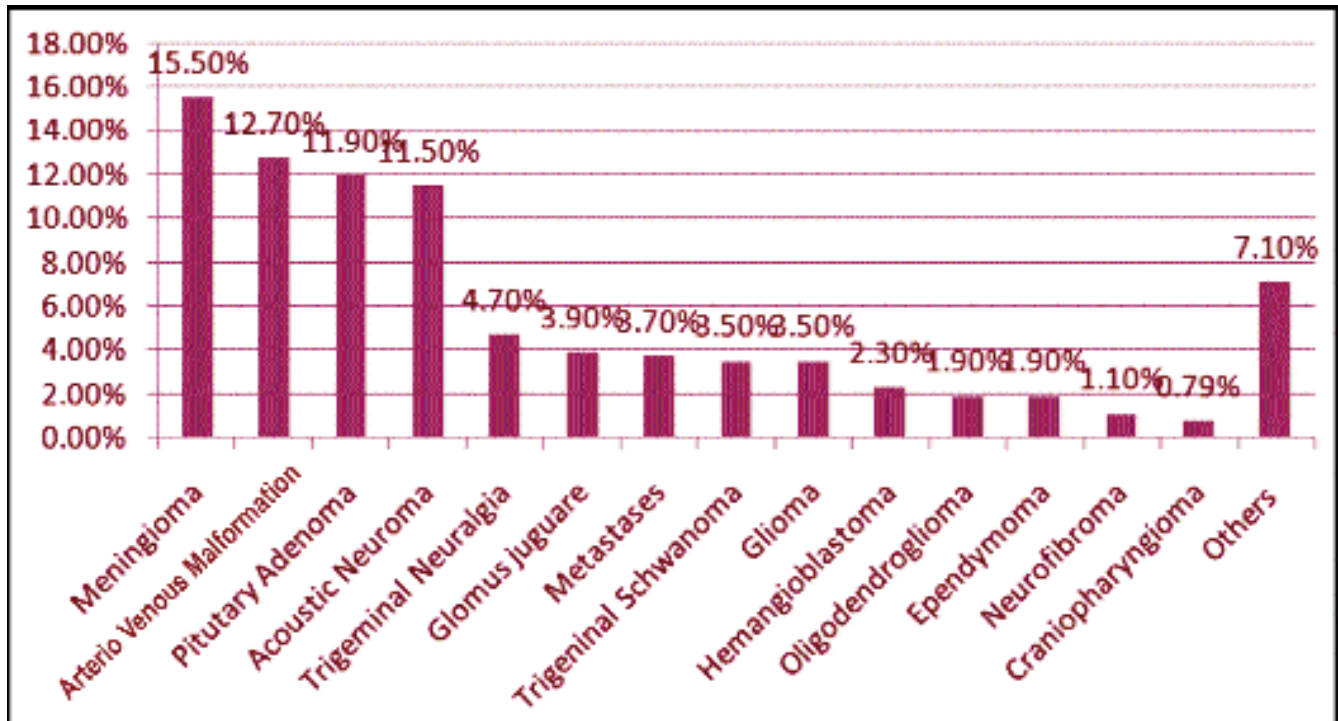


Figure-2: Distribution of disease (%).

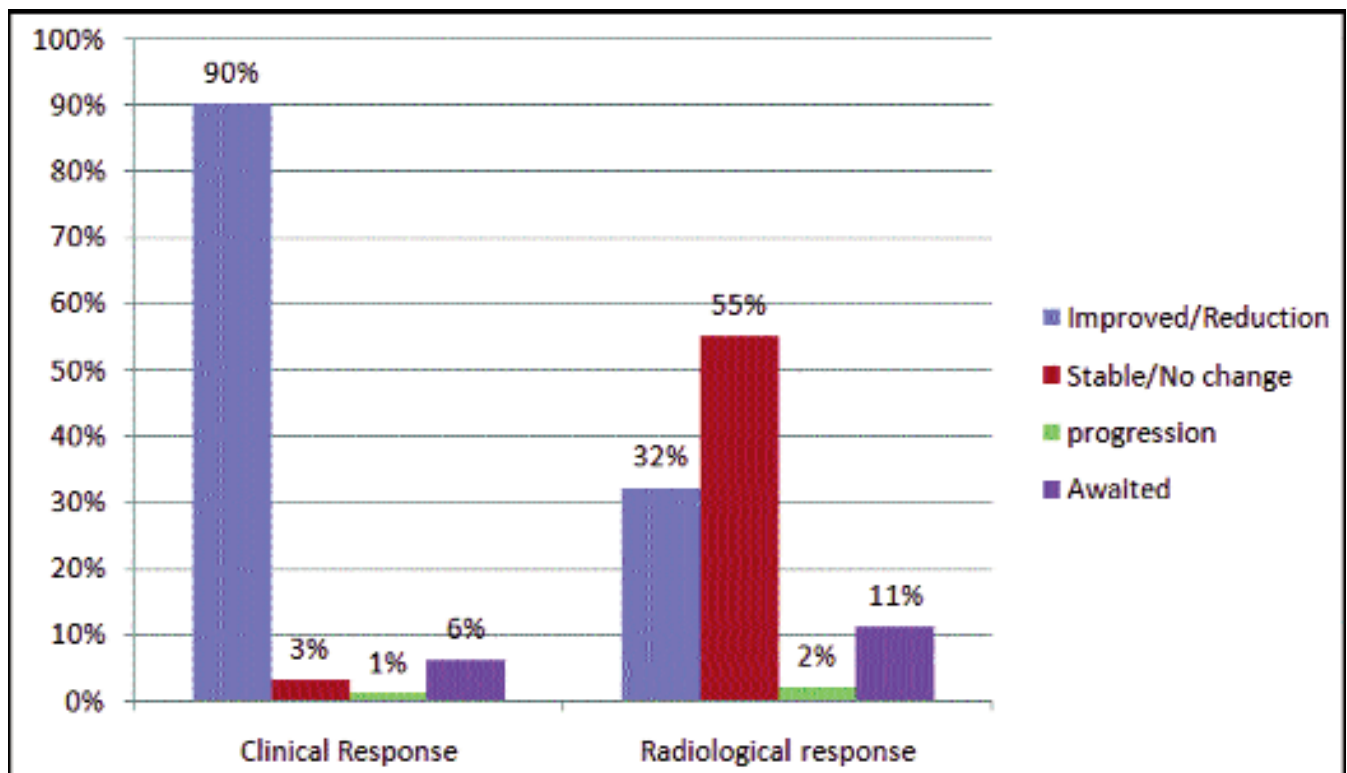


Figure-3: StereotacticRadiosurgeryTreatment Response.

symptoms and 18(7%) patients' follow-up is awaited. Seven (3%) patients died after treatment; 3(1.2%) of them were high-grade glioma with recurrence, and 1(0.3%) was of metastasis.

Radiological improvement was noted in 218(87%); stable disease in 138(55%) and 80(32%) cases showed more than 30% reduction in size after 6-12 months of follow-up. Only 5(2%) cases showed subtle increase in size within 3-month interval due to post-radiation oedema. Acute transient post-radiation changes were seen in 25(10%) patients, sub-acute changes in 4(1.59%) and 1(0.3%) patient showed radionecrosis after 9-month interval. Follow-up MRI of 28(11%) patients treated in the last 3 months of the study is awaited (Figure-3).

Discussion

Brain metastases are a common type of intracranial malignancy derived from the transfer of tumour cells outside the central nervous system (CNS) to the brain tissue.⁷ Stereotactic radiosurgery (SRS), particularly γ -Knife surgery (GKS), affords excellent local tumour control for between 1 and 10 brain metastases.^{8,9} A study¹⁰ assessed the clinical outcomes of 61 patients with >10 brain metastases who had undergone SRS. We have done 10 patients of brain metastases, the primary was in the lung in 2 patients while it was breast in 7 patients and one from primary leiomyosarcoma of the thigh. The maximum number of metastases was 9. Interval reduction in size noted in 5(55.5%) patients, while follow up was awaited in 4(44.4%) patients who

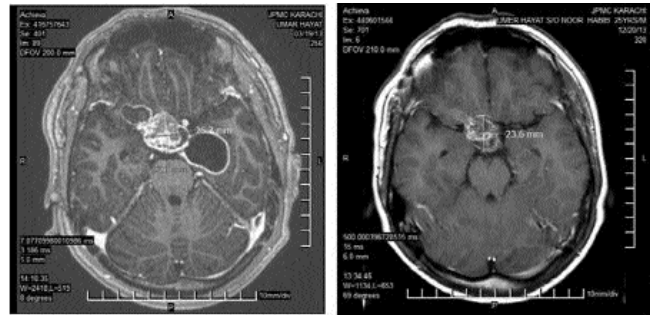


Figure-5: Pre-and post-stereotactic radiosurgery images of Craniopharyngioma show reduction in size of solid component and resolution of cystic components.

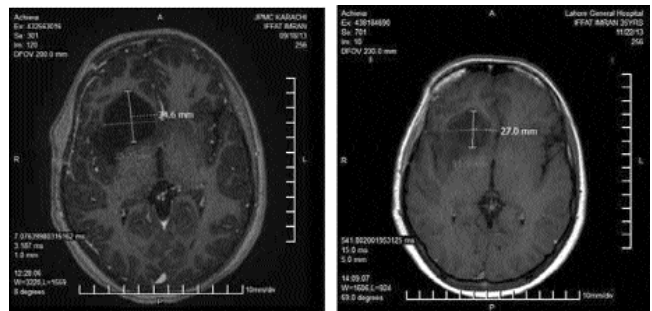


Figure-6: Low-grade glioma.

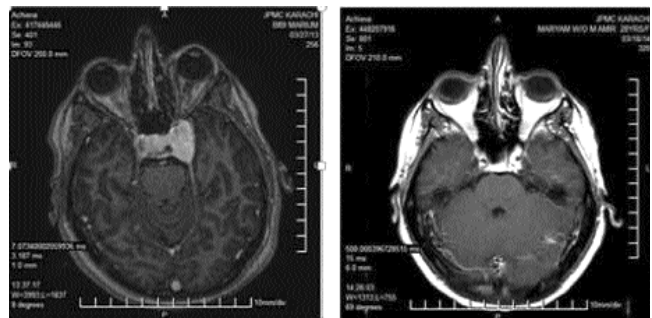


Figure-7: Pre-and post-stereotactic radiosurgery left paracavernous Meningioma.

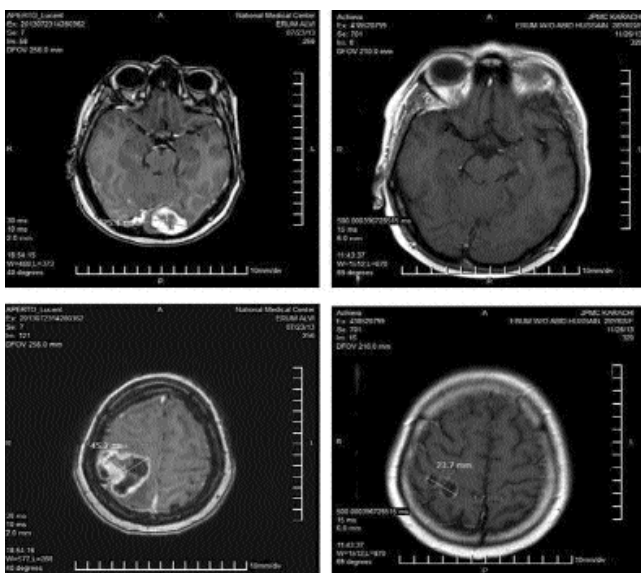


Figure-4: Pre-and post-stereotactic radiosurgery images of brain metastases.

underwent treatment in the last 2 months of the study. One of the patients had 3 large brain metastases with primary breast carcinoma, out of which one was showing interval reduction in size after 3 months, while 2 were completely resolved (Figure-4).

One study had 16 patients of residual or recurrent craniopharyngioma between 2000 and 2007 with SRS at Stanford University Medical Centre. Tumour shrinkage was achieved in 91% patients, with no visual or neuroendocrine complications. Only 1 patient had cystic enlargement of the residual tumour.¹¹ We experienced treating the solid component of 2 craniopharyngioma. Follow-up revealed interval

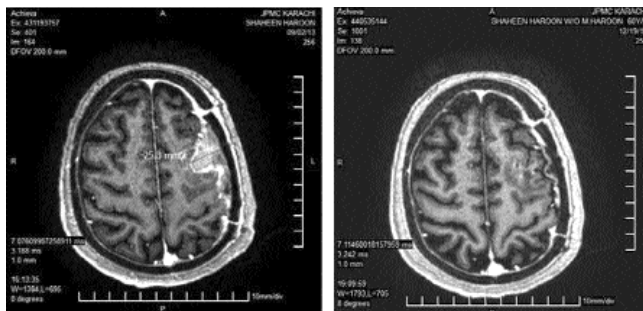


Figure-8: Meningioma post stereotactic radiosurgery resolution.

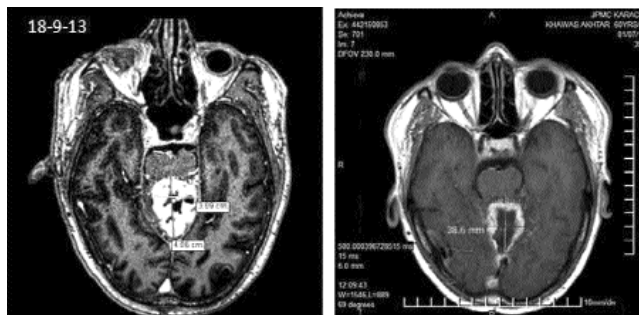


Figure-11: Hemangioblastoma pre and post-stereotactic radiosurgery.

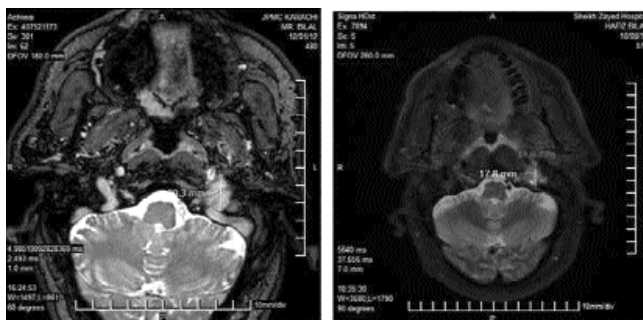


Figure-9: Pre-and post-stereotactic radiosurgery Glomusjugulare.

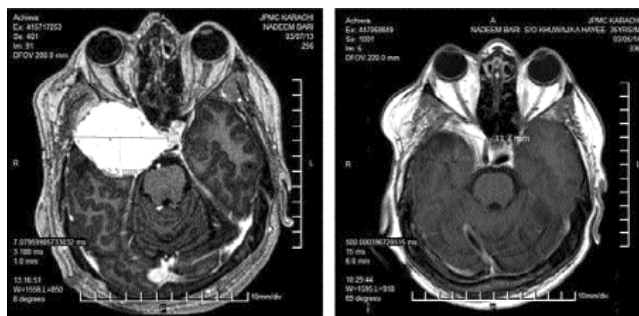


Figure-12: Pre-andpost-stereotactic radiosurgery cavernous Hemangioma.

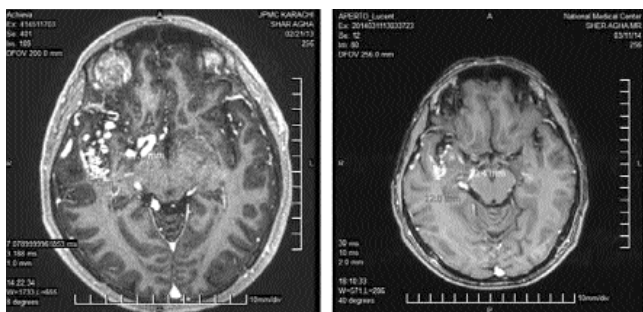


Figure-10: Arteriovenous malformation pre-and post-stereotactic radiosurgery.

reduction in size of the solid component, surprisingly in 1 patient there was not only reduction in size but also complete resolution of two adjacent cystic components (Figure-5).

Another study used CyberKnife in 25 patients with histologically proven malignant gliomas at Konan St. Hill Hospital between June 1998 and November 2002. Their results showed 18 GBM patients with a median survival after diagnosis of 20.7 months. Patients below 70 years of age had a median survival after diagnosis of 37.1 months compared to 12.4 months for older patients. Similarly, patients with well-controlled lesions

had a median survival after diagnosis of 39.8 months compared to 16 months for those with uncontrolled lesions. Late delayed radiation necrosis was seen in 1 GBM patient. No other patient suffered acute or delayed neurological morbidity after CyberKnife therapy.¹² We treated 34 patients of glioma, including 20 GBM/high-grade Astrocytomas, 9 were low-grade/brain stem glioma and 5 were Oligodendrogliomas. Most of them were post-surgery recurrent/residual. Few of them were radiologically diagnosed on MRI and on MR spectroscopy when located on critical locations like thalamic and in the brain stem. Successful outcome was achieved in low-grade gliomas, oligodendroglioma and in high-grade astrocytomas. Follow-up MRI after 3 or 6 months showed stable disease, while 3 patients showed disease progression (Figure-6).

Comparable results were achieved in benign lesions, including meningioma, AVM, neurofibromas, glomus, acoustic neuromas and trigeminal schwannomas. Stable disease occurred in all patients after 3 months, while most of them showed reduction in size after 3-6 months. Two patients of meningioma, one had at paracavernous location and the other at parietal cortex, showed complete resolution (Figures-7,8).

One study summarised first experience of using

CyberKnife system in management of patients with paragangliomas. Between April 2009 and September 2011, 34 patients were treated. Neurological deterioration after radiation treatment was extremely rare and in most cases it was transient.¹³ We treated 10 patients of glomus with 100% successful outcome achieved, as 6 became stable after 6-month follow-up, while 4 shrunk in size with no obvious complication (Figure-9).

Currently SRS has become the treatment of choice in small vestibular schwannomas. A study discussed first experience of application of CyberKnife system for stereotactic irradiation of these tumours between April 2009 and June 2011. We treated 62 patients (35 female and 27 male) with vestibular schwannomas. SRS using CyberKnife system was performed in 33 patients. Stereotactic irradiation using CyberKnife system is effective and sufficiently safe technique for the management of vestibular schwannoma. Literature has demonstrated high rates of tumour stabilisation, hearing preservation and minimal incidence of complications associated with trigeminal or facial nerve.¹⁴

Of the 30 patients with pituitary adenomas, 19 were macroadenomas and 11 were functional microadenomas with growth hormone secreting, adrenocorticotrophic hormone (ACTH) secreting and prolactinomas. In macroadenomas, the visual field improved in 80% patients (pre- and post-radiosurgery perimetry proven), while successful control of hormone was achieved in 85% functional adenomas. (Comparison done with pre- and post-CyberKnife hormone analysis). Results were compared with a study that reported tumour control rate of 92.3%. Hormonal function was improved in all of the 9 (100%) functioning adenomas. Hormonal normalisation was observed in 4(44%) patients with a mean duration of 16 months. In 2(7.6%) patients, visual acuity worsened due to cystic enlargement of the tumour after SRS.¹⁵ No other complications were observed. In our cases no such complication was observed.

We also did inoperable cases of AVM, and satisfactory results were obtained in all cases except one in which there was significant reduction in the size of nidus, but early radiation necrosis developed.

Conclusion

Cyberknife Robotic Radiosurgery is an alternative to

surgical procedure, which is safe, short-duration and effective for benign and malignant tumours if the inclusion criterion is observed. Also, it has a very low risk of post-radiotherapy complication compared to conventional radiation and surgery.

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