ORIGINAL ARTICLE

# The Usefulness of Staged Gamma Knife Radiosurgery (GKRS) in the Management of Large Voluminous Benign Brain Tumours

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**ABSTRACT**
**Background:** Gamma Knife Radiosurgery (GKRS) is a form of surgical ablation, probably, by targeted cell death, without the risks of open surgery. Its application in the treatment of large voluminous benign tumours could result in low efficiency in tumour cell ablation and high risk of damage to contiguous structures. Thus, a staging of the procedure has been advocated.
**Objective:** The aim of this study is to buttress the usefulness of staged gamma knife radiosurgery for benign brain tumours.
**Methodology**: Between June 2008 and November 2013 staged gamma knife radiosurgery (GKRS) was performed on six patients, aged 17-53years, with large voluminous benign brain tumours. All the patients had, at least, one surgical intervention aimed at either diverting cerebrospinal fluid by shunting and/or tumour decompression via surgical intervention. Patients had undergone surgery at least once. The prescription dose of radiation was 9-12Gy (Gray). Follow-up period ranged 2-5years, and except for one, all the patients improved clinically.
**Results**: Tumour control was achieved in 5 out of 6 patients (83%), with one being stable in terms of tumour volume. Of the 5, two had slight tumour reduction and none of them had progression of tumour volume.
**Conclusion**: The GKRS has remarkable benefits in the control of benign brain tumour progression, and has attendant low concomitant morbidity. Staged GKRS procedure represents a safe treatment option for large benign tumours in critical locations (deep seated location with close proximity to neural and vascular structures) following an incomplete surgical resection or as primary treatment for patients with poor medical condition
***Keywords:*** *Deep seated, incomplete surgical resection, low morbidity*

## INTRODUCTION

Gamma Knife Radiosurgery (GKRS) is a form of surgical ablation that competes with microsurgery in the treatment of benign brain tumours by, probably, inducing targeted cell death. This results in shrinkage of tumours (both radiosensitive and radioresistant) as well as the control of hormonal, electrical

dysfunction and thrombosis of dysplastic vessels. This is achieved without the risks of open surgery.[1]

Majority of curable brain tumours are benign and surgical resection is the mainstay of treatment. However, some benign tumours that are deeply seated, located close to neural or vascular structures or those with a history of recurrence are considered for gamma knife radiosurgery (GKRS).[2, 3, 4]

Over 50years ago, Lars Leksell coined the word radiosurgery to describe a non-invasive technique that delivers a precise single high dose of radiation to a targeted area of brain through an intact skull. Few years after this innovation, Leksell in conjunction with Borje Larson introduced Gamma knife.[5]

Gamma knife is a multi-source photon based device that houses 201 fixed cobalt-60 sources. Cobalt-60 emits gamma ray photon which travels as easily predictable, and easily quantifiable high energy beam. The achievable end result of this technique in the treatment of benign brain tumours include shrinkage of the tumour, inhibiting further tumour growth and total tumour obliteration.[5, 6]

Several reports of its use have indicated a single use to relatively small tumours, the place of its use in large voluminous tumours has been acknowledged in several literatures. However, applying this modality in the treatment of large voluminous benign tumours could result in low efficiency in tumour cell ablation and high risk of damage to contiguous structures.[6]

The objective of this study is to assess the usefulness of staged gamma knife radiosurgery (GKRS) in the management of carefully selected benign brain tumours.

## METHODOLOGY

This study recruited six (6) cases of benign brain tumours from June 2008 to November 2013. These patients had GKRS at the Hospital Des Specialites / Hassan 11 Foundation Centre for the Prevention and Treatment of Neurological Diseases.

This represented 0.7% of total patients who had GKRS over this period under review. All cases were discussed in a multidisciplinary meeting involving the neurosurgeons, neuroradiologists and neurologists.

Informed consent was obtained from each patient as regards the option of gamma knife radiosurgery as a veritable means of treatment.

Staged radiosurgery technique was done in dividing original tumour volume above 35cc into two (2) equivalents smaller volume treated with at least six (6) month interval. This technique was made easier with new model Perfexion (PFX model) /new Leksell Gamma Plan (LGP) version.

## RESULTS

This study involved 4 females (66.7%) and 2 males (33.3%) with an age range of 17-53years. These patients presented with large voluminous tumours and/or tumours in close proximity to vital neural and vascular structures.

The tumours included: Petroclival meningioma (3), spheno-orbital meningioma (1), post-operative residual pituitary adenoma (1) and 5th cranial nerve schwannoma (1).

Table1. Pre-GKRS Data

| S/NO | AGE (*years*) | SEX | PATHOLOGY | PREVIOUS SURGERY | VOLUME [*Cubic centimetre (cc)]* |
|---|---|---|---|---|---|
| 1 | 53 | F | Meningioma | 3 VPS | 50.5 |
| 2 | 35 | M | Meningioma | Refused surgery | 45.0 |
| 3 | 41 | F | Meningioma | Had 2 surgeries | 43.0 |
| 4 | 17 | F | Trigeminal schwannoma | Had 2 surgeries and 3 VPS | 56.0 |
| 5 | 40 | F | Meningioma | Had 2 surgeries | 41.0 |
| 6 | 40 | M | Pituitary adenoma | Post-surgery residual tumour | 25.0 |

*VPS (ventriculo-peritoneal shunting)*

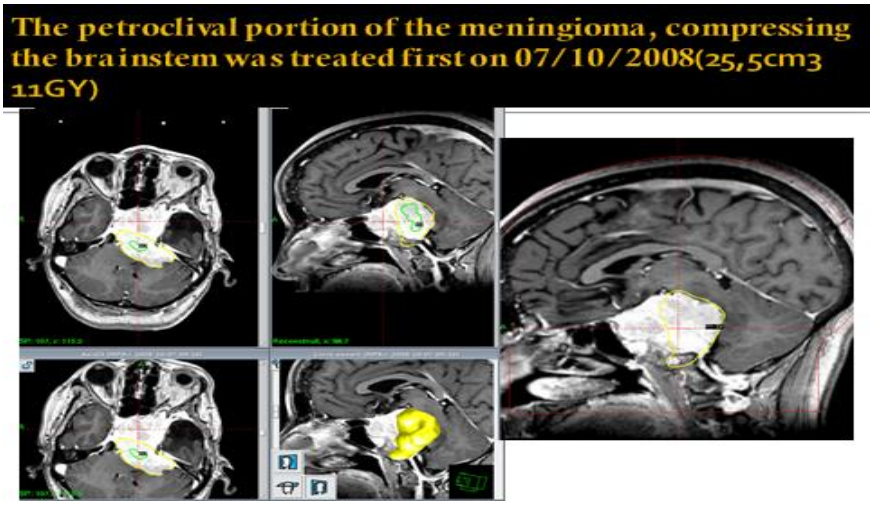
Table 2. Post-GKRS Outcome

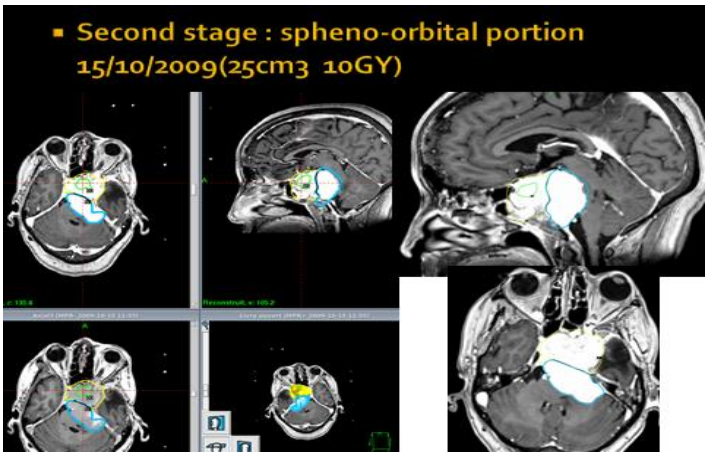
| S/NO | AGE (YRS) | SEX | PATHOLOGY | DOSE | VOLUME CHANGE | CLINICAL STATUS | FOLLOW-UP | COMPLICATION |
|---|---|---|---|---|---|---|---|---|
| 1 | 53 | F | Meningioma | 11Gy | Volume Reduction | Improved | 5 | No |
| 2 | 40 | M | Meningioma | 10Gy | Low volume reduction | Stable | 3 | No |
| 3 | 35 | M | Meningioma | 10Gy | Slight volume reduction | Asymptomatic | 4 | No |
| 4 | 16 | F | Trigeminal schwannoma | | | Improved | 2 | No |
| 5 | 40 | M | Meningioma | 10Gy | Stable | Stable | 3 | No |
| 6 | 40 | M | Pituitary adenoma | 12Gy | Slight volume reduction | Stable | 1 | No |

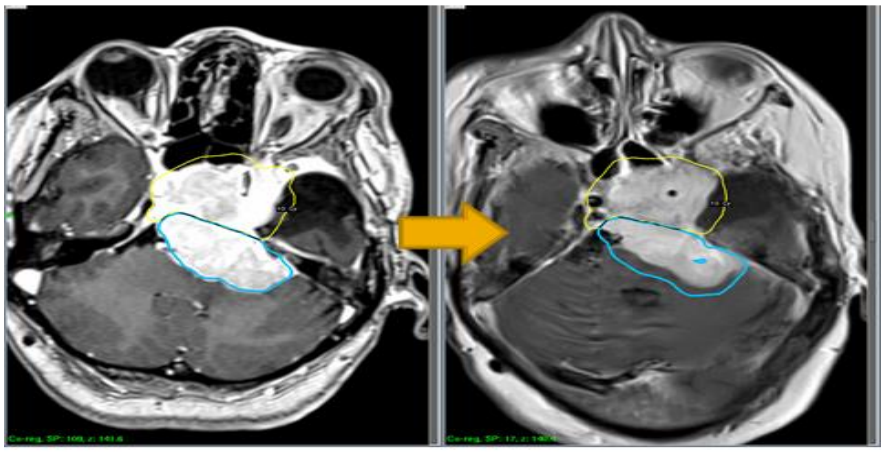
## CASE REPORTS

### Case 1

A 53-year old woman presented with gait disturbances, loss of vision (left eye) and left 3rd nerve palsy. A diagnosis of large petroclival meningioma was made. She had 2 surgical attempts at removal, with ventriculo-peritoneal shunting. The tumour was solid and haemorrhagic on intra-operative evaluation. Tumour volume was 50.5 cc

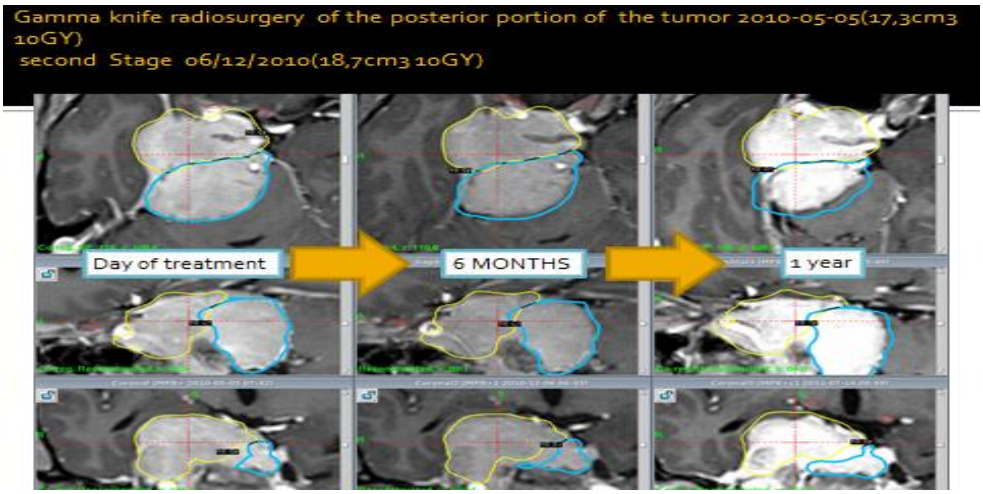


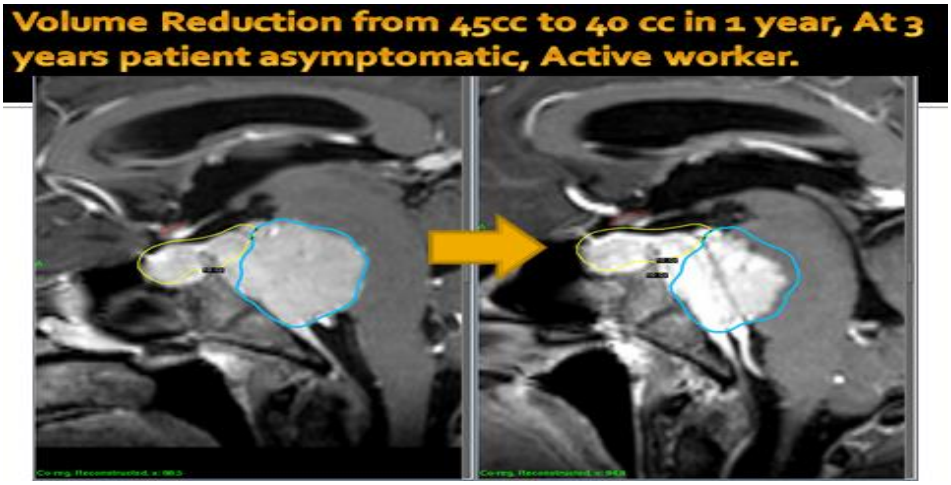





**Case 2**

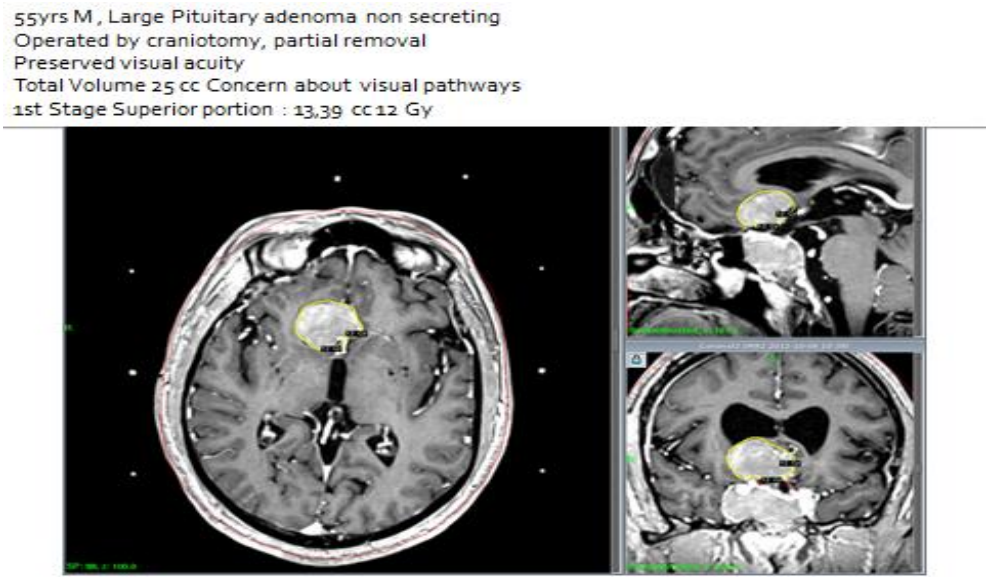
A 17-year old girl presented with loss of left eye vision, gait anomaly and poor school performance which necessitated a stoppage of school. A diagnosis of trigeminal nerve schwannoma (huge) was made. She had 3 attempts at conventional surgical tumour removal. Her tumour volume was 56cc. She had 2-staged SRS - initially, for the posterior fossa component (35cc), and after 1year for the anterior compartment. At 2years of follow-up, there was a marked reduction in tumour volume, improvement in clinical symptoms with gait normalization and patient's resumption of school.

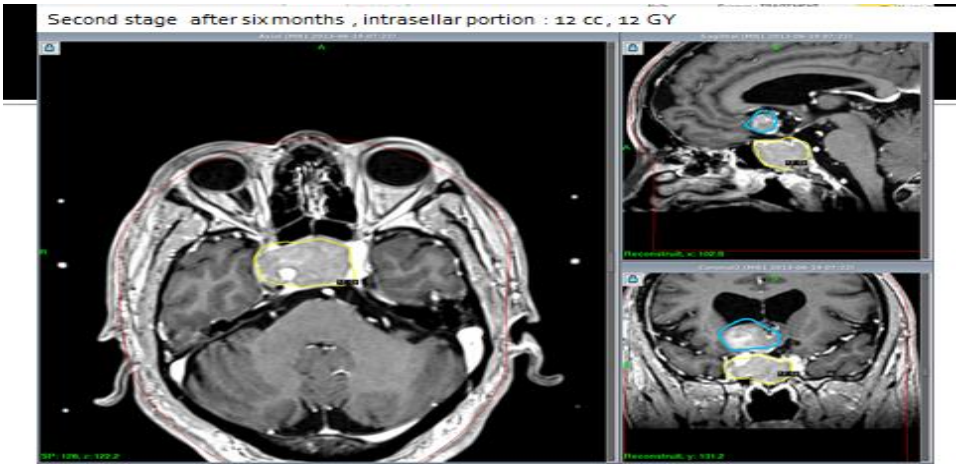


**Case 3**

A 55-year old man, who presented with deteriorating vision and a diagnosis of a non-secreting pituitary macroadenoma for which he had earlier had a craniotomy with partial excision, and preserved visual acuity. The total tumour volume was 25cc. The 1st Stage GKRS was for the superior portion (13.39cc) with 12Gy. Slight volume reduction was noticed at 6months prior to planning the second stage. At 1-year follow up, there was no visual deterioration.




**DISCUSSION**

The use of Leksell Gamma Knife Radiosurgery in the treatment of benign brain tumours has broadened the horizon of neurosurgery over the last 50years, after it found its way into neurosurgery.[2,3,6] Evidence-based findings have been shown to support the safety, efficacy and usefulness of stereotactic radiosurgery (SRS) in the treatment of benign brain tumours.[7] It has a unique design which makes it capable of destroying a targeted area in the brain with a focused high single dose of radiation.

The pattern of steep radiation dose gradient makes it possible to spare the surrounding normal tissues and preserve neuronal function.

Majority of benign brain tumours belong to the radiosurgery target category 2 (late-responding target surrounded by late-responding normal tissue). These tumours are well demarcated and separated from the territory of normal brain tissue, which ensures delivery of appropriate and precise high dose radiation.[8,9,10,11]

The development of modern neuroimaging tools and radiosurgery technique/apparatus has greatly improved radiation accuracy remarkably and enabled its application with various tumours. Gamma knife radiosurgery (GKS) mainly induces coagulative necrosis of tumour parenchyma and stroma with some apoptosis and, ultimately resulting in scar formation. Radiation induced vasculature stenosis and occlusion and tumour degeneration subsequently, results in reduced blood supply.[2,3,4,6]

In our study, involving six patients, age range 17-53years (median 40years), 4 were meningioma (66.7%), 1 was a case of post-operative residual pituitary adenoma, and the other was a 5th cranial nerve schwannoma.

The tumour volumes ranged from 25cc to 56cc (median 44cc), and all, except one, had previous surgical interventions ranging from ventriculo-peritoneal shunt placement and, at least, two surgical procedures aimed at tumour debulking. Radiation dose ranged from 9 to 12Gy. Three of the 6 patients had significant volume reduction (one case of meningioma and the other, 5th cranial nerve meningioma), two had slight volume reduction (one case of meningioma and the other pituitary adenoma), and the last one was stable despite a follow-up period of 3years. Two of these patients were noticed to have improved (meningioma with follow-up of 5years and 5th cranial nerve meningioma with follow-up of 2years) following GKRS.

Three of the 6 patients were noted to be stable, though with follow-up periods ranging from 1 to 5years, and only one became asymptomatic despite a slight reduction in tumour volume with a follow-up period of 4years.

Finding from this our study is not too different from the study by Haselsberger K, *et al*, done over a 16-year period in which staged GKRS was performed in 20 patients with large benign meningiomas, of which 14 of these patients had undergone conventional surgeries, at least once each of them. The patients' ages ranged 26-73 years (median 60.5 years). Tumour volumes were 13.6-79.8cm$^3$ (median 33.3cm$^3$), treatment volumes between 5.4 and 42.9cm$^3$ (median 19.0cm$^3$).

Out of 41 treatments of GKRS, the prescribed dose at the tumour margin was 12Gy for 33 treatments, 10Gy for one, 14 Gy for four, 15Gy for one, and 25Gy for a further two, respectively; (median: 12Gy to a marginal isodose of 45%). Median follow-up was 7.5 years.

Tumour control was achieved in 90% of this series (25% tumour regression, 65% stable size). Only 2 patients (10%) experienced tumour progression outlying the planning target volume treated by an additional radiosurgical procedure. Thereafter, tumour volume decreased in one patient and remained stable in the second one. Clinically, 9 patients (45%) improved within the time of follow-up, 11 (55%) remained unchanged.[12] However, follow-up period in our study ranged 1-5years with varied clinical status.

In a study done by Liu, *et al*, 61 patients underwent neurosurgical intervention for benign brain tumours after GKRS.[13] Of these 61 patients under study, 27 were male and 34 were female. Mean age was 49.1years (range 19–73years). There were 24 meningiomas, 18 schwannomas, 14 pituitary adenomas, 3 hemangioblastomas, and 2 craniopharyngiomas. The interval between GKRS and craniotomy was 2–168months with a median of 24months; for 7 patients, the interval was 10years or longer. For 21 patients, a craniotomy was performed before and after GKRS; in 9 patients, pathological specimens were obtained before and after GKRS. A total of 29 patients had GKRS [13].

In another study by Kano H, *et al*, involving 47 patients who had a multi-stage volumetric management of large AVM, only 16 patients had further retreatment after gamma knife radiosurgery. The mean tumour volume was 11.5(4-26cc) with an initial marginal dose of 16Gy (13-18). Findings from this study show obliteration of tumours in 17 cases after 2-4stages of GKRS; 5 of these cases were near

obliteration, and follow-up period of 5 years showed an obliteration rate of 62%.[14]

From our study, volume of the tumour was an important consideration in staging the treatment, as 35cc was considered a cut-off point in tumours whose volumes were more than 35cc at each session of GKRS. A similar finding was noted in the work of Haselberger K, *et al,* in the management of petroclival and cavernous sinus meningiomata.

From our study, the period of staging was between 6-12months, and this underscores the importance of staged GKRS for benign brain tumours with significant volume reduction and improvement in clinical symptoms in a period of follow-up ranging 1-5years GKRS in the treatment of large voluminous benign brain lesions.

Our finding draws a similarity with the study by DiBiase, *et al,* who identified tumour volume as a significant parameter associated with worse prognosis in patients with meningioma who had GKRS. There were smaller tumour volume residuals in their series with equal results achieved by a Simpson Grade-1 resection with a 9% recurrence rate, and are very close to those obtained by SRS for smaller tumours. [15, 16, 17, 18.] Therefore, a staged procedure for large voluminous benign brain tumours is of characteristic benefit using GKRS in terms of its inherent steep radiation fall off which is maintained in the treatment of larger tumours, thus protecting adjacent brain tissue from radiation-induced injury. [19, 20.]

## CONCLUSION

The gamma knife radiosurgery as an option of treatment of large voluminous benign brain tumour has been documented in our study and other works. Careful selection of patients with clear-cut objective forms the bed rock of this option of treatment of large voluminous benign brain tumours.

It is important that the neurosurgeon when faced with voluminous benign brain tumours, which do not meet the criteria of surgical resection, to consider the option of gamma knife radiosurgery (GKRS) rather than gross total excision for benign tumours closer to neural and vascular structure in view of possible attendant morbidity and mortality. This procedure should be staged to enhance reduction of tumour burden and improved clinical status.

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