International Journal of Pharmaceutical and Bio-Medical Science

ISSN(print): 2767-827X, ISSN(online): 2767-830X

Volume 04 Issue 10 October 2024

Page No: 776-788

DOI: https://doi.org/10.47191/ijpbms/v4-i10-02, Impact Factor: 7.792

Safety and Efficacy of Multisession Gamma Knife Radiosurgery for (Large Benign Intracranial Lesions > 3cm)

Sarah Zuhair kurdi¹, Yasir Mohammed Hasan Hamandi²

¹M.B.Ch.B, F.I.C.M (neurosurgery), Lecturer/neurosurgeon at Al- Kufa university-college of medicine, Al-Sader medical city, Najaf, Iraq

²M.B.Ch.B/F.I.C.M.S (neurosurgery), Professor/consultant Neurosurgeon, Gamma knife department at Saad Al wittry Neuroscience Hospital & Al-Nahrain university-college of medicine, Baghdad, Iraq

ABSTRACT

Background: Stereotactic radiosurgery is delivery of an ablative dose of ionizing radiation to a focused target with 3D localization to elicit a specific radiobiological response and sparing the surrounding normal brain tissue.

Objective: to evaluate safety and efficacy of Gamma knife radiosurgery by volume staging of large benign intracranial lesions.

Patients and methods: prospective cohort study is conducted at Saad Alwitry neuroscience hospital, gamma knife department between June 2017 to February 2021, 60 patients (25 case meningioma,15 case vestibular schwannoma,10 case arteriovenous malformation and 10 patients with pituitary macro-adenoma) having large lesions of >3cm were treated by multisession radiosurgery (2-3 sessions), time between sessions (24hr-6m), follow up time ranged from(6ms-3yr).

Results: rate of growth control for meningioma, vestibular schawannoma, AVM and pituitary macro-adenoma was 76 %,53.3% ,30% and 60% while reduction in lesion size is 20%, 33.3%, 70% and 30% respectively and clinical improvement was 86.4% for meningioma ,52.6% for VS ,73.2% for AVM and 88% for PA and the complications reported were 15.2%.

Conclusion: volume staged multisession GKSR is effective, safe and well tolerated with low morbidity modality for these large lesions.

KEYWORDS: Gamma knife, stereotactic radiosurgery, multisession, gray, volume staged.

INTRODUCTION

Stereotactic radiosurgery is a distinct discipline that utilizes externally generated ionizing radiation in certain cases to inactivate or eradicate (a)defined target(s) in the head and spine without the need to make an incision. The target is defined by high resolution stereotactic imaging. it is performed in a single session, using a rigidly attached stereotactic guiding device, other immobilization technology and/or a stereotactic image-guidance system, but can be performed in a limited number of sessions, up to a maximum of five. Technologies that are used to perform stereotactic radiosurgery include linear accelerators, particle beam accelerators, and multisource Cobalt 60 units. (1)

When tumor size increases >3cm or critical organ lies very close (<2 mm) to the tumor, single session SRS is usually

avoided because of the higher chances of normal tissue toxicity and/or poor local controls. $_{\rm (2)}$

Available on: https://ijpbms.com/

ARTICLE DETAILS

Published On:

04 October 2024

when tumor size increases to >3cm, surgical resection becomes an integral part of treatment. But radiation, perhaps fractionated regimen becomes more preferred treatment if surgery is not possible for any reason such as deep seated / eloquent area tumors, or critical organ is encased, invaded, or lying close to the tumor, or surgically unresectable tumor to avoid gross neurological deficit, medically inoperable (elderly patient, heart disease, uncontrolled diabetes mellitus/hypertension) or patient refuses surgery (either because of the high risk involved in surgery or patient preference. In these situation,multisession SRS becomes an appropriate non-invasive alternative primary treatment option

for this group of patients with adequate therapeutic benefits and minimum normal tissue toxicity. (3)

Multisession SRS is based upon the basic principles of radiobiology concept of fractionated radiotherapy 4 Rs stand for repair, re-assortment, repopulation and re-oxygenation. (4) We investigated group of patients, who had large benign brain lesions (meningioma, VS ,AVM and pituitary macroadenoma) without previous surgery or they may undergo surgical resection but had residual tumors >3 cm.

We assume that multisession stereotactic radiosurgery can be used for these types of patients to reduce the normal tissue toxicity without compromising the therapeutic benefits to achieve good local controls equivalent to or superior to existing standard management strategies.

METHODS

This is a prospective cohort study conducted at Dr. Saad Alwitry Neuroscience Hospital, Gamma Knife Department which conducted for the first time in Iraq.

60 patients were included in this study, meningioma 25 cases in different locations,15 cases of vestibular schwannoma (VS), 10 pituitary macroadenoma (PA) and arteriovenous malformations (AVM) 10 cases.

All are more than 3cm in maximum diameter by radiologist report, 75% were treated primarily by SRS and diagnosed based on their radiological characteristic of the lesions and 15% were residual or recurrent after surgery and diagnosed as WHO grade 1 by histopathological examination.

The study included patients from June 2017 to February 2021 treated by 2-3 sessions, time between sessions range from 24hour to 6months, follow up time ranged from (6ms to 3yr), the lesions were staged according to their volume (volume staged radiosurgery).

History taken and examination done for all cases and were sent for routine investigations in form of complete blood count, renal function test, virology screen, bleeding profile, hormonal assay and visual perimetry for pituitary lesions, pure tone audiometry for vestibular schwannoma and 1.5 or 3 Tesla contrast Brain MRI with Gamma Protocol.

Radiosurgery was performed using the Leksell Gamma Knife® Perfexion[™], Cobalt 60.

The procedure begins with Leksell frame application to patient head which helps to prevent movement of the head under local anaesthetic with 2% lidocaine in four regions (one on each side of forehead and two in the back of the head) where pins will be placed, then measurement taken to be used for planning treatment.

Then patients sent to do CT scan with his frame and during this time patient's information are registered in patient management to insert his name, age, gender, date of birth, type of treatment and also provisional diagnosis with detailed site of lesion and operator ID and Name also included in patient management.

Measurement are entered in planning treatment with selecting (frame cap fit) from skull definition then Patient MRI gamma protocol is inserted and images are imported.

CT scan images which are received from Radiology department are defined and MRI co registered with CT to be merged as one image.

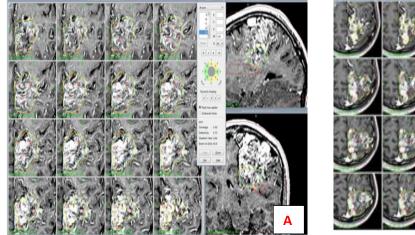
Then we select volume as (target and risk) and manually draw the exact target by dividing the lesion into multiple sections (upper or lower, medial or lateral, anterior or posterior). target volume drawing in the next session skipped the 10-percentile gray zone to avoid radiation necrosis in overlap zone.

The risk volume drawn to shield the nearby critical structures. in addition to sector block, the measurement of radiation is taken to ensure that nearby structures is receiving tolerable dose of radiation.

A new plan dose setting is done as 50% isodose after that apply shots to the selected target with different beam size of 4,8,16 mm. snapshot taken to be printed, then the plan approved and exported to main panel control and patient is guided to the gamma radiosurgery room and operation is completed by removal of frame, sterilizing pin hole sites with iodine.

Most patients discharging home, few of them admitted to the ward for follow up for 1-2 days.

Data of the 60 patients in this study were entered and analyzed using the statistical package for social sciences (SPSS) version 26, IBM, US, 2019.



777 Volume 04 Issue 10 October

Corresponding Author: Sarah Zuhair kurdi

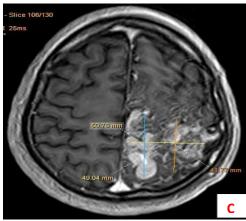


Fig-1 (Case of SM 5 AVM) A-1st session, B- 2nd session, C-post GK *From Dr.Saad Alwittry hospital-GK department*

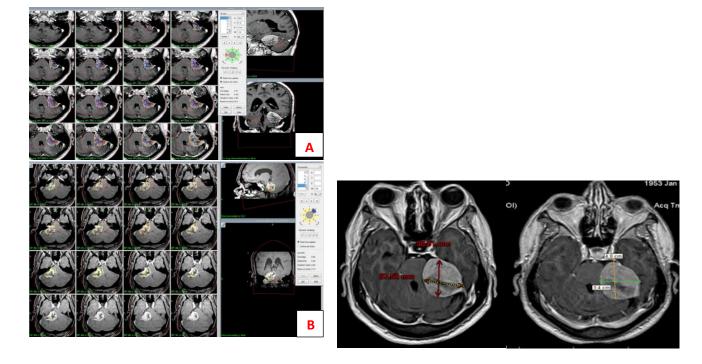
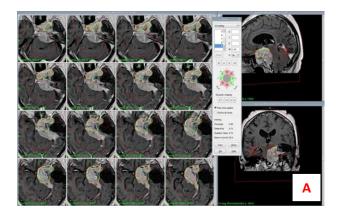


Fig-2 (Case of VS) A-1st session, B- 2nd session, C-post GK From Dr.Saad Alwitry hospital-GK department



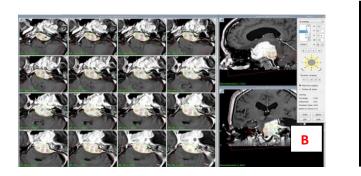


Fig -3 (case of sphenopetro-clival meningioma)

A-1st session, B- 2nd session, C-post GK From Dr.Saad Alwitry hospital-GK department

RESULTS

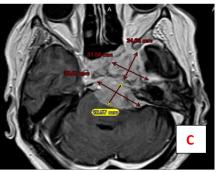
A total of 60 patients were enrolled in this study, 25 of them (41.7%) with Meningioma , 15 (25%) Vestibular Schwannoma, 10 (16.7%) AVM and 10 (16.7%) with Pituitary macro adenoma.

The mean age of the studied group was 48.8 (range: 16-72) years , females were relatively dominant, 51.7% vs. 48.3%, respectively, these baseline characteristics in addition to past medical and surgical history, are shown in (Table 1).

Table 2 shows the Method of diagnosis and Locations of Meningiomas.

In (table 3) the median number of sessions was 2, however, 3

patients performed three sessions, median duration between



sessions ranged 1 to 180 days , and the doses ranged 10 - 14 Gy.

As shown in table 4, no significant change in the size of meningioma after GK sessions(stabilization of growth), (P>0.05), nonetheless, size was decreased in 5 patients (20%).

A significant change was reported in the signs and symptoms after GK sessions, headache and seizures were significantly better , (P<0.05). While no significant change in Neural deficit, (P>0.05), (Table 5).

Unfortunately, Some complications were reported among the 25 meningioma patients with one death , (Table 6).

Similarly, characteristics, responses and outcomes of patients in other groups are summarized in the next tables, (7 - 22).

Variables		No	%
	Meningioma	25	41.7
Diagnosis	Vestibular Schwanoma	15	25.0
Diagnosis	AVM	10	16.7
	Pituitary macro adenoma	10	16.7
C.	Female	31	51.7
Sex	Male	29	48.3
	Hypertension	18	30.0
Dest medical bistom	DM	8	13.3
Past medical history	COPD/Asthma	7	11.7
	IHD	4	6.7
	Craniotomy	6	10.0
Past neurosurgical history	Embolization	1	1.7
	Shunt	3	5.0
	TSS	3	5.0

Table 1. Baseline characteristics of the studied group (N = 60)

No.	
110.	%
22	88.0
3	12.0
6	24.0
5	20.0
3	12.0
2	8.0
2	8.0
2	8.0
2	8.0
1	4.0%
1	4.0%
1	4.0%
	3 6 5 3 2 2 2 2 2 1 1

Table 2. Method of diagnosis and Locations of Meningiomas (N = 25)

Table 3. GK sessions related parameters in meningioma group (N = 25)

	Median	Range
Number of sessions	2	2-3
Duration between session (days)	30	1 – 180
Dose for 1st session (Gy)	14	12 – 14
Dose for 2nd session(Gy)	12	10-14
Dose for 3rd session(Gy)	12	12 - 12

Table 4. Size of meningioma before and after GK session (N = 25)

Size of lesion (mm)		No.	%	Mean Time (months)	P. value
Size before GK	Median	68	-		
Size before GK	Range	50-130	-		
	Decrease	5	20.0%	18	0.824 ns
Size after GK	Same	19	76.0%	11	
	Increase	1	4.0%	9	

Table 5. Signs and symptoms before and after GK sessions in meningioma group (N = 25)

Signal symptoms		Pre GK		Post GK			P. value	
Signs/ symptom	.8	No.	%	Response No. _%		I. value		
Headache	Yes	25	100.0	Better	22	88.0	<0.001 sig	

				Same	0	0.0	
				Worse	3	12.0	
	None	0	0.0	-			
				Better	2	100.0	<0.001 sig
Seizure	Yes	2	8.0	Same	0	0.0	
Seizure				Worse	0	0.0	
	None	23	92.0	-			
				Better	10	71.4	<0.026 sig
Neural deficits	Yes	14	56.0	Same	1	7.2	
Neural deficits				Worse	3	21.4	
	None	11	44.0	-			

Table 6. Complications and outcomes of patients with meningioma after GK sessions (N = 25)

Outcome/ comp	No.	%	
Need Surgery	Craniotomy	1	4.0
	Shunt	1	4.0
	Pinhole infection	1	4.0
Complications	Skin reaction & hair loss	2	8.0
	Edema	1	4.0
	Headache	3	12.0
	Radiation necrosis	2	8.0
	Seizure	1	4.0
	Neural deficit		12.0
	Death	1	4.0
	Malignant tumor	0	0.0

Table 7. GK sessions related parameters in Vestibular Schwannoma group (N = 15)

	Median	Range
Number of sessions	2	2 - 2
Duration between session (days)	60	1 – 180
Dose for 1st session (Gy)	12	12 - 14
Dose for 2nd session (Gy)	12	10 - 12

			Mean time	
Size of lesion (mm)		No.	(months)	%
Size before GK	Median	50		-
Size before GK	Range	38-77		-
	Decrease	5	14.6	33.3
Size after GK	Same	8	9	53.3
	Increase	2	12	13.4

Table 8. Size of lesion before and after GK sessions in Vestibular Schwannoma group (N = 15)

Table 9. Signs and symptoms before and after GK sessions in Vestibular Schwannoma group (N = 15)

Signs/ symptoms		Pre C	GΚ	Post GK			Р.
Signs/ symptoms		No.	%	Response	No.	%	value
				Better	7	77.8	
Vertigo		9	60.0	Same	2	22.2	0.003 sig
				Worse	0	0.0	515
				Better	9	60.0	
Headache	Headache		100.0	Same	4	26.7	0.021 sig
				Worse	2	13.3	
SNHL	Mild	5	33.3	Same	14	93.3	0.992
SINHL	Severe	10	66.7	worse	1	6.7	ns
Facial palsy	Mild	7	46.7	Same	13	86.7	
	severe	7	46.7	worse	2	13.3	0.995 ns
	None	1	6.7	None	0	0.0	110
Long tracs signs	Mild	5	33.3	Better	3	20.0	
	severe	1	6.7	Same	3	20.0	0.871
	None	9	60.0	Worse	1	6.7	ns
				None	8	53.3	

Table 10. Complications and outcomes of patients with Vestibular Schwannoma group (N=15)

Outcome	No.	%	
Need surgery		1	6.7
Need shunt		2	13.4
	Headache	4	26.8
	Pinole site infection	2	13.4
	Skin reaction & hair loss		13.4
	Worsening of facial palsy		13.4
Complications	New or Worsening of brainstem signs	2	13.4%
	hearing deterioration	1	6.7%
	Facial hyposthesia	2	13.4%
	Radiation necrosis		6.7%
	Death	0	0.0
	Malignant tumor	0	0.0

Safety and Efficacy of Multisession Gamma Knife Radiosurgery for (Large Benign Intracranial Lesions > 3cm) Table 11. SM grading of AVM (N=10)

	No.	%
Method of diagnosis		
СТА	8	80.0%
MRI+contrast	2	20.0%
SM grade		
3	2	20.0%
4	5	50.0%
5	3	30.0%

Table 12. GK sessions related parameters in AVM group (N = 10) Image: Non-State State State

	Median	Range
Number of sessions	2	2-3
Duration between sessions (days)	50	1 – 120
Dose for 1st session (Gy)	15	14 – 16
Dose for 2nd session (Gy)	14	12 – 16
Dose for 3rd session (Gy)	13	12 - 14

Table 13. Size of lesion before and after GK session in AVM group (N = 10)

			Mean time	
Size of lesion (mm)		No.	(Months)	%
Size before GK	Median	60		-
Size belore GK	Range	40 - 150		-
Size after GK	Decrease	7	21.8	70.0
Size alter OK	Same	3	18.3	30.0

Table 14. Complications and outcomes of patients with AVM (N=10) Image: Complexity of the second second

Complications	No.	%
Headache	2	20.0
Pinhole site infection	1	10.0
Skin reaction & hair loss	1	10.0
Neural deficit	1	10.0
Hemorrhage	1	10.0
Death	1	10.0
Malignant tumor	0	0.0

Signs/ symptoms		Pre GK		Post GK			Develop
		No.	%	Response No. [%]		P. value	
				Better	6	66.7	0.032 sig
Headache	Yes	9	90.0	Same	3	33.3	
Treatuache				Worse	0	0.0	
	None	1 10.0	-	-			
				Better	7	77.8	0.015 sig
Seizure	Yes	9	90.0	Same	2	22.2	
Seizure					Worse	0	0.0
	None	1	10.0	-	-		
Neural deficit			40.0	Better	3	75.0	0.029 sig
	Yes	es 4		Same	0	0.0	
				Worse	1	25.0	
	None	6	60.0	-	-		

Table 15. Signs and symptoms before and after GK sessions in AVM group (N = 10)

Table 16. Method of diagnosis of Pituitary macro-adenoma (N = 10)

Method of diagnosis	No.	%
Hormonal assay + Histopathology + Imaging	3	30.0%
Hormonal assay + Imaging	7	70.0%

Table 17. GK sessions related parameters in Pituitary macroadenoma group (N = 10)

Parameter	Median	Range
Number of sessions	2	2 - 2
Duration between session (days)	30	1 – 120
Dose for 1st session (Gy)	19	16 – 22
Dose for 2nd session (Gy)	18	12 - 20

Table 18. Size of lesion before and after GK session in Pituitary macro adenoma group (N = 10)

Size of lesion (mm)		No.	Mean time (Months)	%
Size before GK	Median	44		
Size before GK	Range	38 - 55		
	Decrease	3	9	30.0
Size after GK	Same	6	12.2	60.0
	Increase	1	24	10.0

Signs/ symptoms		Pre GK		Post GK			P. value
		No.	%	Response	No.	%	P. value
				Better	8	88.9	0.001 sig
Handasha	Yes	9	90.0	Same	1	11.1	
Headache				Worse	0	0.0	
	None	1	10.0	-			
	Yes	s 4 40.0	Better	4	100	<0.001 sig	
			4 40.0	Same	0	0	
Vision impairment				Worse	0	0	
	None	6	60.0	-			
Cuanial names definit	Yes	0	0.0	Yes	1	10	0.317 ns
Cranial nerve deficit	None	10	100.0	None	9	90	
	Yes	4	40.0	Better	3	75.0	0.029 sig
Hormone related symptoms	1 es	4	40.0	Same	1	25.0	
	None	6	60.0	-	-		

Table 19. Signs and symptoms before and after GK sessions in Pituitary macro-adenoma group (N = 10)

Table 20. Complications and outcomes of patients with Pituitary macro adenoma (N=10)

Complication	No.	%
Pinhole site infection	1	10.0
Skin reaction & hair loss	1	10.0
Headache	2	20.0
Radiation necrosis or apoplexy	0	0.0
Cranial nerve palsy	1	10.0
Visual impairment	1	10.0
Death	0	0.0
Hypopituitarism	0	0.0
Malignant tumor	0	0.0

Table 21. overall clinical status and complications							
Lesion	Clinical improvement	Clinical Stabilization	Clinical worsening	Complications rate			
	rate %	rate%	rate%	%			
Meningioma	86.4	2.4	11	15			
Vestibular	52.6	49.8	6.7	15.6			
schwannoma							
AVM	73.2	18.5	8.3	15			

Pituitary	88	12	6.7	15
macroadenoma				
Overall	75	20.7	8.2	15.2

Table 22. overall Growth control rate **Growth control rate** Lesions **Stable %** Mean time (M) **Decrease %** Mean time(M) **Increase %** Mean time(M) 20 18 9 Meningioma 76 11 4 14.6 VS 53.3 9 33.3 13.4 12 70 AVM 30 18.3 21.8 PA 60 12.2 30 9 10 24 54.8 12.6 38.3 15.9 15 Overall 9.1

DISCUSSION

The LGK was conceived by Lars Leksell as an alternative to an open surgical procedure Which traditionally been a singlefraction treatment modality, now been extended to multiple sessions.

Although surgical resection remain the standard for these large lesions, but some common lesion locations (e.g., skull base meningioma, AVM in eloquent area) are not readily amenable to complete resection because of the proximity of vital neural and vascular structures. Advanced age comorbidities (ischemic heart disease in recent past, uncontrolled diabetes mellitus / hypertension), increasing the morbidity and mortality of surgery.

In our study, 60 patients were engaged in this study, 25 of them (41.7%) with Meningioma , 15 (25%) Vestibular Schwannoma, 10 (16.7%) AVM and 10 (16.7%) with Pituitary macroadenoma.

The mean age of the studied group was 48.8 (range: 16-72) years , females were relatively dominant, 51.7% vs. 48.3%, respectively. 60.5% having comorbidity, 38% were elderly.

In the Majority(75%) of cases the diagnosis is depend on imaging only, about 15% was having histopathological confirmation by previous craniotomy which were residual or recurrent lesions.

The time that used to assess radiological growth control depend on last follow up MRI from the last session of GK.

For meningiomas which were the highest number of cases, mean age was 53.3 years ,62% were more than 65 years,65% having comorbidity. Common locations included in this study were (Sphenoid wing 24% and Sphenopetroclival 20%) which carry high surgical morbidity.

Only 12% (3 cases) had confirmed diagnosis of meningioma WHO grade l by previous craniotomy. Tumors were divided

into sections and given GK ,the median dose was 12 Gy (10-14), duration between sessions were 30 days(1-180) ,mean tumor size were 86mm (50-130) ,tumor growth was stable in 76% of patients in mean time of 11 months and decrease in 20% in mean time of 18months while one case show increase in tumor size due to radiation necrosis according to radiological report after 9months from last session. Clinical signs and symptoms improved in majority of cases ,only one case required surgical resection after increment in tumor size with clinical deterioration.

Complications were 1 pinhole site infection,2 skin reaction, perilesional edema 1, radiation necrosis 2, new neural deficit develop in 3 patients with 1 death case of 70 years old male with huge sphenopetro- clival meningioma develop radiation necrosis and treated conservatively , no new tumor development.

Yoshiyasu Iwai and coworkers (2019) in their study of 27 patients with large skull base meningiomas who underwent volume-staged GK at the Osaka City General Hospital (Osaka, Japan) between March 1995 and September 2018 were reviewed. The mean tumor diameters ranged from 31 to 47.8 mm (median 39.4 mm), The prescribed radiation dose was 8-12 Gy (median 10 Gy). The treatment interval between the first and second session was three to nine months (median 5.5 months). The median duration of follow-up after the first session was 84 months (range 6-204 months), Tumor volume decreased in nine (37.5%) patients, remained stable in nine (37.5%), and increased (local failure) in six (25%). The actuarial progression-free local control rate was 88% at three years, 78% at five years, 70% at 10 years, and 70% at 15 years. Neurological status improved in three (12.5%) patients, was unchanged in 16 (66.5%), and deteriorated in five (21%). Permanent radiation injury occurred in one (4%) patient.(5)

Our study had showed improvement in growth control and clinical status in a shorter period of time.

For vestibular schwannoma, 15 cases were included, mean age was 65.3 years with 41% being more than 65yr. and 70% have co-morbidities. They are koos stage 3 or 4 (53% stage 4) with average size of 50mm (38-77) ,20% had previous retrosigmoid craniotomy confirm VS WHO grade 1 , 20% having VP shunt.

Mass was divided into two segments given two sessions, median dose 12 Gy (10-14), with median time of 60days (1-180).tumor growth was stable in 53.3% in mean time of 9months, decreased in 33.3% after mean time of 14.6months and increased in 13.4% after 12months. headache and vertigo Improved in 60%,77% respectively. Sensorineural hearing loss and facial palsy remain stable in 93.3%, 86.7% respectively.

Complications were 2 pinhole site infection,2 skin reaction, ,radiation necrosis 1,deterioration of facial palsy in 1case and hearing in 2cases and new facial hypoesthesia in 2 cases with no death or new tumor development while 1 patient (6.7%) need surgery after radiation necrosis and worsening of his condition and 2 need VP Shunt.

For pituitary macroadenoma ,mean age was 44.5yr ,1 case more than 65 yr, 30% had co-morbidities. 3 lesions were residual tumor post Trans-sphenoidal surgery ,2 cases were prolactinoma and 2 cases of GH secreting adenoma , others non-functioning adenoma .

Adenoma mean size was 44 mm (38-55) divided into two parts given two sessions with median dose of 18 Gy (12-22) ,in time frame of 30days (1-120) between sessions.

Tumor size was control in 60% in mean time of 12.2months, decrease in 30% of cases after a mean time of 9months and 10% show enlargement by MRI report after 24 months since last session. headache improved in 88.9% ,4 cases were having visual field defect by perimetry which improved by GK. 3 (75%) patients were diagnosed with secretory adenoma show biochemical and clinical improvement.

Pinole site infection ,Skin reaction reported in 1 case, 3rd nerve palsy and Visual impairment developed in one patient, while no Radiation necrosis or apoplexy ,death ,hypopituitarism and Malignant tumor have been reported.

For AVM , 10 patients were included ,50% had spetzler martin(SM) grade 4, 30% SM 5, 20% SM 3. Mean age was 31yr ,10% had co-morbidity. Mean nidus size was 60 mm (40-150), given 2-3 sessions of GK, duration between sessions were 50 days (1-120) ,median dose given was 14 Gy (12-16).

Rate of reduction of nidus size was 70% in mean time of 21.8months while 30% remain the same after a mean time of 18.3 months and no case of complete obliteration. Headache ,seizure and neural deficits were improved in 66.7%, 77.8% and 75% respectively.

Complications reported in 10%(1 case) which were Pinhole site infection, skin reaction & hair loss ,new neural deficits .1

patient develop hemorrhage after 3months of GK and died ,no malignant tumor developed.

Kano and coworkers (2012) reported 47 patients having staged-volume AVM radiosurgery at the University of Pittsburgh. The median AVM volume was 22.2 cm 3 ; the median AVM margin dose used at each procedure was 16 Gy. Obliteration was confirmed in 17 patients (36%) at a median follow-up of 87 months. Ten patients (21%) had bleeding after radiosurgery; five patients died. Two patients (4%) developed symptomatic radiation-related complications.(6)

Pollock and coworkers (2016) Retrospective comparison of 381 AVM patients having SRS during a 20-year period , Obliteration was 59.1% at 4 years and 85.1% at 8 years. The ICH rate was 7.7% at 4 years and 10.6% at 8 years. The rate of permanent radiation induced complications was 4.4% at 4 years and 8.6% at 8 years. (7)

Both of these studies involve large sample size and long duration of follow up that make comparison unreasonable.

Overall rate of growth control was 76% in 11months for meningioma, 53.3% in 9months for VS ,30% in 18.3 months for AVM and 60% in 12.2 months for PA ,while decrease in size was seen in 20% in mean time of 18months for meningioma, 33.3% in 14.6months for VS and 70% in 21.8 months for AVM and 30% in 12.2months for PA, so the staged GK is effective in tumor control and size enlargement was seen in 4% ,13.4 %, 10 % in (9m-12m-24m) for meningioma ,VS and PA respectively.

Overall clinical improvement was seen in 86.4 %,52.6%,73.2% and 88% for meningioma ,VS, AVM and PA respectively that was significant . while clinical worsening was 11%, 6.7%, 8.3% and 6.7% for meningioma , VS, AVM and PA respectively.

Overall complications rate were 15.2%, the radiation induced complications is 5% and mortality was 3%(2 cases).

CONCLUSION

we conclude that volume staged multisession gamma knife radiosurgery is effective in control of tumor growth of these large lesions in following descending order meningioma, PA, VS and AVM and improvement in patient signs and symptoms in following descending order PA, meningioma, AVM and VS.

Volume staged MSRS is safe and well tolerated with acceptable rate of radiation induced complications and mortality.

RECOMMENDATION

mSRS is promising non-invasive approach so we advise volume staged multisession gamma knife for these large benign lesions, long-term follow up is recommended to investigate the impact of mSRS in large brain lesions, comparative study between volume staged and fractionated multisession GKSRS and study of optimal time between multiple sessions and its correlation with growth control and morbidity.

REFERENCES

- I. Ganz C.J ; Introduction and the Nature of Radiosurgery, Gamma Knife Neurosurgery,3rd ed, NewYork: Springer 2011.chap 1 ,p(27-28).
- II. Minniti G. and Scaringi C. ; Fractionated Radiosurgery , Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy,1st ed, Springer 2019, p (94-97).
- III. Rashid A., Memon A. M. Ahmed U., et al, Multisession stereotactic radiosurgery for large benign brain tumors of >3cm- early clinical outcomes, Journal of Radiosurgery and SBRT,, April 19, 2012; Vol. 2, p (29-40).
- IV. Flickinger C. J.; The Radiobiology of Radiosurgery , Intracranial Stereotactic Radiosurgery, 2nd ed, Thieme 2016, p (38-45).
- V. Iwai Y, Yamanaka K, Shimohonji W, Ishibashi K. Staged gamma knife radiosurgery for large skull base meningiomas. Cureus. 2019 Oct; vol 11, p (10).
- VI. Kano H, Kondziolka D, Flickinger JC, Park KJ, Parry PV, Yang HC, Sirin S, Niranjan A, Novotny J, Lunsford LD. Stereotactic radiosurgery for arteriovenous malformations, Part 6: multistaged volumetric management of large arteriovenous malformations. Journal of neurosurgery. 2012 Jan ; vol 116(1) : p (54-65).
- VII. Pollock BE, Link MJ, Stafford SL, Garces YI, Foote RL. Stereotactic radiosurgery for arteriovenous malformations: the effect of treatment period on patient outcomes. *Neurosurgery*. 2016 Apr ; vol 78(4):p (499-509).
- VIII. Hansasuta A., Choi H C., Soltys G.S., et al ; Multisession stereotactic radiosurgery for vestibular schwannomas: single-institution experience with 383 cases, *Neurosurgery*, 2011 Dec, Vol 69(6), P(1200–1209).
- IX. albano l., Losa M., Nadin F., et al; Safety and efficacy of multisession gamma knife radiosurgery for residual or recurrent pituitary adenomas, Endocrine, springer, Feb 2019, vol 64(23), p (639– 647).
- X. McTyre E, Helis CA, Farris M and et al; Emerging indications for fractionated gamma knife radiosurgery. Neurosurgery. 2017 Feb ; vol 80(2): p(210-216).
- XI. Albano L, Losa M, Nadin F and et al ; Safety and efficacy of multisession gamma knife radiosurgery

for residual or recurrent pituitary adenomas, Endocrine. 2019 Jun; vol 64(3) ,p(639-647).

- XII. Casentini L, Fornezza U, Perini Z, Perissinotto E, Colombo F. Multisession stereotactic radiosurgery for large vestibular schwannomas. Journal of neurosurgery. 2015 Apr; vol 122(4), p (818-824).
- XIII. Ilyas A, Chen CJ, Ding D, Taylor DG, Moosa S, Lee CC, : Volume-staged versus dose-staged stereotactic radiosurgery outcomes for large brain arteriovenous malformations: a systematic review. *J Neurosurgy*, 2018 Dec, vol 128, p(154–164).
- XIV. Kirkpatrick JP., Soltys SG. ; The radiosurgery fractionation quandary: single fraction or hypofractionation , *Neuro-Oncology*. 2017, vol 19: p (938–949).
- XV. Jiang B., Hara W. and Li F. G. ; Role of Radiosurgery for Sellar Lesions, Handbook of Radiosurgery in CNS Disease, 1st ed, DEMOSMedical 2013, p (120-126).
- XVI. Lee C., Trifiletti M D. and Sheehan P. J. ; Stereotactic Radiosurgery for Pituitary Adenoma, Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy, 1st ed, Springer 2019, p (121-128).
- XVII. albano l., Losa M., Nadin F., et al; Safety and efficacy of multisession gamma knife radiosurgery for residual or recurrent pituitary adenomas, Endocrine, springer, Feb 2019, vol 64(23), p (639– 647).
- XVIII. McTyre E, Helis CA, Farris M, et al ;Emerging indications for fractionated gamma knife Radiosurgery. Neurosurgery. 2017 Feb ; vol 80(2), p(210-216).
 - XIX. Nguyen JH, Chen CJ, Lee CC, Yen CP, Xu Z, Schlesinger D, Sheehan JP. Multisession gamma knife radiosurgery: a preliminary experience with a noninvasive, relocatable frame. World neurosurgery. 2014 Dec; vol 82(6): p (1256-1263).
 - XX. 20. Flemming D.K. and Brown D.R.; Epidemiology and Natural History of Intracranial Vascular Malformations, Youmans and Winn neurological surgery, 7th ed, Elsevier 2017, p(5512-5515).
- XXI. Choudhri O., Chang D. S., and Steinberg K.G.; Surgical and radiosurgical Management of Grade IV and V Arteriovenous Malformations, Youmans and Winn neurological surgery, 7th ed, Elsevier 2017,p (5593-5607).