OPEN ACCESS

Research Paper

The Role of Gamma Knife in Brain Metastasis. A Clinical Study of 50 Cases

Ahmed Najat Khorsheed Aga[1], Ahmed A Salam Al Atraqchi[2], Ahmed Adnan Al Juboori [3]

ABSTRACT:

BACKGROUND:

Brain metastasis represent a significant source of morbidity and mortality in patients with systemic cancer, they are neoplasms that originate in tissues outside the central nervous system (CNS) and spread secondarily to the brain. SRS is delivered using dedicated radiosurgery platforms such as the Gamma Knife.

OBJECTIVE:

The aim of this study is to evaluate the role of gamma knife radiosurgery as a treatment of secondary metastatic brain tumors.

PATIENTS AND METHODS:

This is a prospective clinical study performed in Dr. Saad Al-Witry Neuroscience Hospital, Gamma Knife Department, to evaluate the role of gamma knife radiosurgery as a treatment of secondary metastatic brain tumors, depending on tumor volume, peritumoral edema and presenting clinical features with their effect on quality of life and survival, between January 2019 to January 2020. Mean age was (63.02± 11.98), 21 patients were >65 years, while 29 patients were ≤65 years. 13 of patients were males and 37 were females. Lung cancer was primary lesion in 68%, breast cancer in 22%, both prostate cancer and RCC were 4%, and unknown origin was 2%. 64% of patients was without previous brain treatment, only 36% was with previous brain treatment. Majority of patients had headache 44%.

RESULTS:

After 12 months of follow up, mean tumor volume post (GKRS) regressed from 6.48cm^3 to 3.38cm^3. Age of patients ≤65 years, KPS >70, patients with small tumor volume and patients without previous treatment (surgery, chemotherapy and WBRT) had good prognosis.

CONCLUSION:

GKRS is efficient and safe in treating patients with secondary brain metastasis, Age groups less than 65 years, KPS more than 70, decrease in tumor volume post . are associated with increased survival rate, improvement in clinical features associated with better quality of life, multiplicity of metastasis is an ominous sign of mortality.

KEY WORDS: gamma knife surgery • brain metastases • small cell lung cancer • non–small cell lung cancer.

[1]MBChB, FICMS Neurosurgery Kirkuk General Hospital, Kirkuk, Iraq.
[2] MBChB, FICMS Neurosurgery, FACS, FICS, FWFNS, IFAANS, Consultant Neurosurgeon, Neurosciences Hospital, Baghdad, Iraq
[3]MB ChB, FICMS Neurosurgery, Neurosciences Hospital, Baghdad, Iraq

Iraqi Postgraduate Medical Journal, 2025; Vol. 24(1): 21-26
DOI: 10.52573/ipmj.2025.144336 *Received: November 6, 2023* *Accepted: November 29, 2023*

INTRODUCTION:

Brain metastasis

Brain metastasis represents a significant source of morbidity and mortality in patients with systemic cancer, they are neoplasms that originate in tissues outside the central nervous system (CNS) and spread secondarily to the brain. In adults, cerebral metastasis is by far the most common intracranial tumors. Treatment of brain metastasis consists of surgical resection, radiation therapy, or a combination of the two modalities. With

advances in surgery and stereotactic radiosurgery (SRS), therapeutic options have increased, and long-term survival has become a reasonable goal.[1] (see figure1).

AIM OF THE STUDY:

The aim of this study is to evaluate the role of gamma knife radiosurgery as a treatment of secondary metastatic brain tumors, depending on tumor volume, peritumoral edema and presenting clinical features with their effect on quality of life and survival.

PATIENTS AND METHODS:

This is a prospective clinical study performed in Dr. Saad Al-Witry Neuroscience Hospital, Gamma Knife Department, to assess the effect of Gamma Knife on 50 patients with brain metastasis, between January 2019 to January 2020, and followed up for 12 months. All patients were assessed according to Tumor volume, peritumoral edema, their clinical features and their KPS, they were obtained 3 tesla brain MRI study with contrast prior to gamma knife. Then performing gamma knife by a procedure mentioned later, these cases were followed up clinically with neurologic examination three weeks later, then after 3 months after GRKS, then with three months interval; All patients were sent for routine investigations in form of bleeding profile, virology screen, complete blood count (CBC), renal function test (RFT).

Brain MRI with gadolinium contrast enhancement was done after 6 and 12 months for the survived patients after gamma knife. Tumor volume was evaluated on contrast-enhanced T1-weighted images. Tumor volume calculated by maximum length, maximum width, number of slices multiply by thickness divided by 2. Peritumoral edema volume was defined as the peritumoral increased signal detected on T2-weighted or FLAIR MRI sequences.

PROCEDURE

Radiosurgery was performed using the Leksell Gamma Knife® Perfexion™, 192 beams of Cobalt 60 radiation are delivered through the intact skull to the metastatic tumor. GKRS procedure begin with Leksell frame is attached to patient head which helps exactly to position patient head and to inject local anesthetic 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 to fasten the Leksell frame to patient's skull, to prevent moving of the head. After that, patient sent to measurement room where measurements are used for planning patient treatment. Then we sent patient to CT scan, and during this time, patient's information are registered in patient management to insert his name, age, gender, and type of treatment and also provisional diagnosis with detailed site of lesion and operator ID and Name also included in patient management. Measurements are entered in planning treatment with selecting (frame cap fit) from skull definition then Patient MRI in form of CD is inserted and images are imported. CT scan images which are received from Radiology department are defined manually and MRI co-registered with CT to be merged as one image. Then treatment planning, the dose prescription between (15-25) Gy, dose limitations to critical structures, then conformal radiosurgical dose planning by the radiosurgery surgeon and his team, radiation delivered to the target volume by positioning of the patient's head inside a collimator system. At the end, Removal of the stereotactic guiding device.

RESULTS:

This study was done on 50 patients with brain metastasis, out of 50 patients, (42%) were in age groups of >65 years and (58%) of them were in age groups of ≤65 years, the mean age was (63.02± 11.98) years; (26%) of patients were males, while (74%) were females, female to male ratio was (2.8:1). According to the number of lesions, in (54%) was solitary tumor, in (46%) were multiple tumor of patients with brain metastasis. The number of lesions was one tumor in (54%) of patients, two tumors in (20%) of them, three tumors in (14%) of them, four tumors in (6%) of them, five tumors was in (2%) of them and six tumors was in (4%) of them, the mean number of lesions (1.94 ± 1.33).

Most of patients with brain metastasis in this study observed that the primary origin for brain metastasis was from lung cancer which was (68%), then the primary origin from breast cancer was (22%), both RCC and prostate cancer were (4%) and unknown primary origin (2%). Patients without previous treatment were (64%), while with previous treatment in (36%); chemotherapy (8%), WBRT (6%), surgery and WBRT (12%), surgery (4%), and surgery and chemotherapy (6%). Mean KPS pre-GKRS for patients with brain metastasis was (76.2±14); the majority of them was KPS 90 in (22%), while mean KPS post-GKRS for patients with brain metastasis was (87.6±12.2); the majority of them was KPS 100 observed in (34%).

According to the clinical features that associated in patients with brain metastasis, the clinical features pre-GKRS were headache/nausea in (44%), seizure was (16%), paresis was (20%), cranial nerve deficit was (12%) and cognitive deficit was (8%). Headache improved in the majority of cases and other symptoms decreased in its severity in (68%), while these symptoms not improved in (32%) of patients. Mean tumor volume Pre-GKRS was (6.48cm^3) which was significantly decreased to (3.38cm^3) 6 months post-GKRS **(p<0.001).** ***(Figure 1).*** Mean KPS Pre-GKRS was (76.2±14) which was increased significantly 6 months post-GKRS to (87.6±12.2) **(p<0.001)**. ***(Figure 2)***

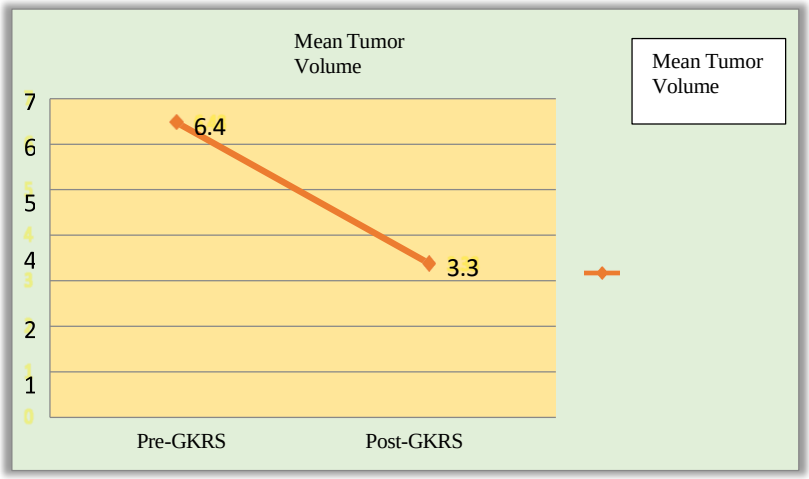

Figure 1: Mean tumor volume distribution pre and post-KRS.

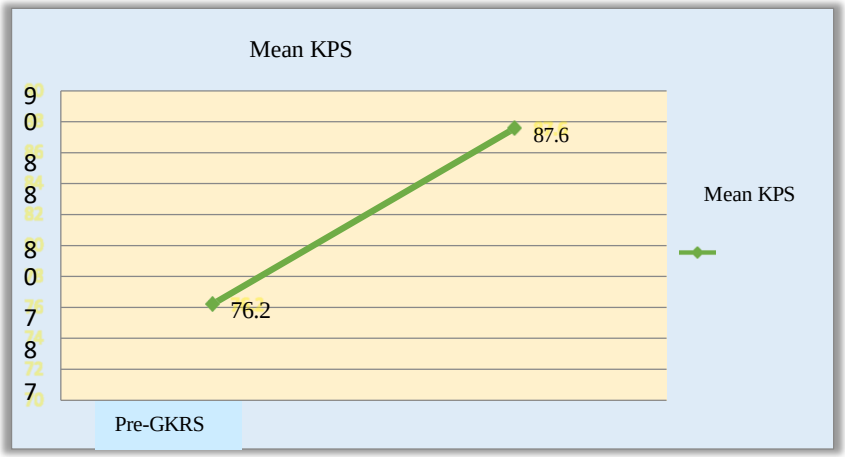

Figure 2: Mean KPS distribution pre and post-GKRS.

Tumor volume pre-GKRS as a significant association with mortality rate in patients with brain metastasis **(P<0.001)**, while reduction in tumor volume post-GKRS as a highly significant association with survival rate in patients with brain metastasis **(p<0.001*). (Table 1).***

Table 1: Final outcome in tumor volume pre and post-GKRS.

Variable	Final Outcome		value*
	Dead	Alive	
	Mean±SD	Mean±SD	
Tumor Volume Pre-GKRS cm^3	7.7±1.63	6.18±1.17	*<0.001 (Highly significant)*
Tumor Volume Post-GKRS cm^3	5.15±2.001	2.94±0.78	*<0.001 (Highly significant)*

**Correlation is significant at the 0.01 level (2-tailed).*

DISCUSSION:

Brain metastasis is devastating stage in the metastasis of CA with 20% (10 patients) of those patients died after GKRS treatment, gender was not significant for mortality. While 80% were alive of them. Matsunaga et al,[2] he found that the mortality rate 20.7% 6 months post-GKRS. Regarding to age groups >65 years were highly significant for mortality (P<0.001), while age groups ≤65 years were highly significant for survival with (P<0.001). Same result was obtained by Shyamal C. et al,[3] who found that survival at 14 months is highly associated with age ≤65 years. Another study done by Jaboin et al,[4] who found that the median survival time for patients of age <65 years was 14.5 months, compared to age ≥65 which was 7.7 months (p = 0.06). Multiplicity of metastasis was a highly significant factor for mortality (P<0.001). Minniti G. et al,[5] who found that the single metastasis (P<0.01) was the only independent prognostic factors associated with a lower rate of distant failure, after a median follow-up of 11 months. Another study done by Jaboin et al,[4] who observed that the patients with a single treated lesion had a median survival time of 16.9 months, and multiple lesions; >3 lesion (MST: 5.9 months) and patients with 2–3 lesions (MST: 14.5 months) compared to patients with a single lesion. Kondziolka D et al,[6] who found patients with increasing numbers of tumors were associated with a lesser chance of surviving. Shyamal C. et al,[3] who found the median survival time for the patients with single BMTs was 38 months and in patients with multiple BMTs was 11 months. Regarding to primary origin of the metastasis was not significant for mortality with (P=0.442); in most of patients the primary origin for brain metastasis was from lung cancer which was (68%), breast cancer was (22%), and others was account (10%). Nayak L. et al,[8] also noted the lung cancer is the most common primary to develop brain metastases. A study done by Wong J. et al,[9] who found that the most common primary cancers were lung (59%) and breast (26%) Previous undergo surgery, chemotherapy and WBRT were showed a highly significant factor for increasing mortality rate (P<0.001). Aoyama H. et al,[10] in his study also observed the median survival time was 7.5 months with WBRT plus SRS and 8.0 months with SRS alone. Motta M. et al,[11] also found that the patients who received WBRT before GKRS fared significantly worse when compared to those receiving GKRS only (p=0.006). Karnofsky Performance Status (KPS) post-GKRS, there was a highly significant survival rate in patients with significant improvement post-GKRS treatment (p<0.001). Al-Khafaji AJ. et al,[12] who found that the role of GKRS treatment increased survival rate with KPS >70 in patients with brain metastasis. Scodan Le. Et al,[13] who found that the KPS <70 was prognostic predictor for poor survival. Another study done by Gaudy-Marqueste C. et al,[14] who found that the survival longer than 6 months was best predicted by KPS 80 and more (p 0.003). Also Lee CC. et al,[15] showed in his study, the better KPS score was significantly related to improved overall survival after GKRS (p = 0.024). Initial tumor volume pre-GKRS and tumor volume post-GKRS was highly significant factor for increasing survival rate (P<0.001). Similar findings done by Baschnagel A.M. et al,[16] who observed the larger total tumor volume all predicted worse overall survival. Al-Khafaji AJ. et al,[14] who found that the smaller tumor volume in patients with brain metastasis were increased survival rate. Also kased N. et al,[17] showed in his study the longer survival rate was associated with smaller total target volume (p = .01 for <3cm^3 vs. ≥3cm^3; p=0.004). Another study by Bragstad S. et

al,[18] found significant decrease in the tumor volume showed was good predictor for survival rate ($p = 0.04$). Patient with brain metastasis post-GKRS regarding to the peritumoral edema, it was decreased or disappeared in 44%. Lee CC. et al,[19] also found the metastatic brain tumor post-GKRS showed brain edema relief in 63% of patients. Clinical features of brain metastasis depend on the site, size, multiplicity and grade of edema. Headache was the most common presenting feature 44%, followed by weakness 20%.Clinical feature post-GKRS improved in 68% of the patients with brain metastasis, while 32% not improved or worsened. A study close to our study done by Lee CC. et al,[19] found most of the patients (83.5%) demonstrated neurological improvement within 3 months. Significant improvement in clinical features post-GKRS was highly significant for survival rate ($p<0.001$).

CONCLUSION:

GKRS is efficient and safe in treating patients with secondary brain metastasis. Age groups less than 65 years, KPS more than 70, decrease in tumor volume post GKRS are associated with increased survival rate. Improvement in clinical features associated with better quality of life. Multiplicity of metastasis is an ominous sign of mortality.

REFERENCES:

1. HR, Winn. Youmans and Winn neurological surgery. 2017.
2. Matsunaga S, Shuto T, Kobayashi N. Gamma Knife Radiosurgery for Metastatic Brain Tumors from Cancer of Unknown Primary. World Neurosurg 2019; 122: e1465-71.
3. BIR, Shyamal C., et al. Long-term outcome of gamma knife radiosurgery for metastatic brain tumors originating from lung cancer. *Surgical neurology international*, 2014, 5.Suppl 8: S396.
4. Jaboin JJ, Ferraro DJ, DeWees TA, Rich KM, Chicoine MR, Dowling JL, Mansur DB, Drzymala RE, Simpson JR, Magnuson WJ, Patel AH. Survival following gamma knife radiosurgery for brain metastasis from breast cancer. Radiation Oncology. 2013;8:1-8.
5. Minniti G, Esposito V, Clarke E, Scaringi C, Bozzao A, Lanzetta G, De Sanctis V, Valeriani M, Osti M, Enrici RM. Stereotactic radiosurgery in elderly patients with brain metastases. Journal of neuro-oncology. 2013;111:319-25.
6. Kondziolka D, Martin JJ, Flickinger JC, Friedland DM, Brufsky AM, Baar J, Agarwala S, Kirkwood JM, Lunsford LD. Long-term survivors after gamma knife radiosurgery for brain metastases. Cancer: Interdisciplinary International Journal of the American Cancer Society. 2005;104:2784-91.
7. Park JY, Moon KS, Lee KH, Lim SH, Jang WY, Lee H, Jung TY, Kim IY, Jung S. Gamma knife radiosurgery for elderly patients with brain metastases: evaluation of scoring systems that predict survival. BMC cancer. 2015;15:1-9.
8. Nayak L, Lee EQ, Wen PY. Epidemiology of brain metastases. Current oncology reports. 2012 ;14:48-54.
9. Wong J, Hird A, Zhang L, Tsao M, Sinclair E, Barnes E, Danjoux C, Chow E. Symptoms and quality of life in cancer patients with brain metastases following palliative radiotherapy. International Journal of Radiation Oncology* Biology* Physics. 2009;75:1125-31.
10. Aoyama H, Shirato H, Tago M, Nakagawa K, Toyoda T, Hatano K, Kenjyo M, Oya N, Hirota S, Shioura H, Kunieda E. Stereotactic radiosurgery plus whole-brain radiation therapy vs stereotactic radiosurgery alone for treatment of brain metastases: a randomized controlled trial. Jama. 2006;295:2483-91.
11. Motta M, Del Vecchio A, Attuati L, Picozzi P, Perna L, Franzin A, Bolognesi A, Cozzarini C, Calandrino R, Mortini P, Di Muzio N. Gamma Knife Radiosurgery for Treatment of Cerebral Metastases From Non–Small- Cell Lung Cancer. International Journal of Radiation Oncology* Biology* Physics. 2011;81:e463-68.
12. Al-Khafaj AJ, Al-Saad HA. Outcomes of Gamma Knife Surgery in the Treatment of Patients with Metastatic Brain Tumors. The Iraqi Postgraduate Medical Journal 2019;18:1-9.
13. Le Scodan R, Massard C, Mouret-Fourme E, Guinebretierre JM, Cohen- Solal C, De Lalande B, Moisson P, Breton-Callu C, Gardner M, Goupil A, Renody N. Brain metastases from breast carcinoma: validation of the radiation therapy oncology group recursive partitioning analysis classification and proposition of a new prognostic score. International Journal of Radiation Oncology* Biology* Physics. 2007;69:839- 45.
14. Gaudy-Marqueste C, Regis JM, Muracciole X, Laurans R, Richard MA, Bonerandi JJ, Grob JJ. Gamma-Knife radiosurgery in the

management of melanoma patients with brain metastases: a series of 106 patients without whole-brain radiotherapy. International Journal of Radiation Oncology* Biology* Physics. 2006;65:809-16.

15. Lee CC, Yen CP, Xu Z, Schlesinger D, Sheehan J. Large intracranial metastatic tumors treated by Gamma Knife surgery: outcomes and prognostic factors. Journal of neurosurgery. 2014;120:52-59.
16. Baschnagel AM, Meyer KD, Chen PY, Krauss DJ, Olson RE, Pieper DR, Maitz AH, Ye H, Grills IS. Tumor volume as a predictor of survival and local control in patients with brain metastases treated with Gamma Knife surgery. Journal of neurosurgery. 2013;119:1139-44.
17. Kased N, Binder DK, McDermott MW, Nakamura JL, Huang K, Berger MS, Wara WM, Sneed PK. Gamma Knife radiosurgery for brain metastases from primary breast cancer. International Journal of Radiation Oncology* Biology* Physics. 2009;75:1132-40.
18. Bragstad S, Flatebø M, Natvig GK, Eide GE, Skeie GO, Behbahani M, Pedersen PH, Enger PØ, Skeie BS. Predictors of quality of life and survival following Gamma Knife surgery for lung cancer brain metastases: a prospective study. Journal of neurosurgery. 2017;129:71-83.
19. Pan HC, Sheehan J, Stroila M, Steiner M, Steiner L. Gamma knife surgery for brain metastases from lung cancer. Journal of neurosurgery.2005;102(Special_Supplement):128-33.