

Gamma Knife Radiosurgery for Resectable Brain Metastasis

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Key words

- Brain metastasis
- Gamma knife radiosurgery
- Non-small cell lung cancer
- Resectable

Abbreviations and Acronyms

GKS: Gamma knife radiosurgery
KPS: Karnofsky performance score
MR: Magnetic resonance
NSCLC: Non-small cell lung cancer
RPA: Recursive partitioning analysis
SRS: Stereotactic radiosurgery
WBRT: Whole brain radiation therapy



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INTRODUCTION

Approximately 20% to 40% of cancer patients eventually develop brain metastases (4, 6, 15). Brain metastases account for a considerable percentage of morbidity in cancer patients and still represent a significant cause of death (42).

Non-small cell lung cancer (NSCLC), accounting for 80% of lung cancer, ranks as the most common origin for brain metastases (40% to 50%) (18). Approximately 120,000 patients develop NSCLC in the United States each year (10, 11, 31, 44). The median overall survival for this group of patients is 1 to 2 months if palliatively managed and approximately 6 months if treated aggressively (10, 16, 26).

Resection is generally utilized for patients who demonstrate a good performance status and have a solitary, accessible (i.e., generally superficial), symptomatic brain metastasis with significant mass effect. Resection is also utilized for those who need a histologic diagnosis and for those in

■ **BACKGROUND:** Surgical resection is most often performed for superficially located brain metastasis. We evaluate the use of gamma knife radiosurgery (GKS) for resectable non-small cell lung cancer (NSCLC) brain metastases located <3 cm away from the outer cortical surface.

■ **METHODS:** Between 1999 and 2009, 306 patients were treated for brain metastasis from NSCLC at the University of Virginia. The current study included patients with 3 or fewer resectable brain metastases, with resectable being defined as <3 cm from the nearest outer cortical surface of the brain. Sixty-four patients with 111 metastatic brain lesions were eligible for the study. Survival, tumor control, and need for a craniotomy and tumor resection after GKS were evaluated.

■ **RESULTS:** The mean overall survival rate in this cohort is 13.5 months (median, 8 months) after GKS, and the mean overall survival after diagnosis of the primary lesion was 31.5 months (median, 19 months). Factors related to prolonged survival after GKS were gender, Karnofsky performance score (KPS), recursive partitioning analysis (RPA) class, age at GKS, number of metastatic lesions, development of new intracranial lesions, and number of lobes involved with metastatic disease. The actuarial local tumor control rate was 84% at 6 months. Two patients (3%) underwent a craniotomy and tumor resection for their progressive superficial metastasis after GKS.

■ **CONCLUSIONS:** GKS for NSCLC brain metastases is effective in patients with 3 or fewer resectable tumors. The need for a craniotomy in this subgroup of patients after GKS is very low.

whom previous radiation therapy has failed. However, unlike an acoustic neuroma or meningioma patient, in whom a complete surgical resection may be curative, extirpation of a brain metastasis is not curative for a stage IV cancer patient.

Stereotactic radiosurgery (SRS) has been used with increasing frequency in patients with 1 to 3 brain metastases <3 cm in diameter (2, 32). Radiosurgery is commonly performed for patients with brain metastases in eloquent areas (24). This study examines the outcome of radiosurgery for treatment of patients with a small number of resectable brain metastases from NSCLC. In particular, we evaluate the efficacy of gamma knife radiosurgery (GKS) for local tumor control, overall survival, and avoidance of a craniotomy in a cohort of patients with a

low number of superficially located metastatic lesions.

MATERIALS AND METHODS

Patient Characteristics

We evaluated NSCLC with brain metastases patients treated with GKS at our center from September 1999 to November 2009. Eligibility criteria for inclusion in this study were 3 or fewer brain metastases, located 3 cm or less from the outer cortical surface of the cerebral hemispheres, no prior open craniotomy, and histologic confirmation of NSCLC. Some of the patients demonstrated mass effect, but the associated neurologic symptoms were responsive to the corticosteroid administration. A total of 64 patients

Table 1. Summary of Initial Tumors and Patient Characteristics

Variable	Number of Patients (%)
Tumor Histopathology	
Squamous cell carcinoma	9 (14%)
Adenocarcinoma	25 (39%)
Large-cell carcinoma	3 (5%)
Unclassified subtype	27 (42%)
Tumor location	
Frontal lobe	21 (33%)
Single	17
2 metastases	2
3 metastases	2
Parietal lobe	8 (13%)
Single	5
2 metastases	2
3 metastases	1
Temporal lobe	7 (11%)
Single	4
2 metastases	3
Occipital lobe	7 (11%)
Single	6
2 metastases	1
Involvement of 2 different lobes	18 (28%)
Involvement of 3 different lobes	3 (5%)
Initial treatment category for the same lesions	
GKS alone	30 (47%)
GKS + contemporaneous WBRT	34 (53%)
Patient gender	
Female	29 (45%)
Male	35 (55%)
Patient age (mean 58.4 years)	
≥60 years	29 (45%)
<60 years	35 (55%)
KPS at GKS	
100	8 (13%)
90	19 (30%)
80	21 (33%)
70	16 (24%)
RPA class at GKS	
I	11 (17%)
II	42 (66%)
Indeterminate	11 (17%)
GKS, gamma knife surgery; KPS, Karnofsky performance score; RPA, recursive partitioning analysis; WBRT, whole brain radiotherapy.	

fulfilled these inclusion criteria. Twenty-nine female (45%) and 35 male (55%) patients constituted this patient cohort, with a mean age at GKS of 58.4 years (range, 20 to 91 years).

Table 1 details the patient characteristics of the entire cohort. Thirty-two patients (50%) had a single tumor, 17 patients (27%) had 2 metastatic lesions, and 15 patients (23%) had 3 metastatic lesions at the time of GKS. Thirty-six patients (56%) underwent whole-brain radiation therapy (WBRT) either before or immediately after GKS. The decision to use a WBRT contemporaneously with GKS was made in conjunction with the patient's treating medical oncologist. In this study, the dose of WBRT ranged from 23.5 Gy to 39 Gy, with a median of 30 Gy. A total of 34 patients underwent a prior WBRT, whereas the remaining 2 patients received WBRT after GKS. In the former group, the median and mean time intervals are 4 months and 6.1 months, respectively (range, 2 weeks to 23 months).

Table 2 details the presenting symptoms of the patients in this series. In brief, 13 patients (20%) were neurologically asymptomatic, 21 patients (33%) had 1 presenting symptom, 15 patients (23%) had 2 symptoms at the time of presentation, and the remaining 15 patients (23%) had 3 or more symptoms. Intracranial metastasis located at eloquent brain areas was defined as those appearing in the primary motor cortex and somatosensory cortex of either hemisphere, speech cortex (posterior left temporal lobe), or primary visual cortex. There were 36 patients (56%) in the eloquent group.

Radiosurgical Technique

Our stereotactic radiosurgical technique for brain metastasis patients has been described previously in detail (7). In brief, patients underwent stereotactic frame placement while under monitored anesthesia. Precontrast and postcontrast thin-slice (1 mm thickness) axial and coronal magnetic resonance (MR) sequences were obtained for the treatment planning. All patients in this series had GKS planning using MR imaging. The dose to the tumor is based on several factors, which include the status of prior WBRT, size of the metastasis/metastases, and radiation tolerance of surrounding critical structure. In general, dose selection was adherent to the RTOG 9508 study,

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