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A Phase II Trial of Stereotactic Radiosurgery Boost Following Surgical Resection for Brain Metastases

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Abstract

Purpose/Objective—To evaluate local control following surgical resection and postoperative stereotactic radiosurgery (SRS) for brain metastases.

Methods and Materials—Forty-nine patients (50 lesions) were enrolled and available for analysis. Eligibility criteria included histologically confirmed malignancy with 1 or 2 intraparenchymal brain metastases, age ≥ 18 , and KPS ≥ 70 . Cox proportional hazard regression model was used to test for significant association between clinical factors and overall survival (OS). Competing risks regression models, as well as cumulative incidence functions, were fit using the method of Fine and Gray in order to assess the association between clinical factors and both

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local failure (LF, recurrence within surgical cavity or SRS target), and regional failure (RF, intracranial metastasis outside of treated volume).

Results—The median follow-up was 12.0 months (mos, range: 1.0–94.1 mos). Following surgical resection, 39 patients with 40 lesions were treated a median of 31 days (range: 7–56 days) later with SRS to the surgical bed to a median dose of 1800 cGy (range: 1500–2200 cGy). Of the 50 lesions, 15 (30%) demonstrated LF after surgery. The cumulative LF and RF rates were 22% and 44% at 12 mos. Patients who went on to receive SRS had significantly lower incidence of LF ($p=0.008$). Other factors associated with improved local control includes NSCLC histology ($p=0.048$), tumor diameter <3 cm ($p=0.010$), and deep parenchymal tumors ($p=0.036$). Large tumors (≥ 3 cm) with superficial dural/pial involvement showed the highest risk for LF (53.3% at 12 mos). Large, superficial lesions treated with SRS had 54.5% LF. Infratentorial lesions were at higher risk of developing RF compared to supratentorial lesions ($p < 0.001$).

Conclusions—Postoperative SRS is associated with high local control, especially for deep brain metastases <3 cm. Tumors ≥ 3 cm with superficial dural/pial involvement demonstrate the highest risk in LF.

Keywords

Brain Metastases; Stereotactic Radiosurgery; Neurosurgery

INTRODUCTION

Brain metastases occur in 20–30% of all cancer patients with systemic cancers [1, 2]. Historically, brain metastases do not respond well to systemic agents, and the outcome for patients with brain metastases is generally poor, with median survivals following whole brain radiation therapy (WBRT) alone in the range of 3–6 months [3–5]. This approach has been gradually changing with use of surgery and stereotactic radiosurgery (SRS). While WBRT remains the main treatment modality for patient with multiple brain metastases, randomized trials support the use of surgery, and more recently, SRS in addition to WBRT in patients with limited intracranial metastases [3, 6–8] in reducing intracranial progression.

Although older series of patients with solitary brain metastasis treated with surgery followed by WBRT showed an overall survival (OS) of less than 1 year with death due to systemic disease in the vast majority of patients [9], updated studies of patients with limited brain metastases have reported longer OS, reflecting, in part, the improved efficacy of modern systemic therapies [10, 11]. As systemic control improves, durable control of CNS metastases is increasingly imperative. Adjuvant WBRT may be effective for improving local control (LC), however neurocognitive deficits associated with WBRT have been reported [12]. Furthermore, WBRT can delay systemic therapy both during the weeks of administration of the radiation treatments and for several weeks afterwards as patients are recovering from the acute side effects.

Adjuvant SRS has been utilized as a method of delivering RT to the post-surgical cavity [13–25]. SRS is established as an effective alternative to WBRT as a primary treatment modality for limited metastases [6, 8]. SRS offers excellent LC and minimal acute and long-term

toxicity as a stand-alone modality [6, 12]. For patients with a single intracranial metastasis, adjuvant radiation in the form of SRS may be beneficial, as it is generally well tolerated with minimal impact on a patient's quality of life and does not significantly interfere with systemic therapy schedules.

The hypothesis for this study was that adjuvant SRS to the surgical cavity for patients with 1 or 2 brain metastases would improve LC over surgery alone and allows for avoiding up-front WBRT. There have been several retrospective studies of postoperative SRS to the resection cavity [13–25], reporting local control between 70 and 90% at 12 months, but this is the first prospective study investigating its efficacy.

MATERIALS AND METHODS

Patient Selection

This phase II study entitled “A Phase II Trial of Stereotactic Radiosurgery Boost Following Surgical Resection for Brain Metastases” was approved by the institutional review board was opened June 8, 2004 and closed to accrual after 50 patients were enrolled in January 27, 2009. Inclusion and exclusion criteria are listed in Table 1. The primary objective of this study was to evaluate the local control of brain metastases with combination therapy of surgical resection followed by post-operative SRS.

Surgery

Study patients were accrued from a population eligible for surgery and for whom surgery was recommended rather than radiation as a primary treatment. Prior to surgery, all patients underwent a complete history and physical examination, an MRI with Gadolinium, and a complete blood count. Contrast-enhancing CT scans of the chest, abdomen and pelvis, or positive emission tomography scan were recommended to determine the extent of extracranial malignant disease. After pretreatment evaluation, patients underwent a craniotomy with the goal of total removal of the metastases. All patients had an MRI acquired (1.5 T GE Excite, GE Medical Systems, Milwaukee, WI) between post-operative days 1 and 3 to determine whether the surgical removal of the tumor was complete, along with the surgeon's operative report.

SRS

SRS was delivered between 2–8 weeks after surgery. A post gadolinium-enhanced T1-weighted MRI with 3 mm slices was obtained 1–7 days before SRS. Patients were immobilized for SRS in a Brown-Roberts-Wells (BRW) frame (Integra Radionics, Burlington, MA) and positioned for treatment using a localizing stereotactic frame. On the treatment day, a 2 mm sliced computed tomography (CT) study was acquired (Philips PQ-500 scanner, Philips Medical Systems, Andover, MA) with Omnipaque (GE Healthcare, Waukesha, WI) intravenous contrast. The CT images were transferred to the BrainLAB treatment planning system (BrainLAB, Feldkirchen, Germany) and fused to the T1-weighted MRI to aid target delineation. The total dose was dependent on the size of the post-surgical cavity as seen on the MRI and planning CT as follows:

<u>Maximal Surgical Cavity Diameter:</u>	<u>Dose:</u>
2.0 cm	2200 cGy
2.1–3.0 cm	1800 cGy
3.1–4.0 cm	1500 cGy

The radiation oncologist and neurosurgeon worked together to define the postoperative cavity and target volumes. The clinical target volume (CTV), defined as the contrast-enhancing post-operative cavity excluding the surgical track, was delineated on T1-weighted MRI and on the planning CT (contrast enhancement on MRI and CT). Surrounding areas of edema were not considered part of the target volume. The planning target volume (PTV) was defined as a three-dimensional 2 mm margin around the CTV. The radiation treatment plans consisted of 8–12 non-coplanar static fields using the micro-multileaf collimator m3 (BrainLAB, Feldkirchen, Germany) with 3 mm leaves for field shaping. The plans were developed such that the 80% isodose line (IDL) encompassed the PTV in the most conformal manner possible, and the determined dose was prescribed to the 80% IDL. Dose volume histograms using a dose grid size of 2 mm were used to document 3-D coverage for tumor and normal structures. Quality criteria and evaluation including dose homogeneity and conformation index were fulfilled according to the Radiation Therapy Oncology Group (RTOG) Guidelines [26]. Institutional normal tissue dose constraints were met (Table 2).

For patients with two brain metastases, each CTV was assigned a prescription dose according to its maximal diameter. To minimize toxicity in patients with multiple metastases, it was also required that if one CTV was ≥ 3 cm in diameter, the second could not exceed 3 cm in diameter for the patient to be eligible.

Statistical Analysis

Patients were followed with MRI imaging 8 weeks following SRS and then every 3–4 months thereafter. Survival time, local failure (LF) rate, and regional failure (RF) rates were measured from the date of enrollment to the date of death or last follow-up. LF and RF were determined by MRI review. LF was defined by the development of recurrence within the post-operative cavity, determined both clinically by the treating physicians' consensus, and radiographically, including the use of advance imaging such as brain positron emission tomography and MRI perfusion imaging. RF was defined by the development of new brain metastasis outside the post-operative cavity. Prognostic factors for overall survival were analyzed by univariate Cox regression analysis. Factors associated with LF and RF were analyzed using the Fine and Gray method of competing risks regression and cumulative incidence functions. Death was considered to be a competing risk for both LF and RF. Univariate analysis for survival and control rates were performed selecting from the following factors: primary histology (non-small cell lung cancer [NSCLC] vs. others), controlled primary tumor (yes vs. no), extracranial metastasis status (yes vs. no), RPA class (1 vs. 2), completion of SRS (yes vs. no), interval between surgery and SRS, RT dose (1500 cGy – 2200 cGy), tumor maximal diameter (≥ 3 cm vs. <3 cm), cavity maximal diameter (≥ 3 cm vs. <3 cm), study lesion location (supratentorial vs. infratentorial), and tumor depth

(superficial with dural/pial involvement vs. deep parenchymal lesion). All of these factors were gathered prospectively with the exception of tumor depth, which was determined by majority consensus of three physicians performing independent, blinded review of pre-surgery MRIs. Tumor depth was classified as superficial/pial if the tumor was seen contacting dura or pia on any MRI series, and otherwise scored as deep. Correlation between clinical factors and incidence of pathologically proven radionecrosis after SRS was determined by Fisher's exact test. Pearson's correlation coefficient was used to determine and test the relationship between tumor max size and cavity size.

RESULTS

Patient Characteristics

From 2004 to 2008, a total of 50 patients enrolled in this prospective study of SRS boost following surgical resection for brain metastases. One patient expired prior to surgery one week after enrollment and was therefore excluded for all analyses. The median age of patients was 59 years. Ten patients did not receive SRS due to early CNS progression (n=4, 3 with local failure and 1 with regional failure), large cavity size (n=2), general medical decline due to systemic progression (n=3), and failure to follow-up (n=1). Following surgical resection, 39 patients with 40 lesions were treated a median of 31 days later with SRS to the surgical bed to a median dose of 1800 cGy. The initial maximal tumor diameter correlated with the surgical cavity maximal diameter ($r=0.49$, $p<0.0001$). Table 3 lists patient and treatment characteristics.

The median follow-up and survival time of the 49 patients was 12.0 months (range=1.0–94.1 months) and survival for the 39 post-operative SRS treated patients was 14.7 months (range=1.0–94.1 months). At the time of our assessment, 5 patients (10.2%) were alive and 44 patients (89.8%) had died. For the patients who were alive at assessment, the median follow-up was 69.5 months (range=63.4–94.1 months). On univariate analysis, no significant clinical variable associated with a longer survival time was identified, including: tumor histology ($p=0.84$), controlled primary tumor ($p=0.33$), extracranial metastasis status ($p=0.29$), RPA class ($p=0.23$), tumor maximal diameter ($p=0.96$), lesion location ($p=0.76$), and tumor depth ($p=0.72$).

Local failure

Of the 50 lesions, 15 lesions demonstrated LF after surgery (prior to any form of salvage therapy). The cumulative LF rate was 22.0% at 12 months. Based on competing risk analysis, patients who completed post-surgical SRS had lower incidence of LF ($p=0.008$, $HR=0.24$), with 15.0% of the 40 irradiated cavities compared to 50.0% of the 10 unirradiated cavities demonstrating LF at 12 months. NSCLC histology was found to be associated with decreased risk of LF compared to brain metastasis from other primaries ($p=0.048$, $HR=0.34$), with 14% demonstrating LF compared to 32% at 12 months (Figure 1). Other factors associated with LF included tumor maximal diameter ≥ 3 cm ($p=0.010$, $HR=4.3$) with 39.1% compared to 7.5% LF at 12 months in lesion with maximal diameter <3 cm, and superficial tumors with dural/pial involvement ($p=0.036$, $HR=9.45$, LF at 12 months= 31.3% vs. 5.6% of the deep parenchymal lesions). Combining tumor maximal

diameter and tumor depth, deep parenchymal lesions that were less than 3 cm (n=7) demonstrated no LF at 12 months. Deep parenchymal lesions that were ≥ 3 cm (n=10) had a LF rate of 10.0% at 12 months. Superficial lesions that were ≤ 3 cm (n=17) showed 11.8% LF at 12 months. Superficial lesions that were ≥ 3 cm (n=15) were at the highest risk for LF, with a rate of 53.3% at 12 months. The difference in LF was highly significant ($p=0.001$, Figure 2) across the various groups. Of the 11 large, superficial lesions treated with post-operative SRS, 6 (54.5%) developed LF.

Factors that were not associated with LF included radiation dose ($p=0.78$) and time interval between surgery and SRS ($p=0.62$). While tumor maximal diameter and tumor depth (superficial vs. deep) were associated with LF, treatment cavity maximal diameter and tumor location (supratentorial vs. infratentorial) were not ($p=0.10$ and 0.26 , respectively). Figure 3 shows an example of the typical pattern of LF after SRS. Of the patients who demonstrated LF, 9 (60.0%) of patients went on to receive salvage whole brain RT (WBRT), and 4 (26.7%) received salvage surgery. Two patients deteriorated medically after the diagnosis of LF and did not receive salvage therapy.

Regional failure

Twenty-three of the 49 patients demonstrated intracranial metastasis at time of study analysis. The cumulative incidence of RF at 12 months was 44.0%. The median time to RF was 4.4 months (range=1.1–17.9 months). The study lesion location significantly predicted for RF, with supratentorial lesions having lower risks of RF compared to infratentorial lesions ($p<0.001$, HR= 4.64). NSCLC histology ($p=0.11$), controlled primary tumor ($p=0.94$), SRS status of the study lesion ($p=0.10$), deep parenchymal lesion ($p=0.76$), and tumor diameter ≥ 3 cm ($p=0.96$) were not associated with improved regional control. Of the patients who developed RF, 15 (65.2%) patients went on to receive WBRT, 5 (21.7%) patients received SRS for the additional lesions, and 1 (4.3%) received partial brain RT. One patient deteriorated medically after the diagnosis of RF, and one patient progressed extracranially and decided to not to proceed with therapy for the asymptomatic intracranial RF.

Radionecrosis

Of the 40 post-surgical cavities treated with SRS, 7 (17.5%) demonstrated pathologically proven radionecrosis with absence of cancer cells. Three cavities demonstrated radionecrosis with 1500 cGy and 4 with 1800 cGy.

DISCUSSION

The importance of whole brain radiation therapy (WBRT) after surgery in patients with limited metastases has been showed in randomized studies showing improvement in local control (LC) in prospective randomized studies. Patchell et al. demonstrated a decrease in local failure rate (LF) from 46% to 10% in patients treated with adjuvant WBRT compared to untreated [9], and Kocher et al. demonstrated a decrease from 59% to 27% at 2 years [8]. Nevertheless, WBRT is associated with an acute decline in quality of life in some patients [27, 28] as well as delayed neurocognitive deficits [29, 30]. Furthermore, the course of

radiation and recovery may delay the onset of systemic therapy for fear of added toxicity. Given these concerns, an alternative to conventional WBRT utilizing stereotactic radiosurgery (SRS) to deliver adjuvant RT to the post-surgical cavities has been investigated in multiple institutions for patients with limited brain metastases. While multiple authors have demonstrated the benefit of this approach through retrospective analysis [13–15, 21–24], to the best of our knowledge, we report the first prospective study on the efficacy of adjuvant SRS in patients with limited intracranial metastases following surgical resection.

We observed excellent LC in this study. Among patients who received SRS after surgical resection, LC approached 85%. Our LC rate in patients treated with SRS was similar to those reported in prior studies: Choi et al. recently reported 90.5% LC at 12 months in a large retrospective analysis of 112 patients with 120 lesions [22], an update from 79% LC in a smaller patient group in 2008 [21]; Hartford et al. showed a LC of 85.5% at 12 months in 47 patients with 49 lesions [24]. In addition to SRS status, we also identified other risk factors associated with LF, such as tumor histology, size, and depth. We found patients with brain metastases from non-small cell lung cancer (NSCLC) demonstrated better LC compared to patients with other histologies. Although the result did not reach statistical significance, similar finding was demonstrated by Choi et al. [22] as the authors reported patients with lung cancer histology had lower LF rate at 12 months on univariate analysis (3.9% vs. 13.7%, $p=0.11$).

In a series of 106 patients, Jensen et al. [23] found preoperative diameters greater than 3 cm to be predictive of LF after adjuvant SRS ($HR=13.6$, $p<0.1$). Similar result was reported by Hartford et al. [24], which the authors found a significantly shorter time to LF in tumors larger than 3 cm. Jagannathan et al. [16] reported a 27% LF in tumor >15 cc compared to a 0% failure in tumor <15 cc. Our analysis found that LF is influenced by the size of initial tumor rather than the postoperative cavity. Recently, Hartford et al. also showed larger tumor size correlated with shorter time to recurrence and time to salvage WBRT [24]. In addition, we also demonstrated superficial tumors with dural/pial involvement were at very high risk of developing LF ($HR=9.45$, $p=0.036$). When combining tumor size and tumor depth in analysis, we found no LF with small, deep parenchymal tumors, where more than 50% of large, superficial tumors had LF at 12 months.

We postulate that LF is more likely in postoperative cavities of large tumors with dural/pial involvement due to both technical inaccuracies and biologic processes. Technical challenges which could contribute to higher failure rates in superficial and large tumors include difficulty in accurately determining both the extent of the radiation target volume of a collapsed large cavity and the extent of superficial surfaces that are at-risk. Biological factors that might lead to higher failure rate in superficial and large tumors include possible dural/pial spread of cancer cells beyond what the MRI indicates, and/or that large tumors are more resistant to radiation, and/or possible contamination of the dural/pial surface during surgery. We noted recurrence at the superficial margin of the resection cavity in most cases of LF. Higher rates of LF have been reported with higher conformity of treatment and smaller treatment margins [16, 21]. While the optimal margin for post-op SRS requires further investigation, a larger margin may be required for larger, superficial tumors for improved LC after SRS.

A concern of single fraction SRS for large metastases is the potential enhanced clinical side effects, therefore a hypofractionated approach could be favorable. In 2012, Wang et al. [31] reported local control rate of 80% at 6 months in 37 patients with 3 cm in diameter cerebral metastases who underwent post-operative hypofractionated SRS. The PTV was a 2–3 mm expansion of the resection cavity. One patient developed radionecrosis, 1 patient experienced prolonged steroid dependence, and 1 patient experienced new-onset seizure. The authors concluded favorable efficacy and toxicity profile of hypofractionated SRS for large tumors after resection. In another study, Steinmann et al. [32] reported local control of 71% at 12 months in 33 patients with single brain metastasis treated with surgical resection followed by hypofractionated SRS. The median PTV, a 4mm concentric expansion of the post-surgical cavity, was 25.6 cc. These studies showed that favorable local control and minimal toxicity can be achieved in the post-surgical setting with a hypofractionated approach in patients with large lesions and cavities. A systematic evaluation is required to determine the optimal treatment technique, dose fractionation, and margin status for patients with large and superficial brain metastases as they are with the highest risks of developing LF after surgical resection and single fraction SRS.

Our observed RF rate of 44% at 12 months is comparable to prior reports [22–24]. Like Choi et al. [22], we did not find lung histology, primary tumor status, or extracranial metastasis status to be associated with RF. While studies suggested that larger tumors are at higher risk in developing RF [23, 24], we did not observe this finding. Interestingly, we found patients with infratentorial tumor are at a higher risk for RF. Iwai et al. [15] reported patients with infratentorial tumors are at higher risk of developing meningeal carcinomatosis, although the total number of patients was small (in the 5 patients who developed meningeal carcinomatosis, 4 had infratentorial tumors). Kitaoka et al. [33] reported that cerebellar metastases had a greater chance of seeding meningeal carcinomatosis due to the proximity of cerebellar cisterns. The biologic cause of higher RF in patients with infratentorial metastases needs to be further delineated.

We observed pathologically-confirmed radionecrosis in 17.5% of our treated patients. Radionecrosis has been reported in up to 24% of patients who received SRS as the primary treatment for metastasis [34–36]. In the adjuvant setting, radionecrosis rate after SRS has been reported to be lower (3–4%) [21–23]. In this small patient cohort, it is difficult to determine significant clinical and dosimetric factors associated with radionecrosis. Identifying risk factors of radionecrosis is the focus of an ongoing investigation at our institution.

Multivariate analysis of factors associated with LF or RF was limited in our study by low failure rates overall. Univariate analysis indicates that tumor size, and pial involvement in particular were significant predictors of failure. These findings are consistent with reported results in literature and should be validated in larger series. Although a significant difference in LC was observed in lesions treated with SRS versus those that were not, this single arm study was not designed for the comparison and is not able to account for all confounding factors associated with LC with or without SRS. Since medical decline was the cause for some patients not to proceed with post-operative SRS, the difference in LC may reflect the higher aggressiveness in patients who did not undergo SRS.

In conclusion, this is the first prospective study of SRS to the post-operative cavity in patients with brain metastases. SRS is associated with high local control after surgical resection of brain metastasis, especially for deep brain metastases <3 cm. Tumors ≥ 3 cm with superficial dural/pial involvement demonstrate the highest risk in LF. In addition to single fraction SRS, other forms of adjuvant radiation therapy utilizing a hypofractionated approach can also be considered, especially in patients with larger tumors.

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SUMMARY

This phase II trial evaluated local control after surgery and SRS in patients with limited brain metastases. With median follow-up of 12 months, we found local control was significantly associated with tumor histology, size of the lesion, and location of the lesion. Postoperative SRS is associated with high local control, especially for deep brain metastases <3 cm. Tumors ≥ 3 cm with superficial dural/pial involvement demonstrate the highest risk in local failure.

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Figure 1.
Comparison of the cumulative incidence of local failure in patients with non-small cell lung cancer primary vs. others.

Figure 2.
Incidence of local failure categorized by tumor depth and size.

Figure 3.

Forty-four year-old gentleman with metastatic melanoma presented with a large (3 cm), superficial brain metastasis (A). He then underwent resection and SRS of post-resection cavity (B), but was then found to have local recurrence at the anterior border of the surgical cavity 7 months later (C). The images are on the same anatomical level. Image B also shows isodose distribution of the treated cavity, prescribed to 1500 cGy to the 80% isodose line. The pink line represents the CTV, and red line represents the PTV.

Table 1

Patients inclusion and exclusion criteria.

Inclusion Criteria	
1	Histologically confirmed malignancy with the presence of one or two intraparenchymal brain metastasis.
2	Age 18 years
3	Karnofsky performance status 70
4	Neurologic function status 0–2
5	Patients may have extracranial sites of metastatic disease
6	Adequate bone marrow reserve (hemoglobin 8 grams, absolute neutrophil count 1000/mm ³ , platelets 50,000/mm ³)
7	Patient must sign a study specific informed consent form. If the patient's mental status precludes his/her giving informed consent, written informed consent may be given to the patient's legal representative
Exclusion Criteria	
1	Major medical illness including poor cardiac, pulmonary or renal status which would result in patient being a high risk candidate for neurosurgical procedure
2	Inability to obtain histologic proof of malignancy
3	Leptomeningeal metastases documented by MRI or CSF evaluation
4	Metastases within 10 mm of the optic apparatus so that some portion of the optic nerve or chiasm would be included in the high dose SRS boost field
5	Metastases in the brainstem, midbrain, pons, or medulla
6	Patients with small cell lung cancer, germ-cell tumors, lymphoma, leukemia and multiple myeloma
7	Prior history of radiation therapy
8	Concomitant use of chemotherapy or targeted biological therapy (within a week of SRS treatment)
9	Patients with 3 metastases in the brain
10	Allergy to both CT and MRI contrast dyes
11	Platelet count <100,000/mcL or coagulation disorders that cannot be corrected or would render the surgery a high-risk procedure.

Abbreviations: CT: computed tomography, MRI: magnetic resonance imaging.

Table 2

Brain SRS Normal Tissue Criteria

Structure	Max Point Dose Constraint
Brainstem	
Midbrain	1800 cGy
Pons	1800 cGy
Medulla	1800 cGy
Spinal Cord	1200 cGy
Optic Chiasm	1200 cGy
Optic Nerve	1200 cGy

Table 3**Patient Characteristics**

Characteristics	Median (Range)	No. (%)
Age (years)	59 (23–81)	
KPS	90 (70–100)	
70–80		23 (47)
80–100		26 (55)
RPA Class		
1		12 (24)
2		37 (76)
Histology		
NSCLC		28 (57)
Breast Cancer		9 (18)
GI Malignancies		4 (8)
Melanoma		4 (8)
Other		4 (8)
Controlled Primary		
Yes		32 (65)
No		17 (35)
Extracranial Metastasis		
Yes		22 (45)
No		27 (55)
Number of Lesion		
1		48 (98)
2		1 (2)
Location of Lesion		
Supratentorial		41 (82)
Infratentorial		9 (8)
Superficial Tumor with Dural/Pial Involvement		
Yes		32 (64)
No		18 (36)
Tumor Maximal Dimension (cm)	2.9 (1.0–5.2)	
3.0 cm		23 (46)
<3.0 cm		27 (54)
Cavity Maximal Dimension (cm)	2.8 (1.7–5.4)	
3.0 cm		18 (36)
<3.0 cm		32 (64)
Resection Status		
Gross total resection		46 (92)
Subtotal resection		4 (8)
Reason for not proceeding to SRS		
Early CNS failure		4 (8)

Characteristics	Median (Range)	No. (%)
General medical decline		3 (6)
Large surgical cavity size		2 (4)
Failure to follow up		1 (2)
Time from surgery to SRS (days)	31 (7–56)	
Dose (cGy)	1800 (1500–2200)	

Abbreviations: CNS= central nervous system; KPS= Karnofsky Performance Status scale; NSCLC= non-small cell lung cancer; PTV= planning tumor volume; RPA= Recursive partitioning analysis; SRS= stereotactic radiosurgery.