Gamma Knife radiosurgery to the surgical cavity following resection of brain metastases

Clinical article

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Object. This study evaluated the efficacy of postoperative Gamma Knife surgery (GKS) to the tumor cavity following gross-total resection of a brain metastasis.

Methods. A retrospective review was conducted of 700 patients who were treated for brain metastases using GKS. Forty-seven patients with pathologically confirmed metastatic disease underwent GKS to the postoperative resection cavity following gross-total resection of the tumor. Patients who underwent subtotal resection or who had visible tumor in the resection cavity on the postresection neuroimaging study (either CT or MR imaging with and without contrast administration) were excluded. Radiographic and clinical follow-up was assessed using clinic visits and MR imaging. The radiographic end point was defined as tumor growth control (no tumor growth regarding the resection cavity, and stable or decreasing tumor size for the other metastatic targets). Clinical end points were defined as functional status (assessed prospectively using the Karnofsky Performance Scale) and survival. Primary tumor pathology was consistent with lung cancer in 19 cases (40%), melanoma in 10 cases (21%), renal cell carcinoma in 7 cases (15%), breast cancer in 7 cases (15%), and gastroenterological malignancies in 4 cases (9%). The mean duration between resection and radiosurgery was 15 days (range 2–115 days). The mean volume of the treated cavity was 10.5 cm³ (range 1.75–35.45 cm³), and the mean dose to the cavity margin was 19 Gy. In addition to the resection cavity, 34 patients (72%) underwent GKS for 116 synchronous metastases observed at the time of the initial radiosurgery.

Results. The mean radiographic follow-up duration was 14 months (median 10 months, range 4–37 months). Local tumor control at the site of the surgical cavity was achieved in 44 patients (94%), and tumor recurrence at the surgical site was statistically related to the volume of the surgical cavity (p = 0.04). During follow-up, 34 patients (72%) underwent additional radiosurgery for 140 new (metachronous) metastases. At the most recent follow-up evaluation, 11 patients (23%) were alive, whereas 36 patients had died (mean duration until death 12 months, median 10 months). Patients who showed good systemic control of their primary tumor tended to have longer survival durations than those who did not (p = 0.004). At the last clinical follow-up evaluation, the mean Karnofsky Performance Scale score for the overall group was 78 (median 80, range 40–100).

Conclusion: Radiosurgery appears to be effective in terms of providing local tumor control at the resection cavity following resection of a brain metastasis, and in the treatment of synchronous and metachronous tumors. These data suggest that radiosurgery can be used to prevent recurrence following gross-total resection of a brain metastasis. (DOI: 10.3171/2008.11.JNS08818)

KEY WORDS • brain metastasis • Karnofsky Performance Scale • surgical cavity

Although brain metastases are one of the most frequently diagnosed sequelae of systemic malignancy, their optimal management is poorly defined.25,35 The primary goals in the initial management of metastatic tumors are relief of neurological symptoms related to mass effect and improvement of patient survival. Although many treatments have been shown to be effective for this purpose,2,8,32,39,40 only surgical extirpation allows the rapid debulking of a tumor, making it beneficial to patients with neurological signs and symptoms related to metastatic disease.10,31,38,43

Following subtotal or gross-total resection, it has become standard practice for patients to receive adjuvant postoperative radiation therapy.1,33,36 Patients who receive radiation therapy are significantly less likely to suffer a treatment failure in the brain, both at the original resection cavity as well as at distant sites, compared with those who do not receive radiation.33 Whole brain radiation therapy, however, is not always a benign process, and it has been associated with short- and long-term sequelae, including radiation-induced edema, leukoencephalopathy, brain atrophy, neurocognitive deterioration, dementia, brain necrosis, neuroendocrine dysfunction, and hydrocephalus.13,24,30,45

Stereotactic radiosurgery is a neurosurgical treatment modality introduced by Lars Leksell in 1951.20 This

Abbreviations used in this paper: GKS = Gamma Knife surgery; KPS = Karnofsky Performance Scale; WBRT = whole brain radiation therapy.
treatment combines stereotactic techniques with focused irradiation, creating a “surgical” margin with a sharp dose fall-off at the margin of the tumor while sparing the normal brain. Brain metastases are ideally suited for radiosurgery, as these neoplasms tend to have clear margins. When used as a primary treatment, radiosurgery has been demonstrated to produce tumor control rates of 73–94%, with an apparently lower rate of neurological sequelae than WBRT. Given these factors, it would appear reasonable that radiosurgery may also be effective in preventing local tumor recurrence following gross-total resection of a brain metastasis. This paper describes our experience using GKS to treat the tumor resection cavity and thereby prevent local recurrence.

Methods

Patient Selection

A review was undertaken of a prospectively acquired database of patients treated at the Lars Leksell Gamma Knife Center at the University of Virginia. Between July 1, 2004, and August 1, 2007, the senior author (J.P.S.) treated 715 patients for biopsy-confirmed brain metastases. Seventy-three patients were identified who underwent prior resection for intracranial metastatic deposits. Patients with radiographic evidence of residual or recurrent tumors on postresection Day 1 using CT or MR imaging with contrast administration, or patients who underwent initial subtotal resection (per the original operative neurosurgeon) were excluded from the analysis, leaving 47 patients who underwent GKS to the surgical cavity of a gross-totally resected brain metastasis (Fig. 1).

Gamma Knife Surgical Technique

The Gamma Knife consists of independent cobalt-60 radiation sources that deliver highly focused ionizing beams to an intracranial target in a single session. All patients underwent stereotactic frame placement under monitored anesthesia in the operating room. After frame placement, stereotactic neuroimaging was performed. If not contraindicated, MR imaging was used. Nonenhanced and contrast-enhanced T1-weighted spin-echo axial images and coronal T1-weighted images with slice separation of 1.5 mm were used. If MR imaging was contraindicated, a stereotactic CT scan with and without contrast administration was performed using thin (1.5-mm) axial slices. At the time of stereotactic MR or CT imaging, no tumor was visible in the surgical cavity in any of the patients included in this study.

All treatments were performed by the senior author (J.P.S.) using the Model C or Perfexion (Elekta AB) Gamma Knife unit. Treatment planning was performed using the GammaPlan software (Elekta AB). For treatment of the resection cavity, the dose pattern was contoured to include the resection cavity along with a surrounding 2–3-mm margin. A 2–3-mm margin was chosen to encompass the resection cavity edge and any microscopic tumor at the margin. Shielding of critical structures was performed as necessary. In cases in which multiple tumors were present (34 cases, 72%), multiple dose matrices were used. Surgical planning was performed to respect the principle of limiting the therapeutic dose entirely within the target and to ensure as steep a dose gradient as possible. To accomplish this goal, multiple isocenters were often used. Dose selection was made on the basis of tumor volume, location, previous fractionated radiation therapy, and the prescription isodose; Radiation Therapy Oncology Group 95–08 dose guidelines were generally used.

Whole Brain Radiation Therapy

To protect patients from unnecessary radiation-induced toxicities, our treatment philosophy involves reserving the option of using WBRT in patients with a small number of tumors (≤ 5) and high functional status. The ultimate decision to administer WBRT following radiosurgery was made on a case-by-case basis depending on the number of tumors, patient performance status, patient wishes, need and timing of additional adjuvant treatment, and extent of control of systemic disease.

Follow-Up Evaluation

Radiographic and clinical follow-up consisted of clinical visits and MR imaging. As a general rule, MR imaging was performed within 3 months of radiosurgery and then at 3-month intervals, unless more frequent imaging was believed necessary by the patient’s oncologist or neurosurgeon. Twenty-six patients (55%) underwent routine clinical follow-up at the University of Virginia, whereas 21 patients (45%) underwent follow-up evaluation elsewhere. For patients who underwent follow-up evaluation elsewhere, clinical updates, neuroimaging studies, and notes were sent to our institution by the referring oncologist and/or neurosurgeon.

Patients Characteristics

A total of 47 patients were treated with GKS delivered...
Gamma Knife surgery to the resection cavity for brain metastasis
to the resection cavity following gross-total resection of a
brain metastasis. Twenty patients (43%) were male and 27
patients (57%) were female. The mean patient age at GKS
was 61 years (range 37–88 years). Pathological results of
the metastases were consistent with non–small cell lung
cancer in 19 cases (40%), melanoma in 10 cases (21%),
renal cell carcinoma in 7 cases (15%), breast cancer in 7
cases (15%), and gastrointestinal malignancies in 4 cases
(9%). The mean duration between resection and GKS was
15 days (range 2–115 days). Three patients (6.4%) received
WBRT prior to radiosurgery. In all cases, this WBRT was
performed at an outside institution (WBRT doses of 38,
40, and 40 Gy, respectively). The mean KPS score at the
time of the initial radiosurgery was 88 (median 90, range
60–100). The mean KPS score at the time of surgery for
these patients (assessed by the surgeon prior to cranioto-
my) was 76 (median 80, range 60–90).

Radiosurgically Treated Cavities
The mean volume of the treated cavity was 10.5 cm
(range 1.75–35.45 cm³). The mean number of isocenters
chosen was 4.5 (range 1–18 isocenters). The mean pre-
scription dose to the cavity margin was 19 Gy (range
6–22 Gy). The mean maximal dose was 42 Gy (range
17–66 Gy). The prescription isodose ranged from 30 to
60% (median 50%).

Synchronous Metastases Treatment
In addition to the resection cavity, 34 patients (72%)
underwent radiosurgery for 116 synchronous metastases
present at the time of the initial radiosurgery (Fig. 2 left).
In these patients the mean number of metastatic deposits
at the time of treatment was 3.5 (median 4, range 1–12).
The mean volume of the synchronous metastases was 7.4
cm³ (range 0.25–19 cm³). The mean number of isocenters
was 3.4 (range 1–8 isocenters). The mean prescription dose
to the synchronous metastasis was 19.7 Gy (range 12–24
Gy), and the mean maximal dose was 44 Gy (range 19–60
Gy). The mean KPS score of patients harboring synchro-

Metachronous Metastases Treatment
Thirty-four patients (72%) underwent additional ra-
diosurgeries (mean 1.7 repeat GKSs in 34 patients; range
1–6 GKSs) for new (metachronous) metastases that ap-
peared after the initial radiosurgery (Fig. 2 right). The
mean duration to follow-up GKS was 5.6 months (range
1–16 months). A total of 140 metachronous metastases
were treated. Mean tumor volume was 5.7 cm³ (range
0.2–12.7 cm³). The mean prescription dose was 19.5 Gy
(range 17–22 Gy), and the mean maximal dose was 44 Gy
(range 21–55 Gy).

Radiographic Follow-up
The mean radiographic follow-up duration was 14
months (median 10 months, range 4–37 months) from the
time of the initial GKS.

Statistical Analysis
The Kaplan-Meier method was used to calculate the
survival time of patients. Differences in treatment out-
comes were evaluated using SPSS version 14.0 (SPSS Inc.)
and Microsoft Office Excel 2003 (Microsoft Corp.). Spe-
cific statistical tests employed are noted in Results. In all
cases, a probability value < 0.05 was considered statisti-
cally significant.

Results
Resection Cavity Tumor Control
An overall summary of the data on radiographic tumor
control is shown in Table 1. Local tumor control at the site
of the surgical cavity was obtained in 44 patients (94%).
Three patients (6%) had radiographic evidence of tumor recurrence at the surgical site. The durations until detection of the recurrence in these 3 patients were 7, 8, and 16 weeks after GKS (9, 13, and 22 weeks postoperatively, respectively; Fig. 3). The pathological results of the recurrent tumor at the resection cavity were consistent with renal cell carcinoma in 1 case, lung cancer in 1 case, and melanoma in 1 case. In 2 cases, the recurrent tumor was retreated using GKS, with a tumor volume decrease of 50% and 65% at the 6-month follow-up evaluation. The third patient died of systemic disease before retreatment could be administered. Although the treatment dose for the recurrent tumors (mean dose 18.1 Gy to the cavity margin) did not appear to differ significantly from those in the rest of the patient series, the treated volumes for the resection cavities in these cases (15.5, 18.4, and 21.1 cm³, respectively) were significantly larger than the volumes treated in the remaining cavities (mean 9.9 cm³; p = 0.04, Student t-test; Table 2).

**Synchronous Metastases**

Radiographic tumor control (stable or decreased size) of treated synchronous metastases was observed in 94 (81%) of 116 metastases. The mean tumor volume at follow-up was 3.7 cm³, and the mean tumor volume reduction was 62%. Sixteen tumors (14%) were radiographically undetectable on follow-up MR imaging. Tumor control appeared to be related to the primary tumor pathology as well as treatment size (Fig. 2 left), although statistical significance was not reached (p > 0.05). The mean duration to radiographic tumor progression was 19 weeks (range 2–94 weeks).

**Metachronous Metastases**

As with synchronous metastases, response to metachronous tumors appeared to be related to the primary pathology and tumor size (Fig. 2 right). Tumor volume control was achieved in 105 (75%) of 140 metachronous metastases. Forty-three tumors (31%) in this category completely disappeared radiographically following radiosurgery. The mean postradiosurgical tumor volume at follow-up was 2.4 cm³, and the mean decrease in tumor volume was 55%. The mean duration to growth for metachronous tumors was 17 weeks (range 2–70 weeks).

**Whole Brain Radiation Therapy**

Thirteen patients (28%) received WBRT in addition to radiosurgery for their intracranial disease. In the majority of these cases (10 patients), the addition of WBRT was due to new tumor deposits or existing tumor progression after radiosurgery, whereas 3 patients received WBRT upfront (Fig. 1). None of the tumor resection cavities in patients treated using GKS and WBRT showed evidence of recurrent tumor.

A total of 70 tumors were treated using GKS and WBRT in 10 patients (mean 7 tumors, range 4–15 tumors). The mean pretreatment tumor volume was 9.6 cm³, and the mean radiation dose received was 40 Gy (range 36–42 Gy). Volume control was achieved in 56 of these tumors (80%). Mean postradiation tumor volume was 4.5 cm³, and the mean change in tumor volume was a decrease of 48%. Fourteen tumors (20%) were radiographically undetectable following treatment. The mean time to growth for tumors that did not achieve growth control was 22 weeks (range 6–22 weeks).

**Patient Survival**

The mean clinical follow-up evaluation was 14 months (median 11 months, range 5–44 months). At the most recent follow-up evaluation, 11 patients (23%) were alive, whereas 36 patients had died. The mean duration until death was 13 months (median 11 months, range 7–36 months) following radiosurgery alone and 11 months (median 9 months, range 5–44 months) for patients who received WBRT in addition to radiosurgery. Six patients (13%) had survival durations > 24 months, and 2 patients (both treated using WBRT for lung cancer) had survival durations of 40 and 44 months, respectively. Thirty-two (89%) of the patients who died showed evidence of progressive systemic disease at the time of death. Ten patients (19%) had progressive CNS disease, 8 of whom died. As demonstrated in Fig. 4, patients who demonstrated good systemic control of their primary tumor tended to survive longer than patients who did not (p = 0.004, Fisher exact test). There was no significant difference in time until death among the 13 patients who received WBRT compared with those who did not undergo WBRT (Fig. 5).

![Graph of Kaplan-Meier curves showing the time to treatment failure at the resection cavity (solid line) versus time to tumor growth for the 57 of 257 tumors (22 synchronous and 35 metachronous metastases) that did not respond to radiosurgery (dotted line).](image-url)
Karnofsky Performance Scale Scores

At the last clinical follow-up evaluation, the mean KPS score for the overall group was 78 (median 80, range 40–100). At the last follow-up evaluation, patients who received radiosurgery alone had higher KPS scores (mean 82, median 90, range 70–100) than those who received radiosurgery and WBRT (mean 66, median 70, range 40–100; Table 3). Overall, however, this difference in KPS scores between groups was not statistically significant and may reflect the overall trend that patients who received WBRT tended to have higher intracranial tumor burden than those who did not (Fig. 6).

Complications

No patient required reoperation for mass effect related to tumor recurrence in the treated resection cavity. In addition, no patients who received GKS to the tumor cavity with or without WBRT had clinical or radiographic signs of radiation necrosis. Two patients (both of whom also received WBRT) required surgery for distant tumor growth after radiosurgery. The pathological results were consistent with active metastatic tumor in both cases. Five patients (11%) required a brief course of steroid treatment following radiosurgery for tumor-associated edema. These patients presented with headaches, but did not have new neurological deficits. The headaches ceased following cessation of the steroids. No evidence of stroke or secondary tumors was observed during the follow-up period.

Discussion

Role of Surgery in the Treatment of Brain Metastases

Surgical extirpation is sometimes viewed as a salvage treatment for patients with brain metastases. However, there are obvious benefits to prompt surgical removal of selected tumors, including relief of mass effect, restoration of CSF flow, and lowering steroid dependence through a reduction in peritumoral-associated edema. Resection has the added benefit of providing or confirming a pathological diagnosis, which can help guide future treatments. Two prospective, randomized, controlled trials have demonstrated a clear benefit of surgery for a single brain metastasis. In a study involving 63 patients randomized to undergo either open surgery (31 patients) or WBRT (40 Gy; 32 patients), Vecht et al. demonstrated a significant increase in patient survival in the surgical group (10 months) compared with the WBRT group (6 months), as well as an increase in functional independence (7.5 vs 3.5 months, respectively). Patchell and colleagues prospectively randomized 48 patients with a single brain metastasis to undergo resection followed by WBRT (36 Gy; 25 patients) or WBRT only (36 Gy; 23 patients). The median survival duration of patients in the surgical group was significantly prolonged compared with the WBRT-only group (40 vs 15 weeks, respectively), as was the length of functional independence (38 vs 8 weeks, respectively).

Our selection of an appropriate treatment algorithm for patients with brain metastases is based on the number and location of tumors, tumor size, patient age, general medical condition, neurological status, and the extent of the systemic cancer, as well as its response to past therapy and its potential response to future treatments. In patients

TABLE 2: Treatment failure at the resection cavity

<table>
<thead>
<tr>
<th>Tumor size (cm³)</th>
<th>No. of Patients</th>
<th>Radiosurgical Margin Around Cavity (mm)</th>
<th>% Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;15</td>
<td>11</td>
<td>2.2</td>
<td>27</td>
</tr>
<tr>
<td>&lt;15</td>
<td>36</td>
<td>2.6</td>
<td>0</td>
</tr>
</tbody>
</table>

Fig. 4. Graph showing the number of patients with systemic disease control and progressive disease control correlated with survival. In the 47 patients treated, those with systemic disease control had the highest correlation with survival (p = 0.03, Student t-test). Ten (83%) of 12 patients with systemic control were alive at the most recent follow-up evaluation, whereas 34 (97%) of 35 patients with progressive systemic disease were dead.

Fig. 5. Graph of Kaplan-Meier curves depicting survival in patients who received postoperative WBRT (solid line) compared with patients who did not (dotted line). No statistically significant difference in survival was observed.
who can safely tolerate radiosurgical treatment, this treatment remains our first choice given the high tumor response rate and low rate of complications compared with surgery.\textsuperscript{28,39} In patients with new or progressive neurological deficits related to a resectable tumor, we advocate open surgery first, to alleviate signs and symptoms related to the tumor burden. Because patients with higher functional status have demonstrated better outcomes after radiosurgery,\textsuperscript{44} the improvement in KPS score (12-point improvement) after surgery in our patients indicates that resection can optimize patients for radiosurgery.

\textbf{Utility of GKS to the Resection Cavity of Brain Metastases}

Even after complete resection, local recurrence of metastatic brain tumors has been reported to be as high as 46\% without postoperative radiation therapy.\textsuperscript{34} The purpose of this study was to evaluate the effectiveness of postoperative GKS even with a radiographically clean resection cavity. Similar to many studies on this subject, we are limited by a fairly heterogeneous patient population, the retrospective nature of the study, and the use of historical controls.

The low rate of tumor recurrence and postradiosurgical complications in our patient series supports previous reports indicating that focused radiation to the resection cavity is efficacious in controlling local tumor growth and maintaining long-term quality of life in surviving patients.\textsuperscript{17,23,42} The fact that no patients suffered from permanent long-term sequelae of radiation, including patients who received additional radiosurgery and those who received GKS, indicates that this treatment strategy can be used safely when further adjuvant treatment is required. The incidence of radiation toxicity following ≥ 1 radiosurgical procedure with or without the addition of WBRT appears to be low. Radiosurgical dose-volume constraints for solid targets (such as unresected brain metastasis, arteriovenous malformations, and others) may not apply to resection cavity radiosurgery because dose is predominantly being delivered to a resected area devoid of brain parenchyma.

As observed by Soltys and associates,\textsuperscript{42} the true tumor control rate for patients who received radiosurgery to the tumor cavity is similar to rates in published reports of low-dose rate brachytherapy, while associated with fewer complications related to device implantation, removal, and technical failure.\textsuperscript{37} It is important to note, however, that the true incidence of radiation-related complications in patients with brain metastases are likely underestimated, both in our patient series and in other reports.

Patients who underwent radiosurgery to larger tumor resection cavity volumes had a higher likelihood of tumor recurrence at the surgical site. Delivering radiation to the resection cavity with a 2–3-mm margin via an extremely precise radiosurgical approach allows a steep fall-off of radiation to the surrounding tissues. In some instances in which the resection cavity may be less distinct, a wider margin may be required to decrease the likelihood of local recurrence following stereotactic radiosurgery.\textsuperscript{42}

The effectiveness of GKS to the tumor cavity is likely also affected by the timing of radiosurgery following open surgery. Immediately performing radiosurgical treatment may make postsurgical changes difficult to differentiate from a residual tumor. Therefore, we generally wait 2–3 weeks after surgery before performing radiosurgery, although Gd enhancement can sometimes be observed in these cases as well.\textsuperscript{44}

\textbf{Addition of WBRT After Metastasis Extirpation and GKS to the Resection Cavity}

Even when local tumor control is achieved, distant tumor recurrence is a treatment conundrum in patients with metastatic brain tumors. Patchell and colleagues\textsuperscript{33} demonstrated a 37\% tumor recurrence rate in patients treated using surgery alone, compared with 14\% in patients who received adjuvant radiation (p < 0.01). This study also indicated that patients treated using radiation therapy were less likely to die of neurological causes than untreated patients (14 vs 44\%, respectively; p = 0.003). The goal of postoperative WBRT in patients with solitary brain metastasis is to destroy microscopic residual cancer cells at the site of resection and at other locations within the brain. Unfortunately, however, this treatment scheme has no way of differentiating the tumor from normal brain tissue, which also has a dose-related susceptibility to radiation.

\begin{table}[h]
\centering
\caption{Clinical follow-up among treatment groups}
\begin{tabular}{|l|c|c|c|}
\hline
Treatment Group & No. of Patients & Median KPS Score at Most Recent Follow-Up & Mean Survival (mos) \\
\hline
GKS only & 34 & 90 & 13 \\
WBRT after GKS & 10 & 70 & 11 \\
upfront WBRT after GKS & 3 & 90 & 16 \\
\hline
\end{tabular}
\end{table}
The relatively short survival of most patients with metastasis has historically made adverse radiation effects a secondary concern because many patients die before becoming symptomatic from radiation sequelae. However, as patients with brain metastasis are now living longer, intermediate and late-term side effects from radiation therapy are now more commonly observed. DeAngelis et al. showed that 11% of patients treated using postoperative radiation therapy with 300 cGy fractions suffered from dementia afterward. Some investigative groups have suggested that reirradiation may be of potential benefit in select patients, and this approach would exceed the typical tolerance of the brain for radiation. The steep dose fall-off of radiosurgery generally allows the safe delivery of radiation either before or after WBRT; the focal delivery of radiosurgery allows for repeat treatments.

The success of GKS in the current patient series raises the question of whether radiosurgery rather than WBRT should be used as adjuvant treatment to prevent recurrence following gross-total resection. New data from colleagues at the M. D. Anderson Cancer Center demonstrates the neurocognitive and neuropsychological effect of WBRT on patients and the apparent avoidance of these deleterious effects when using radiosurgery. Variations on WBRT, such as the recently described “hippocampal-sparing” WBRT, may provide some possible benefit in improving memory function. However, because memory function and neurocognition reside in other areas besides the hippocampus, sparing of the hippocampus using intensity-modulated radiation therapy may prove to be an overly simplified approach to sparing of critical neurocognitive functions. Nevertheless, intracranial disease progression of metastatic cancer may also be a cause for neurological decline.

Given these factors, it appears reasonable to spare patients from WBRT who show a high functional status and a small number of treatable tumors, and instead treat the radiographically visible disease and the previously resected tumor cavity using radiosurgery. In these situations, close radiographic follow-up using brain MR imaging at 3-month intervals is prudent so that new deposits can be retreated quickly when they appear. In patients who demonstrate intracranial disease progression, WBRT can be used at a future time point.

Similar to studies of WBRT, our findings indicate that the greatest benefit of postoperative radiosurgery occurs in patients with controlled extracranial disease (Fig. 5). In their randomized control study, Mintz et al. reported that lack of systemic control was a major causative factor in patients who died of lung cancer, with systemic disease the cause of death in 46% of patients in the surgical group and in 35% of the patients in the radiation group. By contrast, death due to a neurological cause alone was 15% in the surgical group and 28% in the radiation group. These findings are consistent with the concept that the extent of systemic disease largely determines patient survival and overcomes any potential advantage that the addition of surgery may provide in controlling a brain metastasis. An extremely large resection cavity volume or indistinct cavity margins may be another indication to use WBRT in place of directed radiosurgery, as larger resection cavities tended to have a higher treatment failure rate in our experience.

There is clearly variability in the radiosurgical response among histological tumor types (Fig. 2). Experimental models using radiosensitizers for radioresistant tumors (such as melanoma and renal cell carcinoma) may provide improvements in tumor reduction for traditionally radiation-insensitive tumor histopathologies.

Conclusions

Stereotactic radiosurgery delivered to the tumor resection cavity after gross-total resection is useful for preventing local tumor recurrence. The efficacy of GKS in treating synchronous and metachronous tumors argues in favor of using GKS as a primary modality in the treatment of metastases in select cases.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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