Stereotactic radiosurgery for brain metastases

Management of brain metastases typically includes radiotherapy (RT) with conventional fractionation and/or stereotactic radiosurgery (SRS). However, optimal indications and practice patterns for SRS remain unclear.

Significant heterogeneity exists in target volumes for postoperative stereotactic radiosurgery.

The use of radiosurgery as a first-line or salvage treatment for brain metastases continues to expand. As a focal, highly precise treatment option, stereotactic radiosurgery (SRS) provides many benefits, including a short treatment timeline, a low probability of normal tissue complication, and a high probability of treated lesion control 1).

Kann et al. sought to evaluate national practice patterns for patients with metastatic disease receiving brain RT. They queried the National Cancer Data Base (NCDB) for patients diagnosed with metastatic non-small cell lung cancer, breast cancer, colorectal cancer, or melanoma from 2004 to 2014 who received upfront brain RT. Patients were divided into SRS and non-SRS cohorts. Patient and facility-level SRS predictors were analyzed with chi-square tests and logistic regression, and uptake trends were approximated with linear regression. Survival by diagnosis year was analyzed with the Kaplan-Meier method. Results: Of 75,953 patients, 12,250 (16.1%) received SRS and 63,703 (83.9%) received non-SRS. From 2004 to 2014, the proportion of patients receiving SRS annually increased (from 9.8% to 25.6%; P<.001), and the proportion of facilities using SRS annually increased (from 31.2% to 50.4%; P<.001). On multivariable analysis, nonwhite race, nonprivate insurance, and residence in lower-income or less-educated regions predicted lower SRS use (P<.05 for each). During the study period, SRS use increased disproportionally among patients with private insurance or who resided in higher-income or higher-educated regions. From 2004 to 2013, 1-year actuarial survival improved from 24.1% to 49.6% for patients selected for SRS and from 21.0% to 26.3% for non-SRS patients (P<.001). Conclusions: This NCDB analysis demonstrates steadily increasing—although modest overall-brain SRS use for patients with metastatic disease in the United States and identifies several progressively widening sociodemographic disparities in the adoption of SRS. Further research is needed to determine the reasons for these worsening disparities and their clinical implications on intracranial control, neurocognitive toxicities, quality of life, and survival for patients with brain metastases 2).

Complications

With increased adoption of this approach also comes an increase in incidence of treatment failure. Radiosurgical failure, either due to tumor regrowth or radiation necrosis, can occur in about 10% to 15% of patients still alive at 1 yr 3).
Radiation necrosis (RN) may occur after treatment and is challenging to distinguish from local recurrence (LR).

PET is superior to computed tomography and magnetic resonance imaging in the differentiation between recurrence and radiation reaction/necrosis. However, temporary radiation effects may mask remaining tumor tissue, and repeat PET studies may sometimes be necessary.

There are a variety of salvage options available for patients with brain metastases who experience local failure after stereotactic radiosurgery (SRS). These options include resection, whole brain radiation therapy, laser interstitial thermotherapy, and repeat SRS. There is little data on the safety and efficacy of repeat SRS following local failure of a prior radiosurgical procedure.

**Systematic Reviews**

2017

Using Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines, a systematic review was conducted using PubMed and Medline up to November 2016. A separate search was conducted for SRS for larger brain metastases.

Twenty-seven prospective study, critical reviews, metaanalysis, and published consensus guidelines were reviewed. Four key points came from these studies. First, there is no detriment to survival by withholding whole brain radiation (WBRT) in the upfront management of brain metastases with SRS. Second, while SRS on its own provides a high rate of local control (LC), WBRT may provide further increase in LC. Next, WBRT does provide distant brain control with less need for salvage therapy. Finally, the addition of WBRT does affect neurocognitive function and quality of life more than SRS alone. For larger brain metastases, surgical resection should be considered, especially when factoring lower LC with single-session radiosurgery. There is emerging data showing good LC and/or decreased toxicity with multisession radiosurgery.

A number of well-conducted prospective and meta-analyses studies demonstrate good LC, without compromising survival, using SRS alone for patients with a limited number of brain metastases. Some also demonstrated less impact on neurocognitive function with SRS alone. Practice guidelines were developed using these data with International Stereotactic Radiosurgery Society consensus.

Stereotactic radiosurgery (SRS) offers excellent local control for brain metastases (BM) with low rates of toxicity.

It avoids whole brain radiotherapy (WBRT)-associated morbidity.

Studies have clearly established the safety and efficacy of single-dose SRS. However, as patient survival has increased, the recurrence of tumors and the development of metastases to new sites within the brain have made it desirable to repeat treatments over time. The cumulative toxicity of multi-isocenter, multiple treatments has not been well defined.

Postoperative stereotactic radiosurgery to the resection cavity safely and effectively augments local
control of large brain metastases. Patients with <4 metastases and controlled systemic disease have significantly lower rates of distant brain failure (DBF) and are ideal treatment candidates.

In patients with limited brain metastases from non small cell lung cancer (NSCLC), SRS is an effective treatment associated with high local control rate with low morbidity. When performed in isolation, close follow-up is mandatory and radiosurgery can be renewed as salvage treatment for distant brain progression, limiting the use of WBRT.

Significant tumor volume reduction by 6 or 12 weeks post-SRS was associated with long-term local control.

For patients at low risk of distant intracranial failure (such as those with systemic disease control) with early, robust volumetric response, it may reasonable to lengthen imaging intervals to maximize clinical utility.

Although it is necessary to validate the findings in a larger, prospective series, the results are encouraging that a robust early volumetric response is associated with sustained local control for metastatic brain lesions.

Gamma Knife radiosurgery (GKRS) offers a high rate of tumor control and good survival benefits in both new and recurrent patients with MBT. Thus, GKRS is an effective treatment option for new patients with MBT, as well as an adjuvant therapy in patients with recurrent MBT.

There appears to be no consensus regarding the optimal treatment strategy among patients with >3 brain metastases, and practice patterns are heterogeneous. Radiation oncologists, especially high-volume CNS specialists, are treating significantly more brain metastases with SRS than what currently is recommended by published consensus guidelines. Providers struggle with patients with a moderate intracranial disease burden. Further prospective studies are needed to support these practice patterns and guide decision making.

**Case series**

A retrospective analysis reviewed patients treated for ≥15 brain metastases originating from breast cancer, lung cancer, or melanoma. Ninety-three patients met the inclusion criteria. In this study 3,016 tumors were treated. The median number of tumors at the first SRS procedure was 23(15-67) for breast cancer, 21(15-48) for lung cancer, and 21(15-67) for melanoma. The mean aggregate metastases volume was 8.75m³ for breast, 6.89cm³ for lung, and 9.98cm³ for melanoma.

Patients with breast cancer, lung cancer, and melanoma had a median survival after diagnosis of brain metastases of 18.0, 9.4, and 6.3 months, respectively. The survival after SRS was 16 months for breast cancer, 4.6 months in lung cancer and 3.1 months for melanoma. Breast cancer patients had significantly longer survival than lung cancer and melanoma patients after SRS (p=0.001). A higher Karnofsky performance score (KPS) was associated with an increase in survival across all tumor types. Repeat SRS for local or distant progression was performed in 56% of breast cancer, 35% of lung cancer, and 24% of melanoma patients.

Stereotactic radiosurgery is an effective means of managing extensive brain metastases, particularly in breast cancer patients. The primary tumor type, systemic disease and performance status heavily influence survival outcomes.
Patients (n = 41) undergoing single-fraction Gamma Knife SRS following surgical resection of brain metastases from 2011 to 2017 were retrospectively reviewed. SRS included the entire contrast-enhancing cavity with heterogeneity in inclusion of the surgical tract and no routine margin along the dura or clinical target volume margin. Follow-up MR imaging was fused with SRS plans to assess patterns of failure.

The median follow-up was 11.1 months with a median prescription of 18 Gy. There were 5 local failures: infield (n = 3, 60%), surgical tract (n = 1, 20%), and marginal > 5 mm from the resection cavity (n = 1, 20%). No marginal failures < 5 mm or dural margin failures were noted. For deep lesions (n = 13), 62% (n = 8) had the entire tract covered. The only tract recurrence was in a deep lesion without coverage of the surgical tract (n = 1/5).

In this small preliminary experience, despite no routine inclusion of the dural tract or bone flap, no failures were noted in these locations. Omission of the surgical tract in deep lesions may increase failure rates.

References


