

Tile Radiation for Large Brain Mets: A New Approach at ASCO 2026

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Managing large brain metastases (typically defined as >3 cm) presents a clinical challenge, balancing local control with the risk of neurotoxicity from high-dose radiation. Conventional stereotactic radiosurgery (SRS) often struggles with these larger volumes due to dose constraints. The ASCO 2026 meeting introduced a novel tile-based radiation treatment approach, aiming to improve local control while mitigating toxicity.

KEY TAKEAWAYS

- **The Pivot:** Tile-based radiation offers a method to deliver higher cumulative doses to large brain metastases by fractionating the treatment volume.
- **The Data:** Preliminary data suggest improved local control rates compared to historical controls for lesions >3 cm, with acceptable toxicity profiles.
- **The Action:** Clinicians should consider this approach for patients with large brain metastases where conventional SRS is limited, pending further mature data.

Patients with large brain metastases face a difficult prognosis, and treatment options are often limited by the size of the lesion and the proximity to critical structures. Whole-brain radiation therapy (WBRT) offers palliation but is associated with significant neurocognitive decline. Stereotactic radiosurgery (SRS) is effective for smaller lesions, but for metastases exceeding 3 cm, the risk of radiation necrosis increases substantially with conventional single-fraction SRS. This often necessitates either lower, potentially sub-therapeutic doses, or multi-fraction SRS, which can still be limited by the total dose deliverable to the entire volume. The concept of 'tiling' the radiation field aims to overcome these limitations by dividing the large target volume into smaller, contiguous sub-volumes, each treated with a high-dose, spatially fractionated approach. This allows for a higher cumulative dose to the entire lesion over multiple sessions, theoretically enhancing local control while distributing the dose to surrounding healthy tissue more favorably than a single large field.¹

The incidence of brain metastases is increasing, affecting approximately 20-40% of all cancer patients, with lung cancer, breast cancer, and melanoma being the most common primary sources. A significant proportion of these patients present with larger lesions, often exceeding 3 cm, which historically posed a considerable therapeutic challenge due to the balance between achieving local control and minimizing neurotoxicity. The development of advanced radiation techniques, such as SRS, has revolutionized the management of smaller metastases, but large lesions continue to represent an area of unmet need. The rationale behind tile-based radiation therapy stems from the radiobiological principle that fractionating the dose allows for repair of sub-lethal damage in healthy tissues while still delivering a potent cytotoxic effect to tumor cells, especially when combined with spatial separation of high-dose regions. This approach seeks to

leverage the benefits of high-dose per fraction delivery within each tile while mitigating the cumulative toxicity of treating a large volume with a single, uniformly high dose.¹

What the study did

The presentation at ASCO 2026 detailed a prospective, single-arm study evaluating tile-based radiation therapy for patients with brain metastases measuring 3.0 cm to 5.0 cm in maximum diameter. The study enrolled N=85 patients across 5 academic centers. Eligibility criteria included patients with 1 to 3 brain metastases, a KPS of ≥ 0 , and no prior radiation to the target lesion. Patients with active leptomeningeal disease or uncontrolled systemic disease were excluded. The treatment protocol involved dividing the large metastasis into multiple 'tiles,' typically 2 to 4, with each tile receiving a prescribed dose of 7-9 Gy per fraction, delivered over 3 to 5 fractions. The specific number of tiles and dose per tile were determined by the treating radiation oncologist based on tumor size, location, and proximity to critical eloquent brain structures, utilizing advanced treatment planning systems to optimize dose distribution and minimize hot spots in healthy tissue. The total treatment course for a single lesion ranged from 9 to 15 fractions, depending on the number of tiles and the prescribed dose per tile. The primary endpoint was local control at 12 months, with secondary endpoints including overall survival, progression-free survival, and adverse events, particularly radiation necrosis.²

Preliminary results, with a median follow-up of 10.5 months, indicated a 12-month local control rate of 78% (95% CI: 70%-86%). This compares favorably to historical local control rates for conventional multi-fraction SRS for similar-sized lesions, which typically range from 50% to 70%. The incidence of symptomatic radiation necrosis was 8%, with 3% requiring surgical intervention. Grade 3 or higher neurological adverse events were reported in 12% of patients. The median overall survival was 14.2 months. No treatment-related deaths were reported. The study highlighted that the spatial fractionation allowed for higher total doses to be delivered to the entire lesion, with some patients receiving cumulative biological effective doses (BED10) exceeding 100 Gy to the entire target volume, which would be prohibitive with conventional single-field SRS.³

While these initial data are promising, the study is limited by its single-arm design and relatively short follow-up. The absence of a direct comparator arm means that comparisons to historical controls must be interpreted with caution, as patient selection and supportive care may differ. Furthermore, the heterogeneity in the number of tiles and prescribed doses per tile across patients introduces variability that could influence outcomes and makes it challenging to define a single optimal treatment regimen. Longer follow-up is necessary to fully assess the durability of local control and the long-term incidence of radiation necrosis and other late toxicities, such as cognitive decline, which may manifest years after treatment. Future randomized controlled trials comparing tile-based radiation to conventional multi-fraction SRS or surgery for large brain metastases would provide more definitive evidence regarding its efficacy and safety profile. The optimal tiling strategy, including the number of tiles, dose per tile, and fractionation schedule, also warrants further investigation, potentially through dose-escalation studies or adaptive trial designs.⁴

CLINICAL IMPLICATIONS

The introduction of tile-based radiation therapy for large brain metastases at ASCO 2026 presents a pragmatic solution to a persistent clinical problem. For too long, clinicians have been forced to choose between aggressive, potentially toxic, single-fraction SRS for smaller lesions or less effective, palliative WBRT for larger ones. This tiling approach offers a middle ground, allowing for dose escalation to the entire lesion without the

immediate, prohibitive toxicity associated with treating a large volume in a single shot. It is a logical extension of dose painting and spatial fractionation, leveraging existing technology in a novel way.

The industry should take note, particularly manufacturers of linear accelerators and treatment planning systems. While the underlying technology is not new, the specific algorithms and planning tools required to efficiently and safely implement tile-based radiation may need refinement. This could drive innovation in treatment planning software, potentially leading to dedicated modules for such spatially fractionated approaches. Furthermore, the acceptable toxicity profile observed in this preliminary data suggests that this method could expand the population of patients eligible for highly conformal radiation, moving some away from WBRT or extensive surgery.

For patients, this could mean improved local control for challenging lesions, potentially delaying neurological progression and preserving quality of life for longer. The prospect of avoiding WBRT, with its well-documented neurocognitive sequelae, is significant. While the treatment course is longer than single-fraction SRS, the potential benefits in terms of disease control and reduced toxicity may outweigh the inconvenience. As more mature data emerge, this approach could become a standard of care for large brain metastases, offering a much-needed therapeutic advancement in neuro-oncology.

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