Editorial Commentary

MRI-based radiosurgical planning: implications in imaging timing

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Introduction

Stereotactic radiosurgery (SRS) is now an accepted standard of care for patients with brain metastases. Many different platforms and workflows exist for delivering SRS, leading to variations in treatment delivery, such as elapsed time between stereotactic planning magnetic resonance imaging (MRI) and date of first radiosurgery. Salkeld *et al.* attempts to standardize the timing between planning MRI and repeat MRI before radiosurgery to evaluate for differences in target delineation (1). There were remarkable changes over a relatively short period of time, and the authors recommend a short interval between planning MRI and treatment, allowing for more accurate radiosurgical intervention.

Summary

Given the paucity of prospective trials examining the impact of delays between radiation planning imaging and treatment delivery, Salkeld *et al.* conducted a prospective study evaluating repeat verification MRI within 24 hours of SRS. Included were 44 intact brain metastases and 15 tumor resection cavities evaluated in 34 patients. Inclusion criteria for the study included patients at least 18 years of age with less than five brain metastases and/or resected cavities, and excluded patients with hematologic malignancy or germinoma histologies. Imaging was performed with a 1.5 T MRI scanner using 1.25 mm slice thickness with T1 and T2 sequences and single dose 0.1 mmol/kg body weight gadobutrol with 10-minute acquisition delay. Target delineation included calculation of a gross tumor volume (GTV) for intact tumors and a clinical target volume (CTV) for cavities based on MRI anatomy. Planning target volume (PTV) was an institutional protocol-delineated 2 mm circumferential expansion of the GTV/CTV in the setting of mask immobilization. Twenty-four hours prior to SRS the patients underwent repeat MRI for evaluation of intact tumor and/or resection cavity dynamics. The primary endpoint measured was changes in management based on the second MRI (MRI-2) defined as (1) updated GTV/CTV (GTV-2/CTV-2) extending to the edge of or beyond the initial PTV mandating a plan revision and/or (2) increased number of metastases identified requiring an additional SRS target or conversion to whole-brain radiation therapy (WBRT).

Patients enrolled on the study averaged 57 years of age, had preserved functional status, and 82% of the study population had two or less brain metastases. Most common histologies included lung, melanoma, breast, and colorectal. The median time between the first and second MRI was seven days, with 65% and 91% of patients having a less than one week and less than two-week imaging gap, respectively. Overall 25 of 44 intact lesions (56.8%) required repeat planning, 7 of 15 resection cavities (47%) required repeat planning, and 3 of 34 patients (8.8%) progressed rapidly and were treated with WBRT or supportive care alone. When MRI-2 was performed in the 8–14 days range there was a 78% change in management, whereas reimaging within 7 days resulted in 41% change in management. A minority of patients received systemic therapy during study enrollment, however 9 of 15 (60%) had changes

in management, with 2 of these experiencing decrease in size of the metastasis with geometric shift requiring plan revision. More commonly, increasing size of GTV-2/CTV-2 resulted in changes in management with +5% versus +20% mean percentage in GTV changes with 7 or less days versus 8 or greater days between MRIs, respectively.

The authors highlight many of the limitations of the study including small patient population, large percentage metastatic melanoma patients in their Australian patient cohort, and potential image registration differences between the two planning MRIs. Concluding statements highlight the results of the first prospective study on imaging delay in SRS planning to encourage readers to streamline their radiosurgery practices.

Impact on practice

The adoption of SRS in the treatment of intact and resected brain metastases is increasing as randomized data supports decreased rates of cognitive deterioration and improved quality of life, without jeopardizing functional independence or overall survival when compared to whole brain radiation (2-4). There are variabilities in radiosurgical planning MRI techniques including magnet strength (5), contrast delay timing (6), gadolinium dosing (7), slice thickness (8), and timing between planning MRI to radiation delivery (9). Institutional protocols, departmental processes and interdisciplinary workflows, patient social circumstances, care coordination, and insurance prior authorization all compound to result in variability and potential delays in the management of patients with brain metastases. While a common clinical occurrence, there is limited prospective data regarding intact tumor and cavity dynamics during these delays.

This study's findings of changes in management due to cavities dynamics is in contrast to the work of Atalar *et al.* which demonstrated no statistically significant changes in resection cavity volumes from 68 patients with MRIs obtained on days 0–3 versus 9–33, suggesting most changes occur shortly after resection (10). However, multiple other retrospective studies support the prospectively collected data reviewed in this editorial. This includes retrospective data from Jarvis *et al.* who analyzed cavity dynamics in 41 patients with 43 metastasis resections using available post-operative MRI (less than 24 hours) and SRS planning MRI (mean 23.9 days after surgery) with a significant volume change being defined as 2 cm^3. In their patient cohort 20 of 43 cavities (46.5%) were stable in size, 10 of 43 cavities (23.3%) collapsed, and 13 of 43 cavities (30.2%) increased in size (11).

The work conducted by Salkeld *et al.* in 2018 confirms the need to minimize delays between radiation planning MRI and ultimate SRS delivery. There was nearly a halving of the rate of changes in management when planning MRIs were performed less than versus greater than one week apart at 41% versus 78%, respectively. Further delays between planning MRI and treatment delivery increases the risk of geometric miss and under dosing of the target. In a retrospective review by Seymour *et al.* local control was evaluated based on the time delay between planning MRI and SRS delivery with a stratification of 14 days among a group of 82 patients with 151 intact metastases. Local control was 95% at 6 months and 75% at 12 months for metastasis with interval of less than 14 days, in contrast to 56% at 6 months and 34% at 12 months for metastasis with interval of greater than or equal to 14 days (12).

The key driver associated with delays between MRI and SRS is the radiosurgical platform and the workflow associated with it. SRS was pioneered with the Gamma Knife platform (Elekta AB, Stockholm, Sweden), and the most common workflow under this platform involves the placement of a stereotactic headframe, followed by a stereotactic MRI and radiosurgery to follow, all within the same day. While advancements in SRS technology, including the development and validation of linear accelerator-based (LINAC-based) SRS, have grown significantly in recent decades, this technology typically employs an alternative workflow more similar to that of conventional radiotherapy. A LINAC-based workflow typically involves a stereotactic MRI and computed-tomography based (CT-based) simulation scan and thermoplastic mask creation. Following CT-simulation, a SRS plan is created and quality assurance measures are performed, a process that typically results in delays from MRI to radiosurgery on the order of 5–10 days. As such, the adoption of LINAC-based radiosurgical workflows has led to delays that are relatively common, and the results of the trial led by Salkeld *et al.* are more impactful than ever.

This prospective evaluation of target delineation of intact and resected brain metastasis at different time points offers multidisciplinary neuro-oncology teams strong motivation to work within their institutions and beyond to streamline radiosurgery planning and minimize delays in treatment delivery. This study adds to available research that efficiency, in addition to accuracy, precision, and efficacy, is paramount in our daily radiosurgical practices.

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Footnote

Conflicts of Interest: Dr. Trifiletti reports clinical trial research support from Novocure, publishing fees from Springer Inc., unrelated. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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