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AI-Based Quantification of Hippocampal Volume Loss After Whole-Brain Radiotherapy and Stereotactic Radiosurgery

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ABSTRACT

Purpose: Cognitive decline following brain radiotherapy is strongly associated with hippocampal injury, yet scalable methods for assessing treatment-related hippocampal structural change in clinical practice remain limited. This study evaluates hippocampal volume loss following whole-brain radiotherapy (WBRT) versus stereotactic radiosurgery (SRS) using an automated deep-learning segmentation pipeline and examines its relationship with hippocampal radiation dose.

Methods: Patients treated with WBRT (n=15) or SRS (n=15) for brain metastases underwent longitudinal T1-weighted MRI at baseline, 6 months, and 12 months post-treatment. Hippocampal segmentation was performed using FastSurfer, a convolutional neural network–based neuroimaging tool enabling rapid, reproducible volumetric analysis from standard MRI. Hippocampal volumes were extracted at each timepoint, and rates of volume change (%/month) were calculated. Segmentations were co-registered with treatment plans to derive dosimetric parameters, including maximum hippocampal dose (D_{max}). Group comparisons were performed using an unpaired t-test, and dose–response relationships were evaluated using Pearson correlation analysis.

Results: WBRT patients demonstrated significantly greater hippocampal volume loss compared with SRS patients at both 6 and 12 months (p=0.0001). The average rate of hippocampal atrophy following WBRT was approximately sevenfold higher than after SRS. Across all radiotherapy patients, hippocampal volume loss was strongly correlated with hippocampal D_{max} (r=−0.66, p<0.0001), indicating a dose-dependent structural effect. In contrast, cerebellar volume loss showed no significant association with cerebellar dose, supporting regional specificity.

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INTRODUCTION

This work introduces a practical, AI-enabled workflow for quantifying radiation-associated hippocampal injury[1] using standard-of-care MRI and treatment planning data. By integrating FastSurfer deep learning–based segmentation[2] with longitudinal MRI and delivered dose distributions, this study provides a scalable, reproducible method to derive hippocampal morphometric biomarkers without manual contouring. The innovation lies in translating automated neuroimaging analysis into a medical physics context where hippocampal dose–response relationships can be directly evaluated across treatment modalities. This approach enables objective comparison of whole-brain radiotherapy (WBRT) and stereotactic radiosurgery (SRS) with respect to hippocampal toxicity and supports dose-aware treatment selection and hippocampal sparing strategies. The pipeline is readily implementable using routinely acquired MRI and standard planning systems, facilitating adoption across institutions.

METHODS AND MATERIALS

Patients treated with whole-brain radiotherapy (WBRT, n=15) or stereotactic radiosurgery (SRS, n=15) for brain metastases underwent longitudinal T1-weighted MRI at baseline, ~6 months, and ~12 months post-treatment. WBRT prescriptions ranged from 20–30 Gy in 5–10 fractions using parallel-opposed beams. SRS patients received single-fraction treatments of 17.5–20 Gy prescribed to the 50–80% isodose line using a Gamma Knife system. All MR images were resampled to 1x1x1mm^3 resolution and converted to NIFTI format. Automated brain segmentation was performed using FastSurfer, a fully convolutional neural network–based pipeline generating cortical and subcortical parcellations. Bilateral hippocampal volumes were extracted at each timepoint, and rates of volume change (%/month) were calculated between baseline and follow-up imaging. FastSurfer-derived hippocampal segmentations were imported into the treatment planning environment and rigidly co-registered with delivered dose distributions. Hippocampal dosimetric parameters, including maximum dose (D_{max}), were extracted from the registered dose maps. Cerebellar volumes and corresponding dose metrics were analyzed as an internal control region to assess regional specificity. Representative SRS and WBRT cases illustrating hippocampal segmentation, longitudinal volume change, and treatment plans are shown in Figure 1. Comparison of hippocampal volume loss rates was performed using an unpaired t-test, while dose–response relationships between hippocampal volume loss and dosimetric parameters were assessed using Pearson correlation analysis.

RESULTS

Figure 1 demonstrates visibly greater hippocampal volume loss following WBRT compared with SRS over approximately 12 months. In Figure 2, WBRT patients exhibited significantly greater hippocampal volume loss than SRS patients at both 6 and 12 months post-treatment (p=0.0001). The average rate of hippocampal atrophy following WBRT was approximately sevenfold higher than that observed after SRS. Across all radiotherapy patients, hippocampal volume loss showed a strong negative correlation with hippocampal Dmax (r=−0.66, p<0.0001). In contrast, cerebellar volume loss demonstrated no significant association with cerebellar dose (p>0.05), supporting the regional specificity of hippocampal findings.

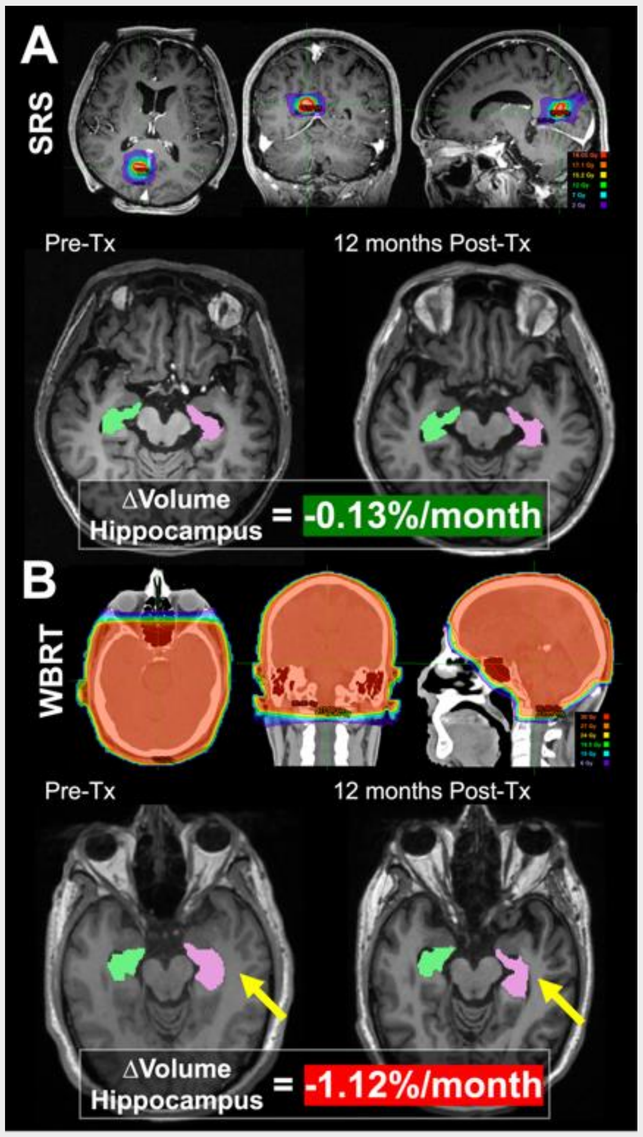

Figure 1. Automated quantification of hippocampal volume change following brain radiotherapy. FastSurfer was used to perform deep learning–based segmentation on standard T1-weighted MRI. Representative cases are shown for patients treated with (**A**) stereotactic radiosurgery and (**B**) whole-brain radiotherapy, including corresponding treatment plans and rates of hippocampal volume loss (%/month) over ~12 months. Yellow arrow highlights hippocampal volume loss in the WBRT case.

DISCUSSION

These findings demonstrate that automated hippocampal volumetry provides a practical imaging biomarker for quantifying radiation-induced brain injury from routine clinical MRI. The marked differences between WBRT and SRS reinforce the importance of minimizing normal brain irradiation whenever clinically feasible. The observed dose-dependent relationship between hippocampal atrophy and radiation exposure further supports hippocampal-sparing treatment strategies and suggests that structural MRI biomarkers may complement longitudinal neurocognitive assessment. Together, these results highlight the potential of AI-enabled volumetric analysis to improve treatment evaluation, toxicity monitoring, and development of neuroprotective approaches.

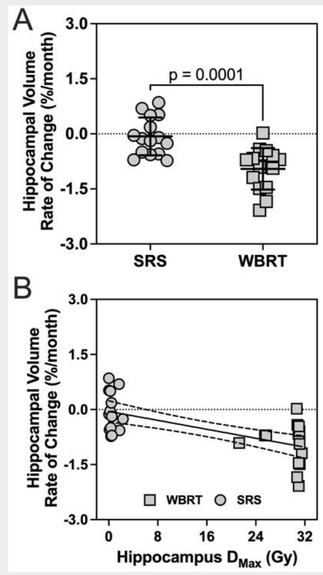

Figure 2. Quantitative analysis of hippocampal volume loss and dose–response. (**A**) Rates of hippocampal volume loss (%/month) in patients treated with stereotactic radiosurgery (SRS) or whole-brain radiotherapy (WBRT). (**B**) Relationship between hippocampal volume loss rate and maximum hippocampal dose (D_{max}), demonstrating a significant dose-dependent effect (r = −0.66, p < 0.0001).

CONCLUSIONS

Deep learning–based hippocampal segmentation using FastSurfer enables robust, high-throughput quantification of radiation-associated hippocampal atrophy from routine MRI. WBRT is associated with substantially greater hippocampal volume loss than SRS, with magnitude tightly linked to hippocampal dose. These findings support hippocampal sparing and dose-aware treatment selection and demonstrate the value of AI-enabled morphometric biomarkers for advancing treatment planning, toxicity assessment, and outcome modeling in contemporary medical physics.

REFERENCES

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WBRT causes sevenfold greater hippocampal atrophy than SRS

AI-based hippocampal volumetry from routine MRI provides a scalable biomarker of radiation-induced brain injury and supports hippocampal-sparing radiotherapy