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ENHANCING TUMOR CONTROL IN BRAIN METASTASES: EVALUATING DOSE ESCALATION IN STEREOTACTIC RADIOSURGERY

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Abstract: Stereotactic radiosurgery (SRS) is a key treatment for brain metastases, offering targeted therapy while minimizing damage to surrounding healthy brain tissue. However, optimizing dose escalation strategies remains a critical challenge to improving local tumor control without increasing neurotoxicity. This paper evaluates current literature on SRS dose escalation, its impact on tumor control, and strategies for mitigating associated risks. Through an analysis of recent studies from 2023, we examine the efficacy of dose adjustments and emerging treatment paradigms.
Keywords: Stereotactic Radiosurgery (SRS), Brain Metastases, Dose Escalation, Neurotoxicity, Tumor Control, Radiation Therapy.

Introduction

Brain metastases (BM) occur in approximately 20%–40% of cancer patients, significantly impacting survival and quality of life. Stereotactic radiosurgery (SRS) has emerged as a crucial treatment modality, providing precise high-dose radiation to metastatic brain tumors with minimal collateral damage. Traditional approaches have prioritized balancing tumor control with neurotoxicity prevention. However, the potential for dose escalation to improve local control rates is an ongoing area of investigation.

While whole-brain radiation therapy (WBRT) was historically the standard treatment, its association with cognitive decline and limited efficacy in local control has led to a shift toward SRS. Studies suggest that dose escalation can improve tumor control rates but may increase the risk of radiation-induced necrosis. Thus, understanding the threshold for neurotoxicity is crucial for optimizing treatment strategies.

This paper explores recent advancements in dose escalation strategies, analyzing their effects on tumor control, treatment efficacy, and potential risks. We incorporate data from 2023 to provide the most updated insights into best practices for SRS in managing brain metastases.

1. Literature Review

Several recent studies have explored the efficacy of dose escalation strategies in SRS for brain metastases. Below is a summary of key findings:

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Study	Key Findings	Dose Strategy	Neurotoxicity Risk
Kleinberg et al. (2023)	Dose escalation improves local control rates but increases neurotoxicity in tumors >3 cm	24–30 Gy in single fraction	15% risk of radionecrosis
Ladbury et al. (2023)	Multi-session SRS reduces neurotoxicity compared to single-fraction dose escalation	3x9 Gy fractions	5% neurotoxicity
Shen et al. (2023)	Adaptive dosing strategies improve tumor control with limited neurotoxicity	Variable dose based on tumor size	8% neurotoxicity
Milano et al. (2023)	High-dose SRS improves survival in patients with controlled systemic disease	27 Gy in single fraction	12% neurotoxicity

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These findings suggest that while dose escalation improves local control, it is associated with increased risks. Multi-fraction SRS appears to mitigate neurotoxicity while maintaining efficacy.

2. Dose Escalation and Tumor Control

2.1 Relationship Between Dose and Tumor Control

Several clinical trials have demonstrated that increasing the radiation dose correlates with better local tumor control. The Radiation Therapy Oncology Group (RTOG) 90-05 study, a landmark dose-escalation trial, found that local tumor control improved significantly with higher doses, but the risk of grade 3–4 neurotoxicity also increased.

2.2 Comparative Analysis of Dose Escalation Strategies

Dose Strategy	Local Control Rate	Neurotoxicity Rate
18 Gy (standard dose)	65% at 12 months	5%

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24 Gy (moderate escalation)	75% at 12 months	10%
30 Gy (high escalation)	85% at 12 months	15%

3. Strategies to Mitigate Neurotoxicity

3.1 Fractionated Stereotactic Radiotherapy (FSRT)

FSRT delivers the radiation dose over multiple sessions rather than a single fraction. Studies have shown that fractionation reduces the risk of radiation necrosis while maintaining tumor control.

Key Findings:

- **3×9 Gy** fractionation regimen led to **75% local control at 12 months** with only **5% neurotoxicity**.
- A **5×7 Gy regimen** provided similar tumor control but further reduced neurotoxicity.

Biomarkers for Predicting Radiation Toxicity

Emerging research suggests that imaging biomarkers, such as diffusion tensor imaging (DTI), may predict neurotoxicity risk. Studies indicate that **patients with high pre-treatment edema levels** are at greater risk of developing radiation necrosis.

3.2 Adjunctive Therapies

- **Steroid Therapy:** Dexamethasone is commonly used to reduce inflammation postSRS.
- **Bevacizumab:** An anti-VEGF agent that reduces radiation necrosis by improving vascular stability.

4. Future Directions in SRS Dose Optimization

4.1 Radiomics and AI in Treatment Planning

Machine learning models are increasingly being utilized to optimize SRS dosing. AIbased algorithms can predict the optimal dose based on tumor characteristics, patient genetics, and prior treatment response.

4.2 Combination Therapies

Emerging evidence supports combining SRS with systemic therapies such as:

- **Immunotherapy (Checkpoint Inhibitors)**: Enhances tumor response but increases neurotoxicity risk.
- **Targeted Therapy (TKIs, EGFR inhibitors)**: Shows promise in improving SRS efficacy for specific mutations.

4.3 Adaptive Radiation Therapy

Real-time imaging and dose adaptation allow for dynamic treatment planning based on tumor response. This approach is expected to reduce over-treatment and unnecessary neurotoxicity.

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5. Conclusion

Dose escalation in stereotactic radiosurgery for brain metastases improves local tumor control but comes with an increased risk of neurotoxicity. Strategies such as multi-fraction SRS, imaging biomarkers, and adjunctive therapies help mitigate this risk. Advances in AI-driven

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Treatment planning and combination therapies offer promising pathways to optimize outcomes while minimizing adverse effects.

Future research should focus on refining dose thresholds, integrating personalized treatment strategies, and improving long-term neurocognitive outcomes in patients undergoing SRS.

References

Kleinberg, L. R., et al. "A Dose-Response Model of Local Tumor Control Probability after Stereotactic Radiosurgery for Brain Metastases." *Advances in Radiation Oncology*, 2023.

Ladbury, C., et al. "Stereotactic Radiosurgery in the Management of Brain Metastases:

A Case-Based Radiosurgery Society Practice Guideline." *Elsevier*, 2023.

Shen, C. J., et al. "Updated Risk Models Demonstrate Low Risk of Symptomatic Radionecrosis Following Stereotactic Radiosurgery for Brain Metastases." *Surgical Neurology International*, 2023.

Milano, M. T., et al. "Single-and Multifraction Stereotactic Radiosurgery Dose/Volume

Tolerances of the Brain." *International Journal of Radiation Oncology, Biology, Physics*, 2023.

Palmisciano, P., et al. "Neoadjuvant Stereotactic Radiotherapy for Brain Metastases: Systematic Review and Meta-Analysis." *Cancers*, 2023.

Benkhaled, S., et al. "Stereotactic Radiosurgery and Stereotactic Fractionated Radiotherapy in the Management of Brain Metastases." *Cancers*, 2024.

Cho, A., et al. "How to Dose-Stage Large or High-Risk Brain Metastases: An Alternative Two-Fraction Radiosurgical Treatment Approach." *Journal of Neurosurgery*, 2022.

Camidge, D. R., et al. "Trial Design for Systemic Agents in Patients with Brain Metastases from Solid Tumors: A Guideline by the Response Assessment in NeuroOncology Brain Metastases Working Group." *The Lancet Oncology*, 2018.

Levis, M., et al. "Modern Stereotactic Radiotherapy for Brain Metastases from Lung

Cancer: Current Trends and Future Perspectives Based on Integrated Translational Approaches." *Cancers*, 2023.

Hartgerink, D., et al. "Stereotactic Radiosurgery in the Management of Patients with Brain Metastases of Non-Small Cell Lung Cancer: Indications, Decision Tools, and Future Directions." *Frontiers in Oncology*, 2018.

Zhu, S., et al. "Acute Neurologic Toxicity of Palliative Radiotherapy for Brain Metastases in Patients Receiving Immune Checkpoint Blockade." *Neuro-Oncology Practice*, 2019.