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Impact of Nodal Stereotactic Body Radiotherapy on Time to Systemic Therapy Initiation: An Emerging Clinical Endpoint in Oligometastatic Disease

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Abstract

The oligometastatic paradigm has introduced metastasis-directed therapies as potential strategies to delay disease progression and postpone systemic treatment initiation. Among these approaches, stereotactic body radiotherapy (SBRT) has demonstrated high local control rates with limited toxicity in oligometastatic lymph node disease. Beyond survival outcomes, the ability of SBRT to defer systemic therapy represents an increasingly relevant clinical endpoint, particularly in patients requiring multiple treatment lines or experiencing cumulative treatment toxicity. Available data indicate a median freedom from systemic therapy of approximately 14 months, with nearly one-quarter of patients remaining systemic treatment–free at five years. Similarly, systemic therapy–free survival around 17.8 months has been reported in some series. These findings highlight the clinical importance of SBRT as a strategy to preserve quality of life while maintaining disease control. This review examines current evidence supporting systemic therapy deferral as a meaningful endpoint in nodal oligometastatic disease management.

Keywords: Oligometastatic disease; Lymph node metastases; Stereotactic body radiotherapy (SBRT); Metastasis-directed therapy; Systemic therapy delay; Treatment-free survival; Quality of life; Personalized oncology.

1. Introduction

The concept of oligometastatic disease has significantly modified the therapeutic landscape of metastatic cancer. Rather than representing a uniformly systemic and incurable condition, limited metastatic burden may reflect a transitional biological state amenable to aggressive local therapies (1,2). In this context, metastasis-directed treatments such as surgery or stereotactic body radiotherapy (SBRT) aim not only to achieve local tumor control but also to influence disease trajectory (2,7).

SBRT has emerged as a key modality due to its ability to deliver ablative radiation doses with high precision and limited toxicity (8,9). In oligometastatic lymph node disease, this approach has demonstrated excellent local control and favorable safety profiles (3–6).

Traditionally, treatment evaluation in metastatic oncology relied primarily on overall survival and progression-free survival. However, increasing attention has been directed toward additional endpoints reflecting patient-centered outcomes, including quality of life and delay in systemic therapy initiation (7). Avoiding or postponing systemic therapy may reduce cumulative toxicity, preserve functional status, and improve overall patient well-being.

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2. Rationale for Delaying Systemic Therapy

Systemic therapies—including chemotherapy, targeted therapy, or hormonal therapy—are associated with significant toxicities that may accumulate over successive treatment lines. Fatigue, hematological toxicity, gastrointestinal complications, and long-term organ dysfunction can markedly impair quality of life.

In oligometastatic settings, effective local control through SBRT may allow postponement of systemic therapy initiation without compromising oncologic outcomes (2,7). This strategy is particularly relevant in patients who have already received multiple systemic treatments or whose tumors exhibit limited sensitivity to available systemic options.

The potential to defer systemic therapy therefore represents an important therapeutic objective in modern oncology.

3. Clinical Evidence Supporting Systemic Therapy Delay

Available data from observational studies and retrospective analyses indicate that SBRT can significantly delay systemic therapy initiation in patients with oligometastatic lymph node involvement **(3–6)**.

One study evaluating freedom from systemic therapy (FFST) reported:

- Median FFST approximately 14 months
- Approximately 23.5% of patients remaining free from systemic therapy at 5 years **(6)**

Similarly, analysis of systemic therapy–free survival (STFS) demonstrated a median duration of approximately 17.8 months following SBRT **(6)**.

These findings suggest that SBRT provides not only local tumor control but also meaningful postponement of systemic treatment exposure.

Such outcomes are clinically relevant because they:

- reduce treatment-related morbidity
- preserve quality of life
- delay cumulative toxicities
- maintain therapeutic options for later disease stages.

4. Integration with Overall Oncologic Outcomes

The ability to delay systemic therapy must be interpreted alongside established oncologic endpoints. High local control rates associated with SBRT contribute to disease stabilization, potentially explaining prolonged systemic therapy–free intervals (3–6).

Randomized clinical trials evaluating SBRT in oligometastatic disease more broadly have demonstrated survival benefits compared with standard care alone (7,10,11). Although these trials were not specific to lymph node metastases, they provide contextual evidence supporting aggressive local treatment strategies.

5. Clinical Implications

- **Quality of Life Preservation:** Avoiding systemic therapy-related toxicity may improve patient comfort, functional independence, and psychosocial well-being.
- **Treatment Sequencing Optimization:** SBRT may serve as an intermediate therapeutic step between initial systemic therapy and later salvage treatments.
- **Personalized Treatment Strategies:** Patients with indolent disease biology or limited metastatic burden may particularly benefit from metastasis-directed therapy **(2,7)**.

5.1. Limitations of Current Evidence

Despite the promising available data, several limitations remain. Most studies evaluating the impact of SBRT on delaying systemic therapy in oligometastatic lymph node disease are retrospective in nature, which may introduce selection bias and limit the strength of conclusions. Additionally, patient populations across studies are heterogeneous in terms of primary tumor histology, metastatic burden, prior treatments, and systemic therapy indications, making direct comparisons challenging. Variability in criteria for initiating systemic therapy further complicates interpretation of outcomes. Moreover, randomized evidence specifically addressing nodal oligometastases remains limited. Prospective clinical trials evaluating systemic therapy delay as a primary endpoint are therefore needed to better define the clinical benefit of SBRT in this setting.

5.2. Future Perspectives

Future research should focus on several key areas to better define the role of SBRT in delaying systemic therapy for oligometastatic lymph node disease. Prospective validation of systemic therapy delay as a clinically meaningful endpoint is essential to strengthen current evidence. In addition, integrating SBRT with novel systemic agents, including targeted therapies and immunotherapies, may further optimize treatment outcomes. The identification of reliable biomarkers to guide patient selection could help personalize treatment strategies and identify patients most likely to benefit from metastasis-directed therapy. Such efforts may ultimately refine therapeutic strategies and contribute to more personalized cancer care.

6. Conclusion

SBRT for oligometastatic lymph node disease offers more than local tumor control. Its capacity to delay systemic therapy initiation represents a clinically meaningful endpoint reflecting modern patient-centered oncology. Median systemic therapy–free intervals exceeding one year and long-term systemic therapy avoidance in a subset of patients underscore the therapeutic value of this approach.

Further prospective studies are required to confirm these findings and establish optimal integration of SBRT within multimodal cancer management strategies.

Compliance with ethical standards

Disclosure of conflict of interest

There are no conflicts of interest.

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