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(REVIEW ARTICLE)

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Toxicity Profile of Stereotactic Body Radiotherapy for Oligometastatic Lymph Node Disease: A Critical Narrative Review

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Abstract

Stereotactic body radiotherapy (SBRT) has emerged as an effective metastasis-directed therapy for oligometastatic lymph node disease, providing high local control with minimal invasiveness. However, the proximity of lymph node metastases to critical organs raises concerns regarding treatment-related toxicity. This narrative review synthesizes current evidence on acute and late toxicity following SBRT for nodal oligometastases, highlighting incidence rates, anatomical risk factors, dosimetric considerations, and technical determinants of treatment safety. Available literature demonstrates a favorable safety profile, with severe toxicity rates generally below 1% when organ-at-risk constraints are respected. Nevertheless, re-irradiation, high biologically effective doses, large target volumes, and central anatomical locations remain significant predictors of complications. Understanding these factors is essential to optimize therapeutic ratio and ensure safe integration of SBRT into multimodal oncologic management.

Keywords: Stereotactic body radiotherapy (SBRT); Lymph node oligometastases; Radiation toxicity; Metastasis-directed therapy; Hypofractionated radiotherapy; Organ-at-risk constraints; Radiotherapy safety; Oligometastatic disease

1. Introduction

The oligometastatic paradigm has reshaped the management of metastatic cancer by identifying a subset of patients with limited metastatic burden potentially amenable to curative local therapies, a concept initially proposed by Hellman and Weichselbaum [3]. Among these approaches, stereotactic body radiotherapy (SBRT) has gained increasing acceptance due to its ability to deliver ablative radiation doses with submillimetric precision while minimizing exposure of surrounding healthy tissues [4].

Lymph node metastases represent a frequent oligometastatic presentation across multiple malignancies. However, their anatomical proximity to critical structures—including gastrointestinal organs, airways, vascular structures, and neural pathways—raises specific concerns regarding treatment-related toxicity [5]. Although SBRT has demonstrated excellent efficacy in local tumor control, safety remains a crucial determinant of its broader clinical adoption.

This review critically examines toxicity outcomes associated with SBRT for oligometastatic lymph node disease, emphasizing incidence rates, risk factors, anatomical considerations, and technical strategies to minimize complications.

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2. Overall Toxicity Profile

2.1. General Tolerance

Available data consistently indicate that SBRT for oligometastatic lymph node disease is generally well tolerated. Large systematic analyses including more than 1,500 patients report extremely low rates of severe toxicity [1,2].

Late toxicity occurring beyond three months after treatment remains rare:

- Grade 3 toxicity approximately 0.6%
- Grade 4 toxicity approximately 0.1%
- No grade 5 treatment-related deaths reported

Most late adverse events are mild, with grade 1–2 toxicities reported in less than 10% of patients [1].

Acute toxicity within three months also demonstrates favorable outcomes, typically limited to fatigue, mild gastrointestinal symptoms, or transient localized pain [2]. These findings confirm that SBRT, when performed under appropriate technical conditions and dose constraints, maintains a favorable therapeutic index.

3. Risk Factors for Severe Toxicity

3.1. Re-irradiation

Re-irradiation represents the strongest predictor of severe toxicity. Several retrospective series report that approximately half of severe late complications occur in previously irradiated regions [6]. Cumulative biologically effective doses exceeding approximately 140 Gy have been associated with fistulas, necrosis, or bowel obstruction [6,7].

3.2. Dose Escalation

Higher biologically effective doses improve tumor control but increase toxicity risk, particularly near radiosensitive organs. Radiobiological studies highlight endothelial damage, vascular compromise, and fibrosis as mechanisms underlying late toxicity following high-dose hypofractionated irradiation [7,8].

3.3. Target Volume

Large planning target volumes increase the likelihood of overlap with organs at risk and therefore elevate complication rates. This relationship has been confirmed in several SBRT cohorts treating nodal oligometastases [1,9].

3.4. Anatomical Location

Central thoracic and abdominopelvic nodal sites present greater risk due to adjacency to critical structures such as esophagus, bowel, ureters, and major vessels [5,9].

4. Site-Specific Toxicity

4.1. Thoracic Lymph Nodes

Pulmonary toxicity, particularly radiation pneumonitis, remains the most frequent complication. Severe pneumonitis is uncommon but has been reported, mainly in re-irradiation contexts [10].

Esophageal toxicity typically manifests as transient esophagitis, although rare fistulas have been described after high cumulative doses **[10]**. Cardiovascular and airway toxicities remain infrequent but possible, especially when mediastinal nodes are treated.

4.2. Abdominopelvic Lymph Nodes

Gastrointestinal toxicity represents the predominant severe adverse event in abdominopelvic nodal SBRT. Although overall incidence remains low (≈0.5%), these events account for the majority of severe late toxicities **[2]**.

Reported complications include:

- Intestinal obstruction
- Gastrointestinal perforation
- Hemorrhage
- Rectovaginal fistulas

Genitourinary toxicity is uncommon but may include ureteral stenosis or bladder irritation **[1]**. Neurological complications affecting lumbosacral plexus structures are rare with modern planning techniques.

5. Technical Determinants of Safety

5.1. Imaging Guidance

Image-guided radiotherapy (IGRT) is essential for accurate dose delivery. Cone-beam CT and MRI-guided radiotherapy improve target visualization and reduce irradiation of normal tissues [11].

MRI-guided adaptive SBRT shows promising safety results, combining excellent tumor control with minimal toxicity in early clinical studies [11].

5.2. Motion Management

Respiratory and interfraction motion can affect nodal positioning. Motion management strategies, including respiratory gating and image guidance, are therefore critical to minimize toxicity **[12]**.

5.3. Organ-at-Risk Constraints

Strict adherence to dose constraints—such as those defined by the AAPM Task Group 101—is fundamental for toxicity prevention **[13]**. Established constraints for gastrointestinal, urinary, and thoracic organs have significantly improved SBRT safety profiles.

5.4. Clinical Implications and Future Directions

SBRT toxicity in oligometastatic lymph node disease remains low when appropriate patient selection, imaging guidance, and technical precautions are applied. Ongoing developments may further improve treatment safety and effectiveness, including the use of MRI-guided adaptive radiotherapy, the identification of biomarkers predicting radiation toxicity, integration with immunotherapy strategies, and prospective randomized trials evaluating long-term safety.

Emerging data suggest that SBRT can be safely incorporated into multimodal oncologic management while maintaining acceptable toxicity levels **[14,15]**.

6. Conclusion

SBRT represents a safe and effective treatment modality for oligometastatic lymph node disease, offering high local control with minimal severe toxicity. Risk factors such as re-irradiation, high biologically effective dose, large target volumes, and central anatomical location require careful consideration.

Advances in imaging, motion management, and adaptive radiotherapy continue to improve safety profiles, supporting broader integration of SBRT into personalized oncologic strategies. Continued prospective research is necessary to refine treatment indications and optimize therapeutic outcomes.

Compliance with ethical standards

Disclosure of conflict of interest

There are no conflicts of interest.

Statement of ethical approval

This review report was conducted in accordance with ethical standards.

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