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Prevention and Management of Osteoradionecrosis in Patients With Head and Neck Cancer Treated With Radiation Therapy: ISOO-MASCC-ASCO Guideline Clinical Insights

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DOI https://doi.org/10.1200/OP.24.00182

Accepted March 13, 2024
Published May 1, 2024

JCO Oncol Pract 00:1-4
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The International Society of Oral Oncology-Multinational Association for Supportive Care in Cancer (ISOO-MASCC) and ASCO recently published a joint guideline to provide formal evidence-based recommendations directed to the prevention and management of osteoradionecrosis (ORN) in patients with head and neck cancer treated with radiation therapy (RT).[1] Clinical guidance included the following:

- Radiation treatment planning considerations to reduce the risk of developing ORN.
- Indications and timing of preradiation dental evaluation and frequency of long-term dental follow-up and management after head and neck RT.
- Indications and timing of teeth extraction before or after head and neck RT.
- Use of systemic therapies and/or hyperbaric oxygen (HBO) to lower the risk of ORN in high-risk patients.
- Surgical indications and techniques for patients with mild-to-moderate and severe ORN.
- Supportive care management of adverse events associated with and/or caused by ORN.

This companion article addresses some of the questions clinicians may face as they implement the recommendations (Fig 1) into clinical practice, especially in settings where coverage for essential dental services is being expanded. For example, the Centers for Medicare and Medicaid Services (CMMS) issued a final rule in November 2023 that included the following key coverage effective January 1, 2024:[2]

> *"Payment for dental services that are inextricably linked to other covered medical services, such as dental exams and necessary treatments prior to organ transplants (including stem cell and bone marrow transplants), cardiac valve replacements, and valvuloplasty procedures."*

For calendar year 2024, the CMMS is finalizing codification of the previously finalized payment policy for dental services for head and neck cancer treatments, whether primary or metastatic. These changes will hopefully increase access to dental services for patients with head and neck cancer and enhance opportunities for reduction of late effects in survivors, including ORN.

This is a significant advance in the United States to improve access to dental care for patients with cancer. It is now essential that private insurers adopt a similar model to expand coverage for essential dental services.

WHAT ARE THE MAIN CONSIDERATIONS IN RADIATION TREATMENT PLANNING TO REDUCE RISK OF ORN?

Head and neck irradiation with doses ≥50 Gy to the maxilla and/or mandible (ie, jaw) leads to increased risk of ORN development. To mitigate this risk, advanced radiation planning techniques such as intensity-modulated radiation therapy should be used to minimize mean radiation dose to the jaw and the volume of jaw receiving ≥50 Gy. Dosimetric parameters associated with reduced ORN risk include mandible V30% <42 Gy, V44Gy <42%, V58Gy <25%, and mean dose <37 Gy.[3] Importantly, coverage of gross tumor volume and clinical/planning target volumes should not be sacrificed to meet maxilla and mandible dose constraints. Disease site, tumor volume, and patient anatomy affect which dosimetric parameters are achievable. However, the overall goal is to reduce the volume of maxilla and mandible receiving high radiation doses without sacrificing target coverage.

Recommendation	Evidence Quality	Strength
1.2. A patient with radiation dose to the jaw of 50 Gy or higher should be considered at risk for development of ORN. Modifiable risk factors including poor oral hygiene, dentoalveolar surgeries, and/or tobacco use, should be considered as further increasing this lifelong risk.	H	S
1.6. Recommended initial evaluation of ORN should include one or more of the following: (1) clinical intraoral examination (including direct visual or endoscopic examination and/or formal periodontal assessment) and/or (2) formal radiographic examination (ie, x-ray orthopanogram, cone-beam or fan-beam computed tomography, magnetic resonance imaging).	M	S
1.7. Recommended serial characterization or surveillance of ORN should include clinical intraoral examination (including direct visual, endoscopic examination, and/or comprehensive periodontal assessment) and comprehensive radiographic examination (ie, x-ray orthopanogram, cone-beam or fan-beam computed tomography, magnetic resonance imaging).	M	S
2.1. Target coverage of tumor should not be compromised to avoid dose to bone.	M	S
2.2. Advanced radiation planning techniques (eg, IMRT, IMPT) should be employed to deliberately reduce radiation dose to the jaw at risk as much as possible.	M	S
2.3. Focused effort should be made to reduce the mean dose to the jaw and the volume of bone receiving above 50 Gy, whenever possible.	M	S
2.4.1. A dental assessment by a dentist (with a dental specialist if possible) is strongly advised before therapeutic-intent radiation therapy to identify and remove teeth which will place the patient at risk of ORN during the patient's lifespan and to comprehensively educate the patient about lifelong risk of ORN.	M	S
2.4.2. Dental extraction, if clinically indicated, should occur at least 2 weeks before commencement of radiation therapy. In the setting of rapidly progressing tumor, extractions should be deferred and not cause a delay in the initiation of radiation therapy.	M	S
5.1.1. In partial thickness ORN (ClinRad Stage I or II), surgical management can start with transoral minor intervention which can lead to resolution. This may include debridement, sequestrectomy, alveolectomy, and soft tissue flap closure.	H	S
5.3. In full thickness ORN or extensive partial thickness ORN where conservative therapy has not yielded appropriate disease control (ClinRad Stage II or III), segmental resection is recommended.	H	S
5.5. Free flaps are recommended over pedicle flaps. Free flaps offer greater versatility and improved outcomes. Pedicle flaps can be used, especially in salvage procedures, with some limitations.	L	S
6.1. Patients should be assessed by their health care providers for presence of adverse events at the time of ORN diagnosis and periodically thereafter until resolution based on patient status including response to intervention.	L	S

FIG 1. Highlighted recommendations. H, high; IMPT, intensity-modulated proton therapy; IMRT, intensity-modulated radiation therapy; L, low; M, moderate; ORN, osteoradionecrosis; S, strong.

WHEN SHOULD PATIENTS AT RISK OF ORN BE SEEN BY A DENTIST AND WHAT IS THE RECOMMENDED FOLLOW-UP FREQUENCY?

Patients at elevated risk for ORN are those with either individual or combinations of modifiable risk factors: uncontrolled diabetes, ongoing tobacco use, poor compliance or low access to dental care, and poor periodontal status. Patients at risk of ORN should be evaluated by a dentist with experience in head and neck oncology more than 2 weeks before starting RT to allow time to identify dental issues and perform needed dental extractions. Ongoing oral surveillance of these patients should occur every 6 months after RT to address modifiable risk factors in addition to lifelong compliance with oral care.

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WHEN SHOULD TEETH BE REMOVED BEFORE AND AFTER HEAD AND NECK RADIATION THERAPY?

Ideally, teeth should be removed at least 2 weeks before RT start date as this has been established as a sufficient healing period to reduce ORN risk from pre-RT extractions in all patients receiving ≥50 Gy to the jaw. Ongoing dental surveillance is essential after RT. After RT completion, a time period when teeth can be safely removed without risk of ORN was not identified. In the post-RT setting, tooth-preserving treatments should be recommended as opposed to extraction, where possible to reduce risk of ORN.

WHAT IS THE PREFERRED SYSTEMIC TREATMENT PROTOCOL FOR PATIENTS WITH OR AT RISK FOR ORN?

If tooth preservation is not possible or has been unsuccessful and dental extraction is indicated, prophylactic use of pentoxifylline and tocopherol may be beneficial. There is limited clinical evidence to support the role of prophylactic antimicrobial use in the setting of post-RT extractions. In the case of established ORN, there are reported benefits of combination pentoxifylline and tocopherol with antimicrobial therapy in mild, moderate, and severe cases of ORN. It is important to note that pentoxifylline and tocopherol should be used only in patients without evidence of active oncologic disease because of the angiogenic effects.

WHAT IS THE ROLE OF HBO THERAPY IN PROPHYLAXIS AND TREATMENT OF ORN?

Routine use of HBO therapy before dental extractions in patients with a history of head and neck RT is not recommended.[4] HBO with or without surgery may improve healing for patients with ORN, particularly for mild cases. However, evidence supporting the therapeutic use of HBO is limited, with promising retrospective data[5,6] but mixed results from prospective randomized trials.[7,8]

WHAT ARE THE GOALS OF TREATMENT AND METHODS AVAILABLE FOR SURGICAL PALLIATION IN PATIENTS WITH ESTABLISHED ORN?

Elimination of pain and infection are the main goals in this patient population. Eradicating the nonviable bone and providing vascularized soft tissue coverage are essential. Surgical debridement and sequestrectomy to bleeding bone can be performed if there is adequate adjacent healthy tissue for tension-free closure over the bone. Regional pedicled or soft tissue free flaps are used depending on the surgical resources available and the health of the patient. When full thickness ORN is present, segmental bony resection is necessary. Local tissue closure or a regional flap can offer palliation in patients who cannot undergo a major surgical intervention recognizing the functional sequelae of a continuity defect in the mandible. Placement of a reconstruction plate with only soft tissue reconstruction should be avoided. If bony continuity is to be restored, a bone-containing free flap is the appropriate choice.

WHAT ARE THE DETERMINANTS OF APPROPRIATE FLAP CHOICE FOR RECONSTRUCTION IN PATIENTS WITH ESTABLISHED ORN?

Microvascular free tissue transfer offers a one-stage procedure to address ORN. Resective margins should be designed to eliminate all affected bone. In the mandible, if the bone is preserved to the inferior alveolar canal, soft tissue coverage is suitable. A radial forearm or anterolateral thigh free flap (or its variations) is most commonly used for coverage. In full thickness resections, the fibula free flap is commonly used as it has adequate bone and the longest vascular pedicle to reach suitable recipient vessels outside of the radiation field for microvascular anastomosis. If the goal is dental rehabilitation with implants, the bone stock of the flap will dictate choice. If microvascular surgery capabilities are unavailable, regional flaps such as the pectoralis major can be adequate recognizing that the bone will not be reconstructed.

WHEN, HOW, AND BY WHOM SHOULD PATIENTS DIAGNOSED WITH ORN BE ASSESSED FOR ADVERSE EVENTS ASSOCIATED WITH AND/OR CAUSED BY ORN?

Several adverse events can occur in patients with ORN. These adverse events as cited in the ORN guideline include but are not limited to pain, impaired mastication, dysphagia, weight loss, trismus, dysarthria, taste alterations, compromised oral hygiene, poor bone health, and psychosocial impairment.[1] Ongoing monitoring of patient status by the interprofessional health care team is essential to ideally prevent or at least diagnose early and treat ORN. Given the current lack of comprehensive high-quality guidance directed to ORN-related adverse events, the Panel recommends using guidelines developed by ASCO[9-11] and other oncology organizations[12-14] for diseases other than ORN for management of these adverse events in patients with ORN.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI https://doi.org/10.1200/OP.24.00182.

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Conception and design: All authors
Collection and assembly of data: All authors
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
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ACKNOWLEDGMENT

Prevention and Management of Osteoradionecrosis in Patients with Head and Neck Cancer Treated with Radiation Therapy: ISOO-MASCC-ASCO Guideline was developed and written by: Douglas E. Peterson, DMD, PhD, FDS RCSEd, FASCO; Shlomo A. Koyfman, MD; Noam Yarom, DMD, MPH; Charlotte Duch Lynggaard, MD, PhD; Nofisat Ismaila, MD, MSc; Lone E. Forner, DDS, PhD; Clifton David Fuller, MD, PhD; Yvonne M. Mowery, MD, PhD; Barbara A. Murphy, MD; Erin Watson, DMD, MHSc; David H. Yang, DDS. FRCD(C); Ivan Alajbeg, DMD, MSc, PhD; Paolo Bossi, MD; Michael Fritz, MD; Neal D. Futran, MD, DMD; Daphna Y. Gelblum, MD; Edward King; Salvatore Ruggiero, DMD, MD, FACS; Derek K. Smith, DDS, PhD, MPH; Alessandro Villa, DDS, MPH, PhD; Jonn S. Wu, BMSc, MD, FRCPC; Deborah Saunders, DMD.

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No other potential conflicts of interest were reported.

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