ORN - DEFINITION

Radiographic lytic or mixed sclerotic lesion of bone and/or visibly exposed bone and/or bone probed through a periodontal probe or fistula

AND

Occurring at an anatomical site previously exposed to radiotherapy (RTx)

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

Douglas E. Peterson, DMD, PhD, FDS RCSEd, FASCO[1]; Shlomo A. Koyfman, MD[2]; Noam Yarom, DMD, MPH[3,4]; Charlotte Duch Lynggaard, MD, PhD[5]; Nofisat Ismaila, MD, MSc[6]; Lone E. Forner, DDS, PhD[7]; Clifton David Fuller, MD, PhD[8]; Yvonne M. Mowery, MD, PhD[9,10]; Barbara A. Murphy, MD[11]; Erin Watson, DMD, MHSc[12]; David H. Yang, DDS, FRCD(C)[13]; Ivan Alajbeg, DMD, MSc, PhD[14]; Paolo Bossi, MD[15,16]; Michael Fritz, MD[2]; Neal D. Futran, MD, DMD[17]; Daphna Y. Gelblum, MD[18]; Edward King, JD[19]; Salvatore Ruggiero, DMD, MD, FACS[20]; Derek K. Smith, DDS, PhD, MPH[21]; Alessandro Villa, DDS, MPH, PhD[22]; Jonn S. Wu, BMSc, MD, FRCPC[13]; and Deborah Saunders, DMD[23]

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TABLE 1. Characteristics of Studies Identified in the Literature Search

Topics	RCT	Prospective (non-RCT)	Retrospective	Total
Grading				
Grading	0	0	2	2
Prevention				
Before RT	0	3	15	18
After RT	0	3	5	8
Mixed	0	0	2	2
Management				
Medication	0	2	6	8
HBO	6	1	4	11
Surgery	0	4	20	24
Combination	0	0	6	6
Laser (PBM)	0	1	0	1
Total	6	14	60	80

Abbreviations: RCT, randomized controlled trial; RT, radiation therapy; HBO, Hyperbaric Oxygen; PBM, photobiomodulation.

KEY STUDY QUESTIONS

1. How should ORN be characterized, graded, and reported?

2. What are the recommended best practices for the prevention of ORN of the head and neck prior to radiation therapy?

3. What are the recommended best practices for the prevention of ORN after radiation therapy?

4. How should ORN be managed nonsurgically?

5. How should ORN be managed surgically?

6. When, how, and by whom should patients diagnosed with ORN be assessed for adverse events associated with and/or caused by ORN?

GRADING

Watson EE, Hueniken K, Lee J, et al: Development and standardization of an osteoradionecrosis classification system in head and neck cancer: implementation of a risk-based model. 2024. J Clin Oncol 10.1200/JCO.23.01951

TABLE 5. ClinRad—A Novel Classification System for ORN

Description	Stage	Radiographic Findings	Clinical Findings	Intervention	ClinRad Clinical Trial Grade Proposal
Distinct from ORN, occurs more often in patients with history of RT	Minor bone spicules	None, aside from superficial sequestra	Superficial mobile spicules/ sequestra within mucosa	None indicated	Grade 0
Radiographic evidence of bone necrosis confined to alveolar bone with no clinical signs of ORN	Stage 0	Bone necrosis confined to alveolar bone including: Bone lysis/sclerosis Widening periodontal ligament (PDL) space Absence of osseous filling of extraction sockets	Intact mucosa	None indicated	Grade 1
Clinical signs of ORN with or without radiographic evidence of bone necrosis confined to alveolar bone	Stage I	None or as stage 0	Exposed bone[a]	Minor surgical intervention[b] and/or medical management[c] may be indicated with or without adjunctive conservative management[d]	Grade 2
Radiographic evidence involving basilar bone with or without clinical signs of ORN	Stage II	Bone necrosis involving the basilar bone or maxillary sinus	Intact mucosa or exposed bone[a]	Intermediate surgical intervention may be indicated[e], with or without adjunctive conservative and medical management	Grade 3
Advanced ORN	Stage III	One or more of the following: Pathologic fracture Orocutaneous fistula Oral antral communication/oral nasal communication	One or more of the following: Pathologic fracture Orocutaneous fistula Oral antral communication/ oral nasal communication	Reconstructive surgical intervention is indicated,[f] with or without adjunctive conservative and medical management	Grade 4

Abbreviations: ORN, osteoradionecrosis; RT, radiotherapy.

[a]Including pinpoint mucosal breach (intraoral fistula) that probes to bone and/or probing to bone along periodontal tissues.

[b]Examples include sequestrectomy.

[c]Examples include pentoxifylline-tocopherol and hyperbaric oxygen.

[d]Examples include chlorhexidine rinses and antibiotics.

[e]Examples include transoral surgical intervention and debridement, alveolectomy, and soft tissue closure.

[f]Examples include segmental maxillectomy/mandibulectomy with vascularized free tissue reconstruction.

Clinical Question	Recommendation	Type	Evidence Quality	Strength of Recommendation
1. How should ORN be characterized, graded, and reported? a. Which patients should be considered at high risk for ORN? b. What is the recommended workup to characterize ORN?	1.1. Osteoradionecrosis of the jaw (mandible, maxilla) should be characterized as a radiographic lytic or mixed sclerotic lesion of bone and/or visibly exposed bone and/or bone probed through a periodontal pocket or fistula, occurring within an anatomical site previously exposed to a therapeutic dose of head and neck radiation therapy	Informal consensus	Low	Strong
	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	Evidence-based	High	Strong
	1.3. Clinicians evaluating ORN should utilize the ClinRad staging system for ORN, as should clinical trials	Evidence-based	Moderate	Strong
	1.4. ORN assessment should have a defined formal characterization for disease evaluation at each visit which is usable across members of the clinical care or provider specialty spectrum. The panel recommends utilizing the ClinRad Classification system for ORN developed by Watson et al[83]	Evidence-based	Moderate	Strong
	1.5. ORN case reporting and diagnosis should include formal informatics, ontology, and lexical standards consistent with the characterization noted in Recommendation 1.1	Informal consensus	Low	Strong
	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)	Evidence-based	Moderate	Strong
	Qualifying statement: If either clinical or radiographic findings are initially detected, suspected or positive, subsequent confirmatory examination or imaging assessment is recommended			
	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)	Evidence-based	Moderate	Strong

PREVENTING ORN PRE-RADIOTHERAPY

1. IMRT to reduce dose to bone to less than 50Gy
2. Comprehensive dental or hospital dentists review prior to RTx
3. Extraction of teeth with poor prognosis, moderate to severe periodontal disease within the field.
4. Consider extraction of teeth with periapical disease, caries, and partially erupted 3rd molars – depending on individual and time for healing
5. Ideally at least 2 weeks of healing prior to Rtx but not at the cost of delaying Rtx
6. Aim exo's prior to mask fabrication if it will alter VD
7. High fluoride toothpaste

PREVENTING ORN POST RTX - SURGICAL

1. Review radiation fields prior to as part of treatment planning
2. Teeth at high risk of ORN – avoid exo's if possible unless patient has recurrent infection, pain or other sx that cannot be alleviated by extractions
3. Avoid implants in high risk zones
4. Oral antibiotics 1 day before and 7 days after dentoalveolar procedures + CHX mouthwash
5. If delayed healing post extractions occurs commence CHX mouthwash and observe with specialist input
6. Pentoxifylline 400mg BD and tocopherol 1000IU 1 week prior and 4 week post exo or preferably until socket is healed in cancer free patients (up to 3 months)
7. Preventive HBOT no longer supported for routine use

TREATING ORN– NON-SURGICAL

1. Pentoxyfylline may be used in cancer free patients. Potential to be beneficial esp combined with tocopherol, antibiotics and prednisolone

Pentoxifylline used in prevention of ORN
- Vasodilation, improves RBC deformation, antifibrotic (by inhibiting TNFa)
- 3 months pre-exo until healed - 400mg BD

Tocopherol: Vitamin E - scavenges free radicals

1. HBOT in conjunction with surgical management may be used in cancer free patients. Most potential benefit in mild cases

TREATING ORN – SURGICAL

1. ClinRad stage 1 or 2 – start with transoral minor intervention – debridement, sequestrectomy, alveolectomy, soft tissue flap closure

2. ClinRad stage 2, 3 or 4– segmental resection and free flap reconstruction is recommended (esp if greater that 2.5cm in length)

3. Removal of superficial bony sequestra should be performed if viewed as low disk by the clinic. Reduction and disease burden and biofilm environment can be synergistic with the ongoing systemic therapy.


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