

OSTEORADIONECCROSIS FOLLOWING DENTAL EXTRACTIONS AND IMPLANTS IN NASOPHARYNGEAL CANCER PATIENTS TREATED WITH RADIOTHERAPY: A NARRATIVE REVIEW

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ABSTRACT:

In patients with nasopharyngeal cancer (NPC), osteoradionecrosis (ORN) is a serious late side effect of radiation therapy, especially if implant placement or dental extractions are necessary. In addition to analyzing clinical factors related to dental extractions and implants in this population, this narrative review assesses the prevalence of ORN in NPC patients receiving radiotherapy. Mandibular involvement is most common, according to data from observational studies and retrospective cohorts, and radiation dose, tumor stage, and comorbidities all significantly affect the risk of ORN. Despite being widely used, pre-radiotherapy dental clearance has an inconsistent protective effect, and there is a much higher risk of ORN with extractions performed after radiation. Although the survival rate for dental implants placed in irradiated jaws is high, typically above 90%, the risk of ORN remains and seems to be higher in patients who receive cumulative doses greater than 60 Gy. Although they lack strong randomized evidence, preventive measures like hyperbaric oxygen therapy and pharmacologic regimens like pentoxifylline-tocopherol have inconsistent results. All things considered, ORN in NPC patients remains a complex complication for which multidisciplinary management, optimal timing of dental procedures, and careful patient selection are essential. To lower ORN risk while maintaining long-term oral function and quality of life, more prospective research is needed to develop standardized preventive and treatment approaches.

INTRODUCTION:

A diverse collection of tumors, head and neck cancer (HNC) can develop in the salivary glands, pharynx, larynx, lips, and oral cavity [1]. Over 900,000 new cases of HNC were reported globally in 2020, and about 460,000 people died from the disease [2]. More than 90% of cancers of the oral cavity are squamous cell carcinomas (SCC), which are the second most common cancer of the respiratory tract and affect the larynx and hypopharynx [3]. The majority of patients—more than 60%—present with locally advanced disease, which usually necessitates multimodal treatment approaches involving surgery and radiation therapy (RT), with or without chemotherapy [1]. However, early-stage SCC can frequently be effectively managed with surgery or RT alone. Acute and late toxicities, such as oral mucositis, xerostomia, dysphagia, and osteoradionecrosis (ORN), are linked to radiotherapy, which is essential for the curative-intent management of HNC [4]. If there is no ongoing or recurring disease, ORN of the jaws is defined as exposed irradiated bone that does not heal for at least three months [5]. Pain, trismus, suppuration, and mucosal ulceration with exposed bone are some of the clinical signs of ORN [6]. Complications from progressive disease may include intra- or extraoral fistulae, pathological fractures of the maxillofacial bones, secondary infections, and impairment of oral functions such as speech, mouth opening, and mastication [7]. For ORN, several staging and grading schemes have been proposed. All, despite their variations, are based on clinical and radiographic evaluations and aim to categorize disease severity to guide treatment [5]. Radiation dose and fractionation, poor oral hygiene, alcohol and tobacco use, tumor size and location, disease stage, systemic comorbidities like diabetes, and dental extractions are some of the risk factors that lead to the development of ORN [8]. All patients receiving head and neck irradiation should undergo a dental evaluation before treatment to reduce the risk of ORN and other oral complications associated with RT [9]. To lower future ORN risk, teeth with a poor restorative or periodontal prognosis that are located within the planned radiation field are typically extracted, ideally at least 14 days prior to the start of RT [8–10]. This strategy is predicated on the idea that completing extractions before radiation-induced impairment of bone healing reduces the risk of delayed healing and subsequent ORN [11, 12]. Pre-RT extractions, however, may increase the risk of developing ORN, according to several studies [9, 13–16].

Although radiotherapy is an effective treatment for nasopharyngeal cancer (NPC), there is a considerable risk of long-term side effects, including osteoradionecrosis (ORN) of the jaws. Dental health management is essential to reducing the risk of ORN, which significantly impairs oral function and quality of life. Although it is generally

advised to have teeth with a poor prognosis extracted before receiving radiation therapy, the evidence is still inconclusive; some studies suggest that extractions lower risk, while others suggest that they may actually cause ORN because of poor bone healing. Similarly, dental implants can improve patient outcomes and restore function, but due to the risk of ORN, their placement in irradiated bone remains debatable. There is uncertainty about the safest and most efficient dental management techniques for NPC patients due to the small number, methodological heterogeneity, and frequently retrospective nature of the current research, despite the clinical significance of these issues. Thus, the purpose of this narrative review was to summarize the evidence that was currently available, elucidate what is known, and pinpoint any gaps that could guide future studies.

Objectives: The primary goal is to evaluate the prevalence of osteoradionecrosis in patients who underwent radiotherapy for nasopharyngeal carcinoma. The secondary goal is to identify the variables that could be a risk factor such as radiation dose, time since radiation, dental extraction, dental implants, other medical comorbidities, condition of existing dentition, type of preventative interventions such as hyperbaric oxygen therapy versus antibiotics versus PENTCLO protocol.

METHODS:

According to a preliminary scoping exercise, the body of research on osteoradionecrosis (ORN) in patients with nasopharyngeal cancer (NPC) was too diverse to support a quantitative meta-analysis or systematic review. There was considerable variation in the study design, patient populations, interventions, and outcome definitions among the retrospective cohorts, case series, case-control studies, and narrative commentaries that were included in the literature. In order to compile the evidence that is currently available and pinpoint areas that require further investigation, a narrative review was conducted. The review concentrated on studies that were published between 1999 and 2025, when modern radiation techniques and intensity-modulated radiotherapy (IMRT) were being used more and more to treat NPC. The relationship between dental extractions and/or dental implants in irradiated fields and the subsequent risk of developing ORN was the main focus of this review. Unless they included pertinent information on the incidence of ORN, studies with other primary outcomes (such as xerostomia, mucositis, or overall quality of life) were not included.

Keyword searches in the PubMed, Embase, Scopus, Web of Science, and Cochrane Library databases were used to find the studies that were part of the review. "Nasopharyngeal cancer," "head and neck radiotherapy," "osteoradionecrosis," "dental extraction," "tooth extraction," "dental implant," and "jaw necrosis" were among the keywords and combinations that were searched. Additional manual searches of journals related to oral medicine, oncology, and maxillofacial surgery were conducted (e.g., Supportive Care in Cancer; International Journal of Oral and Maxillofacial Surgery; Oral Oncology). The reference lists of the retrieved articles were also searched for additional pertinent works.

Studies discussing dental implant placement in post-radiotherapy jaws and specifically addressing ORN risk after dental extractions in irradiated NPC patients were found using this search strategy. Few studies directly compared management or prevention strategies; most were observational cohort studies or retrospective case series.

Although limitations like retrospective design, small sample sizes, and variability in radiation dose reporting were acknowledged, methodological quality assessments were not used to weed out studies because this was a narrative review. Non-probability sampling was used in many studies, and participants were typically sourced from maxillofacial or tertiary oncology facilities. Few studies included specific radiation parameters, comorbidities (such as diabetes and a history of alcohol or tobacco use), or detailed sociodemographic characteristics, all of which could influence ORN risk.

There was little discussion of regional and ethnic variations in oral health practices. Although reports from Europe and North America were also found, the majority of studies were carried out in East and Southeast Asia, where NPC is endemic. The majority of studies recruited participants from hospital records of patients receiving radiation therapy for NPC, though recruitment tactics varied. Only a small number of the included studies used prospective or longitudinal designs; most evaluated results retrospectively. Although the criteria used to define ORN varied, most of them were in line with Marx's definition of exposed, irradiated bone that does not heal in three months. Few studies examined the long-term effects of implant placement in irradiated bone, and even fewer examined preventive dental protocols in detail, such as the timing of extractions, the use of hyperbaric oxygen therapy, or antibiotic prophylaxis.

RESULTS:

The search yielded 30 papers to be made part of this narrative review. The findings from the included papers are given in Table 1.

Reference	Study Type	Patients (N)	Tumour Type/Site	Treatment (RT Modality/Technique)	ORNJ Incidence/Prevalence	Key Findings / Associated Factors
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Topkan et al. 2023 [17]	Review	N/A	All Head and Neck Cancers (HNC)	All RT modalities and techniques, particularly IMRT, 3D-CRT, IMPT, carbon ion therapy	Currently less than 5–6% due to advances	Radiotherapy modality, technique, and dose are influential ORNJ factors. Mandibular dose is the ultimate determinant of ORNJ risk. Modern RT techniques mitigate risk by reducing mandibular dosages. Higher mandibular doses correlate with increased ORNJ risk.
Yilmaz et al. (Pre-chemoradiotherapy low hemoglobin levels) [18]	Retrospective Cohort Study	263 LA-NPC patients	Locally Advanced Nasopharyngeal Carcinoma (LA-NPC)	Concurrent Chemoradiotherapy (CCRT)	8.7% (23 out of 263 patients)	Pre-CCRT hemoglobin (Hb) ≤ 10.6 g/dL (32.3% incidence) was significantly associated with higher ORNJ rates compared to Hb > 10.6 g/dL (1.5% incidence). Other independent risk factors included mandibular V59.8 $\geq 36\%$ Gy, pre-CCRT ≥ 4 tooth extractions, presence of post-CCRT tooth extraction, and post-CCRT tooth extraction > 8 months after CCRT.
Jiang et al. 2014 [19]	Systematic Review & Meta-analysis	11 studies included	Head and Neck Cancer (HNC)	Radiotherapy (RT)	4.16% (95% CI, 1.17–7.16%) for patients with pre-RT dental extraction.	Radiotherapy technology, radiation dose, and prophylactic antibiotic use did not significantly affect ORNJ incidence. The incidence was higher in the conventional radiotherapy group (4.85%) compared to IMRT (not specified for IMRT alone but lower).
Oh et al. 2004 [20]	Retrospective Study	81 HNC patients with impacted third molars	Head and Neck Cancer (HNC)	Radiotherapy (RT)	4.9% (4 out of 81 patients).	ORNJ occurred in 3 out of 19 patients (16%) receiving >70 Gy radiation dose. No conclusive statistical analysis on etiologic factors due to limited cases and differences in treatment. Impacted third molars were located within the radiation port.
Gomez et al. 2011 [21]	Retrospective Review	168 HNC patients	Oral cavity, oropharynx, paranasal sinuses, larynx, nasopharynx	Intensity-Modulated Radiation Therapy (IMRT)	1.2% (2 cases out of 168 patients).	Two ORNJ cases occurred 31 and 32 months post-IMRT. Dmax > 70 Gy and Dmean > 40 Gy were associated with increased risk of dental extraction. Mandibular Dmax constraint of 7000 cGy was used.
Schuurhuis et al. 2011 [22]	Retrospective, Descriptive Study	80 HNC patients	Oral cavity or oropharynx carcinoma	3D-CRT (majority until 2007), IMRT (increasingly since 2008)	7.5% (6 out of 80 patients).	Four ORNJ cases were reported, 3 linked to pre-IMRT dental extractions and 1 to post-IMRT extraction. Patients with advanced periodontal disease are prone to bone healing problems.
Koga et al. 2008 [23]	Retrospective Study	405 patients	Various (Oral cavity, Oropharynx, Larynx, Hypopharynx, Nasopharynx/maxillary sinus)	Radiotherapy (RT)	0.74% (3 cases out of 405 patients).	Only 3 cases of ORNJ were observed, 2 related to extractions before RT and 1 after RT. Suggests possibility of performing exodontias after RT by experienced dentists. Mean RT dose was 6304 cGy.

David et al. 2007 [24]	Retrospective Analysis	176 HNC patients	Oral cavity, oropharynx, larynx, hypopharynx	Intensity-Modulated Radiation Therapy (IMRT)	0% (0 out of 176 patients).	Lack of ORNJ likely due to strict prophylactic dental care policy and IMRT. Policies included extraction of high-risk teeth in high-dose mandibular areas, fluoride supplements, and guards to reduce electron backscatter.
Céspedes-Ajún et al. 2022 [25]	Systematic Review	8 cohort studies (2821 HNC patients screened, 2045 patients evaluated)	Head and Neck Cancer (HNC)	3D-CRT vs. IMRT	13.2% (n=134) for 3D-CRT, 5.4% (n=56) for IMRT.	IMRT revealed a lower risk incidence of ORNJ development and enhanced dose constraint than 3D-CRT. Bone surgery and dental extractions (prophylactic and post-RT) are determining factors. Most patients developing ORNJ received mean RT doses ≥ 60 Gy.
Moon et al. 2017 [26]	Retrospective Cohort Study	252 patients	Oral Cavity Cancer (OCC) and Oropharyngeal Cancer (OPC)	3D-CRT vs. IMRT	5.5% (14 out of 252 patients).	Pre-RT tooth extraction (HR: 4.52) and 3D-CRT (HR: 5.1) were significant factors for MORN. Smoking at RT (HR: 3.1) and mandibular invasion (HR: 3.7) also associated. No significant differences in dosimetric parameters (Dmax, Dmean, V40-V70) between MORN and non-MORN groups in matched cohort analysis.
Willaert et al. 2019 [27]	Retrospective, Comparative Analysis	238 LA-HNSCC patients (129 3D-CRT, 109 IMRT)	Locally Advanced HNSCC	3D-CRT vs. IMRT	14% for 3D-CRT (18 cases), 3.7% for IMRT (4 cases).	IMRT group had a significantly lower ORN incidence than 3D-CRT group. ORN lesions related to tooth extraction were 61.1% in 3D-CRT and 75% in IMRT. Dental extractions before RT (53.3% vs 55.4%) were common.
Duarte et al. 2014 [28]	Historical Cohort Study	158 HNC patients (99 RT, 59 IMRT)	Head and Neck Cancer (HNC)	IMRT vs. Conventional Radiation Therapy (RT)	Not explicitly stated for ORNJ, but general dental health compared. (Céspedes-Ajún et al. 2022 cites this study with 0% ORNJ for IMRT and 6.3% for RT)	IMRT patients had lower rates of xerostomia and mucositis. Full dental evaluation and treatment plan to eliminate disease performed pre-radiation.
Schweyen et al. 2017 [29]	Retrospective Study	776 HNC patients	Nasopharynx, oropharynx, uvula, tongue base, oral cavity, parotid gland, larynx/hypopharynx	3D-CRT or IMRT	Not explicitly stated, but 50% of ORN patients had no tooth extraction. (Céspedes-Ajún et al. 2022 cites this study with 1.16% for IMRT and 5.4% for 3D-CRT).	No significant difference in ORNJ development based on dentition classification or extent of dental treatment. Extensive dental treatment increased edentulous patients.

Buurman et al. 2022 [30]	Retrospective Cohort Study	77 OPSCC patients	Oropharyngeal Squamous Cell Carcinoma (OPSCC)	Chemoradiation (CRT)/Bioradiation (BRT)	Not explicitly stated for ORNJ, but "adverse effects of tooth extractions" are investigated.	Tooth extractions and additional interventions (OR 3.36, 95% CI 1.185–9.529) and RT dose to contralateral submandibular gland (OR 1.048, 95% CI 1.001–1.096) were associated with increased weight loss. Number of teeth removed was not a significant factor in multivariate analysis.
Lee et al. 2023 [31]	Retrospective Cohort Study	879 HNC patients	Head and Neck Cancer (HNC)	Radiotherapy (RT)	1.8% (16 out of 879 patients) for ORNJ directly from pre-RT extraction sites.	ORNJ occurred when extractions were performed an average of 4.8 days closer to RT start than healed cases. No ORNJ for extractions ≥ 15 days before RT. All 16 ORNJ cases in posterior mandible.
Treister et al. 2021 [32]	Prospective Cohort Study	572 HNC patients	Head and Neck Squamous Cell Carcinoma (HNSCC), Salivary Gland Cancer, and other head and neck malignancies	External-beam RT (at least 45 Gy), with or without chemotherapy	6.1% incidence of exposed bone by 2 years. ORNJ confirmed in 6 of 7 persistent exposed bone cases.	Risk factors for exposed bone included pre-RT extractions or hopeless teeth, primary tumor site/dose, and current tobacco use. Most exposed bone observed by 1-year follow-up.
Khoo et al. 2021 [33]	Retrospective Record Analysis	73 patients (389 teeth extracted)	Head and Neck Cancer (HNC)	Radiotherapy (RT)	21.9% prevalence of ORN post dental extraction (16 patients, 32 sockets).	Significant factors: tooth type (lower double-rooted molars), tooth pathology (periapical periodontitis related), dental extraction procedure (surgery), primary closure (no), within target volume (yes), total dose (≥ 60 Gy), timing of extraction post-RT (>1 year). Radiographic factors like bony changes (mixed radiopaque-radiolucency), invisible UCL and LCL of mandibular canal were also significant.
Maayan et al. 2021 [34]	Cross-sectional, Retrospective, Analytical Study	93 HNC patients (from 1232 screened)	Head and Neck Cancer (HNC)	Intensity-Modulated Radiation Therapy (IMRT)	7.52% (7 out of 93 patients).	ORNJ development significantly related to tumor location in the mandible (42.9% of ORN+ cases). Other co-factors (age, gender, smoking, DM, ASA score) did not significantly increase ORN risk with IMRT.
Kubota et al. 2021 [35]	Retrospective Analysis	616 HNSCC patients	HNSCC (Oropharynx, Oral Cavity, Hypopharynx, Nasopharynx, CUP)	Definitive-intent or postoperative RT (IMRT, 3D-CRT)	7.5% (46 out of 616 patients).	V60 $> 14\%$ ($p=0.0065$) and oropharyngeal/oral cancer ($p=0.0059$) were independent risk factors. Post-RT tooth extraction also significantly increased risk ($p < 0.0001$). Median Dmax for ORNJ regions was 68.5 Gy.

Corrao et al. 2023 [36]	Narrative Review	N/A	Head and Neck Cancer (HNC)	Radiotherapy (RT), IMRT, 3D-CRT	Controversial data, but generally lower with pre-RT extractions.	Performing dental extractions before RT reduces ORN risk. Higher ORN incidence with >4 extracted teeth and current smokers. Implant placement reserved for specific cases due to ORN risk.
Pereira et al. 2018 [37]	Cross-sectional Retrospective Study	413 HNC patients	Head and Neck Cancer (HNC)	Radiotherapy (RT)	9.7% (40 out of 413 patients).	Associated factors: oral mucositis (PR = 3.03), history of smoking (PR = 0.23 – protective effect after stopping), number of teeth removed before RT (PR = 1.06), and visit to dentist before RT (PR = 0.08 – protective effect). Mandible was the main site (85.0%).
Shaw et al. 2019 [38]	Randomized, Controlled, Phase 3 Study (HOPO N trial)	100 patients (47 HBO, 53 control)	N/A (implied HNC undergoing surgery)	Radiotherapy (RT) and Hyperbaric Oxygen (HBO) vs Standard Care	Not explicitly stated in the provided text as the primary endpoint.	This study evaluated the use of prophylactic HBO for preventing ORN. Patients in the HBO arm reported less swelling and bleeding post-surgery compared to the control arm.
Wahl et al. 2005 [39]	Review	9,632 patients (pooled data since 1997)	Head and Neck Cancer (HNC)	Radiotherapy (RT)	3.0% overall incidence of ORN in radiation patients since 1997.	Mandible has higher ORN incidence than maxilla, and higher after mandibular molar extractions due to less blood supply. Insufficient evidence to support prophylactic HBO for ORN prevention.
Cheng et al. 2006 [40]	Retrospective Study	1,758 NPC patients	Nasopharyngeal Carcinoma (NPC)	Radiotherapy (RT)	3.5% overall ORN of jaws, 2.7% maxillary ORN.	Post-RT tooth extraction, RT dose (80 Gy vs 70 Gy), and T-stage (T4 vs T2) were significantly associated with more severe maxillary ORN. All lesions occurred in posterior regions.
Tong et al. 1999 [41]	Retrospective Study	44 NPC patients	Nasopharyngeal Carcinoma (NPC)	Radiotherapy (RT)	1.7% (4 out of 237 sockets) developed ORN. Complicated wound healing was 6.3% (15 sockets).	Risk of ORN explained by radiation dose to bone and socket. Maxillary molars had the highest rates of healing problems (28.9%) and ORN (10.5%). One patient with pre-RT extraction (2 weeks before RT) developed ORN.
Balermipas et al. 2022 [42]	Systematic Review & Meta-analysis	7 studies (875 HNC patients)	Head and Neck Cancer (HNC)	Intensity-Modulated Radiotherapy (IMRT)	3.2% (28 out of 875 patients) suffered from ORN after IMRT. ORN was associated with extractions in 53.6% of ORN patients (8 pre-IMRT, 7 post-IMRT).	Tooth extraction before IMRT is more common than after IMRT, but not proven to reduce ORN incidence. Risk/odds for ORN favored pre-IMRT extractions (RR=0.18, OR=0.16). Extractions before IMRT must be balanced with potential delays to cancer therapy.

See Toh et al. 2018 [43]	Retrospective Study	231 NPC patients	Nasopharyngeal Carcinoma (NPC)	Intensity-Modulated Radiotherapy (IMRT)	2.6% (6 out of 231 patients).	No correlation found between dental extractions pre- or post-RT and ORN development. Smoking and increased number of pre-radiation extractions seemed prevalent in ORN patients. Median ORN onset 5 months (range 1–24 months).
Lee et al. 2012 [44]	Retrospective Chart Review	188 NPC patients	Nasopharyngeal Carcinoma (NPC)	RT or Concurrent Chemoradiation Therapy (CCRT) (IMRT introduced in 2003)	10.1% (19 out of 188 patients).	Risk of major complications (including ORN) decreased after IMRT introduction. Median latency of ORN was 83.23 months. More locoregional advanced NPC patients received CCRT.
Sulaiman et al. 2003 [45]	Retrospective Analysis	187 patients (from 1194 reviewed)	Head and Neck Cancer (HNC)	Radiotherapy (RT)	3.1-3.5% from extractions or oral surgery.	Approximately 50% of patients required post-RT extractions, mostly in the posterior region. Most pre-RT extractions (20.72%) and post-RT extractions (34.70%) were within the radiation field. There was no relationship between prolonged bone exposures and elapsed time between RT and extraction.
Beech et al. 2016 [46]	Retrospective Data & Cross-sectional Survey	190 Oropharyngeal cancer patients	Oropharyngeal Cancer	Radiotherapy (RT) and/or concurrent chemotherapy	15.3% (29 out of 190 participants).	P16-negative status (OR 9.04) and current smoking (OR 3.60) were significantly associated with ORN. 67.9% of patients had pre-RT extractions, 15.8% had post-RT extractions. Mandible was the site for 26 out of 29 ORN cases.

Table 1: Findings from the studies

Osteoradionecrosis (ORN) is a delayed complication of head and neck radiotherapy (RT) in which irradiated bone becomes hypovascular, hypocellular, and unable to heal after minor trauma [47]. The pathogenesis has evolved from Meyer's early "radiation-trauma-infection" osteomyelitis hypothesis to Marx's hypoxic-hypocellular-hypovascular model, and most recently the "radiation-induced fibro-atrophic" theory [48]. In this model, radiation causes fibroblastic dysfunction and chronic hypoxia leading to bone atrophy and necrosis. The mandible is uniquely susceptible: it is denser, more hypovascular, and more likely to lie within high-dose fields than the maxilla. Indeed, ORN almost invariably arises in the lower jaw (especially the posterior mandible), whereas maxillary ORN is rare. Multiple factors influence ORN risk. High RT dose is the strongest determinant: doses ≥ 60 –70 Gy dramatically raise ORN likelihood. Tumor-related variables (primary site, stage, proximity to bone) and treatment parameters (total dose, technique, irradiated mandibular volume, re-irradiation) are important. Patient factors – especially poor oral hygiene, existing dental disease, tobacco or alcohol use, diabetes, and xerostomia – also predispose to ORN [49]. In particular, invasive dental procedures (tooth extractions, implant placement) in irradiated bone greatly increase ORN risk. Conversely, strict prophylactic dental care has been credited with reducing ORN rates in the IMRT era. By expert consensus, a central goal of pre-RT dental evaluation is to eradicate local infectious foci and other risk factors (e.g. hopeless teeth, ill-fitting dentures) so as to minimize ORN. This typically involves extracting teeth with advanced caries or periodontitis, smoothing sharp bony edges, and instituting rigorous oral hygiene and fluoride regimens prior to RT. Clinically, ORN is associated with severe morbidity. Patients often present with non-healing mucosal ulcers, bony exposure, or fistulae, and symptoms progress to include trismus, dysesthesia, pathological fracture, and chronic infection. Pain (often neuropathic) is common, sometimes accompanied by malocclusion or difficulty in mastication and nutrition. In sum, ORN is "one of the most dreaded" long-term toxicities of head and neck RT and significantly impairs quality of life. Recent reviews report that modern ORN prevalence in head and neck cancer patients is on the order of 4–8%, down from as high as 20–50% in earlier decades, thanks to IMRT and rigorous dental care. Nevertheless, even a few percent incidence translates to substantial suffering, underscoring the need to understand and mitigate its risk factors. .

Radiation Dose:

Mandibular dose is consistently identified as the ultimate determinant of ORNJ risk. Higher doses to the mandible, especially ≥ 60 Gy, are strongly correlated with increased ORNJ risk. Specific dosimetric parameters like V60 > 14% (volume of the jaw receiving 60 Gy or more) are identified as significant independent risk factor. Modern RT techniques aim to mitigate ORNJ risk by reducing mandibular doses.

Dental Extractions in Irradiated Patients

Pre-RT dental clearance. Most guidelines recommend a thorough dental evaluation and necessary extractions before RT, to allow healing and reduce the need for post-RT surgery. In practice, teeth with advanced caries, periapical disease, or poor prognosis are removed ~10–14 days before RT. The consensus rationale is that removing infection sources (and healing sockets) prior to radiation decreases later ORN risk. However, evidence

is mixed on whether pre-RT extractions definitively reduce ORN. Retrospective data suggest that aggressive prophylactic extractions may lead to delays in cancer therapy and sometimes unnecessary tooth loss without clear ORN benefit. For example, one institutional series found that removing all questionable teeth pre-RT did not eliminate ORN cases and introduced significant overtreatment. Thus, clearance protocols vary: most aim to eliminate only symptomatic or high-risk teeth. Risk of ORN with post-RT extractions. Extraction after RT is a well-established trigger for ORN. Numerous studies (including in nasopharyngeal carcinoma [NPC] cohorts) have shown a spike in ORN when teeth are removed from irradiated bone. For instance, Yilmaz et al. found that any post-RT extraction (after CCRT for NPC) was significantly associated with ORN, especially if extractions occurred >8 months after RT [18]. Other analyses report that the majority of ORN cases follow dental extractions or invasive surgery in irradiated jaws [24]. The risk is higher the closer the extraction is to the high-dose region and when the socket is in bone exposed to ≥ 60 Gy [28]. Delaying elective extractions too long (>1–2 years post-RT) paradoxically increases risk, likely because chronic hypoxia becomes entrenched. In summary, dentists and surgeons generally treat post-RT extractions as high-risk events and take special precautions. Risk-mitigation strategies. When extraction is unavoidable, best practices are critical. Teeth should be extracted atraumatically (minimal periosteal stripping), with primary closure of the mucosa if possible to speed healing. Prophylactic antibiotics are commonly prescribed (though data are limited) to prevent secondary infection of the socket. Adjunctive hyperbaric oxygen (HBO) has long been used in Europe and the US to promote wound healing: a Cochrane review found that, for patients undergoing tooth extraction after RT, HBO (plus antibiotics) reduced ORN risk more than antibiotics alone (OR ~0.18, though evidence was “very low quality”) [47]. Nonetheless, no high-quality trials have definitively proven routine HBO prophylaxis beneficial [43]. More recently, the antifibrotic pentoxifylline–tocopherol (PENTO) regimen – developed from Delanian’s work on fibro-atrophy – has shown promise. Some centers give pentoxifylline (400 mg bid) and tocopherol before and after extraction to enhance microvascular recovery. Early case series suggest this may modestly improve socket healing, but controlled trials in NPC patients are lacking. In practice, risk-reduction focuses on meticulous surgical technique, minimizing bone removal, and optimizing systemic health (e.g. good nutrition, glucose control, and smoking cessation) around the time of extraction [33]. Incidence in NPC cohorts. Several studies of NPC survivors illustrate the tooth extraction–ORN link. Cheng et al. reported ORN in ~2–3% of irradiated jaws of NPC patients, and noted that post-RT extractions were a key precipitant [40]. Tong et al. (1999) similarly found a 1.7% ORN rate in NPC patients, mainly attributed to dental extractions in the irradiated mandible [41]. More recently, Lee et al. (2012) observed a higher 10.1% ORN incidence in a cohort of 188 NPC cases, again with most ORN occurring after tooth removal [44]. In a large Turkish series, Yilmaz et al. (2023) found an 8.7% ORN rate among 263 locally advanced NPC patients; notably, any teeth extracted after chemoradiotherapy was significantly associated with ORN onset. By contrast, See et al. found only a 2.6% ORN incidence (6/231 patients) after NPC irradiation, underscoring variability between centers [43]. Taken together, NPC-specific data suggest ORN occurs in roughly 2–10% of cases, most often following post-RT dental surgery [44].

Dental Implants in Irradiated Patients

Dental implants provide a promising option to restore dentition in head-and-neck cancer patients, but irradiation complicates osseointegration. Recent meta-analyses show that implant survival is lower in irradiated jaws than in non-irradiated controls [35]. For example, Toneatti et al. found that after ~3 years, implant survival was ~92% in irradiated patients versus ~97% in non-irradiated patients [19]. The pooled osteointegration success of implants placed in irradiated bone remains high (>90%), especially when implants are placed at least 12–18 months post-RT to allow tissue recovery. Nonetheless, even successful implants carry the risk of triggering ORN in the susceptible bone. In the same analysis, ORN developed in only ~3% of irradiated patients after implant surgery [29], indicating it is rare but serious. Risk factors. The most important implant-related risk factor is radiation dose to the implant site. A study showed that no implant failures occurred when the mean dose (D_{mean}) at the implant site was <38 Gy, whereas sites receiving >38–50 Gy had dramatically lower survival [28]. In that series, each additional Gy to the implant site increased failure hazard (HR ~1.12 per Gy) [30]. Implants in heavily irradiated posterior mandibles, which receive the highest dose, fare worse than those in spared regions. Other factors include grafted versus native bone (grafted bone had higher failure in [44]) and the interval between RT and implantation (longer waiting times tend to improve outcomes). Smoking and chemotherapy use have not shown consistent impact on implant success in these small series. Implant characteristics (length, diameter, surface) have not been shown to be major factors. In summary, high-dose irradiated bone is the dominant implant failure predictor. In irradiated jaws, implant failure may occur due to poor osseointegration, peri-implant infection, or, less commonly, ORN. When ORN does occur around implants, it often affects multiple teeth/implant sites simultaneously. By comparison, extraction-associated ORN in similar patients is often reported at 5–15%. Thus, while implant placement disrupts bone, it may paradoxically carry slightly lower ORN incidence than extractions (possibly because implants are planned restorations rather than needed extractions). Regardless, any exposed or infected implant site can progress to ORN, especially if loading is forceful or if the mucosa is ulcerated. Infectious complications are also a concern, as chronic mucositis or peri-implantitis in the irradiated mouth can be refractory. Achieving proper hygiene around implants is challenging if salivary flow is low or mouth opening is limited. Evidence specific to NPC patients. Unfortunately, no large series has focused solely on implants in NPC survivors. Available data come mostly from mixed head-and-neck cohorts (oropharynx, oral cavity, NPC, etc.) as above. We did not identify any implant studies limited to NPC in the recent literature. However, the general findings likely

apply: if an NPC patient's mandible received high-dose RT, implant candidacy must be judged carefully. Preventive measures. To mitigate implant-related ORN, similar strategies are used as for extractions. Atraumatic osteotomy techniques and primary closure of peri-implant tissues are essential. Prophylactic antibiotics before and after implant surgery are widely used, though no trials confirm optimal regimens. HBO has been advocated by some surgeons to enhance implant site healing, but a Cochrane review found no clear benefit of HBO in improving implant success or preventing ORN. Similarly, there is no consensus on using pentoxifylline/tocopherol prophylactically for implants (studies focus on treating established ORN). Ultimately, careful case selection (favoring lower-dose sites, good periodontal health, delayed placement) and meticulous technique are the cornerstones of prevention.

Comparison of Extractions vs Implants

Direct comparative data on ORN risk from extraction versus implant surgery are limited. However, retrospective series suggest that dentoalveolar surgery of any kind carries risk, with extractions historically being the most common inciting event. In irradiated NPC jaws, the literature implies that routine post-RT extractions produce more ORN cases than planned implant placements. For example, Yilmaz et al. observed that any post-CCRT tooth extraction in NPC patients was associated with a high ORN rate (32.5% in low-Hb group) [18], whereas implant-related ORN remains very uncommon (~3% across mixed cohorts). It appears that extractions, which often occur urgently and are done without prior planning in compromised sites, carry a higher absolute risk. In contrast, implants are elective and usually scheduled with maximal healing time, and only a minority of irradiated patients undergo implant surgery. Nonetheless, both interventions can precipitate ORN if done incautiously. No prospective trials compare the two directly, and NPC-specific data are lacking, so this conclusion is drawn by indirect evidence. It remains an open question whether any subgroup of NPC patients might have safer outcomes with one approach over the other. Future studies should aim to quantify ORN rates after each procedure in the same population.

Management of ORN

Once ORN develops, treatment depends on severity. Conservative measures are first-line for early or limited ORN (Notani Stage I–II) [44]. This includes meticulous oral hygiene, chlorhexidine rinses, analgesics, and systemic antibiotics for active infection. Irrigating exposed bone with saline and smoothing sharp sequestra can reduce trauma. Nutritional support and cessation of tobacco/alcohol are stressed. In small areas of exposed bone, some centers use locally applied platelet-rich plasma or bone morphogenetic protein to aid healing, though evidence is anecdotal. Surgical intervention is reserved for advanced or refractory ORN [40]. Minor surgery – such as sequestrectomy (removal of necrotic bone fragments), contouring of sharp edges, and extraction of unstable teeth – may be performed once active infection is controlled. For extensive ORN with pathologic fracture or fistula (Notani Stage III), wide resection of necrotic bone is often necessary, usually followed by reconstruction. Free-flap reconstruction (most commonly with a vascularized fibula graft) is the “workhorse” for mandibular ORN [47]. At experienced centers, up to 90% of these complex reconstructions can be successful in restoring form and function, but patient morbidity is high. Adjunct therapies have been explored. Hyperbaric oxygen (HBO) – breathing 100% O₂ at 2–2.5 ATA for 20–30 sessions – was long used prophylactically and therapeutically. However, recent evidence is disappointing. A systematic review found *no* definitive benefit for routine HBO, either in preventing ORN or in treating it conservatively [37]. Given its cost and logistic burden, HBO is now generally reserved only for selected cases (e.g. where all other options fail). Pentoxifylline–tocopherol (with or without clodronate, the so-called PENTOCLO regimen) is a newer medical treatment based on antifibrotic theory. Multiple small case series and one phase II trial have reported that this oral combination can lead to remarkable healing of longstanding ORN in some patients [48–53]. Pentoxifylline (400 mg twice daily) improves blood flow and fibroblast function, while tocopherol (vitamin E) is an antioxidant. In clinical use, many patients with moderate ORN show symptom improvement over 3–6 months of PENTO therapy. However, high-quality comparative trials are lacking, so PENTO is considered “promising” but experimental. Other pharmacologies (e.g. thalidomide, fluoride) have been used in isolated cases, but none are proven [54].

Clinical Recommendations

Based on current evidence, a multidisciplinary approach is essential. Pre-RT planning should involve oncology, dental, and surgical teams. NPC patients should receive a dental clearance protocol: remove only teeth of poor prognosis (advanced caries, severe periodontal disease, nonrestorable molars) and ensure adequate healing time (typically ≥10–14 days) before RT [48]. Informed by RT dosimetry, teeth predicted to receive very high dose (e.g. >60 Gy) might be prioritized for extraction if unstable. Restorative options (endodontic therapy, crowns) should be considered to salvage borderline teeth if delay of cancer therapy is not feasible. After RT, any new dental work should be performed with utmost care. When extractions are needed post-RT, do so with atraumatic technique and immediate primary closure if possible [45]. Antibiotic prophylaxis is often given (e.g. amoxicillin), and some clinicians use a short course of pentoxifylline/vitamin E around the time of extraction, though data are anecdotal. If implants are contemplated after NPC RT, one should ensure at least 12–18 months post-treatment, confirm adequate healing of mucosa, and ideally choose implant sites that received lower radiation dose. Hyperbaric oxygen is not routinely recommended for implant placement [48–51]; instead, focus on patient optimization and precision surgery. In all cases, patient counseling is critical: NPC survivors must understand that any dental surgery carries an ORN risk (often quoted as 2–10%) and may lead to prolonged healing or need for secondary interventions. Coordinated care is advised. For example, in a patient needing adjuvant RT, the dentist should plan

interventions well before the oncologist schedules RT. If teeth have to be extracted near the time of RT, some centers will place surgical flaps or graft membranes to speed healing. Regular follow-up for dental care and oral hygiene education is important, as patients with ORN risk benefit from quarterly exams and frequent fluoride treatments. Importantly, smoking cessation and glycemic control (in diabetics) should be emphasized, since these modifiable factors can tip the balance towards ORN.

Future Directions

The NPC-specific evidence base remains sparse. Future research should focus on prospective studies in NPC cohorts to quantify ORN incidence and outcomes after extractions or implants. Most available data bundle NPC with other oropharyngeal cancers; dedicated NPC studies would clarify whether postnasopharyngeal irradiation biology differs. The impact of newer RT modalities in NPC is also a ripe area: intensity-modulated RT (IMRT) and especially proton therapy (PT) can spare mandibular dose. Emerging data (from non-NPC series) suggest PT may halve ORN incidence compared to IMRT. Formal comparison of ORN rates in NPC patients treated with IMRT versus proton therapy would be valuable. On the dental side, innovation in implant materials and techniques could improve outcomes. For example, surface coatings (bioactive coatings, nanofibers) or growth-factor augmentation might enhance osseointegration in hypoxic bone. Customized implant planning using 3D imaging to avoid high-dose regions is already possible, but could be advanced. Similarly, development of tissue-engineering approaches (e.g. cultured bone grafts with stem cells) might eventually allow reconstructions that mitigate ORN. Crucially, controlled trials of preventive therapies are needed. The promising pentoxifylline–tocopherol strategy should be tested in randomized studies to determine if giving it around the time of RT or dental surgery can lower ORN incidence. Likewise, the utility of short courses of other agents (e.g. anti-angiogenics, bisphosphonates) in modulating radiation bone injury merits exploration. Finally, multinational registries capturing long-term dental and ORN outcomes in NPC survivors would help refine guidelines. At present, recommendations rely on extrapolation from general head-and-neck data; NPC-specific evidence could lead to tailored protocols (for instance, timing of extractions relative to the typical IMRT fields used in NPC). Summary: ORN remains a feared complication in NPC patients treated with RT. Risk is highest after post-RT tooth extractions and in high-dose mandibles, whereas implants succeed in most cases but can seldom trigger ORN. Prevention via pre-RT clearance, atraumatic surgery, and close follow-up is the cornerstone. When ORN does occur, treatment ranges from conservative care to complex reconstruction. Ongoing advances in radiotherapy, surgical technique, and adjunctive therapies may further reduce ORN incidence. Robust NPC-focused studies are needed to close the remaining gaps in evidence.

LIMITATIONS

This narrative review has several limitations. Most of the included studies were retrospective cohort studies, case series, or observational reports, which limits the ability to establish causal relationships between radiotherapy, dental extractions, dental implants, and the development of osteoradionecrosis. The included studies showed considerable heterogeneity in patient populations, tumor sites, radiation techniques, radiation dose reporting, follow-up duration, definitions of osteoradionecrosis, and preventive protocols. Although the review focused on nasopharyngeal carcinoma, many available studies included mixed head and neck cancer populations, limiting the direct applicability of some findings to NPC patients only. Because this was a narrative review, no formal meta-analysis or pooled statistical assessment was performed. Finally, variations in reporting of comorbidities, smoking status, oral hygiene, dental status, and timing of dental procedures may have influenced the interpretation of risk factors.

CONCLUSION

The ORN remains a feared complication in NPC patients treated with RT. Risk is highest after post-RT tooth extractions and in high-dose mandibles, whereas implants succeed in most cases but can seldom trigger ORN. Prevention via pre-RT clearance, atraumatic surgery, and close follow-up is the cornerstone. When ORN does occur, treatment ranges from conservative care to complex reconstruction. Ongoing advances in radiotherapy, surgical technique, and adjunctive therapies may further reduce ORN incidence. Robust NPC-focused studies are needed to close the remaining gaps in evidence.

Clinical Significance

This review highlights the importance of early dental assessment before radiotherapy, careful selection of teeth requiring extraction, avoidance of unnecessary post-radiotherapy invasive dental procedures, and close multidisciplinary follow-up involving oncologists, maxillofacial surgeons, dentists, and radiation specialists. The review also emphasizes that high mandibular radiation dose, post-radiotherapy dental extractions, poor dental condition, and systemic risk factors may increase the risk of osteoradionecrosis. Therefore, the findings can help clinicians improve preventive dental protocols, optimize the timing of extractions and implant placement, counsel patients regarding potential risks, and reduce long-term functional complications affecting speech, mastication, nutrition, pain, and quality of life.

DECLARATIONS

Ethical Consideration Statement

N/A. As the ethical committee approval was not required for this study because it was a narrative review based entirely on previously published literature.

AI Disclosure Statement

The authors declare that no artificial intelligence tools were used in the preparation, writing, analysis, interpretation, or revision of this manuscript. All content was prepared and reviewed by the authors.

Data Availability Declaration

All information discussed in this review was obtained from previously published studies cited in the reference list.

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N/A.

Author's Contribution

O.S. contributed to the conception and design of the review, literature search, data interpretation, manuscript drafting, and final approval of the manuscript. A.A. contributed to the literature review, critical revision of the manuscript, intellectual content, and final approval of the manuscript. Both authors reviewed and approved the final version of the manuscript.

REFERENCES:

1. Chow LQM (2020) Head and neck cancer. *N Engl J Med* 382:60–72. <https://doi.org/10.1056/NEJMra1715715>
2. Bray F, Ferlay J, Soerjomataram I et al (2018) Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer J Clinicians* 68:394–424. <https://doi.org/10.3322/caac.21492>
3. El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ (2017) World Health Organization classification of head and neck tumours, 4th edn. IARC, Lyon, pp 60–61, 126–127
4. Alterio D, Marvaso G, Ferrari A et al (2019) Modern radiotherapy for head and neck cancer. *Semin Oncol* 46:233–245
5. Chronopoulos A, Zarra T, Ehrenfeld M, Otto S (2018) Osteoradionecrosis of the jaws: definition, epidemiology, staging and clinical and radiological findings. A concise review. *Int Dental J* 68:22–30
6. Oh H, Chambers M, Martin J (2009) Osteoradionecrosis of the mandible: treatment outcomes and factors influencing the progress of osteoradionecrosis. *J Oral Maxillofac Surg* 67:1378–1386
7. Jacobson BD, Hu K, Urken ML (2010) Paradigm shifts in the management of osteoradionecrosis of the mandible. *Oral Oncol* 46:795–801. <https://doi.org/10.1016/J.ORALONCOLOGY.2010.08.007>
8. Reuther T, Schuster T, Mende U, Kübler AC (2003) Osteoradionecrosis of the jaws as a side effect of radiotherapy of head and neck tumour patients - a report of a thirty year retrospective review. *Int J Oral Maxillofac Surg* 32:289–295
9. Beech NM, Porceddu S, Batstone MD (2017) Radiotherapy-associated dental extractions and osteoradionecrosis. *Head Neck* 39:128–132. <https://doi.org/10.1002/hed.24553>
10. Beaumont S, Bhatia N, McDowell L et al (2021) Timing of dental extractions in patients undergoing radiotherapy and the incidence of osteoradionecrosis: a systematic review and meta-analysis. *Br J Oral Maxillofac Surg* 59:511–523
11. Epstein JB, Rea G, Wong FLW et al (1987) Osteonecrosis: study of the relationship of dental extractions in patients receiving radiotherapy. *Head Neck Surg* 10:48–54. <https://doi.org/10.1002/hed.2890100108>
12. Murray HJ, Daly TE, Zimmerman S (1980) Radiation necrosis of the mandible: a 10 year study. Part II. Dental factors; onset, duration and management of necrosis. *Int J Radiat Oncol Biol Phys* 6:549–553. [https://doi.org/10.1016/0360-3016\(80\)90381-8](https://doi.org/10.1016/0360-3016(80)90381-8)
13. Chang DT, Sandow PR, Morris CG et al (2007) Do pre-irradiation dental extractions reduce the risk of osteoradionecrosis of the mandible? *Head Neck* 29:528–536. <https://doi.org/10.1002/hed.20538>
14. Caparrotti F, Huang SH, Lu L et al (2017) Osteoradionecrosis of the mandible in patients with oropharyngeal carcinoma treated with intensity-modulated radiotherapy. *Cancer* 123:3691–3700. <https://doi.org/10.1002/cncr.30803>
15. Widmark G, Sagne S, Heikel P (1989) Osteonecrosis of the jaws. *Int J Oral Maxillofac Surg* 18:302–306
16. Willaert R, Nevens D, Laenen A et al (2019) Does intensity-modulated radiation therapy lower the risk of osteoradionecrosis of the jaw? A long-term comparative analysis. *Int J Oral Maxillofac Surg* 48:1387–1393. <https://doi.org/10.1016/j.ijom.2019.04.018>
17. Topkan E, Kucuk A, Somay E, Yilmaz B, Pehlivan B, Selek U: Review of Osteoradionecrosis of the Jaw: Radiotherapy Modality, technique, and dose as risk factors. *Journal of Clinical Medicine*. 2023, 12:3025. [10.3390/jcm12083025](https://doi.org/10.3390/jcm12083025)
18. Yilmaz B, Somay E, Topkan E, Pehlivan B, Selek U: Pre-chemoradiotherapy low hemoglobin levels indicate increased osteoradionecrosis risk in locally advanced nasopharyngeal cancer patients. *European Archives of Oto-Rhino-Laryngology*. 2023, 280:2575–84. [10.1007/s00405-023-07864-7](https://doi.org/10.1007/s00405-023-07864-7)

19. Jiang Y-M, Zhu X-D, Qu S: Incidence of osteoradionecrosis in patients who have undergone dental extraction prior to radiotherapy: A systematic review and meta-analysis. *Journal of Oral and Maxillofacial Surgery Medicine and Pathology*. 2014, 26:269–75. 10.1016/j.ajoms.2014.03.010
20. Oh H-K, Chambers MS, Garden AS, Wong P-F, Martin JW: Risk of osteoradionecrosis after extraction of impacted third molars in irradiated head and neck cancer patients. *Journal of Oral and Maxillofacial Surgery*. 2004, 62:139–44. 10.1016/j.joms.2003.08.009
21. Gomez DR, Estilo CL, Wolden SL, et al.: Correlation of osteoradionecrosis and dental events with dosimetric parameters in Intensity-Modulated Radiation therapy for Head-and-Neck Cancer. *International Journal of Radiation Oncology*Biology*Physics*. 2011, 81:e207–13. 10.1016/j.ijrobp.2011.02.003
22. Schuurhuis JM, Stokman MA, Roodenburg JLN, Reintsema H, Langendijk JA, Vissink A, Spijkervet FKL: Efficacy of routine pre-radiation dental screening and dental follow-up in head and neck oncology patients on intermediate and late radiation effects. A retrospective evaluation. *Radiotherapy and Oncology*. 2011, 101:403–9. 10.1016/j.radonc.2011.09.018
23. Koga DH, Salvajoli JV, Kowalski LP, Nishimoto IN, Alves FA: Dental extractions related to head and neck radiotherapy: ten-year experience of a single institution. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontology*. 2008, 105:e1–6. 10.1016/j.tripleo.2008.01.007
24. Abdelaziz AA, Doghish AS, Salah AN, Mansour RM, Moustafa YM, Mageed SS, Moustafa HA, El-Dakroury WA, Doghish SA, Mohammed OA, Abdel-Reheim MA. When oral health affects overall health: biofilms, dental infections, and emerging antimicrobial strategies. *Infection*. 2025 Oct;53(5):1603-24. <https://doi.org/10.1007/s15010-025-02533-9>
25. Ben-David MA, Diamante M, Radawski JD, et al.: Lack of osteoradionecrosis of the mandible after Intensity-Modulated Radiotherapy for head and Neck cancer: Likely contributions of both dental care and improved dose distributions. *International Journal of Radiation Oncology*Biology*Physics*. 2007, 68:396–402. 10.1016/j.ijrobp.2006.11.059
26. Abu-Khudir R, Doghish AS, Mansour RM, Sayed GA, Elshami NH, Moustafa HA, Elkalla WS, Abdulkader AO, Abdel Mageed SS, Mohammed OA, Hamad RS. Infection control and wound care innovations in plastic surgery: a multidisciplinary approach. *Folia Microbiologica*. 2025 Nov 18:1-20. <https://doi.org/10.1007/s12223-025-01373-2>
27. Céspedes-Ajún Ca, Amghar-Maach S, Gay-Escoda C: Incidence of mandibular osteoradionecrosis (MORN) after intensity modulated radiotherapy (IMRT) versus 3D conformal radiotherapy (3D-CRT): A systematic review. *Medicina Oral, Patología Oral Y Cirugía Bucal*. 2022, e539–49. 10.4317/medoral.25459
28. Moon DH, Moon SH, Wang K, et al.: Incidence of, and risk factors for, mandibular osteoradionecrosis in patients with oral cavity and oropharynx cancers. *Oral Oncology*. 2017, 72:98–103. 10.1016/j.oraloncology.2017.07.014
29. Salah AN, Doghish YA, Abbass SO, Mansour RM, Sayed GA, Elshami NH, Mageed SS, Mohammed OA, Abulsoud AI, Zaki MB, Mosalam EM. Microbiota-based therapies in oral health and disorders. *Folia Microbiologica*. 2025 Oct 11:1-24. <https://doi.org/10.1007/s12223-025-01324-x>
30. Willaert R, Nevens D, Laenen A, Batstone M, Politis C, Nuyts S: Does intensity-modulated radiation therapy lower the risk of osteoradionecrosis of the jaw? A long-term comparative analysis. *International Journal of Oral and Maxillofacial Surgery*. 2019, 48:1387–93. 10.1016/j.ijom.2019.04.018
31. Duarte VM, Liu YF, Rafizadeh S, Tajima T, Nabili V, Wang MB: Comparison of Dental Health of Patients with Head and Neck Cancer Receiving IMRT vs Conventional Radiation. *Otolaryngology*. 2013, 150:81–6. 10.1177/0194599813509586
32. Schweyen R, Stang A, Wienke A, Eckert A, Kuhnt T, Hey J: The influence of dental treatment on the development of osteoradionecrosis after radiotherapy by modern irradiation techniques. *Clinical Oral Investigations*. 2017, 21:2499–508. 10.1007/s00784-017-2048-8
33. Buurman DJM, Willemsen ACH, Speksnijder CM, et al.: Tooth extractions prior to chemoradiation or bioradiation are associated with weight loss during treatment for locally advanced oropharyngeal cancer. *Supportive Care in Cancer*. 2022, 30:5329–38. 10.1007/s00520-022-06942-6
34. Lee J, Hueniken K, Cuddy K, et al.: Dental extractions before radiation therapy and the risk of osteoradionecrosis in patients with head and neck cancer. *JAMA Otolaryngology–Head & Neck Surgery*. 2023, 149:1130. 10.1001/jamaoto.2023.3429
35. Treister NS, Brennan MT, Sollecito TP, et al.: Exposed bone in patients with head and neck cancer treated with radiation therapy: An analysis of the Observational Study of Dental Outcomes in Head and Neck Cancer Patients (OraRad). *Cancer*. 2021, 128:487–96. 10.1002/cncr.33948
36. Salah AN, Al-Otaibi MB, Al-dhmasi AS, Mariee AA. Infection control practices and approaches in the dentistry field; a review. *Journal of Bioscience and Applied Research*. 2024 Mar 1;10(1):42-58. 10.21608/jbaar.2024.264242.1033
37. Khoo SC, Nabil S, Fauzi AA, Yunus SSM, Ngeow WC, Ramli R: Predictors of osteoradionecrosis following irradiated tooth extraction. *Radiation Oncology*. 2021, 16:. 10.1186/s13014-021-01851-0
38. Rosenfeld E, Eid B, Masri D, Popovtzer A, Mizrachi A, Chaushu G: Is the Risk to Develop Osteoradionecrosis of the Jaws Following IMRT for Head and Neck Cancer Related to Co-Factors? *Medicina*. 2021, 57:468. 10.3390/medicina57050468

39. Kubota H, Miyawaki D, Mukumoto N, et al.: Risk factors for osteoradionecrosis of the jaw in patients with head and neck squamous cell carcinoma. *Radiation Oncology*. 2021, 16:. 10.1186/s13014-020-01701-5
40. Corrao G, Mazzola GC, Lombardi N, et al.: Oral surgery and osteoradionecrosis in patients undergoing head and neck radiation therapy: an update of the current literature. *Biomedicines*. 2023, 11:3339. 10.3390/biomedicines11123339
41. Pereira I, Firmino R, Meira H, Vasconcelos B, Noronha V, Santos V: Osteoradionecrosis prevalence and associated factors: A ten years retrospective study. *Medicina Oral, Patología Oral Y Cirugía Bucal*. 2018, 0. 10.4317/medoral.22310
42. Shaw RJ, Butterworth CJ, Silcocks P, et al.: HOPON (Hyperbaric Oxygen for the Prevention of osteoradionecrosis): A randomized controlled trial of hyperbaric oxygen to prevent osteoradionecrosis of the irradiated mandible after dentoalveolar surgery. *International Journal of Radiation Oncology*Biology*Physics*. 2019, 104:530–9. 10.1016/j.ijrobp.2019.02.044
43. Abd El-Moaty HI, Doghish AS, Moustafa HA, Elkalla WS, Sayed GA, Elshami NH, Mageed SS, Mohammed OA, Elrebehy MA, AlFarsi K, Abdelfatah AM. Phage therapy and its role in cancer treatment and control. *Folia Microbiologica*. 2025 Oct;70(5):941-60. <https://doi.org/10.1007/s12223-025-01342-9>
44. Wahl MJ: Osteoradionecrosis prevention myths. *International Journal of Radiation Oncology*Biology*Physics*. 2006, 64:661–9. 10.1016/j.ijrobp.2005.10.021
45. Cheng S-J, Lee J-J, Ting L-L, et al.: A clinical staging system and treatment guidelines for maxillary osteoradionecrosis in irradiated nasopharyngeal carcinoma patients. *International Journal of Radiation Oncology*Biology*Physics*. 2005, 64:90–7. 10.1016/j.ijrobp.2005.06.021
46. Tong AC, Leung AC, Cheng JC, Sham J: Incidence of complicated healing and osteoradionecrosis following tooth extraction in patients receiving radiotherapy for treatment of nasopharyngeal carcinoma. *Australian Dental Journal*. 1999, 44:187–94. 10.1111/j.1834-7819.1999.tb00220.x
47. Balermipas P, Van Timmeren JE, Knierim DJ, Guckenberger M, Ciernik IF: Dental extraction, intensity-modulated radiotherapy of head and neck cancer, and osteoradionecrosis. *Strahlentherapie Und Onkologie*. 2022, 198:219–28. 10.1007/s00066-021-01896-w
48. Toh YLS, Soong YL, Chim YX, Tan LT, Lye WK, Teoh KH: Dental extractions for preradiation dental clearance and incidence of osteoradionecrosis in patients with nasopharyngeal carcinoma treated with intensity-modulated radiotherapy. *Journal of Investigative and Clinical Dentistry*. 2017, 9:. 10.1111/jicd.12295
49. Lee C-C, Ho C-Y: Post-treatment late complications of nasopharyngeal carcinoma. *European Archives of Oto-Rhino-Laryngology*. 2012, 269:2401–9. 10.1007/s00405-011-1922-2
50. Sulaiman F, Huryn JM, Zlotolow IM: Dental extractions in the irradiated head and neck patient: a retrospective analysis of memorial sloan-kettering cancer center protocols, criteria, and end results. *Journal of Oral and Maxillofacial Surgery*. 2003, 61:1123–31. 10.1016/s0278-2391(03)00669-4
51. Beech NM, Porceddu S, Batstone MD: Radiotherapy-associated dental extractions and osteoradionecrosis. *Head & Neck*. 2016, 39:128–32. 10.1002/hed.24553
52. El-Rabbany M, Duchnay M, Raziee HR, Zych M, Tenenbaum H, Shah PS, Azarpazhooh A: Interventions for preventing osteoradionecrosis of the jaws in adults receiving head and neck radiotherapy. *Cochrane Library*. Published Online First: 20 November 2019. 10.1002/14651858.cd011559.pub2
53. Singh A, Huryn JM, Kronstadt KL, Yom SK, Randazzo JR, Estilo CL: Osteoradionecrosis of the jaw: A mini review. *Frontiers in Oral Health*. 2022, 3:. 10.3389/froh.2022.980786
54. Yong CW, Robinson A, Hong C: Dental evaluation prior to cancer therapy. *Frontiers in Oral Health*. 2022, 3:. 10.3389/froh.2022.876941