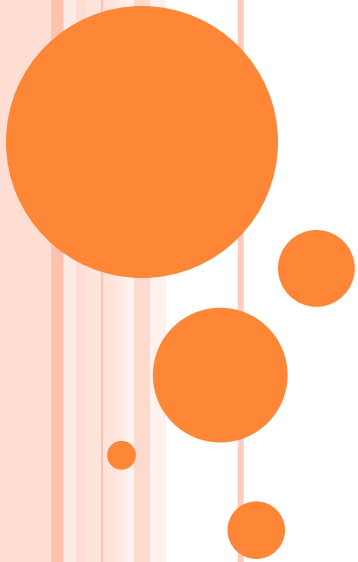


OSTEORADIONECCROSIS

Dr. Simon



- Osteoradionecrosis (ORN), also known as post radiation osteonecrosis (PRON).
- It was first described by Regaud 1920.
- A serious, debilitating and deforming potential complication of radiation therapy



Definitions of osteoradionecrosis

First author	Reference No	Definition
Beumer	6	“When bone in the radiation field was exposed for at least 2 months in the absence of local neoplastic disease”
Marx	8	“An area greater than 1 cm of exposed bone in a field of irradiation that had failed to show any evidence of healing for at least 6 months”
Hutchinson	9	“An area of exposed bone (mandible) present for longer than 2 months in a previously irradiated field, in the absence of recurrent tumour”
Epstein	7	“an ulceration of the mucous membrane with exposure of necrotic bone”
Harris	4	“Irradiated bone becomes devitalised and exposed through the overlying skin or mucosa, persisting without healing for 3 months in the absence of tumour recurrence”



RADIATION INJURY

- **An early and late phase.**
- **Early radiation injury is secondary to depletion of frequently dividing cells (Labile cells)**
- **Late radiation injury occurs in those tissues that proliferate slowly or not at all (Stable cells)**



PATHOPHYSIOLOGY OF OSTEORADIONECCROSIS

○ **Meyer** in 1970 –

Triad of radiation, trauma, and infection
- development of osteoradionecrosis.

○ **Irradiated bone +**

Traumatic event +

Ingress of microorganisms =

Osteoradionecrosis



- **Failure to demonstrate bacterial invasion in compromised bone,**
- **Occurrence with no definable traumatic event,**
- **Poor response to treatment with antibiotic therapy .**

..... Forced to think in another way



PATHOPHYSIOLOGY OF OSTEORADIONECROSIS

○ **Marx** 1983

Osteoradionecrosis - cumulative tissue damage induced by radiation rather than trauma or bacterial invasion of bone.

Complex metabolic and tissue homeostatic deficiency seen in **hypocellular, **h**ypovascular, and **h**ypoxic tissue.**

Three "H" principle.



THREE "H" PRINCIPLE

- Radiation damaged cells not replaced by cells of the same type
- Results in less cellular, more extracellular elements – collagen.
- Fibrotic and poorly vascularized tissue – absent healing ability.
- Absent cellular turnover

Spontaneous breakdown.



EFFECTS OF RADIATION ON BONE

- **Depletion of osteoblasts - Increased osteoclastic resorption of bone**

Reduced bone rebuilding potential

+

- **Progressive endarteritis - reduction of blood flow through the Haversian and Volkmann's canals**

=

OSTEOPOROSIS



OSTEONECROSIS



RADIATION-INDUCED FIBROATROPHIC THEORY

- key event in the progression of ORN is the **activation and dysregulation** of fibroblastic activity that leads to atrophic tissue within a previously irradiated area.



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Surgery

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Review

Osteoradionecrosis of the jaws: current understanding of its pathophysiology and treatment

Andrew Lyons^{a,*}, Naseem Ghazali^b

OSTEORADIONECCROSIS

In the head and neck region

- **Commonest site is mandible.**
- **Also reported in maxilla, temporal bone, sphenoid and base of skull.**



WHY MANDIBLE AT AN INCREASED RISK?

- Generally a bone – with **more tenuous blood supply** and **more mechanically stress** - more susceptible to the development of osteoradionecrosis.
- The craniofacial skeleton receives its blood supply in three distinct manners:
 1. vessels that enter the bone via direct muscular attachments,
 2. periosteal perforators, and
 3. intramedullary vessels



WHY MANDIBLE AT AN INCREASED RISK?

- Mandible - different dominant pattern of blood supply according to various anatomical regions in the bone itself.
- The **posterior segment** of the mandible (condyle process and neck, coronoid, angle, and upper ramus) - **redundant blood supply** from the surrounding musculature, either from direct muscular attachments or through muscular perforators penetrating the periosteum.
- Because of this redundancy, the posterior segment is typically less susceptible to radiation induced ischemia.



- **The anterior segment of the mandible - no prominent nutrient vessel supply through the muscular attachments.**
- **Injection studies in the mandible - primary nutrient source for the body, parasymphyseal, and symphyseal regions is through an intramedullary source, the inferior alveolar artery.**
- **In a study by Bras, et. al., radiation induced obliteration of the inferior alveolar artery was consistently found in osteoradionecrosis of mandible and was felt to be a dominant factor in the onset of the disease.**

INCIDENCE OF OSTEORADIONECROSIS

- The overall incidence of ORN in pooled studies among radiation patients has dramatically declined.

11.8% (391 of 3,312 patients) **before 1968**



5.4% (602 of 11,077 patients) from **1968 to 1992**
due to more efficient techniques in radiation
therapy.

Clayman L. Management of dental extractions in irradiated jaws: A protocol without hyperbaric oxygen therapy. *J Oral Maxillofac Surg* 1997;55:275–281.



TYPES OF OSTEORADIONECCROSIS

- **SPONTANEOUS ORN (39%)** – degradative function exceeds new bone production.
- **TRAUMA INDUCED ORN (61%)** – reparative capacity of bone is insufficient to overcome an insult.
- Bone injury can occur through direct trauma -
 1. tooth extraction [84%],
 2. related cancer surgery or biopsy [12%],
 3. denture irritation [1%]) or
 4. by exposure of the oral cavity to the environment secondary to overlying soft tissue necrosis.

[Remy H Blanchaert, Jr, MD, DDS](#), Osteoradionecrosis of the Mandible
[eMedicine Specialties > Otolaryngology and Facial Plastic Surgery > Head](#)
[And Neck Oncology](#)



CLASSIFICATION OF OSTEORADIONECCROSIS

○ By Marx(1983)

Type I – Develops shortly after radiation,
Due to synergistic effects of surgical
trauma and radiation injury.

Type II – Develops years after radiation and follows a trauma
Rarely occurs before 2 year after treatment &
commonly occurs after 6 years.
Due to progressive endarteritis and vascular effusion.



- **Type III**


**Occurs spontaneously without a preceding a traumatic event.
Usually occurs between 6 months and 3 years after radiation.
Due to immediate cellular damage and death due to radiation
treatment.**



Osteoradionecrosis:

Clinical Experience and a Proposal for Classification

JOEL B. EPSTEIN, DMD, MSD,* FRANCES L. W. WONG, BSc, MD, FRCP(C),† AND
P. STEVENSON-MOORE, BDS, MSD, MRCD(C)‡

- **Stage I** – Resolved healed osteonecrosis
 - (A) – No pathologic fracture
 - (B) – Pathologic fracture
 - **Stage II** – Chronic persistent and non-progressive osteonecrosis
 - (A) – No pathologic fracture
 - (B) – Pathologic fracture
 - **Stage III** – Active progressive osteonecrosis
 - (A) – No pathologic fracture
 - (B) – Pathologic fracture
- 

- grade I, ORN confined to alveolar bone;
- grade II, ORN limited to the alveolar bone and/or mandible above the level of inferior alveolar canal;
- grade III, ORN involving the mandible below the level of inferior alveolar canal and ORN with a skin fistula and/or pathologic fracture.

Notani K, Yamazaki Y, Kitada H, Sakakibara N, Fukuda H, Omori K, Nakamura M. Management of mandibular osteroradionecrosis corresponding to the severity of osteoradionecrosis and the method of radiotherapy. *Head Neck* 2003; 25: 181–186.



Contributing factors of osteoradionecrosis

- **Radiation factors**
- **Tumor factors**
- **Dental factors**
- **Others**



RADIATION FACTORS

- Mechanism of radiation delivery – impact on the development and severity of necrosis.
- Brachytherapy implants have the greatest relative risk in combination with external beam exposures of 6500 cGy (12 - 15 times).

Sanger JR, Matloub HS, Yousif NJ, Larson DL. Management of Osteoradionecrosis of the Mandible. Clinics in Plastic Surgery. 20(3): pg 520. 1993.



TUMOR FACTORS

- Statistically significant incidence of osteoradionecrosis with
 1. more advanced tumors (stage III or IV)
 2. recurrent tumors
 3. tumors involving the tongue, retromolar trigone, and floor of mouth, and
 4. tumors invading bone

Kuluth EV, Jain PR, Stutchell RN, Frich JC. A Study of Factors Contributing to the Development of Osteoradionecrosis of the Jaws. The Journal of Prosthetic Dentistry. 59 (2): pg 200. 1988.



DENTAL FACTORS

- **Presence of carious and periodontally compromised teeth in the irradiated mandible - associated with osteoradionecrosis.**
- **The current school of thought - grossly carious, periodontally "hopeless," or those teeth deemed to have poor prognosis for retention beyond twelve months should be removed prior to the initiation of radiation therapy - this avoids dental manipulations in the post irradiation period.**

Clayman L. Management of Dental Extractions in Irradiated Jaws: A Protocol Without Hyperbaric Oxygen Therapy. Journal of Oral and Maxillofacial Surgery. 55: pg 275. 1997.

DENTAL FACTORS

- **The post surgical healing time prior to starting radiation treatment -under debate.**
- **Marx and Johnson - compared the incidence of osteoradionecrosis in pre-treatment tooth removal patients to the timing of the surgical insult.**
- **From their collected data, most of the osteoradionecrosis developed - in those patents in which treatment was begun within the first two weeks post extraction.**
- **No cases of osteoradionecrosis, when the tissue was allowed to heal for 21 days or more.**


Marx RE, Johnson RP. Studies in the Radiobiology of Osteoradionecrosis and Their Clinical Significance. Oral Surgery Oral Medicine Oral Pathology. 64 (4): pg 384. 1987.

SIGNS AND SYMPTOMS

- **Pain**
- **Swelling**
- **Trismus**
- **Halitosis**
- **Food impaction in the area of the lesion**
- **Exposed bone**
- **Pathologic fracture**
- **Oro-cutaneous fistula**



EVALUATION OF OSTEORADIONECCROSIS

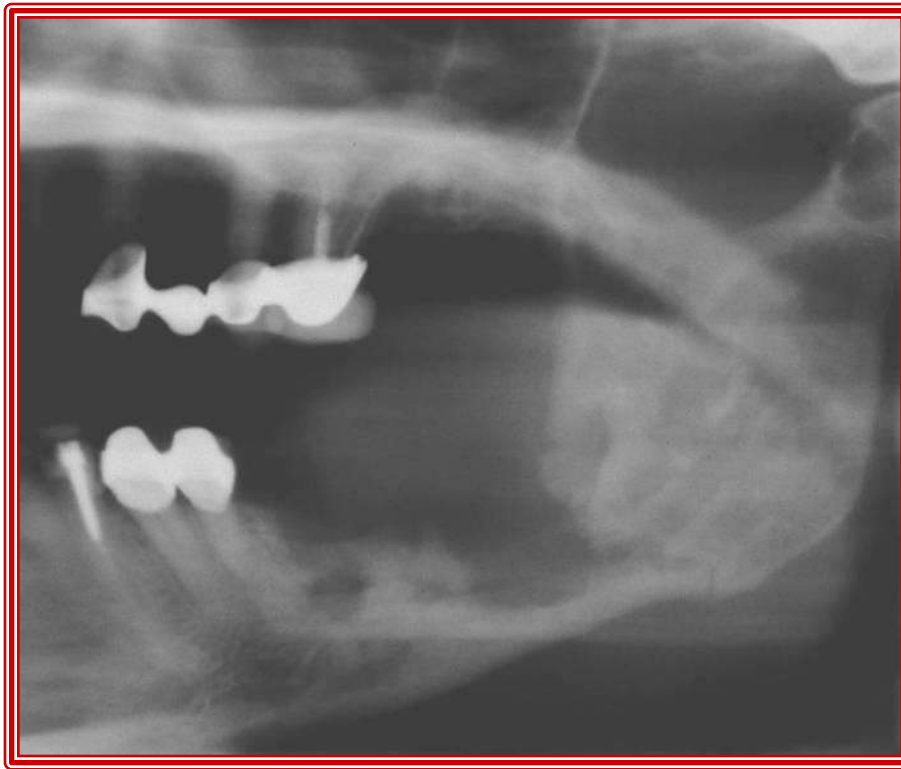
- **A high index of suspicion that this presentation may be recurrent, or persistent, or even metastatic malignancy.**
 - **Deep biopsy of the lesion is helpful**
 - **Review of the pertinent radiation therapy records including the ports of radiation therapy, the total dose, dose per fraction, and timing of therapy.**
 - **A thorough dental examination - in those patients with remaining dentition.**
- 

IMAGING STUDIES

- **Plain radiography of the mandible - depicts areas of local decalcification or sclerosis.**
- **The formation of sequestra or involucra occur late or not at all in irradiated bone because of the severely compromised blood supply.**



PATHOLOGIC FRACTURE



MANAGEMENT OF OSTEORADIONECROSIS

- **Initial treatment – control of infection if present.**
- **Gentle irrigation of the soft tissue margins - removes debris and reduces inflammation.**
- **Supportive treatment with fluids and a liquid or semi liquid diet high in proteins and vitamins.**




HYPERBARIC OXYGEN THERAPY

- The basic mechanism of hyperbaric oxygen therapy is endothelial cell proliferation resulting in neovascularisation and collagen synthesis.**
- It consists of exposing a patient to intermittent short term 100% oxygen inhalation at a pressure greater than 1 atmosphere.**



HYPERBARIC OXYGEN THERAPY

- Marx (1983) presented a new concept in osteoradionecrosis management - **Marx HBO / surgical protocol.**
- The compromised bone and soft tissues are improved and revascularised with HBO and then if necessary, the necrotic bone is surgically removed.
- The patient's response or lack of response to HBO is the main indicator for surgery.
- The primary thrust is to distinguish dead bone from merely compromised bone and to surgically resect all dead bone. 

CONTRAINDICATIONS FOR HBO THERAPY

- 1. Untreated pneumothorax - (Absolute contraindication)**
- 2. Pregnancy**
- 3. Emphysema**
- 4. Upper respiratory tract infection**
- 5. Uncontrollable fever**
- 6. Optic neuritis**
- 7. Ear problems**



Osteoradionecrosis of the Mandible: Treatment Outcomes and Factors Influencing the Progress of Osteoradionecrosis

Hee-Kyun Ob, MS, PhD, Mark S. Chambers, DMD, MS,†
Jack W. Martin, DDS, MS,‡ Hoi-Jeong Lim, PhD,§ and
Hong-Ju Park, MS, PhD||*

Purpose: The present study was undertaken to evaluate our recent experience with mandibular osteoradionecrosis (ORN) and to identify factors that contribute to its progress.

Patients and Methods: The medical records of 114 patients who had been treated for ORN during a 16-year period (1989 to 2004) were reviewed. The patients were then divided into 2 groups according to their response to conservative treatment. Group 1 consisted of patients whose ORN resolved with conservative treatment (n = 47). Group 2 consisted of patients whose ORN was unresolved with conservative treatment or who had required radical resection of the involved tissue (n = 67). The information was obtained from the medical records of the patients and analyzed.

Results: The patients whose ORN was associated with an early-stage tumor or preirradiation extraction had a favorable response to conservative treatment. However, those who had an advanced primary tumor, had continued smoking and drinking after radiotherapy, had received palliative radiotherapy or a radiation dose of more than 6,000 rads, and who had an orocutaneous fistula, a pathologic fracture, swelling, or trismus had a poor response to conservative treatment. In these latter cases, radical resection of the involved tissue proved useful.

Conclusions: The results of the present study have indicated that several factors (ie, the stage of the primary tumor, signs of ORN) can influence the progress of ORN. Our results suggest that radical resection is a useful method for treating mandibular ORN that does not respond to conservative treatment.

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J Oral Maxillofac Surg 67:1378-1386, 2009



Quality of life in osteoradionecrosis patients after mandible primary reconstruction with free fibula flap

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Objectives. To evaluate the quality-of-life outcomes in osteoradionecrosis patients undergoing primary mandible reconstruction with free fibula flap, and to analyze the association between quality of life and demographic and medical characteristics of osteoradionecrosis patients.


Study design. Quality-of-life outcomes of 15 patients after primary mandible reconstruction with free fibula flap for osteoradionecrosis were assessed using a modified University of Washington Quality of Life Questionnaire, version 4.

Results. The best-scoring domain was pain, whereas the lowest scores occurred in chewing, swallowing, speech, and saliva. More than 70% of patients perceived improved health-related quality of life after reconstruction. Men scored significantly higher than women in speech domain, recreation domain, activity domain, and “social function.” The time elapsed from radiotherapy was significantly and negatively correlated with the score of speech, recreation, and global question.

Conclusion. Mandible reconstruction with fibula flap effectively eliminates pain and controls local infection even though radiotherapy-induced complications still influence the quality of life of osteoradionecrosis patients. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:162-168)



PREVENTION OF OSTEORADIONECROSIS

- **Prior to radiation therapy- Dental consultation - To achieve optimal oral health.**
 - **Sleeper (1950) and Meyer (1958) - recommendations before irradiation is started.**
 - 1. The mouth should be made as clean as possible by scaling and irrigation.**
 - 2. All infections of soft tissues should be eliminated.**
 - 3. All infected and non-vital teeth should be extracted. All teeth in the line of irradiation, good or bad, also should be extracted.**
- 

PREVENTION OF OSTEORADIONECROSIS


4. All teeth periodontally involved should be extracted.
5. If the parotid and submandibular glands are to receive heavy irradiation, all teeth should be extracted.
6. If the mouth shows much neglect throughout, all teeth should be extracted.
7. The use of antibiotic prophylaxis b4 extraction, though common practise, has not been validated in any study. However, prophylaxis could be incorporated into the protocol if desired.

PREVENTION OF OSTEORADIONECROSIS

- 8. The patient should be thoroughly instructed in the maintenance of absolute hygienic care of the mouth.**
- 9. Fluoride therapy should be used to prevent irradiation caries of any remaining teeth.**
- 10. No radiotherapy should be attempted for 7-10 days following extractions in the mandible or for 3-6 days in the maxilla. If possible the radiation should start only 21 days after the tooth extractions.**



Instructions after radiotherapy of the jaws

- 1. Strict oral hygiene.**
 - 2. If future work on the teeth or an operation - patients must inform the physician or dentist that their jaws have been previously irradiated.**
 - 3. Preferably no further extractions. If a tooth in the area of irradiation becomes caries - extraction must be done as atraumatically as possible under a course of antibiotics both preoperatively and postoperatively.**
 - 4. Dentures should not be used in the irradiated arch for one year after therapy.**
- 

OSTEORADIONECCROSIS OF THE TEMPORAL BONE

- Following the treatment of nasopharyngeal carcinoma by external-beam radiotherapy.
- **Ramsden** et al classified osteoradionecrosis of the temporal bone as either local or diffuse.
- The local type is characterized by the presence of a bone sequestrum that is confined to the external auditory canal.
- Patients usually present with chronic, offensive otorrhea and occasionally otalgia.



OSTEORADIONECCROSIS OF THE TEMPORAL BONE

- **In the diffuse type - widespread ischemic osteonecrosis of the skull base and adjacent structures.**
- **These patients have usually received higher doses of external irradiation to the temporal bone.**
- **Severe otalgia and pulsatile, offensive otorrhea are common. Cranial nerve palsies might also be present.**
- **Diffuse osteoradionecrosis is associated with a recognized incidence of local or regional complications, such as suppurative labyrinthitis, trismus, meningitis, cerebrospinal fluid leakage, and internal carotid aneurysm.**

MANAGEMENT OF OSTEORADIONECCROSIS IN THE TEMPORAL BONE

- **Controversial.**
- **For localized osteoradionecrosis - Conservative treatment with frequent aural toileting and topical antibiotics.**
- **Rudge** described complete success with the use of hyperbaric oxygen therapy specifically for osteoradionecrosis of the temporal bone.



MANAGEMENT OF OSTEORADIONECSIS IN THE TEMPORAL BONE

- **Other alternatives, such as modified radical mastoidectomy, have been performed in selected cases with good initial results, but no long-term follow up is available to validate this choice of treatment.**
- **Temporal bone resection for diffuse osteoradionecrosis is reported to be an effective treatment.**



BISPHOSPHONATE RELATED OSTEONECROSIS OF THE JAW

- **First recognized in 2003 as a complication of bisphosphonate therapy**
- **Higher frequency in the mandible (63%) than in the maxilla (38%)**
- **Etiology is unclear and is the subject of current research and investigation.**



BISPHOSPHONATE RELATED OSTEONECROSIS OF THE JAW

- **True incidence is difficult to estimate.**
- **Depending on recent retrospective reports could be <1%-9% of cancer patients receiving bisphosphonates.**
- **Seen in cancer patients with multiple antineoplastic medications as well as bisphosphonates.**
- **Multiple myeloma, breast cancer and prostate cancer are the primary neoplasms affected.**



BISPHOSPHONATE RELATED OSTEONECROSIS OF THE JAW

- **Current management is empiric.**
- **A conservative approach is recommended - includes antibiotics, oral rinses, pain control, and limited debridement.**
- **The roles of surgical treatment and hyperbaric oxygen therapy are still under investigation.**



CONCLUSION

- **The aim should be its prevention.**
- **An understanding of the risk factors is important in preventing ORN after radiation therapy.**



THANK YOU