# Objectives:

- History and timeline of bisphosphonate related osteonecrosis of the jaws (BRONJ) as a complication of bisphosphonate therapy.

- Understand the possible mechanisms of action, benefits and risks of bisphosphonate therapy.

- Define osteonecrosis of the jaws, incidence and factors associated with development of BRONJ.

- Know the typical clinical presentation, signs, symptoms, radiographic features and course, of BRONJ.

- Recommendations on Dental Management of Patients Receiving Bisphosphonate Therapy

# History of Bisphosphonates

19th Century: Match factory workers developed "phossy jaw."
Caused by exposure to white phosphorus

## PHOSSY JAW.

### MESSRS. BRYANT AND MAY AT WORSHIP STREET.

### SEVENTEEN CASES OF PHOSPHORUS POISONING NOT REPORTED.

### THE FULL PENALTY INFLICTED.

**[Special to "The Daily Chronicle."]**

Yesterday afternoon, Mr. Corser heard, at Worship-street Police-court, the summonses against Messrs. Bryant and May, Limited, for not reporting cases of phosphorus poisoning which had occurred at their works in East London. Messrs. Bryant and May were not represented by counsel, and their managing director, Mr. Gilbert Bartholemew, admitted the offences with which the firm were charged.

# History of Bisphosphonates

Bisphosphonates and their pyrophosphate analogs:

Have been used in chemical industry since 1900

Used for Anticorrosive and Antiscaling agents

Have the ability to inhibit formation of calcium deposits on various surfaces

# History of Bisphosphonates

1960's that these agents were first considered for medical treatment.

Fleisch et al first reported on the ability of diphosphonate to:

- Inhibit hydroxyapatite dissolution in vitro
- Inhibit bone resorption in tissue culture and in vivo.

This was followed by a companion article in the same issue of *Science by Francis et al*, where diphosphonates were shown to inhibit the formation of calcium phosphate crystals in vitro and pathologic calcifications in vivo.

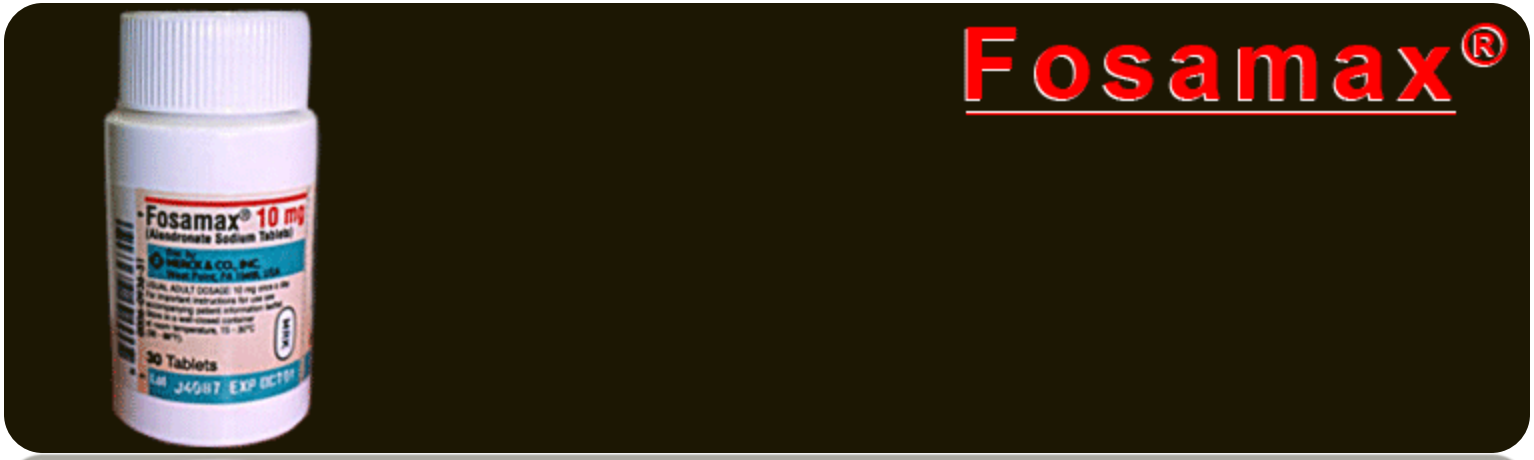
# History of Bisphosphonates

These findings set the foundation for the future use of bisphosphonates for the treatment of a spectrum of disorders related to perturbations in bone remodeling and osteoclast function

# Timeline of BRONJ

Sept. 29, 1995: The FDA approves bisphosphonate drug Fosamax (alendronate sodium) for the treatment of post-menopausal osteoporosis and Paget's disease.

1995: FDA approves Pamidronate ( Aredia) for the treatment of osteolytic metastasis



# Timeline of BRONJ

2001: Oral surgeon Salvatore Ruggiero notices that an unusual number of his patients have osteonecrosis of the jaw.

2002: Submitted his reports to MedWatch

# Timeline of BRONJ

Summer 2003: Robert Marx at the University of Miami, had 36 cases of osteonecrosis of the jaw that he suspected were linked to Aredia and Zometa

Sept. 2003: Marx's article is published in the Journal of Oral and Maxillofacial Surgery **J. 2003 Sep; 61(9):1115-7**

Dec. 2003: By this time, Dr. Ruggiero has 54 patients with osteonecrosis of the jaw. **J Oral Maxillofac Surg. 2004 May;62(5):527-34. Ruggiero SL, Mehrotra B, Rosenberg TJ, Engroff SL.**

# Timeline of BRONJ

Aug. 25, 2004: The FDA reviews new cases of osteonecrosis and recommends labels be changed to warn patients about the risk of osteonecrosis of the jaw.

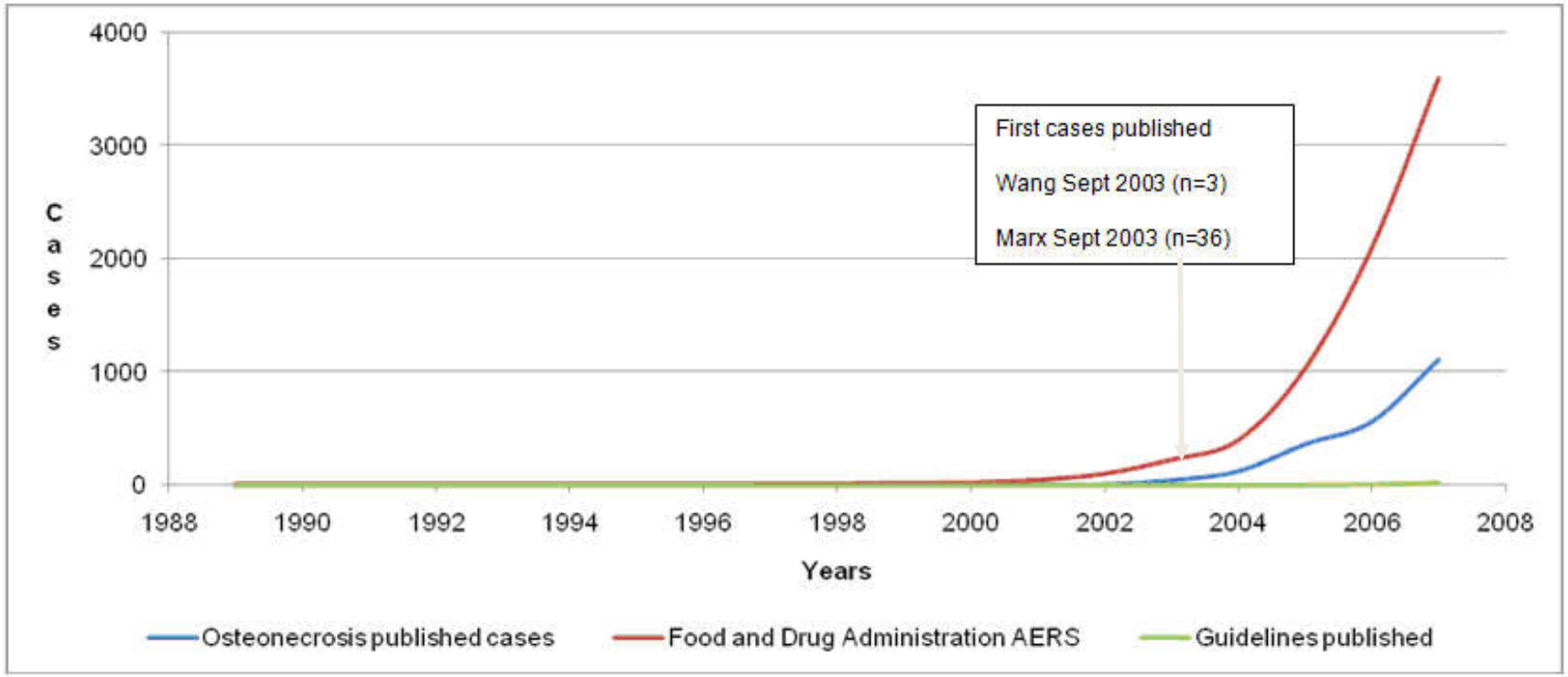
Sept. 2004: By this time, Novartis has received 500 reports.

July 2005: Almost a year after the FDA recommended they do so, Merck adds a warning to Fosamax .

April 2006: Linda Secrest files a class action lawsuit in Florida against Merck for not warning patients about the risk of osteonecrosis of the jaw in patients taking Fosamax. Hundreds of similar lawsuits have since been filed.

# Timeline of BRONJ

**Timeline of Cumulative Cases of Osteonecrosis of the Jaw**




FDA AERS = bisphosphonate associated ONJ logged into the FDA's Adverse Event Reporting System

Published cases= peer review publications

**Pamidronate (Aredia) and zoledronate (Zometa) induced avascular necrosis of the jaws: a growing epidemic.**
**J Oral Maxillofac Surg. 2003 Sep;61(9):1115-7. Marx**

**Osteonecrosis of the jaws associated with the use of bisphosphonates: a review of 63 cases.**
**J Oral Maxillofac Surg. 2004 May;62(5):527-34. Ruggiero SL, Mehrotra B, Rosenberg TJ, Engroff SL.**

**Osteonecrosis of the jaw associated with zoledronate therapy in patient with multiple myeloma.**
**Br J Haematol. 2005 Mar;128(6):738. Vannucchi AM, Ficarra G, Antonioli E, Bosi A.**

# Timeline of BRONJ

Latest PubMed search produced 1473 articles on Bisphosphonate Related Osteonecrosis of the Jaw. (BRONJ)

## Bisphosphonate-induced osteonecrosis of the jaw: a review of 2,400 patient cases.
## J Cancer Res Clin Oncol. 2010 Aug;136(8):1117-24

- METHODS: A PubMed-based review of all of the described cases of BRONJ from January 2003 (the year of the first description) to September 2009. Issues of clinical relevance, such as the primary diagnosis and type of treatment, were evaluated for each patient case.

- RESULTS: 2,408 cases, 88% of which were associated with intravenous therapy, primarily with zoledronate. Of the total number of cases, 89% were associated with the treatment of a malignant condition, particularly multiple myeloma (43% of the cases). Of all the BRONJ cases, 67% were preceded by tooth extraction and only 35% of patients were cured.

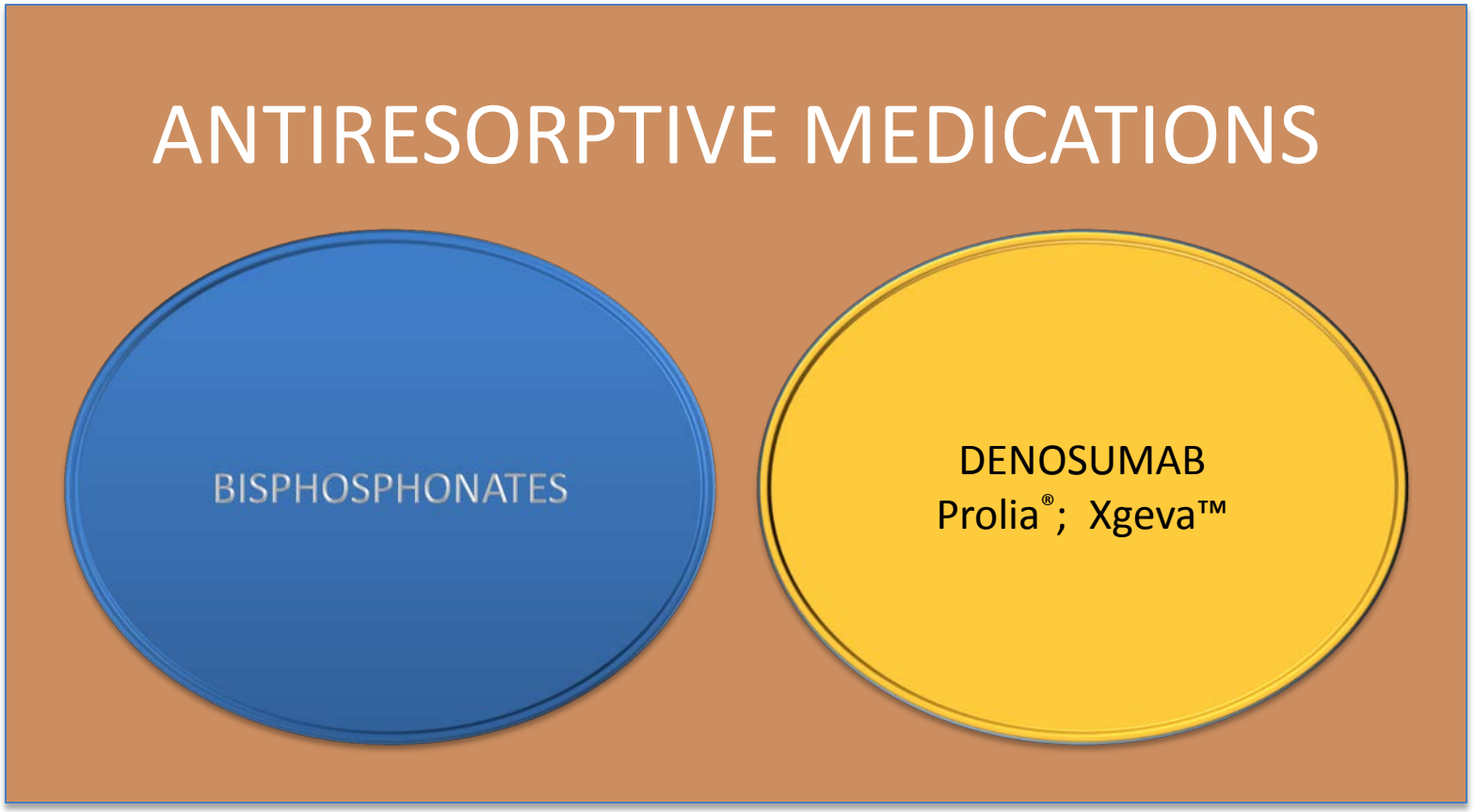
- CONCLUSION: Prevention is better than treatment, and the establishment of meticulous oral hygiene and surgical procedures prior to commencing BP treatment is important for preventing BRONJ.

# What are Bisphosphonates ?

## ANTIRESORPTIVE MEDICATIONS

Osteoporosis
Osteitis deformans (Paget's disease)
Bone metastasis
Multiple myeloma
Primary hyperparathyroidism
Osteogenesis imperfecta

# What are Bisphosphonates ?



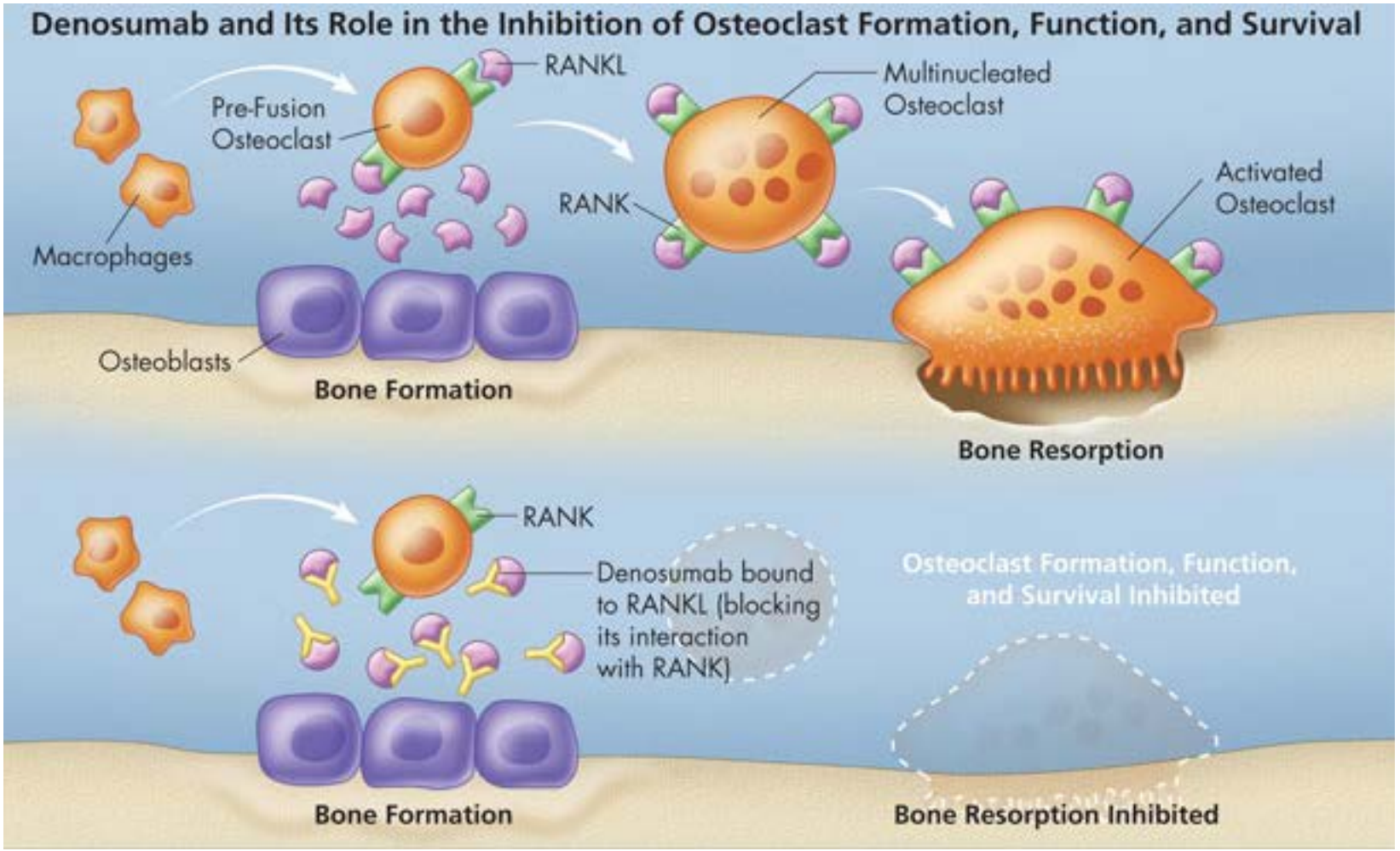
# What are Bisphosphonates ?

**Toxicity comparison for bisphosphonates versus denosumab**

| | Denosumab | Bisphosphonates |
|---|---|---|
| Route of administration | Subcutaneous | Intravenous |
| Osteonecrosis of the jaw | X | X |
| Hypocalcemia | X | X |
| Nephrotoxicity | | X |
| Renal elimination/need for dose adjustment in renal insufficiency | | X |
| Flu-like symptoms (acute-phase reaction) | | X |
| Bone, joint, muscle pain | | X |

Saad F et. al. Ann Oncol 2011

# Denosumab


Denosumab and Its Role in the Inhibition of Osteoclast Formation, Function, and Survival
RANKL
Pre-Fusion Osteoclast
Macrophages
Osteoblasts
Bone Formation
RANK
Multinucleated Osteoclast
Activated Osteoclast
Bone Resorption
RANK
Denosumab bound to RANKL (blocking its interaction with RANK)
Bone Formation
Osteoclast Formation, Function, and Survival Inhibited
Bone Resorption Inhibited

# What are Bisphosphonates ?

- Inhibit osteoclasts
    - Decreased bone turn-over
- Reduce apoptosis in osteoblasts (minor role)
- Reduced mineralization (negative effect and so Etidronate is not used for osteoporosis)
- Direct anticancer effect
    - Induce apoptosis
    - Disrupt cellular adhesion, migration, invasion

# What are Bisphosphonates ?

| Simple bisphosphonates |
| --- |
| Etidronate |
| Tiludronate |
| Clodronate |
| **Nitrogen-containing bisphosphonates** |
| Pamidronate |
| Alendronate |
| Neridronate |
| Ibandronate |
| Risedronate |
| Zoledronic acid |

Metabolized by osteoclasts to metabolites that exchange with the terminal pyrophosphate moiety of ATP, resulting in an ATP that cannot be used as a source of energy. The osteoclasts then undergo apoptosis

- inhibiting the enzyme farnesyl pyrophosphate (FPP) synthase.
- Inhibition of FPP creates cytoskeletal abnormalities in the osteoclast, promotes detachment of the osteoclast from the bone perimeter

# Bisphosphonate Potency

| Simple bisphosphonates |
| --- |
| Etidronate |
| Tiludronate |
| Clodronate |
| **Nitrogen-containing bisphosphonates** |
| Pamidronate |
| Alendronate |
| Neridronate |
| Ibandronate |
| Risedronate |
| Zoledronic acid |

UpToDate

In order of increasing potency

# Bisphosphonates

| | Osteoporosis | Paget's disease of bone | Osteolytic lesions of Myeloma | Osteolytic lesions of Metastasis | Hypercal-cemia of Malignancy |
|---|---|---|---|---|---|
| **Pamidronate (Aredia)** | | x | x | x | x |
| **Zoledronate (Zometa)** | | | x | x | x |
| **Etidronate (Dicronel)** | | x | | | x |
| **Tiludronate (Skelid)** | | x | | | |
| **Alendronate (Fosamax)** | x | x | | | |
| **Risedronate (Actonel)** | x | x | | | |

# Clinical Benefit of Bisphosphonates for Cancer Patients with Metastatic Bone Disease

# Metastatic Bone Disease: Scope of the Problem

- **Extremely common - > 500,000 patients in USA**
  - **Myeloma - > 90%**
  - **Breast - two thirds of patients**
  - **Prostate - two thirds of patients**
  - **Lung - one third of patients**

- **Median survival measured in years, not weeks or months**

- **Major clinical consequences for patients, families, and society**

# Clinical Consequences of Metastatic Bone Disease †

| | % of patients/yr |
|---|---|
| Pathologic fractures | 10 - 25 |
| Spinal cord compression/collapse | 3 - 5 |
| Radiation therapy | 15 - 20 |
| Surgery to bone | 5 - 10 |
| Hypercalcemia | 2 - 10 |
| Bone pain | 50 |
| Use of analgesics | 40 |

SREs = Skeletal-related events.

† From placebo arms of randomized clinical trials with Aredia® or Zometa®.

# Bisphosphonates - BENEFIT

| | % with SRE | | | # SRE per yr | | |
|---|---|---|---|---|---|---|
| | Placebo | BP | %↓ † | Placebo | BP | %↓ |
| Prostate (Saad et al.) | 49 | Z-38 | 22* | 1.5 | 0.7 | 47* |
| Breast (Hortobagyi et al.) | 64 | A-51 | 20* | 3.7 | 2.4 | 35* |
| (Kohno et al.) | 50 | Z-30 | 40* | 1.42 | 0.7 | 50* |
| Myeloma (Berenson et al.) | 51 | A-38 | 26* | 2.0 | 1.0 | 50* |
| Others (Rosen et al.) | 46 | Z-39 | 15 | 2.7 | 1.7 | 37* |

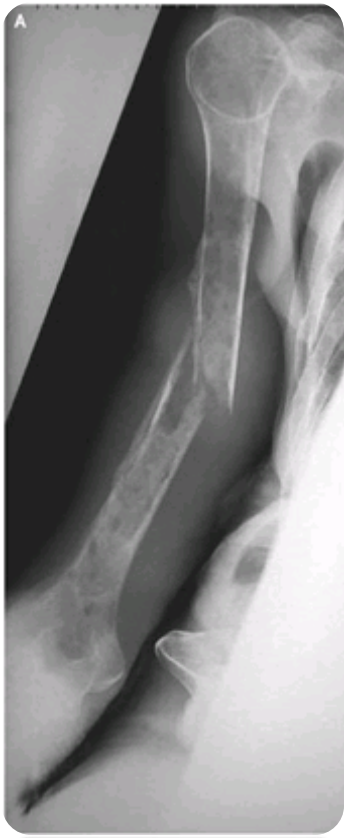
*Aredia® : Breast cancer and myeloma with lytic lesions, Ineffective in prostate cancer*
*Zometa® : Breast cancer, myeloma, and prostate cancer*

* $P < 0.05$; † Relative decrease

# IV Bisphosphonates for Patients With Metastatic Bone Disease—Benefits vs Risks

## Benefits

- ↓ Fractures
- ↓ Radiotherapy
- ↓ Bone pain



Humeral fracture in a myeloma patient

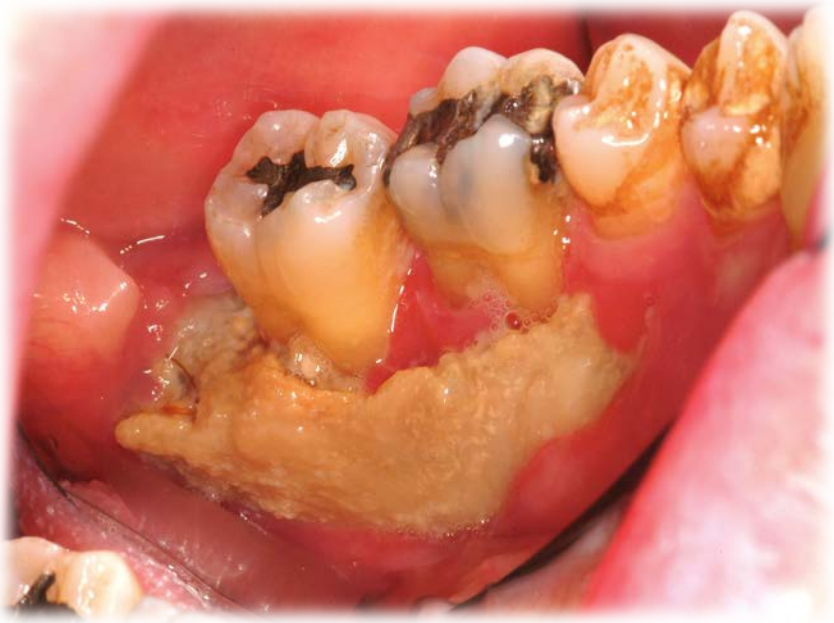
## Risks

**ONJ ?**

**Renal (infrequent)**

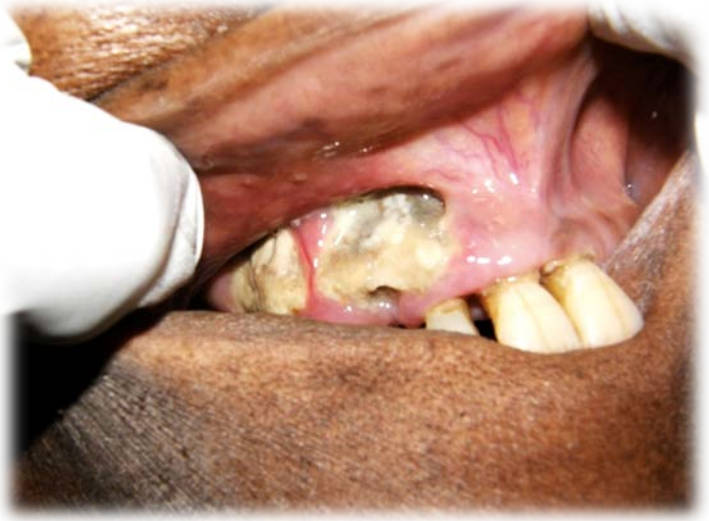
# Bisphosphonates - RISK

Nephrotic syndrome
Renal failure
Acute phase response
Ocular toxicity
Bone joint & muscle pain
ONJ



# What is BRONJ?

- Basic definition
  - **Exposed**, **necrotic** bone in the maxillofacial region for **more than 8 weeks**
  - Current or previous treatment with **bisphosphonates**
  - No history of radiation to the jaws



# Etiology of BRONJ

## Osteoclast inhibition theory

- Altered balance of bone deposition/resorption
- Hypermineralization
- Avascular necrosis
- Exposed intra oral bone
- Superinfection/Fascial space infections

# Bisphosphonates - RISK

IV bisphosphonates and incidence of BRONJ:

- Estimates of the incidence of BRONJ range from 0.8%-12%.
- Patients treated with IV BP who undergo dentoalveolar procedures have a 5 to 21 - fold increased risk for BRONJ.
- Median time to onset of BRONJ = 1yr

Oral bisphosphonates and incidence of BRONJ:

- Considerably lower risk
  - Based on data from the manufacturer of alendronate (Merck),
  - the incidence of BRONJ was calculated to be 0.7/100,000 person/years of exposure.
  - The literature reports varying levels of incidence ranging from .
- Median time to onset of BRONJ = 3yrs

# Bisphosphonates - RISK

Any surgery or procedure that involves the bone of the jaws may result in BRONJ, including, but not limited to: extractions, dental implant placement, periapical surgery and periodontal osseous surgery.

In addition, local anatomy (tori, exostoses, prominent mylohyoid ridges) may predispose to BRONJ due to the possibility of traumatic ulceration of the overlying mucosa.

Periodontal disease and dental abscesses have been associated with a 7 fold increase in the risk of BRONJ.

# Susceptibility of the Jaws to Osteonecrosis

The question often asked is "Why the jaws?"

First,
The jaw bones are separated from a trauma-intense and microbiologically diverse oral environment by thin mucosa and periosteum.

Second,
Tooth roots are separated from bone by no more than 2 mm of periodontal ligament, so dental infections have easy access to the underlying bone.

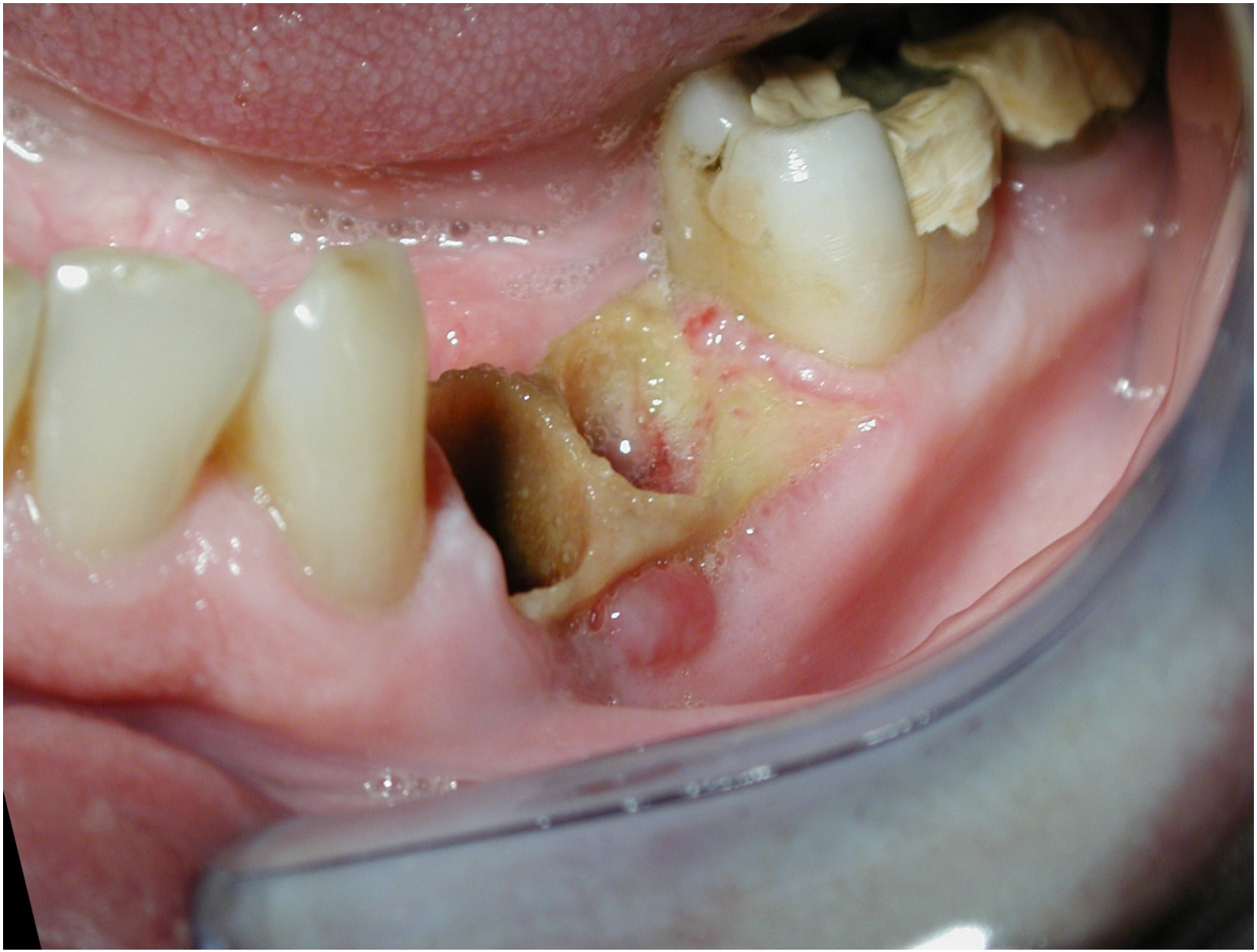
# BRONJ risk factors

## Drug related factors

- IV>Oral
- Zometa>Aredia
- Zometa + Aredia ↑risk
- Risk is related to length of exposure

## Local risk factors

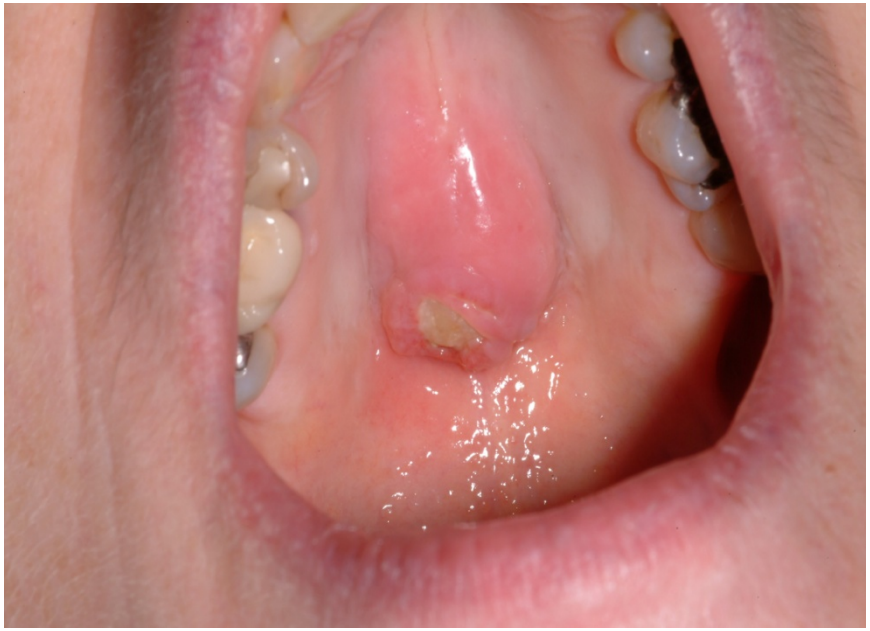
- Extractions
- Dental implant
- Periodontal dis/surgery
- Osseous surgery

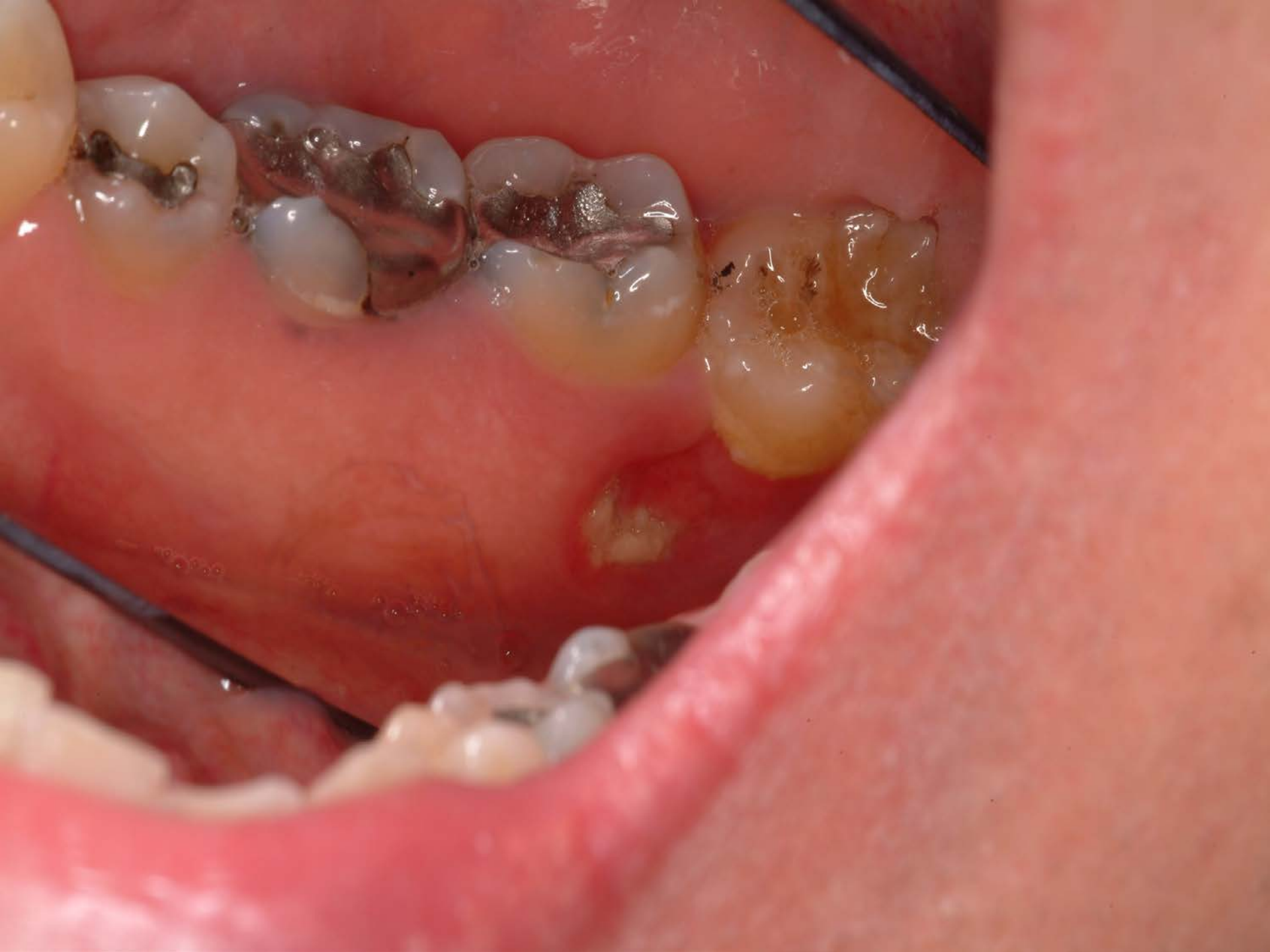


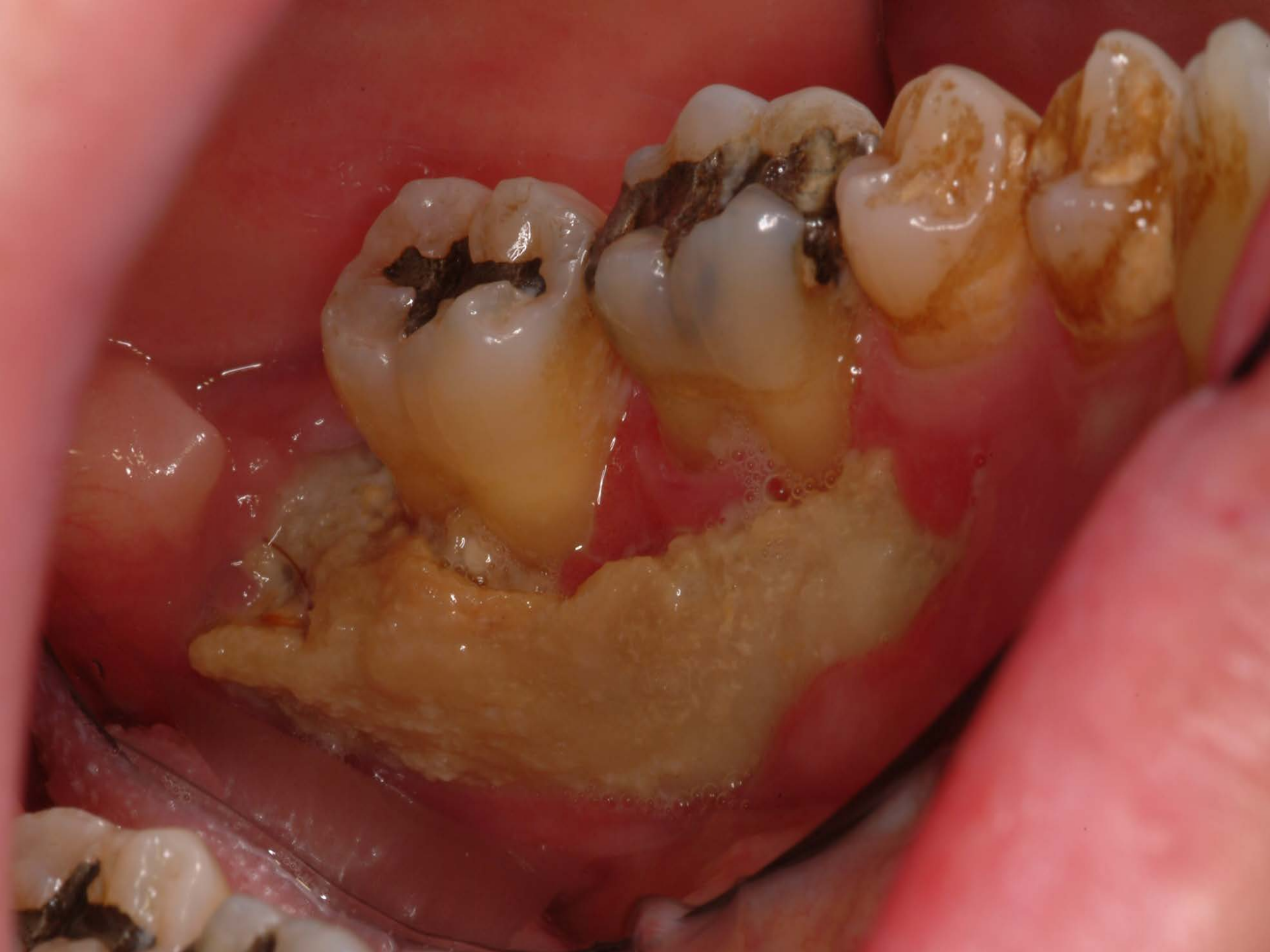
# BRONJ risk factors

## Anatomic risks

- Lingual tori
- Mylohyoid ridge
- Maxillary tori
- Exostoses







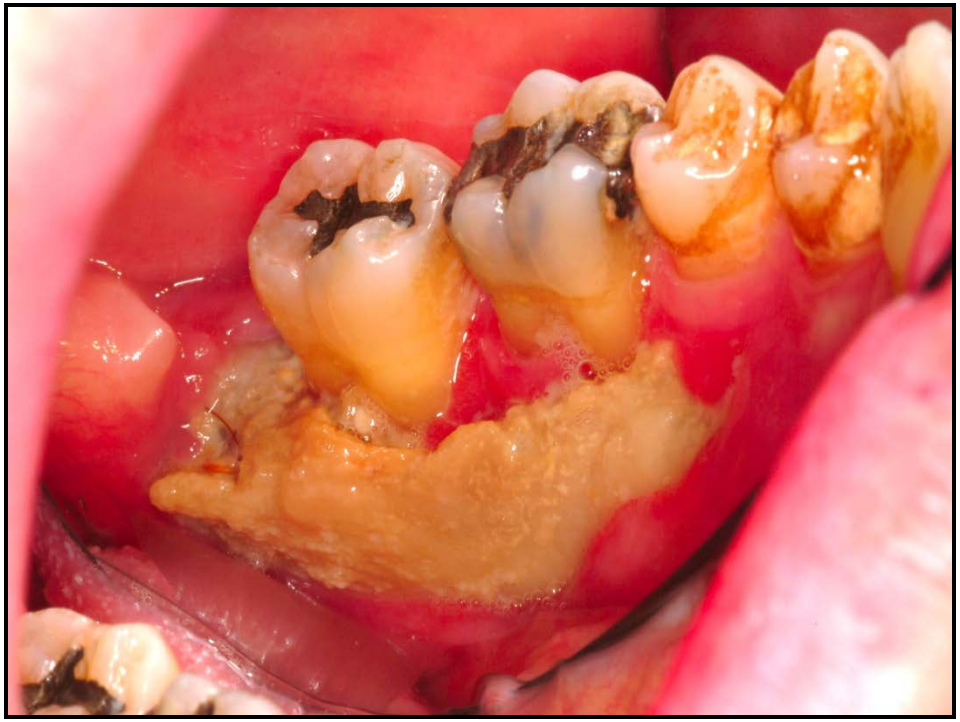
# BRONJ - Treatment Goals

- Prioritization and support of continued oncologic treatment

- Preservation of quality of life through:
    * Patient education and reassurance
    * Control of pain
    * Control of secondary infection
    * Prevention of extension of lesion and development of new areas of necrosis

# Typical signs and symptoms

- Pain
- Soft tissue swelling
- Infection
- Drainage
- Impaired healing
- Loosening of teeth
- Numbness or dysesthesias
- Fracture



# Diagnosis of BRONJ

**Exposed, necrotic for more than 8 weeks**

**Current or previous treatment with bisphosphonates**

**No history of radiation to the jaws**

# Diagnosis of BRONJ

## Other causes of osteonecrosis

Mnemonic = VINDICATE

- Vascular; sickle cell disease, polycythemia vera
- Infection; septic emboli
- Drugs; steroid use, bisphosphonates, antiresorptive meds
- Inflammation; pancreatitis
- Congenital; Gaucher's disease
- Autoimmune; SLE, RA
- Trauma; fracture, radiation
- Endocrine; Cushing's disease

MALIGNANCY

# Radiographic features

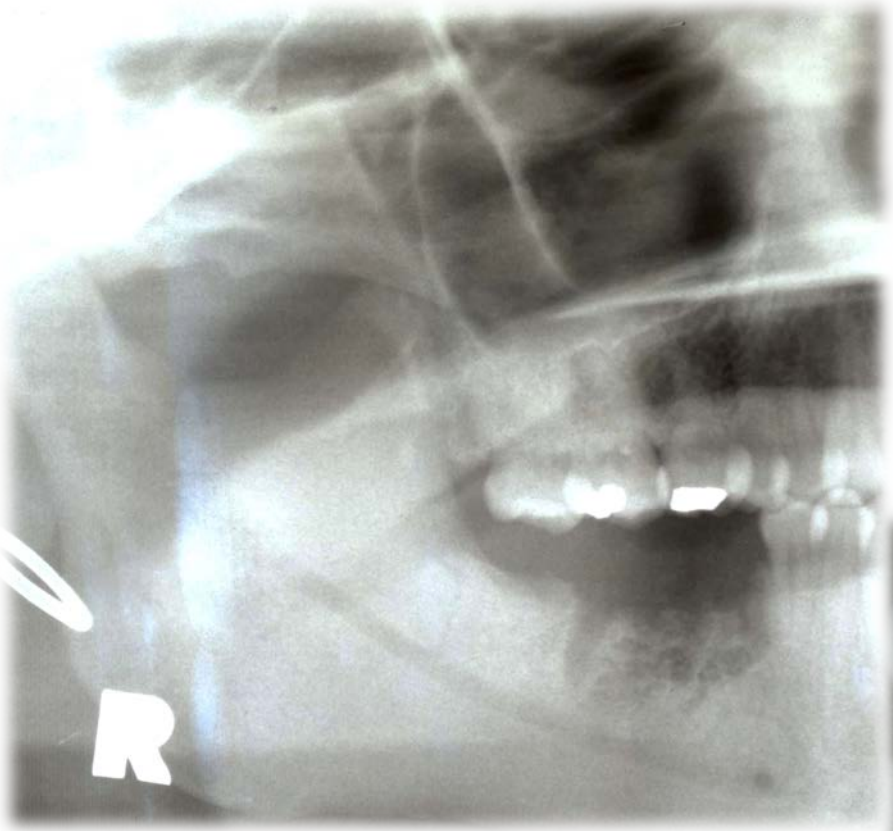
- Periapical and panoramic x-rays allow quick visualization of the areas of concern.
- Computed Tomography provide three-dimensional information and better delineation of the extent of the lesion.
- Magnetic Resonance Imaging assess the bone marrow, surrounding soft tissues, neurovascular bundles, and lymphadenopathy.
- Nuclear Bone Scanning are performed routinely on patients with metastatic disease

# Radiographic features

- Sclerosing osteomyelitis
  - ill-defined margins
  - Hypermineralization
  - Sequestration

- Symmetric widening/thickening of PDL
- Effacement of distinct borders
  - Inferior alveolar canal

- Proliferative periosteal reaction
- Empty socket syndrome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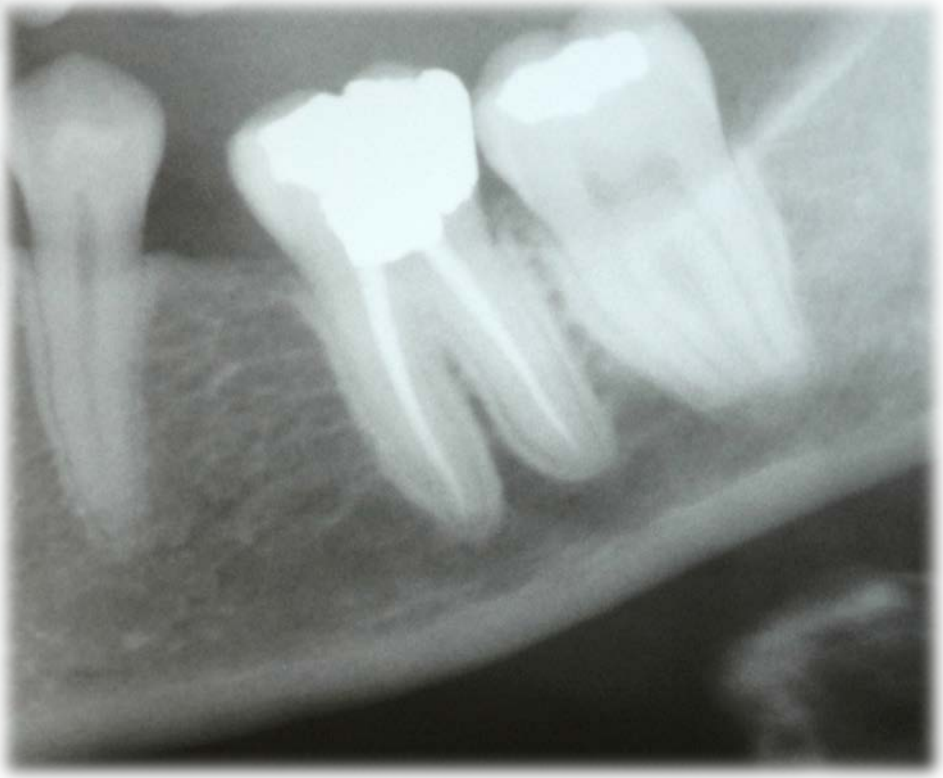

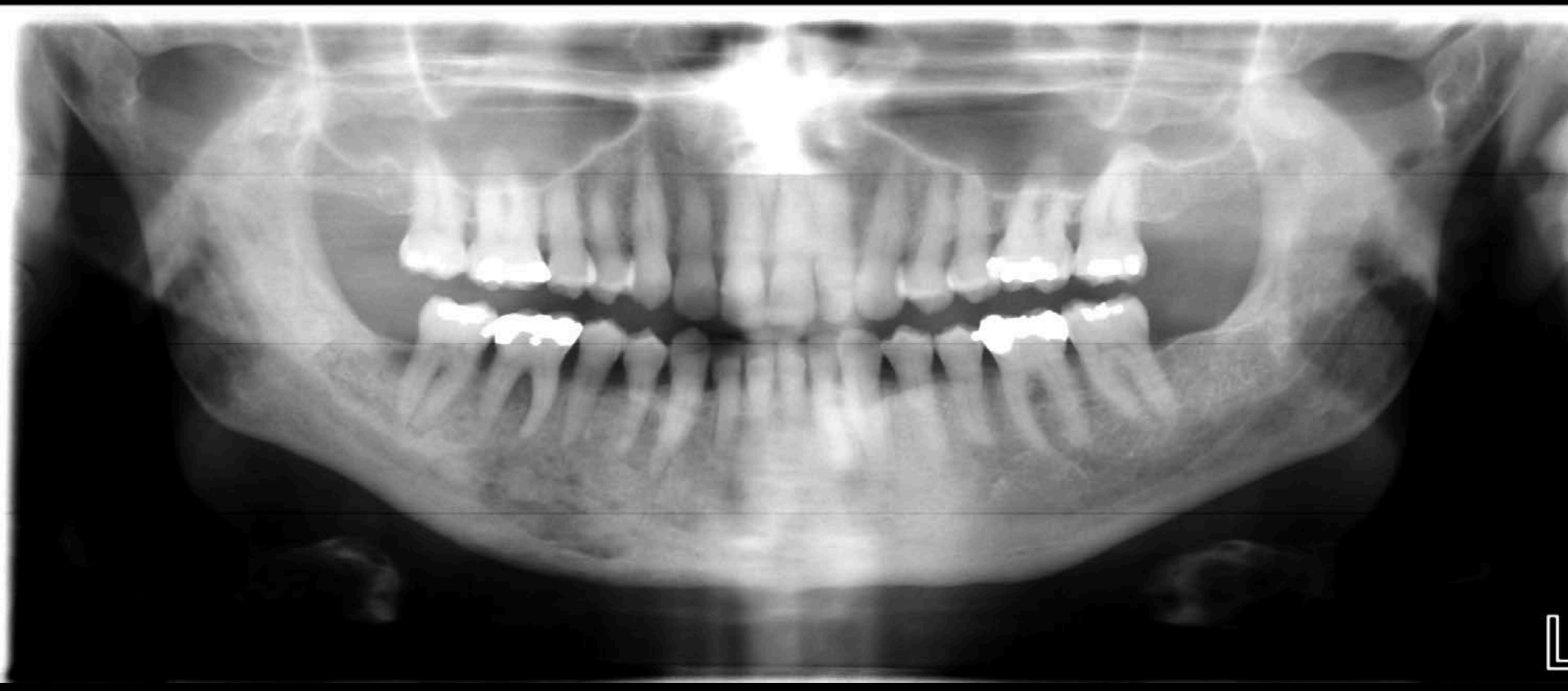

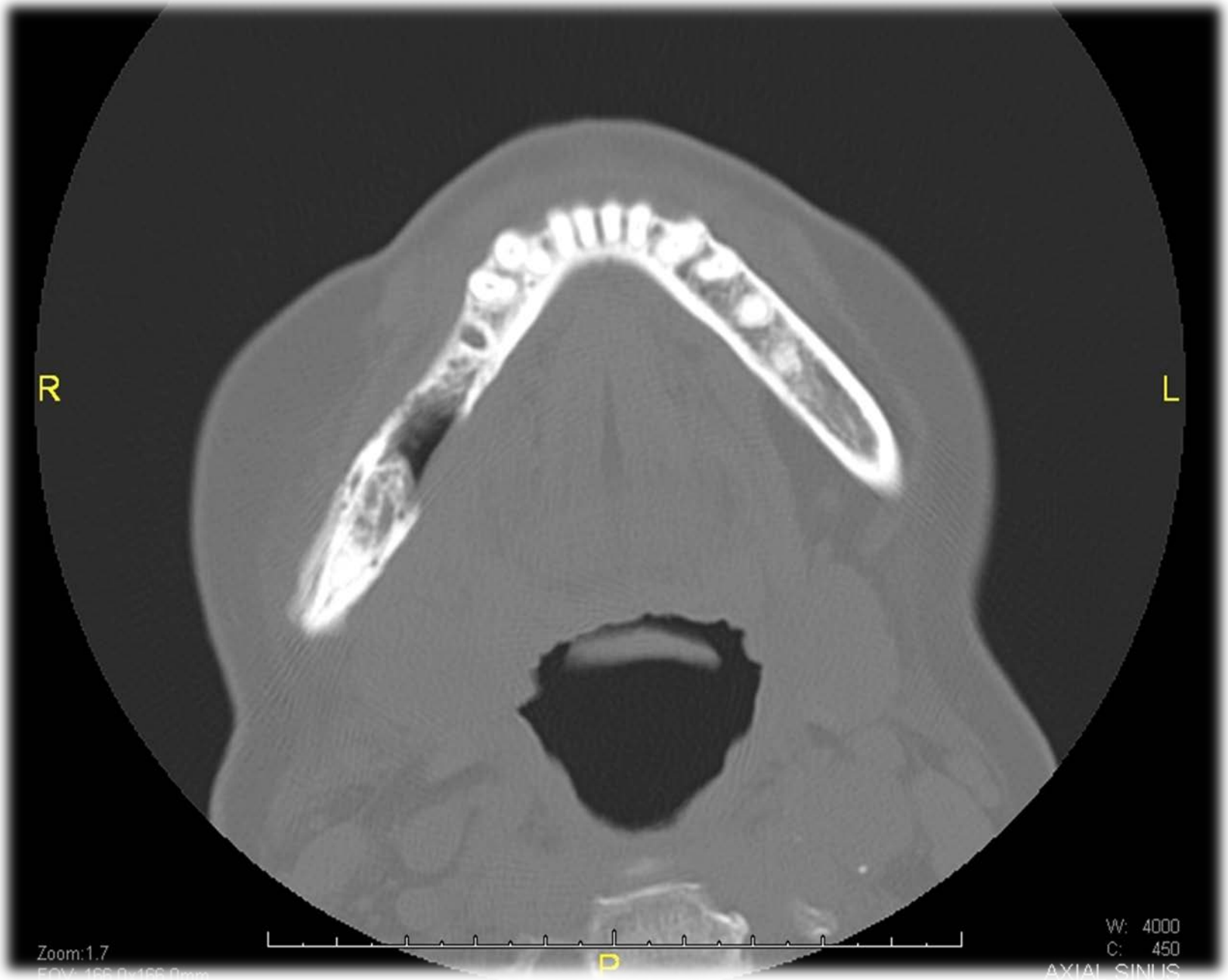
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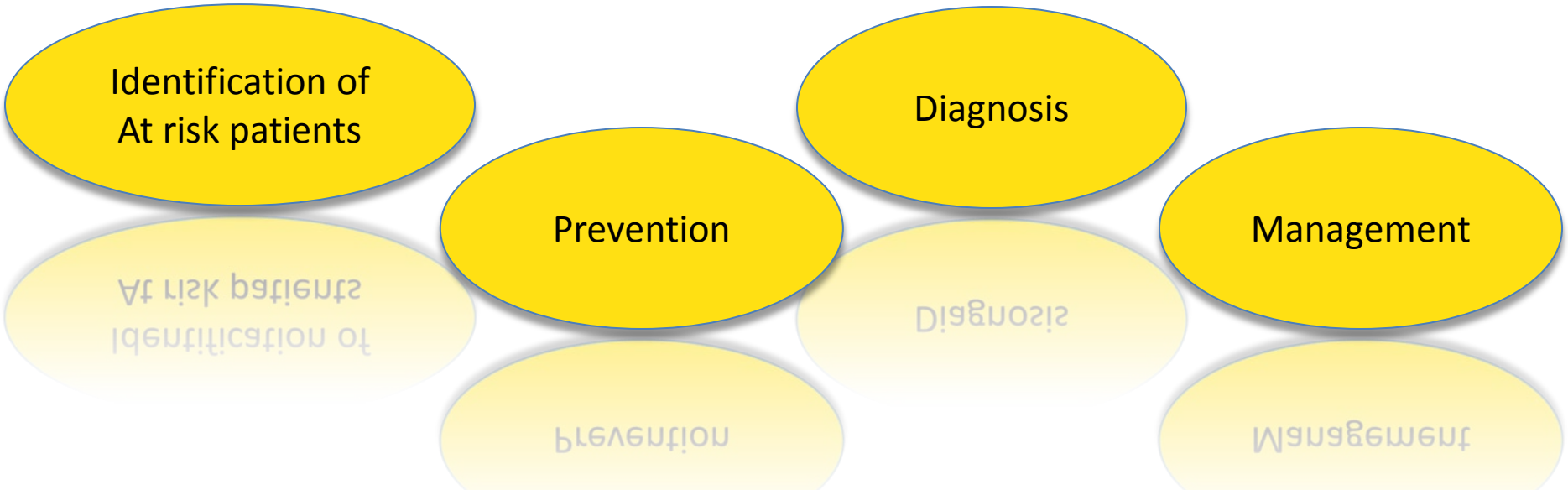
# Guidelines

**Dental Management of Patients Receiving Bisphosphonate Therapy- Expert Panel Recommendations; American Dental Association, July 2008**

**American Association of Oral and Maxillofacial Surgeons Position Paper on Bisphosphonate-Related Osteonecrosis of the Jaws; January, 2009**

**Canadian Consensus Practice Guidelines for Bisphosphonate Associated Osteonecrosis of the Jaw; June 2008**



An ounce of prevention is worth a pound of cure.

# Prevention

**Prior to initiation of bisphosphonate therapy, a thorough dental exam with radiographs should be completed.**

**If any invasive dental procedure (tooth extraction, periodontal surgery) is deemed necessary, it should be completed and optimal dental health achieved prior to initiation of bisphosphonate therapy, if the patient's medical condition permits the delay.**

# My Patient is at risk and now has a dental problem.

## What are the Management Strategies?

- Urgent dental surgery needed
    - Have the dental procedure done
    - Consider interruption of  bisphosphonate therapy if medical condition permits

- Non-emergency dental surgery needed
    - Consider interruption of bisphosphonate therapy for 3 to 6 months prior to the procedure and until the surgical site has healed, if medical condition permits

# Management Strategies:

# Interruption of Bisphosphonate Therapy

- Bisphosphonates have a long-term skeletal retention, and it is not know if stopping treatment will alter the course of an BRONJ lesion

- However, anecdotal reports suggest that cessation of bisphosphonate therapy is beneficial

- While interruption of bisphosphonates may be difficult, other non-bisphosphonate options could be considered for the short-term management of these patients during dental surgery

# Diagnosis & Treatment

| BRONJ† Staging | Treatment Strategies‡ |
|---|---|
| **At risk category No apparent necrotic bone in patients who have been treated with either oral or IV bisphosphonates** | • No treatment indicated<br>• Patient education |
| **Stage 0 No clinical evidence of necrotic bone, but non-specific clinical findings and symptoms** | • Systemic management, including the use of pain medication and antibiotics |
| **Stage 1 Exposed and necrotic bone in patients who are asymptomatic and have no evidence of infection** | • Antibacterial mouth rinse<br>• Clinical follow-up on a quarterly basis<br>• Patient education and review of indications for continued bisphosphonate therapy |
| **Stage 2 Exposed and necrotic bone associated with infection as evidenced by pain and erythema in the region of the exposed bone with or without purulent drainage** | • Symptomatic treatment with oral antibiotics<br>• Oral antibacterial mouth rinse<br>• Pain control<br>• Superficial debridement to relieve soft tissue irritation |
| **Stage 3 Exposed and necrotic bone in patients with pain, infection, and one or more of the following: exposed and necrotic bone extending beyond the region of alveolar bone,(i.e., inferior border and ramus in the mandible, maxillary sinus and zygoma in the maxilla) resulting in pathologic fracture, extra-oral fistula, oral antral/oral nasal communication, or osteolysis extending to the inferior border of the mandible of sinus floor** | • Antibacterial mouth rinse<br>• Antibiotic therapy and pain control<br>• Surgical debridement/resection for longer term palliation of infection and pain |

# Clinical Utility of Serum CTX in Predicting Risk of Osteonecrosis of the Jaw

**C-telopeptide crosslink of type 1 collagen (sCTX)**

# Serum CTX (sCTX)

sCTX is an indicator of skeletal bone turn over

It is a product of the breakdown of type 1 collagen (the major organic matrix of bone >90%)

Patients taking BP have lower sCTX levels

Cessation of BP therapy usually leads to a slow increase in sCTX level.

Bone turnover markers are useful in monitoring patient response to BP and sCTX is used for follow-up of postmenopausal osteoporosis and correlates with fracture risk because of its sensitivity especially when used in conjunction with BDS.

# Oral Bisphosphonate-Induced Osteonecrosis: Risk Factors, Prediction of Risk Using Serum CTX Testing, Prevention, and Treatment

Robert E Marx, Joseph Cillo, Juan Ulloa

J Oral Maxillofacial Surg 2007

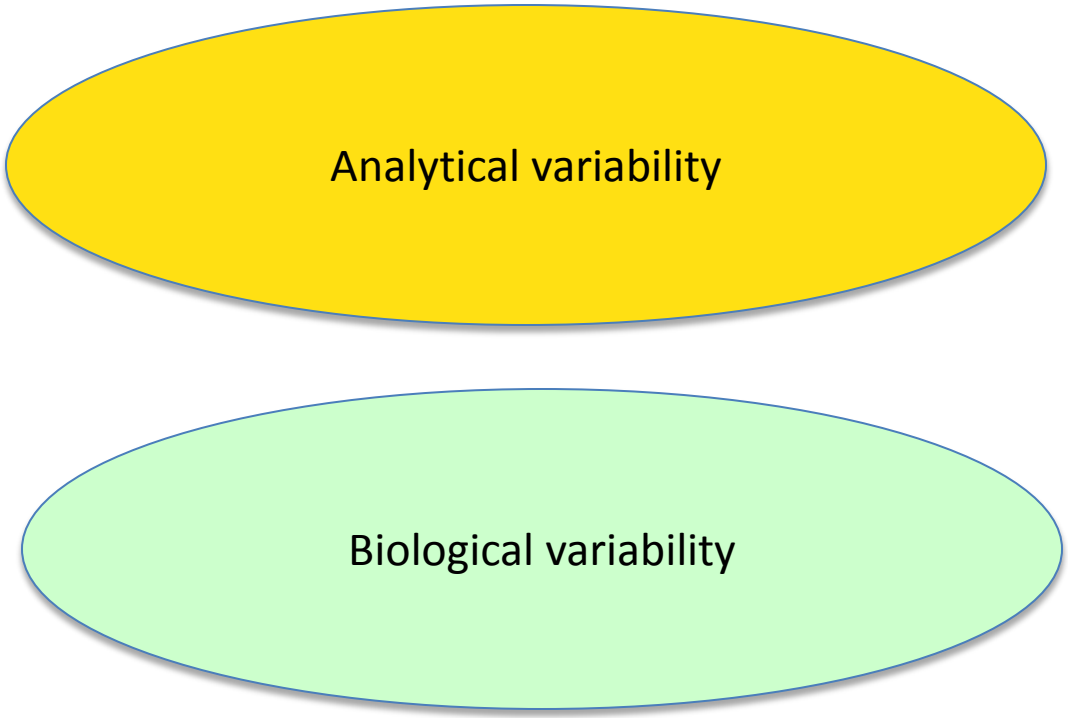
- The serum morning fasting CTX bone turnover marker is a straightforward and useful tool to assess the bone turnover/renewal suppression caused by oral bisphosphonates. Its interpretation of less than 100 pg/mL as high risk, 100 pg/mL to 150 pg/mL as moderate risk, and greater than 150 pg/mL as minimal risk provides the clinician with a useful assessment tool to predict risk and guide treatment decisions.

**CTX**

- For BRONJ associated with Oral bisphosphonates
- CTX < 100 pg/ml high risk
- CTX 100-150 pg/ml medium risk
- CTX >150pg/ml minimal risk
- Increase of 25.9-26.4 pg/ml each month of drug holiday

Marx et al JOMS 2007

# Serum CTX (sCTX)



# Serum CTX (sCTX)

Biological variability:

- Age
- Sex
- Menopausal status
- Fracture status
- Disease states
- Immobility
- Pregnancy
- Lactation
- Medications
- Circadian variation
- Hormonal variation
- Fasting status

# Serum CTX (sCTX)

## Is a level of 150pg/ml meaningful?

- Cases of BRONJ have been reported with levels > 150 pg/ml.
- It is not unusual for patients with osteoporosis to have sCTX levels < 150 pg/ml even before BP therapy.
- The lower limits of healthy premenopausal sCTX reference range is between 40 and 114 pg/ml.

## Oral bisphosphonate-induced osteonecrosis: risk factors, prediction of risk using serum CTX testing, prevention, and treatment. The American Society for Bone and Mineral Research Task Force on Osteonecrosis of the Jaw May 2008

- It is not appropriate to base clinical recommendations on an uncontrolled study of 30 patients without making it clear that the recommendations are based on opinion rather than adequate evidence. This paper may lead many dental health professionals to adopt a set of behaviors (such as measuring serum CTX levels and discontinuing bisphosphonate therapy if the serum CTX level falls below 100 pg/mL) that is not only based on inadequate evidence, but also may deprive patients of much-needed therapy for their osteoporosis.

- Can I place an Implant in patients on Bisphosphonates?

# Dental Implants in Patients Undergoing Bisphosphonate Treatment

Background:
It was suggested that all patients undergoing BP therapy who are expected to receive dental implants should be informed of the possible risks of development of ONJ.

Methods:
Databases were searched from 1995 up to and including February 2010 using the following terms in different combinations: bisphosphonate, dental implant, immediate-loading, implant survival rate, intravenous, oral, osseointegration, and osteonecrosis.

Results:
In 10 studies, the patients were using oral BPs, and in two studies, patients were using IV BPs. Six case reports showed that the placement of implants in patients using BPs could yield a successful osseointegration and function. Four retrospective studies demonstrated
that BPs did not have a negative influence on implant success.
Two studies showed a negative impact of BPs on implant success

Outcomes of Placing Dental Implants in Patients Taking Oral Bisphosphonates: A Review of 115 Cases

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*Purpose:*

•We wanted to ascertain the extent to which bisphosphonate-associated necrosis of the jaw has occurred in our dental implant patients.

• We also wanted to determine whether there was any indication that the bisphosphonate therapy affected the overall success of the implants as defined by Albrektsson and Zarb.

*Patients and Methods:*

•We identified 1,319 female patients over the age of 40 who had received dental implants at Montefiore Medical Center between January 1998 and December 2006.

• A survey about bisphosphonate therapy was mailed to all 1,319 patients.

• Responses were received from 458 patients of whom 115 reported that they had taken oral bisphosphonates. None had received intravenous bisphosphonates.

•All 115 patients were contacted and informed about the risk of bisphosphonate-associated osteonecrosis of the jaw.

• Seventy-two patients returned to the clinic for follow-up clinical and radiological evaluation.

**Results:**

Of the 468 implants, all but 2 integrated fully and meet criteria for establishing implant success. Implant success rates were comparable for patients receiving oral bisphosphonate therapy and those not receiving oral bisphosphonate therapy.

**Conclusions:**

Implant surgery on patients receiving bisphosphonate therapy did not result in bisphosphonate-associated osteonecrosis of the jaw. Nevertheless, sufficient evidence exists to suggest that all patients undergoing implant placement should be questioned about bisphosphonate therapy including the drug taken, the dosage, and length of treatment prior to surgery

# Utility of Hyperbaric Oxygen in treatment of Bisphosphonate-Related Osteonecrosis of the Jaws

Hyperbaric Oxygen Treatment and Bisphosphonate-Induced Osteonecrosis of the Jaw: A Case Series

*John J. Freiberger, MD, MPH et al.*

Purpose:

Bisphosphonate (BP)-associated osteonecrosis of the jaw (ONJ) is an emerging problem with few therapeutic options. Our pilot study of BP-ONJ investigated a possible role for hyperbaric oxygen (HBO2) therapy

Patients and Methods:

A total of 16 patients, ranging in age from 43 to 78 years, with BP-ONJ were treated with adjunctive HBO2 between July 2003 and April 2006. Staging was based on the size and number of oral lesions. Clinical response after treatment and at distant follow-up; the odds of remission, stabilization, or relapse; and time to failure analysis were calculated.

*Results:*

Fourteen of 16 patients (87.5%) improved in stage. The size and number of ONJ lesions were decreased after HBO2 therapy. Immediately after HBO2 therapy, 7 of 16 patients (44%) were in remission and 8 (50%) had stabilized; however, stabilization without remission was sustained in only 2 patients. At follow-up, 10 of the patients (62.5%) were still in remission or had stabilized. The 7 patients
who continued on BP treatment during HBO2 therapy had a shorter time to failure (8.5 months; 95% confidence interval [CI]  7.1 to 9.8) than those who discontinued the drug (20.1 months; 95% CI  17.5
to 23.9; *P  .006 by the log-rank test). Clinical response was not associated with cancer type or* malignancy remission status.

*Conclusions:*

Adjunctive HBO2 therapy may benefit patients with BP-ONJ; however, the outcome is improved with cessation of BP administration.

# What Do We Need to Know about BRONJ

- Take proper medical history on patients & regular updates.
  - Including  list of past and current medications with dosage regiment

- Proper clinical exam and understanding of presentation
  - Is there exposed bone?  Fistula present?  Patient in pain?
  - History of Dental trauma to area?

# What Do We Need to Know about BRONJ

- Radiographic appearance
  - How does it look on a Panorex/CT/MRI/PA

- Focus on Prophylactic care for patients about to undergo tx with nBP.
  - Reconsider elective oral sx, apical sx, periodontal sx, implants, and possibly orthodontics on pts already receiving BP

# What Do We Need to Know about BRONJ

- Focus on Initial Treatment goals
  - Palliative care
  - Use of antibiotics/antimicrobial rinse where applicable,
  - Proper oral hygiene