

## Ischemic Osteonecrosis

Ischemic osteonecrosis is a process that involves impaired outflow of blood from the marrow space, increased intramedullary blood pressure, and reduced blood flow circulation in the bone marrow. This results in the death of osteocytes and other marrow tissues.

Microscopically it is characterized by dilated capillaries with micro clots and infarcts. There are areas of empty lacunae in calcified tissue and loss of integrity of the trabecular structure. There are dead fat cells replaced by loose fibrosis, and oil cysts, or globules, of free lipids. Surprisingly, inflammatory infiltrates are not a factor.

Infection and trauma are known to be the primary factors that predispose bone marrow to this condition, leading a long list of other influences. Click on the topics to the right of this screen for more information on the causes and manifestations of ischemic osteonecrosis.

### Chronic Ischemic Bone Disease (CIBD)

Chronic ischemic bone disease is literally "bone death." It is a process that creates diseased or dead bone marrow resulting from a diminished (abrupt or chronic) blood flow. It can affect any bone; usually from poor outflow from the bone, and usually causes increased marrow pressures and pain, but may be painless. Hips, knees, and jaws are most often affected.

Subsets of this disease include: bone marrow edema (mild form), regional ischemic osteoporosis (mild form), avascular necrosis (severe form), etc.

Characteristics (From [www.maxillofacialcenter.com](http://www.maxillofacialcenter.com)):

- Like inflammation, it is not so much a disease in its own right as it is a generic process.
- A local reaction to a variety of systemic and/or local factors which reduce nutrition, blood flow to marrow.
- Abrupt or very gradual onset.
- May become self-perpetuating.
- Characteristically multifocal 50-80%.
- Characteristically bilateral.
- Mostly hips, knees, jaws

Very difficult to see on radiographs:

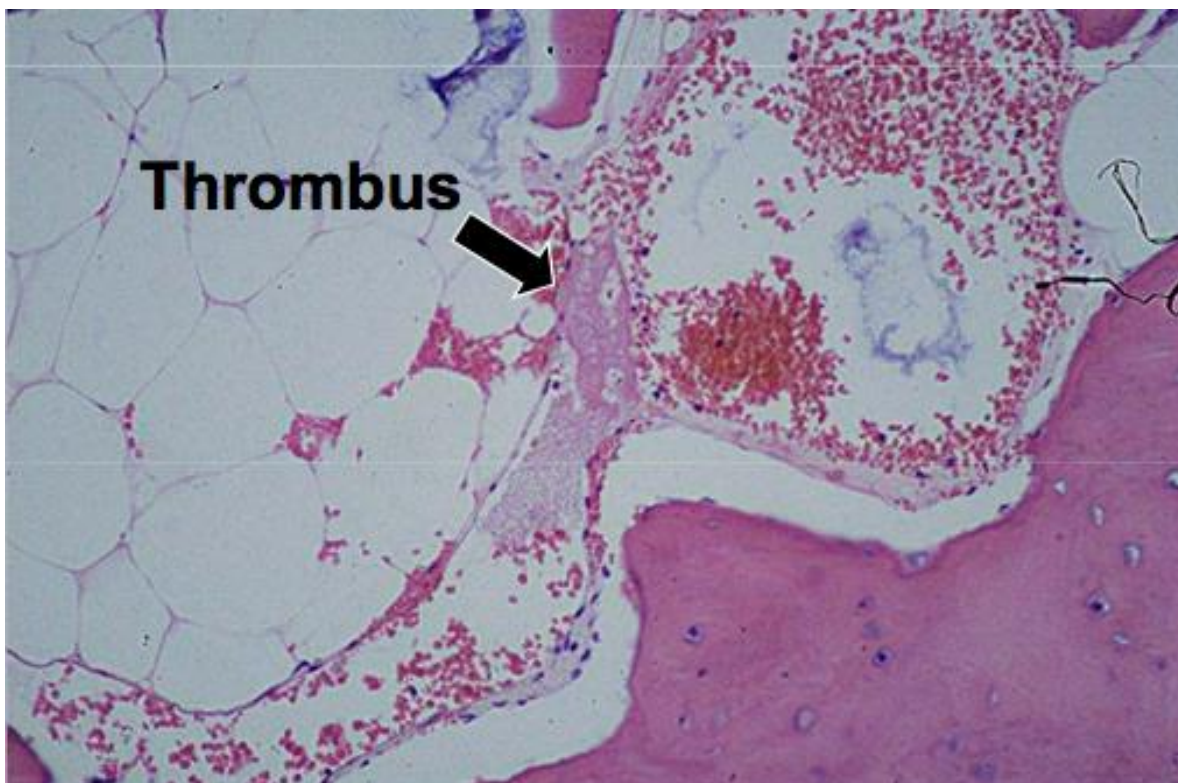
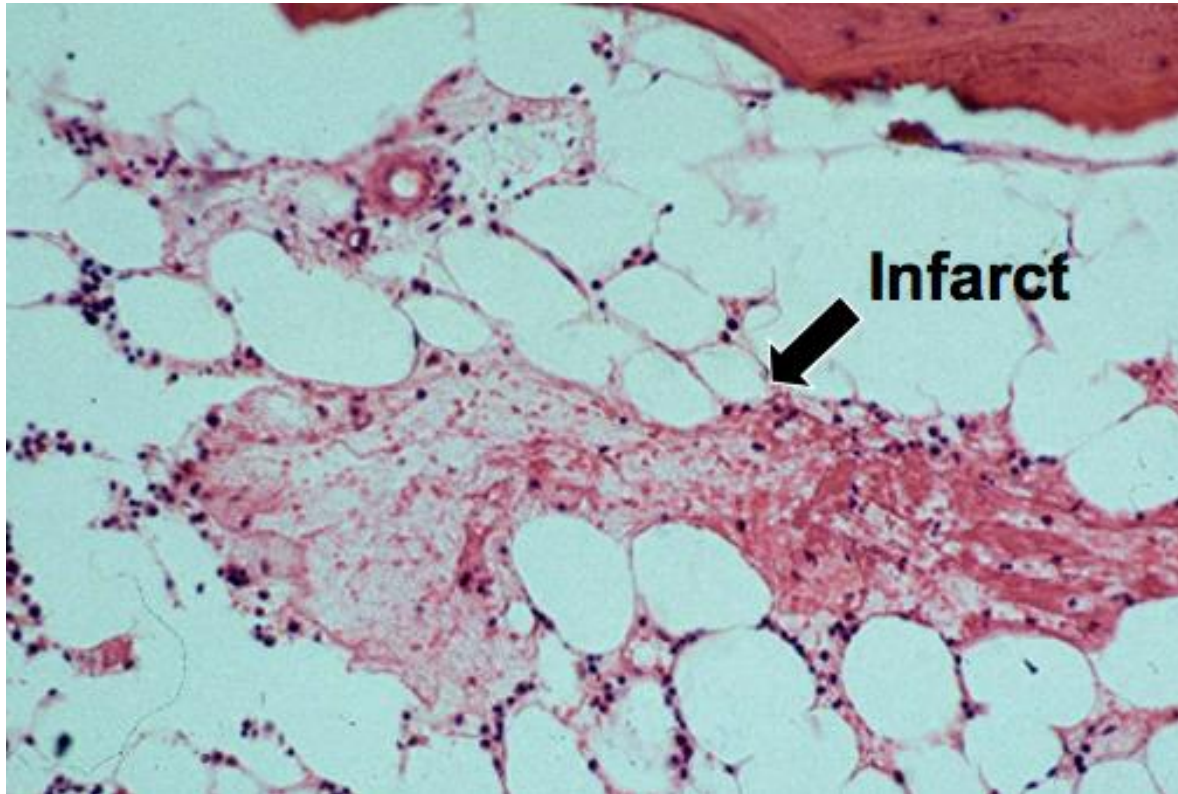
- Need technitium-99 MDP scintigraphy?
- Need quantitative ultrasound (QUS)?
- Need cone beam CT scan?

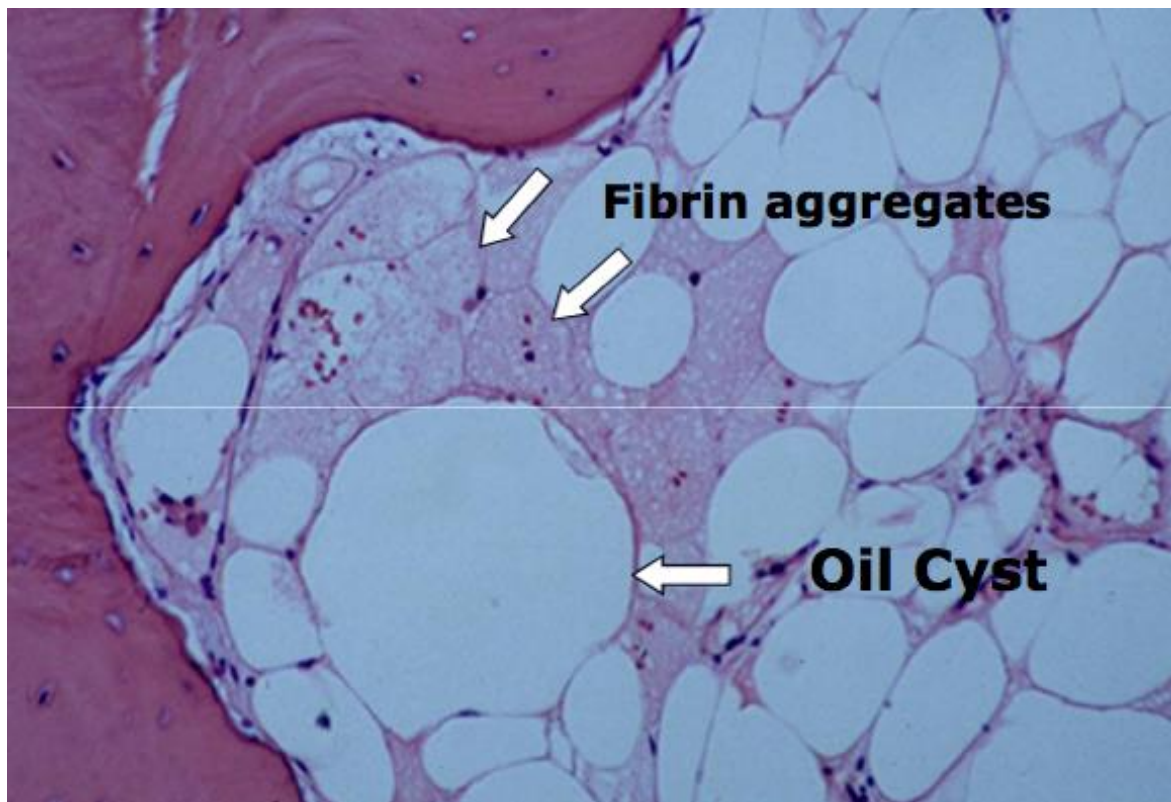
## Learning Aid

Hidden Pathogens in Root and Jawbone

### Micro Clots and Infarcts

Images from [www.maxillofacialcenter.com](http://www.maxillofacialcenter.com).





### Trigger Events

TOP DOZEN FROM A LIST OF MORE THAN 60:

- Infection and trauma
- Estrogen therapy or pregnancy
- Corticosteroid therapy
- Autoimmune diseases (lupus = increased coagulation)
- Malnutrition (starvation, anorexia)
- Anemia
- Alcoholism
- Frequent hyperbaric changes
- Radiation and chemotherapy
- Metastatic cancer
- Bisphosphonates
- Hypothyroidism

From [www.maxillofacialcenter.com](http://www.maxillofacialcenter.com)

### Sluggish Blood Flow

The basic problem is that marrow is especially susceptible to clots and infarcts.

Blood flows sluggishly through marrow, and flows out slowly.

Normal intramedullary pressure is high.

Ischemic disease is the only bone disease in which outflow is even further drastically reduced (80% of cases).



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Intramedullary pressures in osteonecrosis can be 5 times greater than normal because of backup pressure.

Stagnation occurs, increasing risk of clots.

Inherited excess clotting tendencies compound this problem, increasing susceptibility to infarction. Clotting disorders affect 20% of the population. About 4/5 CIBD cases have hyper-coagulation states.

Normal Population	Deep Vein Thrombosis	Osteonecrosis Hips or Jaws
5-9%	20-50%	65-87%

Coagulation Disorder	% in NICO
Increased plasminogen activator inhibitor (PAI)	18
Decreased stimulated tissue plasminogen activator	22
Decreased stimulated tissue plasminogen activator	8
Resistance to activated Protein C	18
Increased lipoprotein A	36
Factor V Leiden gene (heterozygotic)	23
Methylene tetrahydrofolate reductase (MTHFR)	65
Total (including multiple coagulopathies):	78%

\* Data from University of Cincinnati and Indiana University, 2002  
From [www.maxillofacialcenter.com](http://www.maxillofacialcenter.com)

### CIBD: Pain or No Pain

Neuralgia-Inducing Cavitation Osteonecrosis (NICO) is a jawbone version of ischemic osteonecrosis. By definition, NICO is associated with pain. Osteonecrosis itself may or may not be painful. It may or may not affect multiple sites in one bone, or multiple bones.

The disease may or may not produce pain and the intensity of symptoms is not related to the amount of bone destroyed. Recent dental literature has seldom discussed asymptomatic ischemic osteonecrosis of the jaws, but the older literature, including the classic oral pathology textbook by G.V. Black, contains many examples of painless intramedullary "dry rot" or cavitation, usually under terms such as "bone caries" and "chronic osteitis" to distinguish it from osteomyelitis.

In 1915, G. V. Black first described these lesions in jawbones as follows:

***"An osteomyelitis-like bone disease which seemed not to be a true infection, but rather a slow, progressive, unexplained death of cancellous bone and marrow, cell by cell."***

Avascular bone associated with residual or unhealed extraction sockets, with or without pain, was also reported long ago and has recently been cited as a "red flag" or warning sign for medullary ischemia severe enough to prevent proper healing after surgery.

From [www.maxillofacialcenter.com](http://www.maxillofacialcenter.com)

## Detecting Ischemic Osteonecrosis in Jawbone

Detecting lesions of ischemic osteonecrosis in the jawbones of living people has been difficult without specialized techniques. The appearance of these lesions on normal two-dimensional periapical or panoramic radiographs is often indistinct.

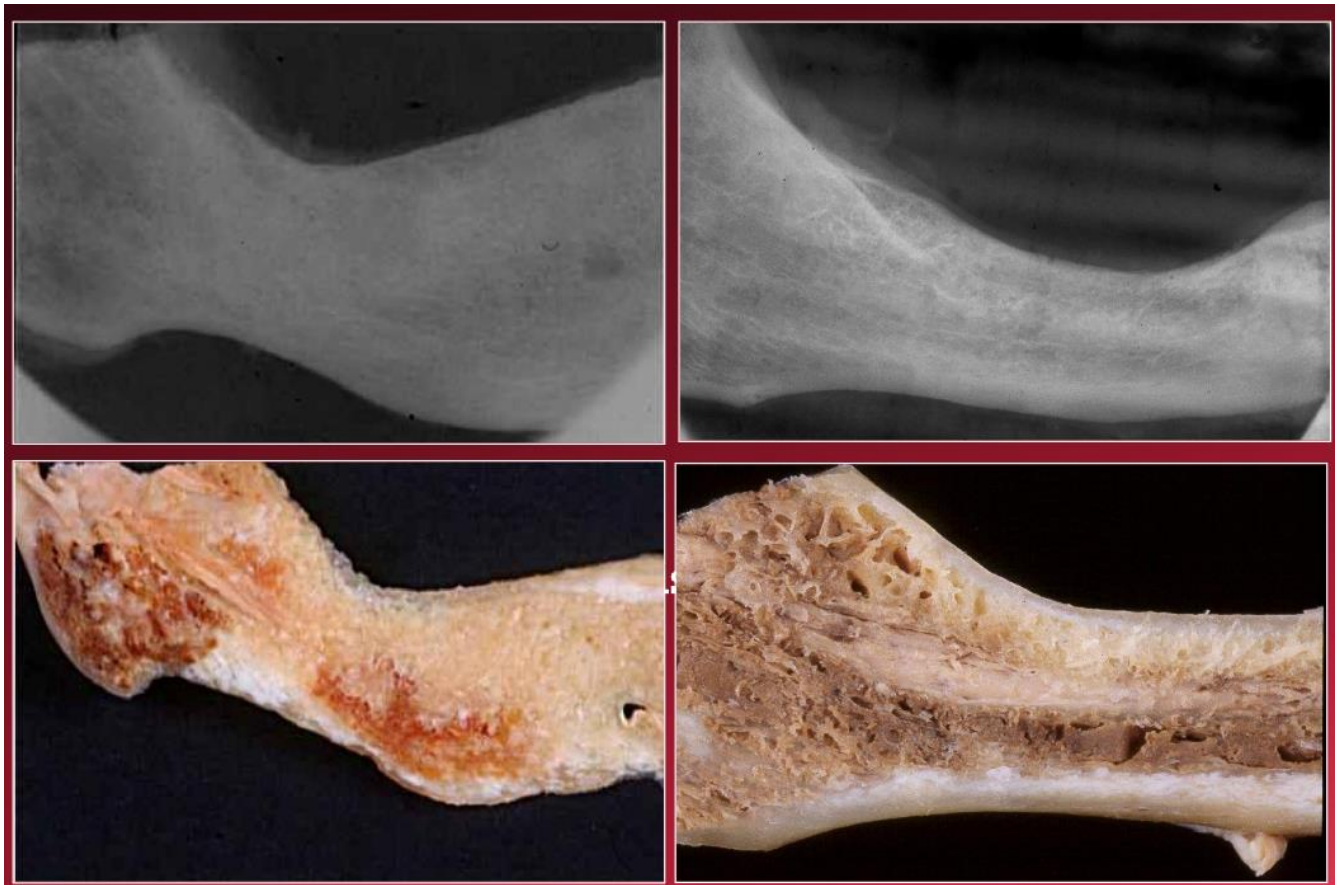
However, once we get used to the idea that the jawbones are particularly likely to be affected and our eyes become alerted to looking for ischemic lesions on normal x-rays, we can begin to see the lesions everywhere.

The vast majority of these very common lesions are not painful. But the very fact that we know the bone is not normal leaves us with questions, such as: Should we consider them pathological? Should they be subjected to some form of therapy? Can they have an impact on the person's general health?

### Specialized Imaging Techniques

The appearance of ischemic osteonecrosis lesions in the jawbones on normal two-dimensional periapical or panoramic radiographs is often indistinct. These lesions can easily be ignored as variants of normal when we're not on the alert to look for them.

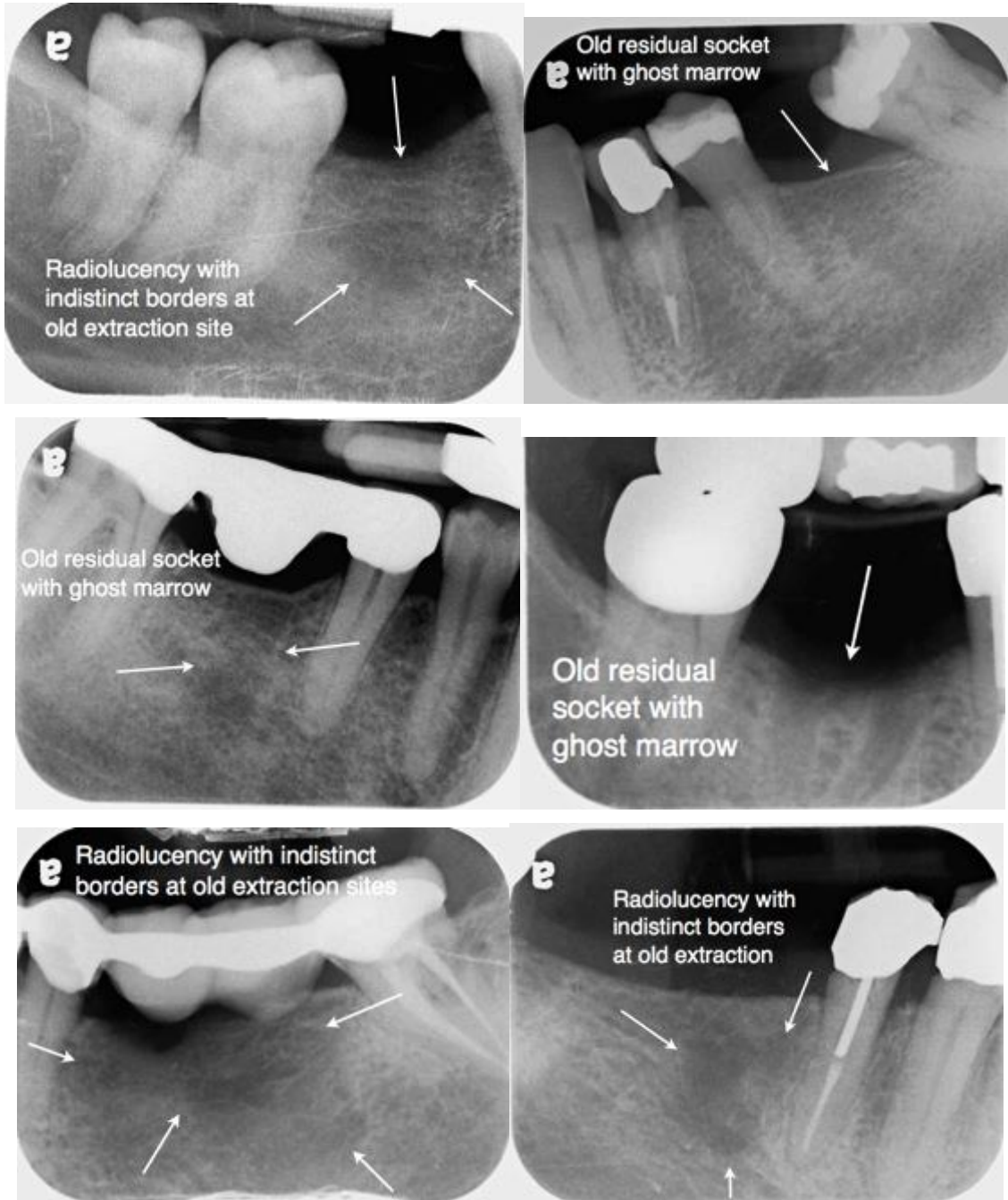
You can see in the following two dramatic examples from the autopsy series that the radiographs may not show any evidence of the osteonecrosis that actually exists inside the bone.



from [www.maxillofacialcenter.com](http://www.maxillofacialcenter.com)

### Ischemia on 2D Radiographs

Radiographic features that were considered variants of normal, or merely unexplainable, can be recognized as being of ischemic origin when we get used to the idea. Normally, an extraction site should completely remodel and heal in 6-12 months. The following images suggest that the sites are affected by ischemia to a degree that full healing is impaired.

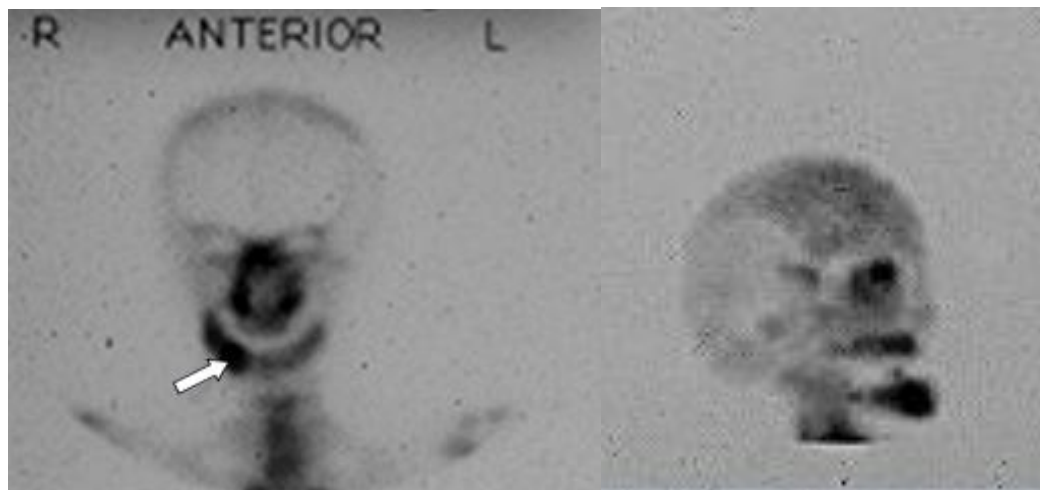






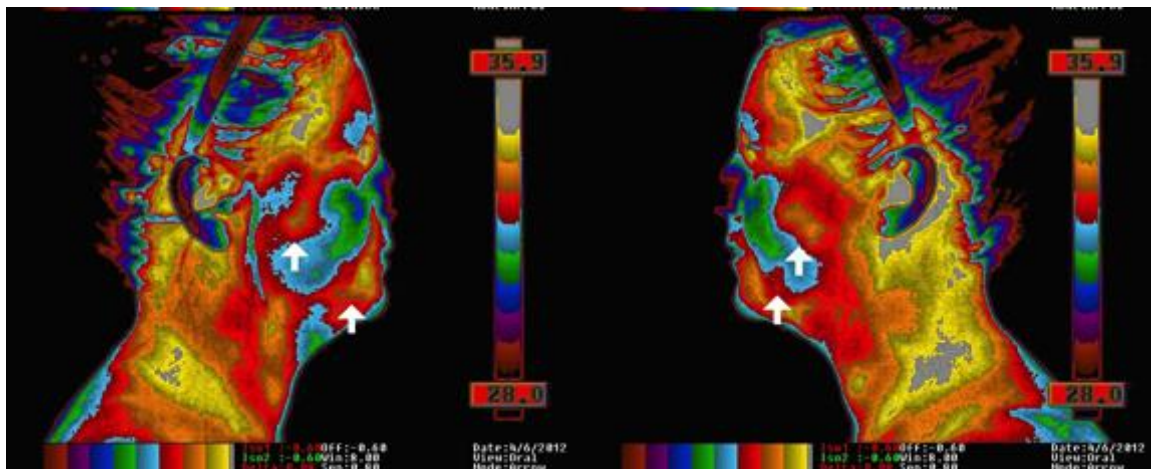
## Bone Scans

Technecium-99, or SPECT bone scans are used to find areas of the skeleton where bone is either being formed or destroyed more actively. The osteonecrotic region, where mineralized crystals are more exposed, attracts the <sup>99m</sup>Tc-bisphosphonate tracer more avidly than surrounding normal bone. Some amount of blood perfusion is necessary. Occasionally there will be an image where the affected area is whiter than normal, indicating no circulation at all.



## Thermography

Thermographic imagery of the skin can be used to give evidence of a general region that is under stress, inflammation, or infection. There seems to be a phenomenon of increased circulation around an area that may be affected by diseased bone.



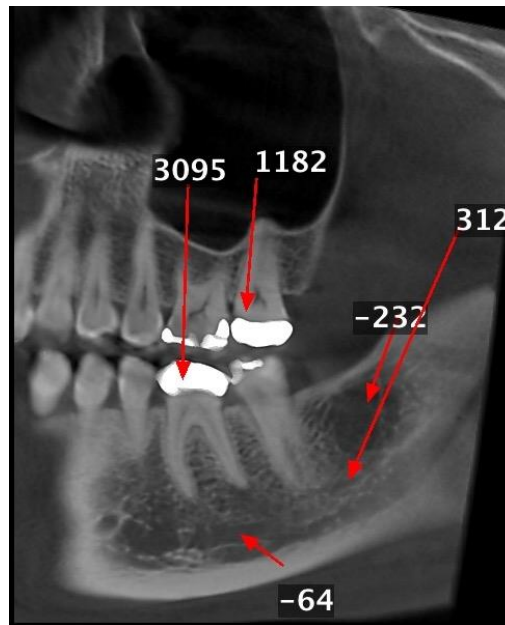
## Cone Beam Tomography

Of course, our new age of cone beam CT imagery gives us a better view of the contents of the marrow spaces. We can find condensing osteitis and cavitated empty zones with much greater accuracy than ever before. Following is a particularly clear example of a residual hollow in the jawbone, where a lower third molar had been extracted years before. The numbers are Hounsfield radiographic density measurements, which are produced by many CBCT software packages. Often the Hounsfield scores will resolve an area of reduced bone density better than the graphic appearance.



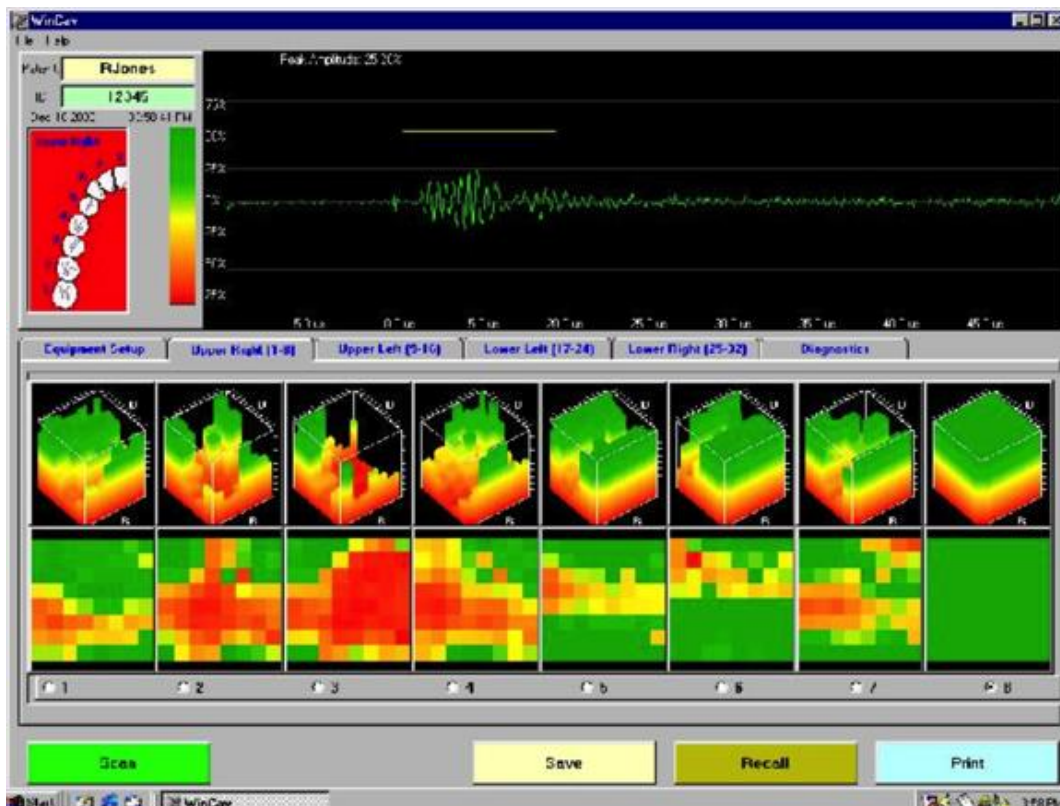
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Hidden Pathogens in Root and Jawbone



### Cavitat

Until the company went out of business in 2005, there was a through-transmission ultrasound system available, called the Cavitat. The system was based on the fact that dead bone, with its disconnected trabecular structure, could not conduct sound the way intact bone does. A signal generated between a sending and a receiving contact, held on either side of the alveolar process, would be converted to a three dimensional image of a volume of jawbone. Damaged bone was rendered in red, while normal bone would be seen as green. Some very useful clinical and research work was done with this instrument, and its absence has negatively impacted further work in this area.

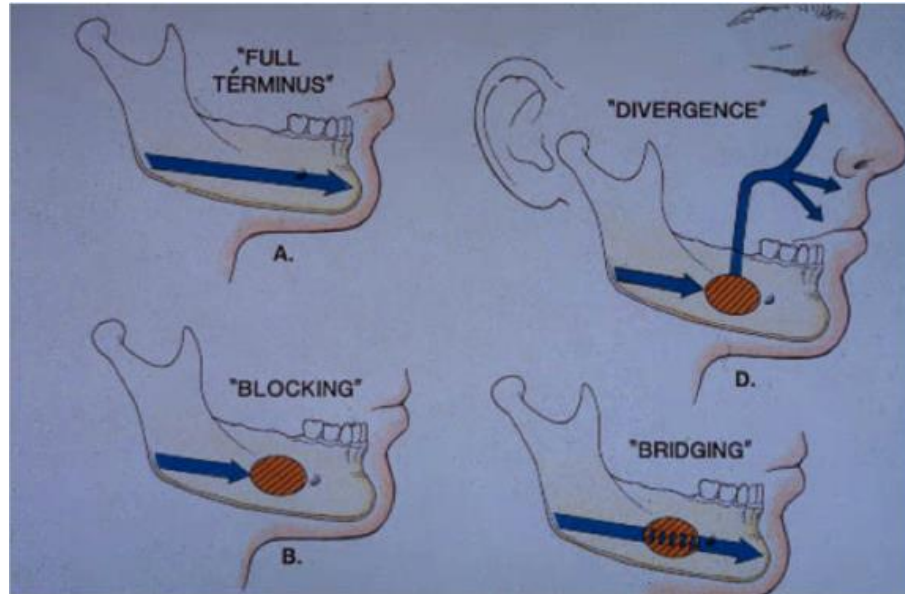


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### The McMahon - Ratner Method

The McMahon - Ratner method is by detecting lesions by derangement of the inferior alveolar block.

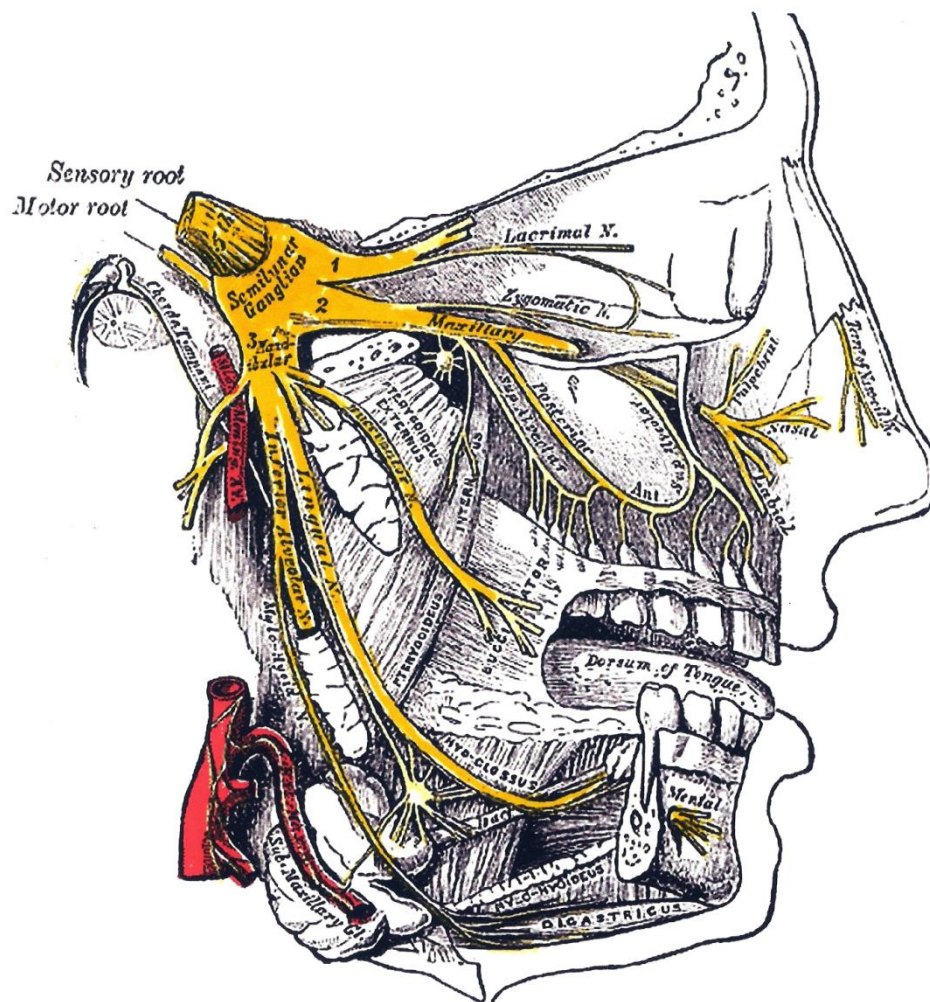


## Ischemic Osteonecrosis and Neuralgia

Besides the upper and lower jawbones, no other bone in the body is traversed by such large sensory nerves. So, it's not surprising that ischemia and necrosis in the jawbones can affect the nerves, and in some cases cause pain. In fact, about 85 percent of neuralgias are associated with the trigeminal nerve, and many appear to derive from sites of ischemic bone in the jaws.

The term we use for jawbone osteonecrosis associated with pain is NICO, or "neuralgia-inducing cavitation osteonecrosis." As biological dentists we constantly look for strategies to treat, and possibly to prevent, NICO and other ischemic lesions.

### Jawbone Sensory Nerves



### Ischemic Jawbone Neuralgic Pain

Most of the scientific inquiry into jawbone osteonecrosis was done in regard to its relationship with pain: facial neuralgias, atypical facial pain, trigeminal neuralgia, migraine, and pain referred to distant sites. Several surgeons, starting with Dr. E. J. Ratner in 1976, have reported high rates of relief from neuralgic pain when ischemic jawbone sites are identified and treated. The first step, as Ratner recommended, is to confirm the connection between the site and the pain with local anesthetic. After that, the sites would be opened surgically and curetted of the necrotic contents. Reliable relief of neuralgias has been reported, although it sometimes would take repeated surgical treatments to reach that final result.

Ratner EJ, et al. Oral Surg Oral Med Oral Pathol. 1979 Jul;48(1):3-20.



## Learning Aid

Hidden Pathogens in Root and Jawbone

### NICO Treatment Methods

NICO is the acronym for “neuralgia-inducing cavitation osteonecrosis.” You can find an extensive discussion of NICO at the [Maxillofacial Center for Education & Research](#) website. The Maxillofacial Center is a private research laboratory and consultation service started in 1994 by Dr. J. E. Bouquot as a national service to the dental and medical professions. We have included a video of one of Dr. Bouquot’s lectures to IAOMT in the [Supplemental Reading and Video](#) page for this course.

#### Surgical Curettage

The success of surgical curettage of painful lesions seems to follow the old adage that where there is more bleeding provoked, bone will follow. Repeated procedures were required to reach the final result in many cases. Surgical curettage remains the standard for definitive treatment.

NICO: IT'S IMPORTANT TO FIND THE LESION  
BECAUSE CURETTAGE OF CANCELLOUS LESION SEEMS TO WORK!

Authors	Country	Year	# Patients	Median Post-op Pain Reduction
Ratner et al.	USA	1976	26 *	100%
Ratner et al.	USA	1979	61 *	93
Roberts et al.	USA	1979	42 *	100
Shaber et al.	USA	1980	8	100
Mathis et al.	USA	1981	8	100
Wang et al.	China	1982	103	100
Demerath, Sist	USA	1982	29	50
Roberts et al.	USA	1984	208 *	95
Grechko, Puzin	Russia	1984	65	100
Ratner et al.	USA	1986	1300 *	85
McMahan et al.	USA	1992	48	80
Bouquot et al.	USA	1995	102	72 **

\* Probably overlapping patients in various studies  
\*\* Average follow time: 4.8 years

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#### Anti-coagulation

Some rate of relief of pain in long bones and jawbone neuralgias has been achieved with anti-coagulation therapy, counteracting the effects of the patients’ endogenous hypercoagulation tendencies. It can provide relief in up to 40% of NICO cases, especially surgical failures. (Glueck, 1996)

#### Ozone Therapy

Oxygen/ozone gas injected in a dose controlled manner into identified lesions, through a trephine (X-tip, Dentsply-Maillefeur) can be a profound disinfectant. Many of the anaerobic waste products of microbial metabolism are themselves pro-thrombotic, and tend to perpetuate the ischemic problem. Ozone can also provoke a number of healing mechanisms that result in the generation of new circulation.

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### Infrared Led Therapy

Low level lasers and near infrared LED devices have been shown to promote bone healing and regeneration of circulation over a period of months.



### Shock Wave Ultrasound

Shock wave therapy is based on the principles of ultrasonic lithotripsy and success in treating orthopedic neuralgias. Inducing micro-trauma by treatment of ischemic jawbones with an extra-oral ultrasonic wand can induce new circulation and bone regrowth.



### Preventing Ischemic Bone Damage

Is there such a thing as a simple extraction? It appears that some undetermined percentage of the population will experience ischemic bone healing of routine dental extractions due to their underlying hypercoagulation states, but dentists don't test for them before proceeding. Nor do we take into account the load of infection and trauma the site has accumulated. We just assume they'll heal.

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Here are some strategies that biological dentists have come up with in an effort to mitigate these risks:

- Minimize the use of vasoconstrictors, even for surgery. This avoids the transient ischemia that can be so damaging to osteocyte viability. “Where there is more bleeding, more bone will follow.”
- Curette the socket with a bur to remove remnants of the periodontal ligament. The ligament is a barrier that normally prevents the root surface from getting involved with the bone replacement cycle, so it may block the bone remodeling system from fully accessing the socket.
- Perforate or decorticate the lamina dura with a bur. This gives the marrow cells, macrophages and stem cells, better access to the organizing blood clot in the socket. It follows the concept that micro-injuries to bone stimulate better healing, too. *Lee TC, et al. Bone adaptation to load: microdamage as a stimulant for bone remodeling. J. Anat. (2002) 437-446.*



from [www.maxillofacialcenter.com](http://www.maxillofacialcenter.com)

- Irrigate the extraction site copiously as you are curetting and burring. Use lots of saline, ozone-saturated water or saline, or other disinfecting solution. Try to reduce the local burden of infection.
- Employ good socket grafting to reduce dry sockets. Especially in favor now is the use of **autogenous platelet-rich fibrin** dressings.



## Hidden Pathogens

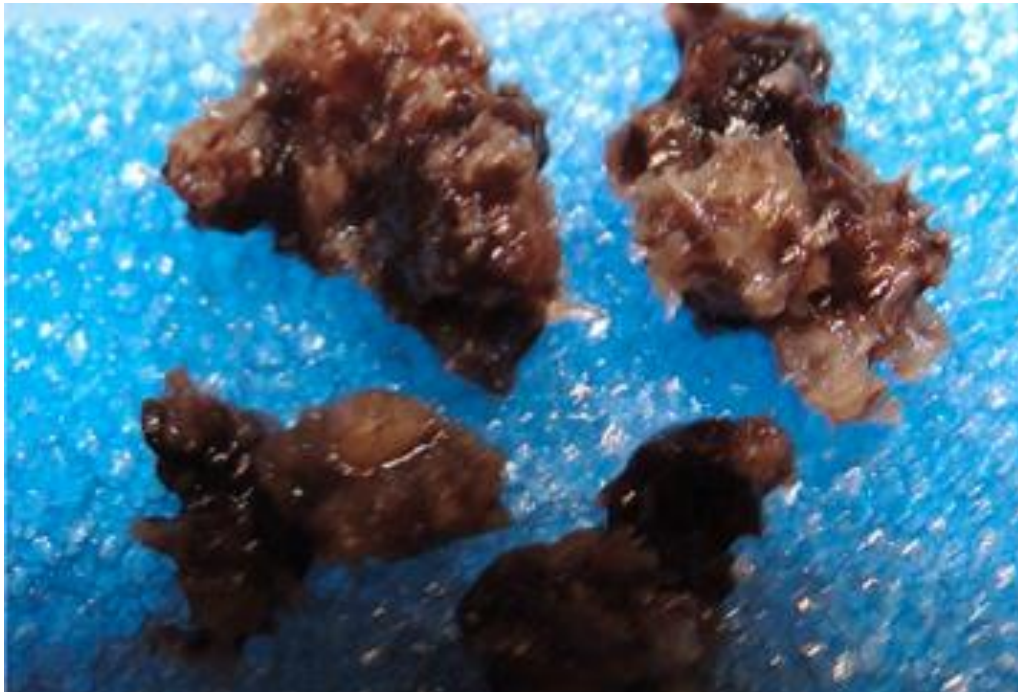
If we can find evidence for ischemic bone lesions so often, and the majority of them are not painful, why should we be concerned?

The reason is – they are toxic. They universally harbor anaerobic microbes: bacteria, fungi, and viruses. And these microbes may or may not be culturable, but they can be identified by their DNA. As well, the waste products that those microbes leave behind have also been shown to contain a number of toxic compounds.

Cytokine ratios are altered in ischemically damaged jawbone. Some investigators wonder if these jawbone lesions, affected as they are by microbes, microbial waste products, and altered physiology, are not a hidden source of systemic stress and immune disease.

### Dental DNA

Dental DNA is a laboratory that dentists can use to document microbial DNA in surgically curetted osteonecrotic material. The lab reports that they have never had a sample that did not show evidence of at least three species of anaerobic microbes, and that they find most samples usually contain more. For more information see the Dental DNA website: <http://www.dentaldna.us/>



from [www.maxillofacialcenter.com](http://www.maxillofacialcenter.com)

### Toxic Compounds

Anaerobic microbes found in ischemic bone lesions leave behind waste products that have also been shown to contain a number of toxic compounds. These compounds have been shown to strongly inhibit a number of essential enzymes, and therefore are toxic to human physiology.

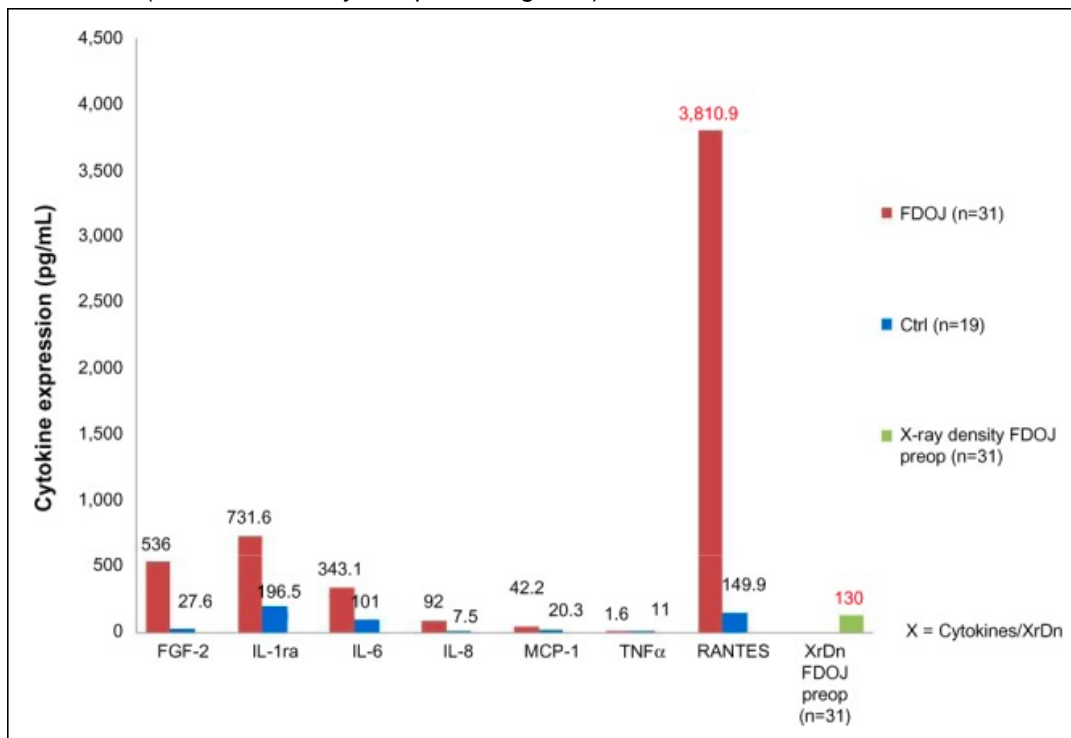
Toxins identified in osteonecrotic material:

- endotoxins
- fungal gliotoxins
- sulfides
- thioethers
- methyl mercaptan
- polyamines: putrescine and cadaverine

## Cytokine Ratios

Cytokine ratios are altered in ischemically damaged jawbone. We don't know why there is so little inflammatory infiltrate, or why pro-inflammatory cytokines are generally not elevated. But uniquely, chemokine CCL-5, otherwise known as RANTES, and Fibroblast Growth Factor FGF-2 have been found to be consistently very high in these bone samples.

- Elevated chemokine CCL-5, or RANTES
- Elevated fibroblast growth factor FGF-2
- Elevated IL-1ra, (anti-inflammatory receptor antagonist)



Lechner J. Validation of dental X-ray by cytokine RANTES - comparison of X-ray findings with cytokine overexpression in jawbone. *Clin Cosmet Investig Dent*. 2014 Aug 21;6:71-9.

Overexpression of RANTES is found in many immune diseases, leading some investigators to wonder if these jawbone lesions are not a hidden source of systemic stress and disease in this way.

Lechner J, von Baehr V. Chemokine RANTES/CCL5 as an unknown link between wound healing in the jawbone and systemic disease. *EPMA J*. 2015 May 6;6(1):10.

## Root Treated Teeth Don't Always Heal

Some biological dentists actually reject the whole concept of root canal therapy. They say there is no justification for leaving dead organs embedded in the body.

### X-Rays Not Reliable

The classic definition of endodontic success (statement of its uncertainty) goes back to the early days:

"[The case] in which the periapical bone structure and the periodontal membrane appeared normal on the roentgenogram and the tooth was entirely comfortable. A case was judged unsuccessful if an area of rarefaction had developed where none had existed before, if a previous area of rarefaction had not repaired, or if, on checkup, the tooth was sensitive to percussion or was uncomfortable."

Goldman M, et. al. Reliability of radiographic interpretations.  
Oral Surgery 1974, 38:287-293.

"It is clear that the radiograph is a very questionable means of determining success and failure. This is not surprising, for we interpret radiographs – we do not read them."

Goldman M, et. al. Endodontic success – who's reading the radiograph.  
Oral Surgery 1972, 33:432-437.

There is a huge literature on the meaning of radiographic interpretation of endodontic treatments. The reliability of radiographs to prove success is always in doubt.

For example, in an autopsy study that examined block sections of 29 root treated teeth, ten had radiographic rarefactions, and histologically verified periapical inflammation. Of the nineteen that were radiographically normal, five had periapical inflammation when examined histologically.

Green T, et. al. Radiographic and histologic periapical findings of root canal treated teeth in cadavers, Oral Surgery 1997, 83:707-711

### CBCT Uncovers Many More Failures

"...CBCT imaging appears to provide a superior validity and reliability in the detection of periapical lesions."

Venskutonis T, et. al. The importance of cone beam computed tomography in the management of endodontic problems: a review of the literature.  
J Endod 2014, 40:1895-1901.

In a study of treated and untreated dogs' teeth, 93% had histologically confirmed apical periodontitis. PA radiographs found 71% of them, while CBCT found 84%. Diagnostic accuracy (true positives + true negatives) was 0.78 for PA's, and 0.92 for CBCT.

De Paul-Silva FW, et. al. Accuracy of PA radiography and CBCT scans in diagnosing apical periodontitis using histological findings as a gold standard.  
J Endod 2009, 35:1009-1012.

Following is an example of an endodontic treatment that would have been acceptable until the CBCT reveals the extent of its failure.

An upper left second molar, PA at the time of treatment:



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A follow up PA, eighteen months later, shows a reasonable degree of healing:



A CBCT scan taken the same day, rotated into the coronal plane, shows how the healing was illusory. Yet the tooth was entirely comfortable. Is it a treatment failure?



### Toxicity of Treated Roots

Beyond massive numbers of anecdotes, and the percentage that smell bad when finally extracted, evidence for toxicity of root canal treatments is sparsely documented. The best documented phenomenon is the ability of dilute extracts from the surface of extracted, treated roots to inhibit critical enzymes. It is explained in detail in a lecture to the IAOMT by Dr. Boyd Haley, and also in the article “Enzymatic Inhibition Associated with Asymptomatic Root Canal Treated Teeth” by Dr. Nunnally. This lecture and article are included on the [Supplemental Reading and Videos](#) page for this course.

## Learning Aid

Hidden Pathogens in Root and Jawbone

The Dental DNA lab ([www.dentaldna.us](http://www.dentaldna.us)) reports that they find high levels of pathogen DNA associated with the roots of extracted root treated teeth. As of this writing in 2015, these reports suffer from a lack of data from untreated controls.

Recent scientific literature has shown that having one or more root canal procedures is associated with an increased incidence of coronary heart disease. Another recent (2013) study examined the blood clots that caused heart attacks (myocardial infarction) and found a high concentration of the DNA found in the pathogens most commonly seen in root canal-treated teeth, as well as in chronic gum disease. The same types of oral pathogen DNA have also been identified in a majority of ruptured intracranial aneurysm specimens obtained from patients, as well as in a majority of the samples of pericardial fluid surrounding the hearts of chronic coronary artery disease patients.

### References:

Frisk F, Hakeberg M, Ahlqvist M, Bengtsson C, (2003) "Endodontic variables and coronary artery disease," *Acta Odontologica Scandinavica*, 61:257-262. PMID: 14763775

Joshi K, Pitiphat W, Hung H et al, (2006) Pulpal inflammation and incidence of coronary artery disease," *Journal of Endodontics*, 32:99-103. PMID: 16427454

Pessi T, Karhunen V, Karjalainen P et al, (2013) "Bacterial signatures in thrombus aspirates of patients with myocardial infarction," *Circulation*, 127:1219-1228. PMID: 23418311

Pyysalo M, Pyysalo L, Pessi T et al (2013) "The connection between ruptured cerebral aneurysms and odontogenic bacteria," *Journal of Neurology, Neurosurgery, and Psychiatry*, 84:1214-1218. PMID: 23761916

Louhelainen A, Aho J, Tuomisto S et al (2014) "Oral bacterial DNA findings in pericardial fluid," *Journal of Oral Microbiology*, November 19. PMID: 25412607