TRATTAMENTO DELLA ONJ: UPDATE DELLA LETTERATURA

(2014-2018)

UNIVERSITÀ DI PARMA

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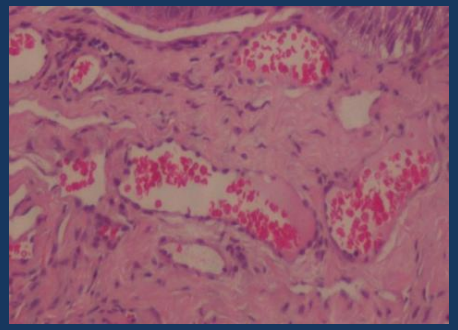
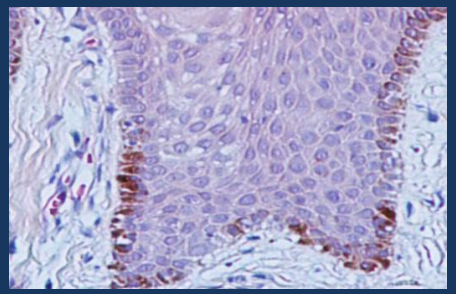
LASER PER IL TRATTAMENTO DELLA ONJ

NON CHIRURGICI

FOTOCOAGULAZIONE E SBIANCAMENTO

ESSICCAZIONE DI LESIONI VASCOLARI– DISTRUZIONE DEI PIGMENTI





ATTIVITA' FOTOCHIMICA

LOW LEVEL LASER THERAPY
(LLLT –"BIOMODULAZIONE")
TERAPIA FOTODINAMICA

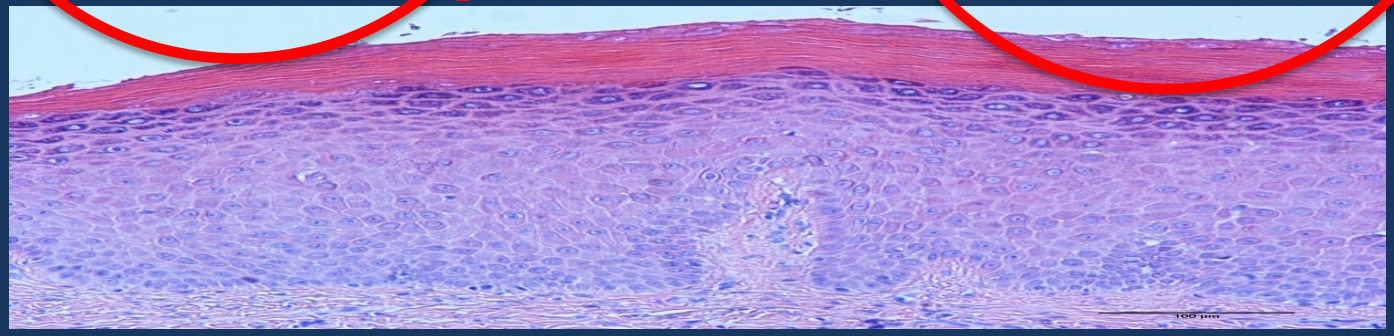
CHIRURGICI

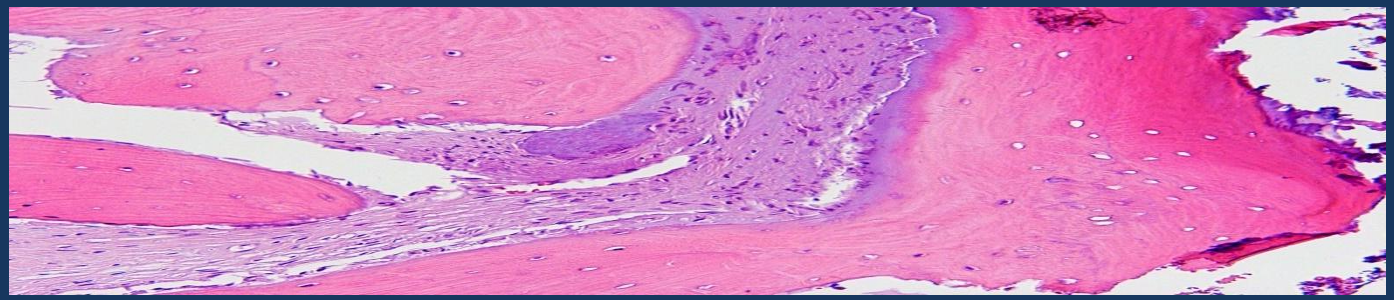
DIAGNOSI

BIOPSIA (Incisionale ed escissionale)

TRATTAMENTO

RIMOZIONE TISSUTALE (taglio e vaporizzazione tissutale)





Lasers in chirurgia orale (più utilizzati)

TIPO DI LASER	LUNGHEZZA D'ONDA	PROFONDITA' DI PENETRAZIONE	ASSORBITO DA
Nd:YAG	1064 nm	3-5mm	Melanina/Hb
DIODE	810-980 nm	2-4mm	Melanina/Hb
Er:YAG	2940 nm	0.1mm	Acqua/HA
KTP	532 nm	0.7mm	Melanina/Hb
CO_2	10600 nm	0.2mm	Acqua
Er, Cr:YSGG	2780 nm	0.1 mm	Acqua

LASER FOR THE TREATMENT OF OSTEONECROSIS

REVIEW OF THE ENGLISH LITERATURE (WOS – Scopus - PubMed)

SEARCHING CRITERIA

TIME:
JAN 2014 - APR 2018

ENTRY TERMS:
"LASER" or "LLLT"
and
- "OSTEONECROSIS"
- "ONJ"
- "BRONJ"
- "MRONJ"

46 PAPERS

EXCLUSION OF 17 PAPERS

29 PAPERS

8 REVIEWS

9 CASE REPORTS

3 CASE SERIES

6 IN VITRO STUDIES

2 STUDIES ON ANIMAL MODEL

LASER AND OSTEONECROSIS (2014 – 2018)

9 CASE REPORTS

AUTHORS – JOURNAL - YEAR	MEDICATION	SITE - STAGE	TREATMENT	LASER
Migliario *et* al. - Dent J (Basel) - 2017	Alendronate	Upper/lowe Jaw Stage ?	Laser Sugery Antiobiotics + LLLT	Er:YAG Diode
Fornaini *et* al. Laser Ther - 2017	Zoledronate - Sunitinib	Lowe Jaw Stage II	Laser Surgery + PRP Antibiotics + LLLT	Er:YAG Diode
Momesso *et* al. J Lasers Med Sci - 2017	Alendronate	Upper Jaw Stage II	Debridment Antibiotics – antiseptics + LLLT	Diode (AlGaInP)
Giovannacci *et* al. J Oral Maxillofac Surg – 2017	Alendronate	Lower Jaw Stage II	Laser Surgery (AF guided) Antibiotics + LLLT	Er:YAG Nd:YAG
Minamisako *et* al. Case Rep Dent - 2016	Alendronate	Upper Jaw Stage II	Debridment PDT (methylene blue) - LLLT	Diode
Giovannacci I *et* al. Minerva Stomatol - 2016	Zoledronate	2 Upper Jaw - 1 Lower Jaw Stage III	Laser Sugery (Autofluorescence-guided) Antiobiotics + LLLT	Er:YAG Nd:YAG
Heggendorn *et* al. Spec Care Dentist - 2016	Zoledronate	Lower Jaw Stage II	Antiseptics + LLLT	Diode
Vescovi P *et* al. Photomed and Laser Surg 2015	Zoledronate	Upper Jaw Stage III	Laser Ssurgery (Autofluorescence guided) Antibiotics + LLLT	Er:YAG Nd:YAG
Porcaro et al. Oral Surg Oral Med Oral Pathol Oral Radiol - 2015	Zoledronate	Lower Jaw Stage III	Laser Surgery (Doxyxycline fluorescence guided) Antibiotics + LLLT	Er:YAG Nd:YAG Diode

LASER AND OSTEONECROSIS (2014 – 2018)

3 CASE SERIES

AUTHORS – JOURNAL - YEAR	NUMBER OF CASES	TREATMENT	TYPE OF LASER	RESULTS
Favia G. *et* al. *Oral Dis* - 2017	24 (out of 131) All stages	Antiseptic + antibiotics + LLLT	DIODE	2 cases – downgrading 1 case - upgrading
Altay *et* al. *Photomed Laser Surg* - 2014	11 All Stages	Surgery + antibiotics + LLLT	GaAlAs (Diode)	Complete mucosal healing in all cases
Vescovi *et* al. Int J Dent - 2014	63 (Stage I) Unresponsive to conservative treatment including LLLT	Surgery (traditional or Laser) Antibiotics + LLLT	Er:YAG Nd:Yag	Complete healing in 96.2% of cases

2 STUDIES ON ANIMALS

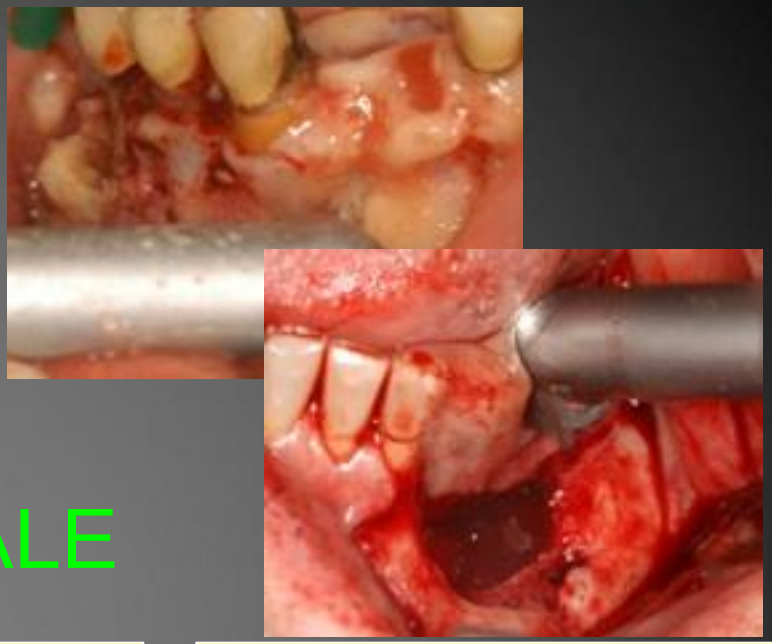
AUTHORS – JOURNAL - YEAR	ANIMAL MODEL	TYPE OF LASER	MAIN RESULTS
Weber *et* al. J Biomed Opt - 2017	Rats treated with Zoledronate and Dexamethason	Diode	Faster wound healing No ONJ
Mergoni *et* al. Support Care Cancer - 2016	Rats treated with Zoledronate	Nd:YAG	LLLT promotes osteoblasts differentiation (increasing of OCN)

LASER AND OSTEONECROSIS (2014 – 2018)

6 *IN VITRO* STUDIES

AUTHORS – JOURNAL - YEAR	TARGET	TYPE OF LASER	MAIN RESULTS
Mergoni *et* al. *Laser Med Sci* -2018	Osteoblasts	GaAs (diode)	LLLT improves the formation of bone nodules
Hafner *et* al. *J Oral Maxillofac Surg* - 2016	Actinomyces naeslundii (from osteonecrosis)	Diode (Methylene blue activated – PDT)	PDT is the most effective method of bacterial inactivation compared to Clorhexidine, polyhexanyde and Laser alone or dye alone
Lee JY *et* al. *Laser Med Sci* - 2015	Oral keratynocites (alendronate treated)	GaAlas (diode)	LLLT Increases of IL-8 and VEGF (which are downregualted by alendronate)
Walter C *et* al. *Biomed Rep* - 2015	Keratinocytes Fibroblasts Endothelial Cells Osteoblasts (treated with Clodronate, Ibadronate, pamidronate and zoledronate	Diode	LLLT significantly increase cells viability
Pansani *et* al. Int J Oral and Maxillofac Surg - 2014	Gingival fibroblasts (treated with zoledronate)	InGaAsP (diode)	LLLT increases cell proliferation (but not in zoledronate treated cells) LLLT induces a decrease of apoptosis but not in zoledronate treated cells
Basso *et* al. *Support Care Cancer* - 2014	Osteoblasts (zoledronate –treated)	InGaAsP (diode)	LLLT increases Col-I expression in osteoblasts treated with zoledronate No increase of bone nodules formation

LASER - 1
FUNZIONE CHIRURGICA



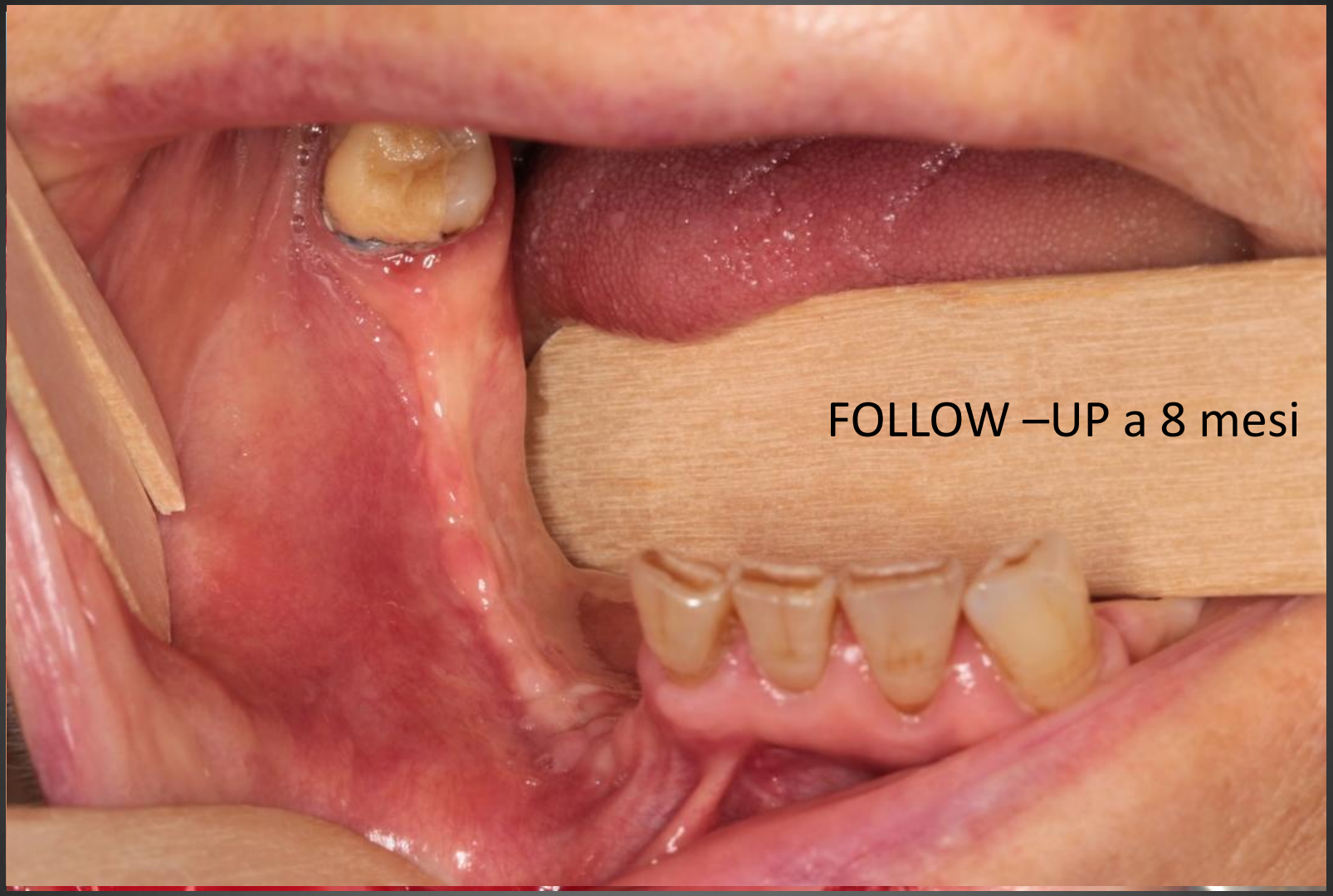
OSTEOTOMIA

VAPORIZZAZIONE TISSUTALE

STAGE 1	STAGE 2	STAGE 3

Efficacy of laser therapy in the management of bisphosphonate-related osteonecrosis of the jaw (BRONJ): a systematic review.
Weber JB, Camilotti RS, Ponte ME.
Lasers Med Sci. 2016 Aug;31(6):1261-72. Epub 2016 Mar 30. Review.

Osteonecrosi Stage II - forma non-exposed



CM, F, 65 anni
osteoporosi, - acido alendronico 84 dosi *im*
estrazione di 4.4 - 4.5 - 4.6

2. LASER
FUNZIONE DI SUPPORTO

"Biostimolazione" – Azione antibatterica

TERAPIA MEDICA

TERAPIA CHIRURGICA

(OCCASIONALMENTE) DA SOLA

STAGE 1

STAGE 2

STAGE 3

Bisphosphonate-related **osteonecrosis** of the jaw: a review of the potential efficacy of low-level **laser** therapy.

Latifyan S, Genot MT, Klastersky J.

Support Care Cancer. 2016 Sep;24(9):3687-93. Epub 2016 Mar 31. Review.

1. LASER
FUNZIONE DI SUPPORTO ALLA CHIRURGIA

"Biostimolazione"

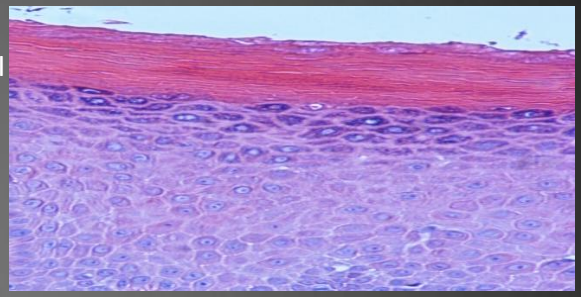
Lasers Med Sci (2015) 30:635–643
DOI 10.1007/s10103-013-1382-6

ORIGINAL ARTICLE

Effect of low-level laser therapy on oral keratinocytes exposed to bisphosphonate

Jae-Yeol Lee · In-Ryoung Kim · Bong-Soo Park · Yong-Deok Kim · In-Kyo Chung · Jae-Min Song · Sang-Hun Shin

OVERCOMING DEGLI EFFETTI INIBITORI DI
ALENDRONATO SULLA VITALITA' DEI CHERATINOCITI
ESPRESSIONE DI IL-8, VEGF E COLLAGENE TIPO I

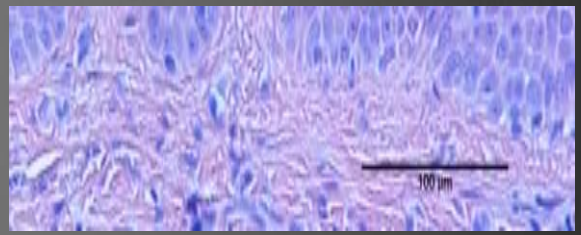


Research Paper
Wound Healing

Effects of low-level laser therapy on the proliferation and apoptosis of gingival fibroblasts treated with zoledronic acid

T. Nogueira Pansani[1], F. Gonçalves Basso[1], A. P. Silveira Turrioni[1], C. Kurachi[2], J. Hebling[1], C. A. de Souza Costa[1]
[1]Araraquara School of Dentistry, UNESP – Universidade Estadual Paulista, Araraquara, SP, Brazil; [2]Physics Institute, USP – Universidade de São Paulo, São Carlos, SP, Brazil

AUMENTO DELLA PROLIFERAZIONE FIBROBLASTICA
MA NON SOSTANZIALE NEI FIBROBLASTI CON AC. ZOLEDRONICO



Support Care Cancer (2014) 22:2741–2748
DOI 10.1007/s00520-014-2267-3

ORIGINAL ARTICLE

Low-level laser therapy for osteonecrotic lesions: effects on osteoblasts treated with zoledronic acid

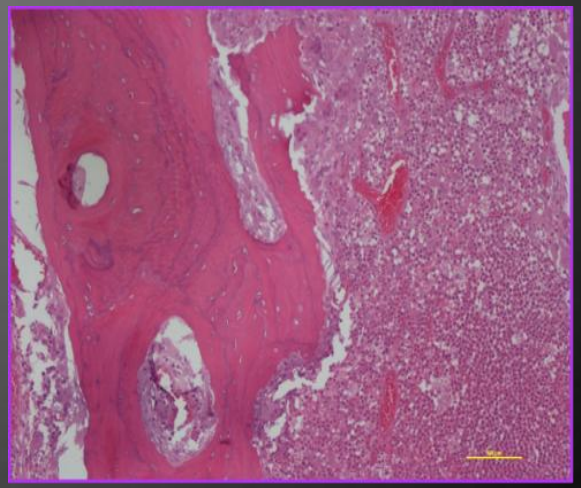
Fernanda Gonçalves. Basso · Ana Paula Silveira. Turrioni · Diana Gabiela Soares · Vanderlei Salvador Bagnato · Josimeri Hebling · Carlos Alberto de Souza Costa

AUMENTO VITALITA' OSTEOBLASTI
AUMENTO ESPRESSIONE DEL GENE COL-I NEGLI OSTEOBLASTI STIMOLATI CON ACIDO ZOLEDRONICO

The effect of laser therapy on the expression of osteocalcin and osteopontin after tooth extraction in rats treated with zoledronate and dexamethasone

Giovanni Mergoni[1] · Paolo Vescovi[1] · Roberto Sala[2] · Elisabetta Merigo[1] · Pietro Passerini[1] · Roberta Maestri[3] · Domenico Corradi[3] · Paolo Govoni[4] · Samir Nammour[5] · Massimiliano G. Bianchi[2]

PROMOTING DELLA DIFFERENZIAZIONE OSTEOBLASTICA E INCREMENTO DELLA PRODUZIONE DI OSTEOCALCINA



1. LASER
FUNZIONE DI SUPPORTO ALLA CHIRURGIA
Azione antibatterica

SCIENTIFIC REPORTS

OPEN

The association of medication-related osteonecrosis of the jaw with *Actinomyces spp.* infection

Received: 26 January 2016
Accepted: 21 July 2016
Published: 17 August 2016

Guenter Russmueller[1], Rudolf Seemann[1], Kathrin Weiss[2], Victoria Stadler[1], Manuel Speiss[1], Christos Perisanidis[1], Thorsten Fuereder[2], Birgit Willinger[3], Irene Sulzbacher[4] & Christoph Steininger[2]

J Biol Regul Homeost Agents. 2015 Oct-Dec;29(4):977-83.

Microbiological investigation of medication-related osteonecrosis of the jaw: preliminary results.

Crincoli V1, Ballini A2, Di Comite M2, Tettamanti L3, Coscia MF2, Mastrangelo F4, De Vito D2.
Author information

ORIGINAL ARTICLE — INFECTIOUS DISEASES

Analysis of the factors affecting the formation of the microbiome associated with chronic osteomyelitis of the jaw

A. Goda[1]*, F. Maruyama[2,3]*, Y. Michi[1], I. Nakagawa[2] and K. Harada[1]
1) Section of Maxillofacial Surgery, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, 2) Section of Bacterial Pathogenesis, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University and 3) Section of Microbial Genomics and Ecology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Bunkyo-ku, Tokyo, Japan

RESEARCH — Open Access

Systemic immunity shapes the oral microbiome and susceptibility to bisphosphonate-associated osteonecrosis of the jaw

Shirin Kalyan[1], Jun Wang[2,3], Elgar Susanne Quabius[1,4], Jörn Huck[5], Jörg Wiltfang[5], John F Baines[2,3] and Dieter Kabelitz[1]*

Clinical Study

Bisphosphonate Related Osteonecrosis of the Jaw: A Study of 18 Cases Associated with Fungal Infection

V. Aftimos,[1] T. Zeinoun,[2] R. Bou Tayeh,[2] and G. Aftimos[1]

Review Article

Is Bisphosphonate-Related Osteonecrosis of the Jaw an Infection? A Histological and Microbiological Ten-Year Summary

A. M. Hinson,[1] C. W. Smith,[2] E. R. Siegel,[3] and B. C. Stack Jr.[4]

RESEARCH REPORTS
Biological

A Role of Oral Bacteria in Bisphosphonate-induced Osteonecrosis of the Jaw

H. Mawardi[1,2,3], G. Giro[1,4], M. Kajiya[1,2], K. Ohta[1,2], S. Almazrooa[1,2,3], E. Alshwaimi[5], S.-B. Woo[2], I. Nishimura[6], and T. Kawai[1,2]*

Eur J Clin Microbiol Infect Dis (2014) 33:1873–1880
DOI 10.1007/s10096-014-2160-5

REVIEW

***Actinomyces* osteomyelitis in bisphosphonate-related osteonecrosis of the jaw (BRONJ): the missing link?**

J. De Ceulaer · E. Tacconelli · S. J. Vandecasteele

ARCHIVES OF ORAL BIOLOGY 59 (2014) 790–799

Review

Important aspects regarding the role of microorganisms in bisphosphonate-related osteonecrosis of the jaws

Renata Chiapinotto Boff, Fernanda Gonçalves Salum, Maria Antonia Figueiredo, Karen Cherubini *
Postgraduate Program, Dental College, Pontifical Catholic University of Rio Grande do Sul – PUCRS, Brazil

RUOLO DELLE INFEZIONI

MEDICATION RELATED OSTENECROSIS OF THE JAWS

- High prevalence of *Actynomices* in MRONJ lesions in retrospective series (73.2%)

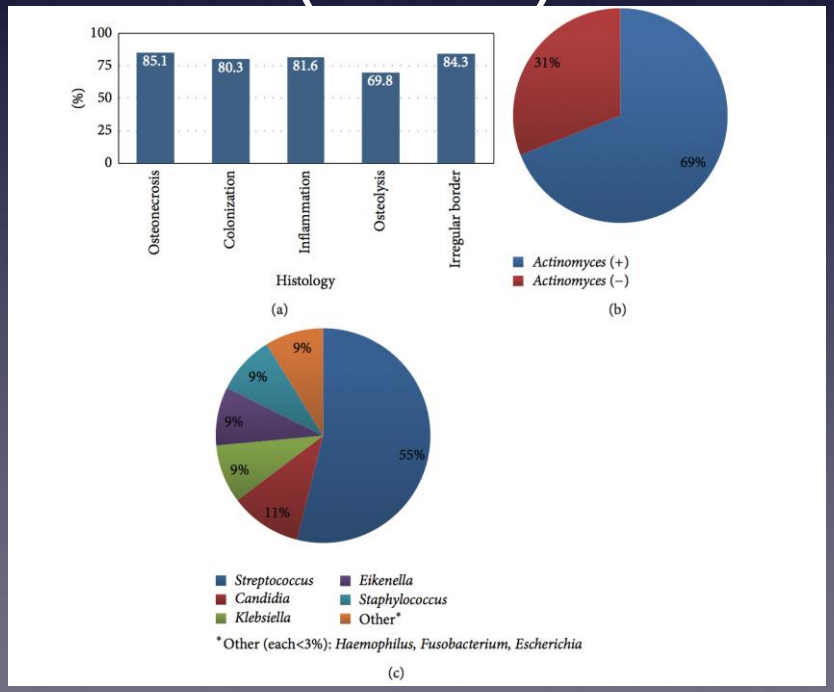


Table 1 – Reports on microorganisms involved in bisphosphonate-related osteonecrosis of the jaws (BRONJ).

Microorganisms	*n* of positive cases/total *n* (%)	Bisphosphonate	Method	Reference
Actinomyces spp *Candida* spp	8/8 (100%) 1/8 (12.5%)	Pamidronate, zoledronic acid, ibandronate	Clinical study, histopathology (H&E, PAS, Gram, Grocott)	Hansen et al.[1]
Actinomyces spp	46/64 (72%)	Zoledronic acid, pamidronate, alendronate, ibandronate, risedronate	Clinical study, histopathology	Jacobsen et al.[21]
Actinomyces spp. *Actinomyces* spp	10/10 (100%) 4/10 (36.4%)	Zoledronic acid Alendronate	*In vivo* study (rats), histopathology (H&E)	Maahs et al.[23]
Fusobacterium, Bacillus, Actinomyces, Candida spp., Staphylococcus, Streptococcus, Selenomonas, Treponemas	4[a]	Pamidronate (1), zoledronic acid (1), alendronate (2)	Clinical study, histopathology (H&E), SEM	Sedghizadeh et al.[58]
Actinomyces spp Yeast colonies	13/13 (100%) *Common finding*[a]	Zoledronic acid, alendronate, risedronate, ibandronate	Retrospective study, histopathology, SEM	Lee et al.[59]
Actinomyces spp *Actinomyces israelii* *Candida* spp	26/26 (100%) 7/7 (100%) 3/26 (11.54%)	Zoledronic acid, pamidronate	Clinical study, histopathology (H&E, Grocott, Gram, PAS, Goldner or Elastica-van Gieson) PCR, SEM	Hansen et al.[68]
Actinomyces spp. *Candida* spp	1/4 (25%) 2/4 (50%)	Pamidronate and zoledronic acid ($n = 2$) Zoledronic acid ($n = 2$)	Clinical study, histopathology (H&E, PAS) and microbiology	Merigo et al.[69]
Actinomyces spp	28/30 (93%)	Pamidronate, zoledronic acid, alendronate, risedronate, clodronate	Clinical study, histopathology (Gram and PAS)	Lazarovici et al.[70]
Actinomyces spp	1/1 (100%)	Clodronate	Clinical study, histopathology: (H&E)	Senel et al.[71]
Actinomyces spp	7/20 (35%)	Zoledronic acid, pamidronate	Clinical study, histopathology Culture	Badros et al.[72]
Peptostreptococcus, Streptococcus, Eikenella, Prevotella, Porphyromonas, Fusobacterium	9/20 (45%)			
Actinomyces, Lactobacillus, Candida glabrata and other microorganisms	6[a]	Zoledronic acid, pamidronate	Clinical study, microbiology	Dannemann et al.[73]
Streptococcus intermedius, Peptostreptococcus spp, Bacteroides melaninogenicus	1/3 (33.3%)	Zoledronic acid, alendronate	Clinical study, culture	Wongchuensoontorn et al.[74]
Actinomyces israelii, Bacteroides fragilis	1/3 (33.3%)			
Enterococcus faecalis, Bacteroides fragilis	1/3 (33.3%)			
Actinomyces spp, Streptococcus spp, Prevotella, Klebsiella, Pseudomonas	12[a]	Alendronate, ibandronate, etidronate	Retrospective study, histopathology	O'Ryan & Lo[75]

H&E, haematoxylin and eosin; PAS, periodic acid-Schiff; SEM, scanning electron microscopy.
[a] Without other specification.

LASER – FUNZIONE DI SUPPORTO

PAZIENTI NON TRATTABILE A CAUSA DELLE CONDIZIONI SISTEMICHE

F – 77 A
METASTASI OSSEE TRATTATE CON ACIDO ZOLEDRONICO

Bisphosphonate-related **osteonecrosis** of the jaws: Report of a case using conservative protocol.

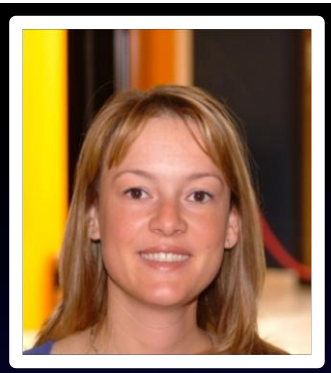
Heggendorn FL, Leite TC, Cunha KS, Junior AS, Gonçalves LS, da Costa KB, Dias EP. Spec Care Dentist. 2016 Jan;36(1):43-7. Epub 2015 Nov 24.

RISULTATI OTTENUTI NEL TRATTAMENTO DI 111 ONJ
CHIRURGIA LASER (Er:YAG) + LLLT

STAGE	NUMERO DI CASI	MIGLIORAMENTO CLINICO
I	44	42 (95.4%)
II	54	52 (96.3%)
III	13	13 (100%)
TOTALE	111	**107 (96.4%)**

EUROPEAN MASTER DEGREE: ORAL LASER APPLICATIONS

EMDOLA



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GRAZIE PER L'ATTENZIONE