

# SIPMO

Società Italiana di Patologia e Medicina Orale

## ONJ UPDATE 2018:

# I TRATTAMENTI CHIRURGICI NON ESTESI

*Alessandria, Sabato 5 Maggio 2018*



**Giacomo Oteri**



# Obiettivi del trattamento

- ▶ Ridurre lo stadio della patologia



# Obiettivi del trattamento

- ▶ Ridurre lo stadio della patologia
- ▶ Arrestarne la progressione



# Obiettivi del trattamento

- ▶ Ridurre lo stadio della patologia
- ▶ Arrestarne la progressione
- ▶ Migliorare la Qualità della vita



# Obiettivi del trattamento


- ▶ Ridurre lo stadio della patologia
- ▶ Arrestarne la progressione
- ▶ Migliorare la Qualità della vita



# Appropriatezza dei trattamenti chirurgici:



Position Paper



saving faces | changing lives  
**American Association of Oral and Maxillofacial Surgeons**

## Medication-Related Osteonecrosis of the Jaw—2014 Update

**Special Committee on Medication-Related Osteonecrosis of the Jaws:**

Salvatore L. Ruggiero, DMD, MD, Clinical Professor, Division of Oral and Maxillofacial Surgery, Stony Brook School of Dental Medicine, Hofstra North Shore-LIJ School of Medicine, New York Center for Orthognathic and Maxillofacial Surgery, Lake Success, NY

Thomas B. Dodson, DMD, MPH, Professor and Chair, Associate Dean for Hospital Affairs, University of Washington School of Dentistry, Department of Oral and Maxillofacial Surgery, Seattle, WA

John Fantasia, DDS, Chief, Division of Oral Pathology, Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY

Reginald Goodday, Professor, Department of Oral and Maxillofacial Sciences, Dalhousie University, Halifax, NS

Tara Aghaloo DDS, MD, PhD, Associate Professor, Oral and Maxillofacial Surgery, Assistant Dean for Clinical Research, UCLA School of Dentistry, Los Angeles, CA

Bhoomi Mehrotra, MD, Director, Cancer Institute at St. Francis Hospital, Roslyn, NY

Felice O’Ryan, DDS, Division of Maxillofacial Surgery, Kaiser Permanente Oakland Medical Center, Oakland, CA

**Introduction**

The Special Committee recommends changing the nomenclature of bisphosphonate-related osteonecrosis of the jaw (BRONJ). The Special Committee favors the term **medication-related osteonecrosis of the jaw (MRONJ)**. The change is justified to accommodate the growing number of osteonecrosis cases involving the maxilla and mandible associated with other antiresorptive (denosumab) and antiangiogenic therapies.

MRONJ adversely affects the quality of life, producing significant morbidity. Strategies for management of patients with, or at risk for, MRONJ were set forth in the American Association of Oral and Maxillofacial Surgeons (AAOMS) updated *Position Paper on Bisphosphonate-Related Osteonecrosis of the Jaws* and approved by the Board of Trustees in 2009.<sup>1</sup> The *Position Paper* was developed by a Special Committee appointed by the Board and composed of clinicians with extensive experience in caring for these patients and basic science researchers. The knowledge base and experience in addressing MRONJ has expanded, necessitating modifications and refinements to the previous *Position Paper*. This Special Committee met in September 2013 to appraise the current literature and revise the guidelines as indicated to reflect current knowledge in this field. This update contains revisions to diagnosis, staging, and management strategies, and highlights current research status. AAOMS considers it vitally important that this information be disseminated to other relevant health care professionals and organizations.

**Purpose**

The purpose of this updated position paper is to provide:

1. Risk estimates of developing MRONJ
2. Comparisons of the risks and benefits of medications related to osteonecrosis of the jaw (ONJ) in order to facilitate medical decision-making for the treating physician, dentist, dental specialist, and patients
3. Guidance to clinicians regarding:

PAGE 1 Medication-Related Osteonecrosis of the Jaw – 2014 Update



# Appropriatezza dei trattamenti chirurgici:

**25° CONGRESSO NAZIONALE  
COLLEGIO DEI DOCENTI UNIVERSITARI  
DI DISCIPLINE ODONTOSTOMATOLOGICHE**

**SESSIONI SIdCO - SIPMO**  
Parco dei Principi Grand Hotel, Roma

SIdCO  
SOCIETÀ ITALIANA DI CHIRURGIA  
ODONTOSTOMATOLOGICA

SIPMO  
Società Italiana di Patologia e Medicina Orale

**SABATO 14 APRILE**
**PRATICHE A RISCHIO INAPPROPRIATEZZA  
IN TEMA DI ONJ: OPEN MEETING**

**08.30** Lavori ONGOING congiunti SIdCO-SIPMO  
Scelte tematiche e metodologiche  
*G. Campisi, G. Oteri*

**08.45** Inappropriatezze in diagnosi clinica di ONJ e proposta di indicazioni  
*O. Di Fede, G. Favia, L. Lo Russo, A. Santarelli\**

**09.30** Inappropriatezze in diagnosi radiologica di ONJ e proposta di indicazioni  
*G. Bettini\*, U. Consolo, A. Lo Casto, D.M. Mignogna*

**10.00** Inappropriatezze in prevenzione ONJ e proposta di indicazioni  
*F. Bertoldo, V. Fusco, A. Marciánò, V. Panzarella\**

**10.30** Inappropriatezze nel management odontoiatrico e proposta di indicazioni per paziente a rischio ONJ  
*M. Biasotto, O. Di Fede\*, G. Favia, U. Romeo, P. Vescovi*

**11.00** Drug holiday (sospensione temporanea vs sospensione terapeutica). SI vs NO  
*A. Bedogni, F. Bertoldo, V. Fusco\*, M. Meleti*

**11.30** Inappropriatezze terapeutiche per ONJ e proposta indicazioni per chirurgia minore e maggiore  
*A. Bedogni\*, G. Colella, M. Gabriele, R. Mauceri, P. Vescovi\**

**12.30** Conclusioni  
*G. Campisi, G. Oteri*

SALA TORLONIA

\*Relatori





# TOPICS

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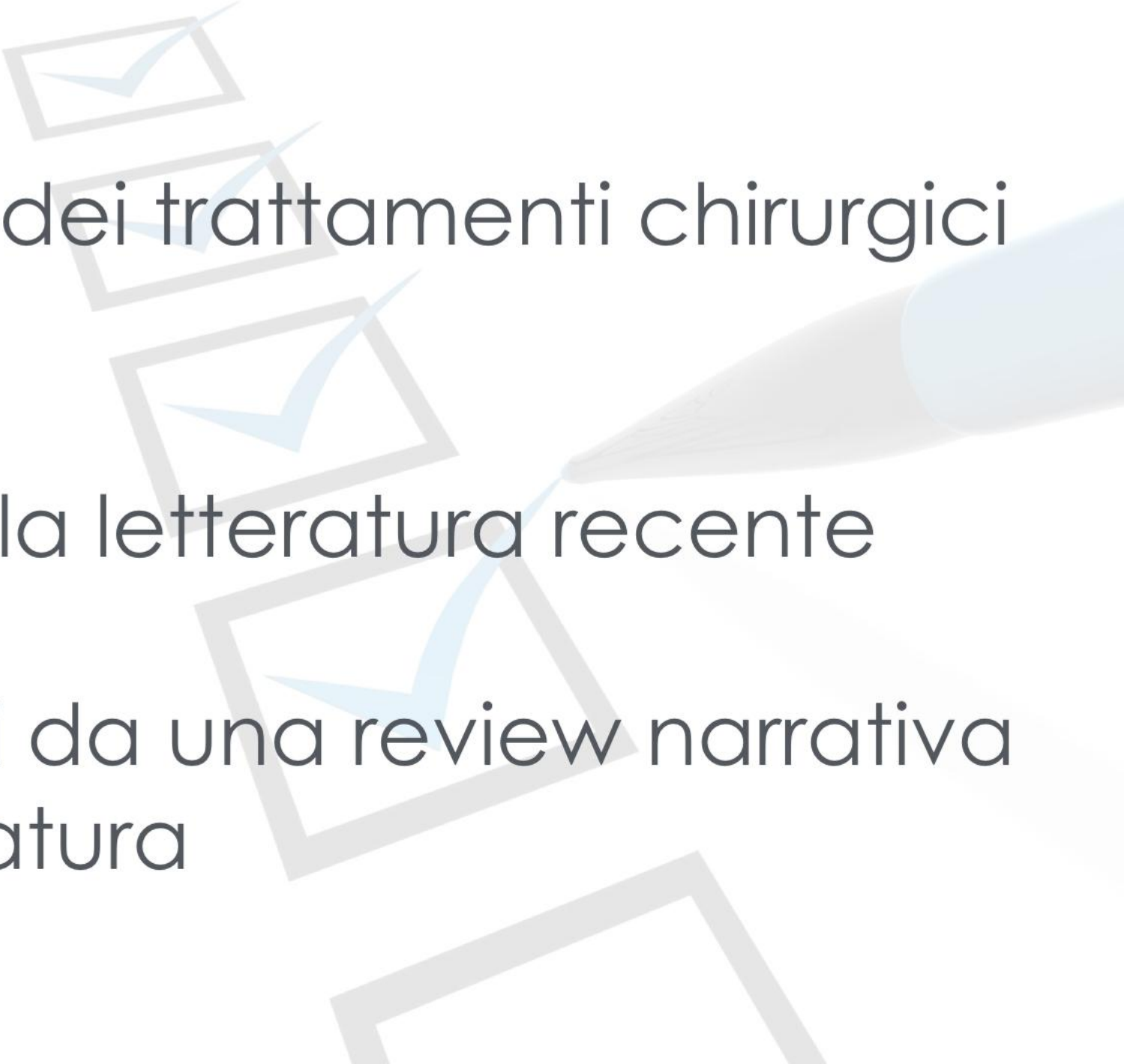
- Definizione dei trattamenti chirurgici non estesi



# TOPICS

- Definizione dei trattamenti chirurgici non estesi
- Update della letteratura recente

# TOPICS

- Definizione dei trattamenti chirurgici non estesi
  - Update della letteratura recente
  - Conclusioni da una review narrativa della letteratura
- 
- The background features a light blue pencil pointing towards the right, positioned behind a series of overlapping, semi-transparent rectangular boxes. Each box contains a blue checkmark, suggesting a checklist or a list of items. The overall aesthetic is clean and professional.

# TOPICS

- Definizione dei trattamenti chirurgici non estesi
- Update della letteratura recente
- Conclusioni da una review narrativa della letteratura

TRATTAMENTI

CHIRURGICI NON ESTESI

# Chirurgia non estesa



# Chirurgia non estesa

- ▶ Indicata per lesioni osteonecrotiche **focali**
- ▶ Approccio chirurgico **marginale** e **non segmentale**
- ▶ Stadi I - II AAOMS  
Stadio I SIPMO



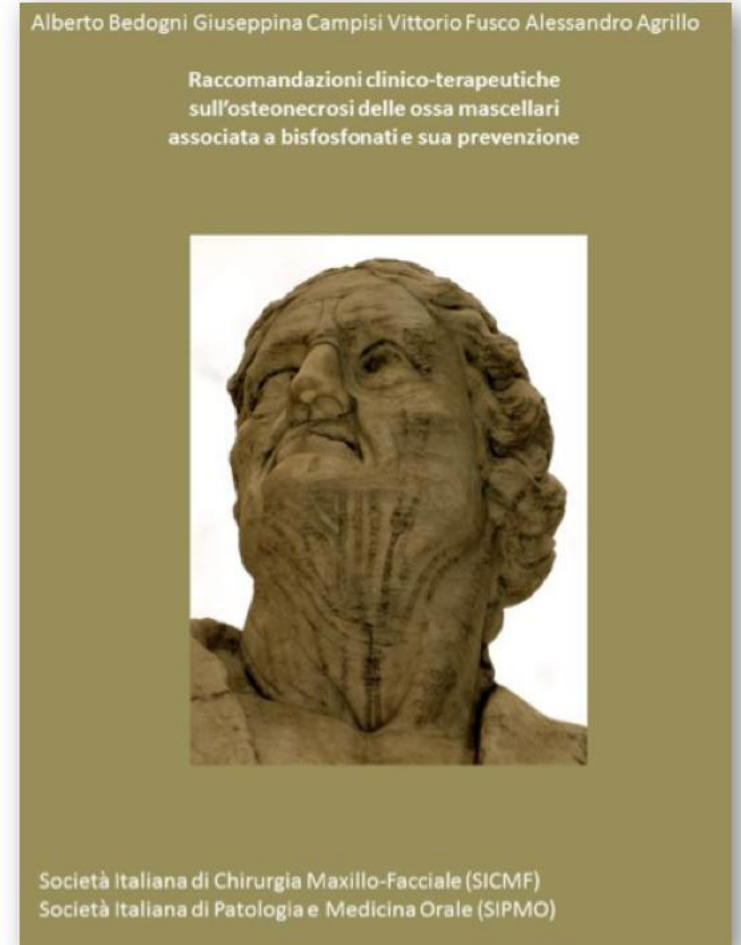
Kim HY et al. Extensive Surgical Procedures Result in Better Treatment Outcomes for Bisphosphonate-Related Osteonecrosis of the Jaw in Patients With Osteoporosis. *J Oral Maxillofac Surg.* 2017 Jul;75(7):1404-1413

Nisi M et al. Conservative surgical management of patients with bisphosphonate-related osteonecrosis of the jaws: a series of 120 patients. *Br J Oral Maxillofac Surg.* 2016 Oct;54(8):930-935

# Obiettivo della chirurgia non estesa

## Rimozione di osso necrotico:

- ▶ Fino al rilievo di tessuto osseo **sanguinante**
- ▶ **Con/senza** inclusione di margine predeterminato di tessuto sano





TRATTAMENTI

CHIRURGICI NON ESTESI

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TRATTAMENTI  
CHIRURGICI NON ESTESI

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**Includono:**



## Includono:

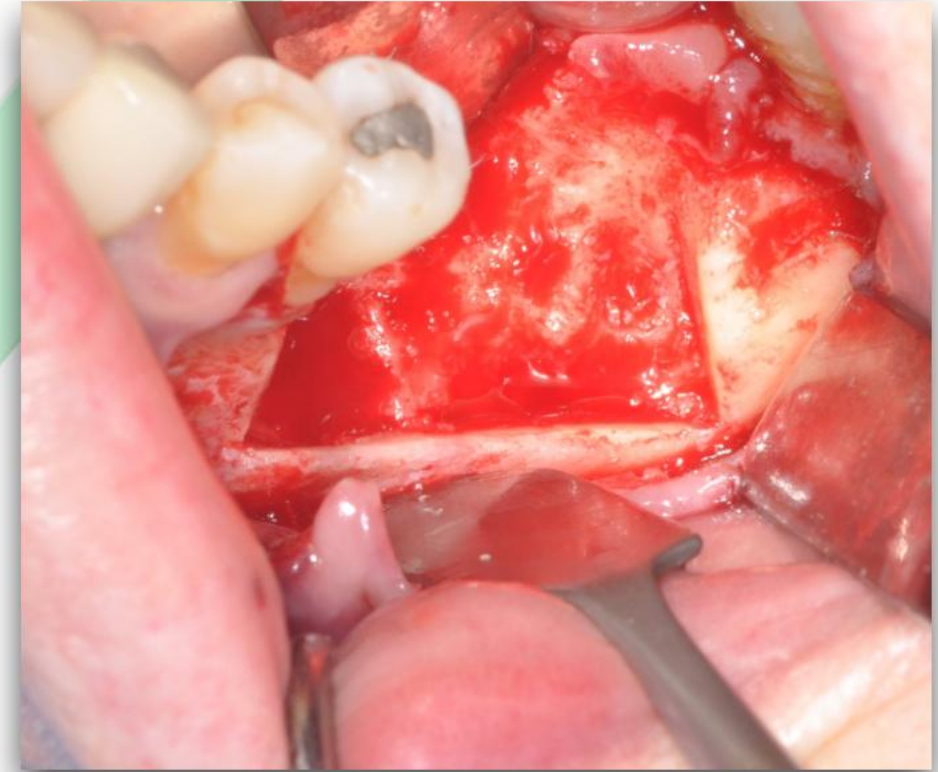
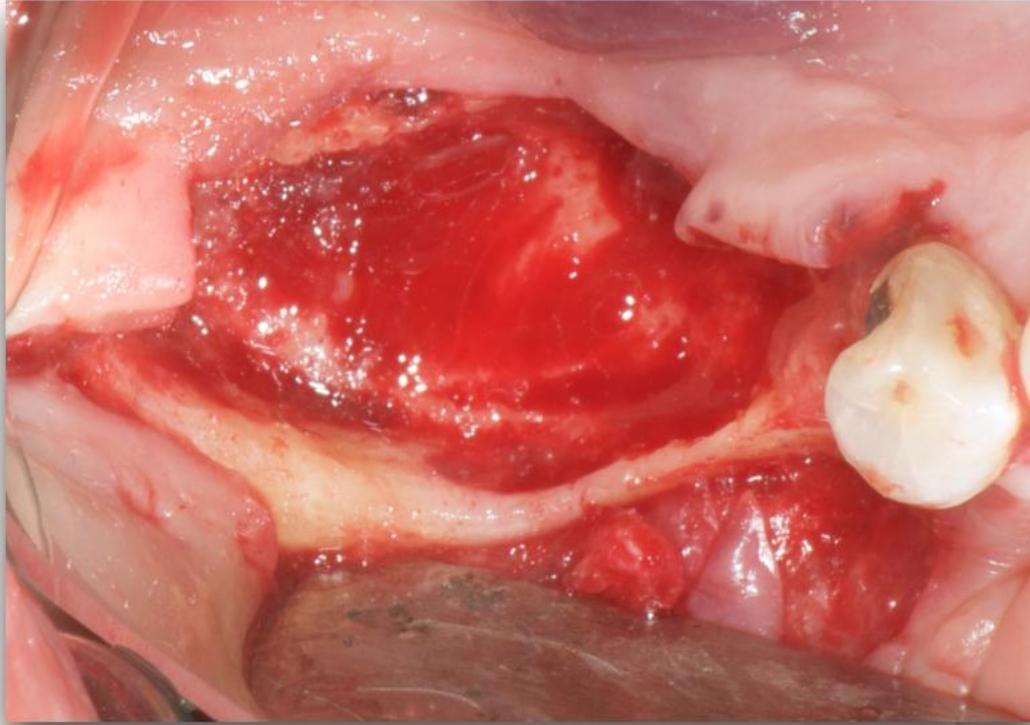


Chirurgia conservativa  
alveolare



Chirurgia resettiva  
alveolare

# Obiettivo chirurgico:



Rimozione totale del tessuto necrotico per evitare recidive

# Obiettivo chirurgico:



Chiusura per prima intenzione

Stockmann P<sub>1</sub>, Vairaktaris E, et al. "Osteotomy and primary wound closure in bisphosphonate-associated osteonecrosis of the jaw: a prospective clinical study with 12 months follow-up", *Support Care Cancer*. 2010 Apr;18(4):449-60.

TRATTAMENTI

CHIRURGICI NON ESTESI

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**Non includono:**



## Non includono:

- ▶ Debridment superficiali



## Non includono:

- ▶ Asportazione di sequestri mobili





# TOPICS

- Definizione dei trattamenti chirurgici non estesi
- Update della letteratura recente
- Conclusioni da una review narrativa della letteratura

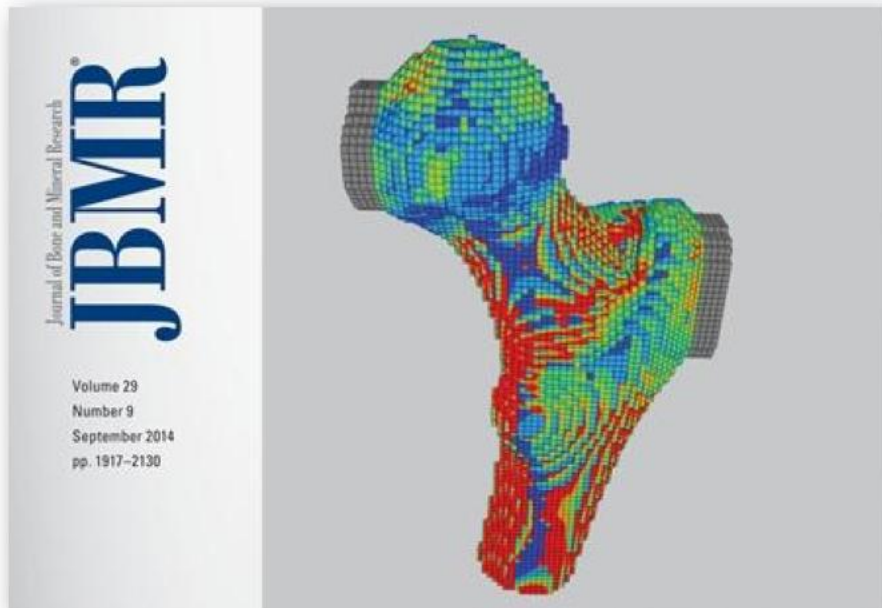
# Review narrativa 2014 - 2018



## Review narrativa 2014 - 2018

- ▶ Studi clinici retrospettivi
- ▶ Studi di coorte
- ▶ Studi prospettici
- ▶ No RCT/studi caso-controllo
- ▶ Review sistematiche a bassa evidenza

# Studi clinici



**ORIGINAL ARTICLE** **JBMR**

**Evaluation of the Treatment Strategies for Medication-Related Osteonecrosis of the Jaws (MRONJ) and the Factors Affecting Treatment Outcome: A Multicenter Retrospective Study with Propensity Score Matching Analysis**

Saki Hayashida,<sup>1,2</sup> Sakiko Soutome,<sup>3</sup> Souichi Yanamoto,<sup>2</sup> Shigeyuki Fujita,<sup>1</sup> Takumi Hasegawa,<sup>4</sup> Takahide Komori,<sup>4</sup> Yuka Kojima,<sup>5</sup> Hironori Miyamoto,<sup>6</sup> Yasuyuki Shibuya,<sup>5</sup> Nobuhiro Ueda,<sup>7</sup> Tadaaki Kirita,<sup>7</sup> Hirokazu Nakahara,<sup>8</sup> Mitsuyo Shinohara,<sup>9</sup> and Masahiro Umeda<sup>2,3</sup>

<sup>1</sup>Department of Oral and Maxillofacial Surgery, Wakayama Medical University, Wakayama, Japan  
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<sup>9</sup>Department of Oral and Maxillofacial Surgery, Juntendo University Faculty of Medicine, Tokyo, Japan

Tipologia di studio	Retrospektivo multicentrico
N° Pazienti	<b>361</b>
Stadiazione	I - II - III
% Successo chirurgico	<b>76,7%</b> 159 pazienti trattati - 94,6% non-oncologici, 51,5% oncologici
Note	Successo della terapia medica <b>25,2%</b> 59,2% non-oncologici, 6.9% oncologici

# Studi clinici



Journal of Cranio-Maxillo-Facial Surgery 45 (2017) 1183–1189

Contents lists available at ScienceDirect

**Journal of Cranio-Maxillo-Facial Surgery**

journal homepage: [www.jcmfs.com](http://www.jcmfs.com)

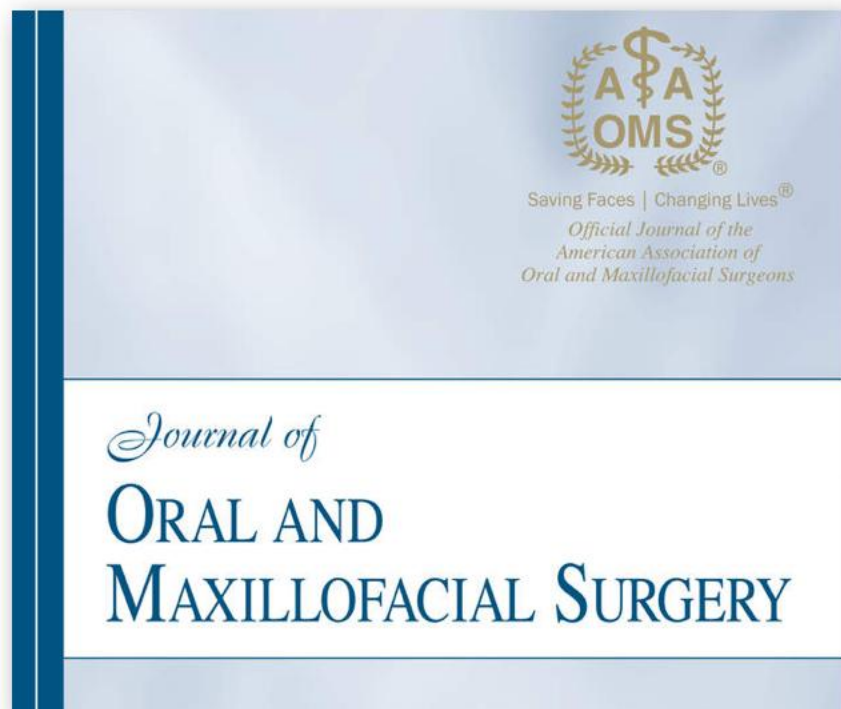
**The impact of surgical intervention and antibiotics on MRONJ stage II and III – Retrospective study**

Matthias Zirk <sup>a,\*</sup>, Matthias Kreppel <sup>a</sup>, Johannes Buller <sup>a</sup>, Julij Pristup <sup>a,c</sup>, Franziska Peters <sup>c,d</sup>, Timo Dreiseidler <sup>a,b</sup>, Max Zinser <sup>a</sup>, Joachim E. Zöller <sup>a</sup>

<sup>a</sup> Department for Oral and Craniomaxillofacial and Plastic Surgery, University of Cologne, Germany  
<sup>b</sup> Dreiflügel-Krankenhaus Wesseling, University Teaching Hospital, Germany  
<sup>c</sup> Department for Dermatology, University of Cologne, Germany  
<sup>d</sup> Institute for Medical Microbiology, Immunology and Hygiene, University of Cologne, Germany  
<sup>e</sup> Department for Operative Dentistry and Periodontology, University of Cologne, Germany

Tipologia di studio	Retrospektivo
N° Pazienti	143
Stadiazione	II - III
% Successo chirurgico	95,1% (cumulativo dei reinterventi)
Note	La terapia antibiotica perioperatoria influenza la recidiva

# Studi clinici



Extensive Surgical Procedures Result in Better Treatment Outcomes for Bisphosphonate-Related Osteonecrosis of the Jaw in Patients with Osteoporosis

Hui Young Kim, BS, DDS, Shin-Jae Lee, DDS, MS, PhD, PhD, Soung Min Kim, DDS, MS, PhD, Hoon Myoung, DDS, MS, PhD, Soon Jung Hwang, MD, DDS, PhD, Jin-Young Choi, DDS, MD, PhD, Jong-Ho Lee, DDS, MS, PhD, Pill-Hoon Choung, DDS, MS, PhD, Myung Jin Kim, DDS, MS, PhD, Byoung Moo Seo, DDS, MS, PhD

PII: S0278-2391(16)31283-6

DOI: [10.1016/j.joms.2016.12.014](https://doi.org/10.1016/j.joms.2016.12.014)

Reference: YJOMS 57576

Tipologia di studio	Retrospettivo
N° Pazienti	325
Stadiazione	II - III
% Successo chirurgico	<p>70% (1 intervento)</p> <p>89,3% (2 interventi)</p> <p>95,5% (3 interventi)</p> <p>100% (&gt;3 interventi)</p>
Note	<p>Pazienti sottoposti a <b>terapia medica preliminare</b>;</p> <p><b>drug holiday</b> non influenza l'outcome</p>

# Studi clinici



Available online at [www.sciencedirect.com](http://www.sciencedirect.com)  
**ScienceDirect**  
 British Journal of Oral and Maxillofacial Surgery xxx (2016) xxx–xxx

**ELSEVIER**

**BRITISH Journal of Oral and Maxillofacial Surgery**  
[www.bjoms.com](http://www.bjoms.com)

**Conservative surgical management of patients with bisphosphonate-related osteonecrosis of the jaws: a series of 120 patients**

M. Nisi <sup>a,1</sup>, F. La Ferla <sup>a,2</sup>, D. Karapetsa <sup>a,2</sup>, S. Gennai <sup>a,\*</sup>, L. Ramaglia <sup>b</sup>, F. Graziani <sup>a,2</sup>, M. Gabriele <sup>a,2</sup>

<sup>a</sup> Department of Surgical Pathology, Medicine, Molecular and Critical Area, University of Pisa, Pisa, Italy  
<sup>b</sup> Department of Neurosciences, Reproductive and Odontostomatological Sciences, School of Medicine, University "Federico II" of Naples, Via S. Pansani 5, 80131 Napoli, Italy

Accepted 17 June 2016

Tipologia di studio	Retrospettivo
N° Pazienti	120
Stadiazione	I - II - III
% Successo chirurgico	<p>84% guarigione completa + regressione</p> <p>Down-staging a seguito della chirurgia:</p> <p>56% stadio III;                      97,1% stadio II;                      100% stadio I</p>
Note	94 pazienti oncologici

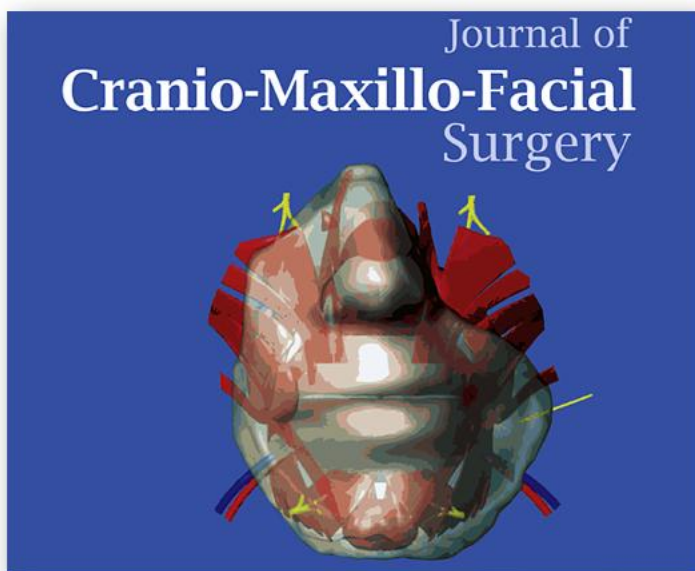
# Studi clinici



Tipologia di studio	Retrospettivo
N° Pazienti	52
Stadiazione	II
% Successo chirurgico	89,3% (28 pazienti trattati)
Note	Chiusura per 1 <sup>a</sup> o 2 <sup>a</sup> intenzione Successo della terapia medica <b>33%</b> Drug holiday condiziona il successo solo della <b>terapia medica</b>

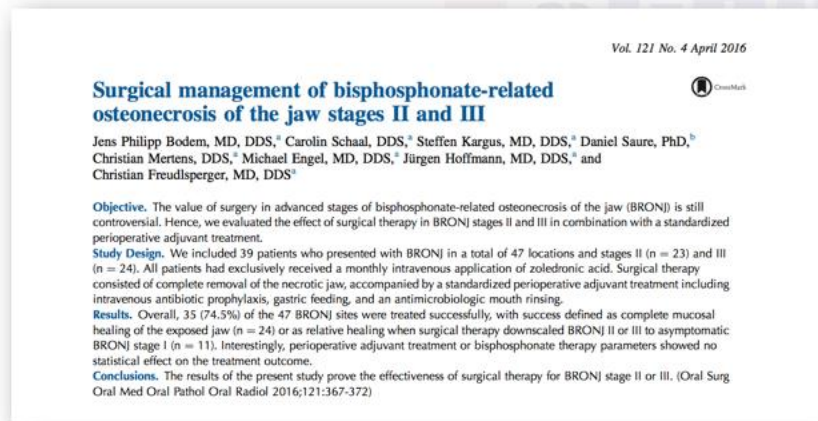
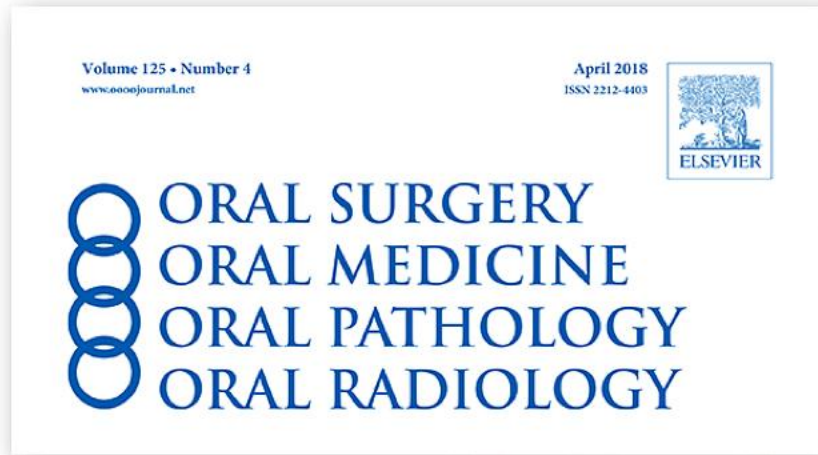


# Studi clinici

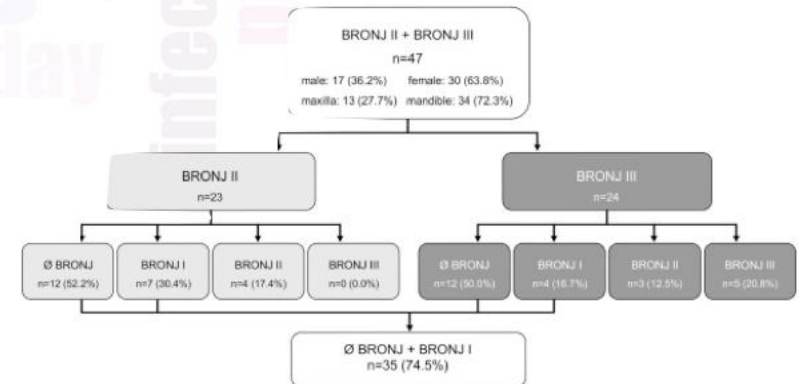


Tipologia di studio	Retrospettivo
N° Pazienti	17
Stadiazione	I - II - III
% Successo chirurgico	80% (6 pazienti trattati)
Note	Solo pazienti trattati con denosumab; successo della terapia medica 20% drug holiday non influenza l'outcome

# Studi clinici



Tipologia di studio	Studio di coorte
N° Pazienti	39
Stadiazione	II - III
% Successo chirurgico	51,06% (guarigione mucosa completa a 6 mesi) 74,5% guarigione completa + regressione a stadio I

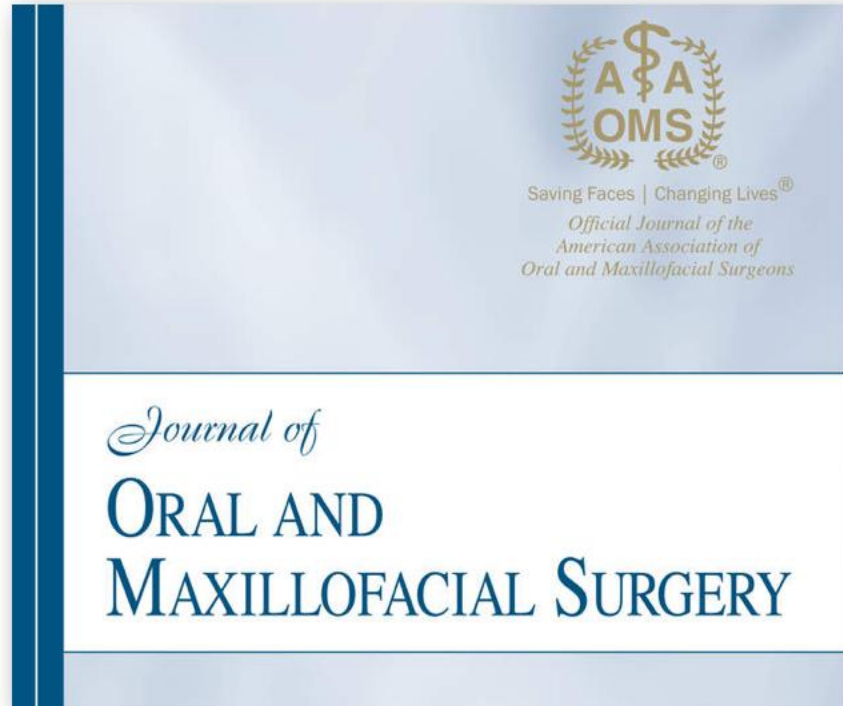


# Review sistematiche



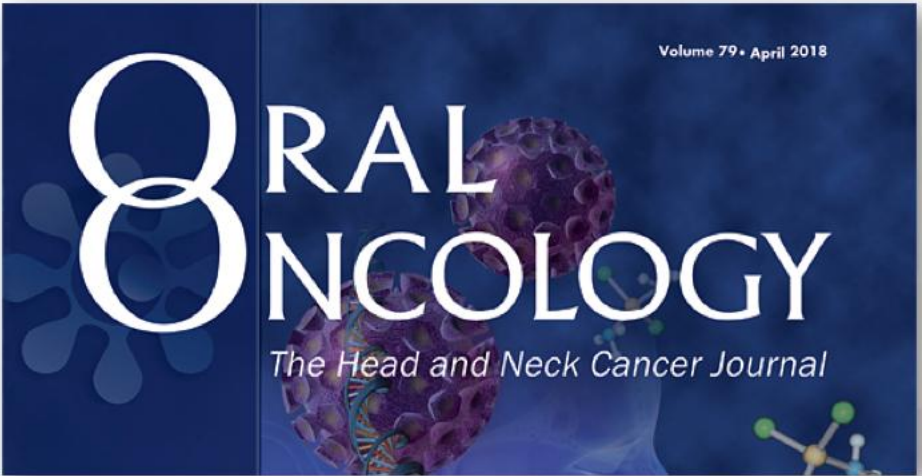
Tipologia di studio	Review
N° studi	13 (da 1480)
RCT	0
% Successo chirurgico	Risultati eterogenei: 0-100% stadio I; 52-100% stadio II; 50-100% stadio III
% Successo terapia medica	Risultati eterogenei: 100% stadio 0; 81-97% stadio I; 63,6-100% stadio II; 73% stadio III
Note	È cruciale una accurata valutazione dei singoli casi

# Review sistematiche



Tipologia di studio	Review
N° studi	67 (da 345)
RCT	0
% Successo chirurgico	Risultati eterogenei tra le diverse tecniche (debridement, sequestrectomy bone resection, and bone reconstruction): <b>23,1-100</b>
Note	Necessità di studi con follow-up più lunghi e campioni più grandi

# Review sistematiche



Tipologia di studio	Review
N° studi	40 (da 1216)
RCT	1
% Successo	Chirurgia conservativa: <b>75%</b> Chirurgia estesa: <b>84%</b> LTT: <b>85%</b> Terapia medica: <b>33%</b> ( <b>52%</b> con HBO)
Note	Migliori risultati con chirurgia estesa e laser

# Terapie aggiuntive e outcome chirurgico

Lasers Med Sci  
DOI 10.1007/s10103-016-1929-4



REVIEW ARTICLE

## Efficacy of laser therapy in the management of bisphosphonate-related osteonecrosis of the jaw (BRONJ): a systematic review

João Batista Blessmann Weber<sup>1</sup> · Renata Stiefman Camilotti<sup>1</sup> · Monique Estér Ponte<sup>1</sup>

Received: 16 December 2015 / Accepted: 18 March 2016  
© Springer-Verlag London 2016

**Abstract** Bisphosphonate-related osteonecrosis of the jaw is a well-known potential side effect of long-term bisphosphonate therapy; the primary objective of the treatment should be to improve patient quality of life through pain and infection management, to prevent the development of new lesions, and to slow disease progression. In recent years, the use of laser for bisphosphonate-related osteonecrosis of the jaw has become more widespread, due to its use of administration and widely reported beneficial effects on tissue healing. The present systematic review of the literature sought to elucidate whether low-level laser therapy has positive effects on the treatment of bisphosphonate-related osteonecrosis of the jaw. We conducted a systematic search of the PubMed, EMBASE, and Cochrane Library electronic databases, with no restrictions on language or year of publication. Search strategies were formulated using keywords and Boolean operators. The electronic search strategy retrieved 55 records. From 55 articles, 16 were selected for full-text review, and of these, 10 were ultimately included for data analysis in this review. Our findings show that treatment modalities including laser were associated with superior outcomes in terms of cure or improvement of bisphosphonate-related osteonecrosis of the jaw

lesions as compared with conventional surgical and/or conservative drug therapy. It can be concluded that combined treatment with antibiotics, minimally invasive surgery (including Er:YAG laser surgery), and low-level laser therapy in the early stages of the disease should be the gold standard for bisphosphonate-related osteonecrosis of the jaw management.

**Keywords** Bisphosphonate-related osteonecrosis of the jaw · Laser therapy · Neoplasm · Neoplasm metastasis · Osteoporosis

### Introduction

Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is a well-known potential side effect of long-term bisphosphonate (BP) therapy. BRONJ is a result of bone resorption and remodeling and is defined as an area of exposed bone in the maxillofacial region [1–7]. The first reports of jaw necrosis associated with BP therapy were published in 2003 [2, 4].

The American Association of Oral and Maxillofacial Surgeons (AAOMS) adopted criteria for the differential diagnosis of BRONJ, to distinguish it from other delayed healing conditions. A diagnosis of BRONJ requires that all of the following three characteristics be present simultaneously: (1) current or previous treatment with a BP, (2) exposed bone in the maxillofacial region that has persisted for more than 8 weeks, and (3) no history of radiation therapy to the jaws [6]. Additional clinical manifestations may be included, such as ulceration and edema surrounding the soft tissues, purulent discharge, fistulas, halitosis, and severe pain. Although less commonly, abscesses, pathologic fractures, and nerve dysfunction may also be associated with BRONJ lesions [7, 8].

The AAOMS originally described three disease stages for the assessment of BRONJ: stage 1, exposed/necrotic bone in

Odontology  
DOI 10.1007/s10266-017-0295-4



ORIGINAL ARTICLE

## Treatment of stage II medication-related osteonecrosis of the jaw with necrosectomy and autologous bone marrow mesenchymal stem cells

Pit Jacob Voss<sup>1</sup> · Akihiko Matsumoto<sup>2</sup> · Esteban Alvarado<sup>3</sup> · Rainer Schmelzeisen<sup>1</sup> · Fabian Duttenhöfer<sup>1</sup> · Philipp Poxleitner<sup>1</sup>

Received: 7 July 2016 / Accepted: 19 December 2016  
© The Society of The Nippon Dental University 2017

**Abstract** Treatment strategies for medication-related osteonecrosis of the jaw (MRONJ) remain controversial. Although the AAOMS suggests a conservative approach, a surgical management with necrosectomy is often required when conservative management has failed. Moreover, recent studies have shown promising results using an early stage surgical treatment. Over the past decade, cell-based bone regeneration utilizing bone marrow mesenchymal stem cells (MSCs) received increased attention. MSCs are known to promote wound healing and induce new bone formation in compromised tissue. Accordingly, the aim of this study was to assess the role of MSCs in the management of MRONJ. This study included 6 patients referred to our department with the diagnosis of MRONJ. Upon informed consent, the patients underwent surgical resection of necrotic bone followed by MSCs grafting. The MSCs were separated from bone marrow cells aspirated from the iliac crest using a bone marrow aspirate concentrate system. The MSCs were grafted into the defect with

autologous thrombin and the defect was covered with a collagen membrane. In all cases, bony edges were rounded and the wound was closed using a three-layered technique. In the follow-up from 12 to 54 months, all patients including those who had impaired conditions, sepsis, or pathological fracture, showed satisfactory healing with no signs of wound infection. This pilot study indicated that surgical management in combination with MSCs transplantation seems to be a promising treatment modality in the therapy of MRONJ.

**Keywords** Medication-related osteonecrosis of the jaw · Bisphosphonate · Mesenchymal stem cells · Stem cell transplantation

### Introduction

Medication-related osteonecrosis of the jaws (MRONJ) is a serious complication in patients treated with antiresorptive medications, such as bisphosphonates (BPs) and human monoclonal antibodies to RANKL (i.e., denosumab) [1–3]. Since the first report in 2003 [4], a large number of MRONJ cases have been reported with a growing tendency [5]. Although a wide range of treatment modalities has been described, the treatment strategies of MRONJ remain controversial. Most guidelines recommend management of affected patients with a conservative approach including chlorhexidine mouth wash, long-term antibiotics, periodic minor debridement of sequestrums and wound irrigation in order to control pain, infection, and progress of exposed bone [3]. However, in many cases, conservative treatment has failed. Hoff et al. [6] described that only 23% of their patients healed after conservative treatment. To address this low success rate, several clinicians proposed a surgical

Akihiko Matsumoto have contributed equally to this work.

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International Journal of  
Oral &  
Maxillofacial  
Surgery

Clinical Paper  
Clinical Pathology

## Surgical treatment of osteonecrosis of the jaw with the use of platelet-rich fibrin: a prospective study of 15 patients

S. E. Nørholt, J. Hartlev  
Department of Oral and Maxillofacial Surgery,  
Aarhus University Hospital and Section of  
Maxillofacial Surgery and Oral Pathology,  
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S. E. Nørholt, J. Hartlev: Surgical treatment of osteonecrosis of the jaw with the use of platelet-rich fibrin: a prospective study of 15 patients. *Int J Oral Maxillofac Surg* 2016; xxx: xxx–xxx. © 2016 International Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

**Abstract** The objective of this study was to evaluate the outcome of the surgical treatment of osteonecrosis of the jaw (ONJ) with the additional use of autologous membranes of platelet-rich fibrin (PRF). The study population consisted of 15 patients with ONJ lesions in the maxilla ( $n = 3$ ), mandible ( $n = 11$ ), or both ( $n = 1$ ). Eight patients had malignant disease and were treated with high-dose anti-resorptive medication, seven were treated with low-dose anti-resorptive drugs for osteoporosis. Thirteen patients had grade 2 ONJ lesions and two had grade 3 lesions. The following standardized surgical technique was applied: resection of necrotic bone, mobilization of mucoperiosteal flaps, and multiple layer coverage of bone with PRF membranes. At follow-up 7–20 months after surgery, complete mucosal healing and an absence of symptoms were found in 14 of the 15 patients (93%). The patient with persistent bone exposure had a grade 3 ONJ lesion before surgery. This study suggests that the use of PRF membranes in the surgical treatment of grade 2 ONJ may be a contributing factor to a successful outcome.

**Key words:** anti-resorptive drugs; bisphosphonate-related osteonecrosis of the jaw; Denosumab; membranes; platelet concentrates; platelet-rich fibrin.

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Osteonecrosis of the jaw (ONJ) is a complication of treatment with anti-resorptive medications and has been recognized since 2003 [1]. The condition appears in patients with malignant diseases on high-dose anti-resorptive drug treatment and in patients with osteoporosis treated with low-dose anti-resorptive drugs. The necrotic bone itself is typically asymptomatic, but the frequent occurrence of infection causes pain and discomfort, leading to impaired

quality of life and oral health profile [2]. Furthermore, the exposed bone is often associated with daily discomfort from sharp edges, food retention, and odour, and extra hygiene measures have to be taken. According to international recommendations, the first choice of treatment is a conservative approach including local debridement and disinfection with antimicrobial solutions (e.g. chlorhexidine) or systemic antibiotic treatment (American

Association of Oral and Maxillofacial Surgeons (AAOMS) position paper 2014, International Consensus 2015 [3]. This can result in cure or improvement in many patients, [4] however a number of patients will continue to experience symptoms from the lesions and recurrent infections, which tend to increase the extent of the osteonecrosis. When these factors are present, a surgical intervention to eliminate the bone is attractive to the patient. [5]

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# Come identificare i limiti della necrosi ossea?

**PATHOLOGY**

## Clinical Differences in Autofluorescence Between Viable and Nonvital Bone: A Case Report With Histopathologic Evaluation Performed on Medication-Related Osteonecrosis of the Jaws

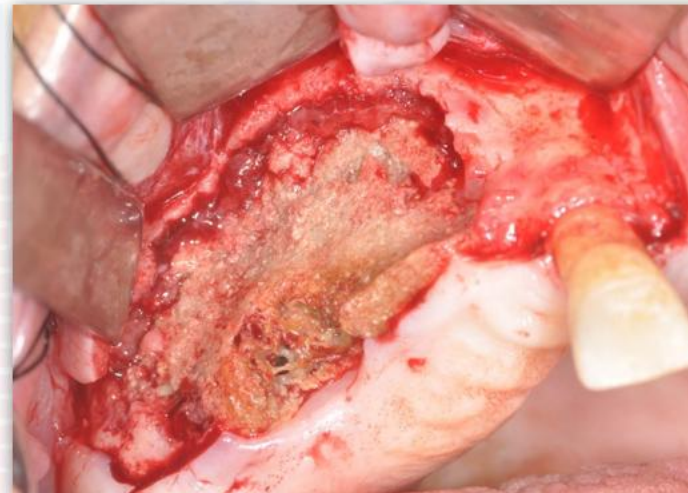
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Medication-related osteonecrosis of the jaws (MRONJ) is an adverse side effect of several drug therapies, including bisphosphonates (BPs). Osteonecrosis of the jaw specifically related to BP therapy is usually referred to using the acronym BRONJ. However, no consensus has yet been reached regarding the most appropriate management of BRONJ. The greatest success rates have been recorded with surgical removal of necrotic bone. In particular, erbium:yttrium-aluminum-garnet (Er:YAG) laser-assisted surgery has shown significantly better results than conventional surgical approaches. According to a position paper reported by the American Association of Oral and Maxillofacial Surgeons in 2007, the identification of necrotic bone margins during osteonecrosis removal can be very difficult. In 2015, a review of treatment perspectives for MRONJ reported that both surgical debridement and resection cannot be standardized owing to the lack of guidance to define the necrotic margins. Recently, the use of autofluorescence (AF) of the bone as a possible suitable guide to visualize necrotic bone during surgical debridement or resection was proposed. It seems that vital bone could be highlighted by its very strong AF. In contrast, necrotic bone loses AF and, thus, appears much darker. The molecular sources of the phenomenon of AF are the specific amino acids of the collagen molecules that show AF when irradiated by ultraviolet or blue light. The use of AF as an intraoperative diagnostic tool is entirely new in the management of MRONJ, although it has been used for several years in other fields (eg, intervertebral disc surgery). The aim of the present report was to describe a case of mandibular BRONJ treated with a new surgical approach performed with an Er:YAG laser and guided by AF. The histopathologic evaluation of the removed hypofluorescent bone block and hyperfluorescent surrounding bone has also been reported in detail.

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ORIGINAL RESEARCH  
 HEAD & NECK

## Bisphosphonate-Induced Osteonecrosis of the Jaw: Comparison of Disease Extent on Contrast-Enhanced MR Imaging, [<sup>18</sup>F] Fluoride PET/CT, and Conebeam CT imaging

R. Guggenberger, D.R. Fischer, P. Metzler, G. Andreisek, D. Nanz, C. Jacobsen, and D.T. Schmid

**ABSTRACT**

**BACKGROUND AND PURPOSE:** Imaging of bisphosphonate-induced osteonecrosis of the jaw is essential for surgical planning. We compared the extent of BONJ on contrast-enhanced MR imaging, [<sup>18</sup>F] fluoride PET/CT, and panoramic views derived from standard conebeam CT with clinical pre- and intraoperative examinations.

**MATERIALS AND METHODS:** Between February 2011 and January 2012, ten subjects with written informed consent (9 women; mean, 69.6 years; range, 53–88 years) were included in this prospective ethics-board-approved study. Patients underwent CEMR imaging, [<sup>18</sup>F] fluoride PET/CT, and CBCT and were clinically examined pre- and intraoperatively. Surgery was performed, and BONJ was histologically confirmed in 9 patients. Location and extent of BONJ on different modalities/examinations were graphically compared (0 = no pathologic finding, 1 = smallest, 5 = largest extent of BONJ). Rank tests were used to assess overall and paired differences of ratings in 9 patients. A P value < .05 was considered statistically significant.

**RESULTS:** Significant differences in BONJ extent among different modalities and examinations were found (P < .001). The highest median rank was seen in PET/CT (4 ± 1.2) and CEMR imaging (4 ± 1.0), followed by intraoperative examinations (3 ± 0.7), CBCT (2 ± 0.33), and preoperative examinations (1 ± 0). No significant differences were found between PET/CT and CEMR imaging (P = .23), except when comparing PET/CT to either CBCT, pre- and intraoperative examinations (all P < .05). Preoperative examinations showed significantly less extensive disease than all other modalities/examinations (all P < .05).

**CONCLUSIONS:** [<sup>18</sup>F] fluoride PET/CT and CEMR imaging revealed more extensive involvement of BONJ compared with panoramic views from CBCT and clinical examinations.

**ABBREVIATIONS:** BONJ = bisphosphonate-induced osteonecrosis of the jaw; CBCT = conebeam CT; CEMR = contrast-enhanced MR; MDCT = multidetector CT; STR = short-t inversion recovery

Osteonecrosis of the jaw is a known complication in patients treated with bisphosphonates.<sup>1,2</sup> The prevalence of bisphosphonate-induced osteonecrosis of the jaw depends on whether patients are receiving intravenous bisphosphonate treatment (eg, for cancer) or less powerful oral bisphosphonates (eg, for osteoporosis) and has been reported to be 1%–10% and 0.0004%–0.04%, respectively.<sup>3,4</sup> The mandible is more often affected than the maxilla, and rarely are both bones affected at the same time.<sup>5</sup> Although the exact pathophysiology of BONJ is not clear, poten-

tial causes include inhibition of bone turnover at sites of oral trauma (eg, tooth extraction), infection with *Actinomyces israelii*, soft-tissue toxic effects of bisphosphonates resulting in mucosal ulceration, direct toxic effects on bone, impaired bone remodeling, high masticatory forces, and exposure of the tooth socket to an infected environment.<sup>6</sup> Antimicrobial rinses and systemic antibiotics are used for therapy, but sometimes surgery is required to remove necrotic bone.

In addition to clinical examinations, radiologic imaging is the key to an assessment and quantification of the extent of BONJ. Usually panoramic radiography and, more recently, conebeam CT are part of a standard preoperative imaging work-up.<sup>7</sup> Multi-detector CT or contrast-enhanced MR imaging might be performed to diagnose early stages of BONJ, rule out malignancy, diagnose pathologic fractures, monitor disease progression, or evaluate the extent of necrotic bone areas preoperatively.<sup>8</sup> Literature is sparse regarding which imaging technique should be used, however; and little is known about the use of new imaging mo-

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## Considerazioni

- ▶ Trial clinici retrospettivi con protocolli eterogenei
- ▶ Review sistematiche senza RCT/studi caso-controllo
- ▶ Ruolo non univoco di terapia antibiotica e drug-holiday
- ▶ Assenza di comparazione tra le tecniche chirurgiche
- ▶ Limitata attenzione a "*patient-centered outcome*" e qualità della vita



# TOPICS

- Definizione dei trattamenti chirurgici non estesi
- Update della letteratura recente
- Conclusioni da una review narrativa della letteratura

## Trattamenti chirurgici non estesi e MRONJ

- ▶ nelle forme focali
- ▶ supportati da terapia medica perioperatoria
- ▶ più promettente nei pazienti non oncologici
- ▶ esperienza clinica dell'operatore

**CONGRESSO NAZIONALE**



**Chirurgia orale  
minimamente invasiva:**

*una scelta appropriata?*



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