TRATTAMENTO DELLA ONJ:
UPDATE DELLA LETTERATURA

Terapia chirurgica non estesa

G. Colella

Dipartimento Multidisciplinare di Specialità Mediche e Chirurgiche

OBBIETTIVI DELLA TERAPIA

- Ripristino funzionale
- Risoluzione del quadro sintomatologico
- Controllo dell'infezione
- Ridurre la progressione o evitare la comparsa della necrosi
- *Guarigione*

Position Paper

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American Association of Oral and Maxillofacial Surgeons

Medication-Related Osteonecrosis of the Jaw—2014 Update

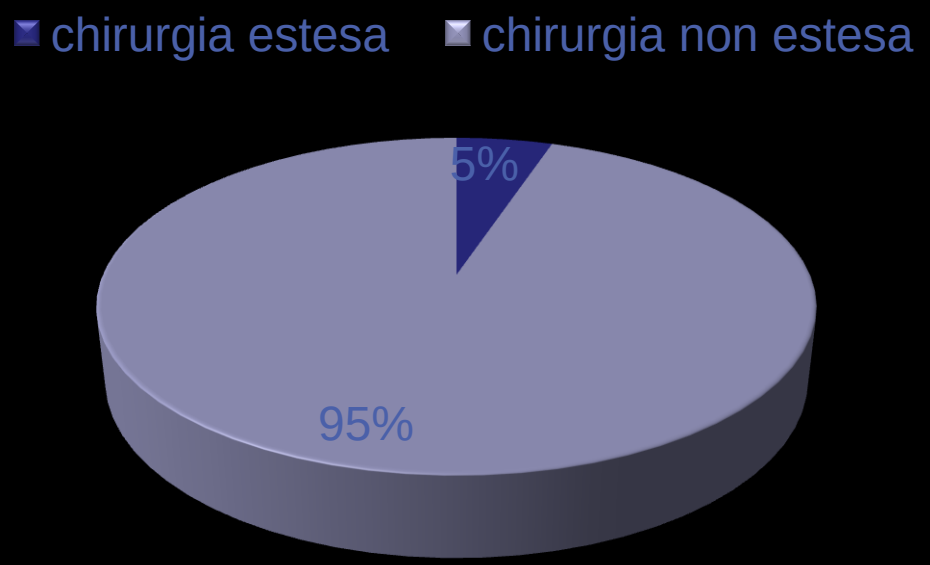
MRONJ† Staging	Treatment Strategies‡
At risk category No apparent necrotic bone in patients who have been treated with either oral or IV bisphosphonates	• No treatment indicated • Patient education
Stage 0 No clinical evidence of necrotic bone, but non-specific clinical findings, radiographic changes and symptoms	• Systemic management, including the use of pain medication and antibiotics
Stage 1 Exposed and necrotic bone, or fistulae that probes to bone, in patients who are asymptomatic and have no evidence of infection	• Antibacterial mouth rinse • Clinical follow-up on a quarterly basis • Patient education and review of indications for continued bisphosphonate therapy
Stage 2 Exposed and necrotic bone, or fistulae that probes to 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 • Oral antibacterial mouth rinse • Pain control • Debridement to relieve soft tissue irritation and infection control
Stage 3 Exposed and necrotic bone or a fistula that probes to 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 • Antibiotic therapy and pain control • Surgical debridement/resection for longer term palliation of infection and pain

Regardless of the disease stage, mobile segments of bony sequestrum should be removed without exposing uninvolved bone. The extraction of symptomatic teeth within exposed, necrotic bone should be considered since it is unlikely that the extraction will exacerbate the established necrotic process.

CHIRURGIA NON ESTESA PRINCIPALE OPZIONE TERAPEUTICA

CASISTICA MULTICENTRICA

chirurgia estesa	18
chirurgia non estesa	331
terapia medica	226
nd	98
totale	673



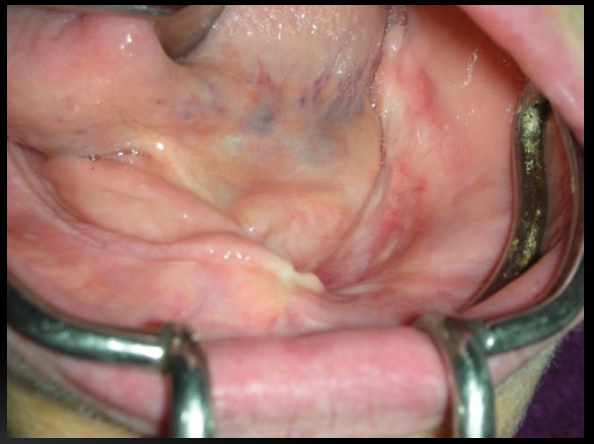
CHIRURGIA NON ESTESA

- Local Debridement
  - Debridement
  - Sequestrectomy
  - Soft tissue debridement
  - Curettage
- Resective procedures
  - Corticotomy
  - Marginal resection

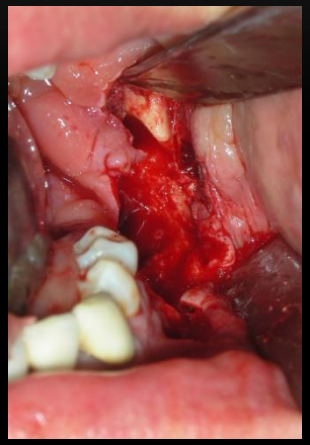
(without prejudice for the continuity of the mandible/maxilla)

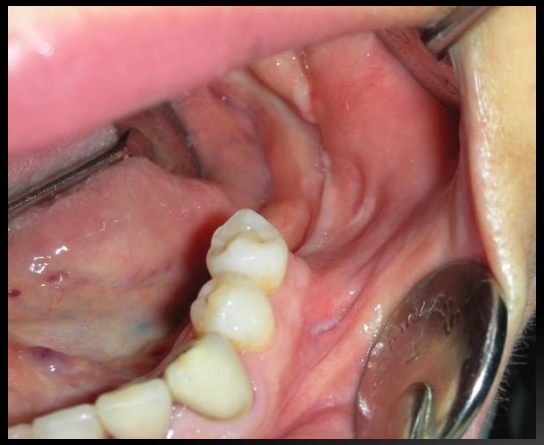
QUALI I LIMITI ?

SEQUESTRECTOMIA

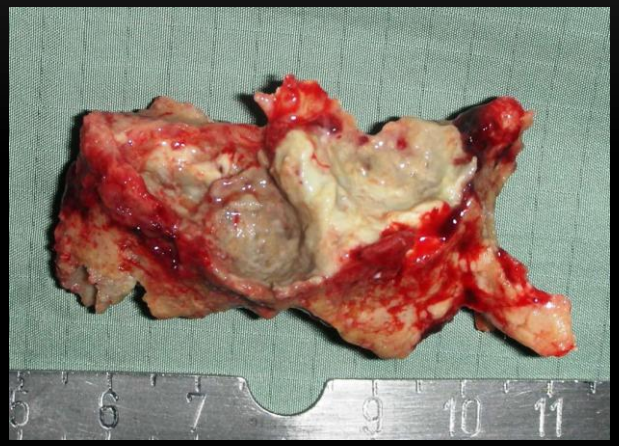


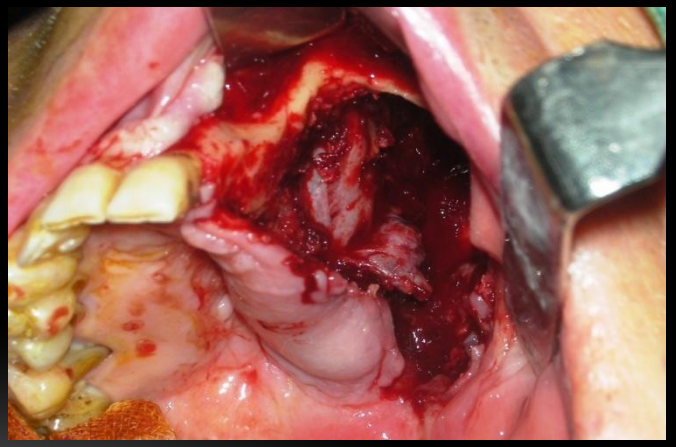
RESEZIONE MARGINALE



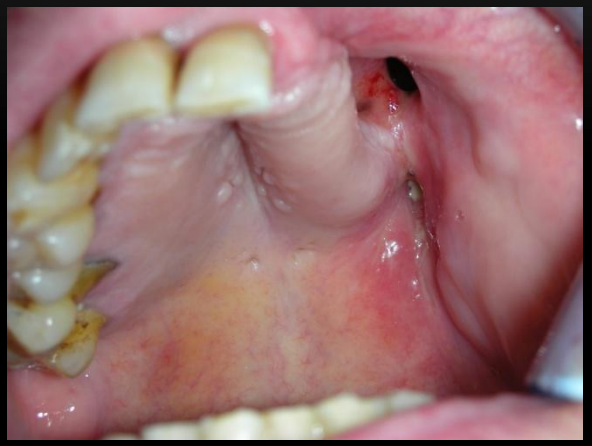


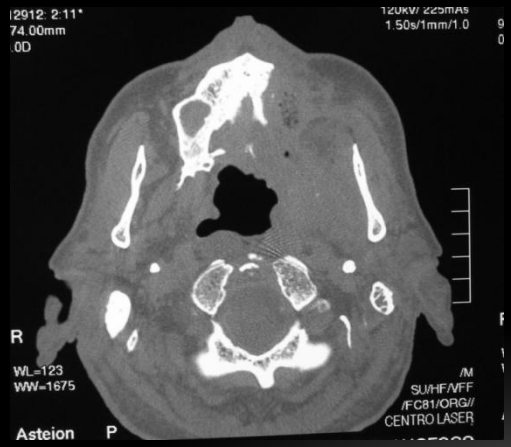
SEQUESTRECTOMIA
RESEZIONE MARGINALE - MAXILLECTOMIA ?

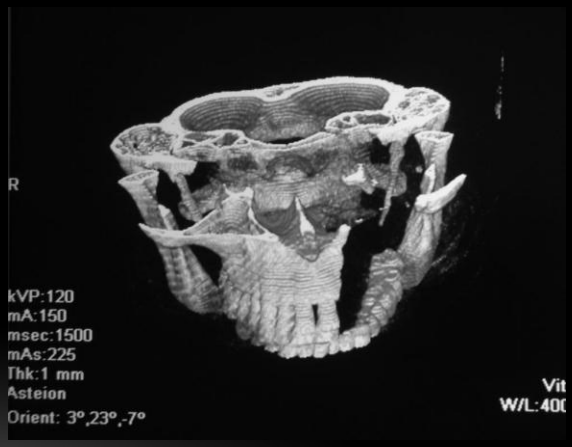




SEQUESTRECTOMIA
RESEZIONE MARGINALE - MAXILLECTOMIA ?







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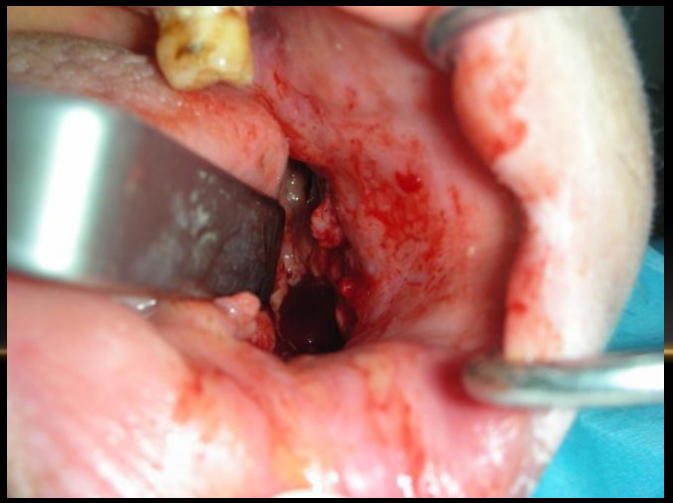
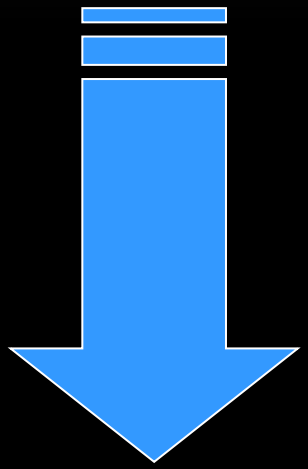


MASSIMO TOLLERABILE



MINIMO EFFICACE

TOPICS

- I pazienti
- La malattia
- I tempi
- Le tecniche
- I presidi
- I risultati
- I limiti

Oral Oncology 48 (2012) 938–947

Contents lists available at SciVerse ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Review

Bisphosphonate-related osteonecrosis of the jaws – A review

Sebastian Kühl [a,*], Christian Walter [b], Stephan Acham [c], Roland Pfeffer [a], J. Thomas Lambrecht [a]

Publications listed according to the year of appearance and grade of evidence.[170]

Year	Level Ia	Level Ib	Level IIa	Level IIb	Level III	Level IV
2003						168
2004					10,15	
2005				48	73–78	24
2006		33	32	49,50	79–92	9,17,26,169–174
2007		31,34	40	51–53	12,93–118	16,18,22,28,102,175,176
2008		35–37		54–60	119–141	19,21,177–179
2009	30	38,39	41–45[a], 46[a], 47[a]	61–64[a], 65–67[a], 68–72	142–151[a], 152,153[a], 154–163[a], 164–167	26,27,180–186

[a] Published in the year 2010 but epub ahead in 2009.

Treatment of bisphosphonate-related osteonecrosis of the jaws: presentation of a protocol and an observational longitudinal study of an Italian series of cases

Sebastiano Ferlito [a], Sergio Puzzo [a,*], Filippo Palermo [b], Placido Verzì [a]

The aim of this study was to evaluate the efficacy of a treatment protocol for bisphosphonate-related osteonecrosis of the jaws (BRONJs). We conducted a longitudinal observational non-controlled study in 94 patients with confirmed BRONJ. Treatment was in two phases: supportive (antimicrobial mouth rinses, antibiotics, and anti-inflammatory steroids) to minimise infection and pain before the formation of a bony sequestrum; and surgical plus pharmacological treatment (sequestrectomy with antibiotic prophylaxis) after the sequestrum had developed. We did a Kaplan–Meier analysis (survival curve) to evaluate the time from the initial assessment until the formation of the bony sequestrum (endpoint), and a log-rank (Mantel–Haenszel) test to compare the formation times of the sequestra in men and women. Ninety-one of the 94 patients developed sequestra and were operated on. Three patients were withdrawn from the study because of severe pain and were treated by debridement before the sequestra developed. The results showed that sequestra developed within 15 months in all 91 patients. The Kaplan–Meier analysis showed that the mean time to formation of a sequestrum was 8 months (range 5–11). The difference between the mean time for men (5 months, range 2–8) and women (9 months, range 6–12) was highly significant ($p < 0.0001$). Within the limits of this study, we conclude that by waiting for the formation of bony sequestra while controlling infection and pain, it is possible to do a conservative resection, unless pain is severe or there is a risk of fracture. This non-aggressive approach permits the removal of all necrotic bone, avoids damage to adjacent healthy bone, and does not result in recurrences.

British Journal of Oral and Maxillofacial Surgery 50 (2012) 425–429

Clinical Study

Conservative Surgical Management of Stage I Bisphosphonate-Related Osteonecrosis of the Jaw

Paolo Vescovi,[1] Elisabetta Merigo,[1] Marco Meleti,[1] Maddalena Manfredi,[1] Carlo Fornaini,[1] Samir Nammour,[2] Giovanni Mergoni,[1] Amin Sarraj,[1] and Jose V. Bagan[3]

Table 7: Number and percentage of healed sites after BRONJ treatment.

	Sites	%
Stage I		
Nonsurgical treatment		
Complete healing	4	11.2
No healing	32	88.8
Surgical treatment		
Complete healing	25	92.6
No healing	2	7.4
Stage II		
Nonsurgical treatment		
Complete healing	13	25
No healing	39	75
Surgical treatment		
Complete healing	50	75.5
No healing	16	24.25
Stage III		
Nonsurgical treatment		
Complete healing	0	0
No healing	7	100
Surgical treatment		
Complete healing	3	75

5. Conclusions

When making the decision to perform surgical procedures for the treatment of BRONJ, the deal between benefit and potential risks according to clinical circumstances of each patient should be considered. Surgical operations for advanced stages of BRONJ are invasive and extensive and must be performed under general anaesthesia. Only few patients may undergo this type of surgery. On the other hand a minimal and faster intervention under local analgesia is useful also for aged and immunocompromised patients. Less invasive surgery may determine a complete mucosal healing containing the microbial infection and the risk of spread of the disease.

Our result confirms that treatment of patients affected by minimal bone exposition, (stage I of BRONJ), through conservative surgical strategies, possibly with laser, may determine a higher control of lesions in the long term.

International Journal of Dentistry
Volume 2014, Article ID 107690, 8 pages

The outcome after surgical therapy of bisphosphonate-associated osteonecrosis of the jaw—results of a clinical case series with an average follow-up of 20 months

Philipp Stockmann · Moritz Burger · Cornelius von Wilmowsky · Tobias Ebker ·

Materials and methods Eighty patients suffering from BRONJ were included in the study. All patients received intravenous bisphosphonate therapy and underwent osteotomy and primary wound closure according to a standardised protocol. After discharge, the patients were reviewed on a regular basis over an average time period of 20 months.

Results During follow-up in 11 patients, a recurrence of BRONJ occurred in the former operation field. Seventeen patients died due to their underlying disease. The success rate of osteotomy and primary wound closure in the treatment of BRONJ was calculated at 84.2 % 20 months after surgery. The results showed non-significant difference concerning the outcome of surgery in the different clinical stages of BRONJ.

Conclusions In accordance with previous studies, stage-independent osteotomy and primary wound closure combined with antibiotics shall be deemed a viable treatment option in patients suffering from BRONJ.

Clinical relevance With a high success rate, osteotomy in combination with primary wound closure seems to be a viable alternative to more conservative protocols in the treatment of BRONJ.

conclusion that a stage-dependent treatment decision, as recommended by the AAOMS [2], is not necessary in this protocol.

Clin Oral Invest Springer-Verlag Berlin Heidelberg 2013

Conservative surgical treatment in the management of BRONJ: a case series of 129 consecutive cases

M. Gabriele, F. La Ferla, S. Cei, M. Nisi, F. Graziani
Department of Surgical, Medical, Molecular Pathology and Critical Area, University of Pisa, Italy

Aim. Aim of this case series was to evaluate the out comes of conservative surgical treatment of bisphosphonate-related osteonecrosis of the jaw (BRONJ).
Materials. 119 subjects affected by 129 BRONJ and surgically treated in our unit were enrolled. Surgical treatment (sequestrectomy, soft tissue debridement, and bone curettage with no or limited extension) was delivered only to sites that did not respond to medical treatment. Age, gender, underlying disease, tabagism, comorbidity were also analysed. Main outcome was improvement of clinical stage and disease resolution (passage to stage 0). Subjects were followed for at least 6 months.
Results. *Sample*: oncologic diagnoses was made in most of the cases (77%). Breast cancer was the primary pathology (36 subjects, 30%), followed by multiple myeloma (26 subjects). Sixty-three percent of the lesions were located in the mandible (81 subjects). The main event leading to BRONJ was tooth extraction (76 subjects, 59%). A reasonable explanation for BRONJ was detected in 82%. The most frequent stage of BRONJ was stage II (77 subject, 60%), whereas stage I (26 subject, 20%) and stage III (26 subject, 20%) were less common.
Effect of surgical treatment: during follow-up, one subject died. 84% of subjects showed improvement after surgery, 15% showed no modification, and 1% exhibited a worsening of their clinical condition. Stratification indicated improvement for 100% stage I (and therefore total disease resolution), 87% stage II and 52% stage III. Disease resolution was noted in the 75% of Stage II and 40% of Stage III. Interestingly, a learning surgical curve was effect noted for disease resolution.
Conclusion. Our data suggest that conservative surgery may be the possible treatment of choice in stage I and II. Conversely, stage III subjects might be treated with either a resective surgical approach or clinical monitoring according to the clinical medical scenario of the patient.

Annali di Stomatologia 2013; Suppl. 2: 1-48

Journal of Cranio-Maxillo-Facial Surgery xxx (2013) 1–8

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

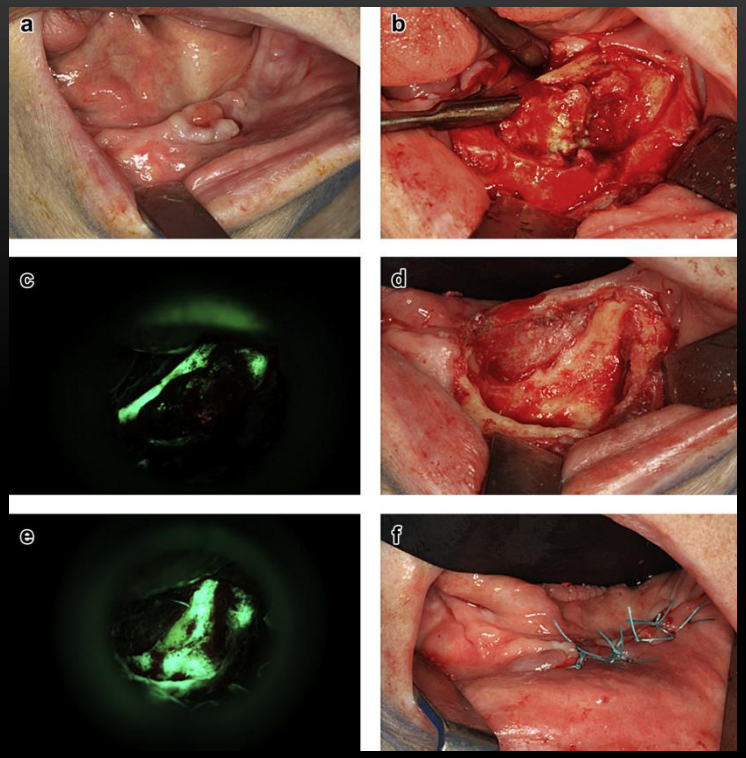
journal homepage: www.jcmfs.com

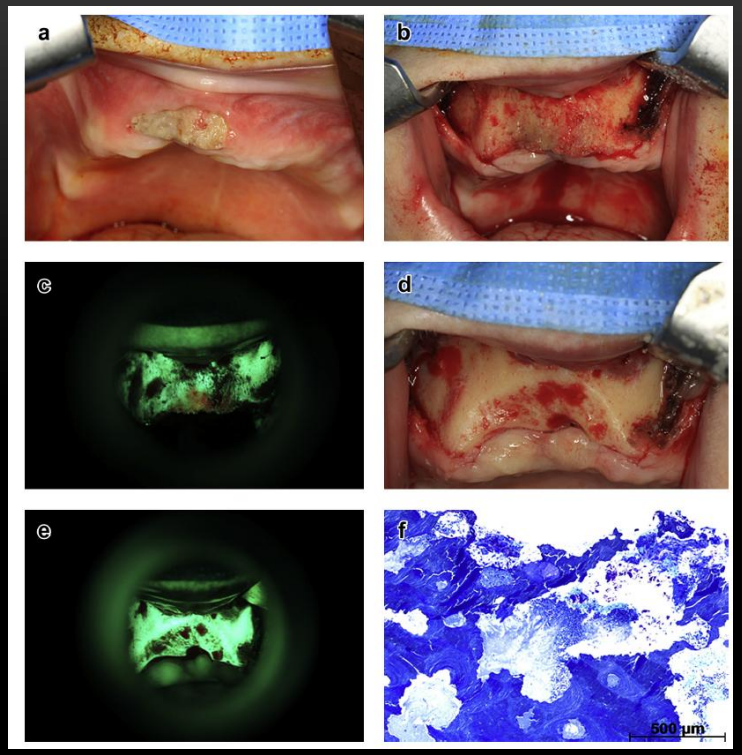
Intraoperative efficiency of fluorescence imaging by Visually Enhanced Lesion Scope (VELscope®) in patients with bisphosphonate related osteonecrosis of the jaw (BRONJ)

Alexandre T. Assaf[a,*,1], Tomislav A. Zrnc[a,1], Björn Riecke[a], Johannes Wikner[a],

Methods: We investigated 20 patients (11 females and 9 males; mean age 74 years, standard deviation ± 6.4 years), over a period of 18 month with the diagnosis of BRONJ in this prospective cohort study. All patients received doxycycline as a fluorescending marker for osseous structures. VELscope® has been used intraoperatively using the loss of fluorescence to detect presence of osteonecrosis. Osseous biopsies were taken to confirm definite histopathological diagnosis of BRONJ in each case.

Results: Diagnosis of BRONJ was confirmed for every patient. In all patients except one, VELscope® was sufficient to differentiate between healthy and necrotic bone by visual fluorescence retention (VFR) and visual fluorescence loss (VFL). 19 cases out of a total of 20 showed no signs of recurrence of BRONJ during follow-up (mean 12 months, range 4–18 months).





VELscope® examination is a suitable tool to visualize necrotic areas of the bone by VFL in patients with BRONJ. As demonstrated, VFL in the necrotic areas of the bone is useful intraoperatively as a guide for fluorescence-guided bone resection with relevant clinical interpretation. In our opinion, surgical procedures are indicated in almost all patients with BRONJ stage II or III and also in many with stage I disease. Using the VELscope® device, excellent results can be reached regarding complete resection of necrotic bone areas, and postoperative outcome after mucosal closure and wound healing. Further studies should follow, e.g. to evaluate the selective effect of fluorescence-guided bone resection, in patients with BRONJ stage I.

Contents lists available at SciVerse ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

Successful surgical management of osteonecrosis of the jaw due to RANK-ligand inhibitor treatment using fluorescence guided bone resection

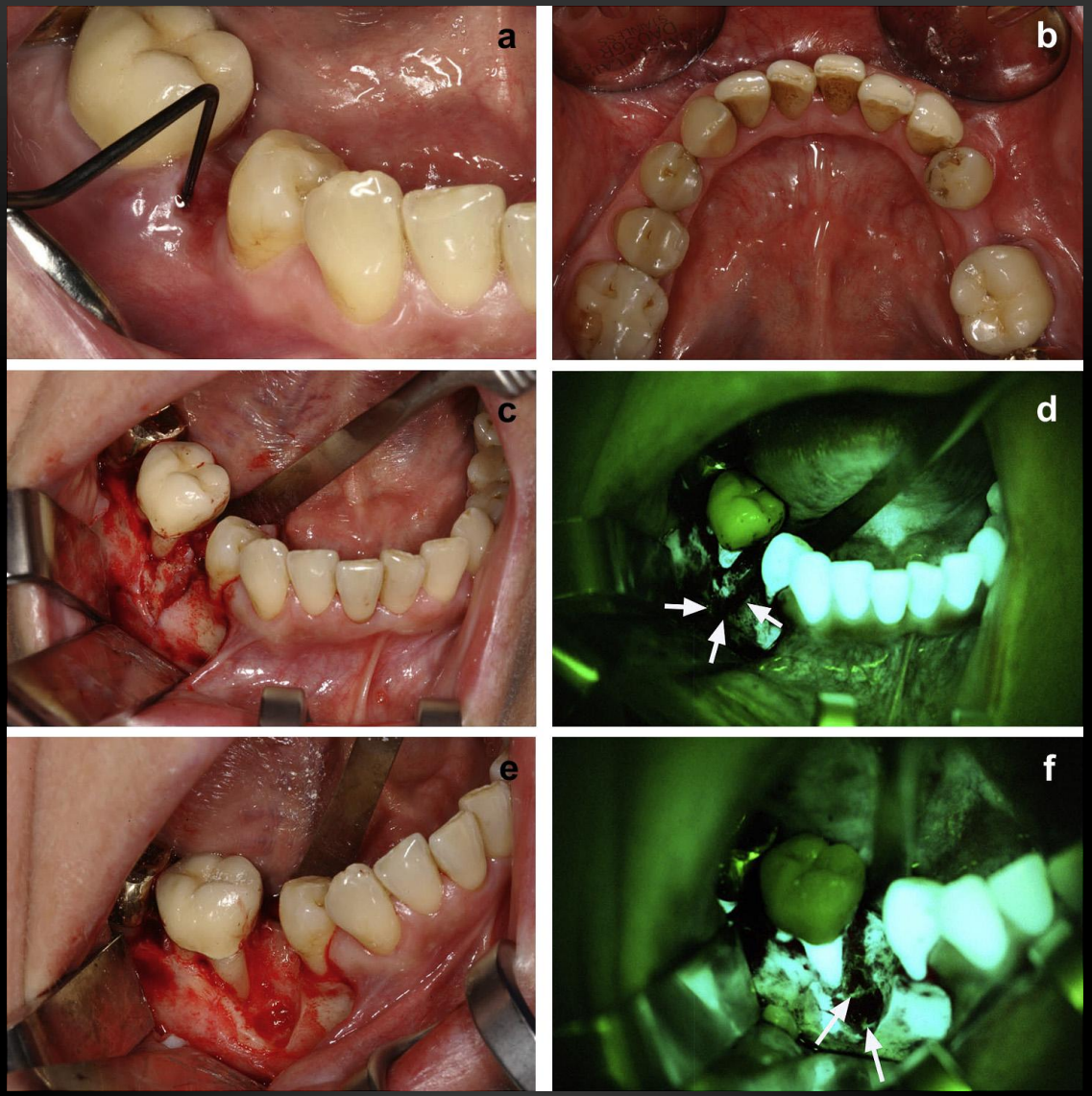
Sven Otto [a,*], Sebastian Baumann [a], Michael Ehrenfeld [a], Christoph Pautke [a,b]

Osteonecrosis of the jaw has recently been described in patients receiving subcutaneous administration of RANKL-inhibitors (denosumab). However, due to promising study results, more patients will receive denosumab in order to avoid skeletal complications due to metastatic bone disease and osteoporosis. Therefore, this has the potential to become a comparable challenge to the bisphosphonate induced jaw necrosis in the area of Oral and Maxillofacial Surgery. Indeed, so far no convincing surgical technique has been described to overcome the non-healing mucosal lesions with exposed bone due to RANKL-inhibitor therapy.

In this technical note, we report two successful cases of surgical treatment of jaw-bone necrosis under RANKL-inhibitor treatment using fluorescence guided bone resection.

In conclusion, the technique is suggested as treatment option for this entity of osteonecrosis of the jaw.

Journal of Cranio-Maxillo-Facial Surgery 41 (2013) 694-698



Journal of Cranio-Maxillo-Facial Surgery 41 (2013) 694-698

Use of Ultrasonic Bone Surgery (Piezosurgery) to Surgically Treat Bisphosphonate-Related Osteonecrosis of the Jaws (BRONJ). A Case Series Report with at Least 1 Year of Follow-Up

Cornelio Blus[1,2], Serge Szmukler-Moncler[1,3], Giulio Giannelli[4], Gloria Denotti[1] and Germano Orrù[1,*]

Abstract: This preliminary work documents the use of a powerful piezosurgery device to treat biphosphonate-related osteonecrosis of the jaw (BRONJ) in combination with classical medication therapy. Eight patients presenting 9 BRONJ sites were treated, 2 in the maxilla and 7 in the mandible. Reason for biphosphonate (BiP) intake was treatment of an oncologic disease for 5 patients and osteoporosis for 3. The oncologic and osteoporosis patients were diagnosed with BRONJ after 35-110 months and 80-183 months of BiP treatment, respectively. BRONJ 2 and 3 was found in 4 patients. Resection of the bone sequestrae was performed with a high power ultrasonic (piezo) surgery and antibiotics were administrated for 2 weeks. Soft tissue healing was incomplete at the 2-week control but it was achieved within 1 month. At the 1-year control, soft tissue healing was maintained at all patients, without symptom recurrence. One patient with paraesthesia had abated; of the 2 patients with trismus, one was healed, severity of the second trismus abated. This case report series suggests that bone resection performed with a high power ultrasonic surgery device combined with antibiotics might lead to BRONJ healing. More patients are warranted to confirm the present findings and assess this treatment approach.

The Open Dentistry Journal, 2013, 7, 94-101

The use of pedicled buccal fat pad combined with sequestrectomy in bisphosphonate-related osteonecrosis of the maxilla

Lorena Gallego [1], Luis Junquera [2], Alejandro Pelaz [3], Josué Hernando [4], Joaquim Megías [4]

The use of pedicled buccal fat pad flap (BFP) has proved of value for the closure of oroantral and oronasal communications and is a well-established tool in oral and maxillofacial surgery. Otherwise, the perceived limitations of surgical therapy for bisphosphonate-related osteonecrosis of the jaws (BRONJ) have been widely discussed, and recommendations have largely been made to offer aggressive surgery only to stage 3 patients refractary to conservative management. Oroantral communication may be a common complication after sequestrectomy and bone debridement in upper maxillary BRONJ. We report a case series of stage 3 recalcitrant maxillary BRONJ surgically treated with extensive sequestrectomy and first reconstruction using pedicled BFP. All the cases presented an uneventful postoperative healing was uneventful without dehiscence, infection, necrosis or oroantral communication. We postulate that managing initially the site with BFP and primary closure may ensure a sufficient blood supply and adequate protection for an effective bone-healing response to occur. This technique may represent a mechanic protection and an abundant source of adipose-derived adult stem cells after debridement in upper maxillary BRONJ. We evaluate in this work results, advantages and indications of this technique.

Med Oral Patol Oral Cir Bucal. 2012 Mar 1;17 (2):e236-41.

Platelet-rich plasma (PRP) in dental and oral surgery: from the wound healing to bone regeneration

Antonino Albanese*, Maria E Licata, Bianca Polizzi and Giuseppina Campisi

Curi et al.	2007	3	Jaw lesions		6-8	Resolution of all lesions	strong
Lee et al.	2007	2	Complications of dental implants: oral sinus communication and lesion on the jaw ramus	Closure of the oroantral communication by rotating a large palatally-based pedicle flap over the defect; surgical debridment of the lesion of the ramus	6-9	Resolution of pain and complete closure of exposed bone	strong
Adornato et al.	2007	12	Soft tissue ulcerations and bone exposure	Marginal resection limited to the alveolar bone	6	Ten patients showed complete soft tissue healing	strong
Cetiner et al.	2009	1	Exposed necrotic bone in the alveolus	Marginal resection of the mandibular necrotic bone	6	Complete healing of the oral mucosa and alveolar bone at the surgical site	strong
Bocanegra et al.	2012	8	Exposed necrotic bone in the mandibula and maxilla	Removal of necrotic bone and curettage of the underlying bone	14	Fast mucosal healing, reduced need for analgesics and resolution of mouth lesions, without evidence of exposed bone.	strong
Mozzati et al.	2012	32	Jaw lesions	Resection of the necrotic bone		The orthopanoramic X-ray and computed tomography performed before and after surgery showed successful outcomes	strong
Coviello et al.	2012	7	Jaw lesions	Surgical debridement and sequestrectomy	3	Improvement in wound healing and reduction of bone exposure	strong

Albanese et al. Immunity & Ageing 2013, 10:23

Curr Pharm Biotechnol. 2012 Jun;13(7):1131-7.

In search of a consensus terminology in the field of platelet concentrates for surgical use: platelet-rich plasma (PRP), platelet-rich fibrin (PRF), fibrin gel polymerization and leukocytes.

Dohan Ehrenfest DM[1], Bielecki T, Mishra A, Borzini P, Inchingolo F, Sammartino G, Rasmusson L, Evert PA.

Author information

Abstract

In the field of platelet concentrates for surgical use, most products are termed Platelet-Rich Plasma (PRP). Unfortunately, this term is very general and incomplete, leading to many confusions in the scientific database. In this article, a panel of experts discusses this issue and proposes an accurate and simple terminology system for platelet concentrates for surgical use. Four main categories of products can be easily defined, depending on their leukocyte content and fibrin architecture: Pure Platelet-Rich Plasma (P-PRP), such as cell separator PRP, Vivostat PRF or Anitua's PRGF; Leukocyteand Platelet-Rich Plasma (L-PRP), such as Curasan, Regen, Plateltex, SmartPReP, PCCS, Magellan, Angel or GPS PRP; Pure Plaletet-Rich Fibrin (P-PRF), such as Fibrinet; and Leukocyte- and Platelet-Rich Fibrin (L-PRF), such as Choukroun's PRF. P-PRP and L-PRP refer to the unactivated liquid form of these products, their activated versions being respectively named P-PRP gels and L-PRP gels. The purpose of this search for a terminology consensus is to plead for a more serious characterization of these products. Researchers have to be aware of the complex nature of these living biomaterials, in order to avoid misunderstandings and erroneous conclusions. Understanding the biomaterials or believing in the magic of growth factors ? From this choice depends the future of the field.

PMID: 21740379 [PubMed - indexed for MEDLINE]

Use of platelet-rich plasma in the treatment of bisphosphonate-related osteonecrosis of the jaw

S. Bocanegra-Pérez,
M. Vicente-Barrero*, M. Knezevic,
J. M. Castellano-Navarro,
E. Rodríguez-Bocanegra,
J. Rodríguez-Millares,
D. Pérez-Plasencia,
A. Ramos-Macías

Hospital Universitario Insular de las Palmas de Gran Canaria, Universidad de Las Palmas de Gran Canaria, Spain

Abstract. Platelet-rich plasma is a concentrate of growth factors and osteoconductive proteins, which can play a major role in bone biology by accelerating and enhancing bone repair and regeneration. This paper describes the results of using platelet-rich plasma in the management of bisphosphonate-associated necrosis of the jaw. Eight patients with a diagnosis of bisphosphonate-associated necrosis of the jaw were surgically treated for debridement and removal of necrotic bone, followed by application of autologous platelet concentrate enriched with growth factors and primary suture of the wound. Patients underwent periodic clinical and radiological follow-up examinations. All patients showed clinical improvement and oral lesions resolved 2–4 weeks after treatment. After an average 14-month follow up period, patients remained asymptomatic. Although not conclusive, the combination of necrotic-bone curettage and platelet-rich-plasma to treat refractory osteonecrosis of the jaw yielded promising results.

Int. J. Oral Maxillofac. Surg. 2012; 41: 1410–1415

Platelet-rich therapies in the treatment of intravenous bisphosphonate-related osteonecrosis of the jaw: A report of 32 cases

Marco Mozzati, Giorgia Gallesio *, Valentina Arata, Renato Pol, Matteo Scoletta

Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is an important complication in cancer patients taking intravenous BPs (BPs). In most cases, BRONJ is associated with an oral surgery procedure involving jaw bone. Currently, BRONJ management remains controversial, and there is no definitive standard of care for this disease. In fact, several articles in the recent literature discuss treatments that range from topical to surgical treatment, without definitive conclusion about treatment. A clinical study was conducted on 32 patients treated with i.v BPs for oncologic pathologies affected by BRONJ. The patients were treated by resection of the necrotic bone with primary closure of the mucosa over the bony defect using plasma rich in growth factors (PRGF). Orthopanoramic and computed tomography were performed before and after surgery. No intraoperative complications were observed, and all 32 cases were treated successfully. Our data on the use of PRGF demonstrate positive results for this surgical treatment. PRGF may enhance vascularization and regeneration of osseous and epithelial tissues.

Oral Oncology 48 (2012) 469–474

Management of Bisphosphonate-Related Osteonecrosis of the Jaw With a Platelet-Rich Fibrin Membrane: Technical Report

Sıdıka Sinem Soydan, DDS, PhD, * *and Sina Uckan, DDS, PhD* †

Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is a challenging complication resulting from the long-term application of bisphosphonates. In most cases, BRONJ occurs after a surgical procedure involving the jawbone. Currently, the management of BRONJ remains controversial, and there is no definitive treatment other than palliative methods. Platelet-rich fibrin (PRF) represents a relatively new biotechnology for the stimulation and acceleration of tissue healing and bone regeneration. This technical note describes the total closure of moderate bone exposure in persistent BRONJ in 2 weeks with a double-layer PRF membrane. PRF may stimulate gingival healing and act as a barrier membrane between the alveolar bone and the oral cavity. PRF may offer a fast, easy, and effective alternative method for the closure of bone exposure in BRONJ.

J Oral Maxillofacial Surg
72:322-326 , 2014

Journal section: Oral Medicine and Pathology
Publication Types: Research

doi:10.4317/medoral.19458
http://dx.doi.org/doi:10.4317/medoral.19458

Alternative treatments for oral bisphosphonate-related osteonecrosis of the jaws: A pilot study comparing fibrin rich in growth factors and teriparatide

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Abstract

Objective: The aim of this study is to describe and compare the evolution of recurrent bisphosphonate-related osteonecrosis of the jaws (BRONJ) in patients treated with plasma rich in growth factors or teriparatide.

Material and Methods: Two different types of treatments were applied in patients diagnosed of recurrent BRONJ in a referral hospital for 1.100.000 inhabitants. In the group A, plasma rich in growth factors was applied during the surgery. In the group B, the treatment consisted in the subcutaneous administration of teriparatide. All the cases of BRONJ should meet the following conditions: recurrent BRONJ, impossibility of surgery in stage 3 Ruggiero classification and absence of diagnosed neoplastic disease. Clinical and radiographic evolution of the patients from both groups was observed.

Results: Nine patients were included, 5 in group A and 4 in group B. All the patients were women on oral bisphosphonate therapy for primary osteoporosis (5 patients) or osteoporosis-related to the use of corticosteroids (4 patients). Alendronate was the most common oral bisphosphonate associated with BRONJ in our study (four patients in group A and two in group B). The mean age was 72,8 years in the group A and 73,5 years in the group B. All the patients from group A showed a complete resolution of their BRONJ. Only one patient in the group B showed the same evolution.

Conclusion: In our series, the plasma rich in growth factors showed better results than the teriparatide in the treatment of recurrent BRONJ.

Cella et al. Head & Face Medicine 2011, 7:16
http://www.head-face-med.com/content/7/1/16

HEAD & FACE MEDICINE

CASE REPORT Open Access

Autologous bone marrow stem cell intralesional transplantation repairing bisphosphonate related osteonecrosis of the jaw

Methods: Under local anesthesia a volume of 75 ml of bone marrow were harvested from the posterior superior iliac crest by aspiration into heparinized siringes. The cell suspension was concentrated, using Ficoll - Hypaque® centrifugation procedures, in a final volume of 6 ml. Before the injection of stem cells into the osteonecrosis, the patient underwent surgical toilet, local anesthesia was done and spongostan was applied as a carrier of stem cells suspension in the bone cavity, then 4 ml of stem cells suspension and 1 ml of patient's activated platelet-rich plasma were injected in the lesion of BRONJ.

Results: A week later the residual spongostan was removed and two weeks later resolution of symptoms was obtained. Then the lesion improved with progressive superficialization of the mucosal layer and CT scan, performed 15 months later, shows improvement also of bone via concentric ossification: so complete healing of BRONJ (stage 0) was obtained in our patient, and 30 months later the patient is well and without signs of BRONJ.

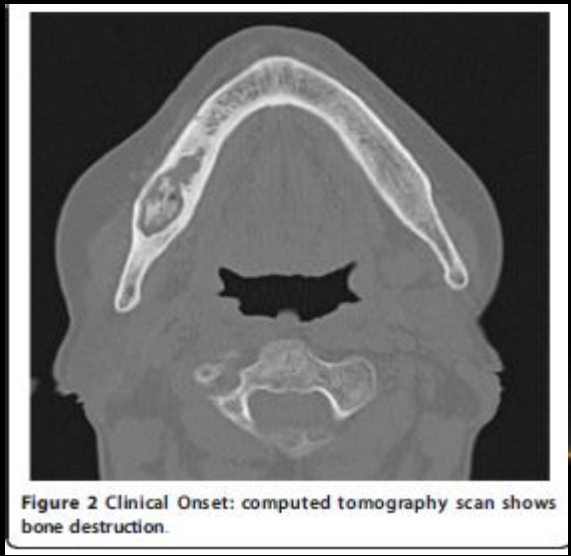

Figure 2 Clinical Onset: computed tomography scan shows bone destruction.

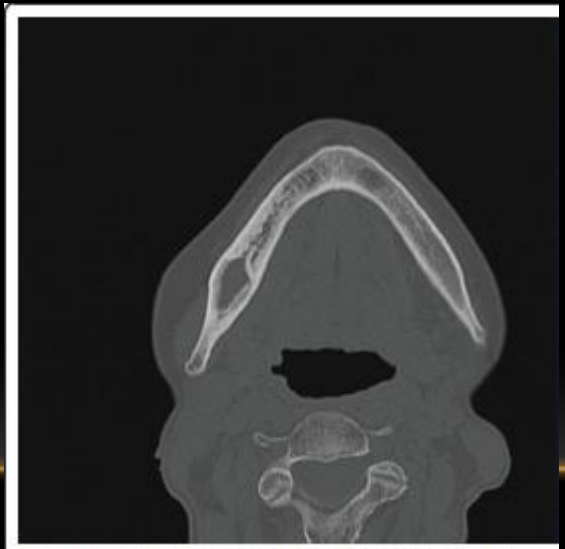

Figure 5 Computed Tomography scan, 15 months later, shows a concentric ossification of the bone lesion.

Commento:

- Caso singolo
- Sequestro osseo
- Senza stem cell?

ORAL DISEASES

Oral Diseases (2012) 18, 823–824 doi:10.1111/j.1601-0825.2012.01941.x

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LETTER TO THE EDITOR

Mesenchymal stem cells and bisphosphonate-related osteonecrosis of the jaw: the future?

These data are important when considering these cells for potential use in cell therapy protocols. We envision a primary clinical application for this type of mesenchymal cells to facilitate the bone regeneration for refractory cases of BRONJ.

Resective Surgical Approach Shows a High Performance in the Management of Advanced Cases of Bisphosphonate-Related Osteonecrosis of the Jaws: A Retrospective Survey of 347 Cases

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Franco Peluso, MD, DDS,‡‡ Matteo Scoletta, DDS,§§
Luigi Solazzo, MD, ‖‖ and Giuseppe Colella, MD, DDS¶¶

Purpose: The aim of this study was to evaluate the results of the surgical treatment of bisphosphonate-related osteonecrosis of the jaw (BRONJ) in a large cohort.

Materials and Methods: A retrospective cohort multicenter study was designed. Patients were enrolled if they were diagnosed with BRONJ and received operative treatment. Data on demographic, health status, perioperative, and surgical factors were collected retrospectively. The primary outcome variable was a change in BRONJ staging (improvement, worsening, or no change). Interventions were grouped by local debridement and resective surgery. Data were collected for other variables as cofactors. Univariate analysis and logistic regressions were then performed.

Results: Of the 347 BRONJ-affected subjects, 59% showed improvement, 30% showed no change, and 11% showed worsening. Improvement was observed in 49% of cases treated with local debridement and 68% of cases treated with resective surgery. Multivariate analysis indicated that maxillary location, resective surgery, and no additional corticosteroid treatment were associated with a positive outcome.

Conclusions: Surgical treatment of BRONJ appeared to be more effective when resective procedures were performed. Nonetheless, other factors, such as the absence of symptoms and the types of drug administration, should be taken into account before clinical decisions are made.

J Oral Maxillofac Surg 70:2501-2507, 2012

Oral Oncology 49 (2013) 66–70

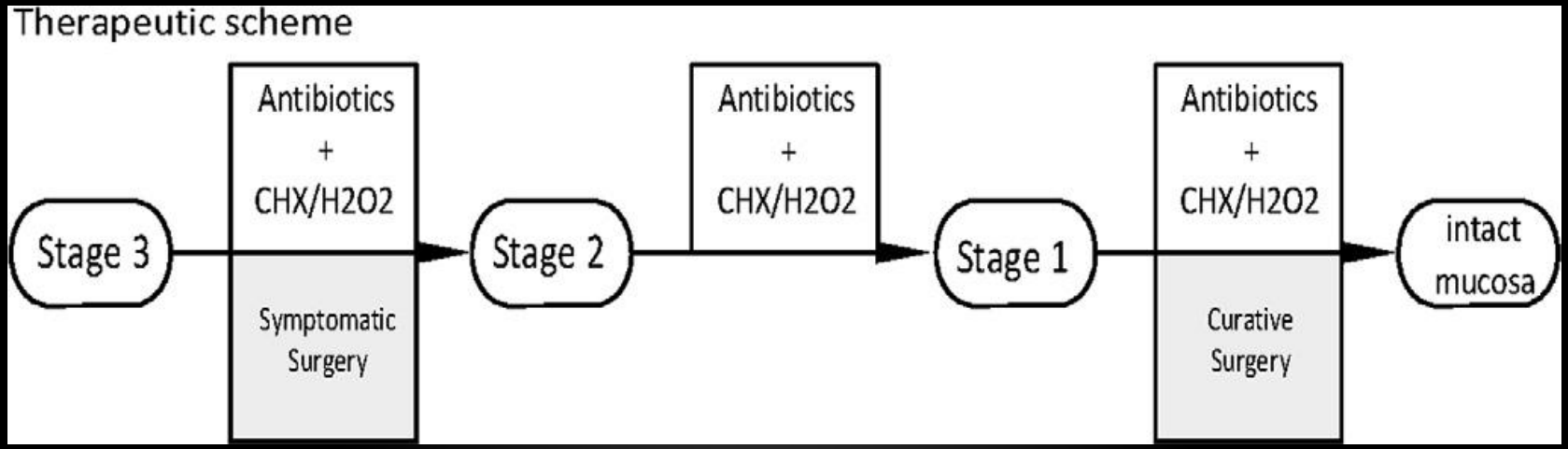
Contents lists available at SciVerse ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Long-term success of surgery in bisphosphonate-related osteonecrosis of the jaws (BRONJs) ☆

Daniel Holzinger *, Rudolf Seemann, Clemens Klug, Rolf Ewers, Gabriele Millesi, Arnulf Baumann, Arno Wutzl



Results: Surgical treatment improved the stage distribution from 19% stage I, 56% stage II and 25% stage III to 59% intact mucosa, 19% stage I and 13% stage II and 8% stage III. The improvement in the stage of disease achieved by surgery was statistically significant.

FACTORS INFLUENCING SURGICAL TREATMENT OF BISPHOSPHONATE-RELATED OSTEONECROSIS OF THE JAWS

Arno Wutzl, MD, DMD,[1] Sebastian Pohl, MD,[1] Irene Sulzbacher, MD, PhD,[2] Rudolf Seemann, MD, DMD,[1]

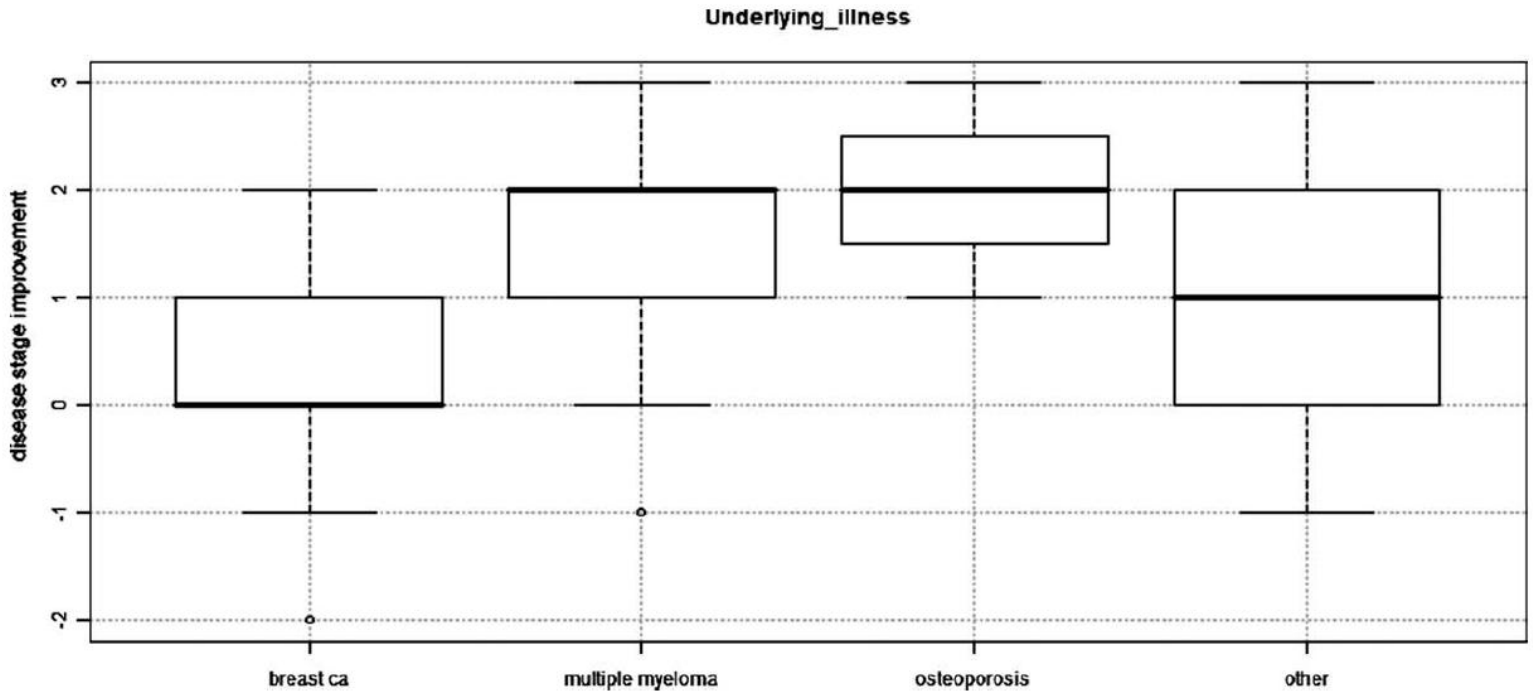


FIGURE 3. The underlying illness plays a significant role in the surgical outcome of patients with BRONJ ($p < 0.05$). Osteoporosis and multiple myeloma patients with BRONJ showed better improvements in BRONJ due to surgical treatment than did patients with breast cancer or those with other types of cancers. Box plots show the improvement in stage disease.

Head Neck 34: 194–200, 2012

MUCOSA

Ben vascolarizzata

Evitare stripping del periostio

Copertura conpleta del difetto senza tensione

British Journal of Oral and Maxillofacial Surgery 47 (2009) 294–297

MUCOSAL OUTCOME

- The primary pathology appeared to be a decisive factor.
- Most osteoporotic patients (87.50 %) showed a clinical mucosa stabilization compared with patients with malignancies

		Healing	Improvement	Spreading	Fisher exact test
Primary pathology	Malignant $n=31$	29.03	45.89	25.08	$p=0.0128$
	Osteoporotic $n=8$	87.50	12.50	–	
ONJ severity	Mild $n=10$	80.00	20.00	–	$p=0.0053$
	Moderate $n=21$	38.10	42.86	19.05	
	Severe $n=8$	–	50.00	50.00	
Local ONJ treatment	Conservative $n=8$	25.00	12.50	62.50	$p=0.0096$
	Mini-invasive $n=8$	50.00	25.00	25.00	
	Extensive $n=23$	43.48	52.17	4.35	

Clin Oral Invest (2014) 18:391–399

BONE OUTCOME

- The primary pathology appeared to be a decisive factor.

		Healing	Improvement	Spreading	Fisher's exact test
Primary pathology	Malignant $n=31$	3.69	24.38	71.93	$p=0.00021$
	Osteoporotic $n=8$	75.00	12.50	12.50	
ONJ severity	Mild $n=10$	40.00	40.00	20.00	$p=0.0319$
	Moderate $n=21$	14.29	14.29	71.43	
	Severe $n=8$	–	25.00	75.00	
Local ONJ treatment	Conservative $n=8$	25.00	12.50	62.50	
	Mini-invasive $n=8$	25.00	37.50	37.50	
	Extensive $n=23$	13.04	21.74	65.22	

Clin Oral Invest (2014) 18:391–399

RISULTATI

- IMPREDICIBILI

  Valutazione estremamente complessa per

  - Patologia di base e BPH usato
  - Tipo di chirurgia conservativa
  - Ampia variabilità dei protocolli terapeutici
  - Correlazione agli stadi (ampiezza stadio 2)
  - Definizione di risultato

CONCLUSIONS…….

- More patients are warranted to confirm….
- We are aware that a case report can be of limited interest…
- This series, although small in number….
- Further clinical studies are needed…..
- Prospective multicenter, controlled trials following specific management algorithms are necessary….
- Further studies should follow….
- Further studies on individual factors….
- Future research involving a larger cohort is needed….
- More comprehensive studies are needed….
- Within the limits of this study….
- Although not conclusive requires further research, based on prospective randomized double-blind controlled trials….