Alessandria
5 Giugno 2010

# Osteonecrosi dei mascellari (ONJ): Prevenzione, Diagnosi, Trattamento "Update 2010"

## Bifosfonati endovena: misure preventive per i pazienti oncologici ed ematologici


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# PREVENTIVE MEASURES – Position papers

Bisphosphonate-related osteonecrosis of the jaw: position paper from the Allied Task Force Committee of Japanese Society for Bone and Mineral Research, Japan Osteoporosis Society, Japanese Society of Periodontology, Japanese Society for Oral and Maxillofacial Radiology, and Japanese Society of Oral and Maxillofacial Surgeons.

Yoneda T, Hagino H, Sugimoto T, Ohta H, Takahashi S, Soen S, Taguchi A, Toyosawa S, Nagata T, Urade M.

J Bone Miner Metab. 2010 Mar 24. [Epub ahead of print]

American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaws—2009 update

Ruggiero SL, Dodson TB, Assael LA, Landesberg R, Marx RE, Mehrotra B; American Association of Oral and Maxillofacial Surgeons.

J Oral Maxillofac Surg. 2009 May;67(5 Suppl):2-12

Oral bisphosphonates as a cause of bisphosphonate-related osteonecrosis of the jaws: clinical findings, assessment of risks, and preventive strategies.

Assael LA.

J Oral Maxillofac Surg. 2009 May;67(5 Suppl):35-43.

1. Patients scheduled for BP treatment should undergo oral examination by a dentist before BP administration. In particular, patients who will receive parenteral BPs should be examined for periodontal diseases (including radiography), and dental treatments should be conducted on a priority basis.

2. Before dental treatments, in BP patients, thorough oral cleaning is essential. Oral care should be conducted by a dental hygienist in parallel with dental treatments. Cessation of smoking and restriction of alcohol intake are also required .

3. For oral treatments for BRONJ patients, alleviation of acute symptoms, including pain (regional cleaning, antibacterial gargle, etc.), should first be conducted, followed by prevention of secondary infection (administration of antibacterial drugs) and removal of necrotic tissues. Conservative procedures are desirable, and unnecessary aggressive curettage is contraindicated .

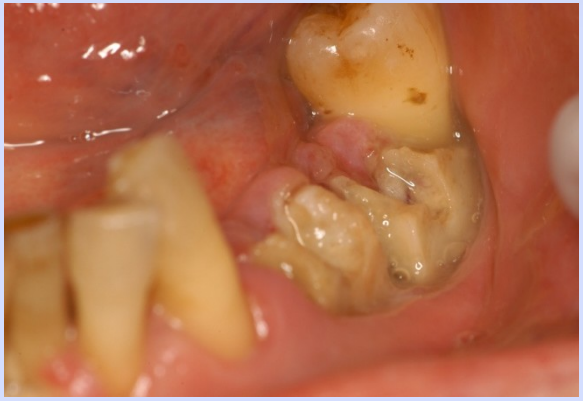
Maintenance of good oral hygiene is important through education and instruction of patients receiving parenteral BP, such that dental treatments can be avoided as much as possible. If dental treatments are desperately required, nonsurgical treatments are suggested rather than surgical treatments such as tooth extraction or dental implants.

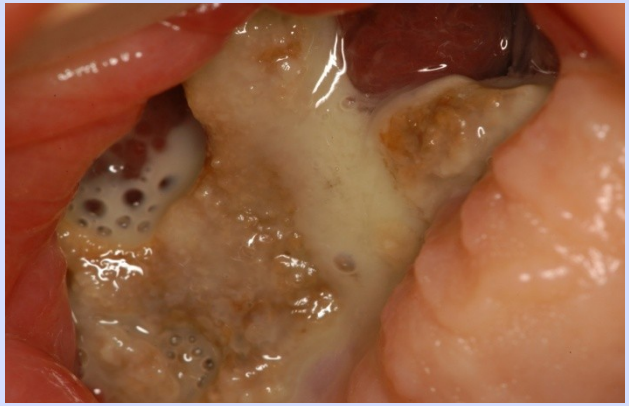
Bisphosphonate-related osteonecrosis of the jaw: position paper from the Allied Task Force Committee of Japanese Society for Bone and Mineral Research, Japan Osteoporosis Society, Japanese Society of Periodontology, Japanese Society for Oral and Maxillofacial Radiology, and Japanese Society of Oral and Maxillofacial Surgeons.

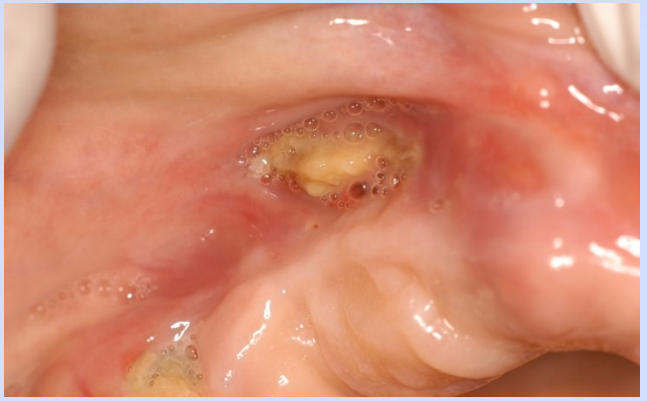
Yoneda T, Hagino H, Sugimoto T, Ohta H, Takahashi S, Soen S, Taguchi A, Toyosawa S, Nagata T, Urade M.

J Bone Miner Metab. 2010 Mar 24. [Epub ahead of print]

# SURGERY: When and why?







The incidence of BRONJ increases with dose, dosing frequency, and dosing duration. It has been reported that the incidence of BRONJ begins to increase approximately 1 year after intravenous zoledronic acid treatment and 2–3 years after oral BP administration

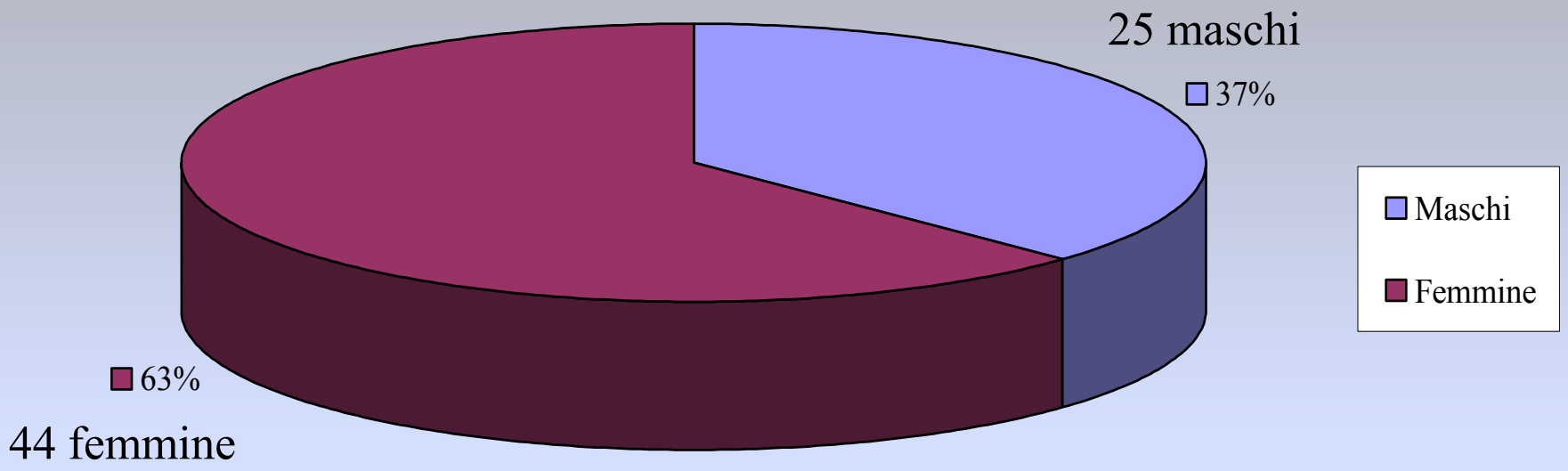
Mavrokokki T, Cheng A, Stein B, Goss A (2007)
Nature and frequency of bisphosphonate-associated osteonecrosis of the jaws in Australia.
J Oral Maxillofac Surg 65:415–423

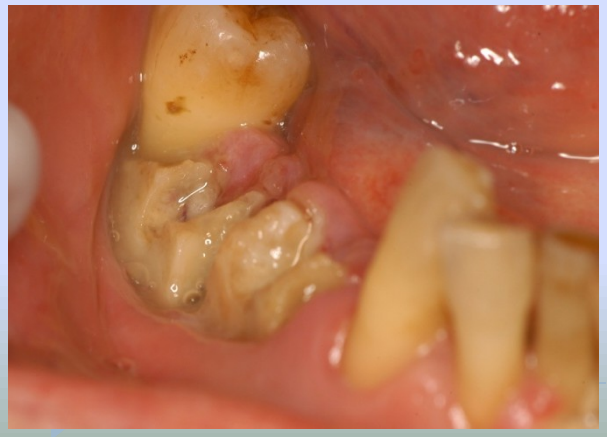
*Studio osservazionale: Tre anni di esperienza*

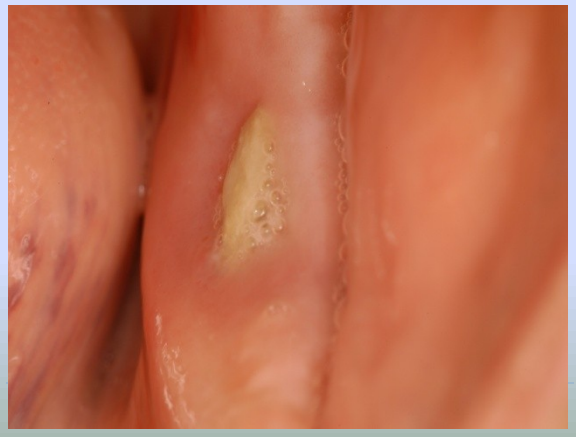
Tra il 2005 ed il 2009, presso l'Area Funzionale di Patologia Speciale Odontostomatologica, dell'Università "Federico II" di Napoli, sono stati trattati 69 pazienti affetti da BRONJ.

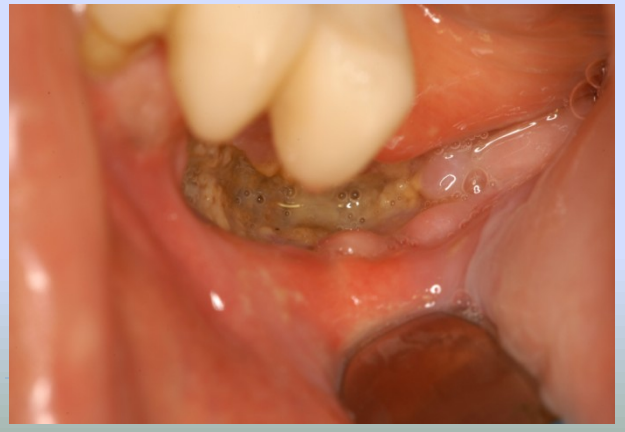
Età dei pazienti compresa tra 39-85 anni (media: 67.5 ± 8.3)

## Distribuzione del sesso

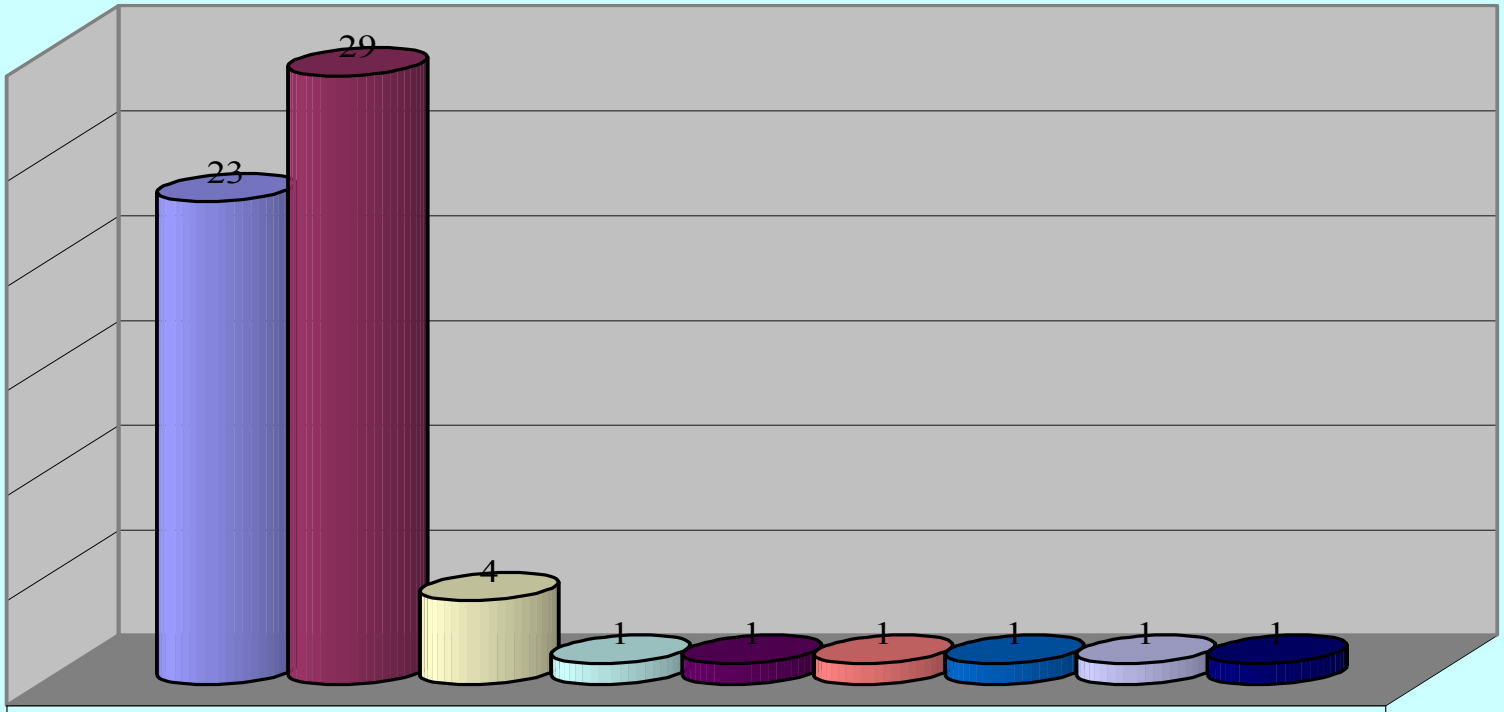




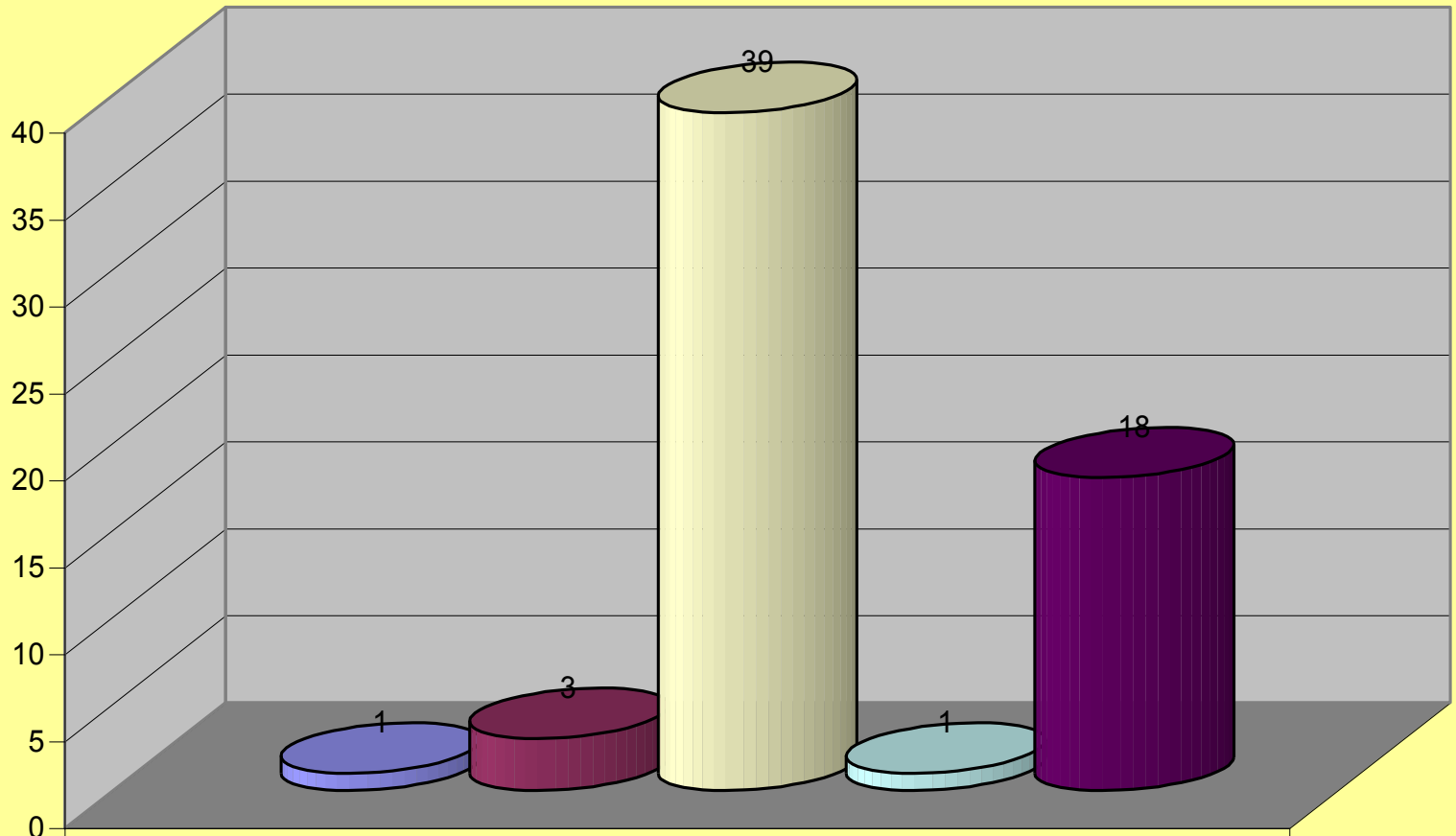


# Patologie di base



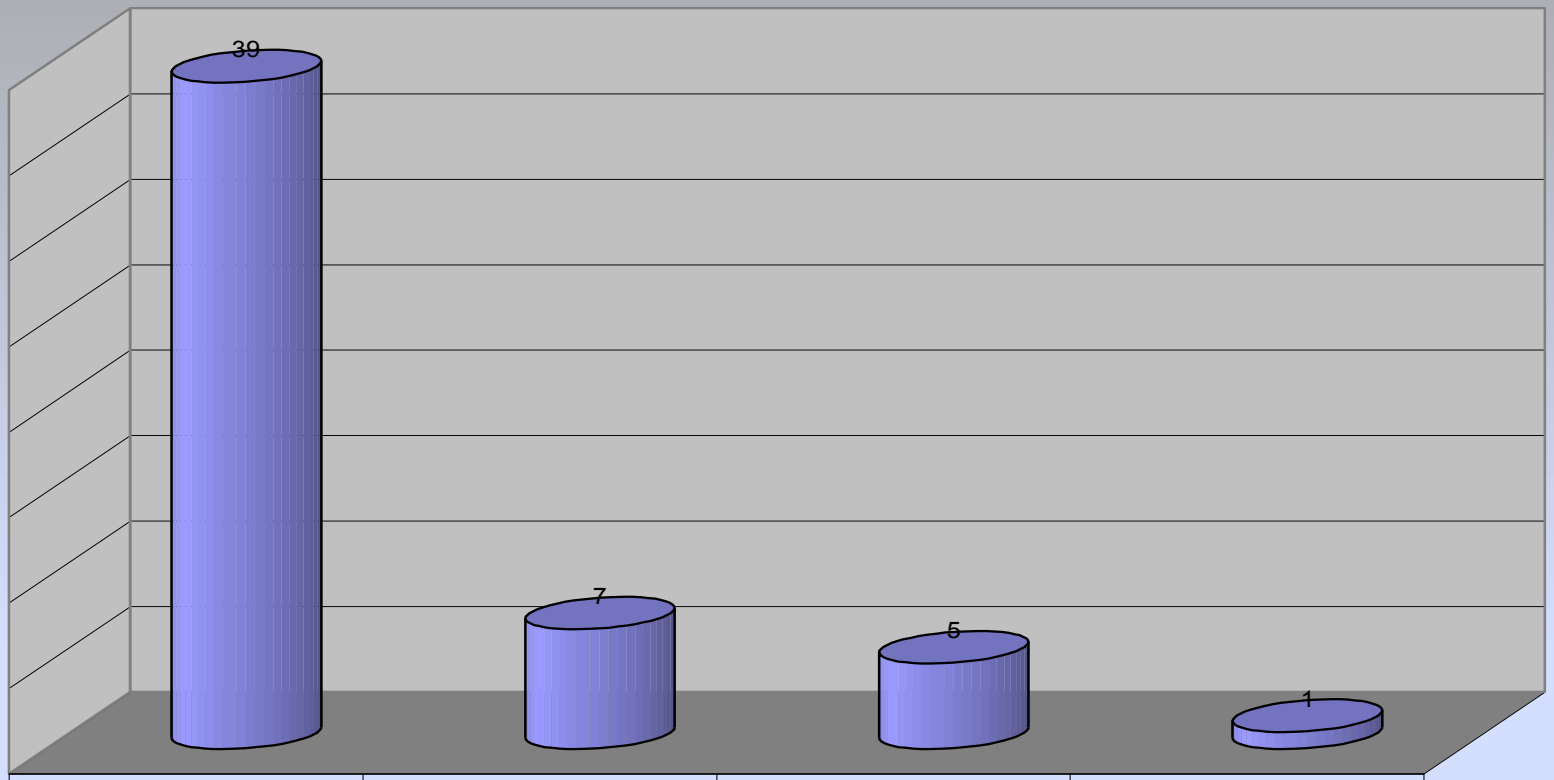

| | |
|---|---|
| mieloma multiplo | 23 |
| ca mammario | 29 |
| ca prostatico | 4 |
| ca polmonare | 1 |
| ca gastrico | 1 |
| artrite reumatoide | 1 |
| non-hodgkin linfoma | 1 |
| sarcoma di kaposi | 1 |
| osteoporosi | 1 |

# Farmaci BPH assunti

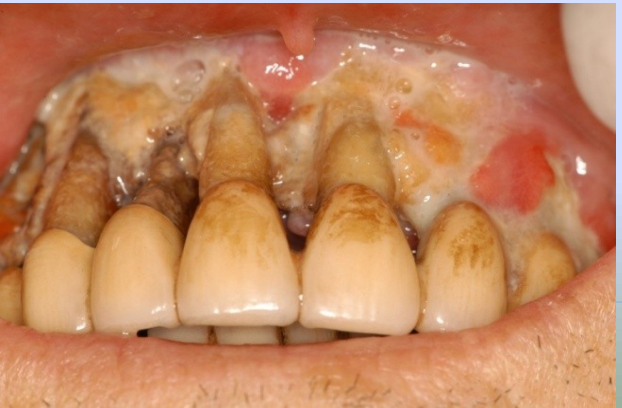


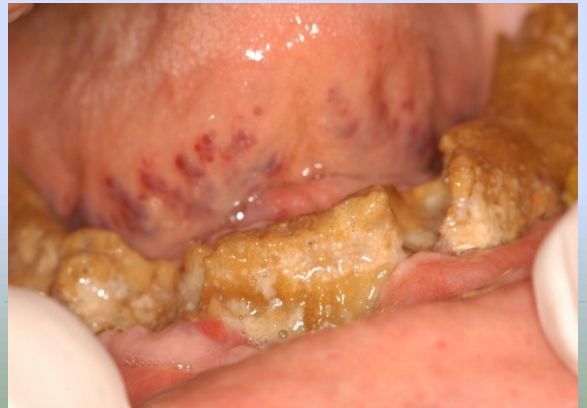

| | |
|---|---|
| | - |
| alendronato | 1 |
| pamidronato | 3 |
| zolendronato | 39 |
| clodronato | 1 |
| pamidronato + zolendronato | 18 |

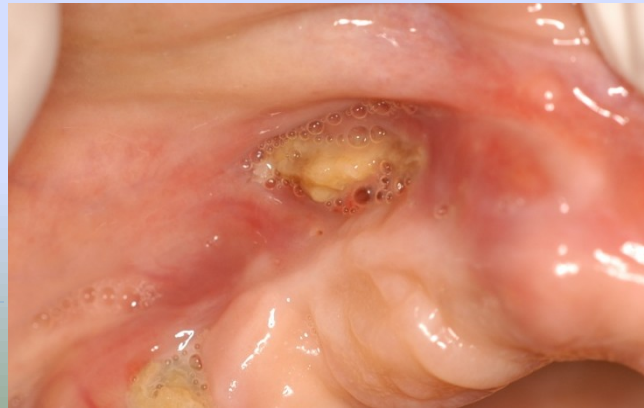
# Sede della necrosi



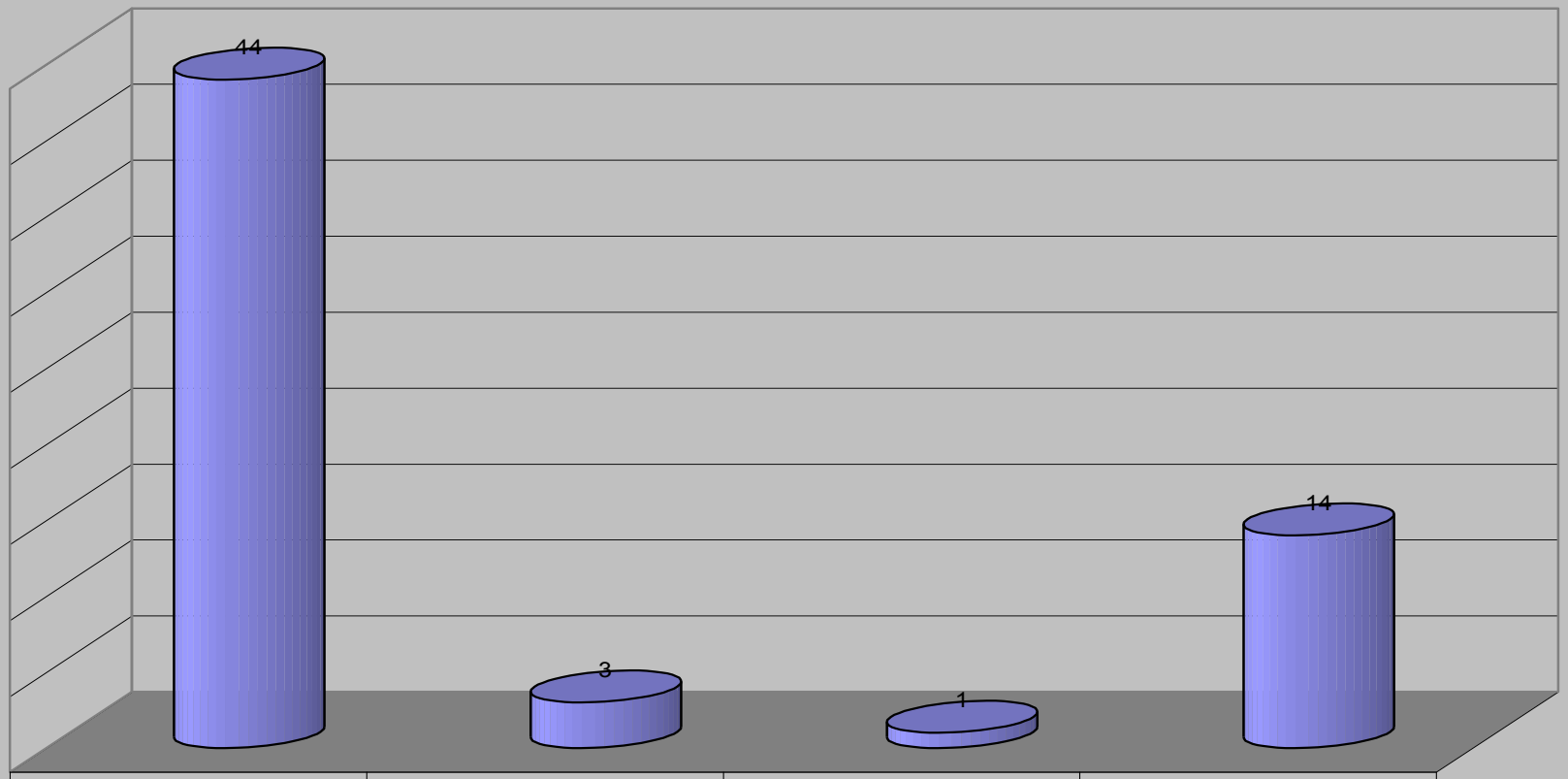

| | mandibola | mascellare superiore | mand+max | mand+condilo |
|---|---|---|---|---|
| numero pazienti | 39 | 7 | 5 | 1 |

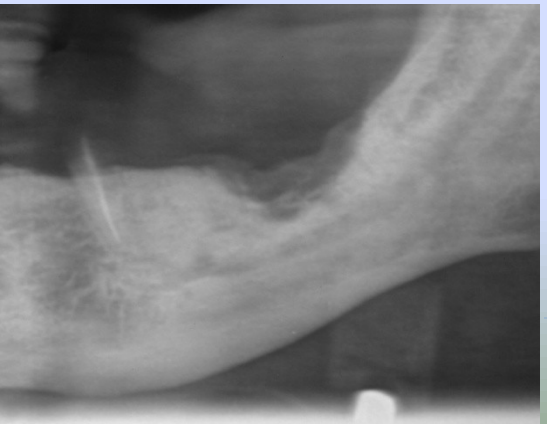


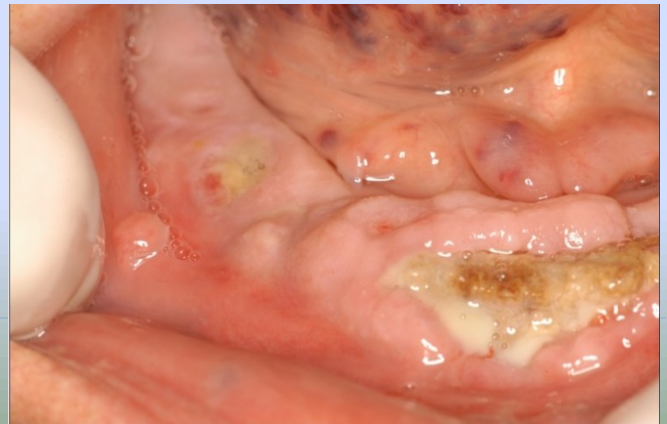


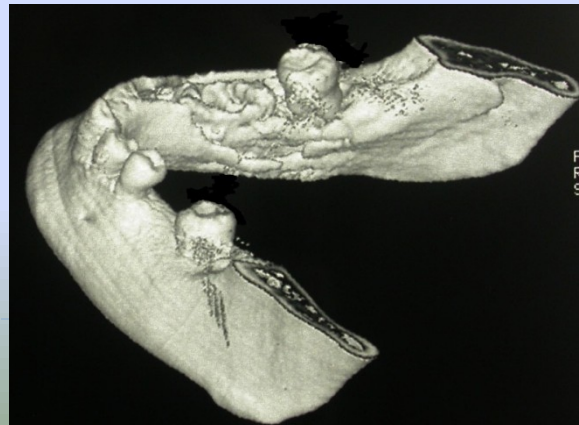


## Fattore scatenante la necrosi





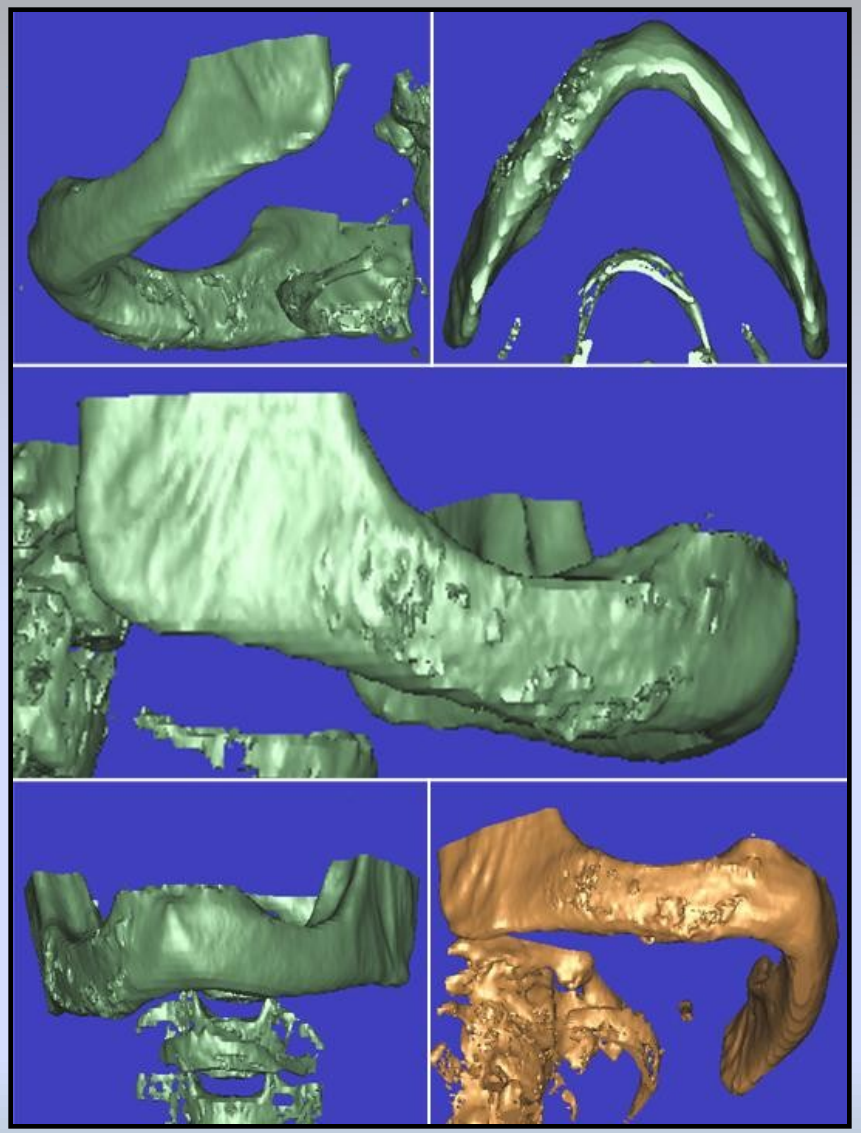


Cancer patients exposed to IV bisphosphonates with a history of inflammatory dental disease (eg, periodontal and dental abscesses) are at a 7-fold increased risk of developing BRONJ.

American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaws—2009 update

Ruggiero SL, Dodson TB, Assael LA, Landesberg R, Marx RE, Mehrotra B; American Association of Oral and Maxillofacial Surgeons.

J Oral Maxillofac Surg. 2009 May;67(5 Suppl):2-12



# EFFICACIA DI PROTOCOLLO TERAPEUTICO SISTEMICO E TOPICO IN 13 PAZIENTI CON MIELOMA MULTIPLO E CANCRO MAMMARIO AFFETTI DA BRONJ

| | Multiple Myeloma | | Breast cancer | | |
|---|---|---|---|---|---|
| **Characteristics** | **No. of patients** | **%** | **No. of patients** | **%** | ***P*** |
| | | | | | |
| Age. years | | | | | .093 |
| Range | 59-76 | | 49-79 | | |
| Median | 70 | | 63 | | |
| Mean | 68.4 | | 63.1 | | |
| Std Deviation | 4.85 | | 9.85 | | |
| Std Error | 1.34 | | 2.63 | | |
| CI 95% interval | 65.45 – 71.32 | | 57.33 – 71.32 | | |
| Location of BRONJ | | | | | .824 |
| Maxilla | 5 | 38.5 | 4 | 30.8 | |
| Mandible | 6 | 46.1 | 7 | 53.8 | |
| Maxilla and mandible | 2 | 15.4 | 2 | 15.4 | |
| Concurrent systemic diseases | | | | | .121 |
| Hypertension | 3 | 23 | 6 | 46.1 | |
| Osteoporosis | 0 | 0 | 8 | 61.5 | |
| Diabetes | 1 | 7.7 | 3 | 23 | |
| Precipitating events | | | | | .768 |
| Dental extraction | 9 | 69.2 | 11 | 84.6 | |
| Periodontal disease | 2 | 15.4 | 2 | 15.4 | |
| Dental prosthesis | 1 | 7.7 | 0 | 0 | |
| Implants | 1 | 7.7 | 0 | 0 | |
| Surgical treatment | 2 | 15.4 | 2 | 15.4 | .967 |
| Smoke | 2 | 15.4 | 3 | 23 | .652 |

# FATTORI PREDITTIVI DI GUARIGIONE

| **Variables** | **Score** | ***P*** |
|---|---|---|
| Cancer (Gender) | .076 | .783 |
| Site per Extent of BRONJ | 2.769 | .429 |
| Time of BP exposure per Extent of BRONJ | 1.107 | .575 |
| Stage at admission | .017 | .896 |
| Concurrent systemic diseases | 9.669 | .139 |
| Smoke | .027 | .869 |
| Major surgery | .445 | .505 |

| **Predictors** | **B** | **SE** | **Wald** | ***P*** | **HR (95% CI)** |
|---|---|---|---|---|---|
| Age | -.054 | .030 | 3.261 | .071 | .947 (.893 – 1.005) |
| Events | | | 8.560 | .036 | |
| PD vs Ex | 1.359 | .630 | 4.643 | .031 | 3.891 (1.131 – 13.388) |
| Prosthesis vs Ex | -13.145 | 690.054 | .000 | .985 | .000 |
| Implants vs Ex | 2.114 | 1.151 | 3.371 | .066 | 8.278 (.867 – 79..31) |

In contrast to patients with ONJ after dental procedures, patients with spontaneous, unprovoked ONJ fared poorly and were at increased risk of nonhealing and of recurrent lesions.

Bedros et al. Natural history of osteonecrosis of the jaw in patients with multiple myeloma.
2008. JCO 26: 5904-5909

# PAZIENTE ONCOLOGICO NON ANCORA IN TRATTAMENTO CON BP PER VIA ENDOVENOSA

GOLD STANDARD:

1) Trattamento odontoiatrico e riabilitazione da effettuare prima della terapia con BP per via endovenosa

LIMITI

1) Trattamento odontoiatrico in genere non effettuabile se non al momento della diagnosi oncologica, dove la necessità di terapie è impellente.
2) Opportuno quindi concentrare il trattamento all'interno dei primi 6 cicli di BP per via endovenosa

# PAZIENTE ONCOLOGICO GIA' IN TRATTAMENTO DA ANNI CON BP PER VIA ENDOVENOSA

1) Fase pre-chirurgica: Riduzione della carica batterica mediante igiene orale professionale, utilizzo di antisettici topici e terapia antibiotica sistemica
2) Fase chirurgica: estrazione con allestimento di lembo e chiusura per prima intenzione, protezione del sito con presidi locali (es: gel piastrinico)?
3) Fase post-chirurgica: utilizzo di antisettici topici e terapia antibiotica sistemica fino alla completa riepitelizzazione del sito chirurgico

Occurrence of bisphosphonate-related osteonecrosis of the jaw after surgical tooth extraction.

Saia G, Blandamura S, Bettini G, Tronchet A, Totola A, Bedogni G, Ferronato G, Nocini PF, Bedogni A.

J Oral Maxillofac Surg. 2010;68(4):797-804.

Recently, the European Myeloma Network has proposed that BP treatment should be discontinued when BRONJ develops in patients with multiple myeloma and resumed when myeloma starts to progress again

Terpos E, Sezer O, Croucher PI, Garcı´a-Sanz R, Boccadoro M, San Miguel J, Ashcroft J, Blade´ J, Cavo M, Delforge M, Dimopoulos MA, Facon T, Macro M, Waage A, Sonneveld P (2009).

The use of bisphosphonates in multiple myeloma: recommendations of an expert panel on behalf of the European Myeloma Network.
Ann Oncol 20:1303–1317

# OPEN QUESTIONS

1. Biopsia ossea
2. Terapia parodontale versus Estrazioni
3. Metodiche di riduzione della carica batterica
4. Necrosi spontanea