



UNIVERSITÀ
DEGLI STUDI
DI PALERMO

OSTEONECROSI DELLE OSSA MASCELLARI (ONJ) DA BIFOSFONATI E ALTRI
FARMACI: PREVENZIONE, DIAGNOSI, FARMACOVIGILANZA, TRATTAMENTO -
UPDATE 2014

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What happens to the BRONJ patients when re-classified according to the novel SICMF-SIPMO recommendations? OUR EXPERIENCE

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Prevenzione e Ricerca sull'Osteonecrosi dei Mascellari da Bifosfonati

Oral Communication

CATEGORY: Descrizione di casistiche di ONJ (n ≥10 casi) – Epidemiologia

BRONJ: Bisphosphonates Related Osteonecrosis of the Jaws



Proposal of definition and staging system 2012

“BRONJ is an adverse drug reaction described as the progressive destruction and death of bone that affects the mandible or maxilla of patients exposed to the treatment with nitrogen-containing bisphosphonates, in the absence of a previous radiation treatment” [1].

Major clinic sign

Necrotic bone exposure in oral cavity

Minor clinical signs and symptoms

- Abscess
- Displaced mandibular stumps
- Extra-oral fistula
- Gross mandible deformity
- Hypoesthesia/paraesthesia of the lips^a
- Mucosal/gingival fistula
- Nasal leakage of fluids
- Non-healing post-extraction socket

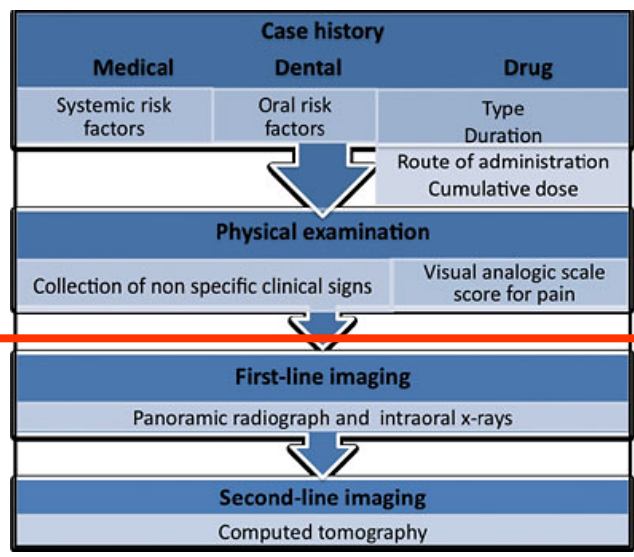


Table 2 Non-specific computed tomography (CT) findings associated with bisphosphonate-related osteonecrosis of the jaws (BRONJ)

Early signs

- Cortical disruption
- Focal bone marrow sclerosis^a
- Markedly thickened and sclerotic lamina dura
- Persisting alveolar socket
- Trabecular thickening^a

Late signs

- Diffuse osteosclerosis^b
- Oro-antral fistula
- Osteolysis extending to the sinus floor
- Osteosclerosis of adjacent bones (zygoma, hard palate)
- Pathologic fracture
- Periosteal reaction
- Prominence of the inferior alveolar nerve canal
- Sinusitis

[1] Bedogni, A et al. (2012). Learning from experience. Proposal of a refined definition and staging system for bisphosphonate-related osteonecrosis of the jaw (BRONJ). *Oral Dis* 18(6): 621-623

SICMF SIPMO Staging System – SS-SS

(Clinical-radiological stadiation of BRONJ)

Stage 1

FOCAL

CLINICAL SIGNS AND SYMPTOMS: bone exposure; sudden dental mobility; nonhealing postextraction socket; mucosal fistula; swelling; abscess formation; trismus; gross mandibular deformity and/or hypoesthesia/paraesthesia of the lips

CT FINDINGS: increased bone density limited to the **alveolar bone** region (trabecular thickening and/or focal osteosclerosis), with or without the following signs: markedly thickened and sclerotic lamina dura; persisting alveolar socket; and/or cortical disruption

1a. Asymptomatic

1b. Symptomatic (pain and purulent discharge)

Stage 2

DIFFUSE

CLINICAL SIGNS AND SYMPTOMS: same as Stage 1

CT FINDINGS: increased bone density extended to the **basal bone** (diffuse osteosclerosis), with or without the following signs: prominence of the inferior alveolar nerve canal; periosteal reaction; sinusitis; sequestra formation; and/or oro-antral fistula

2a. Asymptomatic

2b. Symptomatic (pain and purulent discharge)

Stage 3

COMPLICATED

Same as Stage 2, with one or more of the following:

CLINICAL SIGNS AND SYMPTOMS: extra-oral fistula; displaced mandibular stumps; nasal leakage of fluids

CT FINDINGS: **osteosclerosis of adjacent bones** (zygoma, hard palate); pathologic mandibular **fracture**; and/or osteolysis extending to the **sinus floor**

BRONJ: Bisphosphonates Related Osteonecrosis of the Jaws



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American Association of Oral and Maxillofacial Surgeons

POSITION PAPER 2009

POSITION PAPER 2014

“Patients may be considered to have BRONJ if all of the following three characteristics are present:

1. Current or previous treatment with a bisphosphonate;
2. Exposed bone in the maxillofacial region that has persisted for more than 8 weeks
3. No history of radiation therapy to the jaws.” [1].

“...associated with other antiresorptive (denosumab) and antiangiogenic therapies” [2].

[1] Ruggiero SL et al. AAOMS position paper on bisphosphonate-related osteonecrosis of the jaws--2009 update. J Oral Maxillofac Surg. 2009 May;67(5):2-12.

[2] Ruggiero et al. Medication osteonecrosis of the jaws- update 2014. (http://www.aaoms.org/docs/position_papers/mronj_position_paper.pdf?pdf=MRONJ-Position-Paper)

Medication Related Osteo Necrosis of the Jaw

AAOMS Staging System – (AAOMS-SS) (Clinical staging of BRONJ/MRONJ)

At risk category	No apparent necrotic bone in patients who have been treated with either oral or IV bisphosphonates
Stage 0	Non exposed bone variant No clinical evidence of necrotic bone, but non-specific clinical findings, radiographic changes and symptoms
Stage 1	Exposed and necrotic bone, or fistulae that probes to bone, in patients who are asymptomatic and have no evidence of infection
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
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

any stage according SS-SS

STAGE 1a according SS-SS

STAGE 1b according SS-SS

STAGE 2a, 2b and 3
according SS-SS

1. Abolition of stage “0”
2. Description of three stages (1–3) based on clinical and CT findings
3. Pain and purulent discharge are no longer used to distinguish between different disease stages (to avoid the “ping pong” effect).
4. The presence of clinically detectable sequestra is no longer regarded as a sign of complicated disease



Aim of the study:

To re-classify BRONJ cases in order to evaluate the diagnostic efficiency of the novel staging system and to define the most adequate managements accordingly.

Method:

A **retrospective database analysis** of BRONJ cases observed at the Sector of Oral Medicine-University of Palermo **from 2005 to 2012** was performed.

The patients previously classified according 2009 AAOMS staging system (AAOMS-SS) were reclassified according 2012 SICMF-SIPMO staging system (SS-SS).

93 patients
(mean age 69 yy \pm 7 yy)

♂ 27 ♀ 66

Results

1. RE-CLASSIFICATION

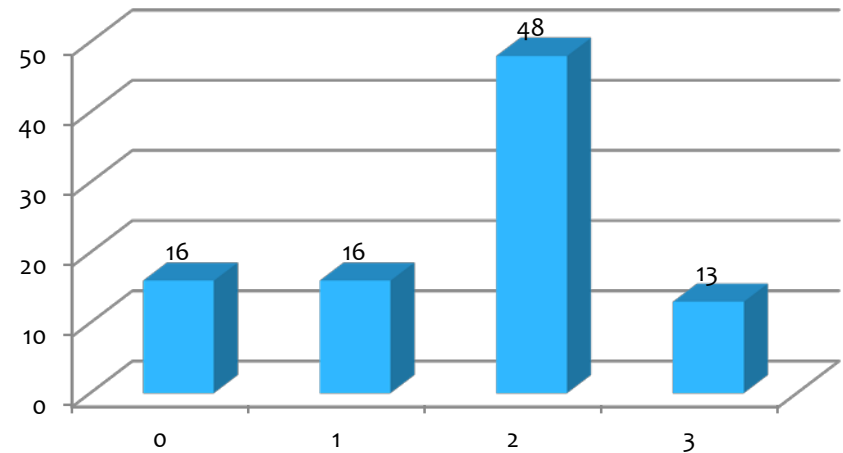
AAOMS - SS

- * stage **0**: 16/93 (17.2%)
- * stage **1**: 16/93 (17.2%)
- * stage **2**: 48/93 (51.6%)
- * stage **3**: 13/93 (14%)

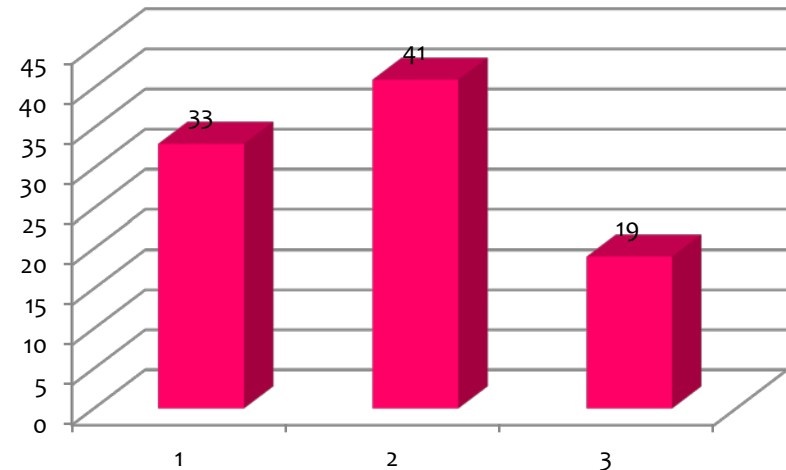
SICMF SIPMO – SS

- * stage **1**: 33/93 (35.5%)
 - * **1 a**: 10/33
 - * **1 b**: 23/33
- * stage **2**: 41/93 (44.1%)
 - * **2 a**: 8/41
 - * **2 b**: 33/41
- * stage **3**: 19/93 (20.4%)

Staging system AAOMS 2009



Staging system SICMF SIPMO 2012

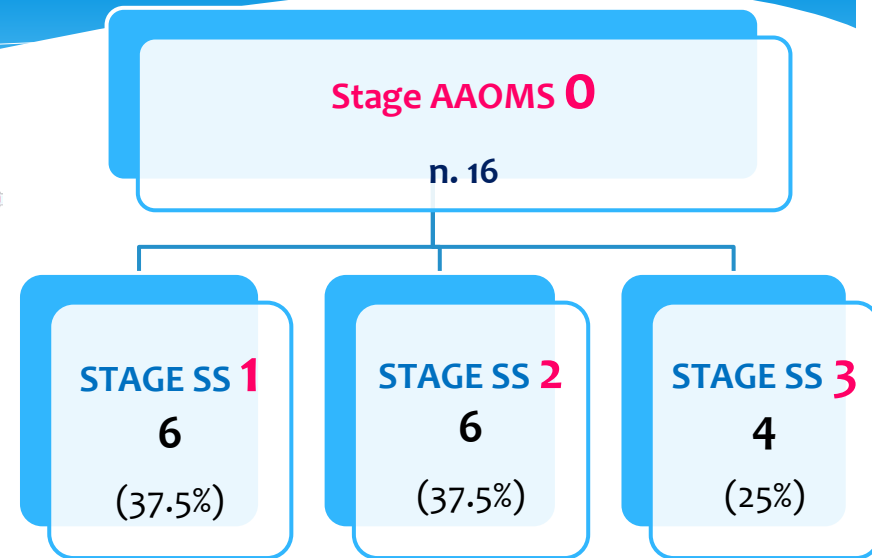


Results

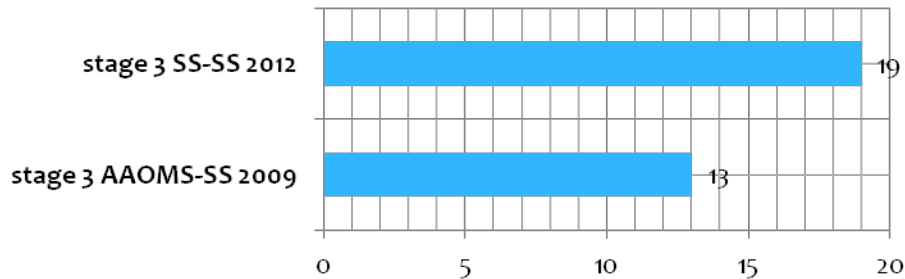
2. RE-DISTRIBUTION EX «STAGE 0»

AAOMS-SS

The 16 cases previously classified as “stage 0” according **AAOMS-SS**, were reclassified according SS-SS as following:

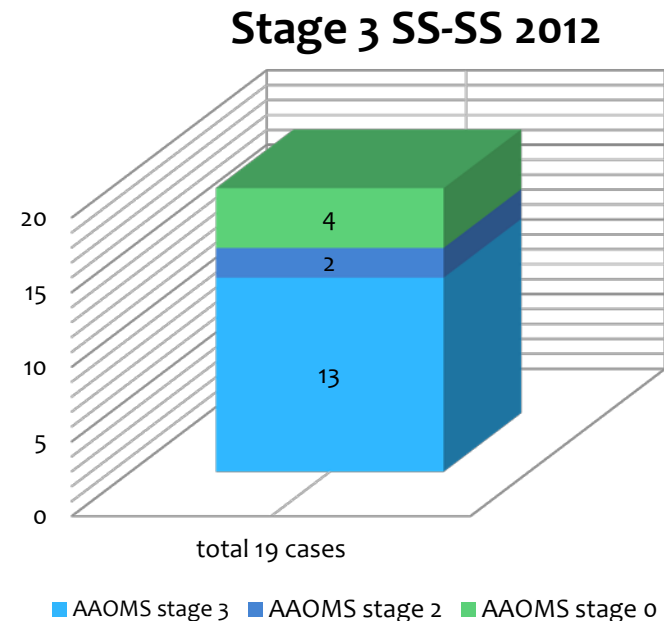


3. COMPOSITION OF «STAGE 3» SS-SS



The **new 6 cases** classified as “stage 3” according **SS-SS**, were previously classified according AAOMS-SS as following:

- * stage 0: 4/16 (25%)
- * stage 2: 2/16 (12.25%)



Case # 1

AAOMS Staging System 2009

(Clinical stadiation of BRONJ)

Stage 0

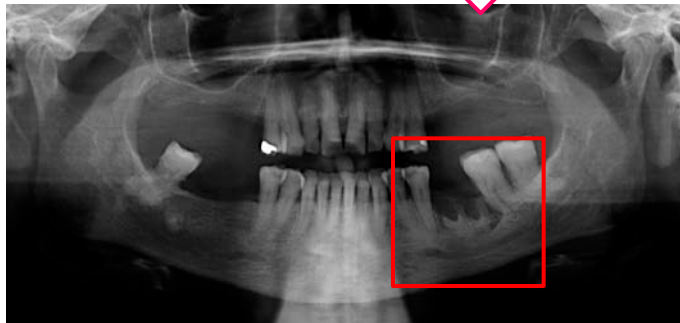
Non exposed bone variant

No clinical evidence of necrotic bone, but non-specific clinical findings, radiographic changes and symptoms

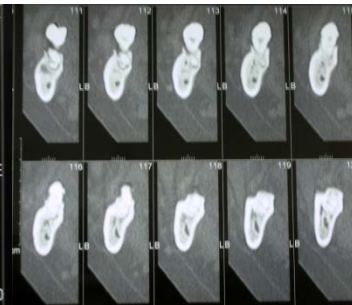
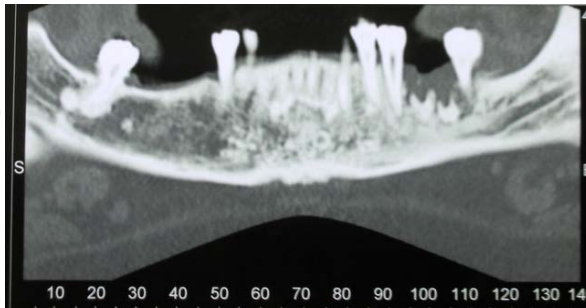
AFTER INTEGRATION WITH RADIOLOGIC SIGNS



OPT



CT



SICMF SIPMO Staging System – SS-SS

(Clinical-radiological stadiation of BRONJ)

Stage 2

Diffuse BRONJ

Clinical signs and symptoms: same as Stage 1

CT findings: increased bone density extended to the basal bone (diffuse osteosclerosis), with or without the following signs: prominence of the inferior alveolar nerve canal; periosteal reaction; sinusitis; sequestra formation; and/or oro-antral fistula

2a. Asymptomatic

STAGE 2A
(DIFFUSE BRONJ)

Case # 2

AAOMS Staging System 2009

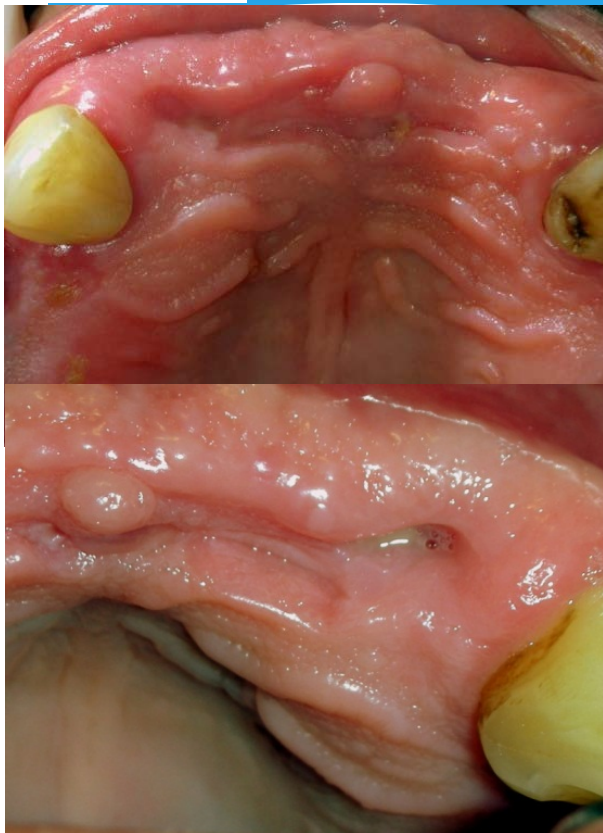
(Clinical stadiation of BRONJ)

Stage 0

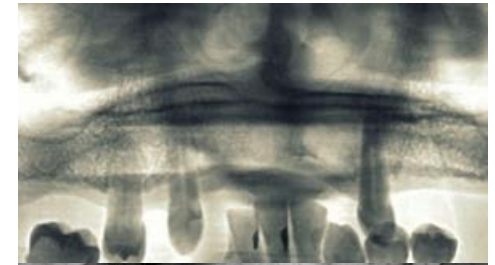
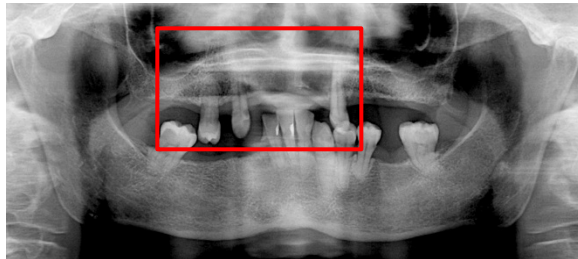
Non exposed bone variant

No clinical evidence of necrotic bone, but non-specific clinical findings, radiographic changes and symptoms

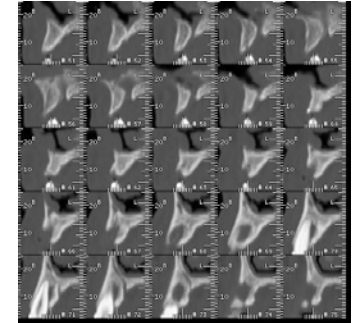
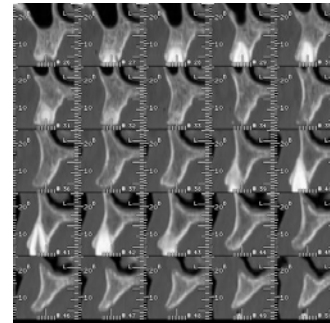
AFTER INTEGRATION WITH RADIOLOGIC SIGNS



OPT



CT



SICMF SIPMO Staging System – SS-SS

(Clinical-radiological stadiation of BRONJ)

Stage 3

Complicated BRONJ

Same as Stage 2, with one or more of the following:

Clinical signs and symptoms: extra-oral fistula; displaced mandibular stumps; nasal leakage of fluids

CT findings: osteosclerosis of adjacent bones (zygoma, hard palate); pathologic mandibular fracture; and/or osteolysis extending to the sinus floor

**STAGE 3
(COMPLICATED
BRONJ)**

Conclusions

What happens to the BRONJ patients when re-classified according to the novel SICMF-SIPMO recommendations?

OUR EXPERIENCE

... and in multicentric study?

1. UNDERESTIMATION OF NON-EXPOSED DIFFUSE / COMPLICATED BRONJs WITH AAOMS-SS

After the re-classification, a large quote of BRONJ cases (>60%) previously underestimated as “stage 0”, was properly diagnosed as diffuse-complicated cases.

2. SS-SS ANTICIPATE BRONJ DIAGNOSIS AND THERAPY

According to our experience, the updated staging system provides important clinical benefits, such as **anticipating BRONJ diagnosis**, performing **therapies earlier and adequate to the correct staging**, in order to increase treatment effectiveness.

Otto S, Abu-Id MH, Fedele S et al. Osteoporosis and bisphosphonates-related osteonecrosis of the jaw: not just a sporadic coincidence-a multi-centre study. J Craniomaxillofac Surg. 2011 Jun;39(4):272-7

Osteonecrosis of the jaws in patients assuming oral bisphosphonates for osteoporosis: a retrospective multi-hospital-based study of 87 Italian cases. Di Fede O, Fusco V, Matranga D, Solazzo L, Gabriele M, Gaeta GM, Favia G, Sprini D, Peluso F, Colella G, Vescovi P, Campisi G.



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grazie



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