



CONGRESO
DE LA
SOCIEDAD CHILENA DE OSTEOLÓGIA
Y METABOLISMO MINERAL - SCHOMM

Osteonecrosis mandibular: evidencia

Dr. Luis A. Córdova



Disclosure: sin conflictos de interés con la industria

O: Compartir evidencia sobre ONJ Relacionada con Medicamentos en 25'

1. Contexto
1. Por qué los maxilares?
1. Desafíos para la terapia de ONJ

ONJ: hueso max/mand. expuesto crónicamente que forma secuestro(s)

1. ON por infección ósea
(osteomielitis)



1. ON inducida por RT
(ORN)

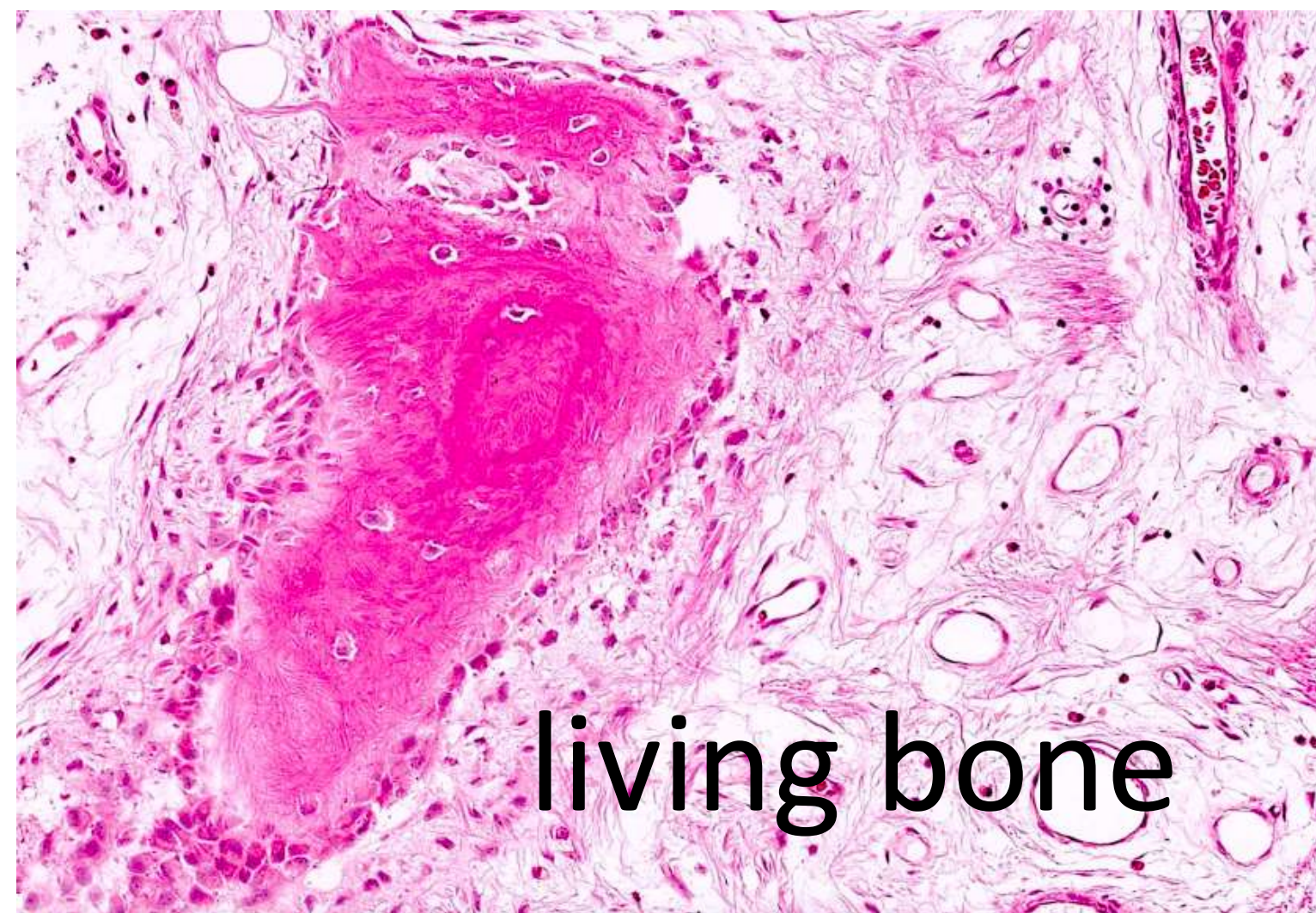


1. ONJ relacionada a medicamentos
(MRONJ)



Confusión diagnóstica!

Cambios comunes en ON:
ausencia de células óseas, lagunas vacías, cambios en matriz ósea, y
espacios medulares acelulares



living bone



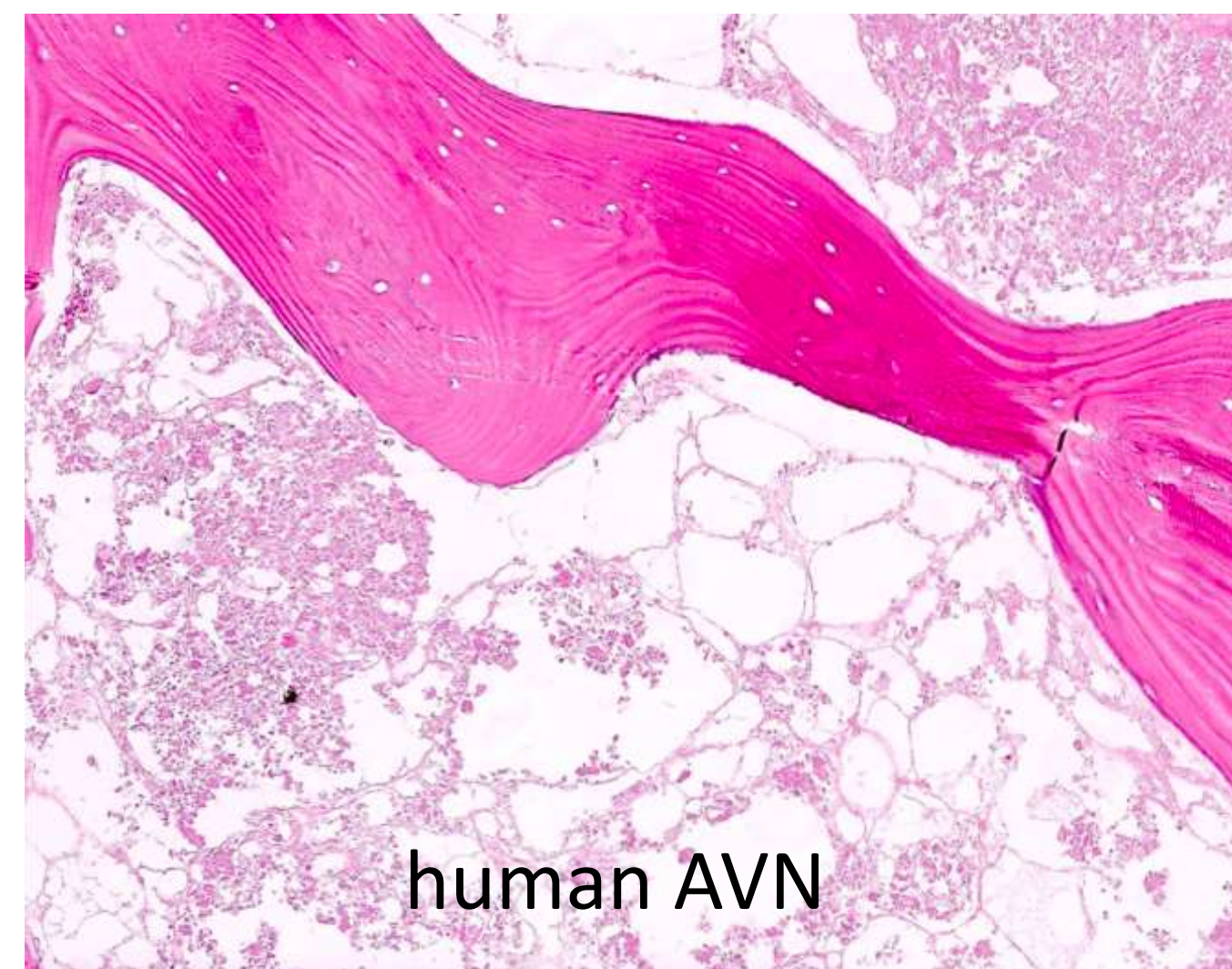
Secuestro mouse BRONJ-like



Submucosa mouse BRONJ-like



dead bone



human AVN



mouse Tibia – 100 Gy

(n=119) 26% Aredia, 40.3% Zometa, 30.2% Aredia then Zometa, and 3 (2.5%) Fosamax.

Bisphosphonate-Induced Exposed Bone (Osteonecrosis/Osteopetrosis) of the Jaws: Risk Factors, Recognition, Prevention, and Treatment

Robert E. Marx, DDS, Yoh Sawatari, DDS,†*

Michel Fortin, DMD, PhD,‡ and

Vishtasb Broumand, DMD, MD§

(n=119) 97.5% cancer patients
2.5% osteoporotic patients

J Oral Maxillofac Surg
63:1567–1575, 2005

Definición (2022 AAOMS) de MRONJ

1. Exposición ósea
MF > 8 semanas
(*)

1. Sin historia de RT
en C-C

1. Bajo tratamiento
con AR o
antiangiogénico



Incidencia MRONJ (n= 2.8MM): 0.06% OP y 1.47% cancer

Table 2. PREVALENCE AND INCIDENCE RATE OF DEVELOPING MEDICATION-RELATED OSTEONECROSIS OF THE JAW

	No. of Antiresorptive Agent Users	Median Observational mo (IQR)	MRONJ (Definition 1)			MRONJ With Surgical Treatment (Definition 2)			MRONJ (Definition 3)		
			No. of Events	Prevalence (%)	Incidence Rate (per 100,000 Person-yr)	No. of Events	Prevalence (%)	Incidence Rate (per 100,000 Person-yr)	No. of Events	Prevalence (%)	Incidence Rate (per 100,000 Person-yr)
All patients	2,819,310		3,877	0.138	1,254.6	2,144	0.076	29.8	9,963	0.353	138.9
Patients with osteoporosis	2,664,104	31.0 (20-43)	1,603	0.060	22.9	1,144	0.043	16.3	5,725	0.215	81.9
Patients with cancer	155,206	9.0 (3.0-22.0)	2,274	1.465	1,232	1,000	0.644	538	4,238	2.731	2,332

Miho Ishimaru, JOMS 2022

Los pacientes oncológicos y osteoporóticos tienen riesgo diferencial de desarrollar ONJ

Osteoporosis International (2024) 35:1677–1678

Oral treatment	Osteoporosis patients	Oncology patients
Tooth extraction	Low risk (Using perioperative considerations)	High risk
Implant surgery	Low risk (Oral antiresorptive therapy) High risk (Intravenous antiresorptive therapy)	High risk
Soft tissue periodontal surgery	Low risk (Protective factor for ARONJ)	Questionable risk
Non-surgical periodontal treatment for periodontitis and/or peri-implantitis	High risk (Risk associated with periodontal/peri-implant infection)	High risk
Endodontic treatment	Low risk (Long-term oral antiresorptive treatment)	Questionable risk
Apical surgery	Questionable risk	Questionable risk

Etapificación clínica

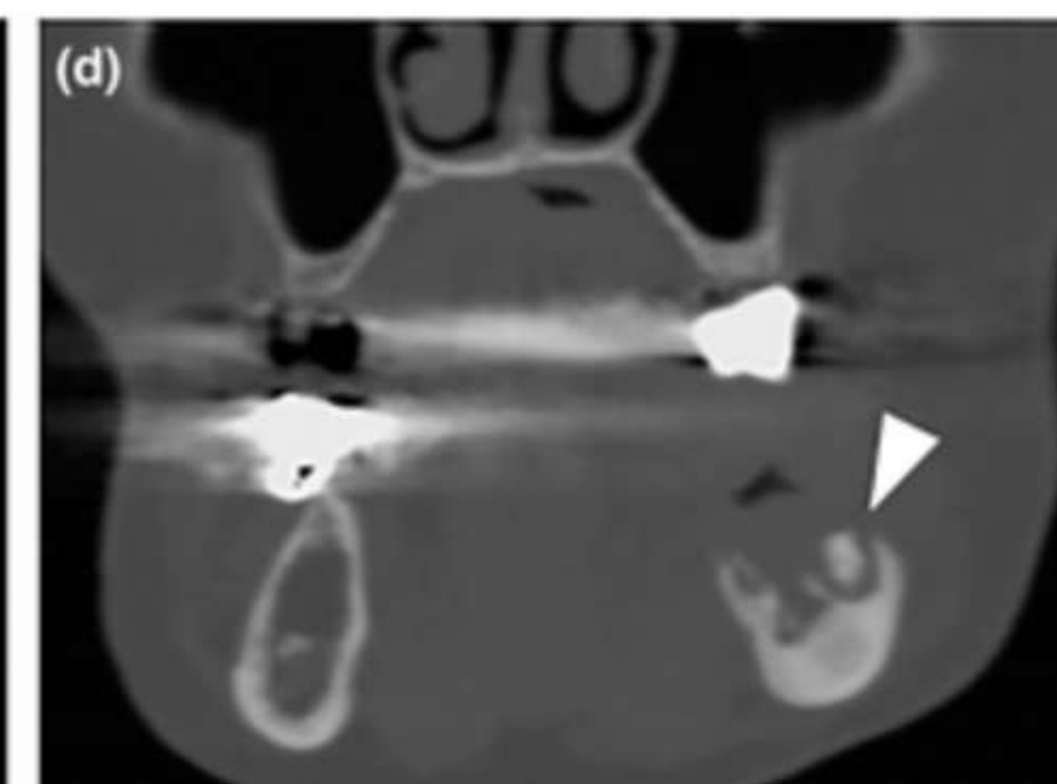
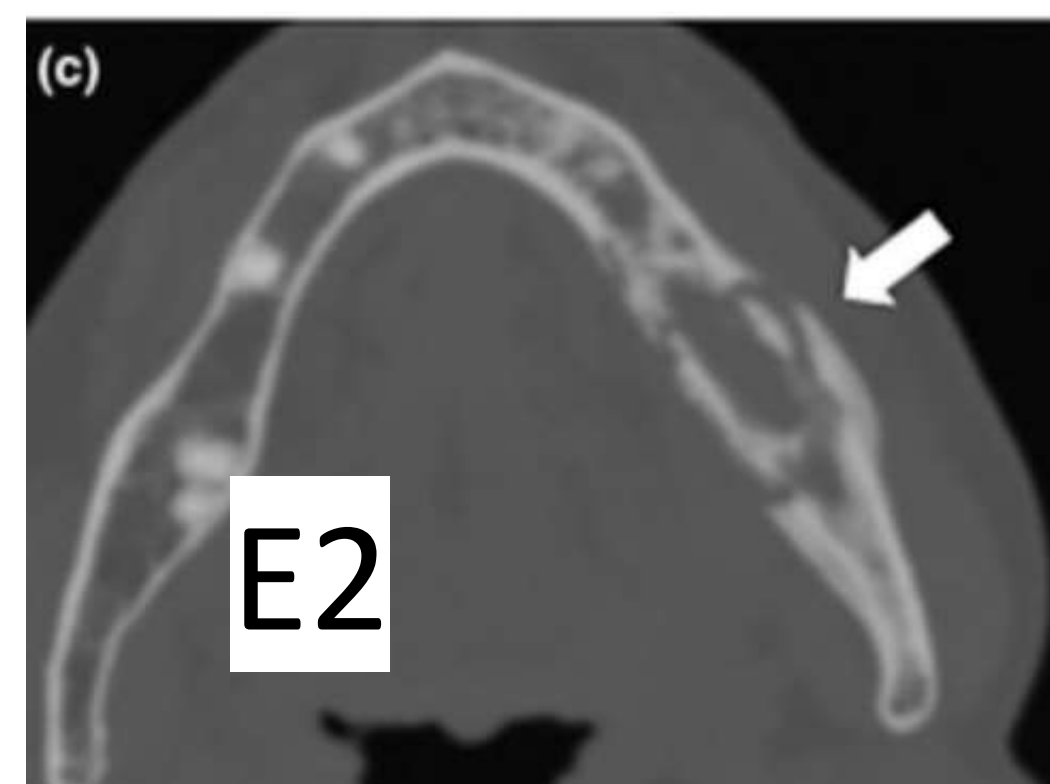
En riesgo

Etapa 0

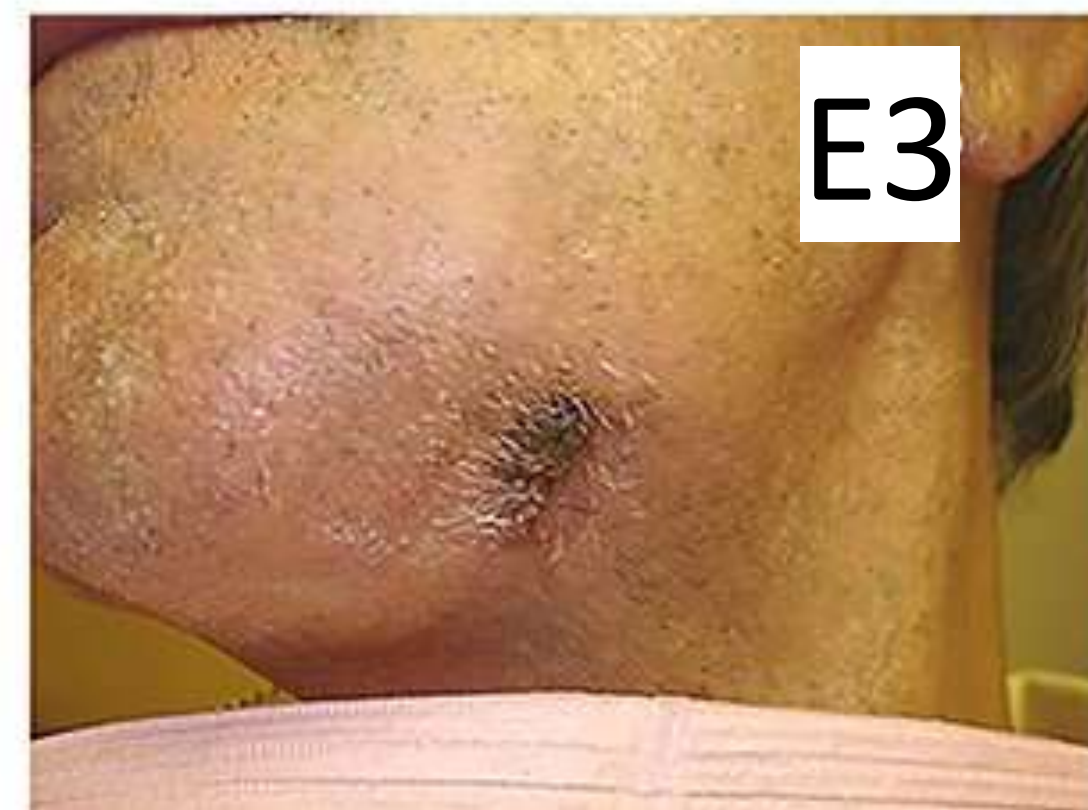
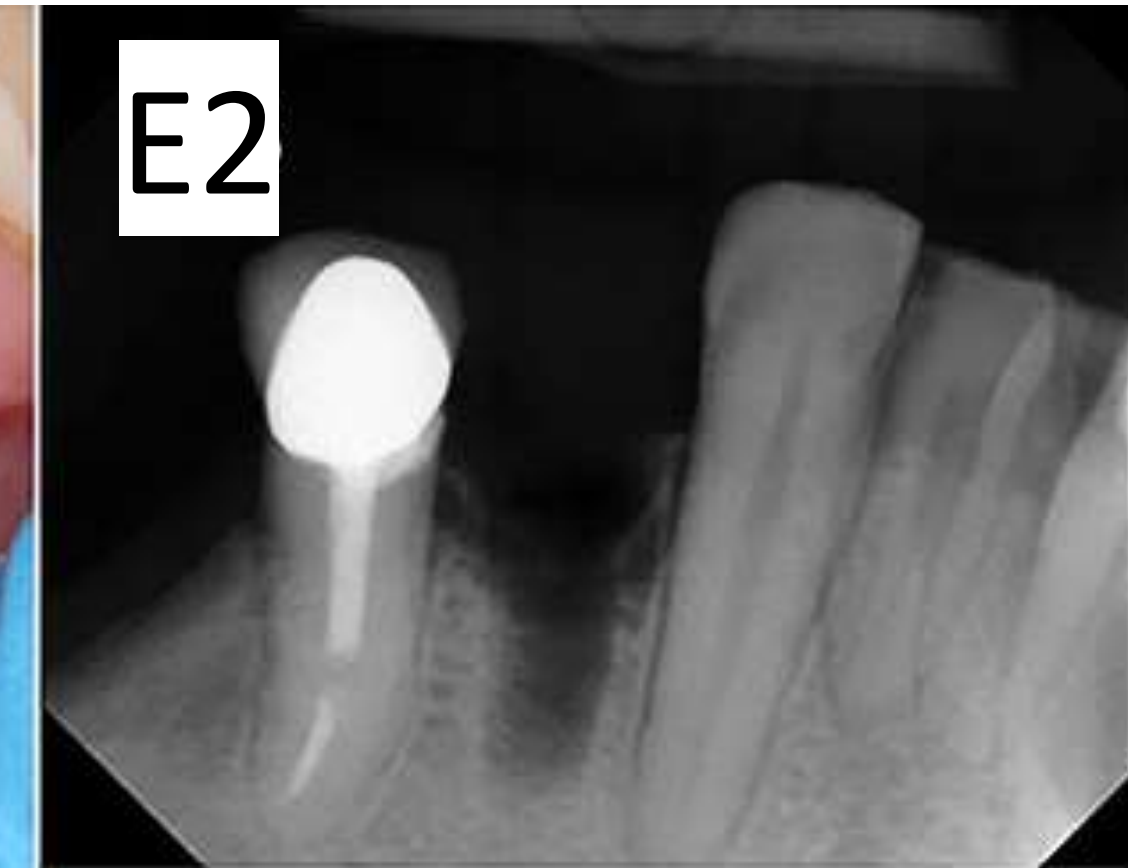
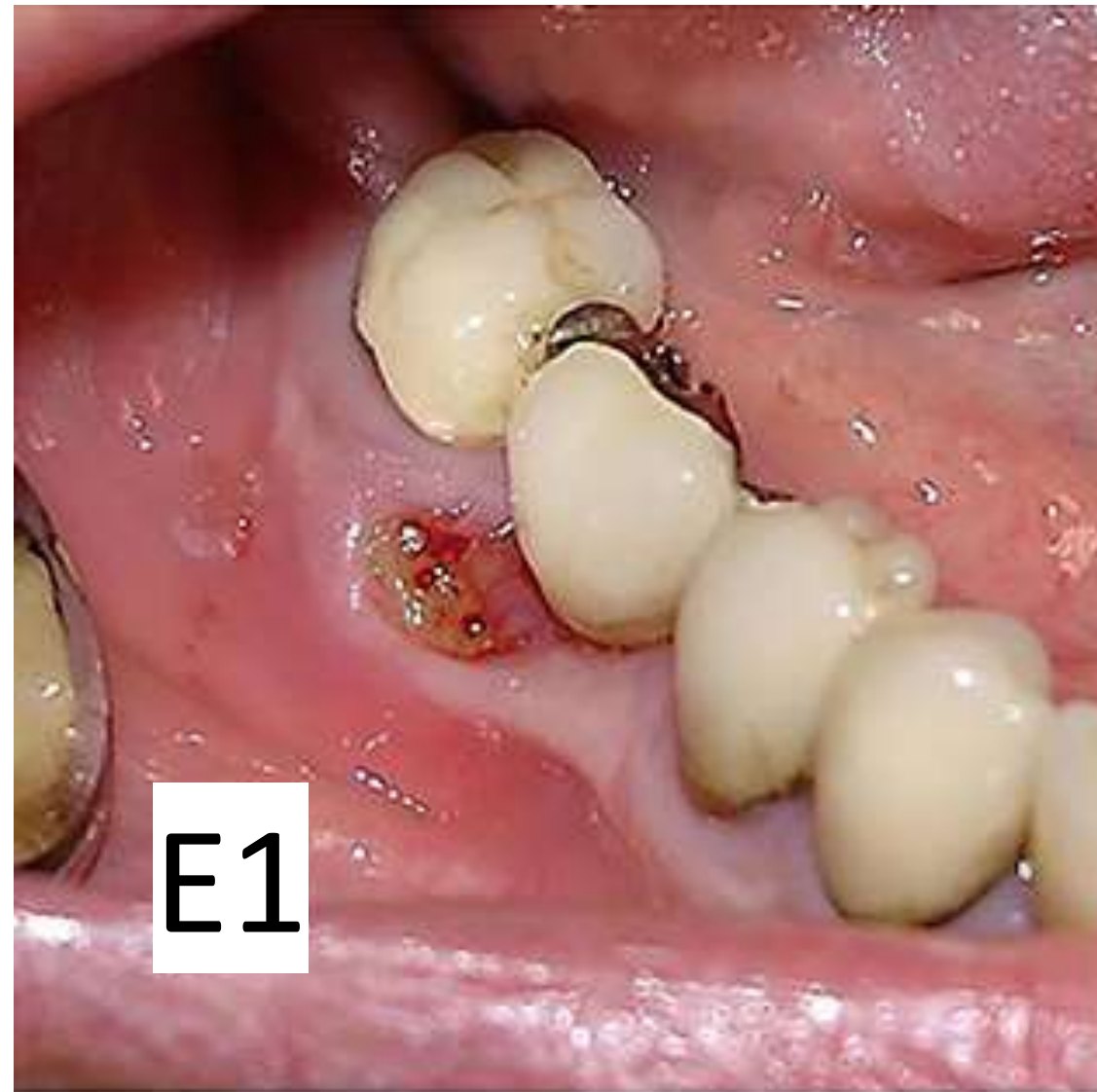
Etapa 1

Etapa 2

Etapa 3



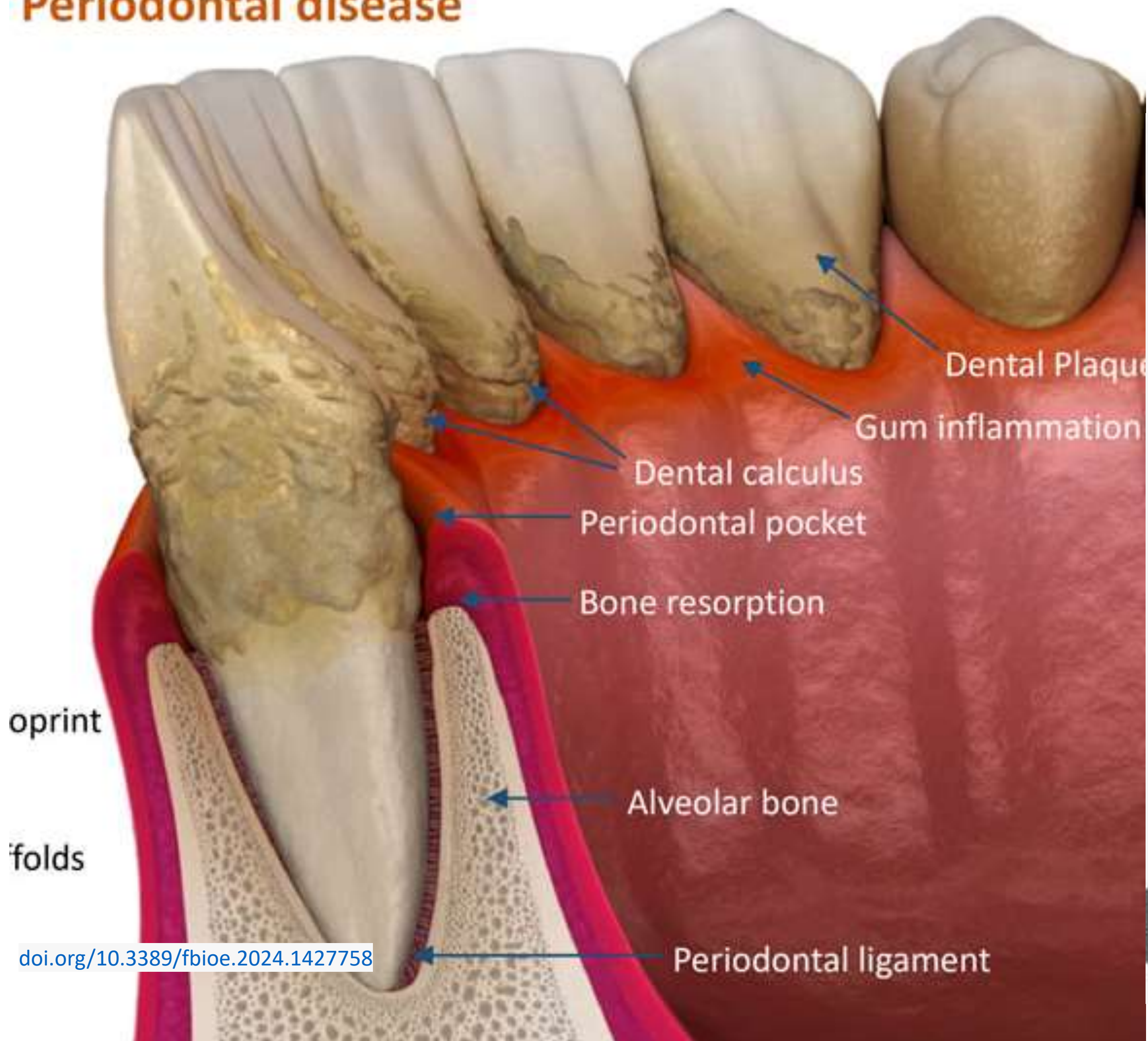
etapificación es operador-dependiente y muy subjetiva (controversial en etapas iniciales)



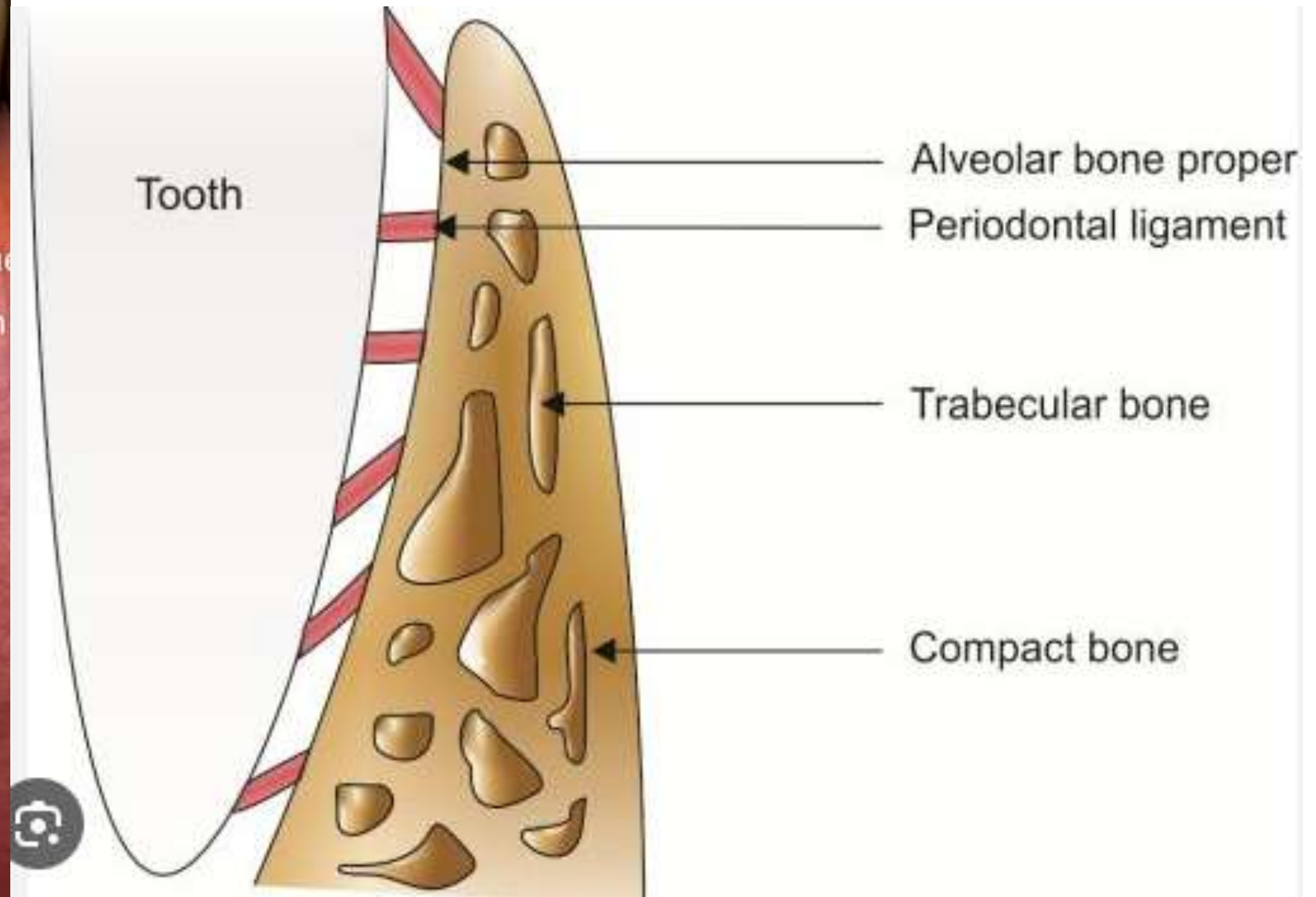
2.- Por qué ON en los maxilares?

a) **Periodonto:** Sitio único de interacción inmune entre *patógenos* y hueso alveolar (x32!)

Periodontal disease

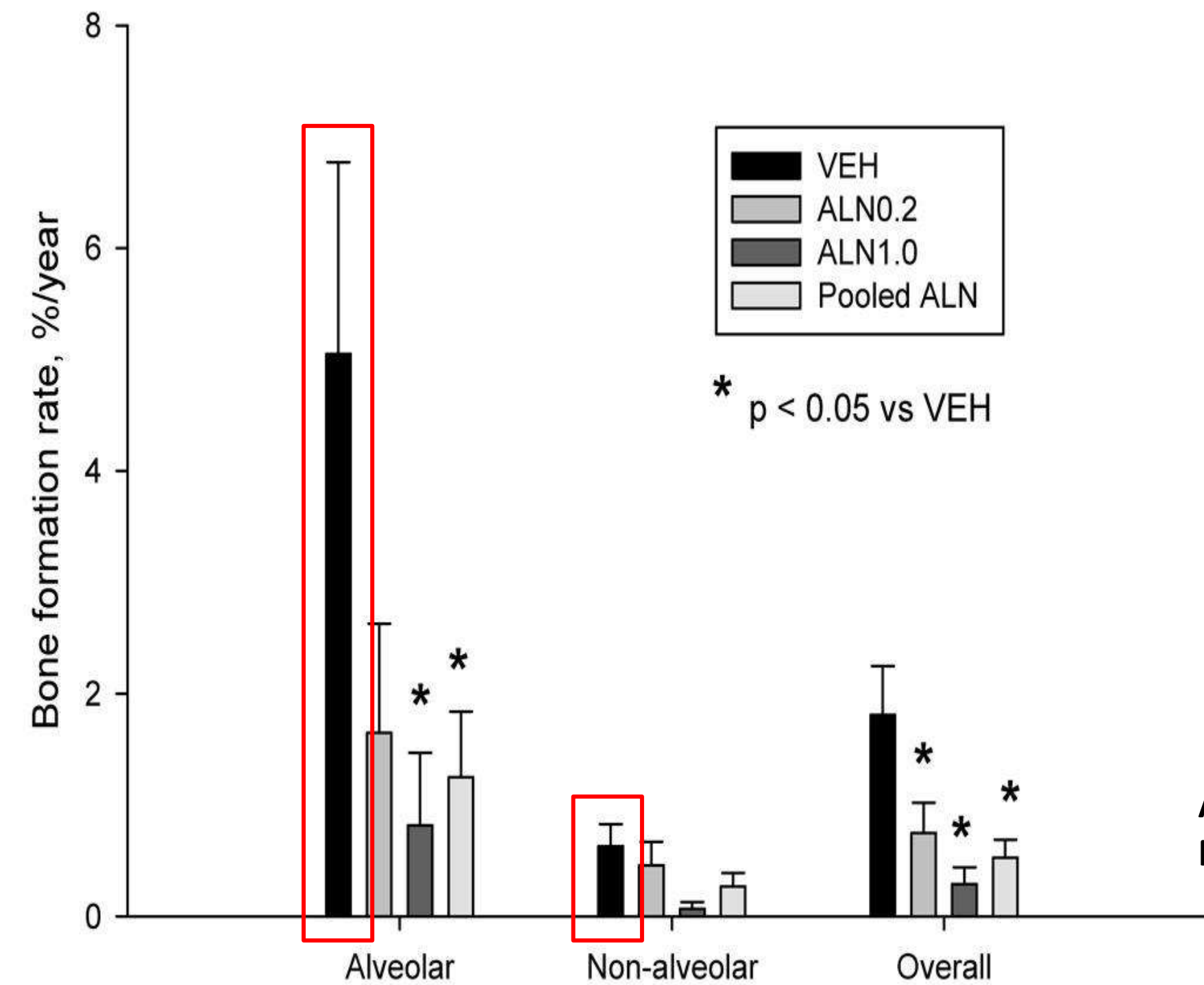
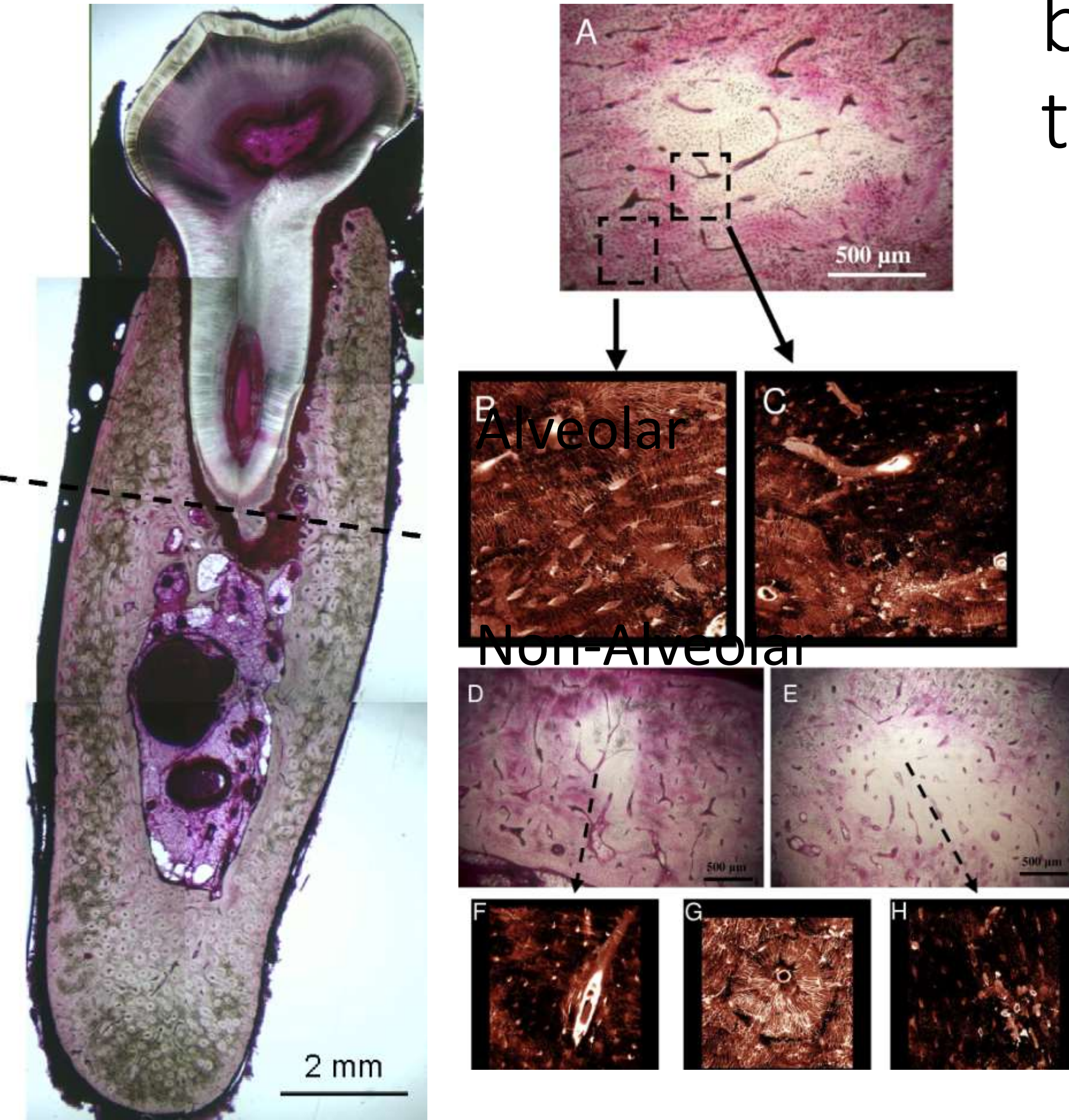


(Muy) alta tasa de recambio óseo alveolar



Bacterias orales

b) ALN reduces alveolar bone turnover inducing ONJ *in vivo*



Allen MR et al, J. Oral
Maxillofac. Surg 2008

b) Ac. Zoledrónico altera el equilibrio OC/OB alveolar *in vivo* -

Córdova LA et al, 2016 JCMFS

L.A. Córdova et al. / Journal of Cranio-Maxillo-Facial Surgery 44 (2016) 1387–1394

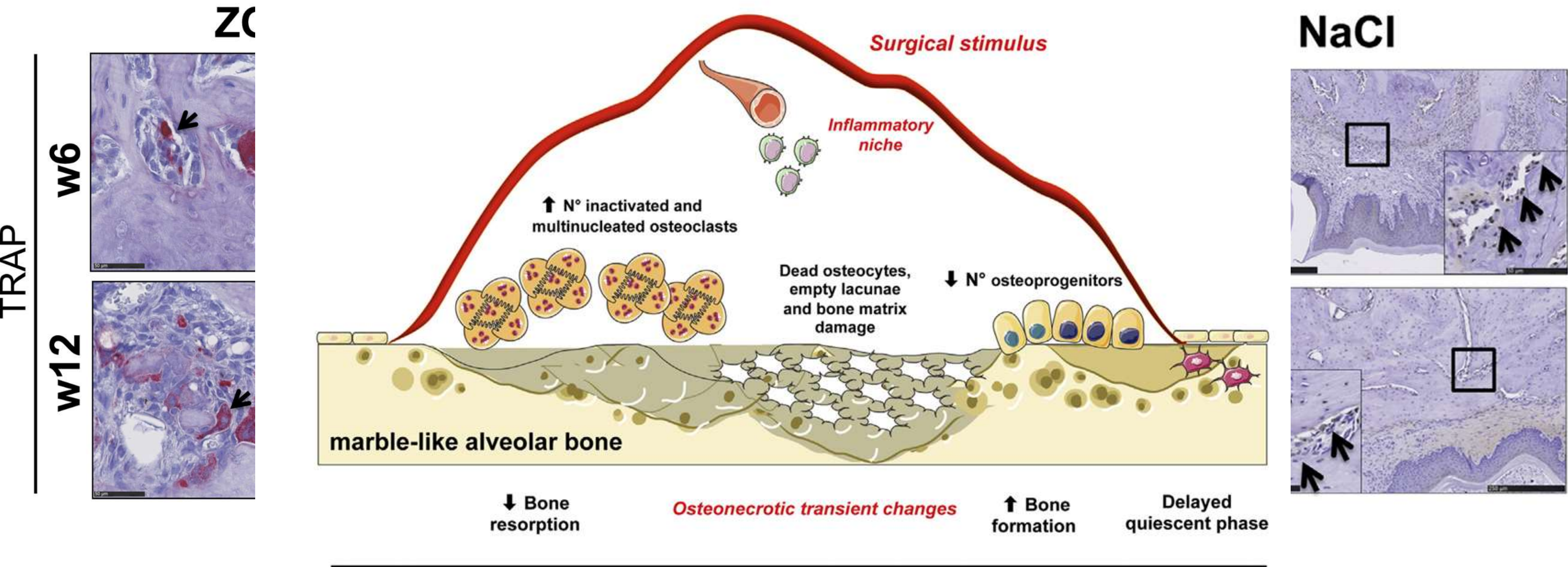
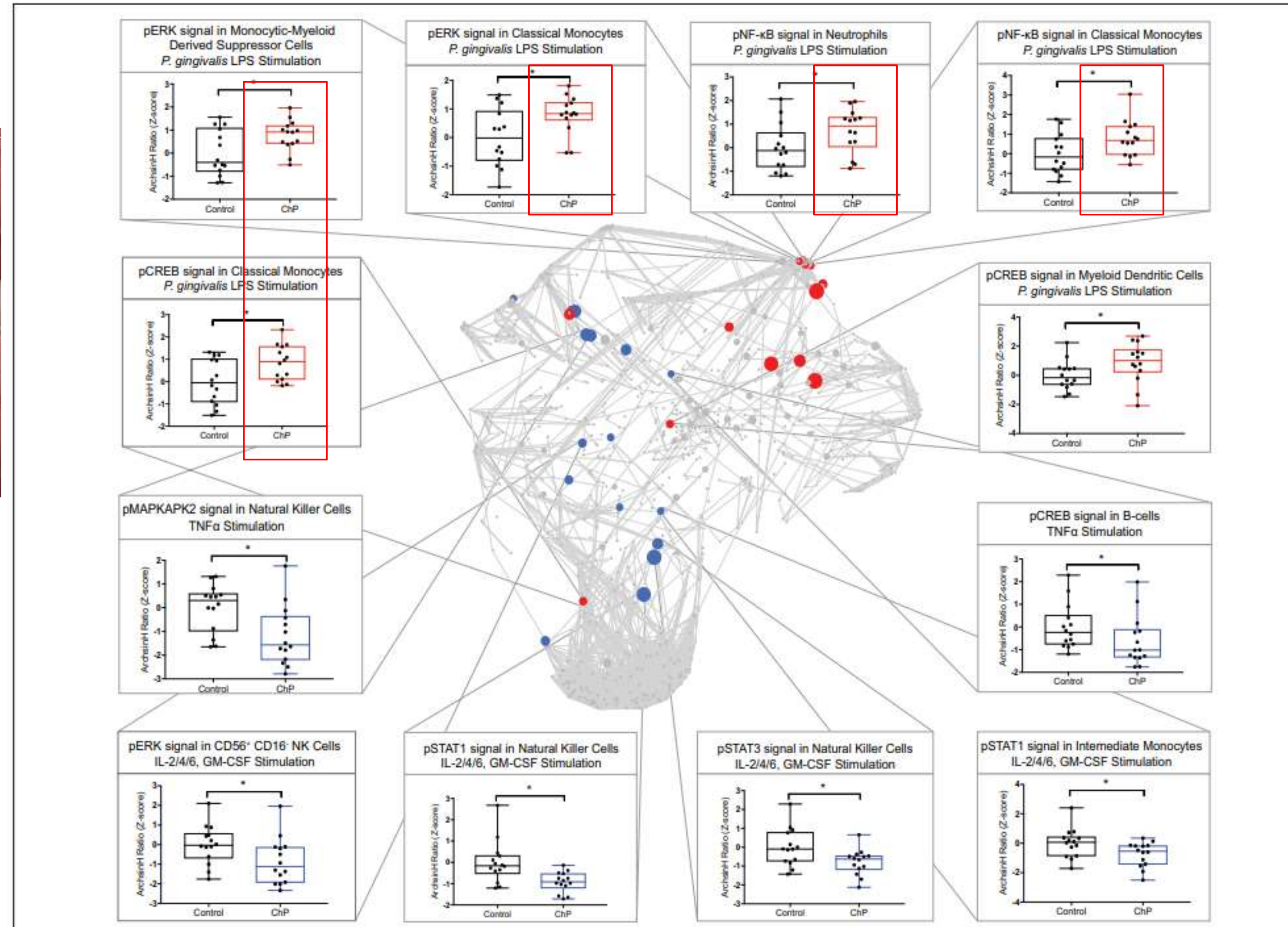


Fig. 5. Scheme representing the disruption of cell components of alveolar BMUs induced by zoledronic acid.

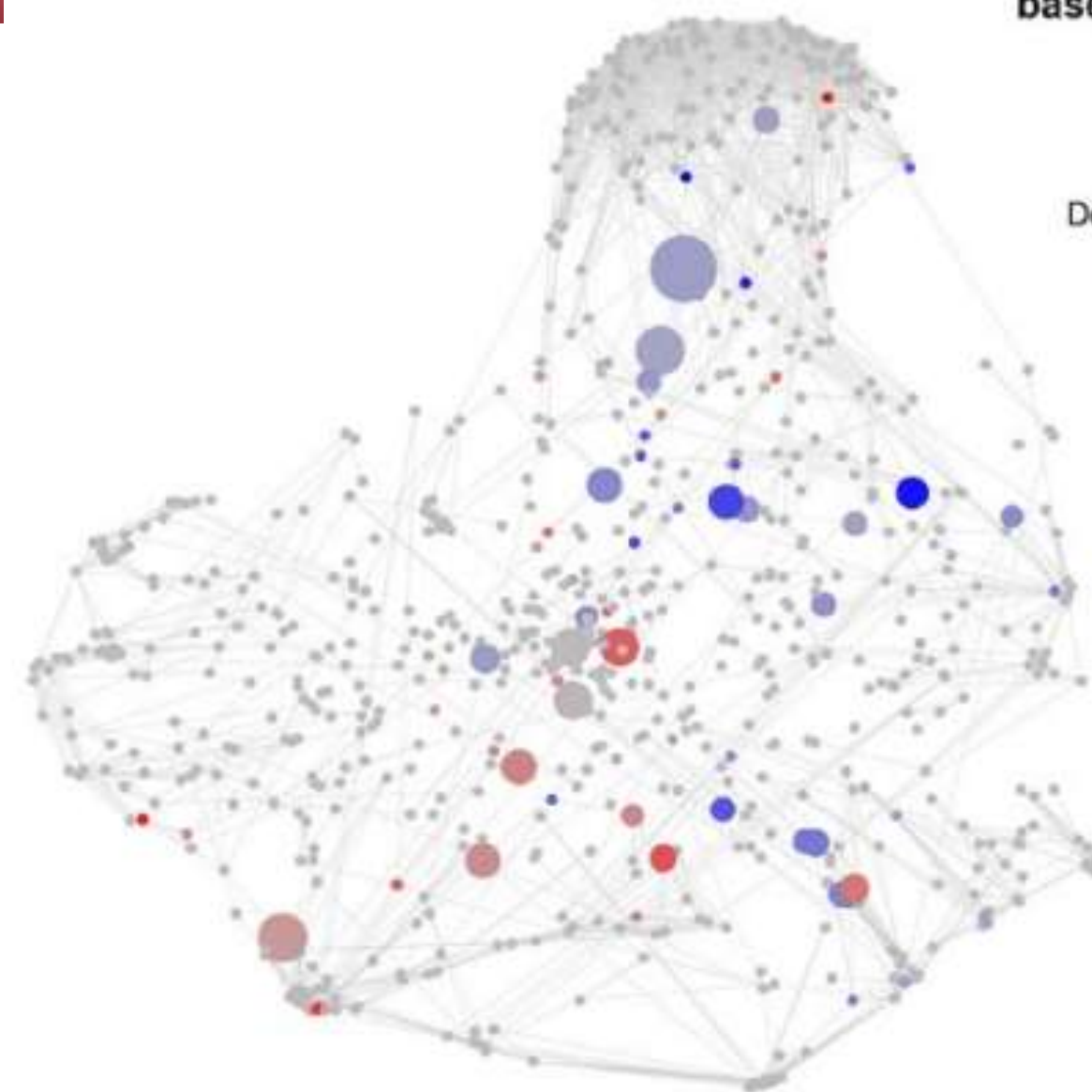
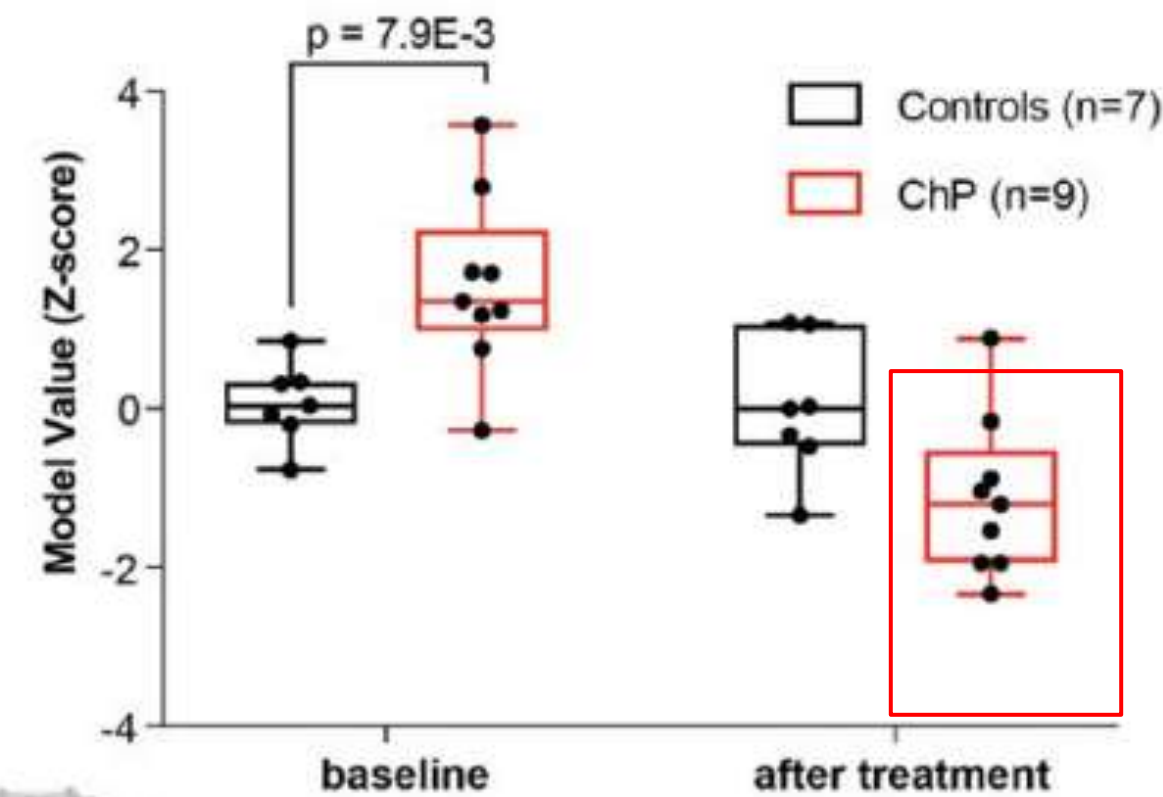
c) Periodontitis se relaciona con **elevación de señales inflamatorias sistémicas** (monocito/neutrófilos) (Gaudilliere et al, JDR 2019)



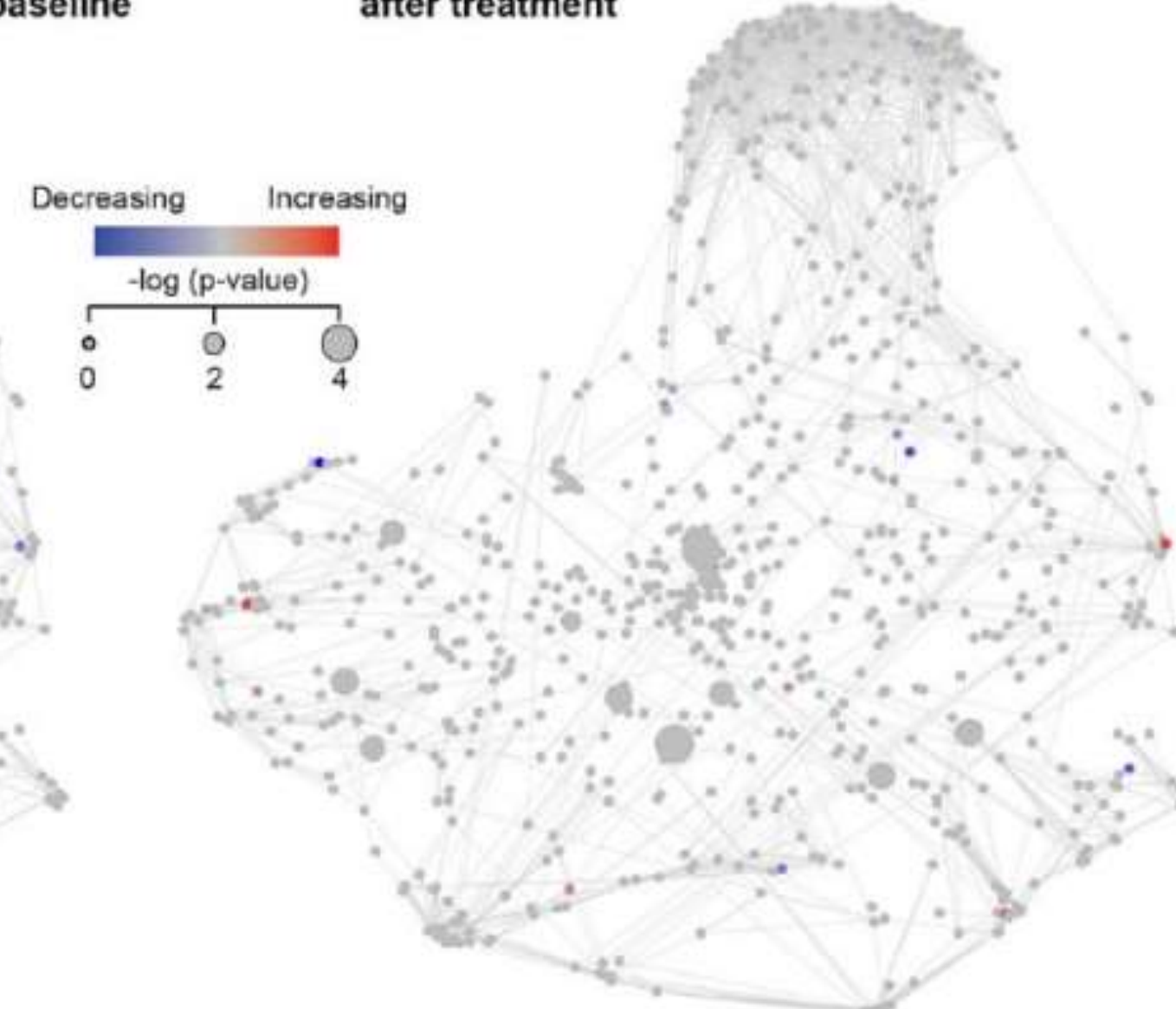
El tratamiento periodontal disminuye la expresión de señales inflamatorias sistémicas (Gaudilliere et al, JDR 2019)



A. csEN model values before and after ChP treatment

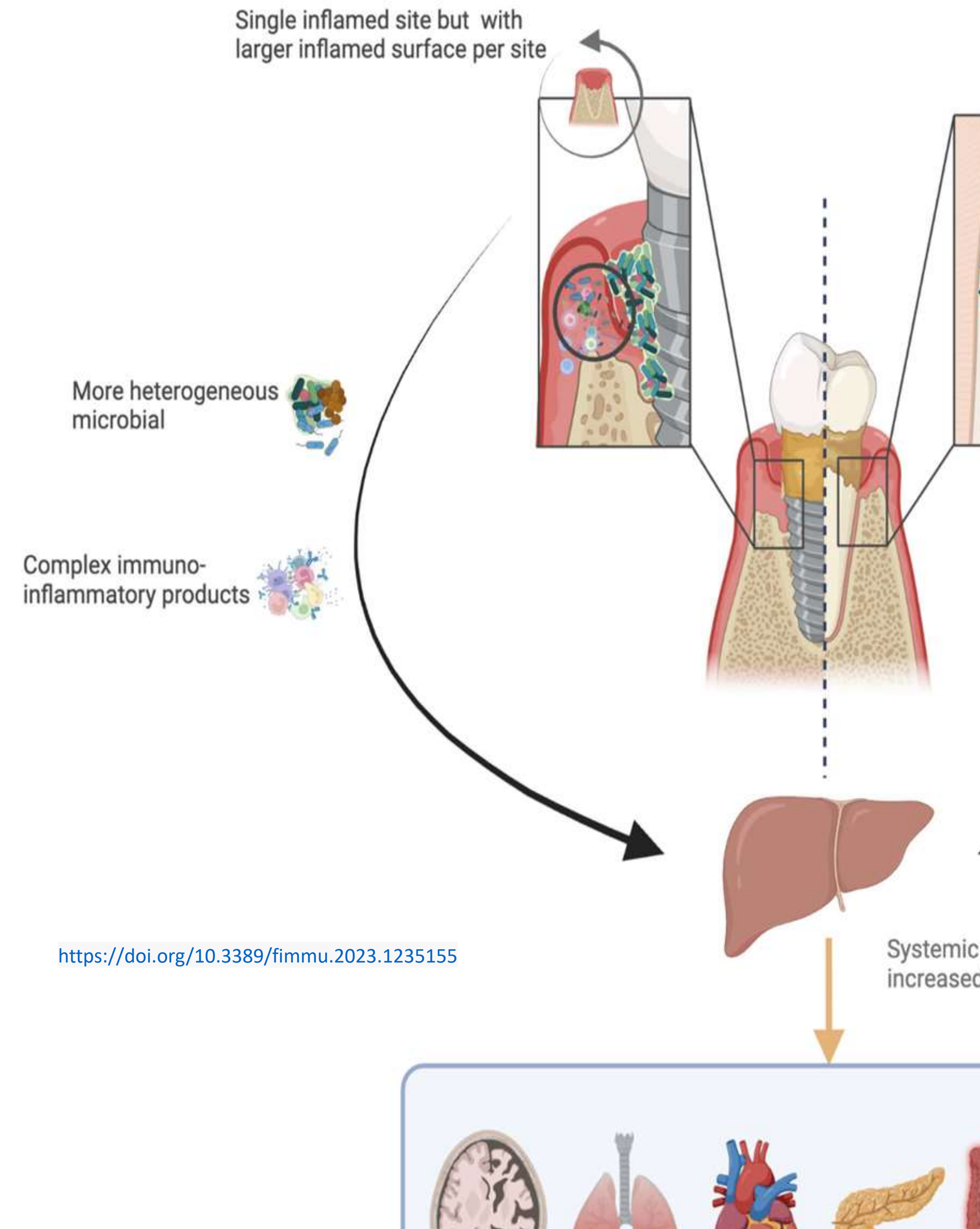


B. csEN model features at baseline



C. csEN model features after ChP treatment

c) **Inmunidad** local/sistémica de la peri-implantitis?



d) La invasión de tejidos orales es muy frecuente debido la alta prevalencia de enfermedades bucales



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Oral health data portal



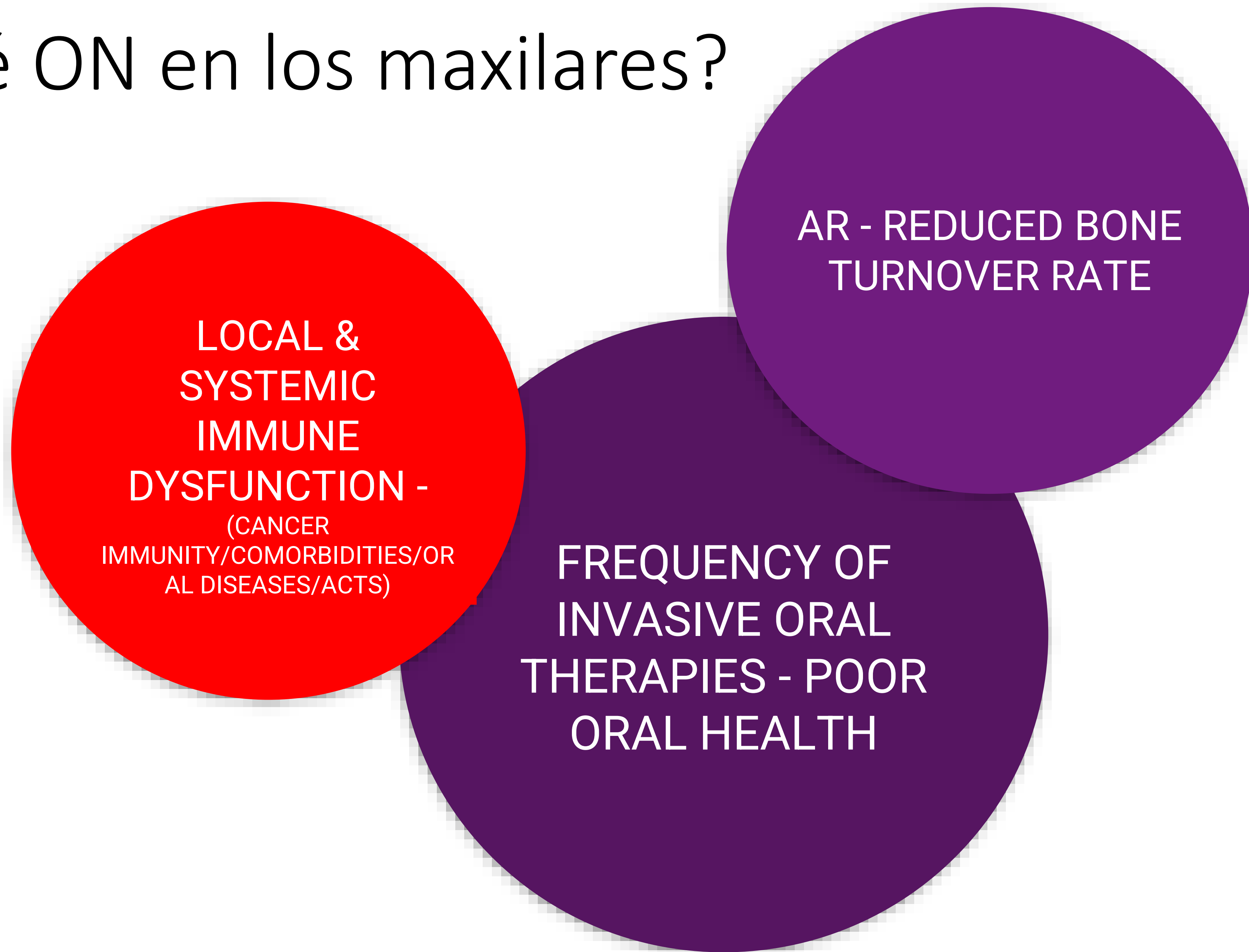
© WHO / Anne Sturm Guerrand

The World Health Assembly approved a Resolution on oral health in 2021, which affirms that oral health should be firmly embedded within the NCD agenda and that oral health-care interventions should be included in universal health coverage programs. This resolution on oral health requested WHO to translate the Global Strategy on Oral Health A75/10 Add.1 into an action plan for public oral health by 2023, including a framework for tracking progress with clear measurable targets of oral health to be achieved by 2030. WHO's Global oral health status report (GOHSR) provides the first-ever comprehensive picture of oral disease burden and highlights challenges and opportunities to accelerate progress towards universal coverage for oral health. This includes introducing oral health profiles of countries based on the latest available data from the Global Burden of Disease (GBD) project, the International Agency for Research on Cancer (IARC) and global WHO surveys. The GOHSR is part of WHO's series of data reports and an important milestone in the larger process of mobilizing political action and resources for oral health. Nearly 20 years after the publication of The World Oral Health Report 2003 and in alignment with the Resolution, the GOHSR will serve as a reference for policy-makers and provide orientation for a wide range of stakeholders across different sectors; and guide the advocacy process towards better prioritization of oral health in global, regional and national contexts. The data in this oral health data portal is from country profiles of the GOHSR.

Key figures

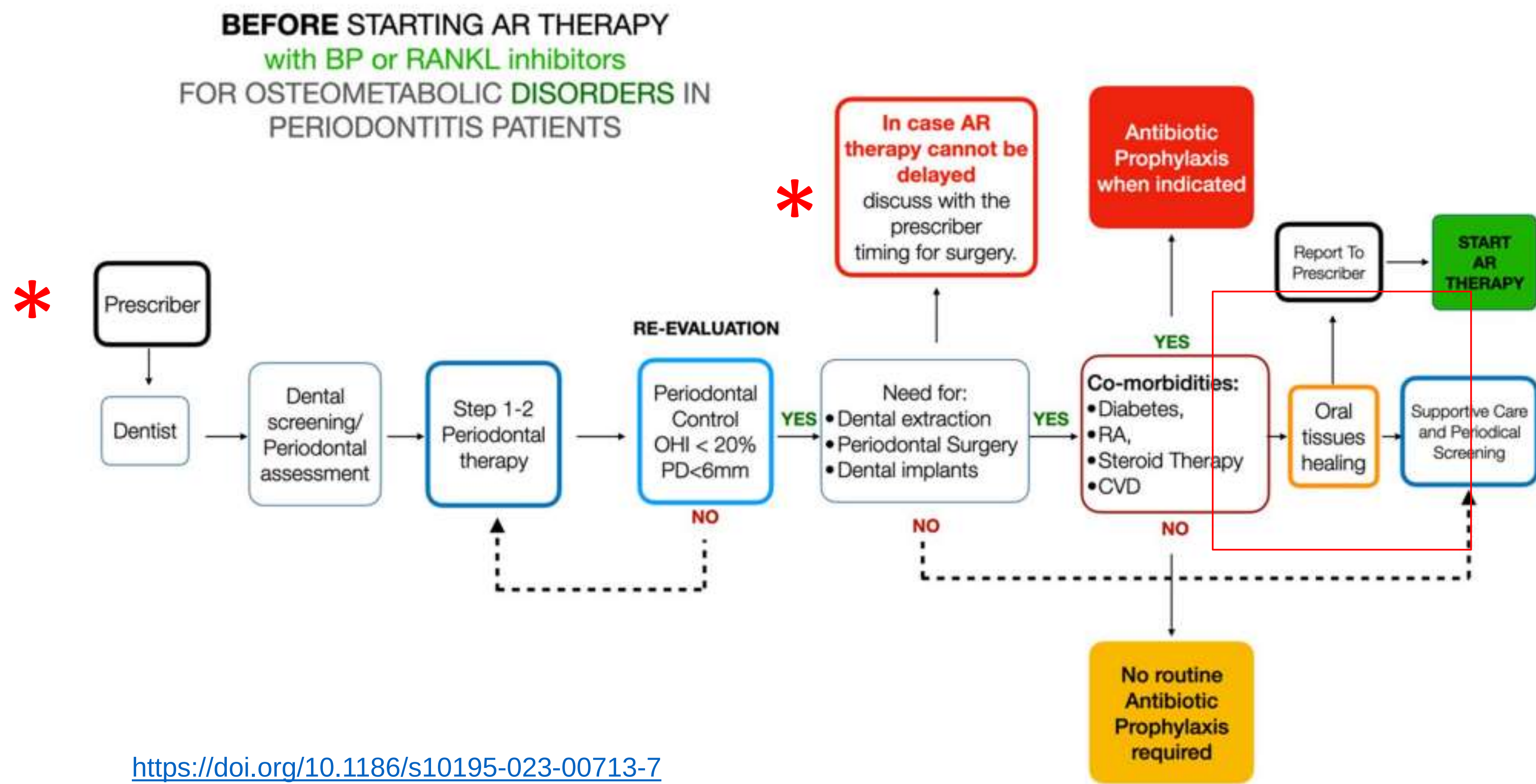
Oral disease burden 3.5 billion people globally are affected by oral diseases in 2019	Oral health inequality 3 out of 4 people affected living in middle-income countries in 2019	High economic burden of oral diseases > 380 billion US\$ is spent for the main oral diseases in 2019
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Por qué ON en los maxilares?

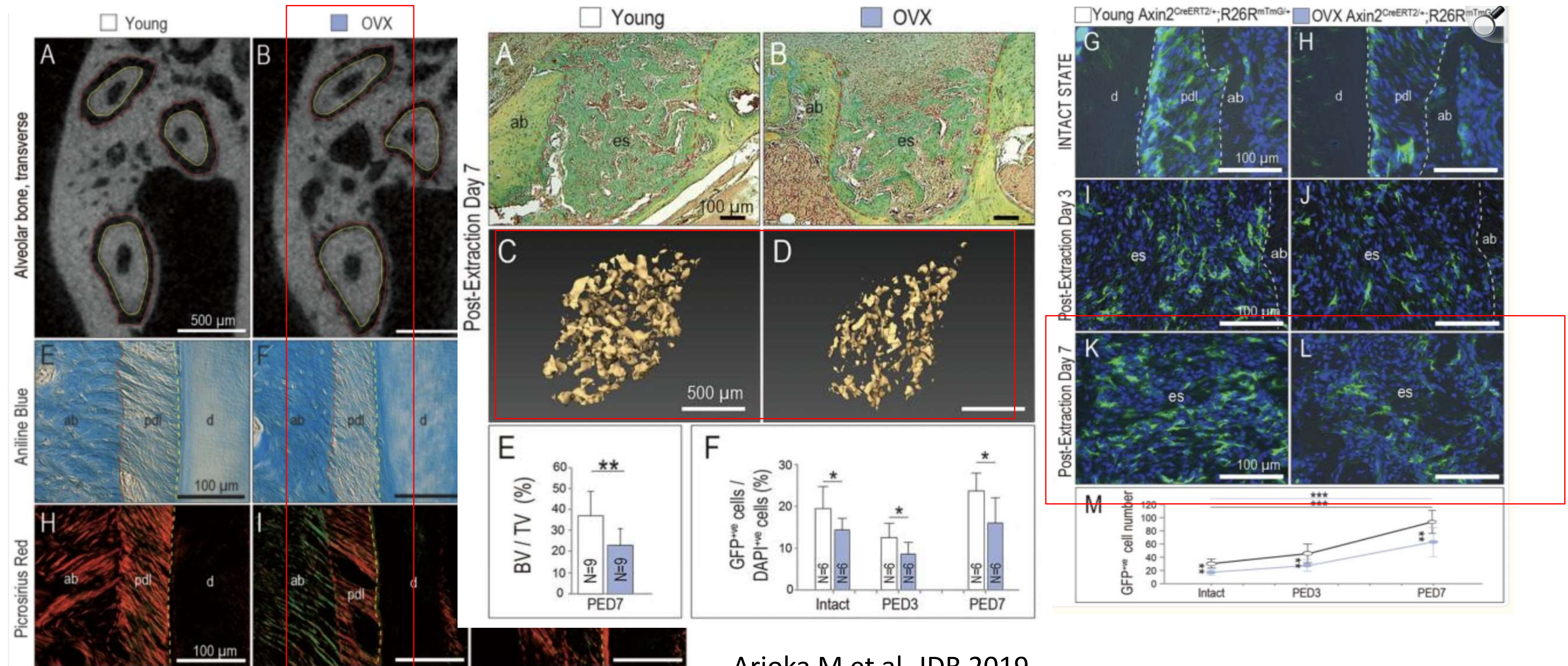


3.- Desafíos para la terapia de ONJ

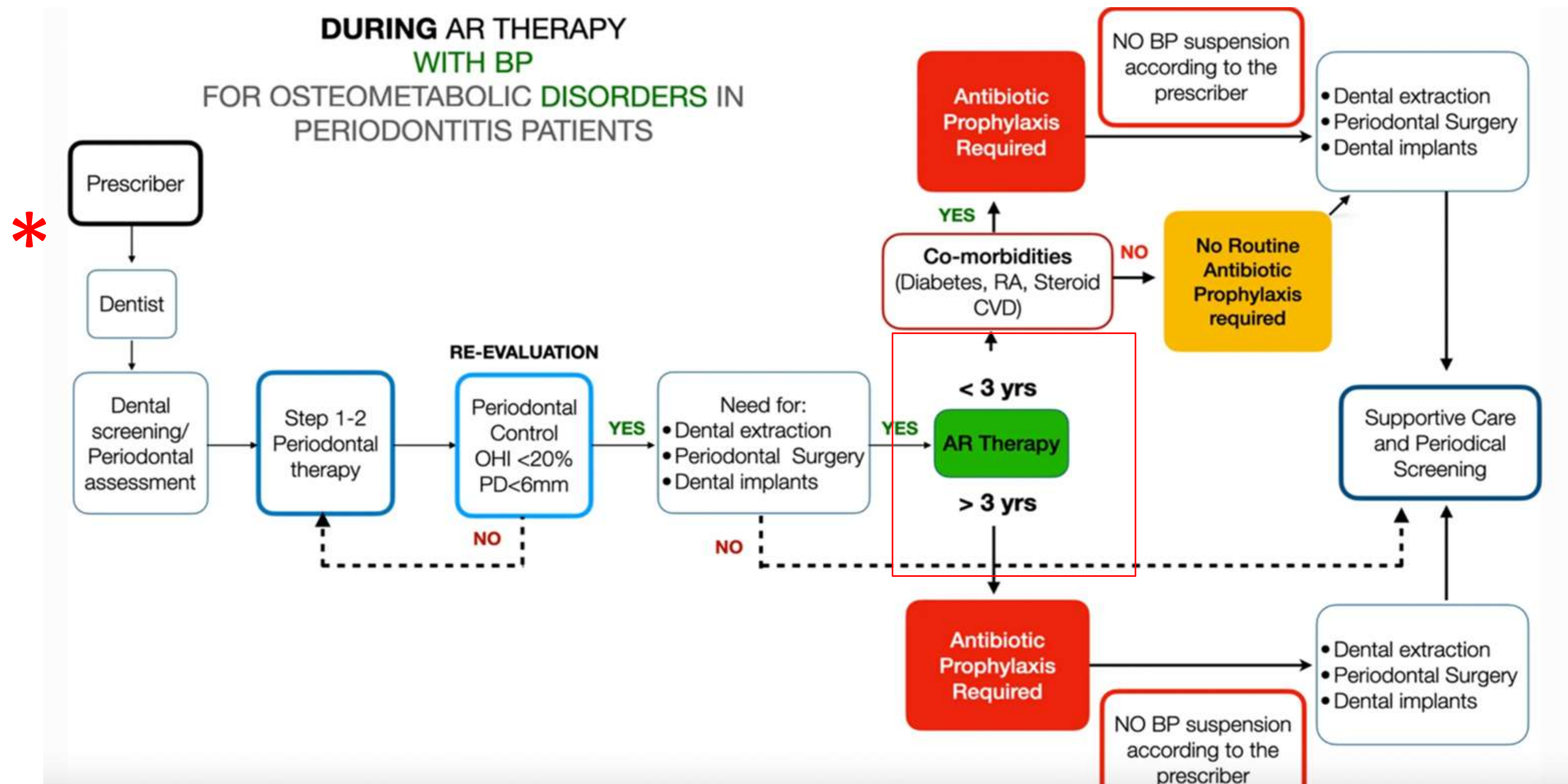
Antes del inicio de terapia con AR - la importancia de los 2 meses para la cicatrización de un alvéolo post extracción osteoporótico



OP induce cambios en periodonto que ralentizan la cicatrización del alvéolo post extracción



Durante la terapia con AR: paciente en riesgo de MRONJ. La ventana de los 2-3 años



El protocolo preventivo PENTOXIFILINA-TOCOFEROL pareciera reducir la severidad de MRONJ (en investigación)

Supportive Care in Cancer (2023) 31:462
<https://doi.org/10.1007/s00520-023-07906-0>

RESEARCH



Pentoxifylline and tocopherol as prophylaxis for osteonecrosis of the jaw due to bone-modifying agents in patients with cancer submitted to tooth extraction: a case series

Jackeline Mayara Inácio Magalhães¹ · Fabiana Moura da Motta Silveira¹ · Luciana Silva Regueira¹ · Douglas Felipe de Lima e Silva¹ · Samuel Rodrigo de Andrade Veras¹ · Maria Júlia Gonçalves de Mello²

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Abstract

Purpose To assess the prophylaxis effect of pentoxifylline and tocopherol (PENTO) on the frequency and severity of medication-related osteonecrosis of the jaw (MRONJ) diagnosed at three months in patients with cancer submitted to tooth extractions during the treatment with bone-modifying agents.

Methods This case series was conducted at the outpatient dental clinic of the Instituto de Medicina Integral Prof. Fernando Figueira (IMIP) between April 2021 and April 2022. Patients ≥ 18 years old were included; those with maxillary metastasis or who performed head or neck radiotherapy were excluded. The PENTO protocol was prescribed two weeks before and two weeks after the tooth extraction, and patients were reassessed one week, one month, and three months after the extraction. The main outcome was the development of MRONJ.

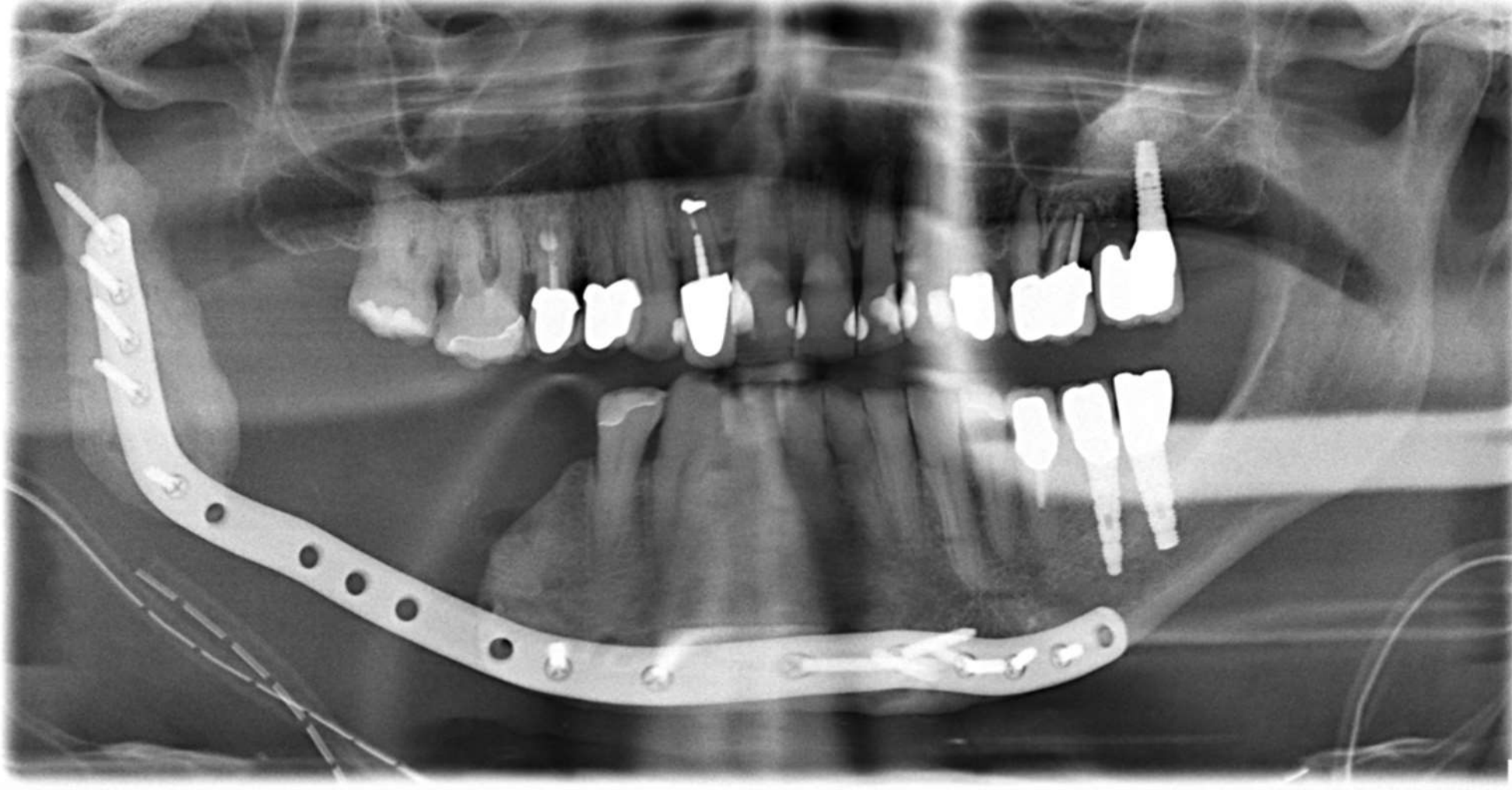
Results Of the 114 screened patients, 17 were included; they were aged between 43 and 73 years and were mostly female (88.2%). Thirty-two tooth extractions were performed (22 in the maxilla and 10 in the mandible). Breast cancer was the most predominant neoplasm (70.6%), being metastatic in 35.3% of patients. Also, all patients used intravenous bisphosphonates. Stage I MRONJ was diagnosed in three patients (17.6%), representing three (9.4%) of all tooth extractions. The repair of MRONJ was achieved 30 days after the PENTO protocol.

Conclusion The prophylaxis use of PENTO reduced the severity of injuries, was well-tolerated, and showed patient compliance.

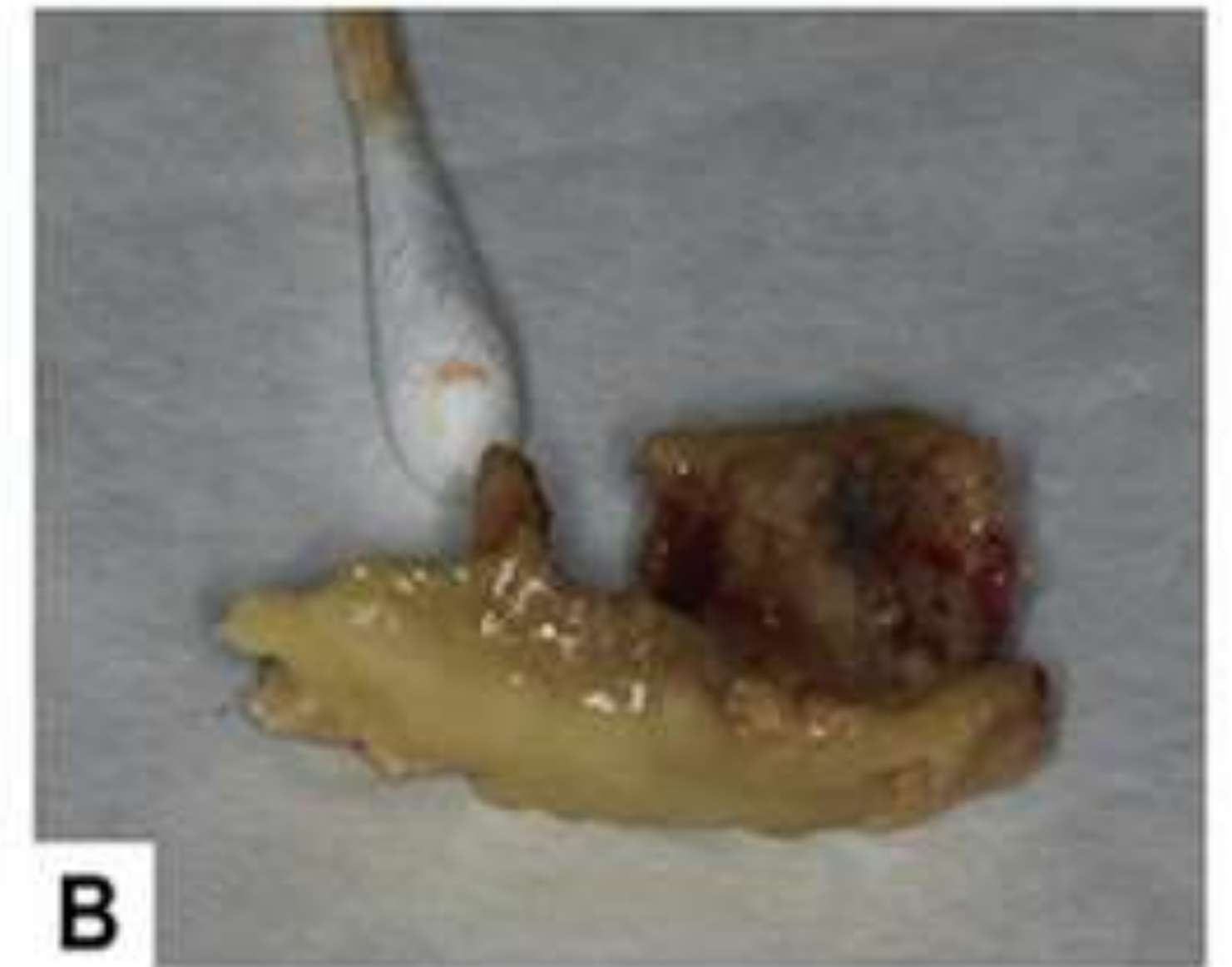
Keywords Pentoxifylline · Tocopherols · Tooth extraction · Osteonecrosis

Durante la terapia con AR: el paciente con MRONJ

a) Tratamiento quirúrgico: Resección marginal + reconstrucción



a) Tratamiento conservador: + secuestrectomía

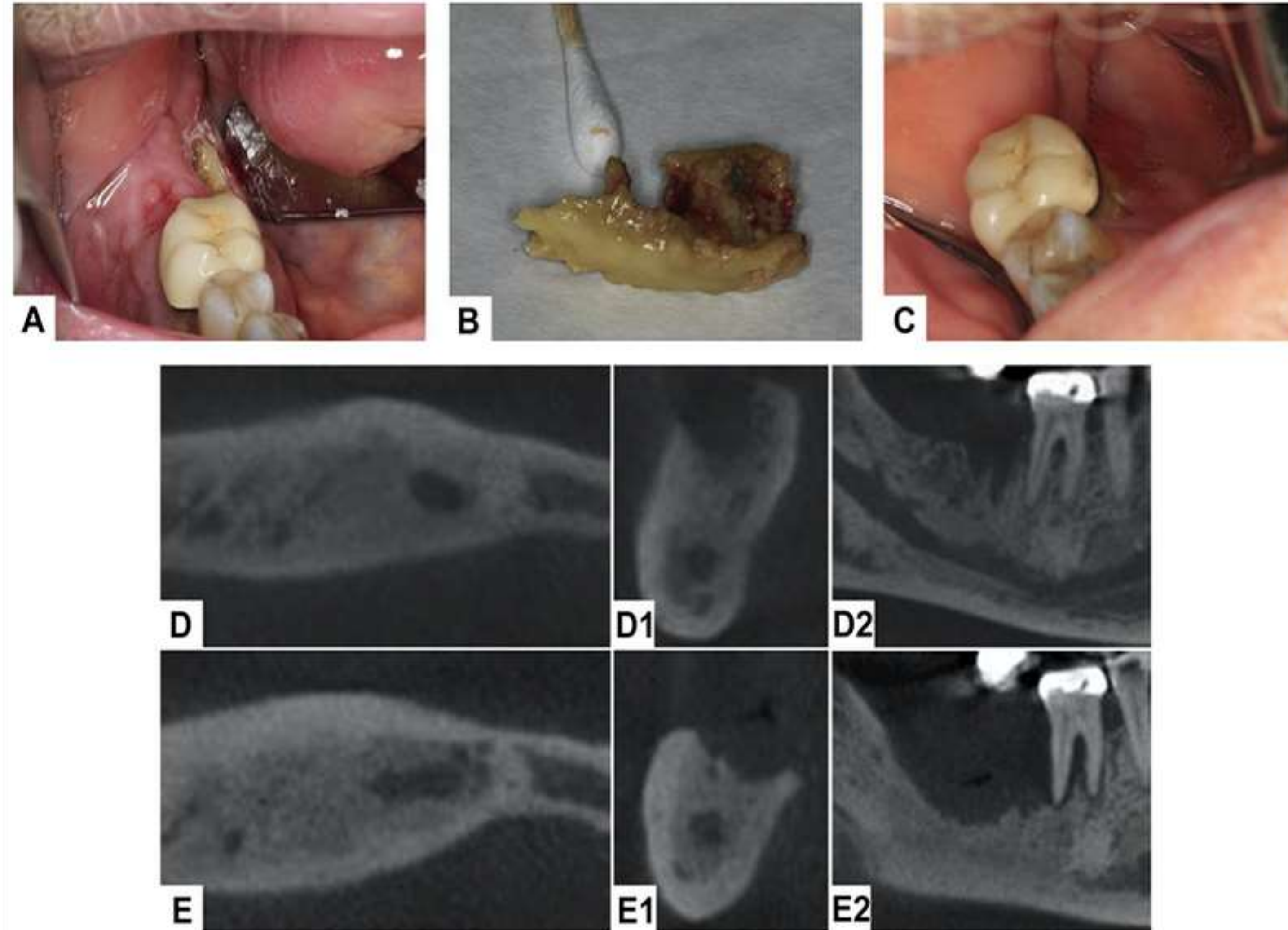


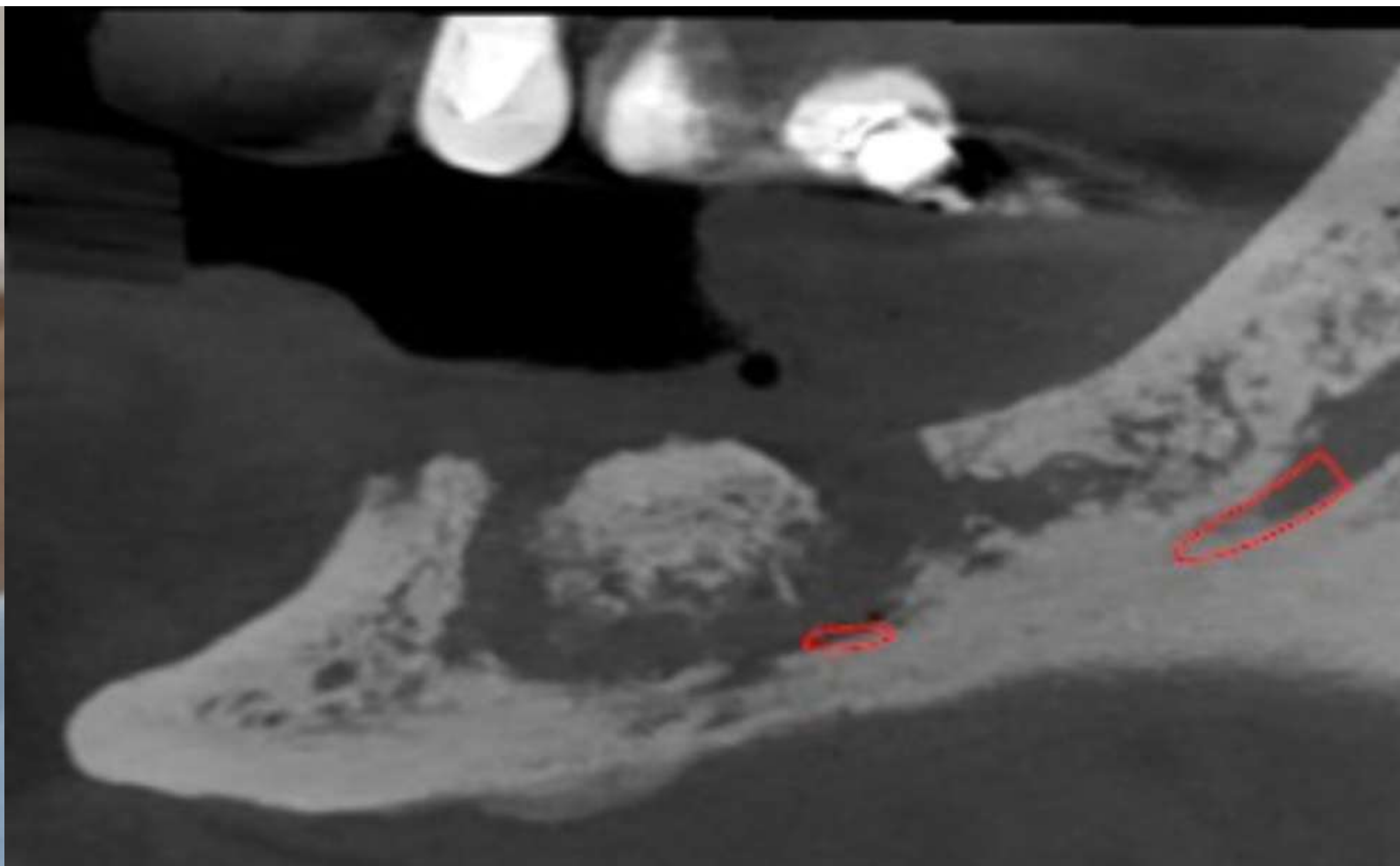
Pathology

Nonsurgical Management of Medication-Related Osteonecrosis of the Jaws Using Local Wound Care

Danny Hadaya DDS *, Akrivoula Soundia DDS †, Earl Freymiller DMD ‡, Tristan Grogan MS §, David Elashoff PhD ||, Sotirios Tetradis DDS, PhD ¶ ☒ ☒, Tara L. Aghaloo DDS, MD, PhD # ☒ ☒

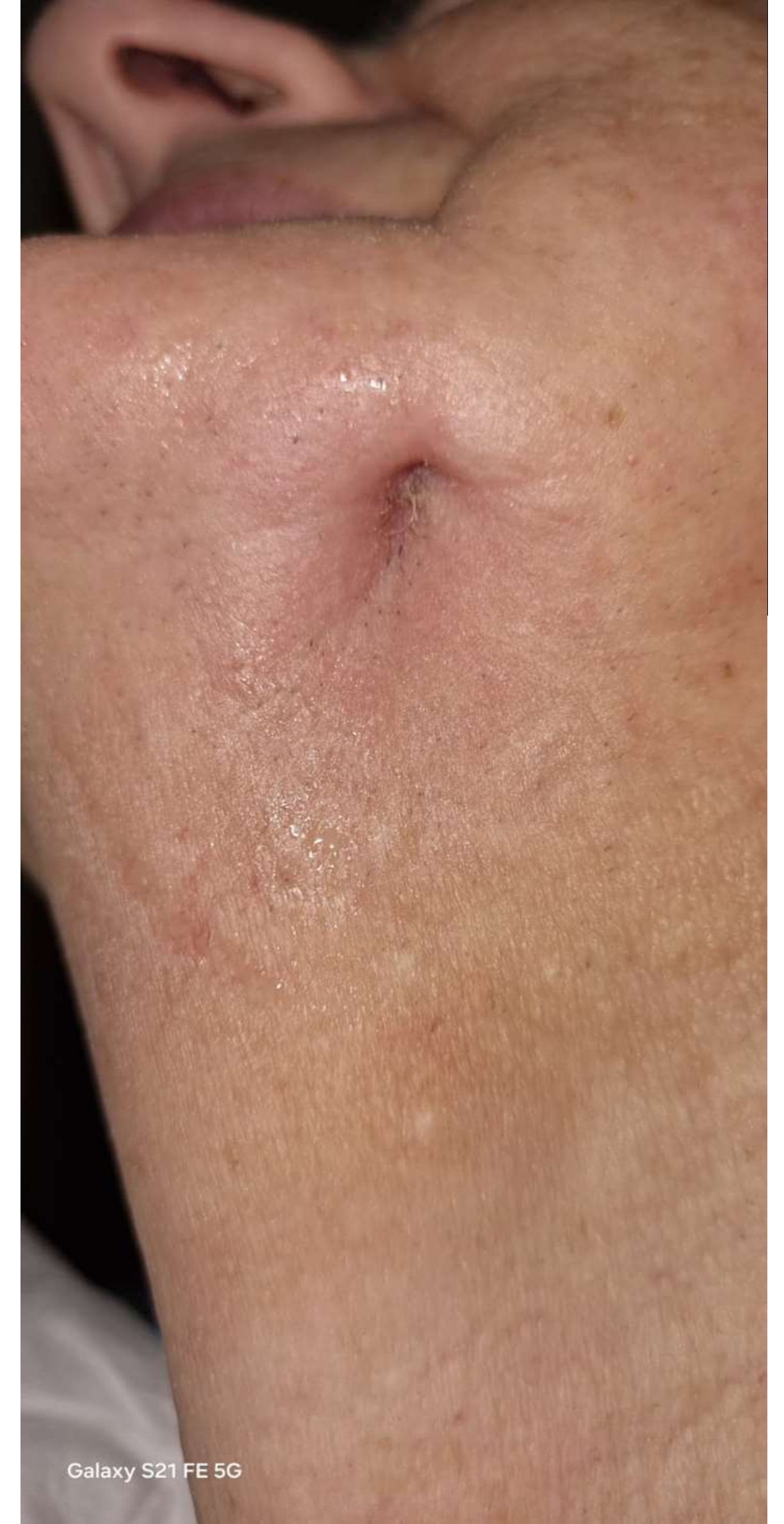
77% resolution and 22% improvement in 106/177 MRONJ patients





88a - Dmab - Meta ósea Ca próstata - MRONJ Etapa 3

Tratamiento conservador por 18 meses



Plasma Rico en Fibrina para MRONJ: siempre ayuda!



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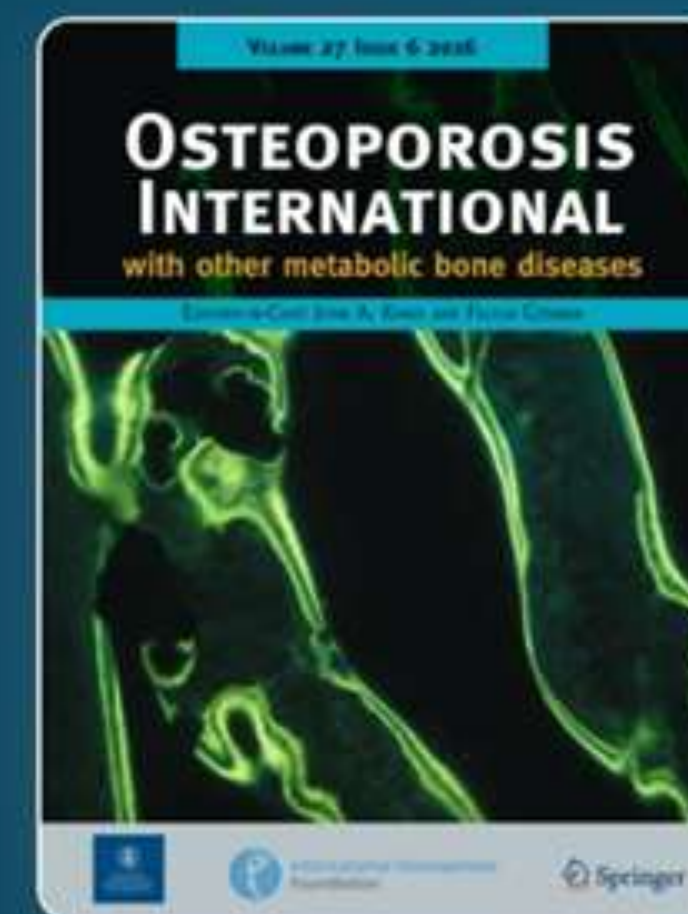
Why are osteoporosis patients treated with antiresorptive therapies considered like oncology patients regarding their oral health care?

Letter to the Editor | Published: 27 June 2024

Volume 35, pages 1677–1678, (2024) [Cite this article](#)

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Avoid common mistakes on your

Adherencia a AR y salud oral?



Preguntas útiles durante entrevista por prescriptores...

- Caries evidentes?
- Gingivorragia?
- Movilidad dental?
- Usa prótesis dental removable?



Es de gran utilidad un paciente que tenga una
radiografía panorámica actual



Centro Radiológico Maxilofacial!

Comentarios finales...

- MRONJ es infrecuente pero es un problema complejo de resolver...
- Los beneficios de la terapia con AR son inmensamente superiores al riesgo de desarrollar MRONJ
- Rol del consentimiento informado
- Rol de la formación continua de médicos prescriptores y dentistas

Osteonecrosis mandibular (ONJ): evidencia

Dr. Luis A. Córdova



Este es un título

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