Medication Related Osteonecrosis of Jaw

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Medication Related Osteonecrosis of Jaw (MRONJ)

- a rare but serious adverse effect of antiresorptive medication
- **Bisphosphonates** and **Denosumab**
- lead to bone death in the jaw

History

- Adverse effect of BP was first described in 2003
- *"BRONJ"* was set in American Association of Oral and Maxillofacial Surgeons' (AAOMS) position paper in 2007
- In 2014, AAOMS suggested to change the nomenclature to **"MRONJ"**

Definition

- Current or previous treatment with antiresorptive therapy alone or in combination with immune modulators or antiangiogenic medications
- Exposed bone or bone that can be probed through an intraoral or extraoral fistula(e) in the maxillofacial region that has persisted for more than 8 weeks
- No history of radiation therapy to the jaws or metastatic disease to the jaws.

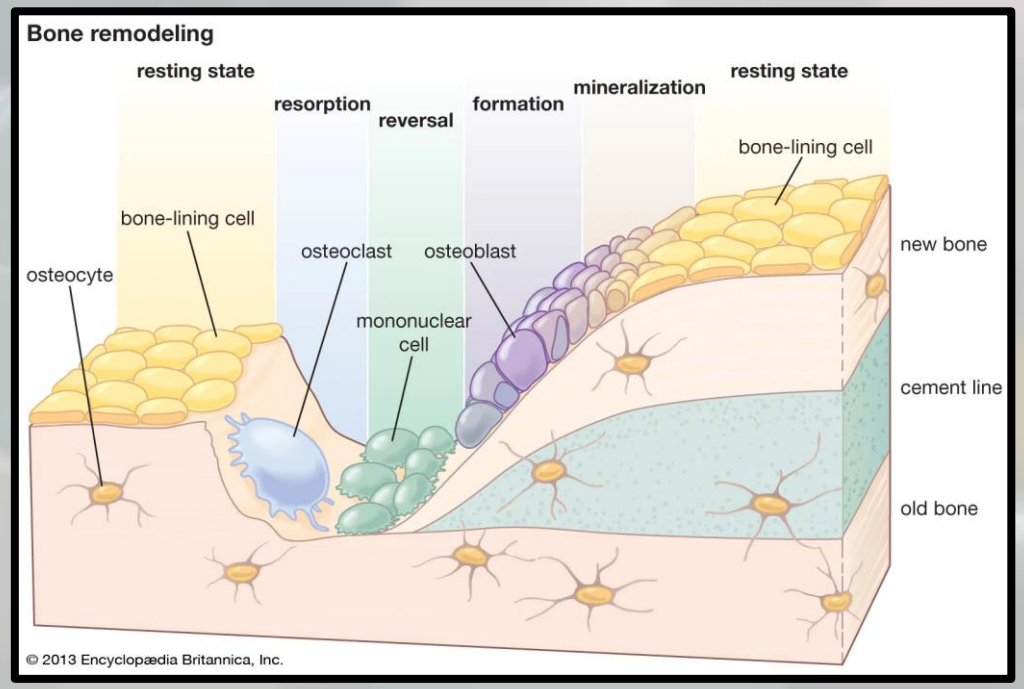
Antiresorptive Medication

- are effective in managing cancer-related conditions and the prevention of osteoporosis-related fractures
- Bisphosphonates (BPs) : via IV and orally
- Denosumab : via Sc

Pathophysiology

- Bone Remodeling inhibition
- Inflammation and infection
- Angiogenesis inhibition
- Innate or acquired immune dysfunction

Bone Remodeling



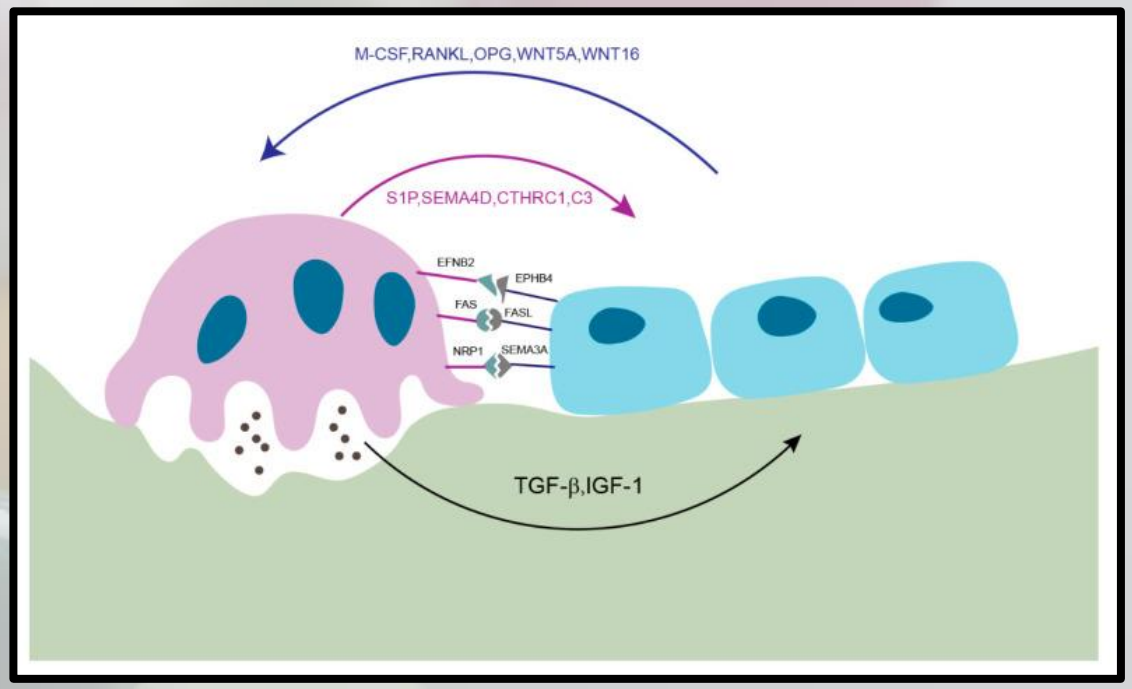


Illustration from : Kim, J.-M., Lin, C., Stavre, Z., Greenblatt, M. B., & Shim, J.-H. (2020). Osteoblast-Osteoclast Communication and Bone Homeostasis. Cells, 9(9), 2073. doi:10.3390/cells9092073

Bone Remodeling Inhibition

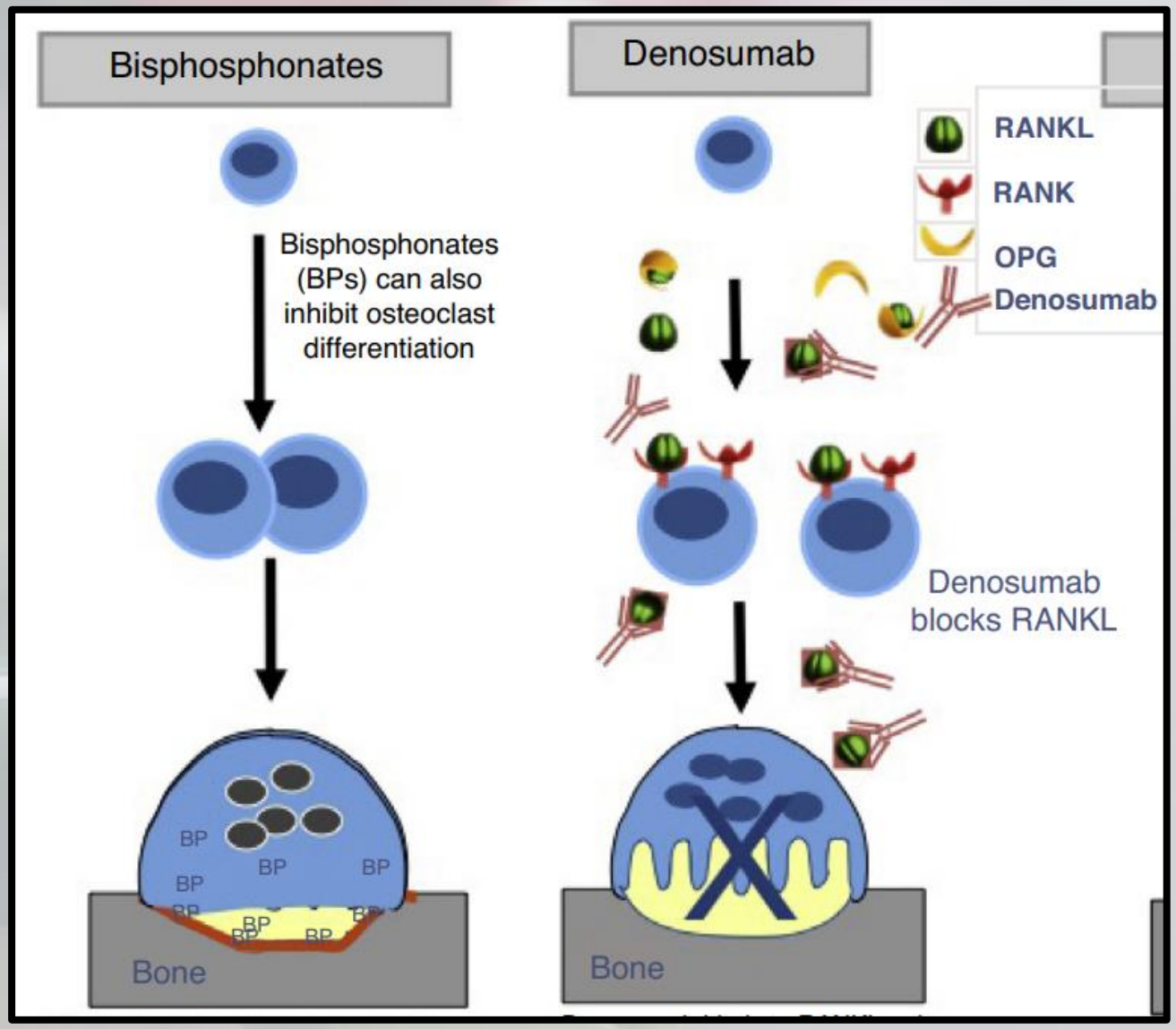


Illustration from : Russell, R. G. G. (2015). Pharmacological diversity among drugs that inhibit bone resorption. Current Opinion in Pharmacology, 22, 115–130. doi:10.1016/j.coph.2015.05.005

Staging

	Symptoms	Exposed Bone/Fistula	Inflammation /Infection	Stage 3 Features*
Pt. at Risk	-	-	-	-
Stage 0	✓	-	-	-
Stage 1	-	✓	-	-
Stage 2	✓	✓	✓	-
Stage 3	✓	✓	✓	✓

**Stage 3 Features : Exposed necrotic bone extending beyond the region of alveolar bone (ie, inferior border and ramus in the mandible, maxillary sinus, and zygoma in the maxilla), Pathologic fracture, Extraoral fistula, Oral antral/oral-nasal communication, Osteolysis extending to the inferior border of the mandible or sinus floor.*

Risk Factors

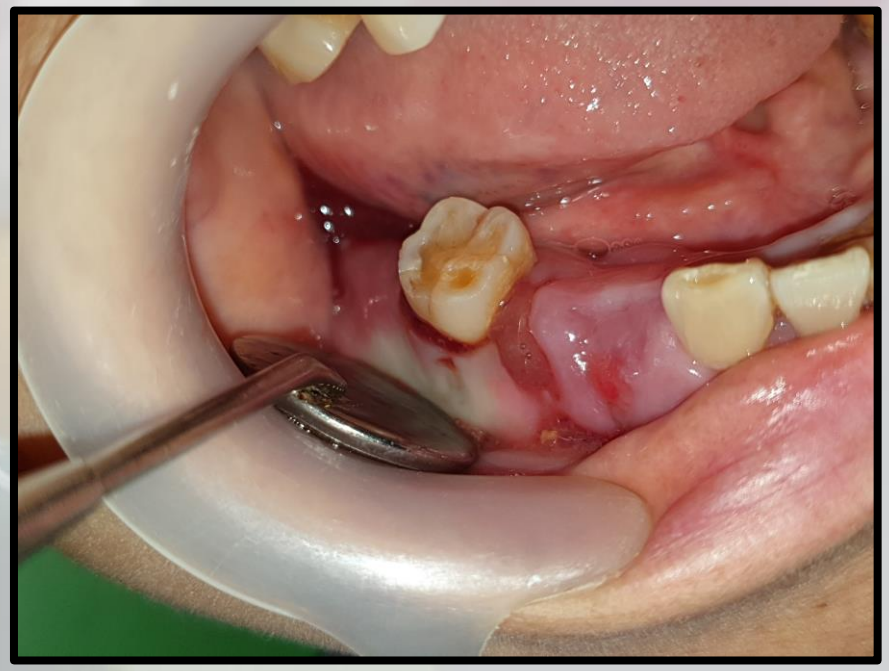
- Medication-related risk factors
  - among cancer / osteoporosis / bone disease
  - duration
- Local factor :- dentoalveolar surgery, anatomic factor, concomitant oral disease, demographic and systemic factors and other medications

History

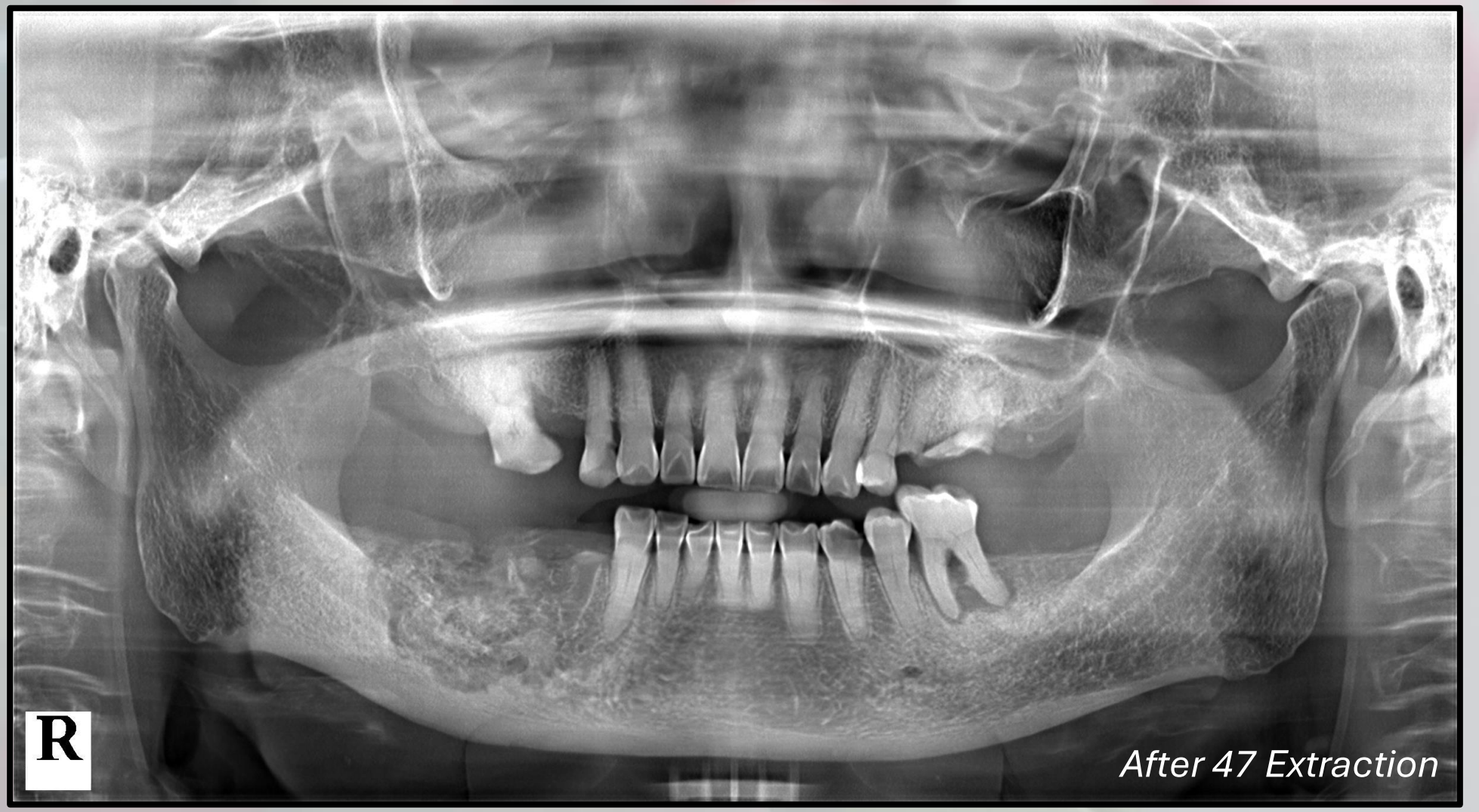
- Thai Female 70 yr. old
- Pain and swelling at Right posterior area of the lower jaw (site of prev. tooth extraction - 3 months ago)
- U/D : HT DLP Osteoporosis
- On Alendronate 70 mg once a week (1 yr. 6 mo.)

Physical Examination

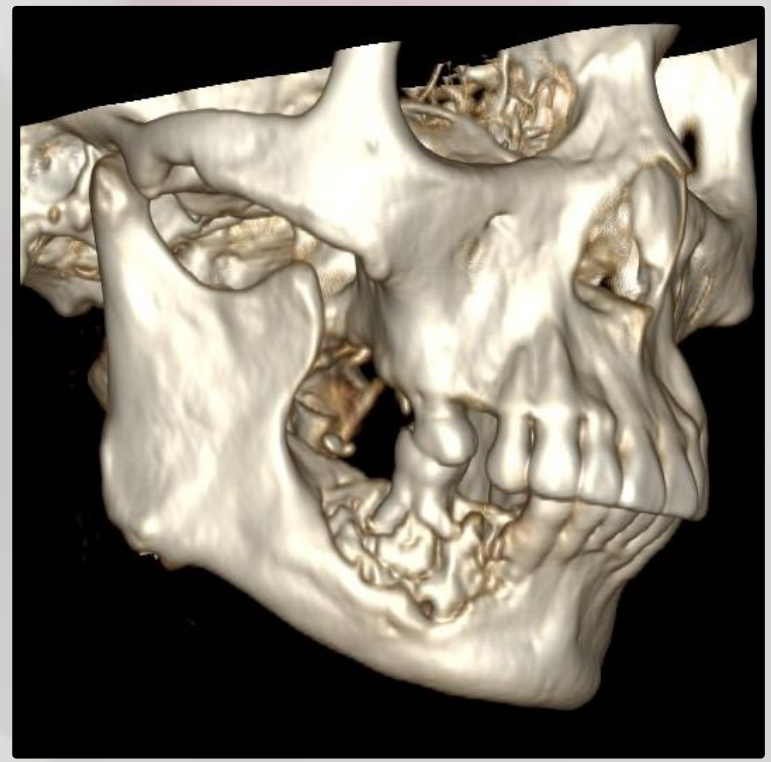
Physical Examination



Radiographic



Radiographic



Diagnosis

Stage 2 MRONJ

Treatment

- Medical Consultation
- **Conservative Treatment**
  - Exfoliation of the exposed, necrotic bone
  - Oral ATB (Amoxicillin + Clavulanate)
  - Wound irrigation twice a day
  - Follow-up once a week

Treatment

1 - Conservative

3 months after Conservative Treatment

- Pus discharge and fistulae from 46 47 area

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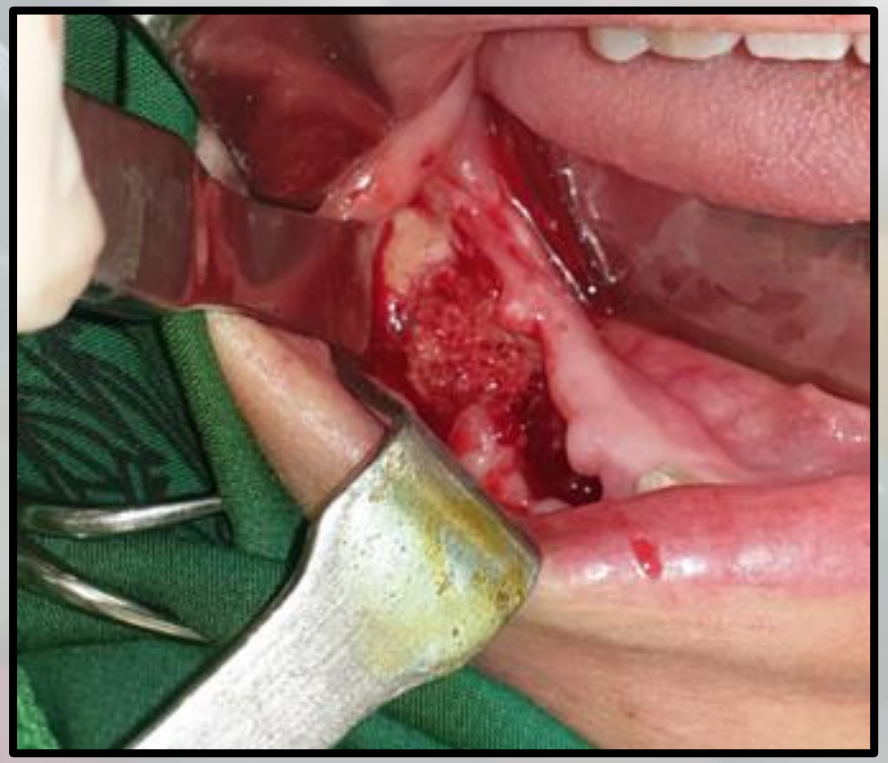
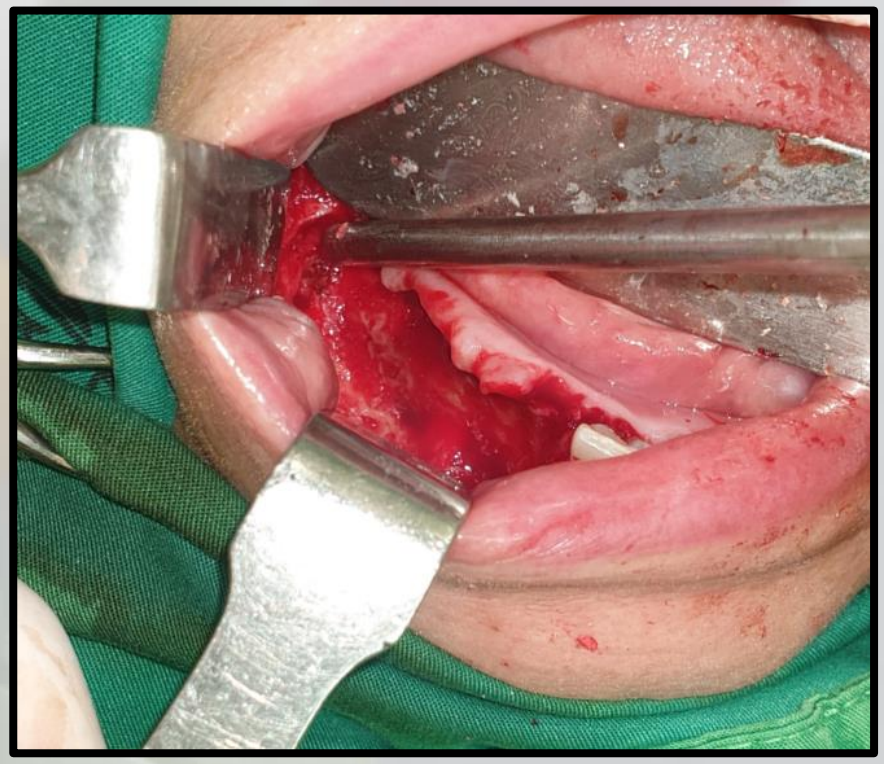
Sequestrectomy under GA

Treatment

2 - Sequestrectomy





Treatment (Pathologic Result)

DIAGNOSIS : Necrotic bone from the right mandible;
- **Mixed empty osteocytic lacunae ,necrotic bone ,neutrophils infiltrate**
- **Consistent with Medical related osteonecrosis**

GROSS DESCRIPTION :

The formalin fixed specimen consists of a piece of irregular green brown bony tissue, measuring 2.2x0.8x0.8 cm. Serial sections are totally submitted as A.

MICROSCOPIC :

Section reveals mixed bone necrosis ,empty osteocytic lacunae and inflammatory cells of neutrophils infiltrate.

Fig.1

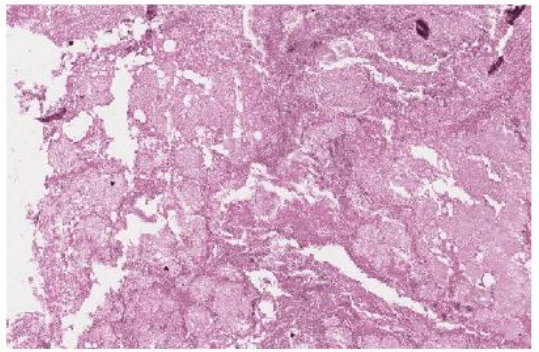
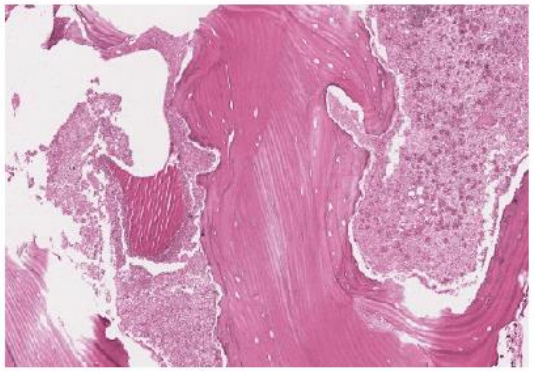
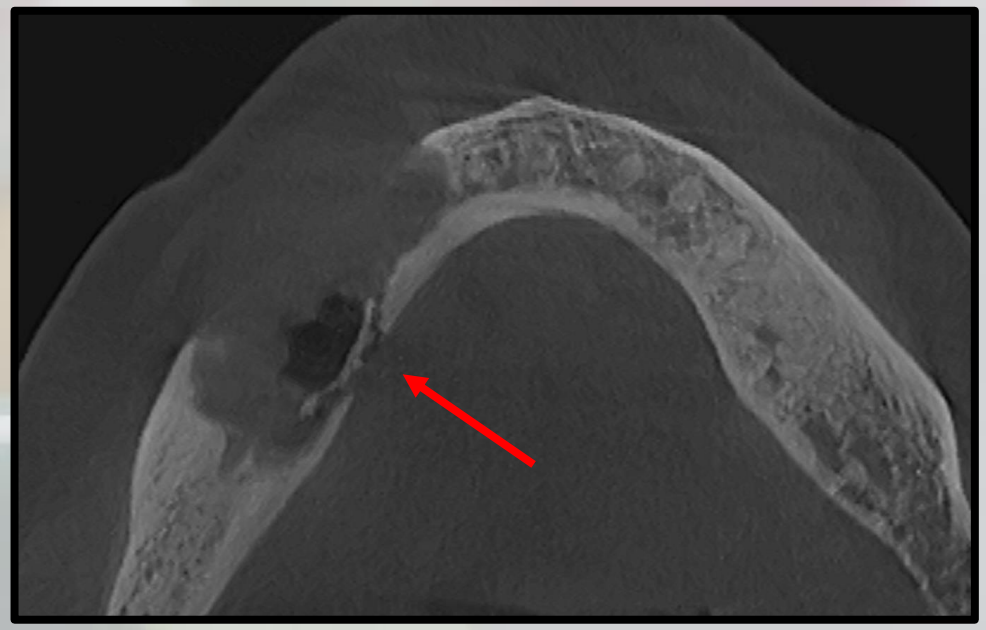


Fig.2



Treatment

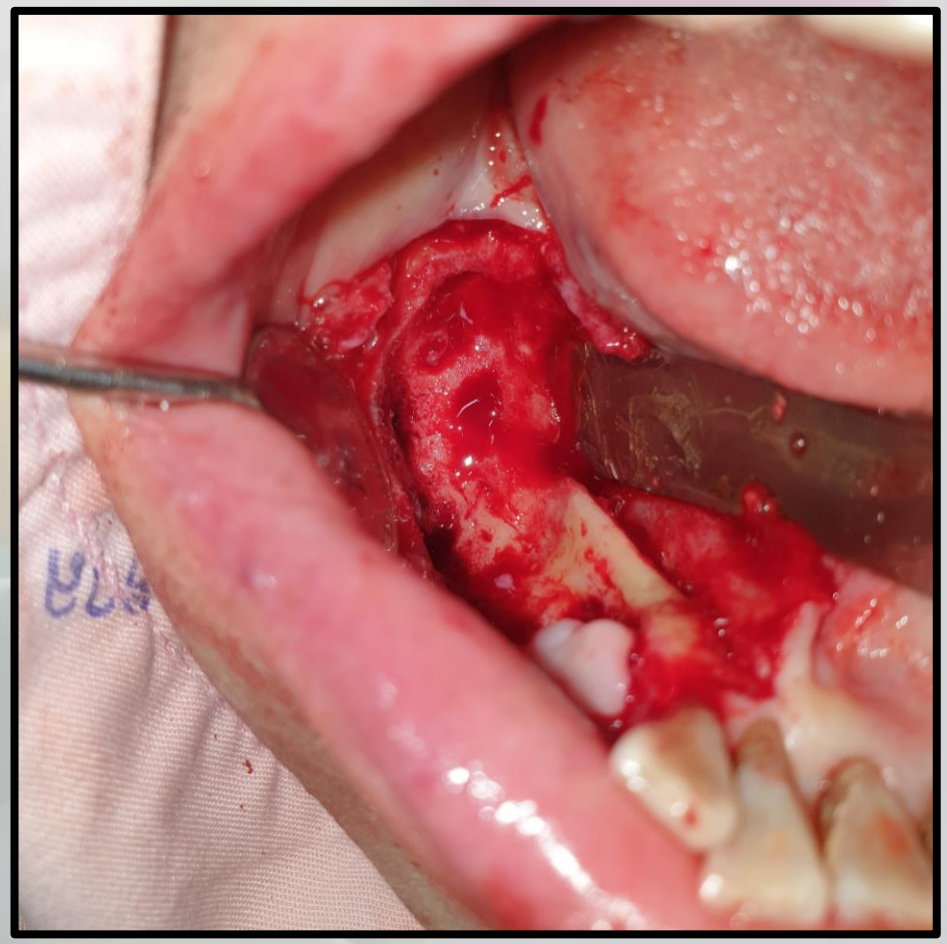
2 - Sequestrectomy



8 weeks after Sequestrectomy

Treatment

3 – Marginal Resection



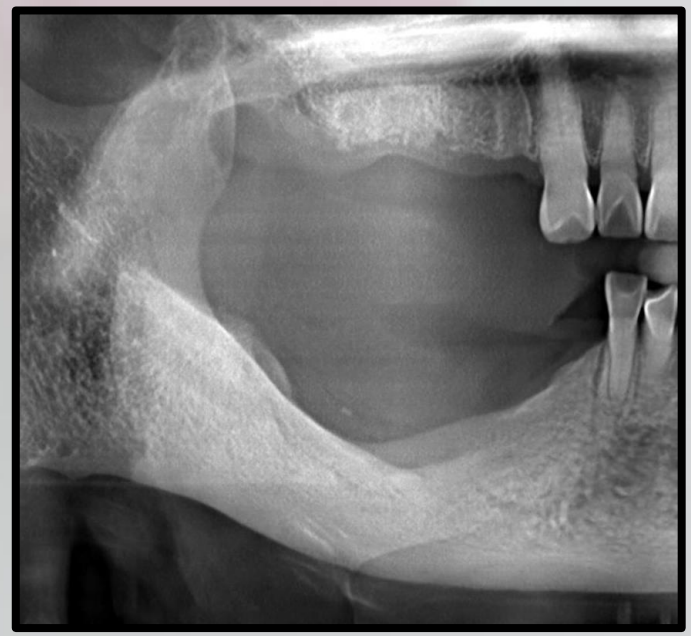
under Local anesthesia

Treatment

3 – Marginal Resection

5 months

8 months after Marginal Resection



Treatment

3 – Marginal Resection

Complication

The patient had fragility fracture after 15 months discontinuation of BP

“Drug holiday”

Discussion

- MRONJ is now well-known complication that in affecting a growing number of patients
- Updated treatment guideline most recently in 2022 that modified from the 2014 position paper

Discussion

1 - Prevalence

- Early in 2014, The prevalence of BRONJ increases over time from near 0 at baseline to 0.21% after four or more years of BP exposure
- More recent data, No significant increase in MRONJ in patients treated for up to 9 years

Discussion

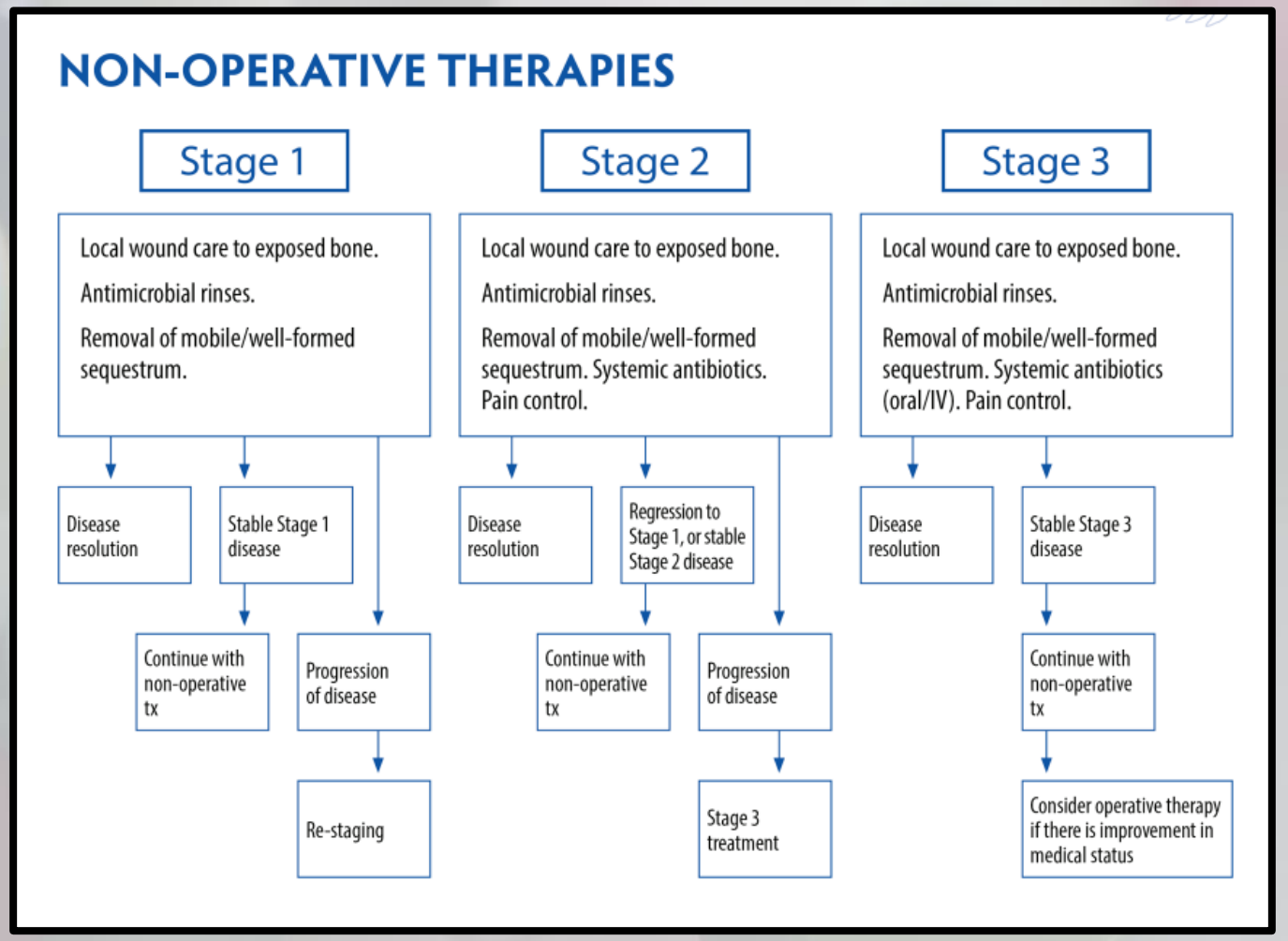
2 - Treatment Strategies

Nonoperative VS Operative

- Both management being acceptable for all stages based on surgical judgment and patient factors in a shared decision making model
- Goal of both remains the same: curative therapy and quality-of-life improvement.

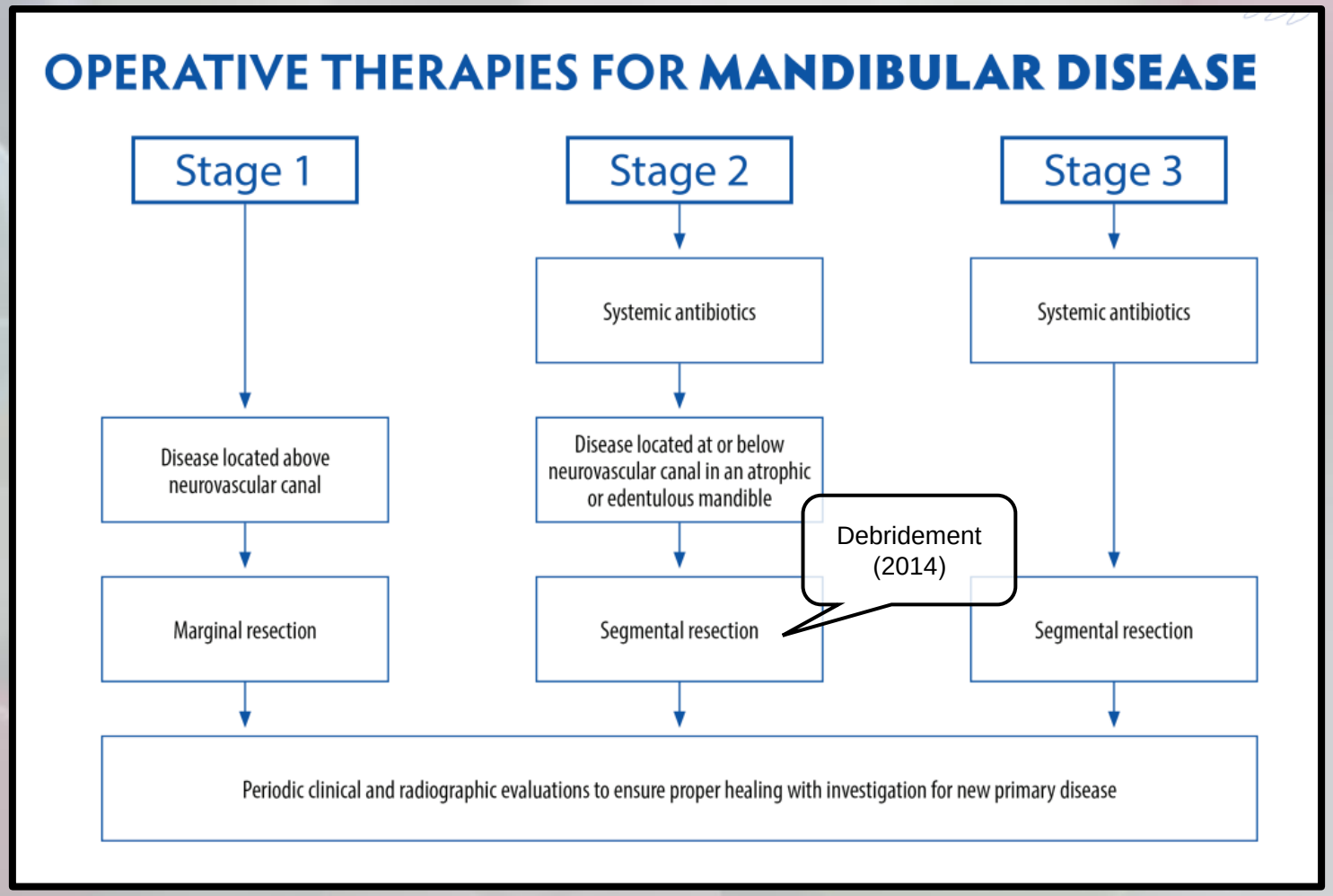
Discussion

2 - Treatment Strategies



Discussion

2 - Treatment Strategies



Discussion

3 – Drug holiday

and expedient resumption of antiresorptive therapy for all stages of MRONJ disease.[245] The benefit of drug holidays for the operative intervention of MRONJ has not been substantiated.

Discussion

3 – Drug holiday

Thank you
For your attention