

Supplementary Material 2

Clinical Decision Pathway for Suspected Stage 0 MRONJ (Based on CBCT Findings)

Step 1: Begin by identifying patients currently or previously treated with antiresorptive (AR) or antiangiogenic (AA) medications who do not present with clinical signs of bone exposure. These patients are at potential risk of developing MRONJ and warrant radiographic screening. **References:** Ruggiero et al., 2022; Shibahara et al., 2019; Moreno-Rabié et al., 2023; Shin et al., 2024.

Step 2: Conduct a CBCT scan of the entire maxillomandibular complex to assess bony structures in both jaws comprehensively. Full-arch imaging is essential to detect subclinical or early-stage MRONJ features. **References:** Ko et al., 2024; Wongratwanich et al., 2021; Zhou et al., 2021; Shimamoto et al., 2018; Ristow et al., 2023, present study)

Step 3: Evaluate each quadrant for CBCT findings suggestive of early MRONJ, including:

- Focal or diffuse osteosclerosis
 - Increased trabecular bone density (especially crossing the midline)
 - Cortical thickening (mandibular inferior border or ramus)
 - Thickening or irregularity of the mandibular canal cortex
 - Mixed radiolucent-radiopaque osteolytic areas
 - Persistent extraction sockets (with delayed bone remodeling beyond 8 weeks)
- These features have been reported as early or subclinical radiographic markers of MRONJ in both symptomatic and asymptomatic regions. **References:** Soundia et al., 2018; Moreno-Rabié et al., 2022, 2023, 2024; Kajihara et al., 2024; Simpione et al., 2020; Zhou et al., 2021; Shin et al., 2024, presente study

Step 4: Count the number of radiographic alterations per site or quadrant. A greater number of findings in a given area may indicate increased risk of disease progression, even in the absence of clinical signs. **References:** Soundia et al., 2018; Badabaan et al., 2023, presente study

Step 5: Determine the appropriate clinical management based on the number and distribution of findings:

- If 0–1 alteration is present, routine follow-up and annual CBCT are recommended.
- If 2 or more alterations are found in a single region, avoid invasive procedures and schedule CBCT re-evaluation in 3–6 months.
- If 2 or more alterations are found in multiple quadrants or bilaterally, the patient should be classified as high risk. Referral to a specialist and close CBCT monitoring (every 3–6 months) is advised. **References:** Shimamoto et al., 2018;

Aghaloo & Tetradis, 2014; Simpione et al., 2020; Pimolbutr et al., 2018; Moreno-Rabié et al., 2024; Campisi et al., 2020, present study

Rationale to include presente study in the steps above

Step 2 – CBCT Imaging

Rationale:

The present study employed **full-arch CBCT imaging** in patients at risk of MRONJ and demonstrated that **radiographic alterations (osteosclerosis, trabecular coarsening, cortical thickening, etc.) were present even in clinically unaffected areas**. This directly supports the use of CBCT as an early detection tool for Stage 0 MRONJ, in alignment with Step 2's rationale. It provides empirical validation for using CBCT beyond symptomatic regions, contributing to early identification in asymptomatic patients.

Step 3 – CBCT Radiographic Findings

Rationale:

The study identified **all major radiographic features** outlined in Step 3—osteosclerosis, thickened lamina dura, mandibular canal alterations, delayed socket healing, and increased trabecular density—in asymptomatic sites. These findings confirm the diagnostic value of such features even outside clinically evident lesions. Thus, the present study supports the inclusion of these findings as Stage 0 indicators.

Step 4 – Number of Alterations & Risk Stratification

Rationale:

Through **multivariate logistic regression**, the study showed that the **presence of multiple radiographic features** was significantly associated with clinical risk factors (e.g., antiangiogenic therapy, oncologic diagnosis). This supports the concept that **cumulative imaging findings correlate with higher MRONJ risk**, validating the risk stratification logic described in Step 4.

Step 5 – Management Guidance Based on Imaging Severity

Rationale:

Although not an interventional study, the present work proposes that **early identification of imaging changes in asymptomatic patients** should influence management strategies. It supports **conservative monitoring or altered surgical**

planning based on CBCT findings, reinforcing the need for **severity-based clinical decision-making**, as proposed in Step 5.

References

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