



Development of Medication-Related Osteonecrosis of the Jaw (MRONJ) Associated with Dental Implant : Report of 3 Cases with Literature Review

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Introduction

- Medication-related osteonecrosis of the jaw (MRONJ) is a severe complication associated with anti-resorptive and anti-angiogenic therapy, with ongoing debate regarding its relationship with dental implants.
- Recently, several studies^{1,2} have reported that implant placement itself does not increase the incidence of MRONJ in patients with osteoporosis.
- However, some^{3,4} have reported the occurrence of MRONJ in implanted implants, which has been named implant-presence triggered MRONJ.
- Peri-implantitis can lead to micro-damage, mechanical stress, and delayed bone remodeling, potentially increasing MRONJ susceptibility.
- In this study, we report three cases of MRONJ associated with dental implants in various clinical situations and provide precautions.

Methods

- Three patients, each diagnosed as MRONJ associated with dental implants, were retrospectively analyzed.
- The patients varied in their medical backgrounds, including osteoporosis and cancer treatments with anti-resorptive medications.
- After undergoing radiographic and clinical examinations, Surgical procedures such as sequestrectomy and explantation were performed, and clinical outcomes were monitored postoperatively.
- The dental notation in Case Reports was recorded using the FDI system.





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Case Report 1

- A 68-year-old female patient who had been taking Fosamax for osteoporosis for 2 years when she underwent implant placement in the lower left molar region (i36, i37) in 2011 at the Local Clinic.
- After osseointegration and prosthodontic treatment, she developed persistent pain and underwent two periodontal surgeries. On November 26, 2015, explantation of i37 was performed at the Department of Periodontology of Gangnam Severance Hospital
- However, the symptoms did not improve, and on December 3, 2015, she was referred to the Department of Oral and Maxillofacial Surgery for further evaluation and management.



- Following the referral, she underwent multiple surgical interventions due to progressive bone loss and osteonecrosis.
- March 8, 2016: Sequestrectomy, i36 implant removal, and #35 extraction.
- November 16, 2016: Sequestrectomy of the mandible under general anesthesia.



- After these surgical procedures, the lower left molar region showed satisfactory bone healing.
- Notably, a lesion was observed after the explantation of i37, yet the patient continued anti-resorptive therapy (Fosamax) without interruption, which may have played a role in preventing significant bone loss.
- It is possible that the patient already had an underlying MRONJ-like condition, which was exacerbated after the removal of i37.
- Alternatively, the explantation itself may have triggered the disease progression, rather than merely worsening a pre-existing condition.



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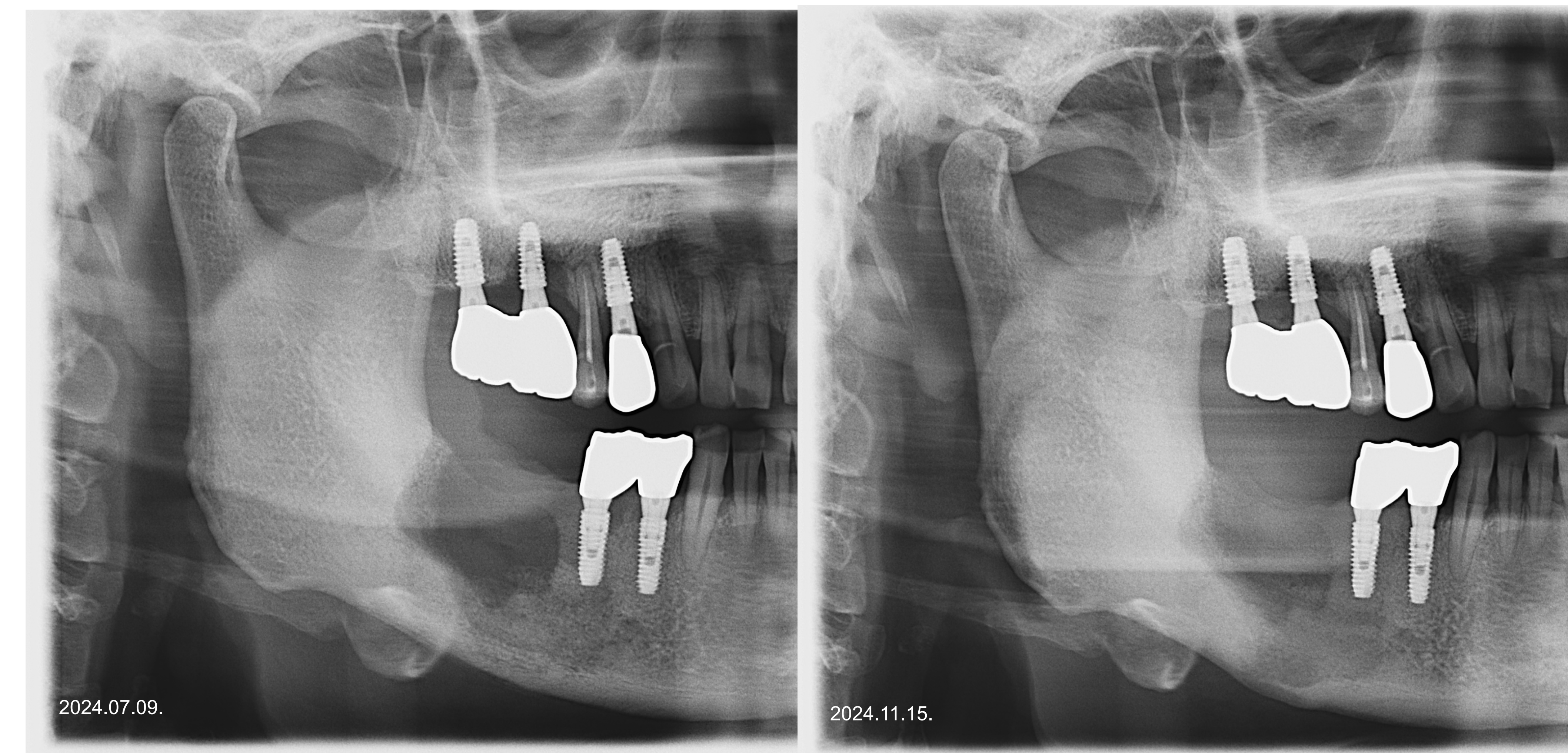


Case Report 2

- A 56-year-old male visited our clinic in November 6, 2023, complaining of pain in the right mandible that had developed a few months earlier around a dental implant placed at a local clinic between 2016 and 2017.
- In November 2023, he underwent explantation of i46 and i47 at the same local clinic.
- His medical history included a hemi-hepatectomy for hepatocellular carcinoma (HCC) in 2007, which recurred in 2022.
- In April 2023, he received three cycles of chemotherapy (atezolizumab + bevacizumab), but the treatment failed.
- In June 2023, he was placed on lenvatinib therapy (12 mg orally, once daily for one month).
- Notably, Mauceri et al.⁵ (2019) reported a case of lenvatinib-related osteonecrosis, highlighting the potential risk of medication-related osteonecrosis of the jaw (MRONJ) in such patients.
- A panoramic radiograph revealed sequestration around the implant



- On April 24, 2024, he underwent sequestrectomy of the right mandible under general anesthesia.
- On April 25, 2024, he underwent periodontal curettage of the maxillary right and left regions under local anesthesia.





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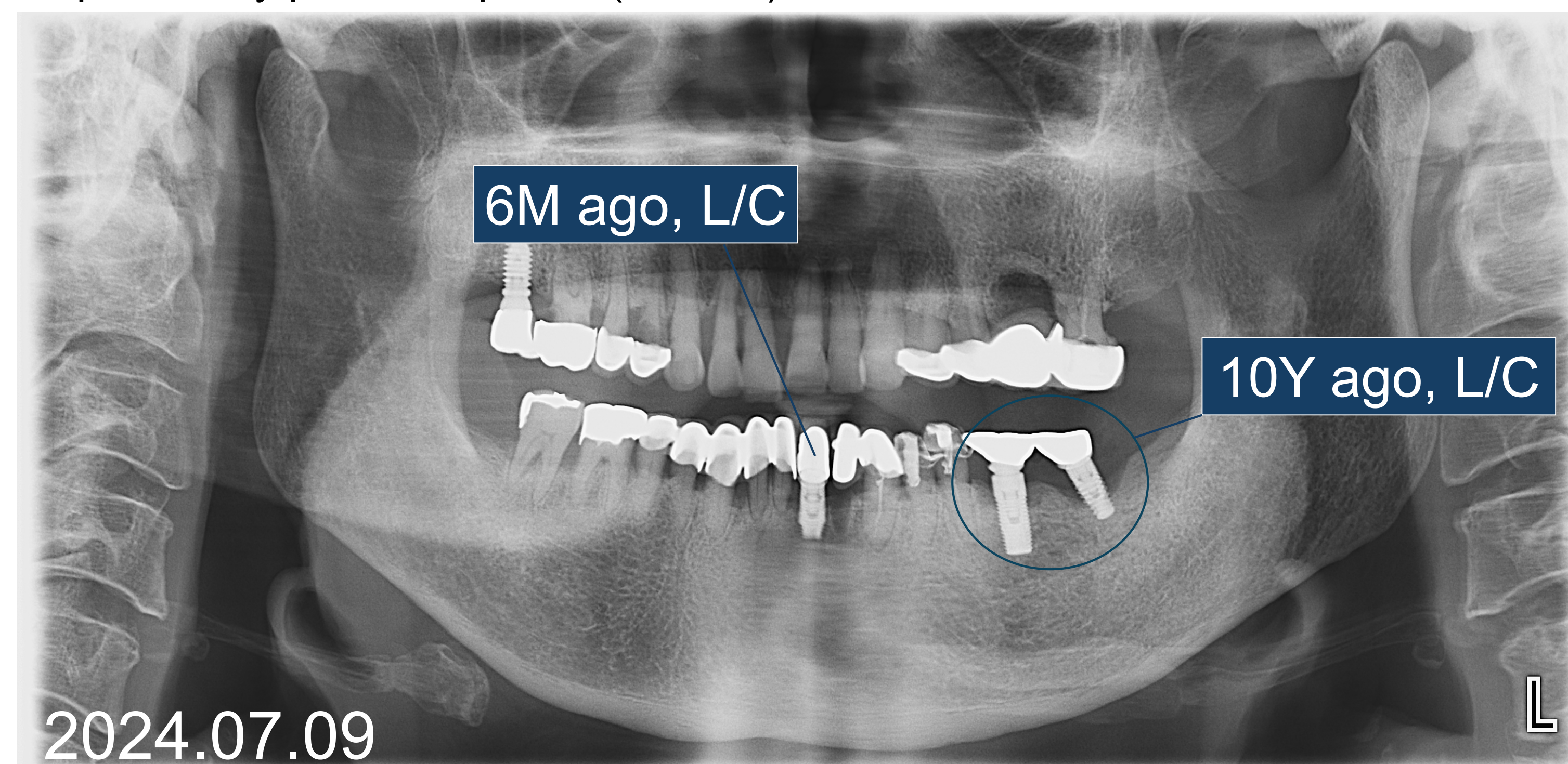
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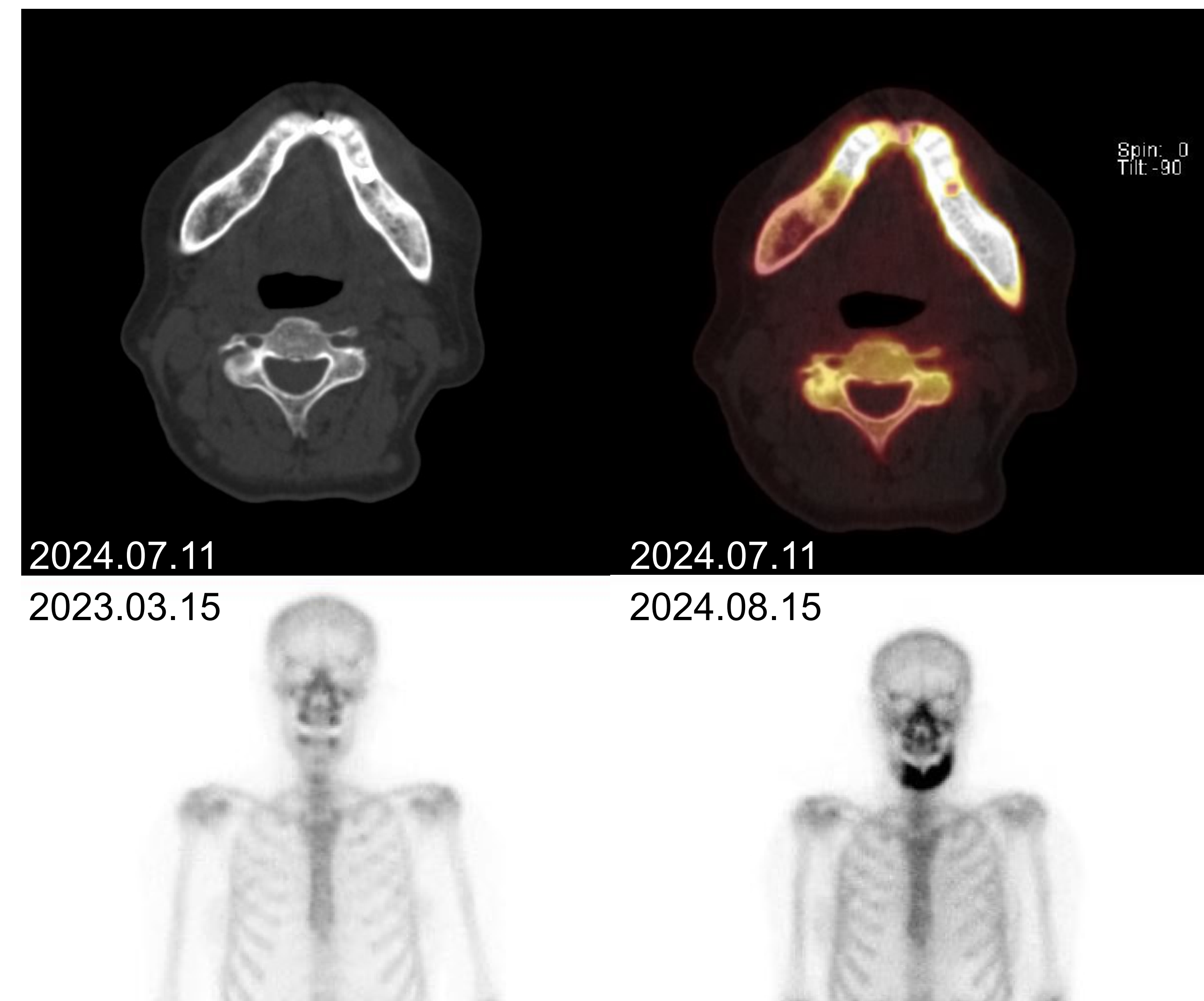


Case Report 3

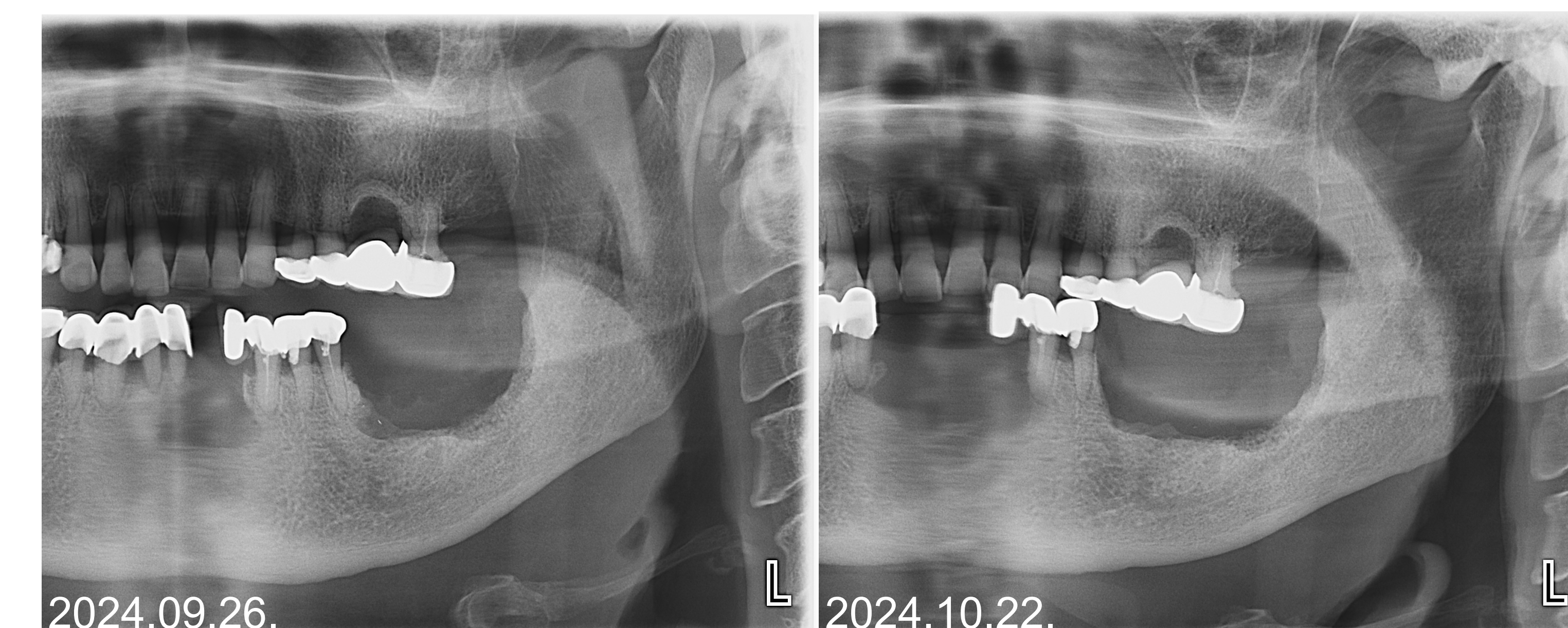
- A 69-year-old female underwent extraction and mandibular anterior implant placement (i31) in June 2023 at a local clinic while receiving chemotherapy and denosumab for breast cancer.
- She had implants in i36 and i37, which had been placed more than 10 years ago at a local clinic.
- Her past medical history (PMH) included breast cancer, managed by the breast surgery department at Gangnam Severance Hospital, with monthly denosumab injections since March 2023 and targeted chemotherapy since January 2023.
- Six months after the i31 implant placement, she visited our clinic complaining of pain in the mandibular anterior region and around the previously placed implants (i36, i37).



- A nuclear medicine examination revealed increased uptake in the lower two-thirds of the mandible, suggesting inflammatory change.
- Given the extent of bone involvement, segmental mandibulectomy with fibular free flap (FFF) reconstruction was recommended; however, the patient preferred more conservative approach, leading to staged surgical interventions instead.



- September 25, 2024: Explantation of i31, i36, and i37 under general anesthesia, along with sequestrectomy of the left mandible.
- October 22, 2024: Admission for sequestrectomy of the mandibular anterior region under local anesthesia.
- November 20, 2024: Extraction of #43 34 35 under general anesthesia, along with sequestrectomy.
- December 12, 2024: Sequestrectomy of the mandibular anterior and left mandibular regions under local anesthesia.



- On February 5, 2025, she underwent additional sequestrectomy of the mandibular anterior and right mandibular regions under general anesthesia, along with the extraction of #44 and the placement of a customized reconstruction plate to prevent pathological fractures.





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Discussion & Conclusion

- Peri-implantitis may act as a local triggering factor for MRONJ, particularly in patients receiving anti-resorptive or antiangiogenic therapy, contributing to progressive bone loss and delayed healing.
- Patients with a history of denosumab, bisphosphonates, or chemotherapy require careful monitoring before and after implant placement, as these medications may compromise bone remodeling and increase the risk of implant-related complications.
- Early diagnosis and appropriate management of peri-implant inflammation are essential in reducing the risk of MRONJ and improving treatment outcomes. Further research is needed to better understand the association between peri-implant disease and MRONJ and to establish effective preventive measures and treatment protocols for at-risk patients.

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