# Computed tomography imaging features of osteomyelitis of the jaw: comparison between antiresorptive medication-related conditions and medication-unrelated conditions

Jeong Won Shin, DDS, MS,[a] Jo-Eun Kim, DDS, PhD,[b] Kyung-Hoe Huh, DDS, PhD,[c] Won-Jin Yi, PhD,[d] Min-Suk Heo, DDS, PhD,[d] Sam-Sun Lee, DDS, PhD,[d] and Soon-Chul Choi, DDS, PhD[d]

**Objectives.** The aim of this study was to analyze and compare the imaging features of osteomyelitis according to the presence or absence of antiresorptive medications by using computed tomography (CT).

**Study Design.** We retrospectively reviewed the records of 270 patients with osteomyelitis (83 males and 187 females; average age 66.6 years). CT imaging features were analyzed, and imaging and demographic features were compared between the medication-related osteomyelitis (MROM) group and the medication-unrelated osteomyelitis (MUOM) group.

**Results.** Trabecular defects, cortical defects, sclerosis, and sequestra were detected in the majority of patients, whereas periosteal new bone formation was less common. The MROM group exhibited sequestra and periosteal new bone formation more frequently on CT images, but the size and appearance of the sequestra and type of periosteal new bone were not significantly different between the 2 groups.

**Conclusions.** Sequestra and periosteal new bone formation were characteristic CT features of osteomyelitis more commonly found in the medication-related condition. These findings may be useful in the evaluation of osteomyelitis and medication-related osteonecrosis of the jaw. (Oral Surg Oral Med Oral Pathol Oral Radiol 2020;129:629−634)

Osteomyelitis is an inflammatory lesion of bone, usually caused by infectious microorganisms; it involves the medullary cavity and extends to the adjacent cortical bone, overlying periosteum, and soft tissues.[1] The jaws are especially susceptible to osteomyelitis because of the frequent opportunities for odontogenic infections and trauma. Bone vascularity−altering conditions, such as osteoporosis, osteopetrosis, exposure to therapeutic radiation, specific medications, and malignancy, may predispose patients to osteomyelitis.[2]

Over the past 2 decades, antiresorptive medications have been associated with progressive destruction of the jaws. Bisphosphonates (BPs) are antiresorptive drugs that inhibit osteoclastic activity. They are effective in treating osteoporosis and other metabolic bone diseases and in preventing osteolysis associated with metastatic malignant tumors, such as breast, prostate, and lung cancers.[3] Although BPs have been used effectively for more than 40 years, their main side effect is bisphosphate-related osteonecrosis of the jaw (BRONJ).[4] More recently, denosumab and other antiresorptive and antiangiogenic medications employed to reduce the risk of skeletal complications in malignant disease have been linked to similar jaw destruction.[5,6] As a result, the term *medication-related osteonecrosis of the jaws* (MRONJ) has been used to represent necrotic alterations in the maxillae and the mandible associated with the use of these drugs.[5] MRONJ is considered to result from noninflammatory drug toxicity.[7] However, some reports have posited that MRONJ might be an infectious disease or an infection triggered by exposed bone. Some microorganisms (e.g., *Actinomyces*) have been discovered in the lesions of MRONJ and might be involved in the chronic and nonhealing state characteristic of the lesion.[8-10]

Overall, MRONJ and osteomyelitis are closely related, with similar clinical, radiographic, and histopathologic features. It is very difficult to distinguish MRONJ from osteomyelitis, especially in advanced stages. Recent studies have attempted to categorize the differences by using histopathologic comparison, but

## Statement of Clinical Relevance

Osteomyelitis and medication-related osteonecrosis of the jaw are hard to differentiate with images. Sequestra and periosteal new bone formation were more commonly observed in the medication-related condition, which can help in differentiating the 2 conditions.

[a]Clinical Assistant Professor, Department of Orthodontics, Institute of Oral Health Science, Ajou University School of Medicine, Suwon, Republic of Korea.
[b]Clinical Assistant Professor, Department of Oral and Maxillofacial Radiology, Seoul National University Dental Hospital, Seoul, Republic of Korea.
[c]Professor, Department of Oral and Maxillofacial Radiology and Dental Research Institute, School of Dentistry, Seoul National University, Seoul, Republic of Korea.
[d]Professor, Department of Oral and Maxillofacial Radiology, School of Dentistry, Seoul National University, Seoul, Republic of Korea.
Received for publication Jun 12, 2019; returned for revision Nov 7, 2019; accepted for publication Nov 9, 2019.

2212-4403/$-see front matter
https://doi.org/10.1016/j.oooo.2019.11.006

there were no significant differences between osteomyelitis and MRONJ.[11,12] It is important to distinguish MRONJ from osteomyelitis because even though the treatment of these diseases is similar, specific recommendations about management might be different. Clinical diagnosis of MRONJ depends on a history of antiresorptive medication and visual examination. Several methods have been suggested for the early diagnosis of MRONJ, including specific serum markers.[13] Radiographic examination is important; however, evidence has not revealed pathognomonic imaging features of MRONJ, and the known features of MRONJ are difficult to differentiate from those of osteomyelitis.[13-16]

This investigation was designed to analyze and compare computed tomography (CT) imaging findings of large numbers of cases of medication-related osteomyelitis (MROM) and medication-unrelated osteomyelitis (MUOM) in an attempt to discover features that might differentiate the diseases. The null hypothesis stated that there are no significant differences in imaging findings between MROM and MUOM.

## MATERIALS AND METHODS

### Patients

The Seoul National University Hospital Institutional Review Board exempted this retrospective study from review (IRB066/05-19). Multidetector computed tomography (MDCT) scans and charts of patients diagnosed in Seoul National University Dental Hospital with osteomyelitis of the jaws from January 1, 2014, to December 31, 2015 were evaluated. The final diagnosis was made through the consensus of 2 radiologists on the basis of clinical, radiologic, and histologic information. MDCT examination was performed within 2 weeks from the day that the patients visited the clinic with the presence of symptoms. Recurrent lesions and cases located adjacent to previous sites of cancer surgery were excluded. Patients with site-specific causes, such as osteoradionecrosis, orthognathic surgery, and trauma, were also excluded. In total, 270 patients were accepted for the study: 83 males (30.7%) and 187 females (69.3 %). The average age was 66.6 years (females = 69.5 years and males = 60.2 years; age range 10−91 years).

### Analysis of clinical records

Each patient's electronic dental record (EDR) was reviewed to identify patient age and gender; duration of symptoms; jaw involved, with specific location in the jaw; and duration of therapy.

### Image analysis

Imaging features were analyzed on 270 MDCT images obtained from a variety of scanners, as most patients were referred from other hospitals or clinics. However, most images had been made with the Somatom Sensation 10 MDCT unit (Siemens AG, Erlangen, Germany). Imaging findings were based on the consensus reached between 2 oral and maxillofacial radiologists, with more than 15 years of experience, who conducted the imaging analyses. They retrospectively interpreted the findings by using the Infinitt picture archiving and communication system (Infinitt Healthcare, Seoul, Korea). During analysis, images were set to a window width/level of 4000/800 for hard tissue assessment and 300/45 for soft tissue analysis. The distribution of the lesions was evaluated. Hard and soft tissue changes were analyzed.

Hard tissue changes included the presence of trabecular defects, cortical defects, sclerosis, sequestra, and periosteal new bone formation. Trabecular or cortical defects represented osteolysis in the trabecular and cortical bones, respectively. Sclerosis was defined as dense trabeculation, which was mostly located adjacent to osteolytic lesions. Sequestra were classified as trabecular, cortical, and trabecular and cortical (Figure 1). The observers also measured the size of each

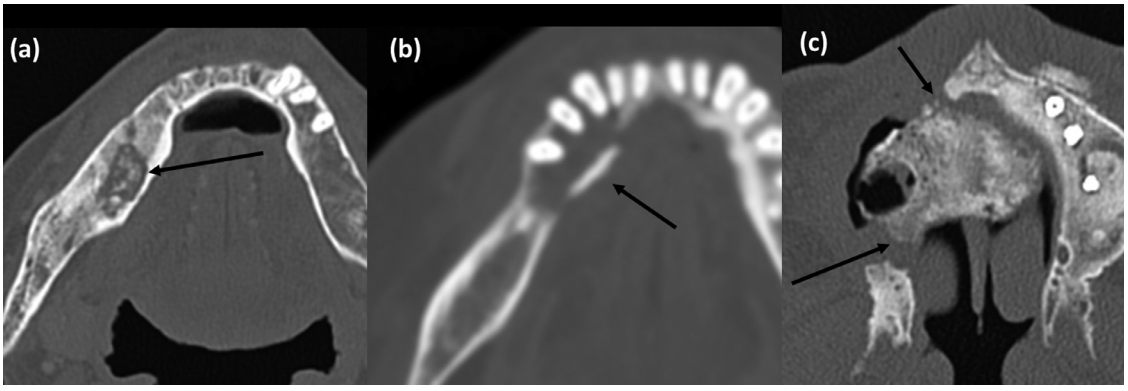


Fig. 1. Computed tomography (CT) bone window images illustrating 3 types of sequestra. **(A)** Trabecular sequestrum. **(B)** Cortical sequestrum. **(C)** Trabecular and cortical sequestrum.

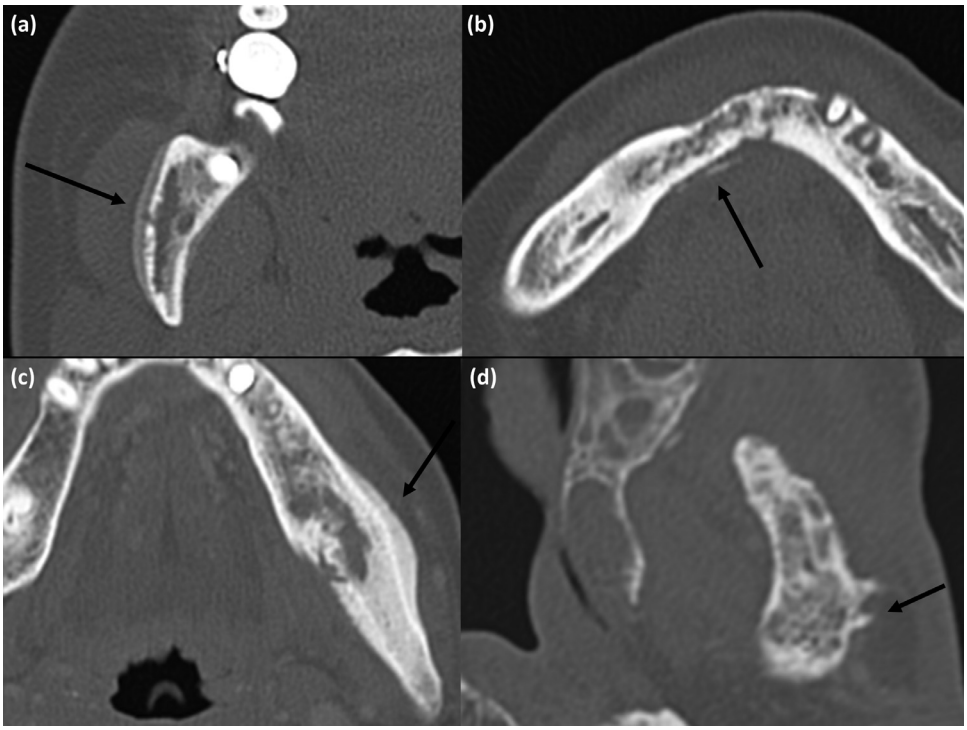


Fig. 2. Images of periosteal new bone. Computed tomography (CT) images with bone window showed 4 types of periosteal new bone formation on the related cortical bone surface. **(A)** Continuous lamellar type. **(B)** Interrupted lamellar type. **(C)** Solid type. **(D)** Spiculated type .

sequestrum. Periosteal new bone was classified as continuous lamellar, interrupted lamellar, solid, and spiculated (Figure 2). A sequestrum in association with an osteolytic lesion is illustrated in Figure 3. Soft tissue changes were evaluated on CT images for the presence of swelling, cellulitis, granulation tissue, sinusitis or mucositis, abscess, myositis, fistula, and sialadenitis.

### Statistical analysis

After the analysis of demographic and CT imaging findings, the patients were divided into 2 groups, according to their history of antiresorptive medication use: MROM and MUOM groups. Pearson's $\chi^2$ test and Student *t* test were performed to evaluate the significance of differences between the 2 groups. A *P* value less than .05 was considered statistically significant. All statistical analyses were performed by using SPSS version 21.0 (SPSS Inc., Chicago, IL).

## RESULTS

Demographic data for patients with osteomyelitis and the differences between the 2 groups are presented in Table I. Of the 270 patients, 133 patients (49.3%) had a history of antiresorptive medication (mostly bisphosphonates) use: oral administration in 108 patients (81.2%) and intravenous administration in 25 (18.8%) patients. In the MROM group, intravenous therapy was given to 3 patients with multiple myeloma,

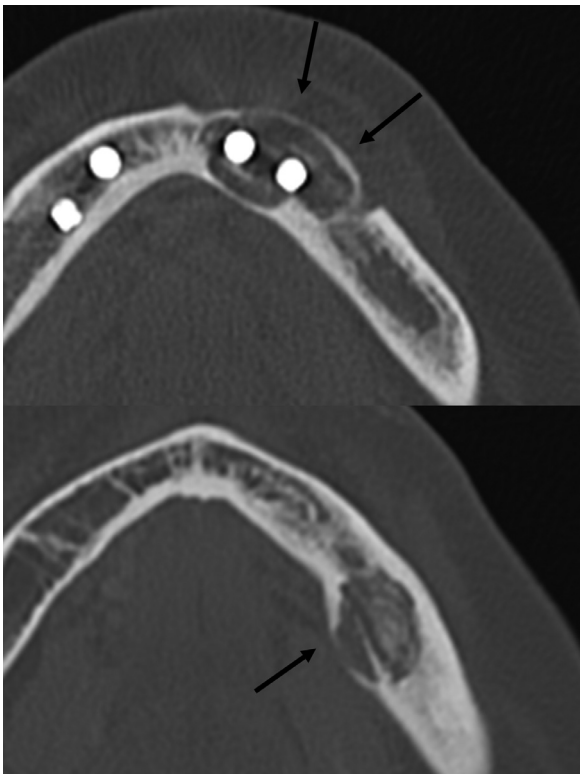

Fig. 3. Axial computed tomography (CT) bone window image demonstrates sequestrum formation within an expansile lytic lesion involving the left body of the mandible.

**Table I.** Differences between the medication-related osteomyelitis (MROM) and medication-unrelated osteomyelitis (MUOM) groups

| *Characteristic* | *MROM (n = 133)* | *MUOM (n = 137)* | *P value* |
|---|---|---|---|
| Age (years)* | 73.0 | 60.5 | < .001 |
| Gender (M:F)† | 8:125 | 75:62 | < .001 |
| Duration of symptoms (months)* | 4.2 | 4.6 | .706 |
| Jaw (maxilla: mandible) | 19:114 | 25:112 | .378 |

*By *t* test analysis.
†By Pearson's $\chi^2$ test; significant at $P < .05$.

10 patients with breast cancer, 1 patient with prostate cancer, and 11 patients with osteoporosis. The average duration of antiresorptive medication use was 4.5 years. The MROM group included patients who were significantly older ($P < .001$), and there were significantly more females in this group than in the MUOM group ($P < .001$), as shown in Table I. The average duration of symptoms for all patients was 4.3 months (range 2 days to 5 years). Most lesions were located in the mandible (maxilla:mandible; 44:226 patients). The most frequent site was the mandibular body, followed by the mandibular angle area. There were no differences in duration of symptoms or jaw location between the 2 groups ($P \geq .378$).

Imaging features and differences between the 2 groups are presented in Table II. Sequestra and periosteal new bone formation were significantly more common in the MROM group ($P \leq .043$). Twenty patients had no trabecular or cortical defects, and among them, 3 patients did not show any imaging features, such as sclerosis or soft tissue inflammation. Sequestra were observed in 168 patients, with trabecular sequestra being the most common type, followed by trabecular and cortical sequestra and cortical sequestra. There was no significant difference between the 2 patient groups in the type of sequestra ($P = .246$) or size of sequestra ($P = .760$). On the CT images of 91 patients who showed periosteal new bone formation, the continuous lamellar type was most frequently seen, and spiculated periosteal new bone was the least frequent. No significant difference in type of periosteal new bone formation was detected between the MROM and MUOM groups ($P = .066$). Signs of soft tissue inflammation were observed in 187 patients (69.3%), and swelling was the most frequent finding. The difference in soft tissue inflammation between the 2 groups was not significant ($P = .356$).

## DISCUSSION

In this study, we investigated and analyzed the CT imaging features of osteomyelitis of the jaw in a relatively large number of patients to determine the differences in imaging findings between the MROM and MUOM groups, according to patient history of antiresorptive medication use. Approximately half (49.3%) of the patients had a history of antiresorptive therapy. The average age of our cohort (66.6 years) was older than that in previous osteomyelitis studies,[17-19] and patients in the MROM group were significantly older than those in the MUOM group. Moreover, there was a significantly marked preponderance of women over men in the MROM cohort versus the MUOM group.

The number of patients receiving antiresorptive therapy is on the rise with an increase in osteoporosis and cancer in the current aging population. This is true especially for menopausal women because antiresorptive medications are widely used to treat and prevent osteoporosis, and it is not surprising that the rate of MRONJ in women is increasing. This would explain the female predominance in the MROM group compared with the MUOM group in this study. We observed most lesions in the mandible, especially in the mandibular body, which is consistent with the findings of a previous study, but the proportion of lesions in the mandible compared with the maxilla was no different in the MUOM group than in the patients taking antiresorptive medication.[18,19]

Many researchers have attempted to describe imaging findings for the diagnosis of MRONJ.[15,20-25] The use of panoramic radiography to measure widening of the periodontal ligament space was studied, but no correlation was found between the BRONJ and non-BRONJ groups.[25] Torres et al. reported that the measurement of the mandibular inferior cortical bone thickness on panoramic radiographs could be a useful tool for the detection of BRONJ.[15] One investigation examined the CT features of MRONJ compared with those of conventional osteomyelitis.[16] Taniguchi et al. suggested that measuring the cancellous bone radiodensity value on CT images has the potential to assess early changes of BRONJ.[16]

Osteolysis of trabecular and cortical bones, sclerosis, and sequestra were frequently detected in our investigation, with periosteal new bone formation being less common. When comparing the 2 groups, sequestra and periosteal new bone were significantly more frequent in the MROM group. This is consistent with the findings of previous studies.[20-22] Fatterpekar et al. reported that none of the osteomyelitis lesions in their patients showed an expansile lytic process and that expansile lytic lesions with dense central sequestra ("bone-within-bone appearance") is highly suggestive of BRONJ.[26] We looked for such changes in our study patients and found sequestra within expansile lytic bone in 7 patients, 6 of whom had received antiresorptive treatment (see Figure 3), but the sample size was too small to be statistically significant.

Wilde et al. found that periosteal new bone formation usually occurs only in sites with higher-stage

**Table II.** Summary of imaging features and differences between the medication-related osteomyelitis (MROM) and medication-unrelated osteomyelitis (MUOM) groups

| *Characteristic* | *Total number (%)* | *MROM (n = 133)* | *MUOM (n = 137)* | *P value* |
|---|---|---|---|---|
| **Hard tissue changes on CT images*** | | | | |
| Trabecular defects | 238 (88.1) | 118 (88.7%) | 120 (87.6%) | .852 |
| Cortical defects | 201 (74.4) | 105 (78.9%) | 96 (70.1%) | .124 |
| Sclerosis | 220 (81.5) | 114 (85.7%) | 106 (77.4%) | .086 |
| Sequestra | 168 (62.2) | 97 (72.9%) | 71 (51.8%) | < .001 |
| Periosteal new bone | 91 (33.7) | 52 (39.1%) | 39 (28.5%) | .043 |
| **Type of sequestra on CT images*** (n = 168) | | | | .246 |
| Trabecular | 139 (82.7) | 81 (83.5 %) | 58 (81.7%) | |
| Cortical | 5 (3.0) | 1 (1.0 %) | 4 (5.6%) | |
| Trabecular and cortical | 24 (14.3) | 15 (15.5 %) | 9 (12.7%) | |
| **Size of sequestra†** | | 10.9 mm | 10.6 mm | .760 |
| **Type of periosteal new bone on CT images*** (n = 91) | | | | .066 |
| Continuous lamellar | 50 (55.0) | 31 (59.6%) | 19 (48.7%) | |
| Interrupted lamellar | 31 (34.1) | 19 (36.5%) | 12 (30.8%) | |
| Solid | 9 (9.9) | 2 (3.8%) | 7 (17.9%) | |
| Spiculated | 1 (1.1) | 0 (0%) | 1 (2.6%) | |
| **Presence of soft tissue inflammation*** | 187 (69.3) | 96 (72.2%) | 91 (66.4%) | .356 |
| **Type of soft tissue changes on CT images** (n = 187) | | | | |
| Swelling | 129 (69.0) | 74 (77.1%) | 55 (60.4%) | |
| Cellulitis | 39 (20.9) | 14 (14.6%) | 25 (27.5%) | |
| Granulation tissue | 41(21.9) | 18 (18.8%) | 23 (25.3%) | |
| Sinusitis or mucositis | 25 (13.4) | 13 (13.5%) | 12 (13.2%) | |
| Abscess | 27 (14.4) | 9 (9.4%) | 18 (19.8%) | |
| Myositis | 13 (7.0) | 0 | 13 (14.3%) | |
| Fistula | 8 (4.3) | 2 (2.1%) | 6 (6.6%) | |
| Sialadenitis | 1 (0.5) | 0 | 1 (1.1%) | |

*By Pearson's $\chi^2$ test; significant at $P < .05$.
†By *t* test analysis.
*CT*, computed tomography.

BRONJ.[23] The large percentage of our study patients with bone abnormalities suggests that many of them had high-stage disease. Compared with the CT findings in previous studies, the presence of sequestra in our patients was significantly higher.[17,18] However, in the study conducted by Yoshiura et al., periosteal new bone was more common.[24]

MRONJ has been regarded as necrosis caused by drug toxicity. However, some believe that MRONJ could be an infectious disease. Suei used the term *bisphosphonate-related osteomyelitis of the jaw* (BROMJ) to classify osteomyelitis in patients with a history of bisphosphonate therapy; he recognized BROMJ as an advanced condition of BRONJ because infection of the jaw would occur even in cases without bone exposure.[27] We agree with Suei's assessment because most osteonecrotic lesions could occur simultaneously with inflammation due to the frequent opportunity for odontogenic infections and trauma in the oral environment. It is not hard to find patients with clinical suspicion of osteonecrosis of the jaw as well as early changes in trabecular and cortical bones and sequestra, fistula formation, periosteal responses, and involved teeth, as seen on CT images.[28] In the present study, signs of soft tissue inflammation were very common in both patient groups, and there was no significant difference in the frequency of these findings between the MROM and MUOM patients.

We conducted an analysis of CT imaging features of a relatively large number of patients with osteomyelitis and compared the findings in the MROM and MUOM groups. The ability to distinguish the pathognomonic features of MRONJ from those of osteomyelitis could facilitate early detection of MRONJ in patients who are taking antiresorptive drugs. Therefore, this study was the initial step in the prediction of MRONJ development with the use of CT images. Further studies on the radiographic features of all stages of MRONJ are required.

This study had some limitations because patient data were collected retrospectively. Patient selection was performed on the basis of imaging diagnoses, but clinical information was insufficient for accurate staging. Further research and analysis are needed to determine other possible parameters predictive of MRONJ. Such research should be prospective and include exact clinical information, such as the type and dosage of the drug and objective clinical findings, to categorize the stage of MRONJ. Previous studies have revealed greater incidence and severity of MRONJ with intravenous administration than

with oral administration of antiresorptive drugs.[27,28] In this study, however, the majority of patients in the MROM group had a history of oral administration. This could possibly explain the lack of significant differences in some of the imaging features examined.

## CONCLUSIONS

We investigated and analyzed the CT imaging features of osteomyelitis in patients with or without a history of antiresorptive medication. Sequestra and periosteal new bone formation were significantly more common in the MROM cohort than in the MUOM group. Imaging findings, especially on CT, may serve as a useful aid for the evaluation of MRONJ.

## REFERENCES

1. Baltensperger M, Eyrich G. *Osteomyelitis of the Jaws: Definition and Classification*. Berlin, Germany: Springer; 2009.
2. Prasad KC, Prasad SC, Mouli N, Agarwal S. Osteomyelitis in the head and neck. *Acta Otolaryngol*. 2007;127:194-205.
3. Tardast A, Sjoman R, Loes S, Abtahi J. Bisphosphonate associated osteomyelitis of the jaw in patients with bony exposure: prevention, a new way of thinking. *J Appl Oral Sci*. 2015;23:310-314.
4. Qaisi M, Montague L. Bone margin analysis for osteonecrosis and osteomyelitis of the jaws. *Oral Maxillofac Surg Clin North Am*. 2017;29:301-313.
5. Nicolatou-Galitis O, Schiodt M, Mendes RA, et al. Medication-related osteonecrosis of the jaw: definition and best practice for prevention, diagnosis, and treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2019;127:117-135.
6. Khan AA, Morrison A, Hanley DA, et al. Diagnosis and management of osteonecrosis of the jaw: a systematic review and international consensus. Osteonecrosis of the jaw: report from the International ONJ Task Force. *J Bone Miner Res*. 2015;30:3-23.
7. Marx RE, Tursun R. Suppurative osteomyelitis, bisphosphonate induced osteonecrosis, osteoradionecrosis: a blinded histopathologic comparison and its implications for the mechanism of each disease. *Int J Oral Maxillofac Surg*. 2012;41:283-289.
8. Hansen T, Kunkel M, Weber A, Kirkpatrick CJ. Osteonecrosis of the jaws in patients treated with bisphosphonates: histomorphologic analysis in comparison with infected osteoradionecrosis. *J Oral Pathol Med*. 2006;35:155-160.
9. Hansen T, Kunkel M, Springer E, et al. Actinomycosis of the jaws: histopathological study of 45 patients shows significant involvement in bisphosphonate-associated osteonecrosis and infected osteoradionecrosis. *Virchows Arch*. 2007;451:1009-1017.
10. Koerdt S, Dax S, Grimaldi H, Ristow O, Kuebler AC, Reuther T. Histomorphologic characteristics of bisphosphonate-related osteonecrosis of the jaw. *J Oral Pathol Med*. 2014;43:448-453.
11. Shuster A, Reiser V, Trejo L, Ianculovici C, Kleinman S, Kaplan I. Comparison of the histopathological characteristics of osteomyelitis, medication-related osteonecrosis of the jaw, and osteoradionecrosis. *Int J Oral Maxillofac Surg*. 2019;48:17-22.
12. De Antoni CC, Matsumoto MA, Silva AA, et al. Medication-related osteonecrosis of the jaw, osteoradionecrosis, and osteomyelitis: a comparative histopathological study. *Braz Oral Res*. 2018;32:e23.
13. Marx RE, Cillo JE. Jr., Ulloa JJ. Oral bisphosphonate-induced osteonecrosis: risk factors, prediction of risk using serum CTX testing, prevention, and treatment. *J Oral Maxillofac Surg*. 2007;65:2397-2410.
14. Takaishi Y, Ikeo T, Nakajima M, Miki T, Fujita T. A pilot case-control study on the alveolar bone density measurement in risk assessment for bisphosphonate-related osteonecrosis of the jaw. *Osteoporos Int*. 2010;21:815-825.
15. Torres SR, Chen CS, Leroux BG, et al. Mandibular inferior cortical bone thickness on panoramic radiographs in patients using bisphosphonates. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2015;119:584-592.
16. Taniguchi T, Ariji Y, Nozawa M, et al. Computed tomographic assessment of early changes of the mandible in bisphosphonate-treated patients. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2016;122:362-372.
17. Ida M, Watanabe H, Tetsumura A, Kurabayashi T. CT findings as a significant predictive factor for the curability of mandibular osteomyelitis: multivariate analysis. *Dentomaxillofac Radiol*. 2005;34:86-90.
18. An CH, An SY, Choi BR, et al. Hard and soft tissue changes of osteomyelitis of the jaws on CT images. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2012;114:118-126.
19. Choi SC. Clinical and radiographic analysis of 313 cases with osteomyelitis of the mandible. *Oral Radiol*. 1988;4:19-25.
20. Bagan JV, Cibrian RM, Lopez J, et al. Sclerosis in bisphosphonate-related osteonecrosis of the jaws and its correlation with the clinical stages: study of 43 cases. *Br J Oral Maxillofac Surg*. 2015;53:257-262.
21. Klingelhoffer C, Klingelhoffer M, Muller S, Ettl T, Wahlmann U. Can dental panoramic radiographic findings serve as indicators for the development of medication-related osteonecrosis of the jaw? *Dentomaxillofac Radiol*. 2016;45:20160065.
22. Treister N, Sheehy N, Bae EH, Friedland B, Lerman M, Woo S. Dental panoramic radiographic evaluation in bisphosphonate-associated osteonecrosis of the jaws. *Oral Dis*. 2009;15:88-92.
23. Wilde F, Heufelder M, Lorenz K, et al. Prevalence of cone beam computed tomography imaging findings according to the clinical stage of bisphosphonate-related osteonecrosis of the jaw. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2012;114:804-811.
24. Yoshiura K, Hijiya T, Ariji E, et al. Radiographic patterns of osteomyelitis in the mandible. Plain film/CT correlation. *Oral Surg Oral Med Oral Pathol*. 1994;78:116-124.
25. Koth VS, Figueiredo MA, Salum FG, Cherubini K. Interrelationship of clinical, radiographic and haematological features in patients under bisphosphonate therapy. *Dentomaxillofac Radiol*. 2017;46:20160260.
26. Fatterpekar GM, Emmrich JV, Eloy JA, Aggarwal A. Bone-within-bone appearance: a red flag for bisphosphonate-associated osteonecrosis of the jaw. *J Comput Assist Tomogr*. 2011;35:553-556.
27. Suei Y. Radiographic findings of bisphosphonate-related osteomyelitis of the jaw: investigation of the diagnostic points by comparison with radiation osteomyelitis, suppurative osteomyelitis, and diffuse sclerosing osteomyelitis. *Oral Radiol*. 2013;29:121-134.
28. Japanese Allied Committee on Osteonecrosis of the Jaw, Yoneda T, Hagino H, Sugimoto T, et al. Antiresorptive agent-related osteonecrosis of the jaw: Position Paper 2017 of the Japanese Allied Committee on Osteonecrosis of the Jaw. *J Bone Miner Metab*. 2017;35:6-19.

*Reprint requests:*

Jo-Eun Kim Clinical Assistant Professor
Department of Oral and Maxillofacial Surgery
Seoul National University Dental Hospital
Seoul
Republic of Korea.
noel1st@snu.ac.kr