Identifying MRONJ-affected bone with digital fusion of functional imaging (FI) and cone-beam computed tomography (CBCT): case reports and hypothesis

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Surgical debridement of medication-related osteonecrosis of the jaw (MRONJ) lesions is far less predictable than lesion resection. Margins for surgical debridement are guided by surrogate markers of bone viability, such as bleeding and bone fluorescence, which limit debridement to visibly necrotic bone. In contrast, surgical resection is extensive, including a substantial portion of surrounding bone. The concept that the MRONJ lesion is a composite of affected but viable (“compromised”) and necrotic bone is supported by histopathological data. Hence, removing only the necrotic bone during lesion debridement could inadvertently leave behind residual compromised bone in the lesion, subsequently contributing to persistence or reestablishment of the lesion. Using 2 case reports, this manuscript illustrates a novel assessment of the MRONJ lesion to enable demarcation of both the compromised and necrotic portions of the lesion. This assessment uses tumor-surface functional bone imaging data that may already be available for cancer patients with MRONJ and fuses these data digitally with computed tomography/cone-beam computed tomography imaging of the jaw obtained during MRONJ assessment. If validated, preoperative functional imaging–based assessment of the MRONJ lesion could enable surgeons to eliminate both the compromised and nonviable portions of the lesion precisely with conservative debridement, matching surgical resection in outcome. (Oral Surg Oral Med Oral Pathol Oral Radiol 2017;123:e106-e116)

To date, recommendations for conservative management of medication-related osteonecrosis of the jaw (MRONJ) have included palliative management of pain and infection in stage 0-2 lesions and limited sequestrum removal and debridement in early stage 3 lesions, with block resection recommended only for extensive stage 3 lesions, 1 although en bloc resection of MRONJ lesions of all clinical stages from 0-3 has been strongly advocated as well. 2,3

In the absence of an effective nonsurgical option, the lack of an early objective protocol for staging and assessment of MRONJ lesions and lack of definitive diagnostic criteria for early diagnosis, the current recommended protocol is to delay definitive management until the extent and severity of the lesion match the clinical criteria defining stage 3 MRONJ. 4 While the success rates of conservative treatment (including surgical debridement) regimens are poor compared to block resection, 5,7 eliminating the MRONJ lesion with block resection comes with higher morbidity and is more debilitating to the patient. 5

The major weakness of either approach is the inability to precisely delineate the extent of the lesion. Both surgical debridement and block resection are based on subjective assessments of the extent of the MRONJ lesion. Surgical debridement is guided by use of intraoperative bleeding and bone morphology as surrogate markers for bone viability. The assumption that these surrogate markers will clearly differentiate MRONJ-affected bone from bone unaffected by MRONJ may be flawed. 5 For example, surgical debridement guided by the absence of intraoperative bleeding may fail to remove MRONJ-affected but viable (perfused) bone (hereafter referred to as “compromised”). Similarly, the use of morphologic changes evident on conventional imaging to guide debridement may leave behind compromised but morphologically unaltered bone. The suggestion that not all MRONJ-affected bone is necrotic and nonperfused (and therefore nonbleeding) is supported by histopathological studies that document viable bone cells, functional and active osteoclasts, and vascular elements within the MRONJ lesion. 9-11 We hypothesize that such remnants of residual MRONJ-affected bone can be left behind because the surgeon does not have a clear demarcation of the total MRONJ lesion. The residual MRONJ-affected bone may subsequently reestablish the lesion, thereby explaining the high probability of persistence or recurrence after conservative debridement. 12,13

An alternative approach is the use of intraoperative bone autofluorescence with the VELscope to guide surgical debridement of the MRONJ lesion; however,
neither long-term outcomes nor the mechanism of action for this technique have been elucidated.\textsuperscript{3,14,15}

In contrast to the aforementioned strategies, block resection of MRONJ lesions will always include a margin of healthy bone, thus overriding the need to precisely demarcate the MRONJ-affected bone in order to eliminate it. Accordingly, while block resection is highly effective and predictable in its ability to eliminate the lesion, such a strategy is nonconservative and results in greater patient morbidity.

An optimal strategy for surgical elimination of the MRONJ lesion will ideally be conservative, yet effective and predictable. We speculate that an objective and precise delineation of MRONJ-affected bone will indeed render surgical elimination of MRONJ both effective and conservative.

Functional bone imaging (FI) is a nuclear medicine procedure that uses a hybrid imaging platform to superimpose radiolabeled tracer uptake changes with computed tomography (CT) to create a composite image from 2 different imaging modalities that can be viewed as a new registered image with more precise information, thus allowing for a more accurate diagnosis. Such a protocol is typically used to stage the disease of patients with cancer, study the response to therapy, and provide ongoing tumor surveillance.\textsuperscript{16,17}

Using 2 case reports, this manuscript seeks to illustrate the diagnostic potential of using digital fusion of existing FI data from imaging protocols such as fluorodeoxyglucose positron emission tomography ($^{18}$FDG-PET/CT) and technetium-labeled bisphosphonate bone scan ($^{99}$Tc-MDP-bone scan) with single photon emission CT (SPECT), combined with cone-beam CT (CBCT) imaging obtained during patient assessment, to produce FI/CBCT composite images that allow us to visualize both the necrotic and compromised zones within the MRONJ lesion. Using this technique for lesion assessment and surgical planning may allow the surgeon to demarcate the MRONJ lesion in a comprehensive manner before surgery, thereby optimizing the ability to eliminate the entire lesion without the need for block resection.

FI imaging performed during tumor surveillance routinely captures tracer uptake data in the jaw region. During such assessment, non–tumor-related jaw tracer uptake is usually interpreted by the radiologist as dental infection, not necessarily MRONJ, as the occasional case may be. Patients with cancer who develop MRONJ secondary to treatment of bone metastases typically have a series of FI studies such as PET/CT and/or SPECT/CT as part of ongoing tumor surveillance imaging. Using FI tumor surveillance imaging data available from previous cancer studies could enable a comprehensive and meaningful assessment of MRONJ lesions in such patients with minimal additional radiation burden.

In this manuscript, we correlate the successful surgical debridement of an MRONJ lesion corroborated by 8-month follow-up data in such a patient, with complete elimination of the lesion as delineated by this fusion protocol.

**MATERIALS AND METHODS**

**CBCT imaging protocol**

The icat Next Generation CBCT machine (Imaging Sciences International, Hartfield, PA, USA) was used with the following settings: tube voltage 120 kVp, tube current 3-7 mA, slice thickness 1.8 mm, voxel size 300 μm, with contrast adjusted for optimal viewing.

**Protocol for fusion of FI and CBCT of the jaws**

The FI/CBCT image was created by digital fusion of imaging DICOMs from FDG-PET/CT, SPECT/CT, and CBCT, with the aid of MIM 6.3.4 software (MIM Software, Cleveland, OH, USA). This medical imaging software routinely used in radiology and nuclear medicine applications was used to set up a semiautomated workflow macro that permitted manual alignment of the CBCT with the low-dose CT component of the PET/CT and SPECT/CT by aligning corresponding anatomic landmarks (http://www.mimsoftware.com/products/radnuc/). This process juxtaposed the CBCT images with the FI images in a manner similar to the original low-dose CT component of the PET/CT and SPECT/CT. The fused FI/CBCT DICOM file can then be secondarily manipulated with InVivo Anatomage (Anatomage, San Jose, CA, USA) as needed to generate custom oblique slices.

Institutional review board approval was granted for the retrospective analysis of imaging (Pro 2013003217) and for compiling the case reports.

**CASE REPORT 1**

A 69-year-old Caucasian man diagnosed with metastatic multiple myeloma was referred for evaluation of an MRONJ lesion in the mandible. He reported discomfort in his right lower jaw that was compounded by the rough texture of the exposed bone abrading his tongue, causing tenderness. The patient was taking a regimen of levofloxacin and pain medications.

The patient had history of 2 failed stem cell transplants, before which he had received intravenous bisphosphonate therapy for nearly 18 months. After a recent single infusion of zoledronate, he developed MRONJ. Zoledronate therapy was later discontinued.

Clinical evaluation revealed a 1 × 0.5 cm linear exposure of the lingual cortex along the mylohyoid ridge on the right side (Figure 1). The exposed bone appeared necrotic, and the soft tissue margins were tender to touch. The patient was diagnosed with stage 2 MRONJ (“exposed and necrotic
bone associated with infection as evidenced by pain and erythema in the region of exposed bone with or without purulent drainage. Available tumor surveillance FI imaging (18FDG-PET/CT and SPECT/CT) revealed tracer uptake in the region of the MRONJ lesion in the jaw (Figure 2). The CT imaging from the tumor surveillance imaging FI was obtained at a lower milliamperage (80-100 mA) and higher slice thickness (5 mm) compared with CT imaging obtained specifically for diagnostic purposes. This was because the CT component was primarily obtained for attenuation correction (standard procedure to correct distortion and artifacts in PET and SPECT imaging) and anatomic correlation (for spatial alignment of tracer uptake in the body with anatomic landmarks obtained from the CT) in the original hybrid imaging and not for diagnostic purposes. This low-dose protocol routinely enables a substantial reduction in patient radiation dose from CT from 11-30 mSv to 0.5-6 mSv. Furthermore, the CT images are smoothed to match the PET resolution before generation of PET attenuation correction factors. Consequently, CT images taken for attenuation correction are many times noisier than diagnostic CT images; such low-dose CT obtained for attenuation correction is not acceptable for diagnostic interpretation.

In contrast, CBCT imaging of the jaws obtained for assessment of MRONJ lesions renders high-resolution image slices that compensate for the lack of anatomic definition in the surveillance image (Figure 3). The imaging DICOMs from the 2 surveillance hybrid images (18FDG-PET/CT and SPECT/CT fusions) were virtually aligned and overlaid with the CBCT image of the MRONJ lesion to generate the FI/CBCT composite image (as described in the Materials and Methods section). The resultant FI/CBCT composite image clearly delineates what we believe to be the extent of the MRONJ lesion (Figure 2A and 2B).

Unfortunately, the patient succumbed to respiratory complications before any definitive management of the lesion could be initiated; hence, it was not feasible to have histopathological corroboration for our interpretation.

CASE REPORT 2
A 78-year-old African American man diagnosed with metastatic prostate cancer was referred for evaluation of an MRONJ lesion in the mandible. The patient was being treated with leuprolide and denosumab injections every 3 months for over 1 year.

He reported that over a year previously, he had developed spontaneous exposure of bone in the lower left side of the jaw. He later developed pain and discomfort in this region and subsequently experienced loosening of his molars in the same region 2 months later. These teeth were extracted. To address his persistent pain and discomfort, he underwent debridement of the exposed bone. Over a period of observation, the region of exposed bone widened and remained nonresponsive to management with chlorhexidine mouth rinse and an oral clindamycin antibiotic regimen. Eventually, the patient was referred to Rutgers School of Dental Medicine for evaluation and management.

Upon clinical examination, it was noted that the patient’s MRONJ lesion clinically extended linearly along the mylohyoid ridge on the lingual shelf of the mandible. Exposed necrotic bone was surrounded by peripheral erythema and tender, friable mucosa with a tendency to bleed upon palpation (Figure 4). The patient’s pain and discomfort precluded a more detailed examination. The patient was diagnosed with stage 2 MRONJ. The panoramic radiograph revealed sclerotic unremodeled old extraction sockets of teeth 17, 18, and 19 (Figure 5, top panel, left). CBCT imaging confirmed surrounding sclerotic bone in the area of the extractions, accompanied by rarefied areas, yielding ill-defined areas of variable bone density (“moth-eaten appearance”), consistent with MRONJ or osteomyelitis (Figure 5, top panel, right).

Available tumor surveillance FI imaging (18FDG-PET/CT and SPECT/CT) was retrieved and digitally fused to a new CBCT image (less than 3 months had elapsed between FI and dental imaging). Tracer uptake for 18FDG and 99MDP in the region of the lesion revealed nearly nonoverlapping patterns (Figure 5, middle panel). FDG uptake was limited to the lingual shelf of the mandible that was starting to sequester from the dentoalveolar region and body of the mandible (standard uptake value = 6.7) (Figure 5, middle panel, left). In contrast, MDP uptake was intense in the buccal cortex and body of the mandible surrounding the area of exposed bone, suggesting that this region was vital and undergoing remodeling (Figure 5, middle panel, right). From this information, we predicted that the MRONJ lesion was likely limited to the lingual cortex that was beginning to sequester. Although this region was vital (perfused), FDG tracer uptake suggested ongoing inflammatory activity; in addition, the region was only minimally remodeled, given the near absence of tracer uptake on SPECT imaging. We predicted that selective removal of this portion of the bone alone would be successful.

The patient underwent limited marginal mandibulectomy to remove the sequestering bone (Figure 5, lower panel, left). The extent of empirical surgical debridement coincided with the region identified as the MRONJ lesion based on our FI imaging analysis protocol. Although our FI/CBCT digital fusion analysis, being experimental, could not dictate surgical debridement, it fortuitously corresponded to the
region that would be removed by empirical surgical debridement guided by exposed bone. Histopathological analysis confirmed osteomyelitic changes consistent with MRONJ (Figure 5, lower panel, middle). After surgery, the patient experienced rapid alleviation of pain and discomfort, and he continued to remain asymptomatic at 8-month follow-up (Figure 5, lower panel, right).

DISCUSSION
Role of imaging in assessing and managing MRONJ
The fundamental obstacle preventing precise demarcation of the MRONJ lesion is the lack of a sensitive and specific tool to enable such an assessment. Several imaging strategies have been evaluated for diagnostic assessment in MRONJ, ranging from plain film radiographs to CT, magnetic resonance imaging, and FI.24 Intraoral and panoramic radiographs are the imaging modalities most commonly used. These 2 modalities lack sensitivity in identifying the true MRONJ lesion, in both severity and extent.25,26, furthermore, a substantial change in bone mineralization/architecture is required to visualize actual radiographic changes in the bone.26,27 3-D imaging with multidetector or CBCT, although valuable for surgical planning, similarly only documents altered bone architecture and bone mineralization patterns, likely leading to misrepresentation of the extent of the entire MRONJ lesion.28 Neither plain radiographs nor CT images have the sensitivity and specificity needed to detect bone vitality and health.4,24,29-32 Therefore, either 2-D or 3-D anatomic imaging alone may not precisely outline the actual MRONJ lesion. Although magnetic resonance imaging has high specificity for soft-tissue changes, it is often difficult to clearly distinguish between necrotic bone and reactive signal changes in the bone marrow secondary to inflammation.31

FI with 18FDG-PET/CT and Tc-MDP-bone scan with SPECT/CT provide a sensitive 3-D measure of inflammatory changes and concomitant bone remodeling, respectively.33-35 FI using hydroxyapatite-homing tracers, such as sodium fluoride (NaF) or bisphosphonate, reveals bone remodeling activity, and the FDG

Fig. 2. Functional imaging (FI)/cone-beam computed tomography (CBCT) in assessment of the medication-related osteonecrosis of the jaw lesion in case report 1. A. Composite of FI and CBCT findings. Panel A: CBCT changes. Hyperostotic bone in the region of missing nos. 29 and 30 in the panoramic reconstruction, bone sequestration in right mylohyoid ridge corresponding to missing no. 29, mesial portion of no. 30. Panel B: Fluorodeoxyglucose positron emission tomography (FDG-PET) uptake in the region immediately posterior to the sequestrum. Panel C: Diffuse single photon emission computed tomography (SPECT) uptake includes the region demonstrating FDG uptake, minimal overlap with the region identified as abnormal using CBCT; excludes a considerable portion of the region with altered appearance on CBCT. Lower panel: Use of InVivo Anatomage CBCT viewing software to display FI/CBCT fusion imaging facilitates interpretation in oblique slices. B, Three-dimensional reconstruction of mandible depicting differential overlap of the 3 imaging modalities in FI/CBCT.
Tracer is primarily taken up by infiltrating leukocytes (in a nononcologic context), functioning as an indicator of inflammatory activity. The exact pathophysiology of MRONJ is currently unclear, but it is widely accepted that both dysregulated bone remodeling and the immune response to the polymicrobial biofilm play fundamental roles in its pathogenesis. Hence, FI may prove useful in describing and assessing MRONJ lesions.

Evaluating MRONJ lesions by using FI is not new. Established lesions display altered tracer uptake upon functional imaging. Currently, each modality in FI is being evaluated in isolation, making it difficult to interpret all the individual FI imaging findings. We propose that detailed examination of the relationship between partial/nonoverlapping uptake of radiolabeled tracers with each of these FI scans, as well as the

Fig. 3. Comparison of image resolution with cone-beam computed tomography (CBCT) (top panel) versus low-dose computed tomography (bottom panel) used for anatomic correlation and attenuation correction in hybrid positron emission tomography (PET)/CBCT: axial, sagittal, and coronal slices.

Fig. 4. Case report 2: Medication-related osteonecrosis of the jaw lesion extending linearly along the mylohyoid ridge on the lingual shelf of the mandible. (Courtesy of Dr. Mahnaz Fatahzadeh, Division of Oral Medicine, Rutgers School of Dental Medicine.)
occasional lack of FDG uptake in well-established MRONJ lesions, facilitated by the FI fusion protocol described below, will provide important insights into bone remodeling dynamics in MRONJ when the multiple FI scans are examined concurrently.

The potential benefits of FI in MRONJ imaging when the protocol is applied are as follows (Figure 6):

1. Combined interpretation of both modalities of FI, that is, concomitantly assessing both bone remodeling (99mTc-MDP-SPECT or NaF-PET) and inflammatory activity (18FDG-PET), allows comprehension of the biological implications of the composite uptake.

2. Interpreting the digital fusion of FI with dental CBCT (FI/CBCT) synthesizes digital data from 2 individual studies, CBCT and FI, thereby integrating the anatomic precision of CBCT with the functional information of FI to precisely define areas of bone affected by MRONJ. FI is conventionally generated using low-dose CT for anatomic correlation, which lacks the resolution that dental CBCT can provide.

Interpretation of the composite FI/CBCT images is based on the following interpretational metric:

1) Regions within the MRONJ lesion with bone necrosis will not demonstrate uptake on either FDG-PET or SPECT imaging (yellow arrows in Figure 2A, blue outline above overlapping green region in Figure 2B).

2) The actual MRONJ lesion likely encompasses the combined region of necrotic bone and the region of 18FDG uptake (yellow and red arrows in Figure 2A, yellow outline in Figure 2B). In the case of the patient with metastatic prostate cancer and MRONJ (case report 2), there appeared to be no distinct region of necrotic bone in the MRONJ lesion, given its tracer uptake pattern. Considering that the

Fig. 5. Case report 2: Imaging findings, surgical specimen, histopathology, and follow-up. Top panel, left: Panoramic radiograph demonstrating sclerotic unremodeled extraction sockets of nos. 17, 18, and 19. Top panel, right: Cone-beam computed tomography (CBCT) imaging confirming hyperostotic bone in the area of the dental extractions. Middle panel: Functional imaging/CBCT composite of tumor surveillance imaging digitally superimposed with CBCT demonstrating fluorodeoxyglucose positron emission tomography (FDG-PET) (left) and MDP—single photon emission computed tomography (right) uptake along the lingual and buccal cortices, respectively. Lower panel: Surgical debridement limited to the clinically diseased lingual cortical region, also demarcated by FDG-PET uptake (left), histopathology of the medication-related osteonecrosis of the jaw (MRONJ) lesion demonstrating osteomyelitic changes and microorganisms consistent with actinomyces, consistent with MRONJ (middle) and 8-month follow-up clinical picture documenting sustained resolution of the MRONJ lesion (right).
lingual shelf was still continuous with the parent bone, it probably remained perfused and hence vital, albeit with minimal remodeling activity (Figure 5, middle panel, left).

3) SPECT imaging reflects increased remodeling activity in both vital medication/bisphosphonate-affected bone within the MRONJ lesion and reactive healthy perilesional bone. This explains the observation that SPECT (or $^{18}$NaF-PET) tracer uptake is usually more extensive than the lesion’s uptake of $^{18}$FDG.31 Thus, the actual MRONJ lesion excludes perilesional remodeling (green arrows in Figure 2A, green region outside of overlapping red region in Figure 2B). This is evident only with concomitant $^{18}$FDG-PET and SPECT FI images. Viewing the resultant fusion images with the dental CBCT imaging software (yellow arrow, lower panel, Figure 2A) appears to facilitate data interpretation compared with the medical CT imaging software (yellow arrow, second panel, Figure 2A). In the case of the patient with metastatic prostate cancer with MRONJ, the entire MDP tracer uptake was limited to bone that revealed no FDG uptake, suggesting that this uptake entirely denoted perilesional remodeling and hence was normal bone tissue (Figure 5, middle panel, right).

Thus, understanding the biologic events depicted by the various fused FI/CBCT scans for each modality of imaging described—anatomic imaging with CT or CBCT, functional nuclear imaging with FDG-PET, and bone scan/SPECT—could likely be the key to discerning the dynamics of the MRONJ lesion (Table I and Figure 7).

The combined presence of viable (“compromised”) and necrotic regions in the bone associated with the MRONJ lesions, as suggested by functional imaging described, is consistent with the histopathological appearance of these lesions,10 and our model for its pathogenesis centered on dysfunctional bone remodeling.37 This is in contrast to the traditional perception (reinforced by nomenclature) that the ONJ lesion is entirely necrotic, which prompted the use of surrogate markers of bone viability to guide surgical debridement.

The presence of inflammatory infiltrates in MRONJ lesions has been extensively described in histopathological assays.11 MRONJ shares several histopathological similarities to osteomyelitic lesions of the jaw. In osteomyelitis, FDG-PET imaging is the gold standard for diagnosis as well as for documenting its resolution.10,33 Similarly, histopathological studies also confirm ongoing bone remodeling within the viable (compromised) regions of MRONJ lesions, consistent with tracer uptake demonstrated by SPECT/CT and bone scans (scintigraphy).33 Established MRONJ lesions display altered tracer uptake in functional imaging.33,35,50,41,43 The tracer uptake on each of these imaging modalities often appeared to highlight partially nonoverlapping or completely distinct regions of the bone in certain instances.18 However, what was initially thought of as inconsistent FI tracer might actually be a reflection of the biological status of the MRONJ lesion.

Based on earlier observations, we hypothesize that the uptake patterns with FI in MRONJ may be varied, dynamic, and evolving over time/lesion severity, and may additionally explain the seemingly erratic and unpredictable response to surgical debridement guided by surrogate markers of bone viability such as bleeding in bone (Figure 8, left panels). Varying degrees of overlap between FDG and MDP (or NaF) uptake patterns over time may represent changing dynamics...
between reactive remodeling in perilesional bone and MRONJ lesions, with the development of necrosis further affecting patterns of uptake. Progressive necrosis (increasing in extent with time) may be accompanied by diminishing FDG uptake as well as reduced overlap patterns when compared longitudinally. These uptake patterns may have potential value in following patients with MRONJ.

Table 1. Information synthesis with functional imaging/cone-beam computed tomography compared to individual imaging modalities

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<th>Imaging modality</th>
<th>What is detected</th>
<th>How missed information is complemented by additional modality</th>
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| 3-D imaging with CT or CBCT   | Altered appearance due to sequestration/trabecular pattern or mineralization changes  
   - Differentiates vital and necrotic (dead) lesion bone only if altered in morphology  
   - Normal reactive bone around the lesion may also be altered in morphology | 1. Misses early lesion ahead of morphology changes (needs FDG)  
2. Cannot delineate vital from necrotic and reactive from lesion bone (needs comparison with FDG + SPECT imaging) |
| FDG-PET imaging               | Inflammatory uptake by white blood cells/ cells with increased glycolytic activity  
   - Vital lesion bone (compromised)                                                      | 1. Early lesion can be picked up ahead of CBCT/CT changes  
2. Misses necrotic part of lesion (needs SPECT and CBCT or CT as explained above and below) |
| Bone scan with 3-D SPECT       | Increased remodeling activity in bone  
   - Vital lesion bone  
   - Normal reactive bone around lesions                                                   | 1. Can delineate non-FDG avid region into vital and necrotic lesion bone (complements CBCT/CT and FDG imaging)  
2. Within vital bone, comparison with FDG uptake delineates reactive and lesion bone |

CT, computed tomography; CBCT, cone-beam computed tomography; FDG, fluorodeoxyglucose; SPECT, single photon emission computed tomography; PET, positron emission tomography.

Fig. 7. Algorithm to delineate vital and nonvital portions of the medication-related osteonecrosis of the jaw lesion using functional imaging/cone-beam computed tomography fusion.
longitudinally to monitor lesion severity and in planning surgical intervention (Figure 8, left panels). Figure 8, pattern 1 depicts a likely early lesion, with no clinical evidence of necrotic bone, yet symptomatic (stage 0). In the case of a lesion with bone remodeling dynamics as depicted in Figure 8, pattern 2, mere targeted removal of bone that appears necrotic clinically may leave behind residual lesion, resulting in an unpredictable outcome compared with surgical resection that includes adequate margin of surrounding bone. In such a situation, the need for a predictable outcome dictates a wider surgical resection than limited surgical debridement. It is precisely in such a situation that precise delineation of the MRONJ lesion using our prescribed protocol could optimize the outcome after conservative debridement.

Finally, these FI uptake patterns may have potential value in the future for monitoring treatment response in patients with MRONJ during treatment with a therapeutic agent. From our current findings, we propose that by providing a remodeling stimulus with an osteoanabolic medication such as teriparatide, it may be possible to initiate healing of the compromised bone with concomitant replacement of the dead bone in the MRONJ lesion, resulting in resolution of MRONJ (Figure 8, right panels).37,44 Short of a therapeutic agent capable of resolving osteonecrosis, we are limited to aiming for complete...
surgical elimination of the MRONJ lesion in order to manage it successfully.

In conclusion, this manuscript describes the innovative use of existing yet underutilized jaw uptake information from routine tumor surveillance imaging in combination with CBCT imaging to provide a high-resolution, 3-dimensional analysis of MRONJ lesions. Obtaining a limited-volume CBCT encompassing the region of the jaw lesion will help minimize additional radiation exposure for the patient. Given that the majority of MRONJ lesions occur in patients with metastatic cancer, ongoing tumor surveillance imaging may be readily available for the imaging analysis described. The novel assessment of the MRONJ lesion described in this manuscript involves synthesizing and interpreting functional imaging information by fusing PET/CT and SPECT/CT DICOM data with CBCT DICOM data. Such composite image analysis provides high-resolution, anatomically accurate image with interpretative insight into the dynamics of bone viability, bone remodeling, and inflammatory activity in MRONJ lesions. We hypothesize that analyzing such lesions in this manner accurately delineates healthy bone from regions of necrosis and MRONJ involvement, giving us a better visual cue for gauging the true extent/severity of the lesion. Hence, we predict that, if validated, this new FI/CBCT protocol will greatly facilitate surgical planning by demarcating the total MRONJ lesion. With this detailed image information, we envision the design and printing of a 3-D surgical guide to provide surgeons with a definitive surgical plan, aiding in patient management in the future.

REFERENCES


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