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Abstract: **OBJECTIVE** The aim of this study was to compare bone imaging between ultrashort echo-time (UTE) magnetic resonance (MR) imaging and cone-beam computed tomography (CBCT) as the reference standard in patients with medication-related osteonecrosis of the jaw (MRONJ). **MATERIALS AND METHODS** A 1-year retrospective, blinded, and randomized qualitative analysis of UTE MR images and CBCT from 19 patients with clinically diagnosed MRONJ was performed by 2 independent radiologists. Medication-related osteonecrosis of the jaw imaging hallmarks such as osteolysis, periosteal thickening, and medullary osteosclerosis were rated visually (0 and 1 to 3 for normal and mild to severe changes) for defined anatomic regions of the jaw. In addition, segmentation of these regions was performed on coregistered MR/CBCT images for the following quantitative comparison of signal intensity (SI) on MR and gray values (GVs) on CBCT images. Interreader/modality agreement (Cohen kappa), standard testing for significant differences of (non)parametric values, and Pearson correlation of signal intensity/GV were used for statistical analysis. **RESULTS** The anterior corpus of the mandible was most often affected by MRONJ ($P < 0.001$). Overall, interreader agreement of qualitative MRONJ hallmark scores was almost perfect ($\kappa = 0.81$) and without significant differences between modalities ($\kappa = 0.81$ vs 0.82 , CBCT vs MR, respectively). Intermodality agreement for qualitative gradings was substantial for both readers ($\kappa = 0.77$ and 0.70). Signal intensity/GV in MRONJ-affected areas differed significantly from healthy bone ($P < 0.001$) as well as correlation significantly between modalities ($r = -0.77$; $P < 0.001$). **CONCLUSIONS** Qualitative assessment of MRONJ with radiation-free UTE MR imaging is comparable to reference standard CBCT. Quantitative measurements of both modalities significantly distinguish diseased from normal bone with strong correlations among the quantitative values in both modalities.

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Medication-Related Osteonecrosis of the Jaw—Comparison of Bone Imaging Using Ultrashort Echo-Time Magnetic Resonance Imaging and Cone-Beam Computed Tomography

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Objective: The aim of this study was to compare bone imaging between ultrashort echo-time (UTE) magnetic resonance (MR) imaging and cone-beam computed tomography (CBCT) as the reference standard in patients with medication-related osteonecrosis of the jaw (MRONJ).

Materials and Methods: A 1-year retrospective, blinded, and randomized qualitative analysis of UTE MR images and CBCT from 19 patients with clinically diagnosed MRONJ was performed by 2 independent radiologists. Medication-related osteonecrosis of the jaw imaging hallmarks such as osteolysis, periosteal thickening, and medullary osteosclerosis were rated visually (0 and 1 to 3 for normal and mild to severe changes) for defined anatomic regions of the jaw. In addition, segmentation of these regions was performed on coregistered MR/CBCT images for the following quantitative comparison of signal intensity (SI) on MR and gray values (GVs) on CBCT images. Interreader/modality agreement (Cohen kappa), standard testing for significant differences of (non)parametric values, and Pearson correlation of signal intensity/GV were used for statistical analysis.

Results: The anterior corpus of the mandible was most often affected by MRONJ ($P < 0.001$). Overall, interreader agreement of qualitative MRONJ hallmark scores was almost perfect ($\kappa = 0.81$) and without significant differences between modalities ($\kappa = 0.81$ vs 0.82 , CBCT vs MR, respectively). Intermodality agreement for qualitative gradings was substantial for both readers ($\kappa = 0.77$ and 0.70). Signal intensity/GV in MRONJ-affected areas differed significantly from healthy bone ($P < 0.001$) as well as correlation significantly between modalities ($r = -0.77$; $P < 0.001$).

Conclusions: Qualitative assessment of MRONJ with radiation-free UTE MR imaging is comparable to reference standard CBCT. Quantitative measurements of both modalities significantly distinguish diseased from normal bone with strong correlations among the quantitative values in both modalities.

Key Words: bisphosphonate-related osteonecrosis of the jaw, cone-beam computed tomography, magnetic resonance imaging

(Invest Radiol 2019;00: 00–00)

Medication-related osteonecrosis of the jaw (MRONJ) is an adverse side effect of different types of antiresorptive agents, most commonly bisphosphonates and denosumab, which are routinely used to prevent and reduce the risk of fracture in osteoporosis patients as well as skeletal related events in metastatic cancer patients.¹ Recently, several

targeted therapies including antiangiogenic medication (eg, bevacizumab), tyrosine-kinase inhibitor (eg, sunitinib), and mammalian target of rapamycin (mTOR) inhibitor have been associated with an increased risk of MRONJ when used alone or in combination with antiresorptive medications. The list of associated medications is constantly growing, and it is estimated that a large number of cases remain undiagnosed.^{2–6} Despite a substantial increase in the prevalence of MRONJ in recent years,^{7–9} the overall awareness for this condition is still moderate in the medical community, often leading to advanced stages of the disease at first diagnosis and initiation of targeted therapy.¹⁰

Diagnosis of MRONJ depends on patient history and clinical features, as defined by the American Association of Oral and Maxillofacial Surgeons (AAOMS).⁵ Overt jaw bone exposure or positive bone-probing fistula is a prerequisite for a correct diagnosis.⁵ As of today, imaging plays a major role in diagnosis and assessment of disease extension for MRONJ patients, especially in patients without exposed necrotic bone according to the AAOMS. In these patients, subtle radiologic signs, for example, focal osteolysis, widening of the alveolar socket, or thickening of the lamina dura, may precede bone exposure and indicate an increased risk for the development of MRONJ.¹¹

X-ray-based modalities traditionally perform best for bone depiction with panoramic radiographs (PRs) as a first-line imaging modality, followed by cone-beam computed tomography (CBCT) for comprehensive depiction of the jaw in 3-dimensional (3D). In more advanced stages, imaging is required in order to determine disease extent and possible complications. Magnetic resonance imaging is optimal for assessing soft tissue involvement and nerve integrity¹² but lacks the high contrast of bone depiction by PR and CBCT.

Comparison of different imaging modalities in the same MRONJ patients have shown different disease extents,¹³ as different modalities were used to investigate different disease aspects, for example, osseous changes in PR or CBCT versus metabolic/soft tissue changes in positron emission tomography–CT or magnetic resonance (MR).^{13–15} Recent advances in MR with application of ultrashort echo-time (UTE) sequences allow for signal detection in structures with very short echo-time, for example, ligaments, joints, and bones that are usually devoid of signal on standard MR sequences. These UTE techniques have thus sparked new interest in using MR not only for evaluation of disease extent and soft tissue involvement but in addition as a possible alternative to x-ray-based imaging for bone depiction, that is, PR and CBCT, without the use of ionizing radiation.^{16–18}

The aim of this study was to test whether UTE MR could replace CBCT as the reference standard regarding bone imaging in patients with MRONJ.

MATERIALS AND METHODS

Patient Population

A 1-year retrospective evaluation of MR and CBCT scans of patients with clinically diagnosed MRONJ according to AAOMS criteria was performed (Fig. 1). Patients had to have been imaged with the

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FIGURE 1. Differences between medication-related osteonecrosis of the jaw disease extent in clinical examination of the oral cavity and in ultrashort echo-time magnetic resonance. The figure represents an individual with visually overt medication-related osteonecrosis of the jaw (A), which matches perfectly with osteolytic regions (arrowheads) in ultrashort echo-time magnetic resonance (B, inverted MIP reconstruction for better visualization) and in cone-beam computed tomography (C).

clinical standard MR protocol for MRONJ assessment of our institution and additional preoperative reference CBCT. The 2 image modalities had to have been acquired within less than 2 months of each other.

Data search was performed via the internal PACS systems (synedra View; synedra information technologies Ltd, Innsbruck, Austria; and IMPAX 6; Agfa-Gevaert N.V., Mortsels, Belgium) and the hospital information system (blinded). All patients that had not received either the CBCT or the MR examination, or that had undergone oral surgery before any of the imaging examinations, were excluded.

The study was approved by the institutional review board and the local ethics committee (blinded) and conducted in accordance with the Declaration of Helsinki. A written general consent for further use of clinical data for scientific purposes was obtained from each patient.

Magnetic Resonance Imaging

All MR examinations were performed on a 3 T MR unit of the latest generation (Siemens Skyra 3.0 T; Siemens Healthineers, Erlangen, Germany) using a 64-channel head coil (dto.) and the clinical standard protocol for MRONJ assessment (including an axial T1-weighted turbo spin echo; a coronal T1-weighted turbo spin echo; an axial fat-saturated, fluid-sensitive turbo inversion recovery magnitude; and a diffusion-weighted MR sequence). Imaging parameters of the respective sequences are listed in Supplementary File 1, Supplemental Digital Content 1, <http://links.lww.com/RLI/A480>. For virtual bone imaging, a vendor-specific UTE MR sequence using pointwise encoding time reduction with radial acquisition was used (“PETRA,” Siemens Healthineers), as listed in Table 1.¹⁹

CBCT Imaging

For CBCT, a state-of-the-art machine for oro-maxillofacial imaging was used (J.Morita 3D Accuitomo 170; J.Morita Europe Ltd, Dietzenbach, Germany). For CBCT machine and imaging parameters, refer to Table 1.

Qualitative Readout

All images were fully anonymized with regard to patient-specific data before readout. All image series were assessed qualitatively by 2 independent radiologists (with 2 and 12 years of MR experience, respectively), regarding osteolysis, periosteal thickening/apposition, and medullary osteosclerosis²⁰ (see Fig. 2). Each aspect was rated on a 4-point Likert scale (0 to 3, for “normal findings,” “mild changes,” “moderate changes,” and “severe changes”). Five predefined anatomic regions were rated in the mandible and 2 in the maxilla on each side: anterior corpus of mandible (aMa, ie, comprised between mental foramina), posterior corpus of mandible (pMa, between mental foramen and angle of the mandible), ramus mandibularis (rMa), condyloid process of mandible (conMa), coronoid process of mandible (corMa), anterior maxilla (aMx), and posterior maxilla (pMx) of the left and right side. The respective anatomical borders were chosen according to characteristic anatomic landmarks¹⁵ as explained and visualized in Figure 3 (an animated 3D model is presented in Supplementary File 3, Supplemental Digital Content 3, <http://links.lww.com/RLI/A481>). Moreover, anatomic regions with severe susceptibility artifacts leading to nondiagnostic quality were noted as such (“not assessable” vs otherwise “assessable”).

Quantitative Readout

Comparison of quantitative values required previous coregistration of each pair of imaging examinations per patient. Both image series were interpolated to an isovolumetric spatial resolution of 0.5 × 0.5 × 0.5 mm³. Coregistration of the image series was performed by rigid registration of 3 manually defined anatomic landmarks (ie, anterior pole of mandible and most craniodorsal aspects of bilateral conMa) and subsequent manual visual fine tuning (Fig. 3). The CBCT dataset was used as the fixed image, whereas the MR dataset was the moving image.²¹ The coregistration process was performed using proprietary medical image processing software (PMOD v. 3.505; PMOD

TABLE 1. Parameters of CBCT and UTE MR Image Acquisition and Reconstruction Parameters of Coredgistered CBCT/UTE MR Data

CBCT (J.Morita 3D Accuitomo 170)		UTE MR “PETRA” (Siemens Magnetom Skyra)	
Tube setting	90 kV/5 mA	Field strength	3.0 T
Voxel size	0.250 mm ³	Voxel size	0.6989 mm ³
CTDI (mGy)	8.61 ± 0.49	TE	0.07 ms
DAP (mGy·cm ²)	2283 ± 378	TR	5 ms
Field of view	170 mm diameter	Field of view	246 mm
Acquisition time	17.5 s	Acquisition time	315 s
		Coil	64-channel head
		Base resolution	352
		Radial acquisitions	60,000
		Bandwidth	355 Hz/Px
		Interpolation to 0.5 mm ³	

Coregistration options

CBCT indicates cone-beam CT; UTE, ultrashort echo-time.

FIGURE 2. Visual hallmarks of medication-related osteonecrosis of the jaw. Qualitative findings are illustrated on ultrashort echo-time magnetic resonance images (left column) and on cone-beam computed tomography images (right column). The exemplary multiplanar reconstructions show a disease affected left mandible (corpus and ramus): Oblique sagittal (A and B), axial (C and D), and coronal (E and F) reconstructions show diffuse medullary osteosclerosis (asterisks in panels A and B), osteolysis (arrows in panels C and D) and periosteal thickening/apposition (white arrowheads in panels E and F). Note the signal void of exemplary free air in the partially imaged oropharynx and of small air inclusions adjacent to the left hemimandible (black arrowheads in panel C), which here can mimic periosteal apposition.

FIGURE 3. Image segmentation and coregistration. A and B show 3-dimensional reconstruction (using volume rendering technique) of a left hemimandible, segmented, and separated into the defined regions. Note that teeth have been neatly excluded manually for further quantitative assessment of the respective partial bone volumes. Visualization of medication-related osteonecrosis of the jaw-associated osteolysis in the posterior corpus of mandible (arrows) was consistent with clinical findings. Exemplary axial images of coregistered (C) cone-beam computed tomography and (D) grayscale inverted native ultrashort echo-time magnetic resonance of the same patient. Osteolysis (arrows) and medullary sclerosis (asterisks) as disease-typical hallmarks are clearly visible in both modalities. In addition, large bone sequestra (dashed encircled area in panels C and D) as late-stage disease characteristics are visible in both modalities. Partially imaged oropharynx shows signal void and consecutive hyperintensity of free air in grayscale inverted ultrashort echo-time magnetic resonance images (arrowheads).

Technologies LLC, Zurich, Switzerland; a video of fused CBCT and MR series is shown in Supplementary File 2, Supplemental Digital Content 2, <http://links.lww.com/RLI/A479>).

Volume segmentation of the aforementioned anatomic regions was performed on the basis of the coregistered CBCT series with volumes of interest (VOIs). In addition, same-sized regions of interest (ROIs) of 0.3 mm^2 were placed in representative parts of healthy or visually altered parts of all regions where the medullary bone was clearly visible. Subsequently, these 2- and 3-dimensional segmentations were applied as masks on the coregistered CBCT and MR image series to calculate mean and standard deviation (SD) values of gray values (GVs) and signal intensity (SI) for each ROI/VOI. Proprietary software (syngo.via VB30; Siemens Healthineers) and an open-source software package (3D Slicer, v.4.10.1^{22,23}) were used for the image segmentation.

To improve the quantitative comparability within patients and modalities, normalization of SI and GV was performed before all intermodal testing. Therefore, a nondimensional arbitrary reference scale (0–100) was defined for both CBCT and MR per patient, ranging from fat (0) to cortical bone (100). A mean value of 4 different representative

GV and SI measurements in buccal subcutaneous fat and of the highest attenuating part of the mandibular cortex was calculated per patient and modality. Subsequently, all original measurements were recalculated in relation to the range between these 2 reference values.

Statistical Analysis

Overall interreader and intermodality agreement was calculated with Cohen kappa (κ). Interreader agreement was also calculated separately for each modality as well as for mandible and maxilla. Furthermore, we evaluated the impact of image artifacts on agreement by separate analysis of normal and artifact-affected regions. In addition, artifact extent of mandible and of maxilla was calculated with chi-square testing. According to Landis and Koch,²⁴ degrees of agreement were considered poor ($\kappa \leq 0$), slight ($0 < \kappa \leq 0.2$), fair ($0.2 < \kappa \leq 0.4$), moderate ($0.4 < \kappa \leq 0.6$), substantial ($0.6 < \kappa \leq 0.8$), or (almost) perfect ($0.8 < \kappa$). All statistical calculations were done using the original measurements as well as with a binary assessment of radiologically healthy (scores 0 and 1) versus clearly MRONJ-affected regions (rated as 2 or 3).

To reflect differences between radiologic and clinical findings, descriptive statistics were calculated for all qualitative parameters and used for comparison of clinically overt MRONJ regions (ie, osteolysis present, rated 1–3) versus the remaining regions.

Differences between cumulative qualitative ratings of the left and right side of the jaw were assessed with the Wilcoxon signed rank test. Friedman test was used for evaluation of differences in qualitative scores per anatomic region and among the 3 evaluated qualitative criteria, as defined above.

To reveal possible systematic differences between UTE MR and CBCT ratings, we performed a Bland-Altman analysis and computed 95% upper and lower confidence intervals to determine the limit of agreement.

Standard paired *t* testing and analysis of variances was performed for the assessment of differences in quantitative measurements, analogously to the evaluation of qualitative parameters. Pearson correlation coefficient (*r*) was used for comparison of mean SI and GV of ROIs and VOIs that were derived from the coregistered MR and CBCT images. As the ground truth, the highest qualitative rating of osteosclerosis by the more experienced radiologist was used for differentiation between radiologically healthy bone (highest score of 0 or 1) and clearly MRONJ-affected sites (if rating was 2 or 3), similarly to the comparison of qualitative findings.

For all measurements, a *P* value smaller than 0.05 was considered statistically significant. All calculations were performed using proprietary software (IBM SPSS Statistics, version 25; IBM, Armonk, NY).

RESULTS

A total of 28 patients received 29 examinations according to the institute own protocol for MR assessment of MRONJ. Due to exclusion criteria, a remainder of 19 patients was included into the study (8 exclusions due to missing CBCT imaging, 1 exclusion due to postoperative

follow-up). There were 11 female (58%) and 8 male patients, patient age ranged from 57 to 93 years (75.3 ± 10.3 years, mean $\pm$ SD), without sex-related differences (*P* = 0.19). The majority of MRONJ patients received denosumab (denosumab: *n* = 12, bisphosphonates: *n* = 8, other drugs: *n* = 2) as antiosteoporotic therapy (osteoporosis: *n* = 10, prostate cancer: *n* = 4, multiple myeloma: *n* = 2, other: *n* = 2). On average, CBCT and MR examinations of a patient were performed within 25.5 ± 34.7 days of each other (mean $\pm$ SD).

The average radiation dose for CBCT was 2283.3 ± 378.5 mGy·cm² dose area product at a CTDI of 8.6 ± 0.5 mGy (both values presented as means $\pm$ SD).

Comparison of qualitative and quantitative ratings was performed for 221 (83%) regions, the remainder were excluded as they were marked as “not assessable” by at least one reader in CBCT and/or MR due to susceptibility (mainly caused by metallic hardware in the oral cavity) or motion artifacts. Artifacts were more often present in MR (*P* < 0.001) and predominantly affected regions of the maxilla (13.2% in mandible vs 26.3% in maxilla, *P* < 0.001).

Qualitative Readout

Overall MRONJ affected mandible and maxilla in 15 and 4 individuals (*P* < 0.001). Each qualitative parameter was rated significantly more often as pathologic in the mandible (*P* < 0.001 each). The prevalence of osteosclerosis, periosteal thickening, and osteolysis was significantly different among the defined anatomic regions (*P* < 0.001, medians/interquartile ranges from 0/0 in corMa to 1/2 in aMa) and is presented in Table 2. The aMa was most often affected by MRONJ (*P* < 0.001). Furthermore, pathological findings were also present in clinically healthy regions (ie, without overt osteolysis; also Table 2). For both readers, there was no significant side difference regarding MRONJ affected regions (*P* = 0.79 and 0.62).

TABLE 2. Distribution of Qualitative Ratings

Anatomic Region	Osteolysis		Periosteal Thickening/Apposition		Medullary Osteosclerosis	
	MRONJ	Healthy	MRONJ	Healthy	MRONJ	Healthy
UTE MR						
conMa	n/a	0/0	n/a	0/0	n/a	0/0
corMa	n/a	0/0	n/a	0/0	n/a	0/0
rMa	3/2	0/0	2.5/2	0/6	2/2	0/8
pMa	2/13	0/0	2/10	0/8	3/11	0/10
aMa	2/13	0/0	2/13	0/12	3/13	0/11
aMx	3/3	0/0	0/0	0/0	0/3	0/0
pMx	3/2	0/0	0/0	0/0	0/0	0/0
CBCT						
conMa	n/a	0/0	n/a	0/0	n/a	0/0
corMa	n/a	0/0	n/a	0/0	n/a	0/0
rMa	3/1	0/0	3/1	0/6	3/1	0/12
pMa	3/11	0/0	2/11	0/9	3/9	0/10
aMa	2/12	0/0	2/11	0.5/13	3/11	0/12
aMx	3/2	0/0	0/0	0/0	1/1	0/1
pMx	3/1	0/0	0/0	0/0	0/0	0/1

Medians of parameters (0–3, normal severe) and respective incidences (separated by “/”) of pathologic ratings (>0), in ultrashort echo-time (UTE) MR and in cone-beam CT (CBCT). The values are listed separately for “osteolysis,” “periosteal thickening,” and “osteosclerosis” among anatomic regions (aMa, pMa, rMa, conMa, corMa, aMx, and pMx) and separated for clinically overt MRONJ regions (ie, osteolysis was present, rated 0 or 1; “MRONJ”) and for the remaining, clinically unaffected regions (“healthy”).

MRONJ indicates medication-related osteonecrosis of the jaw; UTE, ultrashort echo-time; CBCT, cone-beam computed tomography; aMa, anterior corpus of mandible; pMa, posterior corpus of mandible; rMa, ramus mandibularis; conMa, condyloid process of mandible; corMa, coronoid process of mandible; aMx, anterior maxilla; and pMx, posterior maxilla.

FIGURE 4. Bland-Altman plot for comparison of qualitative ratings in cone-beam computed tomography and in ultrashort echo-time magnetic resonance. Blue reference lines indicate upper and lower 95% confidence intervals.

Interreader agreement for qualitative ratings over all parameters and regions was substantial ($\kappa = 0.70$) for both modalities, with 0.73 and 0.66 for CBCT and MR, respectively. Agreement was higher when calculated for mandibular compared with maxillary regions only ($\kappa = 0.69$ and 0.57, respectively). Intermodality agreement was substantial for both readers ($\kappa = 0.62$). Binary differentiation between normal and MRONJ-altered regions showed almost perfect intermodality agreement overall ($\kappa = 0.83$), as well as for each individual radiologist ($\kappa = 0.75$ and 0.74 for expert and resident).

Upper and lower 95% confidence intervals for comparison of qualitative ratings in CBCT and in UTE MR were 1.2716728 and -1.2554728 , respectively. Linear regression analysis for Bland-Altman plot (Fig. 4) indicated no proportional bias (β value of mean = 0.015, $P = 0.384$).

Quantitative Readout

Concordant with visual impression, mean SI, and GV significantly differed throughout the 5 measured anatomic regions of the mandible of all patients ($F = 27.31$ and 16.79 for SI and GV, respectively, $P < 0.001$). MRONJ affected the left and right side of the mandible similarly ($P = 0.08/0.85$ for SI/GV). Based on the qualitative rating of osteosclerosis as the most prevalent MRONJ hallmark, SI and GV were significantly different in healthy (ratings for osteosclerosis being 0 or 1) and disease-affected (rated 2 or 3) bone ($P < 0.001$). This finding is prevalent in all anatomic regions and measurement methods (VOI or ROI). The respective values are listed in detail in Table 3.

Furthermore, SI and GV always showed excellent intermodality correlation when calculated overall ($r = -0.77$), as well as separately for healthy and MRONJ-affected regions ($r = -0.63$ and -0.68), or for ROI- and VOI-derived mean values ($r = -0.83$ and -0.66 , all $P < 0.001$). Visualization of these correlations is given in Figure 5.

DISCUSSION

Medication-related osteonecrosis of the jaw has increased in prevalence in recent years due to the increasing use of antiresorptive drugs for osteoporosis or bone metastasis such as zoledronate and denosumab.

While the disease is known to show characteristic alterations of the affected bone in dental PR and CBCT even in preclinical stages,¹⁵ the definition of MRONJ does not currently contain imaging-related criteria according to a respective position paper of the AAOMS.^{5,25}

Panoramic radiograph and CBCT are considered first choice and thus reference modalities for the assessment of bone affection, whereas MR is known for its optimal soft tissue contrast and thus assessment of soft tissues in the head and neck region. Different groups have already proven the potential of recent, similar UTE sequences of different vendors for both qualitative and quantitative alterations of bone structure.^{17,26–29} Our study investigated the use of one UTE MR sequence for the

TABLE 3. Distribution of Quantitative Measurements

Anatomic Region	Healthy		MRONJ		Overall
	SI	GV	SI	GV	Pearson Coefficient
Measured by ROI					
aMa	332 ± 29	353 ± 125	190 ± 92	797 ± 318	−0.83
pMa	385 ± 57	328 ± 90	225 ± 95	740 ± 219	
rMa	408 ± 87	303 ± 119	307 ± 63	595 ± 157	
conMa	423 ± 82	260 ± 121	n/a	n/a	
Overall	399 ± 78	298 ± 118	227 ± 97	735 ± 266	
Measured by VOI					
aMa	216 ± 23	763 ± 124	198 ± 56	854 ± 143	−0.66
pMa	274 ± 56	714 ± 120	230 ± 53	809 ± 148	
rMa	302 ± 61	654 ± 103	301 ± 49	752 ± 158	
conMa	353 ± 75	507 ± 222	n/a	n/a	
Overall	303 ± 77	626 ± 190	230 ± 65	817 ± 149	
Overall					
Pearson coefficient	−0.63		−0.68		−0.77

Signal intensities and GV's and respective intermodality correlations among different regions of the mandible (aMa, pMa, rMa, conMa, and corMa), separately for each modality and for each measurement method (ROI or VOI). The values are given separately for sites of osteosclerosis-affected medullary bone (rated 2 or 3; "MRONJ"), and for unaffected regions ("healthy"). The values represent means and standard deviations (SD), unless indicated otherwise. Correlations were considered significant for $P < 0.05$.

SI indicates signal intensities; GV, gray values; VOI, volume of interest; MRONJ, medication-related osteonecrosis of the jaw; aMa, anterior corpus of mandible; pMa, posterior corpus of mandible; rMa, ramus mandibularis; conMa, condyloid process of mandible; corMa, coronoid process of mandible; aMx, anterior maxilla; and pMx, posterior maxilla.

FIGURE 5. Intermodality correlation of quantitative parameters. The histogram plots contain either region of interest–derived (A and B) or volume of interest–derived (C and D) correlations of all corrected mean gray values and signal intensities for healthy bone (ie, normal or slight changes, A and C) as well as for medication-related osteonecrosis of the jaw–affected regions (B and D). Values in the top right image corner indicate linear regression coefficient (R^2) and P value, respectively.

assessment of MRONJ-associated bone changes of the jaw by comparing it with the current CBCT criterion standard.

We found good correlation of both qualitative and quantitative imaging parameters, that is, visual assessment and quantitative measurements in both CBCT and MR. Furthermore, CBCT and MR showed no significant differences regarding qualitative overall scores with substantial intermodality agreement for both readers ($\kappa = 0.62$). Binary differentiation between normal and MRONJ-altered regions showed almost perfect intermodality agreement ($\kappa = 0.83$) highlighting the interchangeability of both modalities for MRONJ detection. Both readers experienced certain difficulties for qualitative assessment during readout of CBCT and MR images due to artifacts. However, distortion by motion and by susceptibility/beam hardening due to dental hardware was noted more often in MR than in CBCT. Small air inclusions in the oral vestibulum adjacent to the alveolar ridge may appear equally dark to bone on UTE MR sequences as demonstrated in Figures 2 and 3. The air inclusions can mimic periosteal bone reaction and thickening, as well as detached osseous fragments in MRONJ foci. Prior mouth rinsing and adequate patient instruction before MR scans may potentially help in reducing these artifacts. The air inclusions were noticed by both readers in some cases; however, they were considered to have a small impact on the qualitative bone assessment. Air-induced artifacts in the oral cavity were also noted in the maxilla in areas where the maxillary sinus is in close contact to the socket. However, MRONJ affects the maxilla significantly less often than the mandible,³⁰ as seen in this patient cohort. Further, reference standard imaging modalities such as PR and CBCT may also be affected by substantial artifacts from dental hardware. In certain individuals, strong artifacts were noted in both CBCT and MR images.

Our results suggest good correlation between quantitative indicators of disease-alteration in CBCT and UTE MR images. Due to flat-panel detector technology, GVs in CBCT are less robust than Hounsfield units in multidetector CT due to flat-panel detector technology.³¹

However, our approach of normalizing SI and GV by using a nondimensional arbitrary reference scale allowed us to directly compare the MRONJ-associated quantitative changes in CBCT with UTE MR images despite different underlying physical effects. The normalized and rescaled values reflected an almost perfect intermodality correlation for both healthy and MRONJ affected regions of the jaw. The higher correlation in ROI measurements, compared with VOI, may be due to a spatial blurring effect. While ROIs were placed in the center of medullary fat (or sclerosis), VOIs also included boarder regions that are adjacent to voxels with completely different values (ie, gingiva), thereby quickly introducing substantial sample error by inaccurate image coregistration.

The following limitations need to be acknowledged. First, there was a slight but nonsignificant sex imbalance in our study population in favor of females. However, this is in concordance with the higher prevalence of osteoporosis among females and the overall incidence of the condition in the general population.³² Second, we focused on the radiologic hallmarks of MRONJ. We therefore compared findings on UTE MR images to a CBCT reference standard. The ideal correlation of imaging findings to a histopathologic reference standard could not be performed as not all patients underwent surgery or information on this was missing. Third, due to advanced disease stages and patient age, quite a substantial amount of jaw regions was affected either by motion or metal artifacts. This was seen in both modalities and does not specifically apply to MR imaging alone. Nonetheless, artifacts were more numerous in UTE MR than in CBCT, which may allow thorough comparison with the reference standard in nondistorted regions only. Last, spatial resolution was lower by a factor of almost 3 in the UTE MR sequences compared with CBCT. This may hamper early detection of subtle changes such as widening of the alveolar socket or densification of the lamina dura. However, in clinically diagnosed MRONJ patients with frank bone exposure, we did not experience any

substantial disadvantage in disease assessment in MR images as compared with CBCT.

In conclusion, qualitative assessment of MRONJ with UTE MR imaging is comparable to reference standard CBCT. Quantitative measurements of both modalities significantly distinguish diseased from normal bone with strong correlations among each other.

Given the benefits of MR for soft tissue evaluation as well as its lack of ionizing radiation, it could serve as an equivalent alternative to standard PR and CBCT in the assessment of MRONJ patients; further prospective studies are needed to prove the diagnostic accuracy of UTE MR for this indication.

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