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7 Tesla MRI of bone microarchitecture discriminates between women without and with fragility fractures who do not differ by bone mineral density

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Abstract

Osteoporosis is a disease of poor bone quality. Bone mineral density (BMD) has limited ability to discriminate between subjects without and with poor bone quality, and assessment of bone microarchitecture may have added value in this regard. Our goals were to use 7 T MRI to: (1) quantify and compare distal femur bone microarchitecture in women without and with poor bone quality (defined clinically by presence of fragility fractures); and (2) determine whether microarchitectural parameters could be used to discriminate between these two groups. This study had institutional review board approval, and we obtained written informed consent from all subjects. We used a 28-channel knee coil to image the distal femur of 31 subjects with fragility fractures and 25 controls without fracture on a 7 T MRI scanner using a 3-D fast low angle shot sequence (0.234 mm × 0.234 mm × 1 mm, parallel imaging factor = 2, acquisition time = 7 min 9 s). We applied digital topological analysis to quantify parameters of bone microarchitecture. All subjects also underwent standard clinical BMD assessment in the hip and spine. Compared to controls, fracture cases demonstrated lower bone volume fraction and markers of trabecular number, plate-like structure, and plate-to-rod ratio, and higher markers of trabecular isolation, rod disruption, and network resorption ($p < 0.05$ for all). There were no differences in hip or spine BMD T-scores between groups ($p > 0.05$). In receiver-operating-characteristics analyses, microarchitectural parameters could discriminate cases and controls (AUC = 0.66–0.73, $p < 0.05$). Hip and spine BMD T-scores could not discriminate cases and controls (AUC = 0.58–0.64, $p = 0.08$). We conclude that 7 T MRI can detect bone microarchitectural deterioration in women with fragility fractures who do not differ by BMD. Microarchitectural parameters might some day be used as an additional tool to detect patients with poor bone quality who cannot be detected by dual-energy X-ray absorptiometry (DXA).

Keywords

7 Tesla; Magnetic resonance imaging (MRI); Femur; Osteoporosis; Microarchitecture

Introduction

Osteoporosis is defined as “a systemic skeletal disorder characterized by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture” [1]. Because there is an association between areal bone mineral density (BMD) as measured by dual-energy X-ray absorptiometry (DXA) and fracture risk, DXA has become the standard-of-care test to diagnose osteoporosis [2, 3]. If a patient’s DXA-derived T-score (number of standard deviations below the mean BMD for a population of healthy young women) is less than -2.5 , then the patient is considered as having osteoporosis [2]. A T-score less than -2.5 also serves as the threshold for treatment with osteoporosis medications [4].

However, there are limitations with the use of DXA to assess bone fragility and determine whether an individual has osteoporosis. First, factors other than BMD contribute to bone quality and risk of fracture [2, 5, 6]. For example, DXA does not assess bone microarchitecture, which is included in the definition of osteoporosis and is an important contributor to bone strength and quality [2, 7, 8]. Indeed, the addition of structural measures to BMD improves the prediction of bone strength in ex vivo studies [9–11]. Second, DXA has poor sensitivity for the detection of patients with bone fragility. There is a large overlap in the BMDs of patients with and without fragility fractures [3, 6, 12, 13], and approximately two-thirds of the patients who suffer low-energy, fragility fractures are misclassified as not having osteoporosis because they have BMD T-scores greater than -2.5 [14–17]. The limitations of DXA in this regard have sparked research into the use of other modalities to assess bone quality and strength in vivo [18, 19].

Over the last 15 years, there has been an increasing number of publications describing the in vivo assessment of bone microarchitecture, either by high-resolution magnetic resonance imaging (MRI) [7, 20], or most recently, high resolution peripheral quantitative computed tomography (HR-pQCT) [21–25]. These studies have been carried out predominantly at the distal radius or distal tibia, because imaging at other locations in the body has been too technically challenging. Via HRpQCT, the small scanner bore size precludes imaging anything but the wrist or ankle. And via MRI, it is challenging to image bone microarchitecture at more proximal locations because of signal-to-noise ratio (SNR) limitations. These SNR limitations arise because in more proximal skeletal locations, the bones are deeper within the body and thus more distant from the radiofrequency coil that is placed on the patient and used for MRI signal detection. For example, the distal radius and tibia are only 1–2 cm from the skin surface, but the distal femur is 2–5 cm from the skin surface, and the proximal femur is 5–8 cm from the skin surface. Since SNR decreases rapidly with increasing distance, imaging microarchitecture for deeper skeletal structures becomes challenging.

The goal of this study was to investigate if high-resolution, 7 T MRI is capable of extending the bone microarchitecture analysis previously only feasible at distal peripheral sites to a more proximal location (i.e., the distal femur), and able to differentiate women with and without osteoporotic fragility fracture. We hypothesized that: (1) subjects with fragility fractures would demonstrate deterioration in bone microarchitecture in the distal femur compared to controls, and (2) microarchitectural parameters could be used to discriminate between subjects with and without fragility fractures. We also examined: (1) differences in DXA-derived BMD T-scores between groups, and (2) the ability of BMD T-scores to discriminate between women with and without fragility fractures.

Materials and methods

Subject recruitment

This study had institutional review board approval, and we obtained written informed consent from all subjects. We followed a case–control study design of subjects with and without fragility fractures similar to the work of Melton and Nishiyama [22, 23, 26]. From the Osteoporosis Center at our institution, we recruited women with radiographically

confirmed, low-energy fragility fractures ($n = 31$, age = 56.9 ± 17.2 years, body mass index (BMI) = 22.2 ± 3.6 kg/m²) and female controls without fragility fractures ($n = 25$, age = 50.0 ± 19.5 years, BMI = 20.5 ± 1.8 kg/m²). The type and distribution of fragility fractures were: spine = 16, forearm = 8, sacrum = 4, hip = 3. We excluded patients with a history of knee osteoarthritis, trauma, Paget's disease, or other musculoskeletal disorder that could affect the distal femur. The differences in age and BMI between groups were not statistically significant ($p > 0.1$ for age and $p > 0.07$ for BMI). As in prior studies, a fragility fracture was defined as a fracture due to a fall from a standing height or less [22, 25]. The average time since fragility fracture was 5.7 ± 3.0 months. Subjects underwent standard DXA testing (GE Lunar, Rahway, NJ, USA) to assess T-scores in the hips (total) and the spine (L1–L4). For any analysis, we used the hip T-score for the same lower extremity that we scanned by MRI.

MRI scanning

The distal femur of the dominant lower extremity of all subjects was scanned on a whole body 7 T MRI scanner (Siemens Magnetom, Erlangen, Germany) using a birdcage transmit, 28-channel receive array coil (Quality Electrodynamics, Mayfield Village Ohio). We used a 3-D fast low angle shot sequence to image bone microarchitecture (TR/TE = 20 ms/5.1 ms, field of view = 120 mm, matrix = 512×512 , in-plane resolution 0.234 mm $\times$ 0.234 mm, slice thickness = 1 mm, 80 axial images, parallel acceleration factor = 2, acquisition time = 7 min and 9 s) [27–29].

MR image analysis

We analyzed bone microarchitecture within volumes of interest (VOIs) in two locations: the distal femoral metaphysis (DFM) and the distal femoral epiphysis (DFE). To identify the DFM and DFE, a musculoskeletal radiologist identified the growth plate on sagittal and coronal localizer MR images. The DFM VOI was designated as the ten slices superior to the growth plate and the DFE VOI was designated as the ten slices inferior to the growth plate (Fig. 1).

To each volume of interest, we applied digital topological analysis (DTA). DTA [30, 31] is a 3-D method that accurately determines the topological class (e.g., surfaces, curves, junctions, and edges) of each individual location in a digitized structure that has been applied for quantifying quality of trabecular bone architectural makeup. Before applying DTA, a binarized trabecular bone image is skeletonized to a network of 1-D and 2-D structures representing rods and plates, respectively. DTA involves three steps; the first one is inspecting each bone voxel's neighboring voxels (i.e., the 26 other voxels within the voxel's $3 \times 3 \times 3$ kernel). A unique topological classification can be achieved using lookup tables solving for local topological ambiguities in digital manifolds and their junctions. These topological classes are used to compute several topological parameters for trabecular bone (TB) networks. We computed: bone volume fraction (BVF) and apparent trabecular thickness (Tb·Th), as well as markers of: trabecular number (skeleton density, Sk.D), the ends of trabecular rod-like structure or trabecular rod disruption (curve edge, CEnorm), trabecular plate-like structure (surface, Surf), trabecular plate-to-rod ratio (surface–curve, Surf–Curv), trabecular network connectivity (junctions, Junc), trabecular network

osteoclastic resorption (Erosion Index), and finally, trabecular isolation (Inorm). These parameters were chosen because in previous bone biopsy studies, they have been shown to deteriorate in patients with osteoporosis [32, 33]. The coefficient of variation for microarchitectural parameters in the distal femur with this image analysis and MRI technique has previously been shown to be 0.8–5.6 % [27].

Statistical analysis

We used SPSS v.20 (IBM, Armonk, New York) to perform statistical analysis. To compare differences between groups, we used the nonparametric Mann–Whitney test, which does not depend on a normal distribution of data (the results of a *t* test may be unduly influenced by outlier values). To assess the correlation between the bone volume fraction and microarchitectural parameters, we used the Spearman non-parametric test. A *p* value less than 0.05 was considered statistically significant. To determine the ability of a parameter to discriminate between fracture cases and controls, we performed a receiver operating characteristics (ROC) analysis and computed the area under the curve (AUC), including confidence intervals and *p* values.

Results

Differences between groups

Figure 2a shows representative axial 7 T MR images of the distal femoral metaphysis in patients with and without fragility fractures. Individual trabeculae are well depicted on the images. At the distal femoral metaphysis, compared to controls, fracture cases demonstrated lower values for markers of trabecular number (skeleton density, −5.7 %), trabecular plate-like structure (Surf, −11.5 %), and trabecular connectivity (Junc, −9.6 %), and higher values for markers of trabecular isolation (Inorm, +450 %) and the disruption of trabecular rod-like structure (CEnorm, +341 %) (Table 1). There were no differences between groups for bone volume fraction, apparent trabecular thickness, or markers of trabecular plate-to-rod ratio (Surf/Curv) and trabecular network resorption (Erosion Index). For both controls and fracture cases at the distal femoral metaphysis, there were moderate to strong correlations between bone volume fraction, a marker of bone mass, and microarchitectural parameters (e.g., trabecular thickness, $r = 0.43$, $p = 0.02$; surf [trabecular plate-like structure], $r = 0.99$, $p < 0.001$) (Table 2). There was also no difference in BMD T-scores between groups (Table 3).

Figure 2b shows representative axial 7 T MR images of the distal femoral epiphysis in patients with and without fragility fractures. Again, individual trabeculae are well depicted on the images. At the distal femoral epiphysis, compared to controls, the fracture cases demonstrated lower bone volume fraction (−3.1 %), and lower values for markers of trabecular number (skeleton density, −5.4 %), trabecular plate-like structure (Surf, −10.3 %), trabecular connectivity (Junc, −9.7 %), and trabecular plate-to-rod ratio (Surf/Curv, −11.4 %). Fracture cases also demonstrated higher values for markers of the disruption of trabecular rod-like structure (CEnorm, +764 %), trabecular isolation (Inorm, +881 %), and trabecular network resorption (Erosion Index, +6.2 %) (Table 1). There was no difference in apparent trabecular thickness between groups. For both controls and fracture cases at the

distal femoral epiphysis, there were moderate to strong correlations between bone volume fraction, a marker of bone mass, and microarchitectural parameters (e.g., trabecular thickness, $r = 0.41$, $p = 0.02$; erosion index (marker of trabecular network resorption), $r = -0.95$, $p < 0.001$) (Table 2).

ROC analyses

At the distal femoral metaphysis, the parameters skeleton density (AUC = 0.67), Inorm (AUC = 0.68), CEnorm (AUC = 0.70), Surf (AUC = 0.66), and Junc (AUC = 0.67) could be used to discriminate between groups ($p < 0.05$ for all, Table 4). Bone volume fraction, apparent trabecular thickness, Surf/Curv, and Erosion Index could not be used discriminate between groups (AUC confidence intervals included 0.5, p values >0.05).

At the distal femoral epiphysis, bone volume fraction (AUC = 0.73), skeleton density (AUC = 0.70), Inorm (AUC = 0.73), CEnorm (AUC = 0.72), Surf (AUC = 0.72), Junc (AUC = 0.67), Surf/Curv (AUC = 0.68), and Erosion Index (AUC = 0.66) could all be used to discriminate between groups ($p < 0.05$ for all, Table 4). Apparent trabecular thickness could not be used to discriminate between groups (AUC confidence intervals included 0.5, p values >0.05).

Finally, hip and spine T-scores could not be used to discriminate between groups (AUC confidence intervals included 0.5, p values > 0.05 , Table 5).

Discussion

In this study, we used high-resolution 7 T MRI to evaluate trabecular bone microarchitecture at the distal femoral metaphysis and epiphysis in women with known poor bone quality (fragility fractures) and female controls without fracture. 7 T MRI was able to detect significant deterioration in bone microarchitectural parameters between groups, but there were no differences in DXA-derived BMD T-scores between groups. In addition, in ROC analyses, bone microarchitectural parameters could be used to discriminate between the two groups, but BMD T-scores could not be used to do this. The results provide further insight into how bone microarchitecture deteriorates in patients with fragility fractures, and also suggests that in vivo monitoring of such microarchitectural alterations might allow clinicians to discriminate between subjects without and with bone fragility who are at risk for fracture.

To the best of our knowledge, this is the first study to examine bone microarchitecture in the distal femur of patients with fragility fractures and the largest 7 T MRI study of patients with fragility fractures to date. MRI of bone microarchitecture was originally performed in the distal extremities [34–36], and it is only within the last few years that imaging of bone microarchitecture in more proximal locations of the skeleton has become possible due to improvements in radiofrequency coils and the arrival of high field and ultra high field MRI scanners [29, 37–39]. This study benefitted from both scanning at 7 T and the use of a 28-channel receive array coil to image the distal femur at high-resolution. Because image SNR is approximately linearly proportional with the magnitude of the main magnetic field, MRI at 7 T provides more than twofold higher SNR compared to MRI 3 T, and can thus permit reductions in imaging time and/or voxel size [40, 41]. In addition, the higher SNR provided

by 7 T facilitates imaging of deeper anatomy such as the femur, since coil sensitivity for detection of the MR signal decreases exponentially as the distance from the coil to the object of interest increases [42]. Finally, the use of a 28-channel coil also facilitates high-resolution imaging, as the 28-channel coil at 7 T provides approximately 17–400 % higher image SNR compared to the use of a conventional 2-channel quadrature coil [43]. We leveraged the higher SNR provided by the 7 T MRI scanner and the 28-channel receive coil to decrease imaging time to 7 min and 9 s via parallel imaging, while still being able to acquire 80 axial images at 1 mm slice thickness. Decreasing imaging time is important for high-resolution exams, as this will decrease the risk of motion artifact on images. In the future, the additional SNR could also be used to improve in-plane spatial resolution or further decrease the slice thickness.

We found that fracture cases had lower values for markers of trabecular number (skeleton density), connectivity (Junc), plate-like structure (Surf), and plate-to-rod ratio (Surf/Curv), and higher values for markers of the disruption/ends of trabecular rod-like structure (CEnorm), trabecular isolation (Inorm), and trabecular network resorption (Erosion Index). All of these trends are consistent with increased osteoclastic (bone resorptive) activity and deterioration of bone microarchitecture/weakening of bone seen in landmark bone biopsy studies of osteoporosis [8, 32, 33]. The results are supportive of previous MRI studies of bone microarchitecture, which were carried out in the distal radius and ankle. Majumdar et al. [34] found that subjects with fragility fractures demonstrated lower bone volume fraction and Tb.N. in the distal radius compared to the controls. In a study of calcaneal microarchitecture, Link et al. [36] found lower bone volume fraction and Tb.N. in fracture cases compared to controls. Finally, Wehrli et al. [44] found that subjects with vertebral deformities demonstrated deterioration in parameters of bone microarchitecture at the distal radius that reflected a conversion of trabecular plates to rods as well as a disruption of trabecular rods. Osteoporosis is a “systemic skeletal disease” and the ideal site for bone quality/microarchitectural assessment remains to be determined. In the future, we hope to extend these methods to the proximal femur, which is the most devastating fragility fracture site (requires major surgery, greatest morbidity and mortality of all fractures), but also the most challenging to image because it is deeper in location (5–8 cm from the skin surface) and limited by low SNR. Both 7 T MRI and multichannel coils may again play a similar role in terms of facilitating high-resolution imaging in this location.

While the ability of 7 T MRI to detect differences between groups is useful from the research perspective in terms of providing insight into the pathogenesis of osteoporosis, clinical value would come from being able to use MRI of bone microarchitecture as a test to discriminate between subjects without and with poor bone quality. This has been a large motivating factor for the use of ultrasound to study calcaneal bone quality or HR-pQCT to study distal tibia/distal radius bone quality. If a clinical test could do this, then in theory if a patient were detected before they suffered a fracture, they could be started on one of the many effective bone-strengthening medications that can reduce fracture risk by up to 50 % [5]. Overall, our results provide evidence that measurement of microarchitectural parameters, even in a more proximal skeletal location such as the distal femur, might be able to detect patients with poor overall bone quality who are not currently detectable using DXA criteria for a diagnosis of osteoporosis. We found that microarchitectural measures in the

distal femur could discriminate between patients with and without fragility fractures. However, there was no difference in BMD T-scores between cases and controls, and BMD T-scores could not discriminate between the two groups. The inability of DXA to do this highlights the poor sensitivity of DXA to identify individuals at risk for fracture, and the large overlap in BMDs of patients with and without fragility fractures [3, 6, 12, 13, 17, 45]. The discriminatory ability of microarchitectural parameters has been recently described in cross-sectional HR-pQCT studies of the distal radius. For example, in Melton et al.'s 2007 study of 18 females with forearm fractures and 18 controls, Tb.N. measured at the distal radius demonstrated an AUC of 0.72 for the discrimination of fracture cases from controls [22]. And more recently, Nishiyama et al. [23], in a study of 44 patients with any type of fragility fracture and 88 controls, found that microarchitectural parameters measured by HR-pQCT at the distal radius had an AUC of 0.67 for the discrimination of all fracture cases from controls. We found AUC values for bone microarchitectural parameters measured in the distal femur to be within a similar range.

Finally, we note that the parameter bone volume fraction (which is actually more akin to a marker of bone mass), when measured in the distal femoral epiphysis, performed as well as microarchitectural parameters for the discrimination of fracture cases and controls. This is reflected by its significant AUC value of 0.73, which was equal to the AUC value for the best performing microarchitectural parameter, Inorm. Furthermore, the confidence interval for this AUC value of bone volume fraction overlapped with confidence intervals for the AUC values of microarchitectural parameters. There was also moderate to very strong correlation between bone volume fraction and microarchitectural parameters (as demonstrated by the results in Table 2), which suggests that there is overlap in the bone quality information provided by bone volume fraction and microarchitectural measures. Overall, these results raise the question of whether bone volume fraction could be used alone to discriminate fracture status, rather than a microarchitectural measure. In the distal femoral metaphysis, bone volume fraction could not discriminate fracture cases from controls, even though microarchitectural parameters could do this. Because of the small sample size in this study, we did not have enough power to perform multivariable logistic modeling to determine which parameter or combination of parameters from which measurement site (metaphysis or epiphysis) would provide the highest AUC value. In the future, it will be necessary to perform larger patient studies in order to determine the measurement site and parameters (bone volume fraction, microarchitectural parameters, or a combination of both) that are most useful for the discrimination of fracture status and ultimately, assessment of fracture risk.

There are limitations to this study. First, because this is not a longitudinal study, we cannot draw any conclusions regarding the association between baseline microarchitectural measures and the occurrence of future fractures. Second, at the voxel size of this study $0.234 \text{ mm} \times 0.234 \text{ mm} \times 1 \text{ mm}$, we cannot depict trabeculae smaller than the voxel dimensions. Nevertheless, we could still visualize individual trabeculae on all images. MRI of bone microarchitecture requires high-resolution, but the long imaging times required by high-resolution MRI scans can increase the risk of patient motion artifact or discomfort. We felt that at the resolution of this study, there was a good balance between having adequate resolution to detect differences between groups and having a tolerable scan time to maintain

patient comfort/low risk of motion artifact. Finally, this study was performed on an ultra high field, 7 T MRI scanner, which is not widely available in the community. However, over the last decade, there has been a steady rise in the number of 7 T MRI scanners being installed at academic medical centers worldwide (at least ten in the United States). Like high-resolution peripheral computed tomography (HR-pQCT) scanners, bone microarchitecture imaging could at least be used for noninvasive clinical research studies (as opposed to bone biopsy studies) at hospitals equipped with the scanners.

In conclusion, we have used 7 T MRI to investigate, for the first time, differences in distal femur bone microarchitecture in patients without and with poor bone quality (fragility fractures). There was deterioration of bone microarchitecture in fracture cases compared to controls, and microarchitectural parameters could be used to discriminate between the fracture subjects and controls even though these subjects did not differ by BMD. Overall, the results provide further insight into the role that bone microarchitecture plays in fracture pathogenesis, and the results suggest that evaluation of bone microarchitecture may allow detection of patients with bone fragility who are at higher risk for fracture and who cannot be detected by DXA. Longitudinal studies are necessary to determine whether microarchitectural parameters have added predictive value for the occurrence of future fracture, and to determine whether microarchitectural parameters can be used as surrogate endpoints for fracture in clinical trials for osteoporosis interventions.

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Fig. 1.

We analyzed two volumes of interest at the distal femur: a 10 mm thick volume of interest at the distal femoral metaphysis, superior to the growth plate, and a 10 mm thick volume of interest at the distal femoral epiphysis, inferior to the growth plate

Fig. 2.

a Axial high-resolution 7 T MR images of the distal femoral metaphysis in a control (*left* T-scores = -1.3 in hip, -2.4 in spine) and a subject with a thoracic spine compression fracture (*right* T-scores = -1.5 in hip, -0.6 in spine). The whole area of trabecular bone was analyzed. The *rectangles* highlight an area of microarchitectural deterioration in the fracture case (fewer trabeculae, which are disrupted and have less connectivity) and for comparison, the same area within the control. In MR images, trabeculae are hypointense (*dark*) and marrow is hyperintense (*white*). **b** Axial high-resolution 7 T MR images of the distal femoral epiphysis in a control (*left* T-scores = -2.6 in hip, -1.6 in spine) and a subject with a thoracic spine compression fracture (*right* T-scores = -2.8 in hip, -2.1 in spine). The whole area of trabecular bone was analyzed. The *rectangles* highlight an area of microarchitectural deterioration in the fracture case (fewer trabeculae, which are disrupted and have less connectivity), and for comparison, the same area within the control. The *ovals* highlight areas of microarchitectural deterioration seen medially both within the control and the fracture case. In MR images, trabeculae are hypointense (*dark*) and marrow is hyperintense (*white*)

Table 1

Differences in distal femur bone microarchitectural parameters (measured at the metaphysis and epiphysis) in subjects with and without fragility fractures

	Controls	Fracture cases	% Difference fracture cases vs. controls (%)	Mann–Whitney <i>p</i> value
Distal femoral metaphysis				
Bone volume fraction	0.31 ± 0.016	0.030 ± 0.025	−3.2	0.08
Apparent trabecular thickness (mm)	0.213 ± 0.006	0.213 ± 0.007	0.0	0.64
Skeleton density	0.35 ± 0.02	0.33 ± 0.034	−5.7	0.034*
Inorm	0.00012 ± 0.00006	0.00066 ± 0.0027	+450	0.026*
CEnorm	0.00077 ± 0.0003	0.0034 ± 0.013	+341	0.014*
Surf	0.26 ± 0.024	0.23 ± 0.053	−11.5	0.038*
Junc	0.083 ± 0.007	0.075 ± 0.018	−9.6	0.031*
Surf/Curv	6.47 ± 1.35	5.86 ± 1.78	−9.4	0.22
Erosion index	1.2 ± 0.27	1.24 ± 0.39	+3.2	0.34
Distal Femoral Epiphysis				
Bone volume fraction	0.32 ± 0.01	0.31 ± 0.02	−3.1	0.004*
Apparent trabecular thickness (mm)	0.215 ± 0.006	0.214 ± 0.007	−0.4	0.94
Skeleton density	0.37 ± 0.01	0.35 ± 0.03	−5.4	0.013*
Inorm	0.000054 ± 0.000032	0.00053 ± 0.002	+881	0.004*
CEnorm	0.00037 ± 0.00016	0.0032 ± 0.014	+764	0.005*
Surf	0.29 ± 0.02	0.26 ± 0.05	−10.3	0.005*
Junc	0.096 ± 0.007	0.087 ± 0.02	−9.7	0.029*
Surf/Curv	7.78 ± 1.19	6.89 ± 1.78	−11.4	0.023*
Erosion index	0.97 ± 0.14	1.03 ± 0.32	+6.2	0.040*

An asterisk (*) denotes statistically significant results

Table 2Correlation (*r* values, Spearman test) between bone volume fraction and microarchitectural parameters

	Controls	<i>p</i> value	Fracture cases	<i>p</i> value
Distal femoral metaphysis				
Apparent Trabecular Thickness (mm)	0.63	0.001*	0.43	0.02*
Skeleton Density	0.82	< 0.001*	0.90	< 0.001*
Inorm	-0.78	< 0.001*	-0.83	< 0.001*
CEnorm	-0.81	< 0.001*	-0.89	< 0.001*
Surf	0.96	< 0.001*	0.99	< 0.001*
Junc	0.57	0.004*	0.78	< 0.001*
Surf/Curv	0.90	< 0.001*	0.87	< 0.001*
Erosion Index	-0.91	< 0.001*	-0.74	< 0.001*
Distal Femoral Epiphysis				
Apparent Trabecular Thickness (mm)	0.73	< 0.001*	0.41	0.02*
Skeleton Density	0.52	0.008*	0.78	< 0.001*
Inorm	-0.35	0.08	-0.77	< 0.001*
CEnorm	-0.57	0.003*	-0.81	< 0.001*
Surf	0.91	< 0.001*	0.93	< 0.001*
Junc	0.19	0.37	0.65	< 0.001*
Surf/Curv	0.90	< 0.001*	0.91	< 0.001*
Erosion Index	-0.95	< 0.001*	-0.74	< 0.001*

Table 3

DXA-derived spine and hip T-scores in subjects with and without fragility fractures

Controls	Fracture cases	% Difference fracture cases vs. controls (%)	Mann–Whitney <i>p</i> value
Spine T-score			
-1.4 ± 1.6	-1.8 ± 1.3	-28.5	0.23
Hip T-score			
-1.1 ± 1.3	-1.6 ± 1.0	-45.4	0.06

An asterisk (*) denotes statistically significant results

Table 4

Discrimination of subjects with and without fragility fractures—areas under the receiver operating characteristics curve (AUC) for bone microarchitectural parameters measured at the distal femoral metaphysis and epiphysis

	AUC	95 % confidence interval	<i>p</i> value
Distal femoral metaphysis			
Bone volume fraction	0.64	0.49–0.79	0.078
Apparent trabecular thickness	0.46	0.31–0.62	0.635
Skeleton density	0.67	0.53–0.81	0.034*
Inorm	0.68	0.54–0.82	0.026*
CEnorm	0.70	0.56–0.83	0.014*
Surf	0.66	0.52–0.81	0.038*
Junc	0.67	0.53–0.81	0.031*
Surf/Curv	0.60	0.45–0.75	0.22
Erosion index	0.58	0.45–0.58	0.34
Distal Femoral Epiphysis			
Bone volume fraction	0.73	0.59–0.86	0.004*
Apparent trabecular thickness	0.50	0.34–0.65	0.946
Skeleton density	0.70	0.56–0.84	0.013*
Inorm	0.73	0.59–0.86	0.004*
CEnorm	0.72	0.58–0.86	0.005*
Surf	0.72	0.59–0.86	0.005*
Junc	0.67	0.53–0.82	0.029*
Surf/Curv	0.68	0.54–0.83	0.023*
Erosion index	0.66	0.52–0.81	0.04*

The asterisk indicates an area under the ROC curve whose 95 % confidence interval did not include 0.5 (diagnostic performance better than chance) and whose *p* value is <0.05

Table 5

Discrimination of subjects with and without fragility fractures—areas under the receiver operating characteristics curve (AUC) for DXA-derived spine and hip BMD T-scores

AUC	95 % confidence interval	<i>p</i> value
Spine T-score		
0.58	0.42–0.74	0.28
Hip T-score		
0.64	0.48–0.78	0.08