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CT bone density analysis of low-impact proximal femur fractures using Hounsfield units

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ABSTRACT

Aim: To quantify and compare changes in bone mineral density (BMD) via CT analysis in patients with and without spontaneous femoral fractures.

Materials and methods: Consecutive series of patients with CT imaging for spontaneous femoral fractures were compared to the age and gender matched controls. Bone density fixed region of interest measurements were obtained at the site of the fracture, proximally at the femoral head, and distally at the lesser trochanter in fracture patients and controls. Inter- and intrapatient comparisons were performed, including Chi-square and *t*-test analyses.

Results: 24 spontaneous fractures and 25 controls were analyzed with no significant differences in mean age, gender, or body mass index. There were differences in the bone density between the fracture and contralateral non-fracture sides at ($p = 0.0001$) and distal ($p < 0.0001$) to the fracture. Proximal and distal bone density differences existed between case fracture and control non-fracture sites ($p < 0.0001$, $p = 0.0001$), and between the case non-fracture and control non-fracture sites ($p < 0.0001$, $p < 0.0001$). The reliability for measurements was good to excellent proximally (ICC = 0.63–0.87), moderate to excellent at the fracture site (ICC = 0.43–0.78), and fair to good distal (ICC = 0.24–0.68) to the fracture site.

Conclusion: Patients with spontaneous femoral fractures exhibit lower bone density than the asymptomatic controls. Bone insufficiency is best demonstrated proximal or distal to, rather than at the fracture site.

1. Introduction

Spontaneous fractures are non-pathological fractures, which occur in the context of zero to minimal preceding physical trauma. Osteoporosis ranks among the most common causes of these spontaneous fractures. The medical costs of treating osteoporosis-associated bone fractures are staggering, totaling an estimated $22 billion in medical costs in the United States alone in 2008 [1]. In particular, among the various types of osteoporosis-related fractures, the commonly encountered femoral fracture was shown to be the most expensive ($16,423) and required the longest length-of-stay (5.8 days) in a recent study [2].

The detection of osteoporosis is facilitated using various imaging modalities. Currently in clinical practice, DXA (dual-energy X-ray absorptiometry) is considered the gold-standard in the diagnosis of osteoporosis as well as the prediction of fracture risk [3]. Despite the associated morbidity and prevalence of these fractures, roughly only 30% of women and 4% of men above the age of 65 have had a DXA study [4]. Relying on BMD quantification from DXA alone can be problematic, as many of these osteoporotic fractures occur in the osteopenic (T-score 1–2.5 SD below the reference), rather than the osteoporotic range. Therefore, capturing earlier differences with greater sensitivity and reliability is critical [5]. In addition to this definitional limitation, DXA suffers from other shortcomings inherent to the imaging modality itself, such as an inability to both estimate true volumetric bone density as well as discriminate between cortical and trabecular bone mass [6]. There is also little evidence for employing repeated DXA imaging to follow a patient's disease and treatment

Abbreviations: 3D, three-dimensional; BMD, bone mineral density; BMI, body mass index; CI, confidence interval; CT, computed tomography; DXA, dual-energy X-ray absorptiometry; EMR, electronic medical record; HU, Hounsfield units; ICC, intraclass correlation coefficient; QCT, quantitative computed tomography; SD, standard deviation

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course due to the delayed progression of observable BMD changes, despite its prevalent usage in clinical practice [7,8]. Finally, DXA is prone to calcification artifacts common in older adults that can elevate the measured BMD, thereby obscuring a true osteoporotic phenomenon [9].

Given these limitations in using DXA to accurately assess bone density in the osteoporotic state, using alternative imaging techniques is paramount. Taking advantage of the ubiquity of CT (computed tomography) scanners as well as the capability of CT imaging to generate precise 3D (three-dimensional) imaging of bony anatomy without partial voluming artifacts with overlapping calcified and sclerotic lesions, 3DCT imaging offers excellent prospects for bone insufficiency imaging apart from fracture analysis for surgical planning and prognostication.

The usage of CT, particularly QCT or quantitative computed tomography, imaging in evaluating osteoporosis has been the subject of several articles. QCT has been shown to effectively distinguish between cortical and trabecular bones; however, such a technique relies on employing phantoms in the acquisition process for calibration [10,11]. QCT has been demonstrated to be the more sensitive of the two techniques (17.1% osteoporosis detection rate for DXA versus 46.4% for QCT) in postmenopausal women in the lumbar spine [12].

Evaluation of Hounsfield units (HU) has been explored in the context of wrist fractures on routine CT. By measuring HU density in the cancellous portion of the capitate, Johnson et al. identified a significant correlation with BMD and T-scores at the hip, femoral neck, and lumbar spine [13]. Routine opportunistic thoracic and abdominal CT imaging has also proven useful to detect reduced BMD as well as the presence of fractures despite unremarkable DXA T-scores [14]. No such imaging evaluation has been performed in femoral neck or hip fractures despite the common occurrence of such fractures.

This project was designed to identify the utility of routine 3DCT imaging in assessing BMD changes in the setting of spontaneous femoral fracture, since it is commonly performed for pre-surgical and management planning. It is not clear where the density would be altered with respect to the fracture site. We hypothesized that spontaneous fracture patients will exhibit reduced bone density as compared to the matched controls. If proven, routine 3DCT performed for fracture assessment could also be used to document the bone insufficiency.

2. Materials and methods

This was a HIPAA-compliant, cross-sectional evaluation of deidentified patients and imaging obtained from the electronic medical record (EMR). This project was approved by the university's institutional review board, and the informed consent was waived.

2.1. Patient population

A total of 522 consecutive patient records for patients with various lower extremity fractures who had received CT imaging orders between 01/2013 and 01/2016 were extracted from the hospital EMR system. Detailed chart review was performed to establish the demographic data such as age, sex, and BMI as well as the fracture etiology and fracture anatomic location.

To keep the data homogeneous with respect to spontaneous fractures, individuals below the age of 18 were excluded, as were those whose fracture history correlated with a traumatic cause (e.g. motor vehicle accident, altercation, etc.). Fractures secondary to known pathology such as metastatic disease (e.g. multiple myeloma) or nonmetastatic disease (e.g. renal disease or osteomyelitis) were similarly excluded as non-spontaneous fracture etiologies. Additional exclusion criteria included removing individuals whose CT data was missing or partial due to incomplete orders or unilateral imaging, as well as individuals who had previously underwent surgery or had implanted prosthetic hardware. Once this was completed, the remaining lower extremity spontaneous fracture cases were subdivided by location as hip (which includes acetabulum and femur), knee, upper leg, and lower leg. Ultimately, 24 femoral fracture cases (12 femoral head and neck cases, 7 intertrochanteric cases, and 5 greater trochanter cases) were obtained through this selection process. Of these cases, 6 had a history of using bisphosphonates such as alendronate; however, the fractures were not typical as seen in mid-femoral shaft in patients with bisphosphonate use. These femoral fractures were then compared to an appropriately age, sex, and BMI-matched group of 25 control CTs performed for renal stone analysis, since similar beam collimation and noncontrast technique are used for abdomen and pelvis imaging for such scans. None of these 25 controls had a known history of osteoporosis, osteomalacia, internal metal, or fractures.

All 3DCTs both in the case as well as in the control groups had been acquired on similar and comparable multislice institutional scanners (GE, Toshiba and Siemens = 16–64 slice scanners) using 0.6–0.625 mm beam collimations and 3 mm axial slice reconstructions in bone and soft tissue windows.

2.2. Image evaluation

Two trained readers independently performed all measurements blinded to each other's reads following a consensus session on 5 such scans. The readers were provided with the knowledge of fracture laterality and location as noted in the EMR. The images were loaded on an independent software, TeraRecon (Aquarius Intuition, Foster City, CA). Bilateral measurements at the fracture side and on the contralateral side were obtained on all the scans from fracture cases as well as controls. The axial images from 3DCT were aligned in the plane of the ischial tuberosities.

2.3. Bone mineral density ROI analysis

To assess the BMD, $3.00\,cm^2 \pm 0.05\,cm^2$ elliptical fixed ROIs were drawn on the axial slices at the site of the fracture, proximal to the fracture (within the femoral head) and distal to the fracture (at the level of the lesser trochanter). These elliptical ROIs were drawn to avoid intersections with any cortical bone, and therefore only sampled trabecular bone and bone marrow. Mean bone densities (HU) were recorded for each of these ellipses (Fig. 1).

2.4. Statistical analysis

Descriptive statistics were shown as means and standard deviations for continuous variables and frequencies for categorical variables. Box plots were used for illustrating the distribution of the variables among different groups. Linear mixed models were used to test the differences in mean values 1. between the fracture side and the non-fracture side in patients with fracture; 2. between the non-fracture side from patients with fracture and either non-fracture side from control patients; 3. Between the fracture side from patients with fracture and either non-fracture side from control patients. Within patient correlation was accounted by a random effect. A general Satterthwaite approximation was applied to adjust for unequal variances (heteroscedasticity). Tukey adjustment was used for multiple comparison. *t*-test and chi-square test were used to test the difference in mean age and gender distribution between case and control groups. p-Values were adjusted if significant differences were found in age and/or gender between case and control groups. p-Values of < 0.05 were considered as statistically significant. Inter-reader agreement of the two students' ROI measurements was tested using intraclass correlation coefficient (ICC) and was considered as poor for ICC < 0.20, fair for ICC between 0.2 and 0.39, moderate for ICC between 0.40 and 0.59, good for ICC between 0.60 and 0.73, and excellent for ICC of 0.74 or greater, respectively.

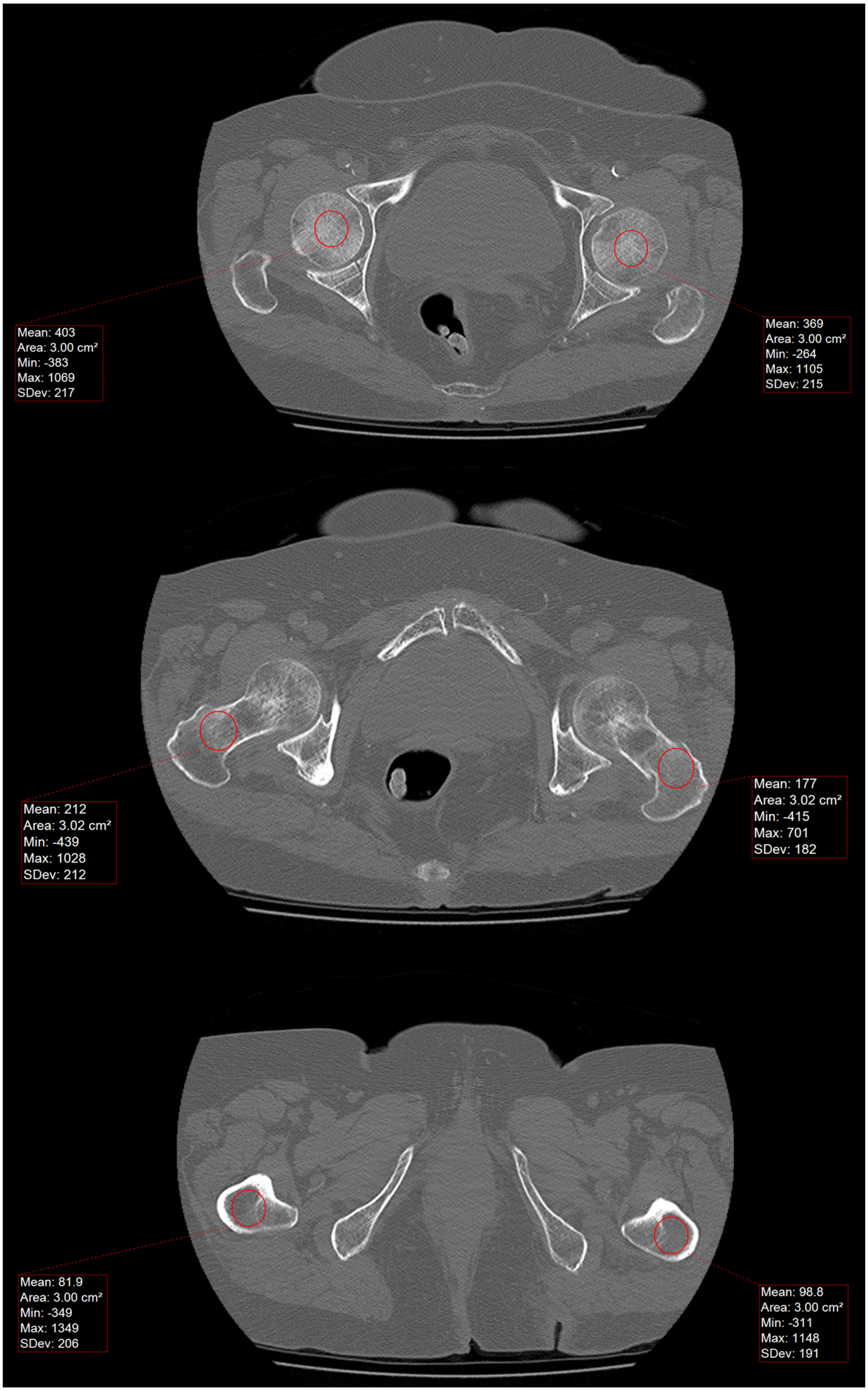

Fig. 1. Examples of ROI drawing in a spontaneous fracture CT. 3.00 cm^2 elliptical ROIs were drawn proximally in the femoral head (top), at the fracture site (middle), and distally at the level of the lesser trochanter (bottom). Note that similar analyses were performed on the contralateral, non-fractured side, as well as bilaterally on the control patients' KUB CTs.

3. Results

There were 24 cases of spontaneous femoral fractures that met the criteria described in the "Patient population" section (mean age = 65.6 years, 12 male, 12 female, mean BMI = 25.3). This case group was compared with 25 controls (mean age = 64.3, 12 male, 13 female, mean BMI = 29.2). No significant differences were seen between the case and the control groups with respect to age (p = 0.86), gender (p = 0.89), or BMI (p = 0.07).

3.1. Inter-patient comparison

Comparing the fractured sides with the 50 control non-fractured sides (the 25 left and 25 right sides were treated independently), it was observed that the mean HU density was significantly ($p \leq 0.0001$) lower proximal (279.7 HU versus 410.6 HU) and distal (58.6 HU versus 140.0 HU) to the site of fracture. However, there was no such difference (p = 0.87) on evaluation at the site of fracture (150.0 HU versus 144.5 HU). Completing an analogous comparison of the non-fractured sides between the case and control groups yielded similar findings, with a difference between the case and control being observed proximally (292.9 HU versus 410.6 HU; $p < 0.0001$), and distally (41.0 HU versus 140.0 HU; $p < 0.0001$), but not at the site of fracture (89.6 HU versus 144.5 HU; p = 0.16). Additionally, it was observed that for every 50 HU decrease in the bone density proximal to the site of fracture and within the femoral head, the odds of fracture risk increased by 74.4% (odds ratio = 1.744, 95% CI (1.291, 2.356)).

3.2. Intra-patient comparison

On examining the bone densities between the site of fracture and the contralateral side in the same cases, we found that the mean HU density was statistically significantly higher ($p \leq 0.0001$) on the side of fracture than on the contralateral non-fracture side at (150.0 HU versus 89.6 HU) and distal to (58.6 HU versus 32.9 HU) the fracture site, but not proximally (279.7 HU versus 292.9 HU; p = 0.59). The results are summarized in Table 1, while summary statistics for both the inter- and intra-patient comparisons are illustrated in Table 2 and Fig. 2.

3.3. Inter-reader agreement

The inter-reader agreement (ICC values) and their corresponding 95% confidence intervals at all 3 locations are shown in Table 3. Proximally at the femoral head, the ICC was 0.78 (95% CI = 0.63–0.87). At the fracture site, the ICC was 0.63 (95% CI = 0.43–0.78). Distally in the lesser trochanter, the ICC was 0.49 (95% CI = 0.24–0.68).

Table 1
Results from fixed ROI measurements. This table presents the means and standard deviations of the average HU densities determined proximal to, at, and distal to the fracture sites bilaterally for both the case as well as the control groups. The size of the standard deviations obtained can be explained by several factors, including the large cross-sections used for the ROIs (3.00 cm^2), the lack of calibration via phantoms prior to acquisition, local heterogeneity in bone density, limited CT image resolution, and partial voluming effect from nearby bone marrow.

	Case						Control		
	Non-fracture			Fracture			Non-fracture		
	N	Mean	Std	N	Mean	Std	N	Mean	Std
Proximal density (HU)	24	292.9	114.8	24	279.7	108.7	50	410.6	113.2
At fracture density (HU)	24	89.6	99.3	24	150.0	101.7	50	144.5	95.2
Distal density (HU)	24	32.9	41.0	24	58.6	51.3	50	140.0	98.5

Table 2
Tabular summary results demonstrating pertinent findings from bone ROI analysis. p-Values for these bone density comparisons are shown, with significant values highlighted in yellow.

	Case fracture vs. case non-fracture	Case fracture vs. control non-fracture	Case non-fracture vs. control non-fracture
Proximal density (HU)	0.59	<0.0001	<0.0001
At fracture density (HU)	0.0001	0.87	0.16
Distal density (HU)	<0.0001	0.0001	<0.0001

4. Discussion

From our findings, many important conclusions can readily be drawn. First, in an individual with existing spontaneous fractures, there seems to be little merit in comparing the fractured and the non-fractured side. Doing so only captures the phenomenon of hemorrhage and trabecular bone compression resulting following the fracture, which artificially and temporarily raises the bone density. Such a deceptive increase could obscure the true osteopenic nature of the bone. In addition, in cases of true spontaneous fractures where no pathology or trauma can be ascribed as the causative agent of the fracture, there is no reason to presuppose that one side would be more susceptible to fracture than the other. Finally, increased bone density at the fracture site shouldn't be taken as a sign of an underlying sclerotic or calcifying lesion.

Another conclusion is that if one is interested in best capturing possible osteopenic status of the femur, rather than measuring elsewhere in the shaft of the femur or at potential future fracture sites distally along the femur, it is best to measure the bone where it should be densest, i.e. at the femoral head. By measuring proximal to the site of fracture, we could best capture any bone insufficiency in our patient group. Fair to excellent inter-observer performance validates the practical use of this simple fixed region of interest measurement during routine CTs performed for pre-surgical assessment.

Several caveats need to be considered in interpreting our data. Besides our limited sample size (n = 24 for cases, n = 25 for controls), one such limitation of this project is our control set. As the healthy general population cannot be ethically screened with CT imaging, our CTs come from individuals who received imaging as part of a workup for nephrolithiasis. These individuals may therefore not accurately reflect the general population, and other suitable control groups could be worked up in the future for an improved comparison with our case group. One possible concern is that given the prior history of bisphosphonate usage in 6 of the 24 spontaneous fracture cases, these individuals could have sustained an atypical femoral fracture. However, these are unlikely to be atypical femoral fractures, as all of the fracture cases included in the study had fractures which were proximal to the lesser trochanter [15,16]. Another limitation of our project is that due to the retrospective nature of the data, we were not able to utilize QCT as the patient scans were not calibrated with phantoms. We wanted to use practical and simple HU criteria as these scans are obtained on routine CT imaging for pre-surgical planning. One additional limiting factor of our analysis was that we could not compare our results to patient DXA scans. Although five of the final CT impressions had indicated that DXA imaging could be considered due to osteopenia qualitatively observed on CTs, no further workup was obtained in those cases.

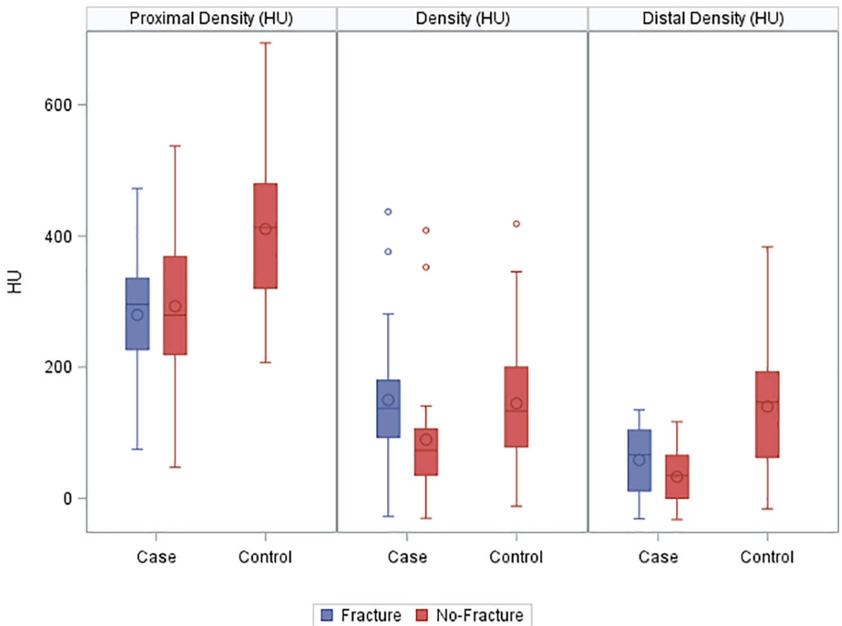

Fig. 2. Box-and-whisker plots of case and control HU densities. Distributions of these densities, along with outliers, are presented here proximal to, at, and distal to the fracture site. Note that measuring density at the site of fracture can be misleading and result in a median density that could be indistinguishable from normal bone.

Table 3
Intraclass correlation coefficient results. ICCs between the two readers in this study were generated. The ICC values proximal to, at, and distal to the site of fracture demonstrate "good" to "excellent", "moderate" to "excellent", and "fair" to "good" inter-reader agreement respectively.

	ICC	95% confidence interval	
Proximal density (HU)	0.78	0.63	0.87
At fracture density (HU)	0.63	0.43	0.78
Distal density (HU)	0.49	0.24	0.68

4.1. Future directions

There are several avenues for additional exploration in this project. In the process of obtaining the cases for this study, we identified other anatomical locations which could be explored in a future project, most notably 88 cases of spontaneous fracture in the knee. This knee subset is being examined to see if similar osteopenic bone density changes occur in individuals with those spontaneous fractures compared to an appropriate control set, and with any obtained DXA scans. It would be of interest to correlate the bone density differences identified in this project with functional survey data. This would be helpful in elucidating possible associations between reduced bone density and other markers readily available to the clinician, such as activities of daily living, Timed Up & Go tests, various Frailty Index measures, etc. Such studies would be of utility to physicians, allowing them to make more informed decisions for their patients with osteopenia who are at risk for falls and future spontaneous fractures.

To summarize, this study expands the understanding of the connection between spontaneous fractures and osteopenic patients. Our data suggests that in patients with spontaneous femoral fractures, decreased bone density is best assessed on routine CT imaging with trabecular bone mineral density measurements proximal to the fracture site in the femoral head.

Disclosures

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The authors do not report any conflict of interest.

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