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ORIGINAL ARTICLE

DXA evaluation of femoral bone mineral density and cortical width in patients with prior total knee arthroplasty

T. Blaty[1] · D. Krueger[1] · R. Illgen[2] · M. Squire[2] · B. Heiderscheit[2] · N. Binkley[1] · P. Anderson[2]

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Abstract

Summary Periprosthetic fractures after total knee arthroplasty (TKA) have devastating consequences. Osteoporosis increases periprosthetic fracture risk, but distal femur bone mineral density (BMD) is not measured post-TKA. This study measured distal femur BMD and cortical width; both were lower in the TKA compared to the non-operated leg. BMD measurement reproducibility was good. Standardized DXA regions of interest are proposed.

Introduction Periprosthetic fractures following total knee arthroplasty (TKA) are not rare. We hypothesized that TKA is associated with low BMD, potentially increasing periprosthetic fracture risk. However, distal femur dual energy x-ray (DXA) measurement is virtually never performed after TKA due to lack of standardized approaches. Thus, this study's aims were to develop standard DXA femur regions of interest (ROIs), assess cortical width, and determine measurement reproducibility in TKA patients.

Methods Thirty adults (15 M/15 F) age 59–80 years with unilateral, primary TKA within 2–5 years had femoral DXA scans performed in duplicate using a Lunar iDXA densitometer. In prior work, we established that femur BMD was lowest in the distal metaphysis and highest in mid-shaft. Thus, BMD and cortical width were measured at 15%, 25%, and 60% of the femur length measured from the distal notch. Femur BMD and cortical width were compared between limbs (TKA vs. non-operated side) by paired *t* test.

Results BMD was 3.2–9.9% lower ($p < 0.001$) in the operated femur at all custom ROIs; substantial between individual differences existed with some up to 30% lower. Cortical width was lower ($p < 0.05$) at the 25% ROI on the TKA side. BMD reproducibility was excellent; CV 0.85–1.33%.

Conclusions Distal femur BMD can be reproducibly measured using DXA and is ~ 10% lower on the TKA leg. Similarly, medial and lateral cortices are thinner at the 25% ROI. These bone changes likely increase periprosthetic fracture risk. Further work to define and mitigate periprosthetic fracture risk after TKA is needed.

Keywords Bone mineral density (BMD) · Cortical width · Dual energy x-ray absorptiometry (DXA) · Total knee arthroplasty (TKA)

Introduction

Total knee arthroplasty (TKA) is a commonly performed and successful surgical technique. As the world population ages, the number of older adults with TKA, and the number of these procedures performed, will increase. Notably, it is reported that ~ 15% of Americans age 70+ have a total knee replacement and estimated that ~ 3.5 million TKA procedures will be performed annually by 2030 [1, 2]. Periprosthetic fractures after TKA, most commonly in the supracondylar area of the distal femur, are increasing in frequency as the number of surviving patients grows and ages [3]. These periprosthetic fractures are not rare with a reported incidence from 0.3 to 2.5% after primary TKA and from 1.6 to 38.0% after TKA revision [4–6]; thus, this is a common problem that will increase for the foreseeable future.

Periprosthetic fractures after TKA may be technically challenging to repair [7, 8] and personally devastating. Indeed, these fractures can cause functional decline and are associated with longer hospitalization, frequent hospital readmission (> 20% within 3 months), major healthcare cost, and high

✉ N. Binkley
nbinkley@wisc.edu

[1] Osteoporosis Clinical Research Program, University of Wisconsin School of Medicine and Public Health, 2870 University Ave. Ste. 100, Madison, WI 53705, USA

[2] Department of Orthopedics and Rehabilitation, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA

mortality (1-year mortality > 20%) [7, 9–11]. Unsurprisingly, osteoporosis predisposes to, and may confound surgical treatment of, periprosthetic fracture [12, 13]. Osteoporosis is extremely common in those undergoing total hip or knee arthroplasty; 26% self-report the condition [14], and 66–85% have low bone mineral density (BMD) when measured by dual-energy x-ray absorptiometry (DXA) [15, 16]. As could be expected, recognized osteoporosis risk factors (glucocorticoid use, female sex, rheumatoid arthritis, and advanced age) are also established risk factors for fracture after joint replacement [3, 4, 17]. Further, severe osteoporosis may preclude adequate fixation potentially contributing to hardware failure [7]. Existing data show that TKA is associated with a rapid and substantial 10–15% decline in distal femur BMD within the first 6 months following TKA [18–22]. In summary, osteoporosis is common prior to TKA, BMD declines following surgery, and low BMD likely contributes to periprosthetic fractures and related adverse outcomes. It is plausible that assessing distal femur BMD will better identify patients at risk for periprosthetic fracture than hip, spine, or forearm DXA. Despite this, distal femoral BMD is virtually never measured prior to or following TKA. This neglect, in part, reflects absence of consensus regarding appropriate distal femur DXA techniques and lack of BMD measurement reproducibility data.

Additionally, it has long been recognized that cortical bone is a major contributor to overall bone strength and fracture risk [23, 24]. Recently, DXA-based methodologies have been developed as an approach to identify signs of atypical femur fracture (AFF) thereby allowing assessment of femoral cortical width and density [25, 26]. To our knowledge, the potential utility of these recent DXA capabilities has not been evaluated following TKA. As such, the purpose of this study was to utilize existing DXA software to evaluate distal femur BMD and cortical width in patients with prior TKA and to assess reproducibility of these measurements.

Methods

Participants

Thirty adults (15 men and 15 women) with a prior unilateral, primary TKA were recruited from a university-based orthopedic joint arthroplasty practice. Patients who were a minimum of two, and a maximum of five, years post-knee arthroplasty with excellent post TKA function, defined as patient-reported outcomes of pain (visual analogue scale (VAS) < 3.0 or SF12 physical component summary (PCS) > 40), were eligible. Potential subjects were excluded for prior hip replacement, bilateral TKA, TKA revision surgery, prior lower extremity fracture, or prolonged immobilization of non-TKA extremity. Further exclusion criteria included potential secondary causes of osteoporosis (such as malabsorption or glucocorticoid use), prior use of an osteoporosis medication, or current use of systemic hormone replacement. Pregnant women were excluded due to use of radiation technology in this study. An award from the University of Wisconsin Department of Orthopedics and Rehabilitation provided funding for this study. The protocol was approved by the University of Wisconsin Health Sciences Institutional Review Board and conducted in compliance with Federal and local regulations.

Study design

As this was exploratory pilot research, the sample size was selected based upon recommendations for routine clinical DXA precision assessment [27]. This study was performed from December 2017 through February 2018 at the University of Wisconsin Osteoporosis Clinical Research Program in Madison, WI. DXA scans were performed using a Lunar iDXA (GE Healthcare, Madison, WI) densitometer with enCORE v17 software and the AFF feature. Subjects' height and weight were obtained prior to DXA scans using a wall-mounted stadiometer and calibrated scale. Each subject underwent standard clinical lumbar spine, forearm, and vertebral fracture assessment (VFA) scans. Bilateral posterior-anterior femur scans were obtained with the AFF feature using a modified acquisition technique. The AFF software allows acquisition of a long femur scan, starting just proximal to the femoral condyle flare and imaging the femur to include the standard proximal femur measurement sites. However, for this study, scans were extended to include approximately 2–3 cm of the proximal tibia and the entire femur. A second set of bilateral whole femur scans was acquired after repositioning (subjects stood from and returned to the DXA table) to acquire precision assessment data.

All scans were acquired and analyzed in the standard clinical manner per manufacturer recommendations by one physician (TB) under the supervision of an International Society for Clinical Densitometry (ISCD)-certified technologist. Vertebral fractures were identified by review of the VFA images by one physician (NB) using the Genant visual semi-quantitative approach [28].

Custom femur analyses

Initially, three 2-cm custom regions of interest (ROIs) to measure BMD were manually placed at the mid-shaft (60% of femur length starting measurement from the intercondylar notch) and distal femur (15% and 25%) of the non-operated leg (Fig. 1). These regions were selected based on prior work investigating femur BMD distribution conducted by stacking 1-cm ROIs from the distal end femur sequentially to the lesser trochanter [29]. Consequently, ROIs at 15% and 25% from the distal end of the femur length were selected as BMD was

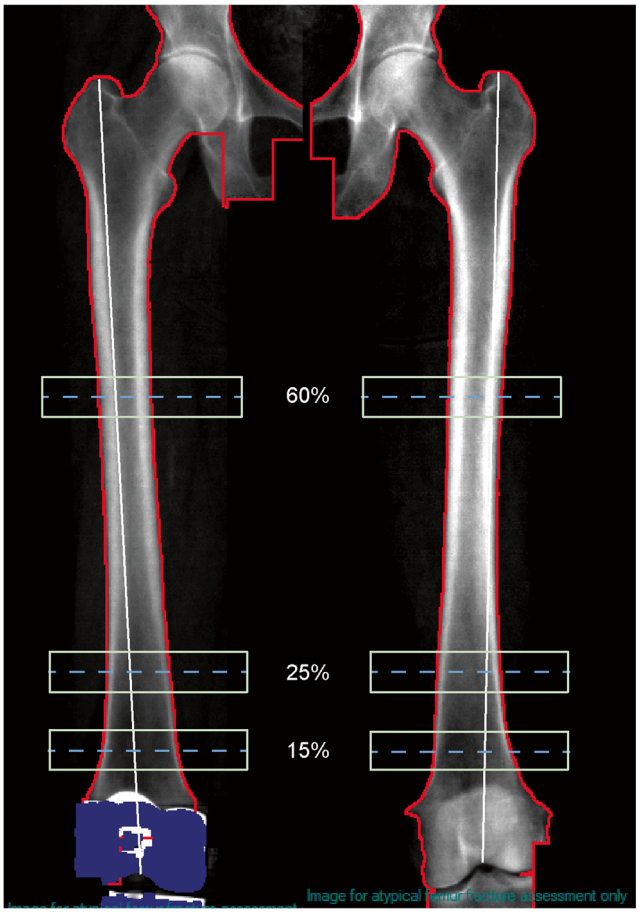

Fig. 1 Custom regions of interest. Distal femur ROI placement is depicted; this was determined by using the DXA software line tool to measure the femur length from the greater trochanter to intercondylar notch on the non-operated leg. Distances from the notch were calculated for 15%, 25%, and 60% of the femur length (dotted lines). A 2-cm ROI was manually centered at these points. Cortical width was measured by the AFF feature of the DXA software at the center of these 2-cm ROIs (dotted lines). This pattern was replicated on the TKA femur and copied to the duplicate scan for precision assessment. *ROI* region of interest, *DXA* dual-energy x-ray absorptiometry, *AFF* atypical femur fracture, *TKA* total knee arthroplasty

lowest at these sites and this supracondylar area is the most common location of periprosthetic fractures following TKA [3]. The 60% ROI was selected to investigate a highly cortical site [30]. This custom analysis template was replicated on the TKA femur.

Detailed methodology for custom ROI placement follows. On the femur of the non-operated side, the line tool was used to determine femur length from the intercondylar notch to the cranial end of the greater trochanter. Based on this measurement, the 15, 25, and 60% locations from the intercondylar notch location were calculated and 2 × 7 cm ROIs placed using the line tool to measure calculated distance. To ensure centering of these 2-cm ROIs, the lines were drawn 1 cm longer than calculated and the proximal end of the ROI superimposed on the tip. To standardize ROI placement, these measurements were used for both legs. This approach was performed on the first set of femur scans acquired; the software copy feature was used to transfer this mask to the second scan pair. This mask was then moved and/or rotated to best fit the anatomy of the second scan set to the duplicate analysis for precision assessment.

Medial and lateral cortical width measurements along the femur were automatically determined by the AFF software at 0.25-mm increments. Values at the 15, 25, and 60% lengths were extracted with manufacturer guidance and used for analyses.

Statistical analysis

Data from the first set of femur scans acquired were used for analyses. Paired *t* tests were used to compare BMD and cortical width measurements at the custom ROIs from the TKA side to the non-operated side. *t* tests were also used to compare BMD differences between legs at the standard versus custom ROIs and also to explore sex differences in BMD (JMP Pro v13, Carey, NC). Linear regression analyses were performed to begin exploring whether lower absolute BMD was associated with greater distal femur BMD difference between the TKA and non-operated leg. Precision of the custom BMD regions and cortical width measurements was determined using the approach described by Baim et al. [27] via the ISCD advanced precision calculator available at www.iscd.org. An accepted level of significance of 0.05 was applied.

Results

Subjects

Thirty subjects (15 men and 15 women) with a mean age of 67.9 years (range 59–80) and mean BMI of 30.0 kg/m^2 (range 23.3–37.1) participated in this study. Demographic data are presented in Table 1; briefly, the group was approximately 3 years post-surgery; five were found to have previously unappreciated osteoporosis by BMD T-score, and three subjects had one prevalent vertebral fracture on VFA, while ≥2 fractures were observed in an additional three. All but one of these ten vertebral fractures (three grade 1, seven grade 2) were in the thoracic spine. Low trauma fractures of the forearm or clavicle as an adult were reported by an additional three subjects, none of whom had vertebral fractures. Women had shorter femurs and lower BMD than men at the 1/3 radius and at all custom distal femur sites; otherwise, the sample did not differ by sex (Table 1).

Table 1 Demographics

	Male ($n = 15$)	Female ($n = 15$)	All ($n = 30$)	p value*
Age (years)	67.1 (5.2)	68.6 (5.5)	67.9 (5.3)	0.44
BMI (kg/m^2)	30.1 (4.3)	29.9 (3.7)	30.0 (3.9)	0.90
Time post-surgery (years)	3.26 (0.82)	3.26 (0.79)	3.2 (0.7)	0.99
Femur length (cm)	45.6 (2.4)	42.1 (2.3)	43.8 (2.9)	< 0.001
L1–L4 BMD (g/cm^2)	1.365 (0.20)	1.335 (0.27)	1.349 (0.24)	0.73
Femur neck BMD (g/cm^2)	0.942 (0.14)	0.904 (0.11)	0.923 (0.13)	0.41
Total proximal femur BMD (g/cm^2)	1.003 (0.13)	0.941 (0.10)	0.972 (0.12)	0.15
1/3 radius BMD (g/cm^2)	0.989 ± 0.10	0.789 ± 0.11	0.889 ± 0.14	< 0.0001
15% distal femur BMD TKA (g/cm^2)	0.894 (0.03)	0.771 (0.03)	0.833 (0.14)	0.01
15% distal femur BMD non-op (g/cm^2)	0.998 (0.03)	0.829 (0.03)	0.914 (0.16)	0.002
25% distal femur BMD TKA (g/cm^2)	1.239 (0.04)	1.053 (0.04)	1.146 (0.18)	0.004
25% distal femur BMD non-op (g/cm^2)	1.384 (0.04)	1.127 (0.04)	1.256 (0.21)	< 0.001
60% distal femur BMD TKA (g/cm^2)	2.282 (0.05)	1.960 (0.05)	2.121 (0.26)	< 0.001
60% distal femur BMD non-op (g/cm^2)	2.236 (0.06)	2.018 (0.06)	2.188 (0.27)	< 0.001
Lowest T-score (of hip, L-spine or 1/3 radius)	− 1.2 (1.01)	− 1.5 (0.97)	− 1.4 (1.0)	0.35
T-score ≤ − 2.5	1	4	5	
Vertebral fracture on VFA	4	2	6	

Data presented as mean (SD)

TKA total knee arthroplasty leg, *non-op* non-operated leg

*Comparison of male and female groups

Femur BMD

Mean BMD was lower ($p < 0.001$) at all ROIs on the TKA leg versus that on the non-operated side (Table 2). Specifically, BMD was 9.9 and 9.8% lower at the far distal femur sites, the 15% and 25% ROIs respectively, compared to 3.3 and 3.7% at the mid-shaft (60%) and standard proximal total femur site (Fig. 2). Substantial between individual variance in distal femur BMD difference was observed, with some subjects having values up to 30% lower in the TKA leg and three demonstrating numerically higher BMD. This is depicted in Fig. 3 using the 15% ROI; a very similar pattern was observed at

Table 2 BMD and cortical width: TKA versus non-operated leg

	TKA leg	Non-op leg	Difference TKA-non-op	p value	CV TKA leg (g/cm^2)	CV non-op leg (g/cm^2)	% CV TKA leg	% CV non-op
BMD (g/cm^2)								
Total proximal femur	0.955* (0.12)	0.988 (0.12)	− 0.033 (0.05)	0.0005	0.008	0.009	0.77	0.90
15% ROI	0.833* (0.14)	0.914 (0.16)	− 0.081 (0.07)	< 0.0001	0.011	0.010	1.05	1.03
25% ROI	1.146* (0.18)	1.256 (0.21)	− 0.110 (0.09)	< 0.0001	0.013	0.011	1.33	1.07
60% ROI	2.121* (0.26)	2.188 (0.27)	− 0.067 (0.08)	< 0.0001	0.009	0.009	0.85	0.91
Cortical width (mm)								
Medial at 15%	2.49 (0.33)	2.51 (0.35)	− 0.02 (0.28)	0.71	0.031	0.048	3.11	4.77
Lateral at 15%	2.51 (0.71)	2.99 (2.09)	− 0.48 (1.97)	0.20	0.123	0.062	12.33	6.24
Medial at 25%	3.29* (0.50)	3.47 (0.43)	− 0.18 (0.40)	0.02	0.046	0.048	4.58	4.81
Lateral at 25%	3.06* (0.40)	3.32 (0.45)	− 0.26 (0.28)	< 0.0001	0.043	0.059	4.25	5.92
Medial at 60%	6.62 (0.94)	6.74 (0.87)	− 0.12 (0.65)	0.32	0.039	0.035	3.86	3.48
Lateral at 60%	6.81 (1.02)	6.98 (0.89)	− 0.17 (0.70)	0.18	0.044	0.038	4.45	3.77

Data as mean (SD)

CV coefficient of variation based on mean and SD of BMD from duplicate scans, *TKA* total knee arthroplasty, *non-op* non-operated, *ROI* region of interest

*TKA side lower than non-operated leg

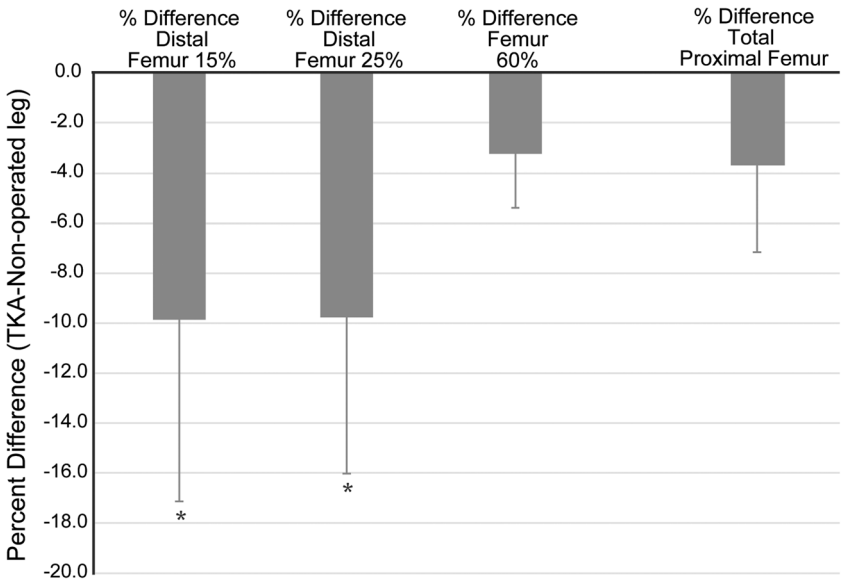

Fig. 2 Mean percent difference in BMD TKA versus non-operated leg. Mean percent difference in BMD between the operated and the non-operated femurs at the 2-cm ROIs centered at 15%, 25%, and 60% of femur length. A greater mean difference was present at the 15% and 25% sites ($p < 0.001$). Data as mean/SD. *Different from 60% and total proximal femur ROIs ($p < 0.001$); *BMD* bone mineral density, *TKA* total knee arthroplasty, *ROI* region of interest

25% (data not shown). No relationship was demonstrated between hip, spine, or forearm BMD and difference between the TKA and non-operated sides (data not shown).

As noted above, with the exception of 1/3 radius, sex differences in BMD at the standard clinical sites were not observed. Conversely, BMD was lower ($p < 0.05$) at all distal femur sites in women compared to the men (Table 1).

Femur cortical width

Mean lateral and medial cortical widths were lower ($p < 0.005$) in the TKA leg at the 25% site compared to those in the non-operated leg (Table 2). Mean cortical width was numerically, but not statistically, lower at the 15% and 60% ROI. Unlike BMD, cortical width measurements were less consistent; the TKA side was numerically less only 65% of the time. It is noteworthy that the software version used was optimized to measure proximal femoral shaft cortices to seek thickening associated with AFF; consequently, identification of the thin distal femur cortices was occasionally beyond the software capabilities to accurately detect the inner and outer cortical edges and were, on visual inspection, occasionally obviously incorrect. By subjective visual assessment, the cortical edge detection could have been improved at the 15% sites in three subjects. These inaccuracies in cortical width measurement confound not only overall results but also exploration of potential sex differences. Medial width was lower ($p < 0.01$) in women at the 15% and all 25% sites ($p < 0.01$), except at the medial cortex of the TKA leg (Table 2). No difference in cortical width was observed at the 60% or lateral cortex at the 15% ROI.

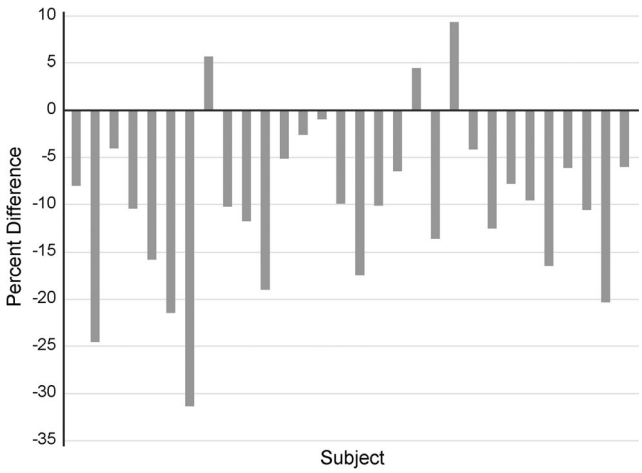

Fig. 3 Percent difference TKA versus non-operated leg at the 15% ROI. The percent difference in BMD at the 15% site between the operated and the non-operated femur in each subject is depicted. This illustrates the substantial between individual variations in BMD and also that not all individuals were lower on the TKA side; a similar pattern was observed at the 25% ROI. *TKA* total knee arthroplasty, *ROI* region of interest, *BMD* bone mineral density

Femur BMD and cortical width reproducibility

BMD reproducibility at the custom ROIs demonstrated %CVs ranging from 0.85–1.33% compared to total proximal femur values of 0.77% and 0.90% on the TKA and non-operated legs respectively (Table 2). For reference, ISCD minimum acceptable precision for the standard clinical total proximal femur and spine is 1.8% and 1.9% respectively [31]. As could be expected from the edge detection issues noted above, cortical width demonstrated more variance between measurements with percent CVs ranging from 3.11–12.33% (Table 2).

Discussion

This pilot study demonstrates that BMD and cortical width can be reproducibly measured at the distal femur using existing DXA software in patients with TKA. It further proposes a standardized approach designed to assess bone density and cortical width in the supracondylar region where periprosthetic fractures commonly occur. As such, standard DXA could potentially be used as a clinical tool to assist in TKA planning, monitor BMD change post-operatively, and evaluate interventions, e.g., exercise, nutrition, and pharmacologic agents to mitigate bone loss post-operatively. It seems plausible/likely that such interventions could ultimately reduce the risk of periprosthetic fracture following TKA. It is likely that DXA measurement techniques distal to the stem of total hip or total shoulder prostheses could be used for similar purposes.

In this cohort, BMD throughout the femur of the TKA side was 4–10% lower than that of the non-operated side, generally replicating findings of other studies [18–20, 32]. It is noteworthy that this difference is most obvious at the distal femur sites, suggesting that measurement of the standard proximal femur sites (e.g., total proximal femur or femoral neck) is likely inadequate to optimally assess periprosthetic fracture risk. Additionally, this is the first study to use DXA for evaluation of distal femur cortical width in TKA patients and demonstrated ~ 8% thinner cortices on the TKA side at the 25% femur ROI. These findings of lower distal femur BMD and thinner femur cortices likely contribute to increased periprosthetic fracture risk [33].

The mechanism(s) leading to lower distal femur BMD and thinner cortices are unknown, but likely multifactorial. Possible mechanisms include decreased loading on the TKA side from chronic pain associated with joint degeneration and therefore present prior to surgery, although prior studies have demonstrated a 12–18% BMD loss after surgery. Additionally, bone loss due to stress shielding, reduced quadriceps strength, immobility, and potentially gait changes post-operatively could contribute to bone loss [34–39]. Unknown effects of impaired proprioception after TKA may affect bone mass. Finally, whether due to the above noted effects on bone loading or to other yet to be defined factors, existing albeit limited, data report changes in bone turnover markers following TKA [40, 41]. Further research is needed to clarify these potential causes of bone loss following TKA. Such work could also potentially explain the substantial between-individual differences observed in this cohort.

An important consideration is pre-existing osteoporosis at the time of TKA, although not addressed in this work, as those with known osteoporosis were excluded. Despite excluding patients likely to have low BMD, 11 of these 30 patients met T-score criteria for osteoporosis or had vertebral fracture (6 had occult vertebral fractures on VFA). It seems probable that those with osteoporosis prior to TKA are more likely to experience periprosthetic fracture. However, in this pilot study, we did not demonstrate a relationship between standard clinically measured BMD and the magnitude of BMD difference between the TKA and non-operated leg at these custom ROIs. The demonstration of BMD sex differences only at the custom and peripheral ROIs may further reinforce the need to measure distal femur BMD in these patients. It is plausible that in addition to our small sample size, degenerative disease of the spine and proximal femur, which can elevate DXA measured BMD [42], is contributing to the inability to detect a sex difference. One could similarly expect to detect sex differences in cortical width, which was observed bilaterally at the 25% ROI; however, the 15% ROI was only different on the medial side. This may reflect small sample size, but as noted above, a contributing factor is use of software designed to measure more proximal femoral cortical bone rather than the thin distal cortices. It seems likely that cortical measurement capabilities could improve with software optimized to detail narrow cortical bone. Regardless of this limitation, these pilot data support the concept that cortical changes may be evaluated in a precise manner at the distal femur.

It is appropriate to consider periprosthetic fractures as osteoporosis-related fragility fractures as the vast majority (~ 80%) occur either with a fall from standing height or with no known trauma [43, 44]. In this regard, there is increasing interest in bone health assessment and optimization prior to major orthopedic procedures in older adults. Thus, it seems prudent to perform BMD measurement prior to TKA performance. Standardization of distal femur DXA regions of interest along the lines proposed here could potentially become part of such an evaluation and treatment program. In this regard, data suggest that pharmacologic agents may be beneficial to mitigate bone loss following joint replacement. For example, anti-resorptive or anabolic medications substantially reduce revision need following total knee and total hip arthroplasty and also improve BMD [45–47]. It is logical that such treatments could reduce periprosthetic fracture risk; studies to test this hypothesis are needed.

A unique strength of this study is that it suggests a standardized, reproducible approach to measuring BMD and cortical width at the distal femur in patients following TKA. However, multiple study weaknesses must be acknowledged. Notably, while the BMD reproducibility was very good, much manual scan analysis (measurement and ROI placement) was required which precludes routine clinical use at this time. However, this work could be viewed as proof of concept in that that such an approach could be optimized and automated with standard regions of interest being automatically placed by the DXA software as is currently done with radius ROIs. Additionally, as noted above, cortical edge detection is currently suboptimal; software enhancement is needed to improve cortical width measurement capabilities and/or offer

the ability for the technologist to adjust these cortical edges. Moreover, although a greater BMD difference is demonstrated at the distal femur, this work does not demonstrate superior sensitivity or specificity to standard hip DXA for assessing periprosthetic fracture risk; however, this is a compelling concept that should be evaluated in future studies. Finally, this study was small, performed only at one research location and with a high-resolution densitometer of one manufacturer; further prospective studies using standardized ROIs with larger numbers and other DXA instruments are needed to evaluate change over time and the utility of distal femur BMD and cortical width measurements.

In conclusion, this study demonstrated a reproducible approach to measuring distal femur bone density and cortical width in patients with TKA. The ROIs studied are logical and should be considered a potential standardized approach to be used in longitudinal studies that evaluate femur change over time following TKA. Optimization of DXA software to automate this process would likely improve the reproducibility and clinical utility. Additionally, investigation of how low distal femur BMD or cortical width impacts periprosthetic fracture risk is indicated. Optimal use of DXA and appropriate interventions to improve skeletal status pre- and post-TKA requires further study; such approaches seem likely to reduce periprosthetic fracture risk, thereby improving long-term outcomes and reducing healthcare costs.

Compliance with ethical standards

The protocol was approved by the University of Wisconsin Health Sciences Institutional Review Board and conducted in compliance with Federal and local regulations.

Conflicts of interest None.

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