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High-Resolution Peripheral Quantitative Computed Tomography (HR-PQCT) and Dual Energy X-Ray Absorptiometry (DXA) Measurements of Proximal Tibia in Patients Undergoing Total Knee Arthroplasty

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The aim of the study was to assess bone morphometric indices of the proximal tibia and compare it with bone mineral density (BMD) at hip and lumbar spine and compare with the pQCT. Fifty consecutive patients who underwent total knee arthroplasty (TKA) had a dual energy X-ray absorptiometry (DXA) scan of the upper femur and lumbar spine. Upper tibial cuts were harvested from the tibial condyles and a DXA of tibial cuts was done during TKA. Bone morphometry studies were carried out using HR-pQCT. The bone mineral density at the hip was 0.54 $\pm$ 0.08 g/cm^2 and spine was 0.73 $\pm$ 0.1 with a T score at the hip –2.23 $\pm$ 0.44 and spine –2.61 $\pm$ 0.45. The bone mineral density of the tibial cut was 0.356 $\pm$ 0.03 g/cm^2 ($P < 0.001$) and T score was –6.58 $\pm$ 2.87 ($P < 0.001$). The average bone volume (BV) was 115.27 $\pm$ 40.45 mm^3, trabecular number (Tb.N) was 1.45 $\pm$ 0.32 (1.009–2.37) and trabecular thickness (Tb.Th) was 0.181 $\pm$ 0.03 mm (0.111–0.268). The mean bone mineral density measured was 206.24 $\pm$ 50.58 mg HA/ccm. This study shows that there is highly significant difference between BMD measured by DXA and pQCT, and that bone morphometric analysis indicates that there is marked decrease in the mechanical properties of the bone in the proximal tibia due to knee Osteoarthritis and Osteoporosis indicating poor bone architecture and quality.

Key words: pQCT – Proximal tibia – Osteoporosis – Osteoarthritis

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Osteoarthritis of the knee (OAK) and osteoporosis (OP) are major health issues world over and affects the quality of life, morbidity, and mortality and ever increasing economic burden. Both conditions are managed differently. In many of the patients, both diseases coexist.[1] Mäkinen *et al*[2] reported the prevalence of OP in 28% of their patients with OA of the hip. The association of OAK and osteoporosis was also reported.[3,4] Terauchi *et al*[5] reported that osteoporosis causes trabecular microfractures, thus increasing the stresses on the cartilage and thereby increasing the severity of OAK. Ding *et al*[6] showed in a study involving 10 cadavers that even in early OAK, deterioration in the architecture of cancellous bone in the sub-chondral proximal tibia decreases mechanical properties.

The clinical survival of joint arthroplasties is associated with the quality of bone at the site of the inserts and normal bone is a key factor for rapid osseointegration of the implant. Gabet *et al*[7] suggested that peri-implant bone should be able to withstand the stresses, otherwise it affects the long-term survival of the implants. Dual energy X-ray absorptiometry is the gold standard technique to measures BMD which gives the quantity of bone. The assessment of the BMD at the hip and spine may not be similar to the periarticular area of the tibia. Soininvaara *et al*[8] studied periprosthetic BMD measurements in patients with osteoarthritis of hip and found precision error between 2.9 and 3.2%. The low BMD has recently been shown to delay the stem osseointegration in patients undergoing cementless total hip replacement.[9] There is frequent observation of soft bone at the subchondral area of the tibia during TKA, which did not correlate with the BMD measurement of the hip and spine. Thus, we hypothesize that there is more extensive bone weakness that meets the eye than the readings of the DXA. Wada *et al*[10] reported that the BMD at the medial condyle of the tibia in the OA was higher, this probably due to compressive forces at the medial condyle. On the other hand, recent studies have questioned this belief. Živković *et al*[11] showed that the main predictor of the BMD is the duration of the postmenopausal period and with longer period is associated with lower BMD, while Goerres *et al*[12] found that their patients with OA had a relatively lower hip BMD on the affected leg.

Recently newer technologies have been applied to study bone morphometric indices in the subchondral area of the tibia to study the trabecular and cortical pattern.[13–16]

With an objective of comparing the BMD of the Spine and Hips with tibial cuts and secondly to assess bone morphometric indices using HR-pQCT and to correlate with the BMD this prospective study was done.

Methods

Fifty consecutive patients who underwent TKA were studied. After informed consent, patient demographic data was collected on a preset pro forma. The data included: age, sex, weight, height, affected knee alignment, and years of OAK. All patients were in the Kellegren and Lawrence grading of ≥ 3. Patients underwent DXA scan of the upper femur and lumbar spine. At surgery of TKA, upper tibial cuts were harvested and the specimen was removed for bone biopsy and a DXA of tibial cuts was done. The tibial cuts of the patients were stored in 2% formalin and shipped to b-cube AG Bio-Technopark, Wagistrasse 13CH-8952 Schlieren-Zurich, Switzerland. The samples were measured with a commercially available cabinet cone-beam micro-CT, (μCT 100, SCANCO Medical AG, Brüttisellen, Switzerland). Micro-CT examinations were captured by the photons and detected by a charge coupled device–based area detector and the projection data was computer-reconstructed into a 3072×3072 image matrix. Individual assessment of the total volume (TV, mm^3); bone volume (BV, mm^3); relative bone volume BV/TV (%); connectivity density (Conn.D); trabecular number (DT-Tb.N, mm); trabecular thickness (DT-Tb.Th, mm); and DT-Tb.Sp: trabecular separation = marrow thickness (DT-Tb.Sp, mm).

Quality control

Calibration tests were carried out every day for the 2 techniques using an external phantom to detect any potential drift of the instrumentation. The same sample was tested twice and we did not observe any drift during the period of the protocol. All examinations of HR-pQCT were analyzed by the same observer. The dual energy X-ray absorptiometry was performed using a commercial system (Discovery, Hologic Inc., Bedford, Massachusetts).

Statistical analysis

For each subject in the reproducibility study, a coefficient of variation (CV) was calculated as the standard deviation of the 3 repeated measurements divided by the subject mean. Furthermore, the

Table 1 Scan settings of pQCT

Scanner	μCT 100
Voxel size	29.3 μm
FOV	90 mm
Image matrix	3072 × 3072
Slices	500 or 600
X-ray voltage	90 kVp
Intensity	18 W
Projections/180°	1500
Integration time	250 ms
Frame average	2
Filter	0.5 mm Al
Scan time	75 min

short-term precision errors were then calculated as root-mean-square (RMS) averages of the precision errors for each of the subjects. Relationships between the young healthy volunteers (reference) and microarchitecture of our patients were compared and estimated using Pearson or Spearman correlations, depending on the distribution of variables (i.e., Pearson for parametric distribution, Spearman for nonparametric distribution). The statistical level of significance was <0.05.

Results

The average age of the patients was 64 ± 7.7 years. There were 11 males and 39 females. Knee alignment range was 0 to 18° of varus. Table 1 gives the scanning details using cone-beam μCT (Scano Medical AG, Bruttisellen, Switzerland). Figure 1 shows the area and the site of where the tibial cut was focused and measured. Table 2 gives the data of the pQCT of the tibial cuts. The average BV was 115.27 ± 40.45 mm^3 (60.05–221); Tb.N was 1.45 ± 0.32 (1.009–2.37); Tb.Th was 0.181 ± 0.03 mm (0.111–0.268); and Conn.D was 6.525 ± 2.57 mm^3 (3.04–13.799). The mean volumetric BMD measured was 206.24 ± 50.58 mg HA/ccm. Table 3 shows the hip and the spine of the patients preoperatively. The bone mineral density at the hip was 0.54±0.08 g/cm^2 and spine was 0.73 ± 0.1 with T score at the hip and spine of –2.23 ± 0.44 and –2.61 ± 0.45, respectively. The bone mineral density of the tibial cut was 0.356 ± 0.03 g/cm^2 ($P < 0.001$) and T score was –6.58 ± 2.87 ($P < 0.001$). Table 4 shows the comparison between the Saudi OAK patients and the controls. Figure 2 gives the 3D reconstruction of patient who had normal BMD and a T score of less than –1. Figures 3 and 4 show the 3D pictures of patients of with a T score of less than –2.6 of the hip and spine. The scans show reduction in the trabecular thickness, trabecular number, and increase in the trabecular spacing. Table 5 shows the

Table 2 Data of age, sex and pQCT analysis

Patients, *n*	50 (males 11, females 39)
Average age, y	64 ± 7.7 (50–85)
Osteopenic	13
Osteoporotic	37
T-score (DXA)	−2.6 (< −1.4 − < 3.8)
T-score (tibia)	−6.58 (< −5.9 − < −7.8)
Total volume	662.77 ± 236.43 mm^3
Bone volume	115.27 ± 40.45 mm^3
Trabecular number	1.452 ± 0.323
Trabecular thickness	0.181 ± 0.038 mm
Trabecular spacing	0.737 ± 0.145 mm
Connectivity density	6.526 ± 2.57 mm^{-3}
Bone mineral density	206.24 ± 50.58 mg HA/ccm

Table 3 Summary of DXA measurements by sex

Variable	Male ($n = 11$), mean (SD)	Female ($n = 39$), mean (SD)
Total hip BMD, g/cm^2	0.694 (0.137)	0.586 (0.151)
Femoral neck BMD, g/cm^2	0.630 (0.123)	0.552 (0.139)
Trochanter BMD, g/cm^2	0.766 (0.104)	0.697 (0.133)
Intertrochanter BMD, g/cm^2	0.858 (0.180)	0.743 (0.187)
L1–L4 BMD, g/cm^2	0.732 (0.160)	0.677 (0.157)
Volumetric BMD, mg/HA/ccm	204.55 (51.03)	184.27 (32.51)

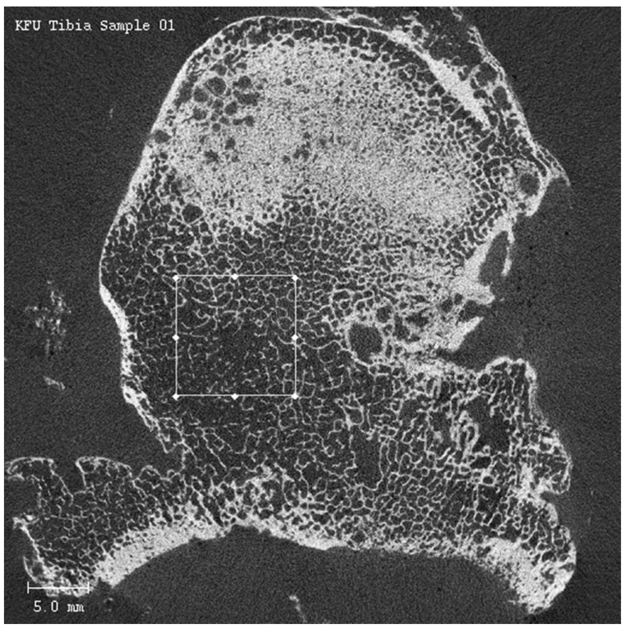

Fig. 1 Grayscale image of the tibia sample, showing the region of interest.

Table 4 Comparison of normal controls of Ding et al (2003) with the study group

Variable	Controls	Study group	*P* value (95% CI)
Patients, *n*	10	50	
Bone volume	21 (17.8–24.3)	18.5 (8.69–26.3)	<0.001 (<8.3016)
Connectivity density, mm^{-3}	8.35 (6.23–10.5)	5.52 (3.43–11.4)	<0.07 (6.5952)
Trabecular spacing, mm	0.588 (0.52–0.63)	0.181 (0.111–0.268)	<0.001 (<0.5452)
Degree of anisotropy	6.56 (2.62–10.5)	1.278 (1.107–1.5)	<0.001 (<5.4537)
Structural model index (range)	1.31 (1.08–1.55)	1.30 (0.53–2.10)	0.1

comparison of the BMD to with HR-pQCT between female patients of osteopenia and osteoporosis.

Discussion

The results of our study confirm our hypothesis that there is a marked significant difference between the BMD at the hip and spine when compared with the proximal tibia. Second, the HR-pQCT findings indicate that subchondral bone quality is much poorer with severe microarchitectural damage and reduced mechanical strength that one could envisage. Dalzell *et al*[17] showed that pQCT confirmed faster deterioration in cortical bone thickness and density in women than in men after ≥50 years. In our study, the mean number was 1.45 ± 0.32 (1/mm) compared with 2.0 ± 0.3.9 (1/mm), which is significantly lower, but the trabecular thickness was 0.181 ± 0.03 mm versus 0.75 ± 0.01 ($P = 0.001$). Due to lack of normal controls in our study, we compared with the data of Ding *et al* (2003).[6]

In the recent past, trabecular bone quantity and quality has received enhanced attention because trabecular bone thickness and number is an important aspect of bone quality; and this quality can increase, due to the influence of hormonal,[16,18] mechanical,[19] and therapeutic strategies. It is also known for some time that it is difficult to assess the trabecular bone by DXA, and it mainly assesses the cortical bone more than the trabecular bone. Second, the size of bone assessed by DXA influences areal BMD (g/cm^2) and thereby gives a positive reading compared with pQCT, which is not influenced by the size and measures volumetric BMD. Thus, it gives a more accurate reading that will help in the correct therapeutic interventions in osteoporosis. Studies have shown the variation of BMD due to age, sex, and grade of OA in proximal tibia not only

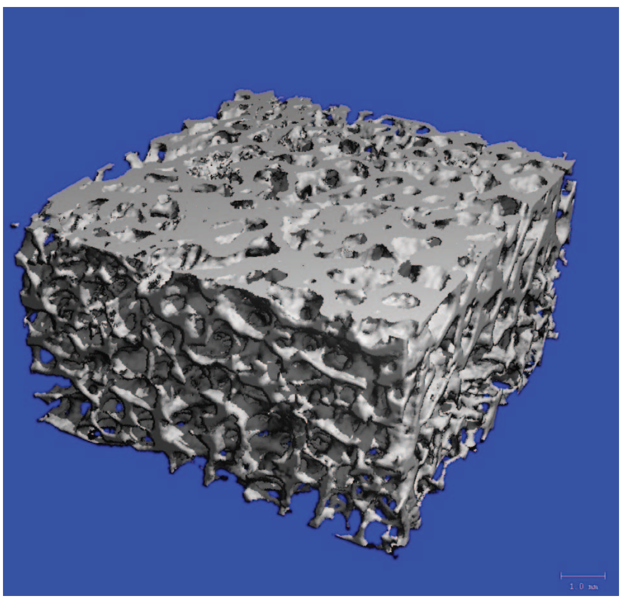

Fig. 2 Patient (51 years) with normal DXA Scan with T score of less than –1.

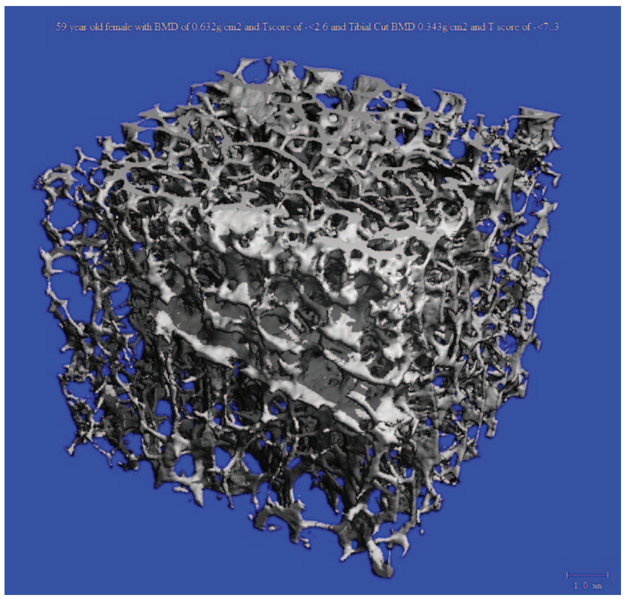

Fig. 3 Female (59 years): the DXA showed BMD of $0.632 g/cm^2$ and T score less than –2.6, while HR-pQCT showed the BMD of $0.343 g/cm^2$ and T score of –7.3.

Table 5 Comparison between female patients of osteopenia and osteoporosis

	Osteopenia	Osteoporosis	$P < 0.05$
Patients, *n*	15	24	
Age	63.5 ± 0.7	64.03 ± 7.01	0.7
BMD FN g/cm^2	0.561 ± 0.28	0.502 ± 0.3	0.4
T score hip	–2.08 ± 0.26	–2.36 ± 0.27	0.7
T score spine	–2.2 ± 0.07	–2.6 ± 0.35	0.6
T score TC	–5.5 ± 0.2	–6.9 ± 0.19	0.001
Total volume, mm^3	761 ± 151.2	593.65 ± 201.3	0.006
Bone volume, mm^3	113.4 ± 32.7	87.9 ± 40.6	0.02
Trabecular number	1.31 ± 0.21	1.01 ± 0.65	0.6
Trabecular thickness, mm	1.1 ± 0.1	0.081 ± 0.0.3	0.002
Bone mineral density, mg HA/ccm	186.15 ± 29.6	112.24 ± 57	0.0002

in the medial and lateral condyles, but also there is influence of the alignment of the limb itself.[20] Hudson *et al*[21] found high medial knee joint load on the medial condyle in OA combined added with the loss of internal rotation of the hip could lead to increased medial versus lateral BMD of the proximal tibia. Even though all our patients had ≤18° of varus deformity, we have taken a part of the medial and lateral condyle of the tibia for analysis (Figure 1).

Bennell *et al*[22] studied the pQCT changes in the different areas of subchondral bone in patients with OA of the knee in control, mild, and moderate OA and found that in the proximal tibia, there was statistical difference between the mild and moderate OA in the volumetric BMD up to 13.9% lower in moderate OA group. This suggests that even in early OA, there are subtle changes in the volumetric BMD that cannot be diagnosed by any other means, hence no treatment is given to such patients. Our study did show significant changes in the parameters of the trabecular bone but all the patients were of severe OA of the knee. On the basis of our results, we believe in situations where severe OAK and osteoporosis coexist HR-pQCT monitoring will give accurate picture for ideal therapeutic interventions to improve bone quality and subsequently better outcome of joint replacement.

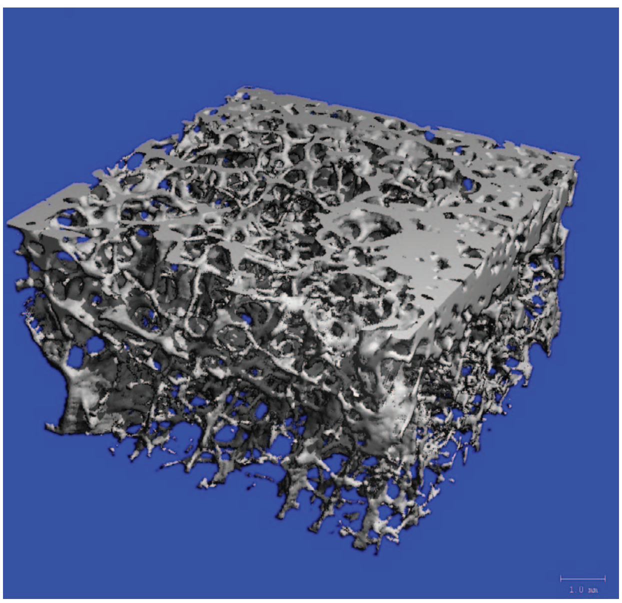

Fig. 4 Male patient (66 years) with T score of less than –2.6.

The implications of this study is that there are severe changes in the bone at the subchondral area which the DXA could not identify, so the correct treatment may not have been instituted early. We suggest that in patients with severe OA and at risk of OP, patients should start antiresorptive medications while waiting for the surgery. Additionally, if patients are predicted to have OP, cemented TKA is more preferred than cementless TKA.

Our study has limitations. The first being the smaller number of patients and the comparison of our patients with what was published of other ethnic groups and it is more so *in vitro* study. Apparently, more studies with a larger number of patients and control groups need to be done. This study shows that there is highly significant difference between bone density measured by DXA at the hip and spine when compared with the upper tibia. Second, the bone morphometric analysis as measured by the pQCT indicates that there is marked decrease in the mechanical properties of the bone in the proximal tibia due to OAK and OP indicating poor bone architecture and quality.

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