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BEYOND DXA: ADVANCES IN CLINICAL APPLICATIONS OF NEW BONE IMAGING TECHNOLOGY

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Abstract

Dual-energy X-ray absorptiometry (DXA) is generally a very useful tool for assessing bone mineral density (BMD) and fracture risk. However, observational studies have shown that in certain instances, BMD as measured by DXA systematically over- or underestimates fracture risk. We herein describe the clinical conundrums encountered when assessing fracture risk by DXA in patients with primary hyperparathyroidism or type 2 diabetes and those of Chinese ethnicity. Furthermore, we discuss how advanced imaging technology that examines skeletal microarchitecture is furthering our understanding of fracture risk in these clinical situations.

INTRODUCTION

Bone mineral density (BMD) using dual-energy X-ray absorptiometry (DXA) is the gold standard for quantitative assessment of bone and an important predictor of fracture risk. This technology is readily available, safe, accurate, and precise (1). Normative BMD population databases exist, and BMD strongly correlates with fracture risk in untreated patients (2). A diagnostic threshold for osteoporosis was established based on the relationship between BMD and fracture risk and the associated lifetime fracture risk. The World Health Organization defines osteoporosis in postmenopausal females who have a T-score at or below -2.5 (3).

According to clinical guidelines, BMD in the osteoporotic range is an indication to commence therapy (4). However, the majority of fractures occur in patients with a T-score higher than -2.5 (5). The greater number of people with the osteopenic classification readily explains this seeming paradox. Nevertheless, this observation raises the important point that other risk factors, besides BMD, modify fracture risk. Subsequently, fracture risk assessment tools that quantify independent fracture risk factors were created. The most widely used

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DISCLOSURE

The authors have no multiplicity of interest to disclose.

fracture risk assessment tool is FRAX[®] (6). While these tools help to account more completely for fracture risk, there may well be additional skeletal features that are important contributors. Three noteworthy examples where additional skeletal features influence fracture risk are the subject of this review: primary hyperparathyroidism (PHPT), type 2 diabetes mellitus (DM2), and ethnicity. Our better understanding of bone microarchitecture through the use of advanced imaging technology has helped to address vexing clinical problems encountered in these patient groups. Table 1 summarizes the key points that follow in this review.

ADVANCED BONE IMAGING TECHNOLOGY

High-Resolution Peripheral Quantitative Computed Tomography (HRpQCT) and Derived Parameters

High-resolution peripheral quantitative computed tomography (HRpQCT) is a noninvasive, in vivo assessment of bone microarchitectural properties at the distal radius and tibia (7,8). The convenience and safety of HRpQCT is realized in the short period of time required to obtain images (about 3 minutes for each site) and the low effective radiation dose (<3 μ Sv per site) (7). This technology combines 110 CT slices of 82-mm voxel resolution to generate 3-dimensional (3D) bone images (Fig. 1), allowing for measurement of volumetric BMD and other specific microarchitectural features (8). An automated threshold algorithm segregates the cortical and trabecular compartments, and microarchitectural properties specific to each compartment are either directly measured or derived (7). With the newest 2.0 version of HRpQCT, in which the voxel resolution is approximately 60 μ m, derived indices can now be measured directly.

Cortical indices include volumetric cortical bone density, cortical porosity, and cortical thickness. Trabecular indices include volumetric trabecular bone density, trabecular bone volume, trabecular number, thickness, and separation (8). In addition, bone stiffness and strength can be calculated from HRpQCT images using microstructural finite-element analysis (μ FEA) to simulate a uniaxial compressive force (9).

The trabecular bone network is comprised of plate and rod-like trabeculae. In simplistic terms, individual trabecular segmentation (ITS) analysis converts HRpQCT images into 3D models of trabecular microarchitecture according to the type of trabeculae (10). This validated methodology permits determination of plate and rod numbers, a plate:rod ratio, composite bone volume fractions, orientation, and interconnectivity (10). Biomechanical principles teach that the trabecular plates contribute more to bone strength than the trabecular rods (11) and that plate parameters correlate positively with bone stiffness, while rod parameters correlate negatively (11,12). Therefore, ITS analysis can add to our understanding of fracture risk. For example, ITS revealed significant difference in trabecular microarchitecture, independent of BMD, in postmenopausal females with previous fracture (10). In these patients, trabecular microarchitecture was typically rod-like, and the more competent horizontal plates were reduced in number. The consequent reduced plate:rod ratio contributed to increased fracture risk (10).

Trabecular Bone Score (TBS)

Trabecular bone score (TBS) is an indirect measure of trabecular microarchitecture derived from DXA images of the lumbar spine. TBS is an attractive technology because it relies on DXA, which unlike HRpQCT, is widely accessible. A software application package permits a rapid assessment of the TBS from the lumbar spine DXA image. The gray-level pixel variation of the 2-dimensional DXA image is used to estimate the 3D structure of trabecular bone (13). In postmenopausal females, a TBS score >1.350 is associated with normal trabecular bone microarchitecture, TBS scores between 1.200 and 1.350 represent partially degraded microarchitecture, and a TBS score <1.200 represents degraded microarchitecture (13). It is important to point out that although TBS is an estimate of skeletal microstructure, and therefore not equivalent to direct assessment of skeletal microstructure, it does provide fracture risk information that is complementary to what can be gleaned from DXA alone. In retrospective analyses of a very large and comprehensive clinical registry of postmenopausal females (The Manitoba Database), TBS predicted major osteoporotic fractures independent of spine and hip BMD, and improved fracture prediction when use in combination with DXA (14). TBS also predicted fractures in an independent but complementary fashion with FRAX[®] (15). As a result, the FRAX[®] 10-year fracture risk assessment tool now accommodates the TBS score.

Bone Microindentation Testing (BMT)

Bone microindentation testing (BMT) is a validated technology that directly measures the ability of bone to withstand fractures (16). Under local anesthetic, a microprobe, approximately 1-mm in diameter, is inserted under the skin of the mid anterior tibia and set to rest on the bone surface. After locally penetrating the periosteum, cycles of indentations, 375- μ m across, are made along the tibia (Fig. 2). These indentations do not harm or cause discomfort to the patient, but they do create microscopic discontinuities that can be extrapolated into measures of resistance. The indentation distance from the periosteal surface to the last-cycle indentation is the total indentation distance (total ID) while the difference between the first- and last-cycle indentation is the indentation distance increase (IDI). Both the total ID and IDI were significantly greater in postmenopausal females with than without osteoporotic fractures indicating increased bone fragility (16). Total ID and IDI showed excellent fracture discrimination (area under the receiver operating characteristic curve >90%), but neither measure correlated well with BMD, indicating that BMT is an independent predictor of osteoporotic fractures (16). Using the same principles as BMT, a handheld device was created that compares the mean IDI of subjects to a calibration phantom. The resulting ratio is called the bone material strength (BMS): a lower BMS indicates lower fracture resistance (17). BMS was lower in males and females with previous fracture than those without, despite similar BMD values (17). These findings support the utility and application of in vivo bone microindentation as an assessment to estimate biomechanical skeletal competence, independent of BMD.

PHPT

The Conundrum

The clinical presentation of PHPT has, over the past several decades, become an asymptomatic disorder. BMD has replaced skeletal X-rays in the assessment of skeletal involvement in PHPT. Using DXA, many studies have shown preferential bone loss at the distal 1/3 radius site, a site of cortical bone, with corresponding protection of the lumbar spine, a site comprised primarily of trabecular bone (18,19). An increased incidence of nonvertebral fractures in PHPT would be expected based on these DXA results; however, abundant epidemiologic data indicate that fracture risk is increased globally in PHPT, not just at nonvertebral sites (20). When postmenopausal females with PHPT were systematically evaluated with spine radiographs, the incidence of vertebral fractures was markedly higher in PHPT than in a matched control cohort: 25% versus 4%, respectively (21). These studies demonstrate a clinical problem, namely that the PHPT bone phenotype established by DXA is discordant with actual fracture data showing increased fragility fractures at sites enriched in trabecular bone, as well as cortical bone. Advanced imaging technology has helped to explain this conundrum, elucidating trabecular bone involvement in PHPT.

Utility of HRpQCT in PHPT

Two recent studies have used HRpQCT to demonstrate that compared to healthy age-matched controls, females with untreated PHPT have net bone loss in both the cortical and trabecular compartments (22,23). Hansen et al reported not only reduced cortical area, volume, and thickness at the distal radius, but also reduced trabecular volume, number and increased trabecular separation (22). There were no significant differences in cortical or trabecular parameters at the tibia, possibly due to limited sample size or site-specific differences in mechanical loading. In a larger study, Stein and colleagues reported reduced cortical volume at both the distal radius and tibia (23). In addition, the distal radius showed reduced trabecular volume, number, and thickness and increased trabecular separation. At the tibia, the abnormalities were less evident with only trabecular volume and separation demonstrating significant reductions. These studies with HRpQCT technology confirm the involvement of trabecular bone in PHPT and are consistent with the clinical observations of increased general fracture risk in PHPT. In addition, neither study reported significantly differing vitamin D levels between patients and, therefore, there was no apparent additional mechanism for microarchitectural differences.

Utility of ITS in PHPT

ITS analysis of distal radius and tibia HRpQCT images has demonstrated further alterations in trabecular microarchitecture among postmenopausal females with PHPT (23). At the radius, patients with PHPT demonstrated reductions in both plate and rod trabecular numbers and respective bone volume relative to controls, with plate trabecular parameters more significantly impacted. At the tibia, the rod trabecular parameters were not significantly different compared to controls, but the plate trabecular number and plate bone volume were reduced. These abnormalities led to an overall reduction in the plate:rod ratio by 22% at the radius and 19% at the tibia. These alterations in trabecular microarchitecture translated to compromised bone strength as demonstrated by μ FEA.

Utility of TBS in PHPT

Trabecular bone involvement in the skeletal disease of PHPT, as documented by HRpQCT and ITS, has also been corroborated by TBS. In one cohort, TBS was “degraded” or “partially degraded” in the majority of patients with PHPT even though DXA did not detect any abnormality in BMD (24). Similarly, in a case-control study, TBS was lower in patients with PHPT than controls, despite no difference in spine BMD and similar vitamin D levels (25). Furthermore, in this patient population, TBS was significantly correlated with many trabecular and cortical HRpQCT parameters (24).

DM2 AND BONE FRAGILITY

The Conundrum

Conventional wisdom has not placed DM2 in the category of a risk factor for fractures. In fact, patients with DM2 often have higher body mass indexes (BMIs) (26–28) and BMD values (14,26,27,29,30) and are expected to have a lower incidence of fragility fracture. On the contrary, multiple studies, including 2 meta-analyses, have shown that despite higher BMI and BMD, fracture incidence in patients with DM2 is increased (26,27,29–31). Furthermore, FRAX[®] seems to underestimate fracture risk in patients with DM2, suggesting that DM-related factors not captured by BMD or by FRAX[®] may be contributing to the increased fracture incidence (30,32).

A number of factors have to be taken into account when explaining increased fracture risk in DM2. These include increased falls due to hypoglycemia and neurovascular complications, a shift in cell lineage from osteoblasts to adipocytes by thiazolidinediones (TZDs) (33), inhibition of bone formation by higher levels of sclerostin (34), and overall decreased bone turnover (34–36). However, even after adjusting for some of these confounders such as falls (26,27) and TZD use (30), DM2 remains a major risk factor for fracture. For example, after multivariate adjustment, postmenopausal females with DM2 from the Women’s Health Initiative Observational Cohort were found to have a 20% increased incidence of all fractures compared to females without DM2 (27). After additional adjustment for higher baseline hip BMD, the risk of hip/pelvis/upper leg fracture and spine/tailbone fracture in females with DM2 was 82% (hazard ratio [HR] 1.82) and 57% (HR 1.57) higher. Clearly, the relationship between BMD and fracture risk is altered in DM2, suggesting that other factors such as impaired bone quality need to be considered.

Utility of HRpQCT in DM2

HRpQCT has been used to study the microarchitectural properties of postmenopausal females with DM2 (37,38). In a pilot study, 19 postmenopausal females with DM2 and 19 age-matched controls underwent HRpQCT imaging (37). At the distal tibia, trabecular thickness and cortical porosity were higher in DM2, but only increased trabecular thickness reached statistical significance. Conversely, cortical porosity was significantly higher at the distal radius in patients with DM2, but there were no other significant microarchitectural differences. In this cohort of subjects with DM2, bone strength was not significantly compromised by cortical porosity. However, results became more impressive when subjects with DM2 who had fractured were compared to controls and to patients with DM2 who had

not fractured. Among those who had sustained a fragility fracture, cortical porosity was decidedly greater (38).

Patsch and colleagues examined HRpQCT images of the standard distal radius and tibia sites (9.5 and 22.5 mm from the reference line, respectively) and at slightly more proximal radial and tibial locations (24.5 and 37.5 mm from the reference line, respectively) in a cohort of 80 postmenopausal females: 20 with DM2 and prior fragility fracture, 20 with DM2 without fractures, 20 controls with prior fragility fracture, and 20 controls without prior fracture (38). Diabetic subjects were well matched for age, BMI, vitamin D, parathyroid hormone (PTH) levels, and hemoglobin A1C. Of all 4 groups, cortical porosity of the peripheral skeleton was greatest in patients with DM2 and prior fracture. Within-group comparison of diabetic subjects revealed that at all 4 sites, cortical porosity volume was significantly greater among patients with a history of fracture as compared to patients without. The relative cortical porosity was also significantly greater at all sites except the standard radial site. These same cortical deficits were not significantly different in the control group of patients with and without fractures, suggesting that among patients with DM2, increased cortical porosity contributes to bone fragility. A deficit in bone strength related to cortical porosity was further supported by μ FEA analyses in DM2 patients.

Utility of TBS in DM2

At the central skeleton, TBS has demonstrated microarchitectural differences in patients with diabetes. A retrospective analysis of the Manitoba Database compared BMD and TBS of postmenopausal females with ($n = 2,356$) and without diabetes ($n = 27,051$) (28). Although the type of diabetes could not be distinguished from the database, presumably most patients had DM2. An additional limitation of the study was that vitamin D level differences between groups could not be ascertained. Nonetheless, females with diabetes had significantly higher BMI and BMD at all sites; however, the incidence of major osteoporotic fractures was also significantly increased (7.4% vs. 5.5%). In females with DM, despite higher lumbar spine BMD, TBS was significantly lower compared with controls (1.17 vs. 1.25), indicating that trabecular microarchitecture was degraded to a greater extent. Differences in TBS and BMD remained significant even after adjusting for multiple covariates such as age, BMI, osteoporosis therapy, and standard fracture risk factors. Furthermore, TBS captured fracture risk more accurately than lumbar spine BMD or BMD at other sites in this patient population.

Utility of Microindentation in DM2

Bone material strength was directly assessed using microindentation technology in 30 postmenopausal females with DM2 of more than 10 years duration and 30 age-matched controls; there was no significant difference in vitamin D levels between groups (39). The measured 3-site BMD by DXA was significantly higher in females with DM2. Similarly, HRpQCT showed greater cortical thickness at both the distal radius and tibia and higher trabecular number at the distal radius. However, BMD by DXA and microarchitectural differences dissipated once groups were adjusted for BMI. Conversely, BMS was significantly lower among females with DM2, both before (-11.7%) and after adjusting for

BMI (−10.5%). Furthermore, BMS and average 10-year glycemic control were negatively correlated, suggesting that poor glycemic control may contribute to the reduction in BMS.

ETHNIC DIFFERENCES IN BONE FRAGILITY

The Conundrum

The vast majority of what is known about osteoporosis and the relationship between BMD and fracture risk is derived from postmenopausal Caucasian females, where for every standard deviation decrease in areal BMD, the fracture risk doubles (2,3). Extrapolating this relationship one would predict that regardless of ethnicity, a lower BMD, as measured by DXA, should equate to a higher fracture risk. However, comparisons of BMD and fracture incidence in subjects with different ethnic backgrounds has called into question this assumption (40). For example, Chinese subjects of both sexes, residing in either China or America, have lower total hip, femoral neck, and lumbar spine BMD values relative to their Caucasian counterparts (41–43). Additionally, BMD at peripheral DXA sites was found to be lower in Chinese-American females (40). However, despite consistently lower BMD, hip fracture incidence is lower in Chinese subjects of both sexes (44), as is wrist/forearm fracture incidence in Chinese females compared to their Caucasians counterparts (40). Therefore, it appears that BMD measured by DXA overestimates fracture risk in Chinese patients. An inherent limitation of DXA is that it measures areal (2-dimensional) density, and thus, BMD will be lower in Chinese patients by virtue of their generally smaller bone size. However, correction for body size does not re-establish the standard relationship between BMD and fracture risk, and Chinese females continue to demonstrate lower nonvertebral fracture risk in relation to their BMD (40).

Utility of HRpQCT in Chinese American Females

In a cross-sectional study, HRpQCT was performed on 31 Chinese-American and 32 Caucasian premenopausal females (45). Before adjusting for covariates including weight, vitamin D levels, and PTH levels, there was no significant difference in lumbar spine, hip, or femoral neck BMD by DXA. Weight was not significantly lower in Chinese-American subjects, but vitamin D was significantly lower and PTH was significantly higher in these patients although no patient had secondary hyperparathyroidism. After adjustment for covariates, areal BMD was slightly higher in the Chinese-American cohort. However, such statistical adjustments are not possible in clinical practice, and decisions are made on the areal BMD measured, which, as demonstrated, may underestimate BMD relative to body size. In contrast, even without statistical adjustment for covariates, the average total, cortical, and trabecular volumetric BMD measurements by HRpQCT were significantly higher at both the distal radius and tibia in Chinese-American females. Furthermore, cortical thickness and trabecular thickness were significantly higher at the radius (23% and 21%) and tibia (9% and 18%), indicating better bone microarchitecture in addition to greater volumetric bone density among Chinese-American females. In a subsequent study, this sample size was expanded to incorporate 49 Chinese-American and 46 Caucasian females, and whole and compartment-specific bone strength was estimated using μ FEA (46). The same vitamin D and PTH differences were observed in this study. Nonetheless, The estimated whole bone

stiffness was 14% greater at the radius and 8% greater at the tibia in Chinese-American females, without any difference in compartment-specific load distribution.

The same study was repeated in 29 Chinese-American and 69 Caucasian postmenopausal females (47). Patients with secondary hyperparathyroidism or other conditions that might affect bone metabolism were excluded. Here areal BMD at lumbar spine, total hip, and femoral neck did not differ between groups, even after adjusting for age and BMI. Cortical thickness and volumetric BMD measured by HRpQCT were higher at the distal radius and tibia in Chinese-American females. Trabecular parameters were not different at the radius, whereas at the tibia, trabecular thickness was higher but trabecular number was reduced. Consequently, unlike their premenopausal counterparts, postmenopausal Chinese-American females did not have greater trabecular volumetric BMD at either site, which may suggest that cortical but not trabecular microarchitecture is preserved with aging. Whole-bone stiffness by μ FEA did not differ between groups; however, a greater proportion of the mechanical load was supported by the cortical compartment in Chinese-American females. Therefore, the favorable cortical microarchitecture of postmenopausal Chinese-American females may compensate for smaller bone size and lower trabecular number resulting in bone strength equivalent to Caucasian females. Based on these findings, Walker et al postulated that lower fracture incidence in Chinese-American females may be attributed to greater bone mechanical competence relative to lower force generated during a fall given that Chinese-American females are generally shorter and lighter than their Caucasian counterparts.

Utility of ITS in Chinese American Females

In the aforementioned study by Liu and colleagues, HRpQCT images were also analyzed by ITS to further delineate the trabecular microarchitectural differences between Chinese-American and Caucasian females (46). In their premenopausal cohort, despite the same areal BMD by DXA, ITS showed that plate-like trabeculae were more numerous and thicker in Chinese-American subjects resulting in nearly double the Caucasian plate bone volume fraction, at both the distal radius and tibia. There was no difference between ethnic groups with regard to rod-like trabecular parameters, but the overall trabecular network connectivity was 37% greater at the radius and 29% greater at the tibia as a result of higher plate density. In another study, tibial plate:rod ratio values for premenopausal Chinese-American and Caucasian females were determined by ITS and separated into quartiles (48). After controlling for covariates such as differences in daily calcium intake and vitamin D levels, those in the highest plate:rod ratio quartile were 85 times more likely to be of Chinese descent than those in the lowest quartile. Therefore, Chinese-American females appear to have a much more favorable trabecular profile, which also likely contributes to stronger, more fracture-resistant bones in this patient population.

CONCLUSION

Although DXA is a very useful clinical tool and surrogate marker of bone strength, it does not account well for fracture risk in certain patient groups. Through advances in bone imaging technologies that go beyond the capabilities of DXA, we now better understand

how bone microstructural features help to account for fracture risk in the PHPT, DM2, and Chinese skeleton.

Abbreviations

BMD	bone mineral density
BMI	body mass index
BMS	bone material strength
BMT	bone microin-dentation testing
3D	3-dimensional
DM2	type 2 diabetes mellitus
DXA	dual-energy X-ray absorptiometry
μFEA	microstructural finite element analysis
FRAX	fracture risk assessment tool
HRpQCT	high-resolution peripheral quantitative computed tomography
ID	indentation distance
IDI	indentation distance increase
ITS	individual trabecular segmentation
PHPT	primary hyperparathyroidism
PTH	parathyroid hormone
TBS	trabecular bone score

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Fig. 1.

High-resolution peripheral quantitative computed tomography images of the left radius of an individual who suffered a low trauma fracture at the right radius (top row) and a fracture-free, age-matched control (bottom row). The figure depicts 2-dimensional grayscale slices, the segmented cortical and trabecular compartments, and a 3-dimensional rendering with highlighted cortical porosity. Figure and legend reproduced from (8).

Fig. 2.

Indentation procedure for measuring material properties of bone in vivo and SEM imaging of an indent on a human bone sample. (A) Illustration of the method for obtaining indentation measurements, including insertion of the test probe assembly, displacing the periosteum with the reference probe, first-cycle indentation, and last cycle indentation, which determines the IDI with respect to the first cycle. (B) SEM image of an indentation (*dashed line*) being compared to a dime (the smallest U.S. coin). (C) This magnified SEM image of the indentation shows microcracks created during the repetitive loading cycles at a constant force. Figure and legend reproduced from (16). *IDI* = indentation distance increase; *SEM* = scanning electron microscopy.

Table 1

Information Emerging from Advanced Imaging that Reconcile Discrepant Fracture Data and Bone Phenotype in Specific Patient Populations

Population	Persons with PHPT	Persons with DM2	Persons of Chinese ethnicity
Bone phenotype	<ul style="list-style-type: none"> • Preferential cortical bone loss • Preservation of trabecular bone 	<ul style="list-style-type: none"> • Patients with DM2 often have higher BMI and BMD than controls 	<ul style="list-style-type: none"> • Chinese and Chinese-American males and females have lower total hip, femoral neck, and lumbar spine areal BMD than Caucasians • Chinese-American females have lower areal BMD at peripheral DXA sites
Fracture data	<ul style="list-style-type: none"> • Increased fragility fractures at cortical and trabecular sites 	<ul style="list-style-type: none"> • Higher fracture incidence despite better BMD • FRAX seems to underestimate fracture risk 	<ul style="list-style-type: none"> • Hip fracture incidence is lower in Chinese males and females compared to Caucasians • Wrist/forearm fracture incidence is lower in Chinese females
Additional HRpQCT-derived information	<ul style="list-style-type: none"> • Reduced trabecular volume, number and increased trabecular separation at distal radius • Reduced plate:rod ratio at distal radius and tibia and reduced bone strength by μFEA 	<ul style="list-style-type: none"> • Among patients with DM2, increased cortical porosity contributes to bone fragility 	<ul style="list-style-type: none"> • Chinese-American premenopausal females have better cortical <i>and</i> trabecular bone microarchitecture, and volumetric bone density than Caucasian controls • Chinese-American postmenopausal females have better cortical thickness and volumetric bone density than Caucasian controls
TBS data	<ul style="list-style-type: none"> • Degraded or partially degraded trabecular microarchitecture not detected by lumbar spine DXA 	<ul style="list-style-type: none"> • Trabecular microarchitecture was more degraded in patients with DM2, relative to controls, despite higher lumbar spine BMD 	<ul style="list-style-type: none"> • N/A
BMT data	<ul style="list-style-type: none"> • N/A 	<ul style="list-style-type: none"> • After adjusting for BMI, patient 	<ul style="list-style-type: none"> • N/A

Population	Persons with PHPT	Persons with DM2	Persons of Chinese ethnicity
		with DM2 had 10% lower BMS, relative to controls with same BMI-adjusted BMD by DXA	
Modified bone phenotype	<ul style="list-style-type: none"> Trabecular bone is also affected by PHPT 	<ul style="list-style-type: none"> At the peripheral skeleton data suggest cortical bone deficits and less favorable trabecular microarchitecture at the spine in patients with DM2 	<ul style="list-style-type: none"> Persons of Chinese ethnicity have more favorable bone microarchitectural properties and volumetric bone density

Abbreviations: BMD = bone mineral density; BMI = body mass index; BMS = bone material strength; BMT = bone microindentation testing; DM2 = type 2 diabetes mellitus; DXA = dual-energy X-ray absorptiometry; μ FEA = microstructural finite element analysis; FRAX = fracture risk assessment tool; N/A = not available; TBS = trabecular bone score; PHPT = primary parathyroidism.