MRI-measured pelvic bone marrow adipose tissue is inversely related to DXA-measured bone mineral in younger and older Adults

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Abstract

Background/Objective—Recent research has shown an inverse relationship between bone marrow adipose tissue (BMAT) and bone mineral density (BMD). There is a lack of evidence at the macro-imaging level to establish whether increased BMAT is a cause or effect of bone loss. This cross-sectional study compared the BMAT and BMD relationship between a younger adult group at or approaching peak bone mass (PBM) (age 18.0-39.9 yrs) and an older group with potential bone loss (PoBL) (age 40.0-88 yrs).

Subjects/Methods—Pelvic BMAT was evaluated in 560 healthy men and women with T1-weighted whole body magnetic resonance imaging. BMD was measured using whole body dual-energy x-ray absorptiometry.

Results—An inverse correlation was observed between pelvic BMAT and pelvic, total, and spine BMD in the younger PBM group (r=-0.419 to -0.461, P<0.001) and in the older PoBL group (r=-0.405 to -0.500, P<0.001). After adjusting for age, sex, ethnicity, menopausal status, total body fat, skeletal muscle, subcutaneous and visceral adipose tissue, neither subject group (younger PBM vs. older PoBL) nor its interaction with pelvic BMAT significantly contributed to the regression models with BMD as dependent variable and pelvic BMAT as independent variable (P=0.434 to 0.928).

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Conclusion—Our findings indicate that an inverse relationship between pelvic BMAT and BMD is present both in younger subjects who have not yet experienced bone loss and also in older subjects. These results provide support at the macro-imaging level for the hypothesis that low BMD may be a result of preferential differentiation of mesenchymal stem cells from osteoblasts to adipocytes.

Keywords

body composition; bone marrow adipose tissue; bone mineral density; dual-energy X-ray absorptiometry; magnetic resonance imaging; aging

INTRODUCTION

Recent studies have reported an inverse relationship between bone marrow adipose tissue (BMAT) and bone mineral density (BMD) in human subjects (6-10). However, it is unknown whether this relationship represents a preferential differentiation of mesenchymal stem cells (MSC) into adipocytes instead of osteoblasts (3-5); or a passive accumulation of BMAT as bone is lost and marrow space increases with aging. In the present study, we compared the association of BMAT and BMD in younger adults who are at or approaching their peak bone mass (PBM) with older adults who have potential bone loss (PoBL). An inverse correlation between BMAT and BMD before the onset of bone loss would support the notion of a preferential differentiation of MSCs into adipocytes instead of osteoblasts. On the other hand, if the inverse relationship between BMAT and BMD is found only in older PoBL adults, either passive accumulation of BMAT or preferential differentiation of MSCs into adipocytes could explain the pathophysiology related to aging.

In the present study, we investigated the relationship between BMAT and BMD in an anatomically matched region (i.e., pelvic BMAT and pelvic BMD), non-anatomically matched region (i.e. pelvic BMAT and spine BMD), and regional and whole body (i.e. pelvic BMAT and whole body BMD). This study design allows us to investigate the relationship between BMAT and BMD not only on a local level (i.e., MSC level) but also on a systemic level (i.e., hormonal level). A clearer understanding of the relationship between bone mineral and marrow fat is a critical first step toward the development of prevention and treatment strategies for bone loss; possibly through enhancing the osteogenic differentiation of progenitor cells.

Bone interacts with both bone marrow fat and total body fat (1-2). It has been shown that bone mass is positively related to body weight. The effect of body weight on bone mass is probably attributed to both fat mass and lean mass (11). In this study we adjusted body composition for whole body MRI measured visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT) and skeletal muscle as well as fat mass index and fat free index ratio (12). Accurate adjustment of body composition allows us to investigate the relationship between BMAT and BMD independent of other body components.

Some previous studies have used magnetic resonance spectroscopy (MRS) to measure marrow fat (7-8, 13). Although MRS is considered a reference method for the measurement of fat content within a small volume of tissue (14), its application to quantifying marrow fat

is limited because marrow fat is not homogeneously distributed in the cavity of one bone or across bones (15). In contrast, magnetic resonance imaging (MRI) overcomes this limitation of MRS by measuring adipose tissue across multiple bones (9, 16). T1-weighted MRI has not only been validated for quantifying regional adipose tissue volume (17-18), it has also been widely applied to adipose tissue measurement and serves as a reference method for adipose tissue quantification (19-22). The recently optimized water-fat imaging methods (23-24), combine the merits of both MRS and volumetric MRI methods. However, to the best of our knowledge, there is no large scale marrow fat dataset measured by water-fat imaging available. The unique large scale T1-weighted MRI dataset (n=560) in the present study enables us to provide timely evidence of the interaction between marrow fat and bone at the human macroscopic imaging level. In the present study we measured BMAT in the pelvic region because of its large quantifiable cancellous bone volume and its high correlation with BMD as shown in our previous studies (9).

SUBJECTS AND METHODS

Protocol and Design

The present study analyzed existing data of healthy subjects archived at the New York Obesity Nutrition Research Center, St. Luke's-Roosevelt Hospital, New York City, New York, USA. Participants were a sample of healthy men and women over the age of 18 yrs and all completed a medical history screening, physical examination, and blood studies. Ethnicity was established for each subject by self-report. Athletes, women within six months of delivery or breast feeding, and subjects with a history of anorexia nervosa or any other disease conditions were excluded by medical history review. Subjects weighing more than 136.2 kg were excluded from the study due to the weight limits of MRI and dual-energy x-ray absorptiometry (DXA) system. Weight, height, and body composition were measured on the same day as the screening examination was done.

In this study, we defined the younger PBM group as ages 18.0-39.9 years and the older group as ages 40.0-88.0 years. The rationale for the cut-off ages of the younger PBM group was to include subjects who reached bone maturity (25) and to exclude peri-menopausal women who may have experienced bone loss (26-27). We used the same cut-off ages in both men and women to simplify comparison between genders in the regression analysis.

Because there are inconsistencies regarding the age at which bone loss begins (26-28), we have also used an age range of 18.0-29.9 years to define the younger PBM group and 50.0-88.0 years to define older PoBL group in order to eliminate the potential overlap between the two groups. Due to the exclusion of a large number of subjects from these defined age ranges (i.e., 306 vs. 560), this part of the analysis was retained as exploratory.

Dual-Energy X-Ray Absorptiometry

DXA (DPX GE Lunar, software version 4.7e, Madison, WI, USA) was used to estimate BMD, total body fat, and %fat using the whole body scan mode. All scans were acquired and read by trained technologists. We report pelvic BMD because this site approximates the pelvic region used to measure BMAT by MRI. In addition, we also report total body BMD and total spine BMD because of their availability. The estimated precision for BMD and

%fat is 1.28% and 3.3%, respectively (29). The system was routinely calibrated and quality control measures were followed as recommended by the manufacturer.

Magnetic Resonance Imaging

Whole-body MRI scans were acquired as previously reported by our group (30-31) using a 1.5 T General Electric system (6X Horizon, Milwaukee, WI, USA). The MRI data were obtained using a T1-weighted, spin-echo sequence with 200-ms repetition time and a 17-ms echo time. A 26-s breath hold was required during abdominal slice imaging. The field of view is 48 cm by 48 cm with a matrix is 256 by 256. The protocol involved acquisition of approximately forty 10 mm thick axial images at 40 mm intervals from fingers to toes. The subject rested in either a prone or supine position during the procedure with the L_4-L_5 intervertebral disc as the point of origin. Following acquisition, the bone marrow, visceral, and subcutaneous adipose tissue compartments, and skeletal muscle were segmented at the New York Image Reading Center by trained, and cross-validated technicians using image analysis software (SliceOmatic, Tomovision Inc., Montreal, Canada). Technicians were blinded to patient demographic information and test results. From a total of 596 subjects, 36 were excluded due to severe inhomogeneity of the MRI adipose tissue signal. The remaining 560 subjects were included in the study. The threshold for BMAT segmentation was set at the same level as SAT on the grey scale (9, 16). The intraclass correlation coefficients for volume rendering of BMAT, subcutaneous adipose tissue, visceral adipose tissue, and skeletal muscle for the same scan by different analysts are 0.99, 0.99, 0.95, and 0.99, respectively. Tissue compartment volume was calculated as:

$$V = (t+h)\sum_{i=1}^{N} A_i$$

where V is volume, A_i is each scan's cross-sectional area, h is the between-slice interval, t is the thickness of each slice, and N is the total number of slices. Pelvic BMAT volumes were calculated from the region that matched the pelvic region of DXA and included ilium, sacrum, ischium, pubis, coccyx and femoral heads. The pelvic region was selected for evaluation because of its large quantifiable cancellous bone volume and its high correlation with BMD as shown in our previous studies (9). Lumbar spine BMAT is not reported separately because the small amount of adipose tissue in the lumbar spine could not be reliably quantified in some subjects with the current MRI protocol (9).

ETHICS

The exempt status of the present study was reviewed and approved by the Institutional Review Board ofSt. Luke's-Roosevelt Hospital. The original study was approved by the Institutional Review Board ofSt. Luke's-Roosevelt Hospital and each subject gave written consent to participate.

STATISTICS

Data are presented as the mean ± SD (**Table 1**). Pearson correlation coefficients among pelvic BMAT, total body, pelvic and spine BMD were calculated separately for the younger PBM group and the older PoBL group. Correlation coefficients were calculated between pelvic BMAT and BMD in the two groups after adjustment by multiple regression for age, weight and total body fat. Correlation coefficients were also calculated between pelvic BMAT and BMD in the two groups after adjustment by multiple regression for age, weight, total body fat, subcutaneous adipose tissue, visceral adipose tissue, skeletal muscle, sex, ethnicity and menopausal status.

Regression models were established with pelvic BMD, total body BMD, or spine BMD as the dependent variable and pelvic BMAT, age, weight, total body fat, subcutaneous adipose tissue, visceral adipose tissue, skeletal muscle, sex, ethnicity, menopausal status, subject group (i.e., younger PBM vs. older PoBL), and biological plausible two-way interactions as potential independent variables. The above regression models were also tested by substituting muscle and fat mass by fat mass index to fat free mass index ratio.

Levene's test was used to evaluate the equality of variance among groups and the Shapiro-Wilk test was applied to test the normality of the residual distributions. When necessary, variable values were mathematically transformed to normalize the residual distributions and to equalize the residual variance across sex and ethnicity. Log transformations were applied initially and followed by Box-Cox transformations when necessary.

The intraclass correlation coefficient was calculated with subjects as a random effect and analysts as a fixed effect.

All statistical analyses were carried out using SAS 9.2 program package (SAS Institute. Inc., Cary, NC, USA). Two-tailed ($\alpha=0.05$) tests of significance were used.

RESULTS

Descriptive Statistics

The characteristics of the subjects are shown in **Table 1**. Of the 380 total women, 254 were pre-menopausal and 115 were post-menopausal. The menopausal status information on 11 women was missing.

Total body BMAT of the younger PBM group ranged from 0.60 to 3.08 L with a mean of 1.52 L. Total body BMAT of the older PoBL group ranged from 0.50 to 3.27 L with a mean of 1.74 L. BMAT ranged from 1.1% to 31.6% of total adipose tissue with a mean of 8.0%.

Relationship between BMAT and BMD in younger PBM and older PoBL group

An inverse correlation was observed between logarithm or Box-Cox transformed pelvic BMAT and BMD in both the younger PBM group (pelvic BMD, r = -0.460; total BMD, r = -0.461; spine BMD, r = -0.420; all P < 0.001, n = 280) and the older PoBL group (pelvic BMD, r = -0.556; total BMD, r =-0.500, spine BMD, r = -0.413; all P < 0.001, n=280) (**Figure 1**). After adjustment for age, weight and total body fat, or additionally adjusted for

subcutaneous adipose tissue, visceral adipose tissue, skeletal muscle, sex, ethnicity, menopausal status, the correlation between pelvic BMAT and BMD dropped in magnitude but remained significant (**Table 2**). There was no significant difference between the correlation coefficient of the younger PBM and older PoBL group with adjustment (P = 0.532 to 0.953) and without adjustment (P = 0.149 to 0.926).

Regression models were developed with pelvic BMD, total body BMD, or spine BMD as the dependent variable; and pelvic BMAT, age, weight, total body fat, subcutaneous adipose tissue, visceral adipose tissue, skeletal muscle, sex, ethnicity, menopausal status, and subject group (i.e., younger PBM vs. older PoBL) as potential independent variables. Biological plausible two-way interactions were also included in the regression model as potential independent variables. Neither subject group nor its interaction with BMAT significantly contributed to the BMD prediction (pelvic BMD, P = 0.438, P = 0.921 respectively; total BMD, P = 0.896, P = 0.451 respectively; spine BMD, P = 0.683, P = 0.500 respectively). In these regression models, pelvic BMAT significantly contributed to BMD measures (standardized regression coefficients = -0.337 to -0.380, P < 0.001).

When fat mass index to fat free mass index ratio substituted fat and muscle mass for body composition adjustment in the above regression, neither subject group nor its interaction with BMAT significantly contributed to the BMD prediction (pelvic BMD, P = 0.464, P = 0.949 respectively; total BMD, P = 0.820, P = 0.373 respectively; spine BMD, P = 0.716, P = 0.492 respectively). In these regression models, pelvic BMAT significantly contributed to BMD measures (standardized regression coefficients = -0.511 to -0.529, P < 0.001).

We also performed the above regression analyses with the younger PBM defined as age 18.0-29.9 years (n=131) and the older PoBL group defined as 50.0-88.8 years (n=175). Neither age group nor its interaction with pelvic BMAT significantly entered into any regression models with BMD as the dependent variable (pelvic BMD, P = 0.856, P = 0.738 respectively; total BMD, P = 0.775, P = 0.958 respectively; spine BMD, P = 0.350, P = 0.167, respectively).

DISCUSSION

Using MRI and DXA, the current findings provide additional support at the macroscopic level for an inverse relationship between BMAT and BMD; which we believe represents the competitive differentiation of MSCs into either osteoblasts or adipocytes. In a diverse population, we observed an inverse correlation between BMAT and BMD in both the older PoBL and younger PBM groups. A strength of the present study is that, unlike most previous studies, we adjusted for body composition measured by whole body MRI, which allows evaluation of interaction between fat and bone independent of SAT or VAT. Although previous studies have reported inverse relationships between BMAT and BMD (7-10), the present study is the first that systematically compares the relationship between BMAT and BMD in a younger PBM group and an older PoBL group of adults. Because our results show an inverse relationship between BMAT and BMD in the younger PBM group, this finding supports the notion that the differentiation of MSCs to either osteoblasts or adipocytes is competitive even before the onset of bone loss. Since only healthy adults were

included in this dataset, we assume that the possibility that we included subjects who had undergone bone loss in the younger PBM group is low. Therefore, the low BMD in the younger PBM group is likely due to either decreased differentiation or decreased proliferation of MSCs (32-33). In the older group of adults, the inverse relationship between BMAT and BMD may also be explained by a competitive differentiation of MSCs to osteoblasts or adipocytes. It is also possible that BMAT passively fills the empty space of trabecular bone loss with aging.

In the present study, we observed an inverse relationship between BMAT and BMD in an anatomically matched region (i.e., pelvic BMAT and pelvic BMD), non-anatomically matched region (i.e. pelvic BMAT and spine BMD), and regional and whole body (i.e. pelvic BMAT and whole body BMD). Therefore, it is plausible that both local level MSC differentiation and systemic level hormonal factors contribute to the observed inverse relationship between BMAT and BMD. Future studies may investigate potential targets to prevent and treat osteoporosis at both the MSC level and hormonal level.

Our results provide *in vivo* human imaging evidence in support of *in vitro* studies that have shown osteoblastogenesis and adipogenesis are competing processes. *In vitro* studies have found that activation of peroxisome proliferator-activated receptor-γ (PPARγ) promotes adipogenesis and that suppression of PPARγ transactivation switches cell fate of bone marrow stem cells from adipocytes into osteoblasts (34-35). Although certain thiazolidinedione derivatives can activate PPARγ and enhance bone marrow adiposity without altering BMD (34, 36), it remains plausible that adipocyte expansion may occur at the expense of bone in the absence of pharmaceutical intervention. In addition, other studies have found that PPARγ and its ligands promote osteoclast differentiation and bone resorption (37-38). *In vitro* studies have shown that mechanical influences enhance osteoblastogenesis through inhibiting adipogenesis (39). Future studies should investigate whether pharmaceutically or mechanically inhibiting adipogenesis in bone marrow could be used to prevent and treat osteoporosis. There are multiple factors that influence the differentiation of bone marrow MSCs through multi-pathways (40) and the ways in which these factors work are not fully understood. The application of combined molecular biology techniques and human imaging methods could further our understanding of the physiological role of bone marrow fat to facilitate the prevention and treatment of osteoporosis (40).

A critical aspect of the present study design was determining the cut-off ages for both maturity of bone and bone loss. Since females reach skeletal maturity at about age 17 and males at about age 18 (41-42), we used age 18 as the cutoff for both genders. The cut-off age between the younger PBM group and the older PoBL group was set at 40 years to avoid including peri-menopausal subjects in the younger PBM group. Since we only included healthy subjects in this dataset, we assume that no major bone loss had occurred in the younger PBM group. Although some studies suggest that bone loss begins as early as the third decade (28), most evidence suggests that bone loss does not begin until menopause in women and approximately age 65 in men (26-27). Setting age 40 as the lower age limit for the older PoBL groups could lead to the inclusion of subjects without bone loss in this group

and could therefore slightly under power the study. However, the large sample size should have compensated for this small loss of power.

Because of the inconsistencies regarding the age at which bone loss begins (26-28), we also examined the BMD and BMAT relationship using ages 18.0-29.9 years to define the younger PBM group, and ages 50.0-88.0 years to define the older PoBL group, and the results did not change. It would have been ideal if the present study also investigated a PBM group of subjects below the age of 25 who had reached sexual and bone maturity. However, we did not have an adequate sample size for subjects below the age of 25. An earlier study reported an inverse relationship between marrow fat and BMD in women below age 25 (10). Our studies and previous ones collectively contribute to the growing evidence supporting a competitive relationship between marrow fat and BMD.

Limitations and future directions

DXA BMD readings can be underestimatd when BMAT is present. This raises the question of whether the observed inverse relationship between BMAT and BMD is an artifact. Previous studies have shown that the underestimation of BMD caused by marrow fat is only severe in osteoporosis with a small amount of extraosseous fat (43). Hangartner et al. reported that a 50% increase in marrow fat content could only cause underestimation of the apparent areal bone density by 5–6% (44). In addition, the same change in soft-tissue fat content (not in the path of the beam traversing the bone) causes overestimation of bone density (6, 43-44). Considering that subjects in the present study had a mean BMD 1.14 g/cm^2 and a mean subcutaneous fat of 17.4 L, it is unlikely that there was a major underestimation of BMD, if at all. More detailed discussion can be found in our previous report (9). A recent study has also shown that the changes in BMAT are not related to changes in BMD during weight loss (16). In addition, the underestimation of BMD caused by the presence of BMAT is unlikely to play a major role in the inverse relationship between BMAT and BMD when BMAT and BMD are measured at different locations (i.e., between spine BMD and pelvic BMAT).

A second limitation of the present study is that the sample is cross-sectional; therefore, we cannot directly evaluate the relationship between BMD loss and BMAT increase. A recent longitudinal study found that bone acquisition is inversely related to marrow fat adiposity changes in cortical bone in young females (45). Future longitudinal studies should ideally investigate whether BMAT contributes to bone quality and fracture risk by examining the relationship with both cortical and cancellous bone density and architecture in a diverse population.

A third limitation is that we did not have DXA measurements available for the femoral neck and lumbar spine; which could have been used to determine which individuals had osteoporosis (46). In addition, studies using Quantitative Computed Tomography (QCT) are advantageous since this method allows for the differentiation of cortical and cancellous bone (47). Future studies should therefore include QCT methods as a means to expand our findings, and it would be especially interesting in an osteoporotic population.

A fourth limitation is that BMAT was semi-quantitatively measured using the single threshold MRI methods applied in the current study. However, less accurate methods reduce observed correlations from their potential maximum. Thus, it is likely that the application of more accurate BMAT measurement methods would strengthen the observed inverse association between BMD and BMAT. In addition, the use of 10 mm skip 40 mm MRI acquisition protocol can induce ~6% error compared to a contiguous protocol (unpublished data, n=27, r = 0.97, P<0.001). We expect that future studies that use contiguous MRI acquisition protocol will strengthen the observed association between BMD and BMAT.

Information on bone turnover biomarkers, hormonal measures, and vitamin D levels was not available in the present study. This serves as a limitation since these factors are known to be related to BMD.

Methods that can accurately quantify BMAT in cancellous bones, both in a single bone and multiple bones, need to be developed to better understand the relationship between BMAT and BMD. These future studies would ideally investigate whether BMAT contributes to bone quality and fracture risk by examining the relationship with both cortical and cancellous bone density and architecture. Longitudinal studies could help clarify whether the relationship between BMAT and BMD is causal in cancellous bone across diverse populations. *In vivo* studies have recently found that biphosphonates reduce marrow fat (48) and *in vitro* studies have found that mechanical influences enhance osteoblastogenesis through inhibiting adipogenesis (39). Future studies could rigorously test whether inhibiting adipogenesis in bone marrow could prevent and treat osteoporosis. There are many factors influencing the differentiation of bone marrow MSCs through multi-pathways (40) and the ways in which these factors work are not fully understood. The application of combined molecular biology techniques and human imaging methods could also help explain the physiological role of bone marrow fat as well as facilitate the prevention and treatment of osteoporosis (40).

CONCLUSIONS

Our findings indicate that an inverse relationship between BMAT and BMD exists in both healthy older adults with potential bone loss and healthy younger adults at or approaching peak bone mass. This result provides macro-imaging level support for the concept that low BMD may be a result of preferential differentiation of MSCs into adipocytes instead of osteoblasts.

ACKNOWLEDGMENTS

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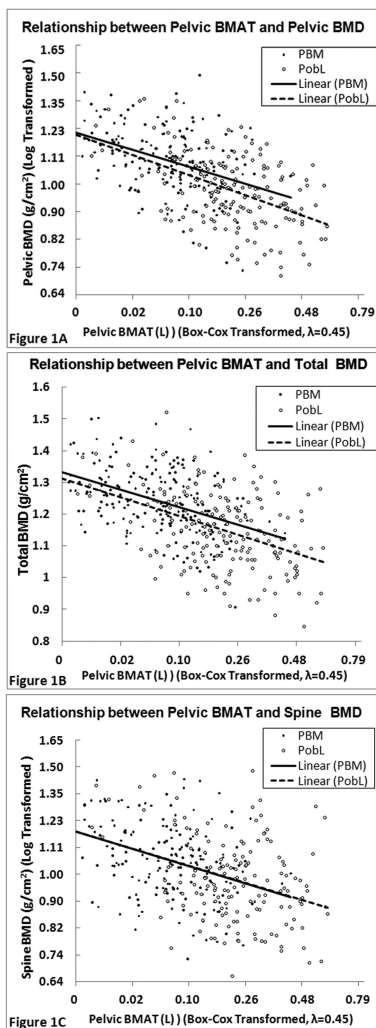
Figure 1.
Correlation between bone mineral density (BMD) (1A, pelvic BMD; 1B, total BMD; 1C, spine BMD) and Pelvic bone marrow adipose tissue (BMAT) in peak bone mass younger (PBM) group and potential bone loss older (PoBL) group. BMD and BMAT was either log or Box-Cox transformed to normalize the distribution of the residuals and to equalize the residual variance among groups.

Table 1

Subject Characteristics

		Younger PBM Group		Older PoBL Group	
		Men	**Women**	**Men**	**Women**
Sample size		98	182	82	198
Ethnicity	**Caucasian**	30	82	49	76
	African American	29	70	22	97
	Hispanic	20	11	3	18
	Asian[1]	17	18	8	7
Age (yrs)		29.4 ± 5.8 (25.0, 29.0, 35.0)	30.3 ± 5.3 (26.0, 31.0, 35.0)	58.4 ± 13.4 (47.0, 58.0, 70.0)	57.1 ± 13.9 (44.0, 55.0, 70.0)
Weight (kg)		78.3 ± 13.0 (69.6, 75.7, 87.8)	70.1 ± 17.5 (55.8, 66.8, 78.6)	79.1 ± 12.5 (71.5, 79.8, 86.3)	71.0 ± 15.5 (58.7, 70.0, 82.0)
BMI (kg/m^2)		25.2 ± 3.7 (22.3, 24.8, 28.0)	26.2 ± 6.2 (21.5, 24.9, 29.7)	26.2 ± 3.9 (24.0, 25.8, 28.2)	27.4 ± 5.4 (23.1, 27.1, 31.9)
Pelvic BMD (g/cm^2)		1.23 ± 0.14 (1.12, 1.21, 1.33)	1.18 ± 0.14 (1.09, 1.18, 1.28)	1.13 ± 0.14 (1.06, 1.12, 1.19)	1.11 ± 0.15 (1.00, 1.10, 1.22)
Whole body BMD (g/cm^2)		1.27 ± 0.09 (1.21, 1.26, 1.33)	1.22 ± 0.10 (1.15, 1.21, 1.30)	1.23 ± 0.09 (1.17, 1.22, 1.28)	1.15 ± 0.12 (1.07, 1.16, 1.24)
Spine BMD (g/cm2)		1.14 ± 0.14 (1.03, 1.12, 1.22)	1.18 ± 0.18 (1.05, 1.18, 1.29)	1.14 ± 0.18 (1.02, 1.12, 1.25)	1.11 ± 0.18 (0.98, 1.09, 1.24)
Pelvic bone BMAT (L)		0.12 ± 0.10 (0.04, 0.11, 0.17)	0.09 ± 0.08 (0.02, 0.08, 0.12)	0.22 ± 0.14 (0.12, 0.20, 0.29)	0.18 ± 0.15 (0.06, 0.15, 0.26)
Subcutaneous adipose tissue (L)		15.9 ± 6.9 (10.9, 15.0, 19.5)	24.9 ± 12.4 (16.2, 21.5, 31.3)	18.8 ± 7.0 (14.0, 17.8, 22.3)	29.2 ± 11.8 (19.9, 27.7, 38.4)
Visceral adipose tissue (L)		1.70 ± 1.29 (0.77, 1.28, 2.41)	1.14 ± 0.86 (0.53, 0.92, 1.54)	3.37 ± 1.91 (1.87, 3.07, 4.71)	2.13 ± 1.33 (1.07, 2.02, 2.83)
Total body fat (kg)		15.3 ± 8.4 (8.9, 13.9, 20.3)	24.3 ± 12.6 (14.5, 21.4, 32.1)	19.9 ± 8.5 (14.2, 18.8, 24.6)	28.2 ± 11.9 (18.9, 27.5, 37.4)

Data are presented as mean ± SD (25 percentile, median, 75 percentile)

[1] the Asian sample is a multi-generation mixture of Chinese, Indian, Korean, and Japanese.

Table 2

Pearson correlation coefficients among BMD and pelvic BMAT with and without adjustment (N = 560).

	Pelvic BMAT[†]					
	Younger PBM group	Older PoBL group	Younger PBM group adjusted[1]	Older PoBL group adjusted[1]	Younger PBM group adjusted[2]	Older PoBL group adjusted[2]
Pelvic BMD[3]	-0.460[5]	-0.556[5]	-0.394[5]	-0.379[5]	-0.242[5]	-0.217[5]
Whole body BMD	-0.461[5]	-0.500[5]	-0.403[5]	-0.367[5]	-0.266[5]	-0.215[5]
Spine BMD[3]	-0.420[5]	-0.413[5]	-0.349[5]	-0.307[5]	-0.150[4]	-0.155[4]

BMD, bone mineral density; BMAT, bone marrow adipose tissue; PBM, peak bone mass younger group; PoBL, potential bone loss older group.

[1] adjusted for age, weight and total body fat

[2] adjusted for age, weight, total body fat, subcutaneous adipose tissue, visceral adipose tissue, skeletal muscle, sex, ethnicity, and menopausal status.

[3] Either log or Box-Cox transformed to normalize the distribution of the residuals and to equalize the residual variance among groups.

[4] Differs from 0, P < 0.05

[5] Differs from 0, P < 0.001.