

The relationship between bone mineral density and biomechanics in patients with osteoporosis and scoliosis

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Abstract Nearly one-third of all women and one-sixth of all men over age 65 have osteoporosis, and this condition is often accompanied by lumbar scoliosis. Previous work has shown that, in a group of postmenopausal women with scoliosis and osteoporosis, both the bone mineral content (BMC) and bone mineral density (BMD) were greater on the concave side than the convex side. The goal of this study was to examine the structure-function relationships in the spines of patients with low bone mass and scoliosis using a patient-specific biomechanical model. We compared the percent change in BMC and the percent change in BMD with axial force, F_a , shear force, F_s , moment, M , local curvature, θ_{rel} , and the patient's age, A . We found that the percent change in BMC depended on the applied moment and the local curvature. The same dependence was observed for the percent change in BMD, but in this case, the shear force was also significantly inversely correlated. A population with femoral neck BMD with a T-score greater than -2.0 was similarly evaluated and yielded similar results. The percent change in BMD was related to M , θ_{rel} , A and negatively to the shear force. These results indicate that the osteoporotic spine is still able to respond to changes in the mechanical environment and provides a useful

comparison between patients with osteoporosis and those with normal bone mass. In addition, this model may be a useful tool for the in vivo assessment of bone density changes in response to mechanical stimuli and drug treatments.

Keywords Biomechanical model · Bone adaptation · Vertebral deformity

Introduction

Osteoporosis is the most common bone disorder found in the elderly. It is estimated that in the United States nearly one-third of all women and one-sixth of the men over the age of 65 have osteoporosis [1]. There are more than 1 million age-related osteoporotic fractures annually in the U.S., and the associated costs are in excess of \$10 billion [2]. This cost is anticipated to increase concomitantly with the elderly population [2]. Epidemiological studies indicate that adults who present with osteoporosis or osteomalacia are six times more likely to exhibit scoliosis [3]. Adult scoliosis is associated with significant morbidity, including low back pain and radicular symptoms [4].

Low mean bone mineral density (BMD) has been correlated to indices of wedging and bi-concavity in the elderly spine [5]. Only recently, however, have attempts been made to consider the variation within the vertebral body with regard to vertebral deformity and bone adaptation [6]. Previous work from our laboratory has shown that the bone mineral content (BMC) and bone mineral density measured by dual energy X-ray absorptiometry (DXA) are both greater on the concave side than the convex side in postmenopausal women with scoliosis [6]. There are many factors that may be responsible for these results, including rotation of the spine, compression of the vertebrae and biomechanical adaptation within the cancellous or cortical bone tissue. Interestingly, the difference between the concave and

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convex sides appeared to be at least as great in patients with a low femoral neck t -score as compared to those with a high femoral neck t -score [6].

While it is well established that cancellous and cortical bone are able to adapt to changes in the mechanical stress applied to the bone, there have been few attempts to quantify the relationship between spine curvature and bone density [7]. Consequently, the goal of this study was to elucidate the structure-function relationships in the spines of patients who presented with both low bone mass and scoliosis. Specifically, we used DXA scans to measure the BMC and BMD of patients in different regions of the L1-L4 vertebrae and compared the data with the prevailing mechanical loads using a patient-specific biomechanical model. We hypothesized that (1) the concave side of each vertebra would have a higher BMD and BMC than the convex side and (2) the differences between the concave and convex sides would be related to the applied mechanical loads. The latter would be evidence for biomechanical adaptation in the osteoporotic-scoliotic spine.

Materials and methods

Population

All experimental protocols were approved by the Institutional Review Board at Ochsner Hospital, New Orleans, La. To collect the bone mineral content and density data, DXA scans of the L1-L4 vertebrae from 87 individuals with both scoliosis and low bone mineral density in the femoral neck were examined. Scoliosis was identified in patients undergoing lumbar spine and hip BMD evaluations from 27 November 2000 to 7 October 2002 using a dual energy X-ray absorptiometry (DXA) system (Hologic Delphi, Bedford, Mass.). The lumbar spine BMD scans were performed in the supine position, and a single physician diagnosed lumbar scoliosis on the basis of the scan. While it has been shown that lateral scans are better able to detect bone loss, they are not recommended for patients with scoliosis [8]. Consequently, we chose to use only the supine anterior-posterior measurements for our analysis. Patients with a femoral neck T-score of less than -2.0 were considered to have osteoporosis. The population for this analysis included Caucasian postmenopausal women with an average age of 74.8 ± 8.8 years and self-reported menopause onset at an age of 45.7 ± 8.2 years.

Each individual provided a maximum of four data points, one for each usable vertebra from L1 to L4. Once the individuals were identified and observed, all vertebrae that had parallel inferior and superior endplates based on the DXA images were removed from the study. These vertebrae did not exhibit concave and convex sides. Once these points were removed, the dataset contained information from 316 vertebrae from the group of 87 individuals, an average of 3.63 vertebrae per individual.

Determination of BMD and BMC

BMC and BMD were determined by using proprietary Hologic Delphi software. Each vertebra was vertically bisected using a feature of the software package that allowed the user to define regions of interest (Fig. 1). The BMC and BMD were then determined for each region of interest. To minimize operator variability, the bisecting process was repeated if the region of interest contained less than 49% or more than 51% of the total vertebral cross-sectional area. The difference between the BMC on the concave and convex sides of each vertebra, ΔBMC , was also calculated:

$$\Delta\text{BMC} = \text{BMC}_{\text{concave}} - \Delta\text{BMC}_{\text{convex}}.$$

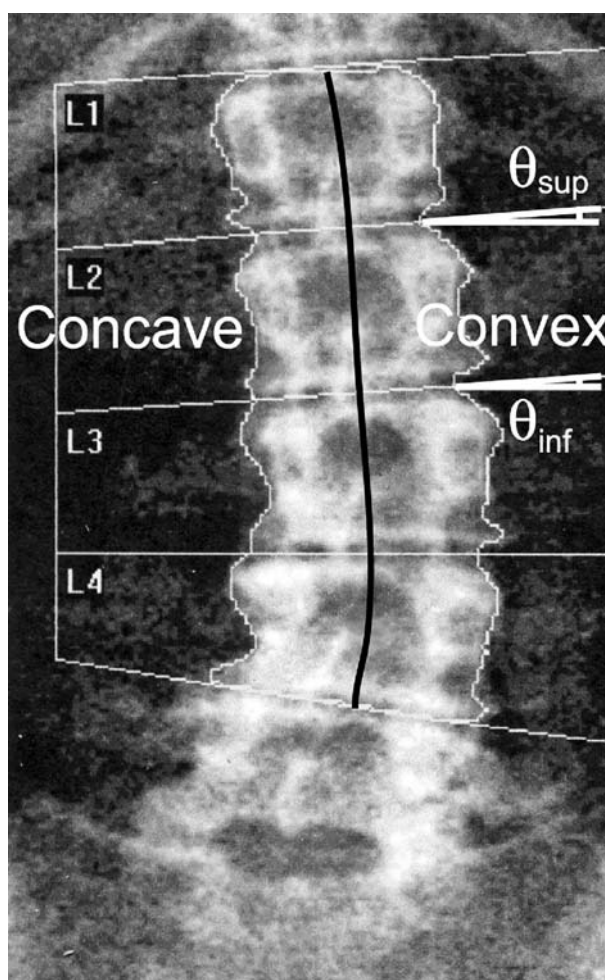


Fig. 1 Bisection of the lumbar spine. Each vertebra was bisected across its width using a feature of the Hologic software package that allowed the user to define regions of interest (indicated by black lines). The software was then used to determine the BMC and BMD for each region of interest. To minimize operator variability, the bisecting process was repeated if the region of interest contained less than 49% or more than 51% of the total vertebral cross-sectional area

The difference between the BMD on the concave and convex sides of each vertebra, ΔBMD , was determined in an analogous manner. In addition, the percent change in BMC, P_{BMC} , was defined as

$$P_{\text{BMC}} = \frac{\Delta\text{BMC}}{\text{BMC}_{\text{convex}}} \times 100\%,$$

and the percent change in BMD was defined similarly.

Vertebral alignment and deformation

A printout of each scan was used to obtain measurements not provided by the Hologic software program. The orientation of the superior and inferior surfaces of each vertebra was measured (Fig. 1). The difference between these two angles, θ_{rel} , was used as the quantitative measurement of deformity for each vertebra. This method was accurate to 0.5° . The average of these two angles, θ_{avg} , was used in the calculation of the axial and transverse forces exerted on the vertebrae. Using a vertical line drawn through the sacrum as a reference the horizontal offset distance, d , to the centroid of each vertebra was measured and scaled to the actual size of the vertebrae. This horizontal offset was used to calculate the net moment exerted on each vertebra as described below.

Force and moment calculations

Several force measurements were made using the data collected. It has been shown that in elderly patients the average weight supported by the lower spine is 46.46% of the patient's total weight, W [9]. Variation in this load from L1 to L4 was neglected. Using this assumption, the axial force, F_a , exerted on each vertebra was

$$F_a = 0.4646 (W \sin(\theta_{\text{avg}}))$$

and the average shear force, F_s , exerted on each vertebra was

$$F_s = |0.4646 (W \cos(\theta_{\text{avg}}))|.$$

The magnitude of the moment exerted on each vertebra was then given by

$$M = |0.4646(Wd)|.$$

Scoliotic patients with normal bone mass

In order to gain some insights into the combined effects of osteoporosis and scoliosis, we repeated the above analysis on a total of 321 vertebrae from 92 post-menopausal Caucasian women (average age 69.4 ± 9.15 years) who had femoral neck T-scores greater than -2.0 . Because the average relative angle was small ($4.59 \pm 3.01^\circ$), it was assumed that changes observed in this set of patients reflected normal adaptive processes.

Statistical analyses

All statistical analyses were performed using StatView v5.0.1 (SAS, Cary, N.C.) on a PC platform. A single factor analysis of variance (ANOVA) was used to evaluate the mean differences in BMC and BMD between the concave and convex sides of the vertebrae. Both single and multivariable linear regressions were used to evaluate the relationships between each dependent variable, P_{BMC} and P_{BMD} , and each of the independent variables, F_a , F_s , M , θ_{rel} and the patient's age, A .

Results

Patients with osteoporosis and scoliosis

When bisected, the average concave BMC for patients with osteoporosis and scoliosis was 6.91 ± 2.08 g and that of the convex side was 6.00 ± 1.85 g. This corresponds to a percent difference of 17.6%. The average BMD on the concave side was 0.992 ± 0.243 g/cm² and that on the convex side was 0.826 ± 0.185 g/cm², a 22.0% change on average. A single factor ANOVA showed that both BMC and BMD were greater on the concave side of the spine than the convex side ($P < 0.0001$ for both).

Multiple linear regression analysis indicated that both P_{BMC} and P_{BMD} depended significantly on θ_{rel} and at least one other mechanical parameter (Tables 1, 2). The r^2 value for P_{BMC} was 0.09 and that of the P_{BMD} regression was 0.36. It should be noted that both P_{BMC} and P_{BMD} were positively correlated to M and θ_{rel} . In contrast, P_{BMD} was negatively correlated to F_s .

Single variable linear regression analysis was performed using P_{BMC} and P_{BMD} as the dependent variables and F_a , F_s , M , θ_{rel} and A as the independent parameters. Only M and θ_{rel} significantly influenced P_{BMC} (Fig. 2) with $P < 0.0001$ for both. The r^2 values, however, were low (0.057 and 0.054, respectively). In contrast, and P_{BMD} exhibited significant dependencies on three variables (Fig. 3), namely, M ($P < 0.0001$), F_s

Table 1 Results of a multiple linear regression between P_{BMC} and axial force, F_a , shear force, F_s , moment, M , angular measure of the deformity, θ_{rel} , and the patient's age, A , for patients with scoliosis and osteoporosis. The R^2 value for the regression was 0.09. The only significant variables were the applied moment, M , and the value of θ_{rel} . Age was nearly significant, but the P value did not improve when the two forces were removed from the regression

Variable	Coefficient	Units	P value
Constant	-15.73	g	0.256
F_a	0.016	g/N	0.432
F_s	-0.067	g/N	0.248
M	1.991	g/(Nm)	0.004
θ_{rel}	0.785	g/degree	0.023
A	0.280	g/year	0.058

Table 2 Results of a multiple linear regression between P_{BMD} and axial force, F_a , shear force, F_s , moment, M , angular measure of the deformity, θ_{rel} , and the patient's age, A , for patients with scoliosis and osteoporosis. The R^2 value of the regression was 0.36. The only significant variables were F_s , the applied moment, M , and the value of θ_{rel} . Again, the patient's age was nearly significant, but the P value did not improve when the two forces were removed from the regression

Variable	Coefficient	Units	P value
Constant	-13.57	1	0.273
F_a	0.006	1/N	0.734
F_s	-0.127	1/N	0.016
M	1.643	1Nm	0.007
θ_{rel}	2.989	1/degree	<0.0001
A	0.242	1/year	0.068

($P < 0.005$) and θ_{rel} ($P < 0.0001$). The r^2 values for these regressions were 0.12, 0.02 and 0.33, respectively.

Patients with normal bone mass and scoliosis

For patients with normal bone mass and scoliosis, a multiple linear regression analysis indicated that both P_{BMC} and P_{BMD} depended significantly on M . In

addition, P_{BMD} was significantly correlated with θ_{rel} and patient age, A (Tables 3 4). The r^2 value for P_{BMC} was 0.05 and that of the P_{BMD} regression was 0.22. Both P_{BMC} and P_{BMD} were positively correlated to the applied moment, M . In addition, P_{BMD} was positively correlated to θ_{rel} and A (Fig. 4).

Discussion

Rumancik et al. [6] were the first to show that adults with scoliosis exhibited higher BMC and BMD readings on the concave side of the vertebrae. Interestingly, P_{BMD} increased with decreasing femoral neck BMD, a measure of overall skeletal bone health [10]. These results suggested that patients with low bone mass might respond to the altered mechanical environment of scoliosis with long-term changes in bone density. Consequently, we examined the relationship between P_{BMC} and P_{BMD} and a geometric parameter, θ_{rel} , three biomechanical parameters, F_a , F_s and M , and the patient's age, A , using a large sample size and patient-specific biomechanical models. We found that changes in BMC and BMD were influenced by geometry and the applied

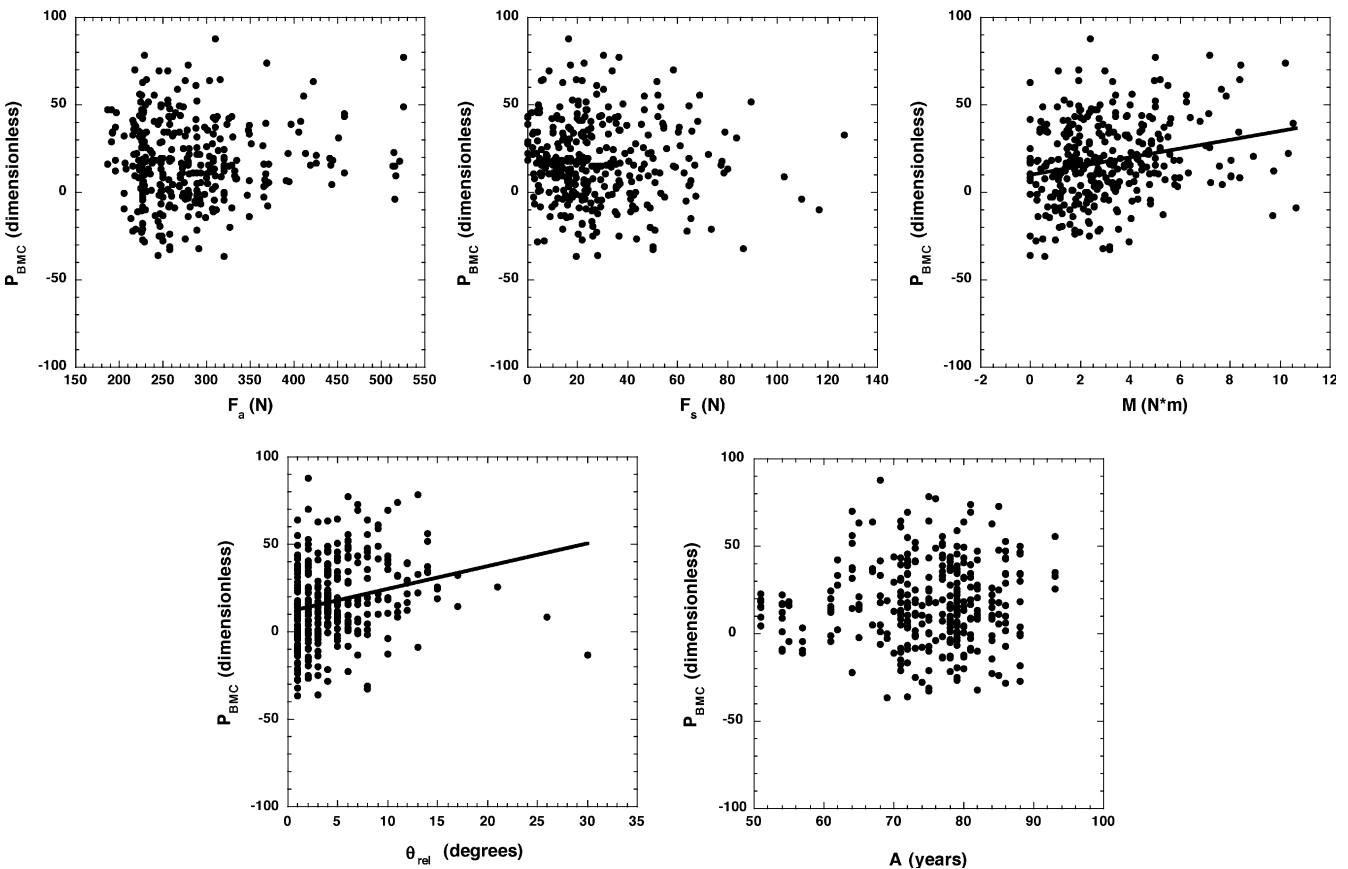


Fig. 2 Percent change in BMC as a function of axial force, F_a , shear force, F_s , moment, M , angular measure of the deformity, θ_{rel} , and the patient's age, A , for patients with scoliosis and osteoporosis. Regression lines are shown only for variables that provided significant correlations (M and θ_{rel})

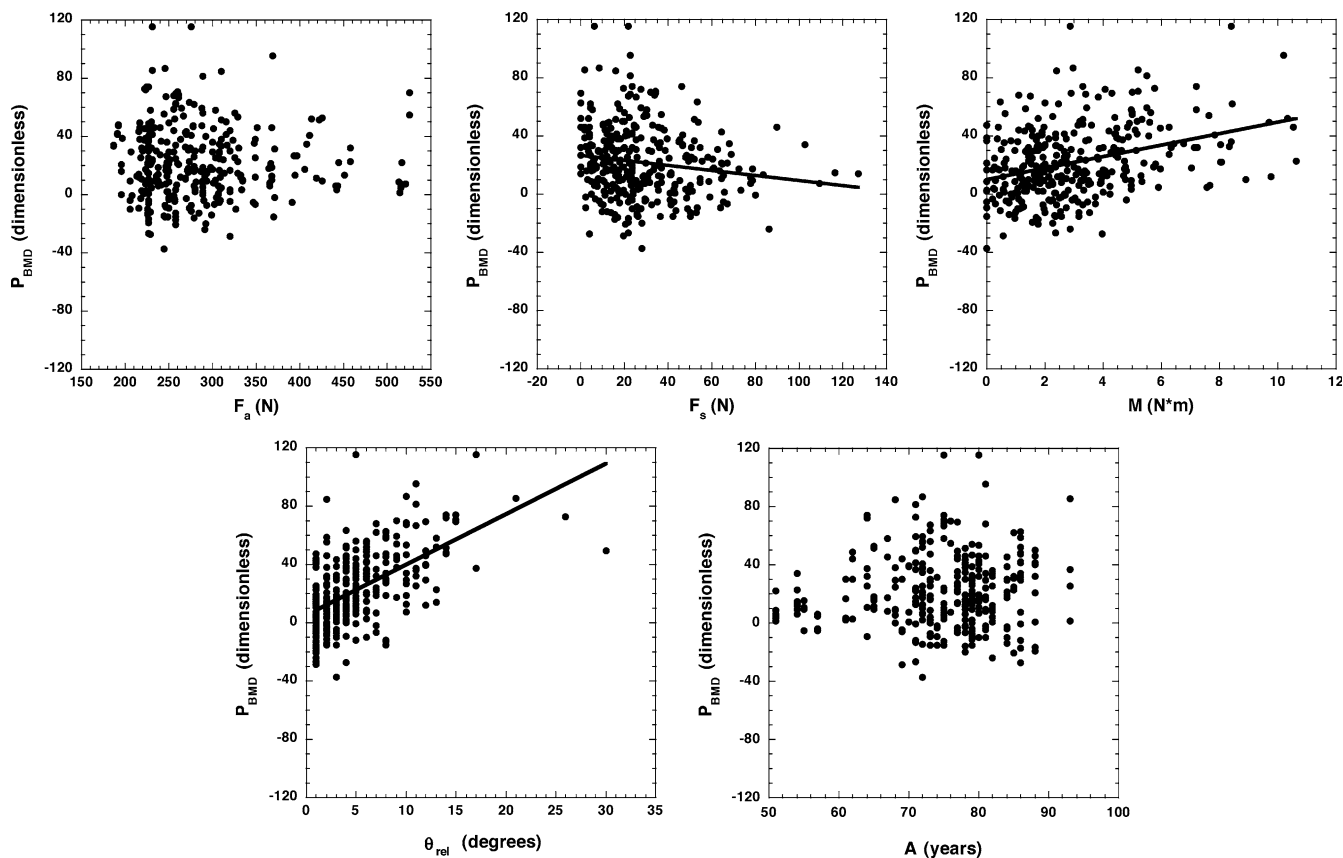


Fig. 3 Percent change in BMD as a function of axial force, F_a , shear force, F_s , moment, M , angular measure of the deformity, θ_{rel} , and the patient's age, A , for patients with scoliosis and osteoporosis. Regression lines are shown only for variables that provided significant correlations (F_s , M and θ_{rel})

moment. In addition, the P_{BMD} was negatively correlated to the shear force.

It is well-accepted that bone adapts to changes in its mechanical loading environment [7, 11, 12], although the precise mechanisms governing this response remain elusive. Patients with scoliosis provide an accessible, in vivo model of an altered mechanical environment that may prove useful in the study of bone adaptation and osteoporosis. Interestingly, Hans et al. [13] showed that one outcome of scoliotic deformity was a decrease in the bone mass of the femur on the convex side of the curve. Shea et al. [14] were the first to demonstrate an adaptive

response in the facet joints of the scoliotic spine. They found that the cortical thickness was higher and the overall porosity was lower on the facets from the concave side as compared to the contralateral controls, although they did not quantify the forces and moments involved. Our results, applied to the whole vertebrae, indicated that the bone did indeed respond to the applied moment and shear force, but not to the axial load. This result was expected because the spine does not normally carry shear loads or moments in the frontal plane, and the change in the magnitude of the axial load caused by this curvature was relatively small.

Table 3 Results of a multiple linear regression between P_{BMC} and axial force, F_a , shear force, F_s , moment, M , angular measure of the deformity, θ_{rel} , and the patient's age, A , for patients with scoliosis and normal femoral neck bone mass. The R^2 value for the regression was 0.05. The only significant variable was M

Variable	Coefficient	Units	P value
Constant	20.58	g	0.147
F_a	-0.012	g/N	0.642
F_s	0.078	g/N	0.391
M	3.421	g/(Nm)	0.0019
θ_{rel}	0.580	g/degree	0.221
A	-0.212	g/year	0.192

Table 4 Results of a multiple linear regression between P_{BMD} and axial force, F_a , shear force, F_s , moment, M , angular measure of the deformity, θ_{rel} , and the patient's age, A , for patients with scoliosis and normal femoral neck bone mass. The R^2 value for the regression was 0.22. The only significant variables were the applied moment, M , the value of θ_{rel} , and the patient's age, A

Variable	Coefficient	Units	P value
Constant	-11.28	1	0.239
F_a	-0.005	1/N	0.753
F_s	-0.117	1/N	0.057
M	2.623	1/Nm	0.0004
θ_{rel}	1.961	1/degree	<0.0001
A	0.257	1/year	0.0194

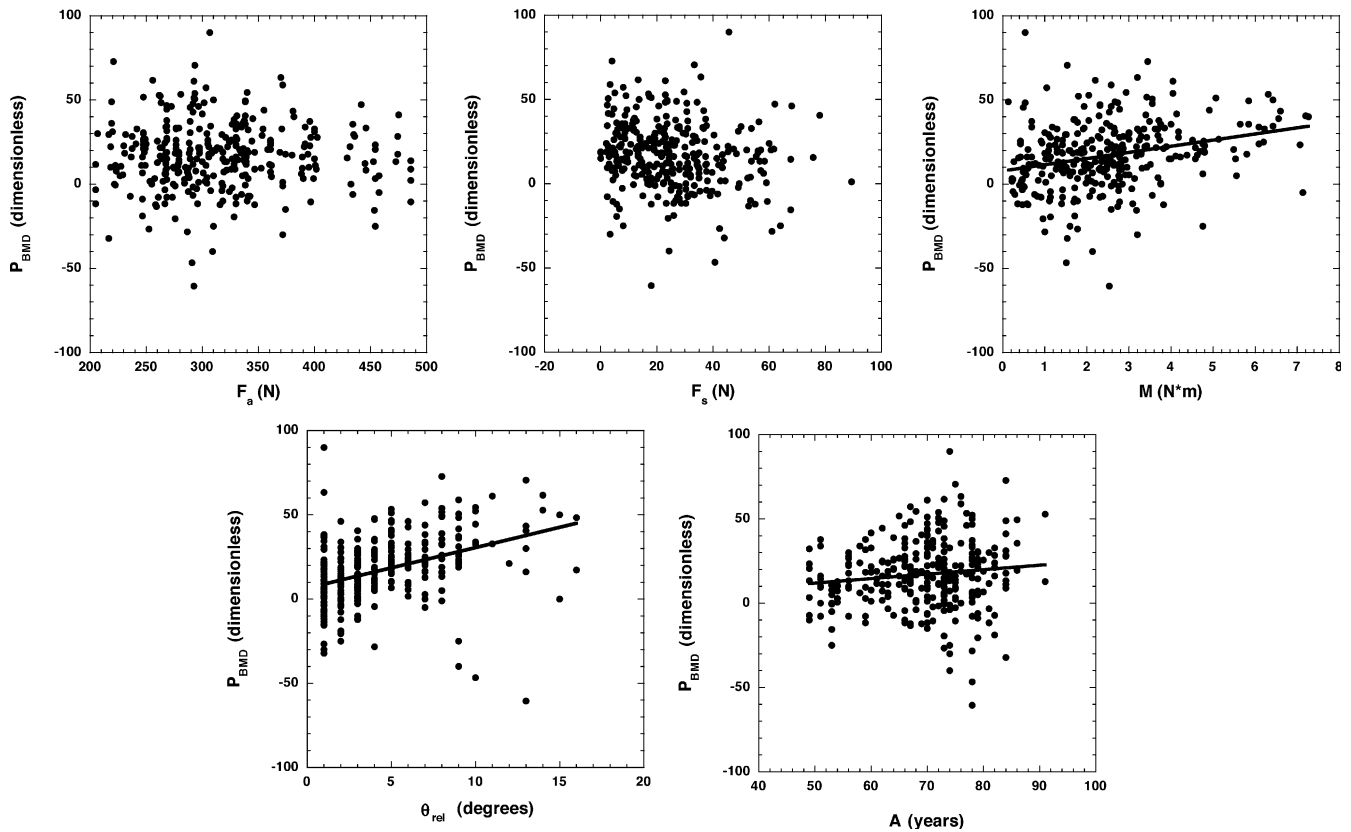


Fig. 4 Percent change in BMD as a function of axial force, F_a , shear force, F_s , moment, M , angular measure of the deformity, θ_{rel} , and the patient's age, A , for patients with scoliosis and normal bone mass at the femoral neck. *Regression lines* are shown only for variables that provided significant correlations (M , θ_{rel} and A)

A limitation of this study was that we did not consider disc degeneration as a possible mediator of the adaptive response. Exaggerated kyphosis has been correlated to degenerative disc disease [15], likely because of the altered mechanical environment, and it is possible that a similar result would be found in this model of increased lateral curvature. A second limitation involved the reporting of the patients' ages. As part of the study protocol approved by the Institutional Review Board at Ochsner Hospital, we only had access to each patient's age in years, yielding a discrete number as opposed to a continuous variable. Because of the large number of data points collected for this study, the subtle adjustments in age would be unlikely to affect the results.

The effect of local curvature, demonstrated here by a dependence on θ_{rel} , could be explained by a variety of mechanisms. It is possible that these patients experienced a vertebral fracture and the increased BMC and BMD are the result of a structural failure that compressed the bone tissue into a smaller volume. Recent follow-up studies on patients with similar degrees of scoliotic deformity, however, indicate that the difference between the concave and convex sides increases with time (data not shown). In the present study, the effect of age on the P_{BMD} and P_{BMC} was nearly significant. This may indicate that the observed changes are the result of long-term adaptation, but when the non-significant

variables were removed from the regression, the significance of patient age did not increase. A high degree of curvature may also disturb the surrounding soft tissue, changing the local blood flow patterns or fracture trabeculae, which could lead to a wound-healing response. All of these factors could mitigate long-term bone adaptation without being directly related to the prevailing mechanical loads.

The fact that the results for the BMC and BMD differed was not surprising. BMC measures the total amount of bone in a given region and is dependent on the size of the vertebrae. BMD accounts for this in part by normalizing the cross-sectional area of the region in question and often exhibits less variability. However, it assumes the depth of the vertebrae is the same for all individuals. Future work should consider the use of computer tomography (CT) scans to measure the changes in bone mineral density more accurately throughout the entire vertebrae.

It should be noted that P_{BMD} was positively correlated with M and θ_{rel} , but negatively correlated with F_s . This result suggests that, while large moments may engender an adaptive response, large shear forces tend to damage the bone or interfere with the remodeling process in some way. Alternatively, the shear forces may stimulate bone formation on the convex side as well as the concave side. Future work should address the effects

of shear stresses independent of the applied moment on the adaptive response of cancellous and cortical bone in the vertebral body in an effort to elucidate the mechanisms responsible for the change in P_{BMD} . While this particular human model is not well-suited for such experiments, animal models exist that may provide additional insights [16, 17, 18].

In this study, patients with normal bone mass and scoliosis also exhibited an adaptive response to the prevailing mechanical loads. In particular, P_{BMC} and P_{BMD} both depended significantly on the applied moment. In contrast to patients with osteoporosis, F_s was not significantly correlated to the change in BMD in patients with normal bone mass. It is possible that susceptibility to shear failure in trabecular struts that make up the cancellous bone plays a role in the eventual development of osteoporosis, but additional studies, likely using animal models, will be needed to further elucidate these relationships.

This is the first study that has shown a relationship between biomechanical forces and scoliosis using DXA technology. It should be noted that our study considered the average forces and moments applied to each vertebral body and did not examine the local variation in any of these parameters. To do so would require patient-specific high resolution finite element models and was beyond the scope of this work. In addition, these results are specific to adult scoliosis in women and may not be generalizable to children or males.

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