

# Densitometric and tomographic analyses of musculoskeletal interactions in humans

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## Abstract

Previous studies with standard densitometry (DXA) have suggested that the bone mass is strongly dependent on the muscle mass in the species, following a similar relationship at any age and sex hormones or related factors potentiate that relationship. Studies with pQCT indicated that the surplus bone mass per unit of muscle mass previously observed in premenopausal women would be stored in skeletal regions with relatively little mechanical relevance, thus avoiding remotion through mechanically oriented remodelling by the bone mechanostat. Scanning the distal radius with pQCT has also showed a highly significant, linear relationship between SSI of the distal radius and the dynamometric maximal bending moment of the forearm in normal men and women. In order to investigate similar relationships in regions that are inaccessible to pQCT, we used spinal radiographs and axial QCT. This study affords additional evidence to the previous references concerning the direct, significant impact of the regional muscle strength on the determination of the tomographic indicators of bone mechanical quality and their indirect repercussion of the skeletal condition (curvature of the spine).

**Keywords:** DXA, pQCT, Musculoskeletal Interactions

## Previous studies with standard densitometry (DXA) and peripheral QCT (pQCT)

We have collected the following experimental evidences of some interesting musculoskeletal interrelationships in human studies.

1. We measured the whole-body bone mineral content (BM), lean mass (LM) and fat mass (FM) by standard densitometry (DXA, Norland XR-26) in 1,500 males and females aged 2-87 years, and found that either the crude or the FM-adjusted BM values correlated linearly and closely with the LM values showing similar slopes regardless of age, sex and body habitus.

However, the intercepts of these correlations were higher in postpubertal than in prepubertal individuals; in menstruating women than in men, and in premenopausal than in postmenopausal women. Multiple regression

analyses showed that the most significant determinant of the BM was the LM, with little or no independent effect of the FM or the body habitus in both genders<sup>1</sup>. This suggested:

- a) that the bone mass is strongly dependent on the muscle mass in the species, following a similar relationship at any age, and
  - b) that sex hormones or related factors potentiate that relationship. That would be an evidence that the endocrine environment somehow disturbs the "mechanostatic" regulation of bone properties by muscles<sup>2</sup> in terms of densitometrical "masses".
2. On scanning the distal radius of normal men and women with pQCT (Stratec QCT 960), we have observed that a) the slope of the correlation between the cross-sectional moment of inertia (CSMI, y) and area (x) of the cortical region was higher in men than in women, while b) the slope of the correlation between the volumetric bone mineral density (vBMD, y) and content (vBMC, x) of trabecular bone was higher in premenopausal women than in men<sup>3</sup>.

This indicated that the surplus bone mass per unit of muscle mass previously observed in premenopausal

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women (supposedly suitable for breeding) would be stored in skeletal regions with relatively little mechanical relevance (as the cortical-endosteal or the trabecular surfaces), thus avoiding remotion through mechanically-oriented remodeling by the bone mechanostat<sup>4</sup>.

3. We have also observed a highly significant, linear relationship between the pQCT-determined Stress / Strain Index (SSI<sup>1,5</sup>) of the distal radius and the dynamometric maximal bending moment of the forearm in normal men and women, showing a single slope for both genders<sup>6</sup>.

In addition to confirm the proposed muscle/bone relationships from a more structural (tomographic) and mechanical (dynamometric) point of view, this suggested the existence of a single "mechanostatical" muscle/bone interaction for any specimen of Homo sapiens, regardless of the gender-related differences in bone mass accumulation during the reproductive life.

4. On analyzing pQCT scans of the calf from normal men

and women, we have also found close correlations between the tibial CSMI or SSI (y) and the calf-muscles cross-sectional area (x), also following single slopes for males and premenopausal females. In postmenopausal females, however, the same correlations showed a comparatively greater dispersion of the data and a significantly lower slope<sup>7</sup>.

These findings further evidenced the disturbing role of the endocrine system on the regulation of the efficiency of bone structure by the bone mechanostat.

### A further study with spinal radiographs and axial QCT

#### Materials and methods

In order to investigate similar relationships in regions that are inaccessible to pQCT, we have measured the curvature angle of the spine between T4 and T12 in lateral radiographs, and the total, cortical and trabecular cross-sectional bone areas, vBMC and vBMD of the vertebral body, as well as the whole and the fat-free areas (MA, FFMA, better indicators of the muscle strength than the densitometrically-assessed lean "masses") of the flexor (ventral) and extensor (dorsal) muscle groups of the spine, in axial-QCT scans (Siemens Somatron Plus '98, slice thickness = 1 cm) taken at the L3 level in a sample of 93 pre- and postmenopausal women aged 35-79 years, to which data from 5 normal men aged 32-74 years were added as a reference.

Subjects showing vertebral deformities in control, frontal radiographs that could have interfered the measurements of the spinal curvature were excluded from the study. None of the individuals, otherwise unselected, had received any kind of treatment known to affect the skeleton.

The interrelationships between the tomographic indicators and their value as predictors of the spinal condition were evaluated by simple and multiple regression analyses.

#### Results

Both the bone and muscle indicators correlated negatively with the curvature of the spine (Fig.1). The vBMC (of the total or cortical, better than the trabecular bone) and vBMD (of the trabecular, better than the total or cortical bone), rather than the cross-sectional bone areas, ranked among the most reliable tomographic indicators of the spinal condition.

The two best predictors were the vBMD of the central core of trabecular bone and the total vBMC of the vertebral body (partial r=0.749 and 0.693, respectively). An independent influence of each of these two factors on the spinal curvature could not be ruled out.

Neglecting the bone variables, the total or dorsal FFMA (rather than the ventral FFMA or any of the "whole" MA determinations) were the best significant predictors of the spine curvature (partial r=0.600 and 0.590, respectively).

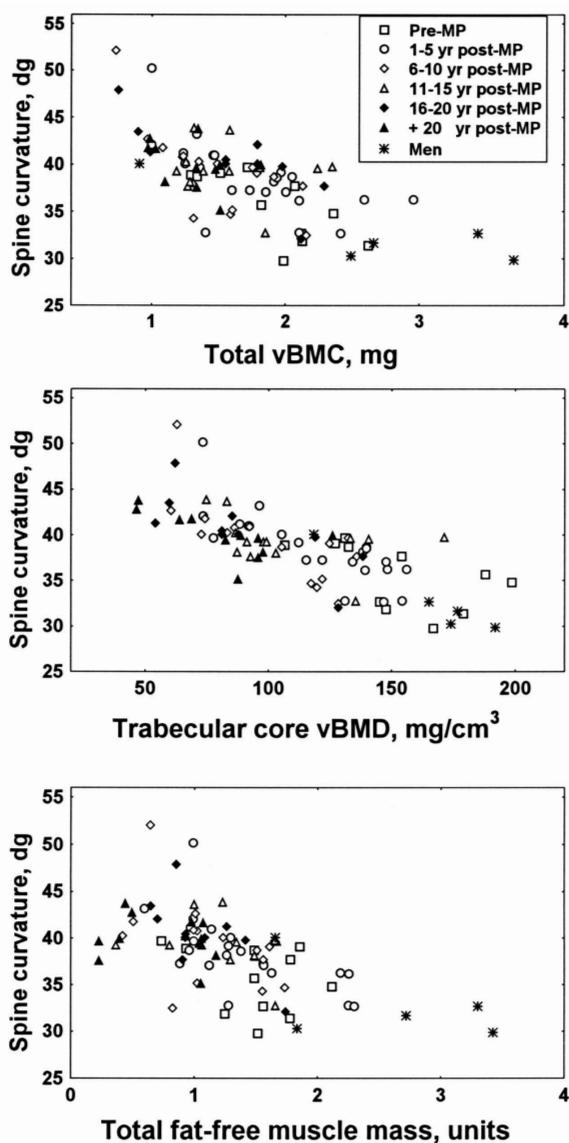


Figure 1.

Accordingly, the dorsal FFMA was also the best predictor of every tomographic indicator of bone health, especially of the vBMD of the trabecular core and the total vBMC (Fig.2; multiple  $r=0.675$  and  $0.656$ , respectively, for the dorsal FFMA).

Successive distribution zones of the data from individuals of increasing ranges of age in the correlation graphs between bone/bone or muscle/bone variables were observed.

However, multiple regression analyses ruled out any significant independent influence of the age or the time since menopause, as well as of the body weight or height on those associations (partial  $r$  below  $0.170$  in every case).

The only exception was a weak, significant correlation between the time since menopause and the vBMD of the central cores (partial  $r = 0.363$ ). The expression of the bone variables as z-scores failed to improve any of the above correlations. The data from the reference men group respected the same associations shown by those of the studied women in all instances.

## Discussion

This study affords additional evidence to the above references concerning the direct, significant impact of the regional muscle strength on the determination of the tomographic indicators of bone mechanical quality, and their indirect repercussion on the skeletal condition (curvature of the spine) in the studied sample, in a region that is being scarcely investigated in this regard.

These findings contrast with the scarce (if any) independent influence of the age, time since menopause, or

body habitus on either the bone or skeletal indicators studied. The demonstration of a higher determining power of the FFMA than that of the MA on the bone mass or mechanical ability or on the skeletal condition should reflect a significant independence of the muscle influences on bone over the obvious, genetically-determined allometric relationships.

According to this interpretation, the peak strains derived from the contractions of the regional muscles, rather than any anthropometric factor or the gender, age or time since menopause by themselves, should be first-order determinants of the biomechanical ability of bone structure, as long as no significant disturbances come from the endocrine-metabolic environment<sup>8</sup>.

## General inferences

The bulk of the referred evidences suggest:

- that the human male and female skeletons do not differ significantly from the biomechanical point of view, as we have previously proposed<sup>1,6</sup>, and
- that the tomographic (and densitometric) data of bone variables should be adjusted to suitable muscle mass (or strength) indicators instead to be referred to gender, age, or body habitus, or expressed as z-scores or similar indices, before applying them to the diagnosis of either an osteopenia (the only bone condition that can be defined by DXA) or an osteoporosis (a disease that could only be defined if other, complementary technologies as those employed in these studies allow measuring some relevant indicator(s) of bone mechanical quality)<sup>8</sup>.

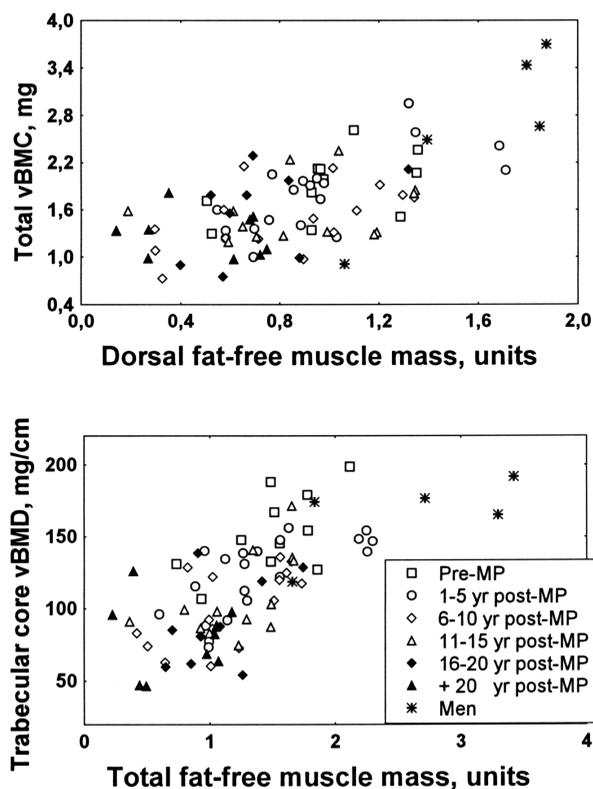


Figure 2.

## References

- Ferretti JL, Capozza RF, Cointry GR, Garcia SL, Plotkin H, Alvarez F. ML, Zanchetta JR. Gender-related differences in the relationships between densitometric values of whole-body bone mineral content and lean mass in humans between 2 and 87 years of age. *Bone* 1998; 22:683-690.
- Frost HM, Ferretti JL, Jee WSS. Some roles of mechanical usage, muscle strength, and the mechanostat in skeletal physiology, disease, and research. *Calcif Tissue Int* 62:1-7,1998.
- Ferretti JL, Zanchetta JR, Capozza RF, Cointry GR, Braun M, Schneider P, Reiners C. The premenopausal accumulation of bone material per unit muscle mass in women would be of little mechanical relevance. *Osteoporosis Int* 1998; 8(S3):83.
- Ferretti JL. Biomechanical properties of bone. In: *Bone Densitometry and Osteoporosis*. Genant HK, Jergas M, Guglielmi G (eds), pp.143-161. Springer Verlag, Berlin, 1998.
- Ferretti JL. Noninvasive assessment of bone architecture and biomechanical properties in animals and humans employing pQCT technology. *J Jap Soc Bone*

- Morphom 1997; 7:115-125.
6. Schiessl H, Tysarczyk-Niemeyer G, Willnecker J, Ferretti JL. Despite a different bone mineral storage per unit muscle mass, the determination of radial bone quality by forearm muscle strength follows the same relationship in men and women at any age. *Osteoporosis Int* 1998; 8(S3):157.
  7. Ferretti JL, Roldan EJA, Capozza RF, Cointy GR, Pasqualini T, Capiglioni R. Muscle / bone interrelationships in the human leg. A pQCT study. *Bone* 1998; 25(5S):S510.
  8. Ferretti JL, Schiessl H, Frost HM. On new opportunities for absorptiometry. *J Clin Densitom* 1998; 1:41-53.