

Introduction

Osteoporosis is defined as "a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture." (1) A major determinant of bone strength is bone microarchitecture. Examining the architecture has been shown to improve the prediction of structural vertebral strength beyond QCT-based bone density (2). Currently, the clinical gold-standard to assess trabecular architecture and the effectiveness of osteoporosis therapy is pathologic analysis of iliac crest biopsies. Decreased bone microarchitecture is also associated with an increase in severity of vertebral fractures in women (3). However, the procedure to obtain the biopsy is invasive and cannot be used for routine screening analysis. Noninvasive high resolution scans (μ CT) of the distal radius (or other relevant bones) may prove useful in routine assessment of trabecular architecture. This imaging would allow for repeated analysis of the same region, which is impossible after iliac crest biopsy.

Since osteoporosis is a systemic disease, it might be assumed to have similar degenerative effects on microarchitecture across osseous sites. Architectural measurements from the appendicular skeleton, such as the distal radius, which are more easily obtained in vivo, could then be used as surrogate markers of axial skeletal architecture. This could potentially lead to a more cost effective and less invasive way to screen patients who may be at risk for osteoporotic fractures. Though it has been shown that vertebral architecture is a good measure of vertebral strength, there have been no studies evaluating the distal radius or other appendicular sites as predictors of vertebral strength. Additionally it is widely assumed, but to our knowledge not tested, that the prevalence of vertebral fractures correlate negatively with vertebral strength.

Aim

The hypotheses tested include: 1) the presence of vertebral fractures will correlate negatively with vertebral strength and 2) the microarchitecture of the distal radius and vertebral bodies will correlate with vertebral strength.

Method

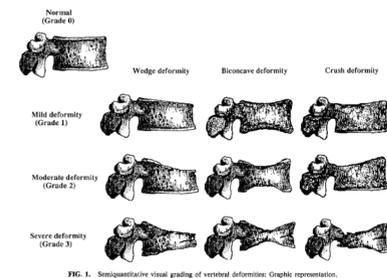
Subjects: Fourteen cadavers donated for medical science research were studied, after formalin fixation. Lumbar vertebrae were dissected in each cadaver and used in image analysis and strength testing.

QCT analysis: Whole body dual energy multi detector CT's were performed with multiplanar reconstruction and were analyzed for bone mineral density (BMD) and determination of fracture prevalence. Vertebral fractures were graded using the Genant Method (4, 5). A spinal Deformity Index (SDI) was calculated as a sum of the Genant scores for each vertebra.

Genant Score:

- 1 = 20-25 % reduction in any height and 10-20% decrease in area
- 2 = 25-40 % reduction in any height and 20-40% decrease in area
- 3 = 40% or more reduction in any height and area

Method (Continued)



Anterior (a), middle (m), posterior (p) heights and the area for each vertebra (T9-L5) were measured on digitized films using J Image. The heights and areas were compared to mean population measurements (6) to determine their Genant score.

μ CT technique: All μ CT completed using Imtek μ CT. Sample Size was determined by the bore size of the Imtek μ CT system. The L2-L4 vertebrae and bilateral distal radii were analyzed with Scanco Medical μ CT. Structural analysis included the determination of bone volume fraction (BV/TV) and an array of architectural parameters including, connectivity density (Conn Dens), marrow star volume, and structure model index (SMI).

Destructive testing: The vertebrae were separated by cuts through the intervertebral discs thus producing flat, parallel, superior and inferior surfaces. The principal dimensions of the vertebrae were measured using a precision dial caliper (accurate to approximately 0.001 in.). Each vertebra was then subjected to compressive loading using an Instron A620 machine: Each specimen was placed between parallel plates and slowly compressed at 1/8 inch/min. until failure. "Failure" was taken to be the compressed state where the force needed to deform (shorten) the specimen decreased dramatically. The compressive force and the resulting specimen deformation were continuously recorded during the compression and the data were compiled and represented by a force-deformation graph. Using the force-deformation data, the graphical representation, and the geometric data the strength for each specimen was calculated.

Statistical Analysis: Statistical Analysis: Mixed effect models were used to compare strength measures and SDI. Mixed linear models with a random effect were used to assess relationships between strength measures and architectural measures, using a random effect to account for within subject correlation of repeated observations.

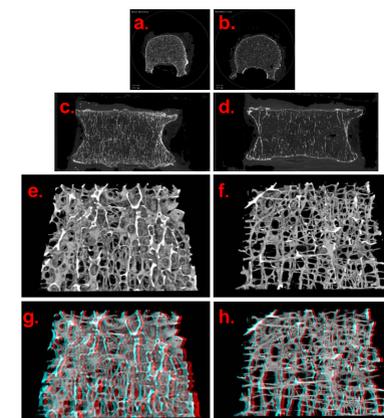
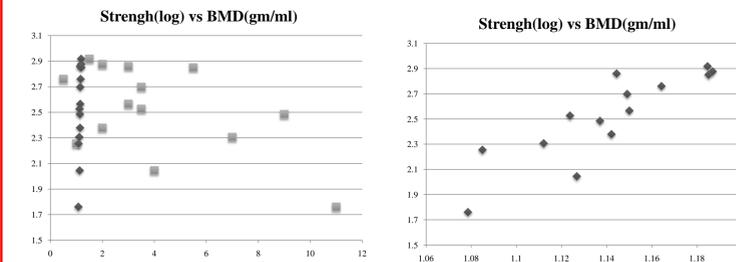
Results

Subjects has median (range) of age 78 (39, 98) years and female:male ratio of 10:4. Mean \pm Std of vertebral strength (log transformed) was $6.01 \pm .66$ for 11 subjects of mild fracture (SDI ≤ 7); higher than that of $5.03 \pm .87$ for the rest of 3 subjects with worse fracture. ($p=.05$). Vertebral strength and BMD shows + correlation ($r=.87$, $p<.001$). Correlations between vertebral strength (log transformed) and architectural parameters (both vertebral and radial) were summarized in table 1. A multivariate linear model showed the vertebral strength (log transformed) could be predicted by many radius architectural parameters and 90% of variability was explained by those predictors.

Results (Continued)

Table 1. Summary of Pearson correlation coefficient between Vertebral Strength (log transformed) and Architectural parameters at both vertebra and radius

Architectural parameters	Statistics *significant	@ Vertebrae	@ Radius
bone volume fraction(BV/TV)	pearson correlation coefficient r (p-value)	0.75*(0.002)	0.70*(0.005)
connectivity density (Conn.D)	pearson correlation coefficient r (p-value)	0.81*(0.001)	0.24(0.408)
structural model index (SMI)	pearson correlation coefficient r (p-value)	-0.65*(0.012)	-0.74*(0.003)
trabecular number (TbN)	pearson correlation coefficient r (p-value)	0.74*(0.003)	0.63*(0.015)
trabecular thickness (TbTh)	pearson correlation coefficient r (p-value)	-0.22(0.455)	0.67*(0.009)
trabecular separation (TbSp)	pearson correlation coefficient r (p-value)	-0.87*(<0.001)	-0.67*(0.009)
bone surface to volume (BS/BV)	pearson correlation coefficient r (p-value)	-0.18(0.548)	-0.71*(0.004)
degree of anisotropy (DA)	pearson correlation coefficient r (p-value)	0.27(0.356)	0.54*(0.048)
Marrow Star Volume	pearson correlation coefficient r (p-value)	-0.89*(<0.001)	-0.64*(0.014)



The images to the left were acquired by the mCT80 Scanner at P&G. Coronal 37mm sections (a,b); Sagittal 37 mm sections (c,d); vertebral reconstruction (e,f) and 3D vertebral reconstruction (g,h).

There appears to be a reduced density and thickness of the trabeculae in subject L as compared to Subject A. Subject L had the highest SDI (11) and the lowest bone density measurements (QCT).

Subject A
Strength =
239.31lb/in²

Subject L
Strength =
57.67 lb/in²

Conclusion

As hypothesized, there was a very moderate correlation between prevalent vertebral fractures and decreased vertebral strength. Both vertebral architecture and distal radius architecture are moderately good predictors of vertebral strength. Vertebral parameters have higher correlation with vertebral strength, while more radial parameters show correlation with vertebral strength. This suggests that microarchitecture across osseous sites show similar degenerative effects and that the distal radius may serve as a surrogate marker of vertebral strength, potentially leading to a more cost effective and less invasive way to screen patients who may be at risk for osteoporotic fractures. The findings also suggest that there is a high correlation between prevalent vertebral fractures and vertebral BMD just as is assumed in the literature. By completing whole body qCT scans of cadavers and then removing the vertebrae for strength testing, we were able to validate this long held assumption.

In conclusion, although various treatment options are becoming available, prevention is still the most important way to reduce the incidence of osteoporosis fractures. This study examined previous held assumptions with respect to analyzing fracture risk. More study is needed to further validate these results as a small sample size is a limitation of this study. More analysis on current sample needs to be done regarding age of cadavers to show if results are more relevant in respect to the age of cadaver.

References

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