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THE MECHANICAL CONSEQUENCE OF ACTUAL BONE LOSS AND SIMULATED BONE RECOVERY IN ACUTE SPINAL CORD INJURY

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Abstract

Introduction—Spinal cord injury (SCI) is characterized by rapid bone loss and an increased risk of fragility fracture around regions of the knee. Our purpose was to quantify changes in torsional stiffness K and strength T_{ult} at the proximal tibia due to actual bone loss and simulated bone recovery in acute SCI.

Methods—Computed tomography scans were acquired on ten subjects with acute SCI at serial time points separated by a mean of 3.9 months (range 3.0 to 4.8 months). Reductions in bone mineral were quantified and a validated subject-specific finite element modeling procedure was used to predict changes in K and T_{ult} . The modeling procedure was subsequently used to examine the effect of simulated hypothetical treatments, in which bone mineral of the proximal tibiae were restored to baseline levels, while all other parameters were held constant.

Results—During the acute period of SCI, subjects lost $8.3 \pm 4.9\%$ ($p < 0.001$) of their bone mineral density (BMD). Reductions in K ($-9.9 \pm 6.5\%$; $p = 0.002$) were similar in magnitude to reductions in BMD, however reductions in T_{ult} ($-15.8 \pm 13.8\%$; $p = 0.005$) were some 2 times greater than the reductions in BMD. Owing to structural changes in geometry and mineral distribution, T_{ult} was not necessarily recovered when bone mineral was restored to baseline, but was dependent upon the degree of bone loss prior to hypothetical treatments ($r = 0.719$; $p = 0.019$).

Conclusions—Therapeutic interventions to halt or attenuate bone loss associated with SCI should be implemented soon after injury in an attempt to preserve mechanical integrity and prevent fracture.

Keywords

Finite element method; Disuse osteoporosis; Bone strength; Bone fracture

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1. INTRODUCTION

Spinal cord injury (SCI) is associated with an abrupt disruption to the bone metabolic process whereby increased osteoclastic activity [1] leads to a rapid loss of bone mineral at sublesional regions [2]. Several mechanisms are responsible for this bone loss, but the removal of mechanical stimuli resulting from the loss of motor function and habitual ambulation is believed to be an important factor [3]. The clinical consequence of this bone loss is an increased rate of low-energy fracture [4–8] that is similar to the rate of fracture in post-menopausal osteoporotic women [9,10]. Although many individuals with SCI are non-ambulatory, these fractures are still a source of considerable morbidity, loss of independence, and increased medical costs [11].

The greatest magnitude of bone loss following SCI is observed around regions of the knee. Within the first 2 to 3 years of SCI, some 50% of the bone mineral is resorbed at the distal femur and proximal tibia [12,13]. Consequently, the distal femur and proximal tibia are the primary locations of fracture in the SCI population [14,15]. Falls from wheelchairs, wheelchair transfers, and rolling over in bed are commonly reported causes of fracture [4,11,16,17]. Torsional loading has been implicated as a principal mode of failure, as spiral fracture patterns are frequently observed around metaphyseal regions of the distal femur and proximal tibia [18,19].

Although the time course and magnitude of bone mineral loss following SCI have been well documented using both dual energy x-ray absorptiometry (DXA) [4,12,20,21] and peripheral quantitative computed tomography (pQCT) [13,22–24], the biomechanical relevance of this bone loss remains unclear. Bone fractures are ultimately biomechanical events, and data from subject-specific finite element models suggests that changes in bone mineral may have large mechanical consequences. For example, annual percent declines in proximal femoral fracture strength associated with aging are some two to three times greater than annual percent declines in bone mineral density [25].

Pharmaceutical treatment represents a potential therapeutic intervention to ameliorate bone loss and reduce fracture occurrence following SCI. In this regard, the acute stages of SCI (< 1yr) are presumably the most productive window for treatment. Indeed the greatest reductions in bone mineral are observed during the first year of SCI [12,13] and drug treatment has not been effective at reversing bone loss in individuals with chronic SCI [26]. In addition to the loss of bone mineral, SCI is associated with structural changes to the geometry and distribution of bone mineral [27,28]. These structural changes will influence mechanical integrity, therefore pharmaceutical treatments that reverse SCI related bone loss alone may not necessarily restore mechanical integrity back to baseline levels.

The purpose of this study was to quantify changes in torsional stiffness and strength of the proximal tibia due to 1) actual bone loss and 2) simulated bone recovery in acute SCI. To this end, a validated subject-specific finite element modeling procedure [29] was used to predict changes in stiffness and strength resulting from an acute period of SCI in ten individuals. The finite element modeling procedure was subsequently used to examine the effect of two different hypothetical treatments, in which bone mineral of the proximal tibiae were restored to baseline levels, while all other parameters were held constant.

2. MATERIAL AND METHODS

2.1 Subjects

Ten subjects with acute SCI were recruited for this study (Table 1). All subjects were older than 18 yrs, non-ambulatory at study entry with an ASIA Impairment Scale level of A, B, or

C, and medically stable in the opinion of their physiatrist. Pregnant females and patients with current or recent (within 12 months) use of drugs that affect bone metabolism (bisphosphonates, PTH, SERMs) were excluded from the study. Prior to participation, subjects provided written informed consent and the study was approved by the necessary institutional review boards.

2.2 Physical and simulated models

Voxel-based models of proximal tibiae from each subject were generated from computed tomography (CT) scans of the knee (Sensation 64 Cardiac, Siemens Medical Systems, Forchheim, Germany, 120 kV, 200 mAs, pixel resolution 0.352 mm, slice thickness 1 mm). The scan length captured the proximal most 15 cm of the tibia and all scans included a calibration phantom (QRM, Moehrendorf, Germany) to convert CT Hounsfield units to calcium hydroxyapatite equivalent density ρ_{ha} . Four models were generated for each subject – two physical (baseline and follow-up models) and two simulated (treatment 1 and treatment 2) models. Physical models were generated directly from CT scans collected at serial time points over an acute period of SCI. These models were used to quantify the mechanical consequence of actual bone loss. Simulated models were generated from follow-up scans and represented hypothetical treatments that restored bone mineral back to baseline levels. These models were used to quantify the mechanical consequence of simulated bone recovery.

2.2.1 Baseline models—Baseline CT scans were performed a mean 2.3 months (range 1.0 to 3.8 months) after SCI. The CT data were imported to Mimics (Materialise, Leuven, Belgium) where images were re-aligned so that the axial direction corresponded to the long axis of the tibia; the mediolateral axis was defined by a line passing through the medial and lateral condyles of the tibia and the anteroposterior axis was oriented orthogonally. Proximal tibiae were segmented from the aligned images using a ρ_{ha} threshold of 0.15 g/cm³ to identify the periosteal surface. The baseline models consisted of all voxels contained within the periosteal surface boundary.

2.2.2 Follow-up models—Follow-up CT scans were performed a mean 3.9 months (range 3.0 to 4.8 months) after baseline scans. The CT data were imported to Mimics and native follow-up images were rigidly registered to their respective aligned baseline images. The rotation matrices for the image registration were determined using ICP-FINITE, an iterative closest point registration algorithm for 3D point clouds available through Matlab Central File Exchange (URL: <http://www.mathworks.com/matlabcentral/fileexchange/24301-finite-iterative-closest-point>). Follow-up models were generated from the registered images using methods identical to those described for baseline models.

2.2.3 Treatment 1 models—The treatment 1 models simulated a hypothetical treatment, in which the ρ_{ha} of voxels of follow-up models were uniformly increased so that integral bone mineral content (BMC) was equal to that of their respective baseline models:

$$\rho_i^{T1} = \rho_i^F + \rho_i^F \left[\frac{BMC^B - BMC^F}{BMC^F} \right]$$

where ρ_i^{T1} is the ρ_{ha} of the i^{th} voxel for the treatment 1 model, ρ_i^F is the ρ_{ha} of the i^{th} voxel for the follow-up model, and BMC^B and BMC^F are the integral BMC for the baseline and follow-up models, respectively. Here, integral BMC was calculated as the total sum of all bone mineral within the periosteal surface boundary:

$$\text{BMC} = \sum_i \rho_i \cdot dV$$

where ρ_i is the ρ_{ha} of the i^{th} voxel and dV is the fixed voxel volume.

2.2.4 Treatment 2 models—The treatment 2 models represented a hypothetical treatment that more realistically simulated the manner by which bone remodeling takes place. Bone remodeling is accomplished by basic multicellular units acting on bone surfaces (e.g., trabecular surfaces, harversian canals, endosteal and periosteal surfaces). Thus, the potential for bone remodeling to occur in a given volume is dependent on the amount of available surface area, or surface area density (S_v). Martin [30] illustrated that bone S_v (mm^2/mm^3) is related to bone apparent density ρ_{app} (g/cm^3) by a 5th order polynomial:

$$S_v = 0.2 + 6.75\rho_{\text{app}} - 2.475\rho_{\text{app}}^2 - 2.25\rho_{\text{app}}^3 + 2.6875\rho_{\text{app}}^4 - 0.9\rho_{\text{app}}^5$$

where $\rho_{\text{app}} = \rho_{\text{ha}}/0.626$ [31]. The polynomial was used to develop a S_v weighting value (k) between 0 and 1 as a function of ρ_{ha} . This was done by normalizing the function to a maximum value of 1 and refitting the data to the range of ρ_{ha} observed in this study (-0.2 to $1.6 \text{ g}/\text{cm}^3$). Negative values of ρ_{ha} are representative of CT voxels comprised primarily of marrow fat [32]. The resulting polynomial for k was (Figure 1):

$$k = 0.3727 + 1.4406\rho_{\text{ha}} - 0.9673\rho_{\text{ha}}^2 - 0.1002\rho_{\text{ha}}^3 + 0.6149\rho_{\text{ha}}^4 - 0.3644\rho_{\text{ha}}^5.$$

For treatment 2 models, the ρ_{ha} of voxels of follow-up models were increased so that integral BMC was equal to that of their respective baseline models, but the amount of mineral apposition for each voxel was dependent on the available surface area for remodeling:

$$\rho_i^{\text{T2}} = \rho_i^{\text{F}} + k_i \cdot \rho_i^{\text{F}} \left[\frac{\text{BMC}^{\text{B}} - \text{BMC}^{\text{F}}}{\sum_i \rho_i^{\text{F}} \cdot dV \cdot k_i} \right]$$

where ρ_i^{T2} is the ρ_{ha} of the i^{th} voxel for the treatment 2 model.

2.3 Prediction of torsional stiffness and strength

Torsional stiffness and strength were predicted for each model using validated subject-specific finite element modeling procedures. Using cadaveric experimentation, the subsequent procedures were able to predict *in vitro* torsional stiffness and strength with an r^2 of 0.95 and 0.91, respectively; both displayed an X=Y type of relationship in which regression slopes and intercepts did not differ significantly from 1 and 0, respectively. For a detailed description of the modeling procedures and validation process the reader is referred to Edwards et al [29].

Briefly, CT images were resampled to isotropic voxels with a 1.5 mm edge length and voxels from segmented bones were directly converted to 8-node hexahedral elements for finite element model generation. The models consisted of a mean 63,791 (range 45,999 – 83,760) elements with a mean 71,658 (range 51,983 – 92,975) degrees of freedom,

depending on bone size. Elements were assigned inhomogeneous, anisotropic, and non-linear material properties based on apparent density ρ_{app} . The pre-yield elastic moduli in the axial direction E_3 was defined using a density-elasticity relationship specific to the proximal tibia [33]:

$$E_3 = 6570 \rho_{app}^{1.37}$$

where E_3 is expressed in MPa, and ρ_{app} is expressed in g/cm³. Anisotropy was assumed to be the same throughout with $E_1 = 0.574 \cdot E_3$, $E_2 = 0.577 \cdot E_3$, $G_{12} = 0.195 \cdot E_3$, $G_{23} = 0.265 \cdot E_3$, $G_{31} = 0.216 \cdot E_3$, $\nu_{12} = 0.427$, $\nu_{23} = 0.234$, and $\nu_{31} = 0.405$ [34]. Here, subscripts 1 and 2 denote the mediolateral and anteroposterior directions, respectively. The non-linear phase was modeled as bilinear elastic-plastic with a post-yield modulus equal to 5% of the pre-yield modulus [35]; yield was defined using Hill's conventional criterion for orthotropic materials. Yield strains were assumed to be isotropic in the normal (0.675%) and shear (1.215%) directions [36] and yield stresses were determined by multiplying yield strains by their respective normal (E_1 , E_2 , E_3) and shear (G_{12} , G_{23} , G_{31}) moduli.

Surface nodes of the proximal most 2 cm of bone were subjected to a torsional displacement and surface nodes distal to the proximal most 13 cm of bone were constrained in translation, i.e., 11 cm of bone was left "exposed". Torsional stiffness K was quantified from the linear portion of the torque-rotation curve and torsional strength T_{ult} was defined as the torque at which 10% of surface elements had failed (Figure 2). A value of 10% was chosen because it minimized the error between experimentally measured and finite element predicted T_{ult} [29]. A maximum principal strain greater than 1.41% was used to define element failure [36] (Figure 3).

2.4 Bone mineral assessment

Integral bone mineral density (BMD) and BMC were calculated for the proximal most 13 cm of bone, i.e., all bone proximal to the distal constraint. Trabecular and cortical BMD and BMC were also calculated, in which, trabecular bone was defined as all voxels having a $\rho_{ha} < 0.626$ g/cm³, and cortical bone was defined as all voxels having a $\rho_{ha} \geq 0.626$ g/cm³. This threshold of $\rho_{ha} = 0.626$ g/cm³ corresponded to a $\rho_{app} = 1.0$ g/cm³ [37].

2.5 Statistics

Statistical analyses were performed using SPSS software (Chicago, IL). Paired t-tests were used to examine differences in bone mineral (integral, trabecular, and cortical BMD and BMC) and mechanical behavior (finite element predicted K and T_{ult}) between baseline and follow-up models as well as baseline and treatment models. Changes in follow-up and treatment measures were calculated and expressed as a percent change relative to baseline. A one-way (4×1) repeated measures ANOVA was used to determine if percent changes in mechanical behavior (finite element predicted K and T_{ult}) were greater than percent changes in integral bone mineral (BMD and BMC) at follow-up. A significant F-statistic was followed by planned comparisons between finite element predicted K and integral bone mineral, as well as finite element predicted T_{ult} and integral bone mineral. Correlation analyses were used to examine potential relationships between percent changes in follow-up measures of bone mineral with percent changes in follow-up measures of mechanical behavior. To determine whether the magnitude of actual bone loss associated with acute SCI was related to the degree to which mechanical behavior was restored following simulated treatment, correlation analyses were used to compare percent changes in bone mineral at follow-up versus percent changes in mechanical behavior after simulated treatment. Again,

all percent changes were expressed relative to baseline. For all statistical tests the alpha level was set to 0.05.

3. RESULTS

Percent changes in bone mineral and mechanical behavior between baseline and follow-up models as well as baseline and treatment models are reported in Table 2. During the acute period of SCI, subjects lost a mean 8.3% of their integral BMD owing to a mean 9.7% decrease in trabecular BMC and a mean 8.0% decrease in cortical BMC. The observed reductions in bone mineral were associated with a mean 9.9% reduction in finite element predicted K and a mean 15.8% reduction in finite element predicted T_{ult} . A significant effect of outcome measure was observed for the repeated measures ANOVA comparing percent changes in mechanical behavior and integral bone mineral at follow-up ($p=0.009$). Specifically, percent changes in finite element predicted T_{ult} were significantly greater than percent changes in integral bone mineral ($p=0.047$), while no differences were observed between percent changes in finite element predicted K with percent changes in integral bone mineral ($p=0.215$). Treatment 1 was associated with a significant decrease in trabecular BMD ($p=0.035$) and trabecular BMC ($p=0.029$), and a significant increase in cortical BMD ($p=0.011$) and cortical BMC ($p=0.030$). In contrast, trabecular and cortical bone mineral parameters after treatment 2 were not significantly different from baseline ($p=0.295$). Despite these discrepancies in bone mineral, finite element predicted K and T_{ult} were not significantly different from baseline for either treatment ($p=0.159$).

Table 3 displays correlations between percent changes in follow-up measures of bone mineral with percent changes in follow-up and treatment measures of mechanical behavior. Percent changes in finite element predicted K at follow-up were positively correlated with percent changes in integral BMD ($p=0.004$), integral BMC ($p=0.003$), and cortical BMC ($p=0.008$) at follow-up. Percent changes in finite element predicted T_{ult} at follow-up were positively correlated with percent changes in integral BMD ($p<0.001$), integral BMC ($p<0.001$), trabecular BMD ($p=0.012$), and trabecular BMC ($p=0.016$) at follow-up. Percent changes in finite element predicted K after treatment 1 illustrated inverse correlations with actual percent changes in trabecular BMD ($p=0.032$) and trabecular BMC ($p=0.028$) indicating that individuals with the greatest losses in trabecular bone mineral had the greatest improvements in K after treatment 1. Both simulated treatments illustrated positive correlations between percent changes in finite element predicted K and percent changes in cortical BMD ($p=0.011$). Additionally, both treatments illustrated positive correlations between percent changes in finite element predicted T_{ult} and percent changes in integral BMD ($p=0.019$) and integral BMC ($p=0.018$). In other words the more bone mineral an individual lost by follow-up, the less effective the simulated treatment was at restoring T_{ult} back to baseline (Figure 4).

4. DISCUSSION

Bone loss following SCI is rapid and profound. The mechanical consequence of this bone loss remains unclear, as does the potential for pharmaceutical treatment to reverse these mechanical changes. To investigate these issues, a validated subject-specific finite element modeling procedure was used to quantify changes in torsional stiffness and strength of the proximal tibia after an acute period of SCI. Hypothetical treatments were then simulated to determine if changes to torsional stiffness and strength after acute SCI could be reversed if bone mineral, but not necessarily bone structure, was restored back to baseline levels.

The findings from this study suggest that changes to bone mineral associated with acute SCI can have large mechanical consequences. Although percent reductions in torsional stiffness K (9.9%) were not significantly different than percent reductions in integral BMD (8.3%),

percent reductions in torsional strength T_{ult} (15.8%) were some 2 times greater than the observed reductions in integral BMD. This discrepancy, between reductions in finite element predicted K and T_{ult} , can be explained by a more rapid initiation and progression of element failure at follow-up that was disproportionate to the observed reductions in stiffness (Figure 5). In other words, SCI-related bone loss had a larger influence on post-yield rather than pre-yield mechanical behavior of the finite element models. It remains unclear if similar reductions in strength after acute SCI would be observed under different modes of loading (e.g., compression or bending) or at other skeletal sites below the neurological lesion (e.g., the proximal or distal femur). However, in a recent study of individuals with acute SCI our group has illustrated similar relative changes in quantitative CT measured strength indices at regional locations of the distal femur and proximal tibia for both compressive and torsional modes of loading [38]. Additionally, bone loss after SCI is largely due to mechanical unloading, and data from human spaceflight has illustrated comparable reductions in finite element predicted fracture strength at the proximal femur. For example, 4–6 month missions aboard the International Space Station were associated with relative reductions in proximal femur strength that were approximately 2 times greater than relative reductions in DXA assessed BMD [39].

Although paired comparisons suggested that proximal tibia mechanical behavior after acute SCI can be reversed if bone mineral is restored back to baseline levels, we caution that this may be an overgeneralization. Substantial scatter in the mechanical behavior after treatment was observed between subjects, and correlation analyses suggested that this scatter was, in part, due to the degree of bone loss prior to treatment. Figure 4 illustrates that the more bone mineral an individual lost by follow-up, the less mechanical integrity he/she recovered following treatment ($r=0.726$). In theory, this is because simply restoring bone mineral content back to baseline did not necessarily lead to mineral accrual at the most “mechanically important” locations, and this limitation appears to be exacerbated proportionally to the degree of bone loss. Variability in the degree of bone loss observed herein may be related to the heterogeneity of our sample population in terms of sex, age, injury level and severity. Unfortunately, this assumption cannot be verified statistically owing to the relatively small sample size of this study.

The two distinct hypothetical treatments used to restore bone mineral back to baseline levels provide some insight into the mechanisms by which bone mineral is resorbed after SCI. Whereas the increase in ρ_{ha} for treatment 1 was uniform across the proximal tibia, the increase in ρ_{ha} for treatment 2 was dependent on the available surface area for remodeling. In contrast to the treatment 1 simulation, trabecular and cortical BMD and BMC after the treatment 2 simulation were not significantly different from their respective baseline levels. These data, therefore, suggest that the bone remodeling response after SCI is dependent to some degree on surface area density. Indeed, peripheral QCT studies of disuse from bedrest and SCI have observed the greatest declines in bone mineral at anatomic regions expressing the largest surface area for remodeling [24,40].

Inclusion of subjects within the first few months after SCI was a strength of this study. Although this limited us to a relatively small number of subjects, it allowed us to quantify actual bone loss during the acute periods of SCI when the rate of bone loss is most pronounced [12,13]. The use of subject-specific finite element modeling procedures allowed us to translate the observed changes in bone mineral to changes in mechanical behavior at a clinically relevant location of fracture. But perhaps the greatest limitation of our clinical CT-based modeling procedure is our inability to account for any microstructural changes to bone that may occur with disuse [28,41] or treatment [42]; for example changes in trabecular architecture, tissue-level mineralization, and remodeling space. Previous studies have investigated the influence of simulated changes in trabecular architecture on localized

changes in stiffness and strength [43,44]. These studies have indicated that loss of trabecular connectivity is much more detrimental to mechanical integrity than trabecular thinning, and that restoring bone mineral following connectively loss does not fully recover mechanical integrity. As anisotropy was held constant in the present study, our follow-up and treatment models more closely represented changes to trabecular thickness rather than trabecular connectivity. This would likely mean that the changes in torsional stiffness and strength observed herein were conservative. On the other hand, the response of whole bone mechanical integrity to disuse and treatment appears to be much more influenced by cortical thinning than trabecular architecture, at least when cortical thinning takes place through periosteal resorption [45]. Changes in cortical bone are explicitly captured within our models, however, it is important to note that cortical bone loss following SCI occurs through endosteal resorption with little to no loss at the periosteal surface [38]. Lastly, it should be noted that our simulated treatments of bone mineral recovery do not reflect the effect of any existing drugs or therapies of which we are currently aware. Rather, these simulations were meant only to illustrate the potential limitations of favorable hypothetical treatment scenarios. Although no direct clinical recommendations can be made on the basis of our simulated treatments, the data suggest that therapies to preserve bone strength after SCI may be more effective if initiated before substantial bone loss has occurred.

In summary, individuals with acute SCI experience a rapid loss of bone mineral at the proximal tibia. This bone loss had large mechanical consequences, with percent reductions in torsional strength being twofold greater than percent reductions in bone mineral. Owing to structural changes in geometry and mineral distribution, torsional strength was not necessarily recovered when bone mineral was fully restored, especially when the magnitude of bone loss prior to treatment was large. Thus, it is imperative that therapeutic interventions to halt or attenuate bone loss associated with SCI are provided early in an attempt to prevent future fracture. The most effective interventions may be those targeting “mechanically important” skeletal regions, perhaps through combined drug and mechanical loading therapy.

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HIGHLIGHTS

- Changes to bone mineral and strength were assessed after spinal cord injury (SCI)
- 4 months of acute SCI was associated with an 8% reduction in proximal tibia volumetric BMD
- Reductions in strength were twofold greater than reductions in volumetric BMD
- Simulating bone mineral recovery did not necessarily restore strength to baseline levels

Figure 1.
The surface-area-density weighting value k as a function of ρ_{ha} .

Figure 2. Finite element predicted torque-rotation behavior for a representative subject. The point of predicted fracture is labeled with a black dot.

Figure 3.

Finite element models for a representative subject illustrating the distribution of maximum principal strain at 100 Nm. For this subject, a torque of 100 Nm corresponded to the predicted T_{ult} at follow-up (i.e., the torque at which 10% of the surface elements had failed, $\epsilon_{max} > 1.41\%$).

Figure 4.
The relationship between percent changes in finite element predicted T_{ult} after treatment 2 with percent changes in integral BMC at follow-up.

Figure 5. Initiation and progression of surface element failure as a function of applied torque for a representative subject. Note the more rapid initiation and progression of element failure at follow-up relative to baseline and treatments (see insert).

Table 1

Subject characteristics and time post-SCI at baseline and follow-up scans.

Subject	Sex	SCI level	ASIA	Age	Months post-SCI at baseline	Months post-SCI at follow-up	Months between scans
1	F	C6	B	21	1.5	4.7	3.2
2	F	C5-6	C	64	1.0	4.9	3.9
3	M	T11	B	44	2.9	6.1	3.2
4	F	T4-T5	B	21	1.4	4.4	3.0
5	M	C4	A	22	3.0	7.7	4.7
6	M	C5-6	B	25	1.7	6.4	4.7
7	M	C4-5	A	24	2.2	7.0	4.8
8	M	C7	B	19	3.8	6.8	3.0
9	M	C5	A	27	3.1	7.7	4.7
10	F	T5	A	25	2.7	6.2	3.5

Table 2

Mean (SD) baseline measures in physical units and percent changes in follow-up and treatment measures relative to baseline.

Parameter	Baseline	Follow-up (%)	Treatment 1 (%)	Treatment 2 (%)
Integral BMD (g/cm ³)	0.34 (0.04)	−8.3 (4.9)*	0.7 (0.3)*	0.7 (0.3)*
Integral BMC (g)	70.06 (18.12)	−8.9 (5.0)*	0.0 (0.0)	0.0 (0.0)
Trabecular BMD (g/cm ³)	0.20 (0.03)	−10.3 (9.2)†	−6.0 (7.8)‡	0.6 (4.8)
Trabecular BMC (g)	33.98 (9.57)	−9.7 (9.2)‡	−7.2 (8.2)‡	−2.9 (8.6)
Cortical BMD (g/cm ³)	1.01 (0.04)	−1.1 (2.2)	5.0 (4.8)‡	0.6 (2.5)
Cortical BMC (g)	36.07 (9.49)	−8.0 (5.3)*	7.0 (7.3)‡	0.4 (4.6)
K (Nm/deg)	50.25 (20.15)	−9.9 (6.5)†	2.2 (4.7)	−0.2 (3.4)
T _{ult} (Nm)	210.15 (74.40)	−15.8 (13.8)†	−5.0 (10.0)	−2.4 (4.7)

Paired t-test significantly different from baseline indicated by *(p < 0.001), †(p < 0.01) and ‡(p < 0.05).

Table 3

Correlations between percent changes in follow-up measures of bone mineral with percent changes in follow-up and treatment measures of mechanical behavior. All percent changes were expressed relative to baseline.

	Relative change at Follow-up			Relative change at Treatment 1			Relative change at Treatment 2		
	K	Tult		K	Tult		K	Tult	
Integral BMD	0.822†	0.914*		-0.351	0.760‡		-0.155	0.719‡	
Integral BMC	0.832†	0.917*		-0.336	0.763†		-0.143	0.726‡	
Trabecular BMD	0.494	0.752‡		-0.677‡	0.610		-0.540	0.496	
Trabecular BMC	0.460	0.731‡		-0.687‡	0.598		-0.563	0.476	
Cortical BMD	0.527	0.176		0.760‡	0.202		0.867*	0.374	
Cortical BMC	0.781†	0.506		0.447	0.426		0.601	0.546	

Significant correlations with percent changes in bone mineral at follow-up indicated by * (p 0.001), † (p 0.01), and ‡ (p<0.05).