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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 ± 4.9% ($p < 0.001$) of their bone mineral density (BMD). Reductions in K (−9.9 ± 6.5%; $p = 0.002$) were similar in magnitude to reductions in BMD, however reductions in T_{ult} (−15.8 ± 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 ($r \geq 0.719$; $p \leq 0.019$).
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.

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 (<1 year) 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]

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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 was restored to baseline levels, while all other parameters were held constant.

Material and methods

Subjects

Ten subjects with acute SCI were recruited for this study (Table 1). All subjects were older than 18 years, 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.

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.

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 anterioposterior axis was oriented orthogonally. Proximal tibiae were segmented from the aligned images using a ρ_{ha} threshold of 0.15 g/cm^3 to identify the periosteal surface. The baseline models consisted of all voxels contained within the periosteal surface boundary.

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.

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 ith voxel for the treatment 1 model, ρ_i^F is the ρ_{ha} of the ith 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:

$$BMC = \sum_i \rho_i \cdot dV$$

where ρ_i is the ρ_{ha} of the ith voxel and dV is the fixed voxel volume.

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, Haversian 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:

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

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