Neurology Section

Online Journal Club-Article Review

Background/Overview	
Article Citation	Dudley-Javoroski, S., P.K. Saha, G. Liang, C. Li, Z. Gao, and R.K. Shields. "High Dose Compressive Loads Attenuate Bone Mineral Loss in Humans with Spinal Cord Injury." *Osteoporosis International* 23 (2012): 2335-346.
Study Objective/Purpose (hypothesis)	The purpose of this study is to compare three doses of bone compressive loads at the distal femur in individuals with complete SCI who receive a novel stand training intervention.
Brief Background (why issue is important; summary of previous literature)	In paralyzed extremities, the absence of muscular contractions deprives the skeletal system of critical stress necessary for bone health. As much as 50% of bone mineral may be lost at certain anatomic sites within the first 4 years post injury. The severe osteoporosis that develops rapidly in people with SCI increases their risk for fracture during routine daily activities. A method to prevent the deterioration of the musculoskeletal system is essential to improve the health of people with SCI. The loss of mechanical stimuli to bone is considered to be a big contributor to bone mineral density (BMD) decline. A body of animal research has demonstrated the adaptive capacity of bone in response to mechanical loading. The recent literature on muscle stimulation protocols to attenuate post – SCI BMD decline in humans has not been straightforward. Mechanical loads delivered to the skeletal system during these studies were not estimated and may have been insufficient to exceed bone's hypothesized remodeling threshold.
Methods	
Study Design (type of trial, randomization, blinding, controls, study groups, length of study, follow-up)	Participants underwent bone mineral density (BMD) assessment between one and six times over a 3-year training protocol. The study was conducted as a mixed cross-sectional and longitudinal design. SCI individuals 1–7 performed unilateral quadriceps stimulation in supported stance ("High Dose" loading) with the knee in 20 degrees of flexion. A second group of five individuals with SCI stood in a standing frame or a standing wheelchair without applying quadriceps electrical stimulation. A final group of 15 individuals with SCI served as a non-training group. To facilitate longitudinal comparisons among cohorts, the study partitioned the dataset into seven time bins based on time post-SCI: 0–0.25 years, 0.25–0.50 years, 0.50–0.75 years, 0.75–1 year, 1–1.5 years, 1.5–2 years, and >2 years.
Target Population (dx, acuity,	

inclusion/exclusion critieria)	28 individuals with motor complete (ASI- A and B) SCI. 14 individuals without a SCI served as a normative control condition. Exclusion criteria were a history of bone pathology (i.e., bone metabolic disease, cancer, etc.), thyroid disorder, previous fracture at the scan sites, pregnancy, and medications known to affect bone metabolism.
Interventions (if applicable): (specificity of interventions, ability to replicate, frequency, duration)	Quadriceps loading protocol SCI individuals 1–7 performed unilateral quadriceps stimulation in supported stance ("High Dose" loading) with the knee in 20 degrees of flexion. During initial visits to the laboratory, the participants developed tolerance for standing in a standing frame under the supervision of a physical therapist. The standing frame incorporated padded plates positioned against the anterior surface of the individual's knees. Velcro straps secured the knees against the plates. A force transducer mounted in series with one plate measured the isometric knee extension force during unilateral quadriceps activation. The experiment was controlled by custom-designed software. The microcomputer output was conveyed via shielded cabling to a muscle stimulator unit. The researchers delivered 60 100-pulse trains to the quadriceps via reusable carbon adhesive electrodes. Each train was followed by 5 minutes of rest, yielding a 1:1 work/rest ratio. Participants performed two stimulation bouts separated by 5 min of rest during each training session. Passive standing protocol A second group of five individuals with SCI stood in a standing frame or a standing wheelchair without applying quadriceps electrical stimulation (Table 1, "Low Dose" loading cohort). We previously determined that modeled femur compressive loads during passive stance approximate 40% of body weight (% BW) (Fig. 1) [25]. Participants were requested to stand for 30 min on five calendar days per week. These individuals logged their training participation in notebooks. In the High Dose group, the limb that did not receive electrical stimulation did perform passive stance during training sessions. Data from the untrained limbs of High Dose participants were therefore added to the Low Dose group. Untrained subjects A final group of 15 individuals with SCI served as a non-training group. These individuals performed no standing or electrical stimulation and underwent bone density assessment between one and three times.
Outcome Measures (relevant to purpose of	

the study; reliable, valid, clinical utility)	Bone mineral density deterioration after the 3 year study.
Statistical Analysis (statistics used, appropriate application)	Quadriceps force and fatigue index and modeled femur compressive loads for the High Dose group were each analyzed using a one-way analysis of variance (ANOVA) across the seven time bins. Pairwise multiple comparisons were used when indicated. Significance was set to alpha <0.05. The study also used a two-way (group x time) ANOVA to compare BMD differences among the High Dose, Low Dose, and Untrained groups at these two time points. Pairwise multiple comparisons were used when indicated. Significance was set to alpha <0.05. The statistics used are appropriate.
Results	
Enrollment/Subject Characteristics (sample size, gender, age, functional level; were groups similar on important variables prior to application of the intervention)	Ages range from 16-64 years old, with a mix of males and females. The level of injuries were reported and ranged from C5/6 through T12. Group dynamics in addition to these characteristics were not discussed.
Summary of Primary and Secondary Outcomes (include aggregate and sub-group findings if reported); note results that were statistically significant; How many reached a level of clinical significance (exceed MCID if known); Was there retention of changes following intervention (if studied)	High Dose group significantly exceeding BMD for both the Low Dose and the Untrained groups (p =0.003 and p =0.019). No significant difference existed between the Low Dose and Untrained groups (p =0.353), indicating that BMD for individuals performing passive stance did not differ from individuals who performed no standing. Retention of changes would need to be further studied.
Authors' Discussion and Conclusions	
Brief Summary of Authors' Main Discussion Points; Authors' Conclusion	Quadriceps loading during stance yielded significantly higher BMD over 3 years of training than the lower dose levels. No significant differences emerged between passive standing (Low Dose) and no standing activity. The results of this study confirm that muscular loads in stance offer a bone-sparing stimulus to the distal femur, a common fracture site after SCI. Study participants in the High Dose group showed rapid adaptations in quadriceps physiology during training. Quadriceps force doubled between 0.25 and 0.5 year due to a combination of training adaptations and gradual intensification of stimulus intensity as the participants acclimated to the protocol. Quadriceps fatigue index showed a

	similar trend, with the greatest gains in the first 6 months of training. The results of the present study support that post-SCI BMD decline can be attenuated with routine application of mechanical loads that meet certain dose criteria (150% BW compressive load). We have previously noted that BMD varies from distal to proximal in the tibia and femur distal epiphyses, and that adaptations to mechanical loading may occur in asymmetric patterns. The extensive BMD-sparing effect of the High Dose load at the femur was less apparent at more distal skeletal sites. **Conclusion**: Over 3 years of training, a high dose of compressive load (150% BW) administered via quadriceps activation in stance significantly attenuated BMD decline at the distal femur when compared to a low dose of load (passive standing) or no loading (no standing) in subjects with SCI. High-resolution CT imaging supports that the high dose compressive load training attenuated trabecular architecture deterioration and that training adaptations occurred in the tibia of the trained limb.
Reviewer's Discussion and Conclusion	
Study Strengths	This study's detailed calculation for proper application of doses creates a high internal validity. The methods are very detailed and could be replicated if researchers were able to attain the proper computer and stander equipment.
Study Limitations and Potential for Bias	Sample sizes were small. To ensure that bone adaptations to various doses of stress are detected, further work with high-resolution imaging is necessary to identify the locations that are most sensitive to change across time. In this study, the quadriceps muscle was activated, which generated the primary stress through the distal femur during stance. Because sites throughout the lower extremity are at risk for fracture, more research with alternative methods (including additional muscles being activated) are necessary before active stance becomes a routine comprehensive method to attenuate bone loss in people with SCI.
Applicability: • Types of patients (dx) that results apply to • Types of settings or patient acuity that the results apply to • Can interventions be reproduced? Can results be applied to other pt. populations?	The results of this study apply to individuals with motor complete (AIS-A and B) spinal cord injury. A setting that is equipped with the computer technology and proper technicians to operate the proper dosages. Further studies would need to be done in order to apply the results of this study to other populations outside of the diagnoses discussed above.

How will study results impact PT management of this patient population?; List suggestions for how to implement changes in your clinic/department to integrate study findings into patient care	This study impacts PT management of the specified patient population due to the evidence that as therapists we need to do more than simply get the patients into a weight bearing position. The study suggests that muscle contractions are also needed to ensure a better chance of slowing the progression of losing BMD in the lower extremities.