INTERNATIONAL SPINAL CORD INJURY

FRACTURE HISTORY EXTENDED DATA SET (Version 1.0)

The working-group consists of:

Leslie R. Morse (US), leslie.morse@ucdenver.edu, chair, William A. Bauman (US), william.bauman@va.gov; Cathy Craven (Canada), Cathy.Craven@uhn.ca; Angela Frotzler (Switzerland), angela.frotzler@paraplegie.ch; William Leslie (Canada), BLESLIE@sbgh.mb.ca; Thomas J Schnitzer (US), tjs@northwestern.edu; Karen Troy (US), ktroy@WPI.EDU; Ekaterina Zivanovic e_zivanovic@yahoo.com; and Fin Biering-Sørensen (Denmark), Fin.Biering-Soerensen@regionh.dk, chair of the International Spinal Cord Injury Data Sets committee under the International Spinal Cord Society (ISCoS) Scientific Committee.

Introduction

The purpose of the International Spinal Cord Injury (SCI) Fracture Extended Data Set is to standardize the collection and reporting of information on osteoporotic fractures in accordance with the purpose and vision of the International SCI Data Sets [1]. In the general population, the World Health Organization (WHO) criteria are used clinically to diagnose osteoporosis based on bone density in men over the age of 50 and postmenopausal women. The WHO Fracture Risk Assessment Tool (FRAX) estimates 10-year fracture risk based on bone density at the femoral neck and clinical risk factors [2]. However, information is not available in persons with SCI on fracture risk based on WHO bone density categories, or any other classification system for the prediction of fracture. Of note, the distal femoral metaphysis and proximal tibial metaphysis are not included in standard clinical DXA scans, and there are no T-scores yet available for these skeletal sites. As a result, there are no guidelines for fracture risk prediction based on bone density in the SCI population. This void in the prediction of fractures in persons with SCI limits clinical care because there are no standards for the diagnosis of osteoporosis or for initiation of medications to treat osteoporosis to prevent fractures. Other than severe immobilization, little is known concerning other potentially relevant clinical risk factors for the prediction of fracture in persons with SCI, or the association between incident fracture and bone density at SCI-relevant skeletal sites, or the possible relationship of fractures to metabolic bone markers. The data that are proposed to be collected in this data set should begin to provide meaningful information necessary to develop specific algorithms to predict risk of fracture in persons with SCI, which can be applied to identify those who are at greatest risk of fracture, and to provide an evidence-based approach to rehabilitation strategies to avoid fracture.

This data set is for the clinician and researcher in the assessment of prevalent and incident fractures, as well as factors (ambulatory status, medication use, putative osteogenic therapies, health habits, and medical comorbidities) that may be associated with fracture risk. This Extended Data Set expands upon factors assessed in the International SCI Endocrine and Metabolic Extended Data Set and includes additional imaging variables (quantitative computed tomography and soft tissue body composition by dual energy x-ray absorptiometry) for standardization of research protocols.

The information collected in this International SCI Fracture Extended Data Set will generally be used in connection with data in the International SCI Core Data Set [3], which includes information on date of birth and injury, gender, the cause of spinal cord lesion, associated injuries, and neurologic status. It will also be used together with the International SCI Endocrine and Metabolic Extended Data Set that includes calcium metabolism and dual energy x-ray absorptiometry (Bauman, et al., In Press). It is recommended that medical comorbidities be recorded using the following International SCI Basic Data Sets: Endocrine and Metabolic [4, 5], Cardiovascular Function [6], Pulmonary Function [7], and Musculoskeletal [8]. It is recommended that mobility be assessed using the Spinal Cord Independence Measure (SCIM) mobility tool [9-11]. In addition, this Data Set may be used together with other relevant International SCI Basic or Extended Data Sets, when appropriate and relevant.

The etiology of a spinal cord lesion may be traumatic or non-traumatic. All lesions to the spinal cord, conus medullaris, and cauda equina are included in the present context.

This document was produced under the auspices and approved by ISCoS and the American Spinal Injury Association (ASIA), and in cooperation with the International Society for Clinical Densitometry (ISCD).

Acknowledgements: Comments and suggestions were provided by Susan Charlifue and Lawrence Vogel, Thomas Bryce, and Marcalee Sipski Alexander.

General remark regarding date of data collection/performing the test

DESCRIPTION:	For each variable in this dataset the date of data collection/performing the test is required.
CODE	YYYY.MM.DD (Year, Month, Day) Unknown
COMMENTS:	Because the collection of data on fracture conditions may be performed at any time following the spinal cord lesion, the date of data collection is imperative for computing the time that has lapsed after the initial spinal cord lesion. This will permit the obtained information to be related to other data collected on the same individual at various time points. However, the exact date of fracture may not be known. The date should be recorded to the extent known (year, year plus month, or year plus month plus day).

VARIABLE NAME:	Fracture History
DESCRIPTION:	This variable will assess the skeletal site, mechanism of injury, medical management, and known complication(s) for each fracture.
CODE	YYYY.MM.DD (Year, Month, Day) Unknown *Fracture location:* skull, face, neck/cervical spine, thoracic spine, lumbar spine, left and right shoulder/humerus, clavicle, elbow, forearm, wrist, finger, hip/proximal femur, midshaft femur, distal femur, proximal tibia, distal tibia, proximal fibula, distal fibula, tarsal, metatarsal, phalanges. *Fracture etiology:* **Fragility fracture:** no event, turning over in bed, caught foot on object while wheeling, dropped object on body, stretching/physical therapy, fall from wheelchair, fall from standing height or less, weight bearing or assisted ambulation activities (exoskeletal-assisted walking, manual or robotic body-weight supported treadmill training, overhead harness systems, functional electrical stimulation, epidural spinal stimulation), other: specify. **Traumatic fracture:** fall from greater than standing height, sports injury, motor vehicle/motor cycle accident, other: specify. **Unable to determine etiology**.

Fracture treatment: none, surgery, bed rest, bracing, casting, medication, other: specify, unknown.

Fracture complications: none, skin ulcer, infection, amputation, fracture non-union/delayed union, deep venous thrombosis, autonomic dysreflexia, new contracture, loss of range of motion, increased spasticity, other: specify, unknown.

COMMENTS: In the general adult population, osteoporosis diagnosis can be established after a hip or vertebral fracture that occurs in the absence of major trauma [12]. Limited information exists on factors associated with incident fracture risk and the prevalence of fracture-related complications after SCI [13]. Moreover, wide fracture treatment variations may exist in this population [14].

VARIABLE NAME: The WHO Fracture Risk Assessment Tool (FRAX)

DESCRIPTION: This tool will estimate 10-year fracture risk based on bone density at the femoral neck and clinical risk factors [2].

CODE

YYYY.MM.DD (Year, Month, Day)
Unknown

Country: specify
Unknown

FRAX calculator used: specify
Unknown

Age (enter 40 if younger than 40 years), gender (male/female), weight (kg), height (cm), previous fragility (non-traumatic) fracture (yes/no), history of fractured hip in parent (yes/no), current smoking (yes/no), glucocorticoids >5 mg prednisolone/prednisone daily for 3 months or more (yes/no), rheumatoid arthritis (yes/no), secondary osteoporosis (yes/no, enter yes for all individuals with SCI), alcohol 3 or more units/day (yes/no), femoral neck BMD (g/cm^2), DXA manufacturer, 10-year probability (%) of major osteoporotic fracture, 10-year probability (%) of hip fracture

COMMENTS: Because FRAX scores may vary widely based on the FRAX calculator used, input variables, country, and FRAX calculator will be recorded to compare and interpret results across regions. FRAX calculator link: http://www.shef.ac.uk/FRAX/. Follow this link to the FRAX website and choose the "calculator tool" specific to your

country. If your country is not represented, choose the country that most closely resembles the epidemiology of osteoporosis in your country from the list. The FRAX algorithm has not been validated in the SCI population. It is unknown the degree to which completeness of neurological impairment and associated degree of immobilization in those with SCI factor into the prediction of sublesional osteoporosis. Furthermore, the FRAX algorithm considers bone density at the hip and it is unknown if this tool will predict fractures at the knee (distal femoral metaphysis and proximal tibial metaphysis). Of note, there is a proposed SCI-specific fracture risk prediction algorithm [15] that has yet to be validated.

VARIABLE NAME: Osteoporosis Treatment

DESCRIPTION: This variable will assess previous (over the last 12 months) and/or current use of medications to treat osteoporosis, medications that potentially affect bone metabolism, and osteogenic physical therapies. Therapy frequency and average daily dose will also be recorded.

CODES

YYYY.MM.DD (Year, Month, Day)
Unknown

Anti-resorptive: alendronate, ibandronate, risedronate, zoledronic acid, denosumab, raloxifene, estrogen, other: specify

Osteo-anabolic: teriparatide, abaloparatide, testosterone, other: specify.

Osteogenic Exercises/Physical Therapy: Functional electrical stimulation-biking, other electrical stimulation, vibration therapy, assisted ambulation, other: specify.

Medications affecting bone metabolism: oral corticosteroids, antiepileptics (carbamazepine, phenytoin, valproate, phenobarbital), other: specify.

COMMENTS: Osteoporosis medications, including the antiresorptive bisphosphonates [16-20] and denosumab (a soluble antibody against receptor activator of nuclear factor kappa-B ligand (RANKL) [21], have been studied in SCI. Additionally, studies have shown new bone formation or reduced bone loss in response to electrical stimulation [22], functional electrical stimulation (FES) biking [23],

or vibration therapy after SCI [24]. For some therapies average daily dose and duration of use should be recorded.

QUANTITATIVE COMPUTED TOMOGRAPHY (QCT) DERIVED BONE MEASURES

COMMENTS: Clinical trials and other research targeting bone health after SCI would benefit from a higher level of detail and precision than that applied to the routine delivery of clinical care. If available, it is recommended that QCT, rather than DXA, measures be adopted as a primary outcome measure for clinical trials that address questions related to osteoporosis in persons with SCI [25]. Bone density assessment by DXA is widely used clinically, is cost-effective, and has been shown to discriminate between those with and without fractures after SCI [26]. Therefore, we recommend these QCT derived measures to be used as an adjunct to the DXA data collected in the metabolic dataset.

CODE	Date: YYYY.MM.DD (Year, Month, Day) Unknown

VARIABLE NAME: Bone Volume

DESCRIPTION: This variable will assess integral (everything within the periosteal surface), cortical, and trabecular bone volume at skeletal sites of interest, including distal femur and proximal tibia. In most cases unilateral scans are sufficient and balance cost/radiation exposure and data collection. Decisions to obtain bilateral knee scans may be made based on muscle/strength asymmetry.

CODES: Integral, cortical, and trabecular bone volume in cm^3.

COMMENTS: Distal-most 30% of the femur or the proximal-most 30% of the tibia is suggested for analysis, but this can vary as long as the exact region to be analyzed is specified per skeletal site.

VARIABLE NAME: Volumetric Bone Density

DESCRIPTION: This variable will assess integral (everything within the periosteal surface), cortical, and trabecular volumetric bone density at skeletal sites of interest, including 30% distal femur and 30% proximal tibia.

CODES: Integral, cortical, and trabecular volumetric bone mineral density in g/cm^3.

COMMENTS: 30% of the distal femur or proximal tibia is suggested for analysis, but this can vary as long as the exact region to be analyzed is specified per skeletal site.

VARIABLE NAME: Volumetric Bone Mineral Content

DESCRIPTION: This variable will assess integral (everything within the periosteal surface), cortical, and trabecular volumetric bone mineral content at skeletal sites of interest, including distal femur and proximal tibia.

CODES: Integral, cortical, and trabecular volumetric bone mineral content in g.

COMMENTS: 30% of the distal femur or proximal tibia is suggested for analysis, but this can vary as long as the exact region to be analyzed is specified per skeletal site.

VARIABLE NAME: Torsional Strength Index

DESCRIPTION: This variable will assess the torsional strength index at skeletal sites of interest, including distal femur and proximal tibia.

CODES: Torsional strength index in N*m/deg.

COMMENTS: Given that torsional (spiral) fractures are commonly observed after SCI [27, 28], torsional stiffness is an accurate and clinically relevant outcome [29]. 30% of the distal femur or proximal tibia is suggested for analysis, but this can vary as long as the exact region to be analyzed is specified per skeletal site.

VARIABLE NAME: Mass-weighted Principle Moments of Inertia of the Cross-Section

DESCRIPTION: This variable will assess the resistance to bending about the axes for which the bone is both strongest (Imax) and weakest (Imin) at skeletal sites of interest, including distal femur and proximal tibia.

CODES: Mass-weighted Principle Moments of Inertia of the Cross-Section (Imin and Imax) are measures of bone resistance to bending in $g*mm^2$

COMMENTS: 30% of the distal femur or proximal tibia is suggested for analysis, but this can vary as long as the exact region to be analyzed is specified per skeletal site.

VARIABLE NAME: Cross-sectional area

DESCRIPTION: This variable will assess the cross-sectional area at skeletal sites of interest, including distal femur and proximal tibia.

CODES: Cross-sectional area in cm^2.

COMMENTS: 30% of the distal femur or proximal tibia is suggested for analysis, but this can vary as long as the exact region to be analyzed is specified per skeletal site.

SOFT TISSUE BODY COMPOSITION BY TOTAL BODY DUAL ENERGY X-RAY ABSORPTIOMETRY (DXA)

CODE Date: YYYY.MM.DD (Year, Month, Day)
Unknown

VARIABLE NAME: Lean Mass

DESCRIPTION: This variable will assess lean mass at skeletal regions of interest, including total body, arms, and legs.

CODES: Lean mass of total body, arms, and legs in kilograms (kg)

COMMENTS: Muscle-bone interactions are poorly defined after SCI. In persons with SCI, the magnitude of the loss of total body lean mass was correlated with the magnitude of the loss of total body or leg bone mineral content (BMC) [30]. An association between muscle and lower extremity bone density [31]or bone quality [32] has been reported after SCI.

VARIABLE NAME: % Fat Mass

DESCRIPTION: This variable will assess % fat mass at skeletal regions of interest, including total body, trunk, legs, arm, android, and gynoid regions. Percent fat mass in each region is reported as the total of the percent

fat on the right and left sides. DXA software is used to define standard gynoid and android regions. FDA-approved software for DXA imaging is available for visceral adipose tissue mass (VAT_{mass}) and volume (VAT_{vol}) measurement. The android fat mass region of interest (ROI) is defined as the area that begins at the top of the iliac crest and has a height that is 20% of the total distance from the top of the iliac crest to the base of the skull with the soft tissue border at the umbilical level of the abdominal region acting as the lateral boundary of the ROI box. VAT_{mass} is transformed to a volume using a constant correction factor yielding a CT validated VAT_{vol} (cm^3) generated from an analyzed total body DXA scan. The upper boundary of the gynoid region below the pelvis cut extends downward from 1.5 times the height of the android region. Lateral boundaries of the gynoid region are the outer leg cuts. Percent fat mass in each region is reported as the total of the percent fat in the right and left sides.

CODES: % Fat mass of total body, trunk, legs, arms, gynoid region, and android region, and VAT_{vol} (cm^3).

COMMENTS: Adipose tissue is a major regulator of bone metabolism [33, 34]. In persons with SCI, a direct association was reported between total body percent fat and leg BMD, and leg fat mass was the single most significant predictor of leg BMD or leg BMC [35]. Visceral fat is metabolically active and is a source of adipose derived hormones, including leptin and adiponectin, which can modulate bone metabolism [36-45]. Android fat is considered an indicator of visceral fat, which is more directly measured, in part, by VAT_{vol}.

Appendix

INTERNATIONAL SPINAL CORD INJURY FRACTURE HISTORY EXTENDED DATA SET (Version 1.0) - DATA COLLECTION FORM

Fracture History Table

Fracture Date YYYY/ MM/DD	Location*	Etiology	Treatment	Complications
	□ Skull □ Face □ Neck/ Cervical spines □ Thoracic spine □ Lumbar spine □ Shoulder/ Humerus (L R) □ Clavicle (L R) □ Elbow (L R) □ Forearm (L R) □ Wrist (L R) □ Finger (L R) □ Hip/proximal femur (L R) □ Midshaft femur (L R) □ Distal femur (L R) □ Proximal tibia (L R) □ Proximal fibula (L R) □ Distal tibia (L R) □ Distal fibula (L R) □ Tarsal (L R) □ Metatarsal (L R) □ Phalanges (L R)	□ **Fragility Fracture** □ no event □ turning over in bed □ caught foot on object while wheeling □ dropped object on body □ stretching/physical therapy □ fall from wheelchair □ fall from standing height or less □ weight-bearing or assisted ambulation activities □ other, specify_____ □ **Traumatic Fracture** □ fall from greater than standing height □ sports injury □ motor vehicle/motor cycle accident □ other, specify_____ □ **Unable to determine etiology**	□ none □ surgery □ bed rest □ bracing □ casting □ medication □ other, specify_____ □ unknown	□ none □ skin ulcer □ infection □ amputation □ fracture non-union/delayed union □ deep venous thrombosis □ autonomic dysreflexia □ new contracture □ loss of range of motion □ increased spasticity □ other, specify _____ □ unknown

Were you hospitalized overnight or longer for the fracture(s)?
□ No □ Yes

Did the fracture(s) interfere with your therapy program or activities of daily living (transfers, walking, dressing, showers, etc)?
□ No-not at all □ Yes, a little □ Yes, a lot

*****Indicate all bones broken per fracture event. One table should be completed and the 2 questions above answered for each fracture event (fractures occurring at the same time due to the same

mechanism of injury).

FRAX Input Variables and Score:
Date YYYYMMDD; □ Unknown _____
Country: _____ □ Unknown_____
FRAX Calculator used:_____ □ Unknown_____

Age (between 40 and 90 years, enter 40 if less than 40 years) or date of birth: _____
Gender: □ male □ female
Weight (kg): _____
Height (cm): _____
Previous fragility (non-traumatic) fracture: □ yes □ no
History of fractured hip in parent: □ yes □ no
Current smoking: □ yes □ no
Glucocorticoids >5 mg prednisolone/prednisone daily for 3 months or more: □ yes □ no)
Secondary osteoporosis (enter yes for all individuals with SCI): **X** yes
Alcohol 3 or more units/day: □ yes □ no
Femoral neck BMD (g/cm^2): _____
DXA manufacturer: _____

Result recorded from the FRAX calculator:
10-year probability of major osteoporotic fracture (%): _____
10-year probability of hip fracture (%): _____

Osteoporosis Treatment Table Date YYYYMMDD; □ Unknown

	Current Use		Past Use (during last 12 months)	
	Check	Average daily dose/treatment frequency	Check	Average daily dose/treatment frequency
Anti-resorptive				
Alendronate				
Ibandronate				
Risedronate				
Zoledronic Acid				
Denosumab				
Raloxifene				
Estrogen				
Other, specify				
Osteo-anabolic				
Teriparatide				
Abaloparatide				
Testosterone				
Other, specify				
Osteogenic Exercises/Physical Therapy				
Functional Electrical Stimulation-biking				
Other electrical stimulation				
Vibration therapy				
Assisted ambulation				
Other, specify				
Medications Affecting Bone Metabolism				
Oral corticosteroid				
Antiepileptic (carbamazepine, phenytoin, valproate, phenobarbital)				
Other, specify				

Bone Measures:

Quantitative computed tomography: Date YYYYMMDD; □ Unknown

Integral bone volume, volumetric bone density (vBMD), and volumetric bone mineral content (vBMC) for each of the skeletal sites of interest:
Distal femur: Integral bone volume _____ (cm^3) Integral vBMD_____ (g/cm^3)
Integral vBMC_____ (g)
Proximal tibia: Integral bone volume _____ (cm^3) Integral vBMD_____ (g/cm^3)
Integral vBMC_____ (g)

Cortical bone volume, vBMD, and vBMC for each of the skeletal sites of interest:
Distal femur: Cortical bone volume _____ (cm^3) Cortical vBMD_____ (g/cm^3)
Cortical vBMC_____ (g)
Proximal tibia: Cortical bone volume _____ (cm^3) Cortical vBMD_____ (g/cm^3)
Cortical vBMC_____ (g)

Trabecular bone volume, vBMD, and vBMC for each of the skeletal sites of interest:
Distal femur: Trabecular bone volume _____ (cm^3) Trabecular vBMD_____ (g/cm^3)
Trabecular vBMC_____ (g)
Proximal tibia: Trabecular bone volume _____ (cm^3) Trabecular vBMD_____ (g/cm^3)
Trabecular vBMC_____ (g)

Torsional strength index for each of the skeletal sites of interest:
Distal femur _____ (N*m/deg)
Proximal tibia _____ (N*m/deg)

Mass-weighted principle moments of inertia of the cross-section for each of the skeletal sites of interest:
Distal femur: I_{max} _____ ($g*mm^2$) I_{min} _____ ($g*mm^2$)
Proximal tibia: I_{max} _____ ($g*mm^2$) I_{min} _____ ($g*mm^2$)

Cross sectional area for each of the skeletal sites of interest:
Distal femur _____ (cm^2)
Proximal tibia _____ (cm^2)

Body Composition:
Dual energy x-ray absorptiometry: Date YYYYMMDD; □ Unknown

Lean mass each region of interest:
Total body _____ (kg)
Arms _____ (kg)
Legs_____ (kg)

% Fat for each region of interest:
Total body _____ (%)

Gynoid Region _____(%)
Android Region _____(%)

Visceral adipose tissue (VAT) area _____(cm^2)

REFERENCES

1. Biering-Sorensen, F., et al., *International Spinal Cord Injury Data Sets.* Spinal Cord, 2006. **44**(9): p. 530-4.
2. Siris, E.S., et al., *The clinical diagnosis of osteoporosis: a position statement from the National Bone Health Alliance Working Group.* Osteoporos Int, 2014. **25**(5): p. 1439-43.
3. DeVivo, M., et al., *International Spinal Cord Injury Core Data Set.* Spinal Cord, 2006. **44**(9): p. 535-40.
4. Bauman, W.A., F. Biering-Sorensen, and A. Krassioukov, *International spinal cord injury endocrine and metabolic basic data set (version 1.2).* Spinal Cord. **50**(7): p. 567.
5. Bauman, W.A., F. Biering-Sorensen, and A. Krassioukov, *The international spinal cord injury endocrine and metabolic function basic data set.* Spinal Cord. **49**(10): p. 1068-72.
6. Krassioukov, A., et al., *International spinal cord injury cardiovascular function basic data set.* Spinal Cord. **48**(8): p. 586-90.
7. Biering-Sorensen, F., et al., *International spinal cord injury pulmonary function basic data set.* Spinal Cord. **50**(6): p. 418-21.
8. Biering-Sorensen, F., et al., *International spinal cord injury musculoskeletal basic data set.* Spinal Cord. **50**(11): p. 797-802.
9. Anderson, K.D., et al., *United States (US) multi-center study to assess the validity and reliability of the Spinal Cord Independence Measure (SCIM III).* Spinal Cord, 2011. **49**(8): p. 880-5.
10. Catz, A., et al., *A multicenter international study on the Spinal Cord Independence Measure, version III: Rasch psychometric validation.* Spinal Cord, 2007. **45**(4): p. 275-91.
11. Itzkovich, M., et al., *The Spinal Cord Independence Measure (SCIM) version III: reliability and validity in a multi-center international study.* Disabil Rehabil, 2007. **29**(24): p. 1926-33.
12. Cosman, F., et al., *Clinician's Guide to Prevention and Treatment of Osteoporosis.* Osteoporos Int, 2014. **25**(10): p. 2359-81.
13. Morse, L.R., et al., *Osteoporotic fractures and hospitalization risk in chronic spinal cord injury.* Osteoporos Int, 2009. **20**(3): p. 385-92.
14. Morse, L.R., et al., *VA-based survey of osteoporosis management in spinal cord injury.* PM R, 2009. **1**(3): p. 240-4.
15. Craven, B.C., Robertson LA, McGillivray CF, Adachi JD, *Detection and Treatment of Sublesional Osteoporosis Among Patients with Chronic Spinal Cord Injury: Proposed Paradigms.* Top Spinal Cord Inj Rehabil, 2009. **14**(4): p. 1-22.
16. Bauman, W.A., et al., *Zoledronic acid administration failed to prevent bone loss at the knee in persons with acute spinal cord injury: an observational cohort study.* J Bone Miner Metab, 2015. **33**(4): p. 410-21.

17. Gilchrist, N.L., et al., *Alendronate prevents bone loss in patients with acute spinal cord injury: a randomized, double-blind, placebo-controlled study.* J Clin Endocrinol Metab, 2007. **92**(4): p. 1385-90.
18. Moran de Brito, C.M., et al., *Effect of alendronate on bone mineral density in spinal cord injury patients: a pilot study.* Spinal Cord, 2005. **43**(6): p. 341-8.
19. Zehnder, Y., et al., *Prevention of bone loss in paraplegics over 2 years with alendronate.* J Bone Miner Res, 2004. **19**(7): p. 1067-74.
20. Schnitzer, T.J., et al., *Zoledronic acid treatment after acute spinal cord injury: Results of a randomized, placebo-controlled pilot trial.* PM R, 2016.
21. Gifre, L., et al., *Denosumab increases sublesional bone mass in osteoporotic individuals with recent spinal cord injury.* Osteoporos Int, 2016. **27**(1): p. 405-10.
22. Shields, R.K. and S. Dudley-Javoroski, *Musculoskeletal plasticity after acute spinal cord injury: effects of long-term neuromuscular electrical stimulation training.* J Neurophysiol, 2006. **95**(4): p. 2380-90.
23. Frotzler, A., et al., *High-volume FES-cycling partially reverses bone loss in people with chronic spinal cord injury.* Bone, 2008. **43**(1): p. 169-76.
24. Davis, R., et al., *The effects of whole body vibration on bone mineral density for a person with a spinal cord injury: a case study.* Adapt Phys Activ Q, 2010. **27**(1): p. 60-72.
25. Troy, K.L. and L.R. Morse, *Measurement of Bone: Diagnosis of SCI-Induced Osteoporosis and Fracture Risk Prediction.* Top Spinal Cord Inj Rehabil. **21**(4): p. 267-74.
26. Lala, D., et al., *Exploring the determinants of fracture risk among individuals with spinal cord injury.* Osteoporos Int, 2014. **25**(1): p. 177-85.
27. Keating, J.F., M. Kerr, and M. Delargy, *Minimal trauma causing fractures in patients with spinal cord injury.* Disabil Rehabil, 1992. **14**(2): p. 108-9.
28. Martinez, A., et al., *Late lower extremity fractures in patients with paraplegia.* Injury, 2002. **33**(7): p. 583-6.
29. Edwards, W.B., T.J. Schnitzer, and K.L. Troy, *Torsional stiffness and strength of the proximal tibia are better predicted by finite element models than DXA or QCT.* J Biomech, 2013. **46**(10): p. 1655-62.
30. Spungen, A.M., et al., *Soft tissue body composition differences in monozygotic twins discordant for spinal cord injury.* J Appl Physiol (1985), 2000. **88**(4): p. 1310-5.
31. Doherty, A.L., et al., *Adiponectin is a candidate biomarker of lower extremity bone density in men with chronic spinal cord injury.* J Bone Miner Res, 2014. **29**(1): p. 251-9.
32. Gibbs, J.C., et al., *Muscle Density and Bone Quality of the Distal Lower Extremity Among Individuals with Chronic Spinal Cord Injury.* Top Spinal Cord Inj Rehabil, 2015. **21**(4): p. 282-93.
33. Duque, G., *Bone and fat connection in aging bone.* Curr Opin Rheumatol, 2008. **20**(4): p. 429-34.
34. Rosen, C.J. and A. Klibanski, *Bone, fat, and body composition: evolving concepts in the pathogenesis of osteoporosis.* Am J Med, 2009. **122**(5): p. 409-14.
35. Bauman, W.A., et al., *Relationship of fat mass and serum estradiol with lower extremity bone in persons with chronic spinal cord injury.* Am J Physiol Endocrinol Metab, 2006. **290**(6): p. E1098-103.
36. Berner, H.S., et al., *Adiponectin and its receptors are expressed in bone-forming cells.* Bone, 2004. **35**(4): p. 842-9.

37. Cornish, J., et al., *Leptin directly regulates bone cell function in vitro and reduces bone fragility in vivo.* J Endocrinol, 2002. **175**(2): p. 405-15.
38. Hinoi, E., et al., *An Osteoblast-dependent mechanism contributes to the leptin regulation of insulin secretion.* Ann N Y Acad Sci, 2009. **1173 Suppl 1**: p. E20-30.
39. Holloway, W.R., et al., *Leptin inhibits osteoclast generation.* J Bone Miner Res, 2002. **17**(2): p. 200-9.
40. Lee, H.W., et al., *Adiponectin stimulates osteoblast differentiation through induction of COX2 in mesenchymal progenitor cells.* Stem Cells, 2009. **27**(9): p. 2254-62.
41. Lee, W.Y., et al., *Identification of adiponectin and its receptors in human osteoblast-like cells and association of T45G polymorphism in exon 2 of adiponectin gene with lumbar spine bone mineral density in Korean women.* Clin Endocrinol (Oxf), 2006. **65**(5): p. 631-7.
42. Luo, X.H., et al., *Adiponectin stimulates RANKL and inhibits OPG expression in human osteoblasts through the MAPK signaling pathway.* J Bone Miner Res, 2006. **21**(10): p. 1648-56.
43. Oshima, K., et al., *Adiponectin increases bone mass by suppressing osteoclast and activating osteoblast.* Biochem Biophys Res Commun, 2005. **331**(2): p. 520-6.
44. Peng, M., et al., *Effects of leptin on the expression of alpha1 (I) collagen gene in human osteoblast-like MG63 cells.* Biochem Cell Biol. **88**(4): p. 683-6.
45. Zeadin, M.G., et al., *Leptin promotes osteoblast differentiation and mineralization of primary cultures of vascular smooth muscle cells by inhibiting glycogen synthase kinase (GSK)-3beta.* Biochem Biophys Res Commun. **425**(4): p. 924-30.