

ORIGINAL ARTICLE

Dual energy X-ray absorptiometry of the knee in spinal cord injury: methodology and correlation with quantitative computed tomography

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Study Design: Comparison of diagnostic tests; methodological validation.

Objectives: Primary: to investigate the precision and reliability of a knee bone mineral density (BMD) assessment protocol that uses an existing dual energy X-ray absorptiometry (DXA) forearm acquisition algorithm in individuals with spinal cord injury (SCI). Secondary: to correlate DXA-based knee areal BMD with volumetric BMD assessments derived from quantitative computed tomography (QCT).

Setting: Academic medical center, Chicago, IL, USA.

Methods: Participants: a convenience sample of 12 individuals with acute SCI recruited for an observational study of bone loss and 34 individuals with chronic SCI who were screened for a longitudinal study evaluating interventions to increase BMD. Main outcome measures: root-mean-square standard deviation (RMS-SD) and intra/inter-rater reliability of areal BMD acquired at three knee regions using an existing DXA forearm acquisition algorithm; correlation of DXA-based areal BMD with QCT-derived volumetric BMD.

Results: The RMS-SD of areal BMD at the distal femoral epiphysis, distal femoral metaphysis and proximal tibial epiphysis averaged 0.021, 0.012 and 0.016 g cm⁻², respectively, in acute SCI and 0.018, 0.02 and 0.016 g cm⁻² in chronic SCI. All estimates of intra/inter-rater reliability exceeded 97% and DXA-based areal BMD was significantly correlated with QCT-derived volumetric BMD at all knee regions analyzed.

Conclusions: Existing DXA forearm acquisition algorithms are sufficiently precise and reliable for short-term assessments of knee BMD in individuals with SCI. Future work is necessary to quantify the reliability of this approach in longitudinal investigations and to determine its ability to predict fractures and recovery potential.

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INTRODUCTION

Spinal cord injury (SCI) has a major impact on systems that regulate bone metabolism,¹ and frequently leads to enhanced bone resorption and accelerated loss of bone mineral density (BMD).^{1–4} Such a decrease in BMD compromises bone strength and predisposes individuals with SCI to fractures, even under minimally loaded conditions.^{5,6} Although hip and spine BMD—known predictors of overall fracture risk in post-menopausal women—have been used as general monitors of bone loss post SCI,^{7,8} the distal femur and proximal tibia are the most common sites of fracture in this population.^{9,10} Indeed, bone loss at these locations is markedly greater than that at the hip and/or spine, rendering the knee a more sensitive and clinically relevant region in which to assess bone loss following SCI.^{11,12}

Despite its potential clinical impact, quantification of BMD in skeletal regions surrounding the knee has yet to become routine practice. In part, this may stem from methodological issues

surrounding the two most common means of BMD assessment, quantitative computed tomography (QCT) and dual energy X-ray absorptiometry (DXA). QCT provides a three-dimensional, or volumetric, measure of BMD (vBMD) that is largely free from artifacts that are potentially introduced by changes in limb position and/or ectopic bone formation as a consequence of heterotopic ossification. However, lingering concerns over the high costs and radiation exposure have limited the use of QCT to the research setting rather than in the clinic for routine BMD assessments in this population. DXA provides an alternative measure of BMD, but no widely accepted standardized protocol exists for computing knee BMD using DXA. In addition, its two-dimensional, or areal, measure of BMD (aBMD) may be subject to more artifacts from limb repositioning and/or ectopic new bone formation. Nevertheless, its widespread availability, low cost and minimal radiation exposure make DXA an appealing option. As a result, the development and validation of a DXA-based knee protocol would greatly facilitate

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routine assessment and monitoring of knee BMD in both clinical and research settings.

A modest but growing body of research indicates that existing DXA acquisition algorithms intended for measurements of aBMD at other skeletal regions are capable of providing reliable estimates of distal femur and proximal tibia aBMD.^{13–15} However, this finding has yet to be systematically investigated in individuals with SCI, where optimal limb positioning may be difficult to achieve and heterotopic ossification may be present. Consequently, the primary goal of this study was to establish the precision and intra-/inter-rater reliability of a standard DXA acquisition algorithm for assessment of distal femur and proximal tibia aBMD in both acute and chronic SCI populations. In addition, we quantified the correlation between DXA-based aBMD and QCT-based vBMD estimates in these cohorts, given that QCT is generally considered to be a more robust technique for BMD analysis.

MATERIALS AND METHODS

Study participants

Forty-six individuals with SCI were included in this study; all were recruited from the inpatient and outpatient populations at the Rehabilitation Institute of Chicago. Twelve of these individuals were recruited for an observational study of bone loss beginning acutely post SCI (acute cohort), whereas the remaining thirty-four individuals were screened for a longitudinal study evaluating interventions to increase BMD (chronic cohort; ClinicalTrials.gov identifier: NCT01225055) in chronic SCI. All participants were medically stable and non-ambulatory with an ASIA level of A, B or C at the time of study entry. Pregnant females and/or individuals with current or recent (within 12 months) use of drugs that affect bone metabolism were excluded from participation.

DXA acquisition and analysis

DXA scans were obtained using a Hologic QDR4500A instrument that was calibrated daily (Hologic, Inc., Bedford, MA, USA). A modified forearm algorithm was elected for scan acquisition,¹⁵ with the imaging field comprising the distal two-third of the femur and the proximal one-third of the tibia (Figure 1). During scans, participants were placed in a supine position and the lower limb was stabilized in full extension. When possible, both knees were imaged, with duplicate scans per knee. The lower limb was repositioned and restabilized between adjacent scans on each knee.

Two individuals independently analyzed all DXA images, using the Hologic APEX software (Hologic, Inc.) to quantify aBMD. Three skeletal regions were analyzed that permitted direct comparison to a previously described QCT protocol:³ two regions of interest (ROIs) corresponding to the first 0–10% and 10–20% of the femur as measured from the distal end (R1, R2, respectively), and one region corresponded the first 0–10% of the tibia as measured from the proximal end (R3; Figure 1). These regions anatomically correspond to the distal femoral epiphysis, distal femoral metaphysis and proximal tibial epiphysis. Segment lengths were estimated from self-reported stature using standard proportionality constants. This method of segment length was chosen in place of direct stature or segment measurement because of difficulties in reliably assessing these parameters in the SCI population.

QCT acquisition and analysis

Participants also received a QCT scan within 2 weeks of their corresponding DXA scans. All computed tomography images were acquired on the non-dominant knee using a Sensation 64 Cardiac scanner (Siemens Medical Systems, Forchheim, Germany; 120 kVp, 280 mAs, pixel resolution 0.352 mm, slice thickness 1 mm). Each scan was 30 cm in length and captured approximately 15 cm each of the distal femur and proximal tibia. All computed tomography scans included a phantom—placed on the side of, or underneath, the subjects' knee—with known calcium hydroxyapatite concentration (QRM, Moehrendorf, Germany). The phantom allowed conversion of computed tomography Hounsfield units into hydroxyapatite equivalent density for the

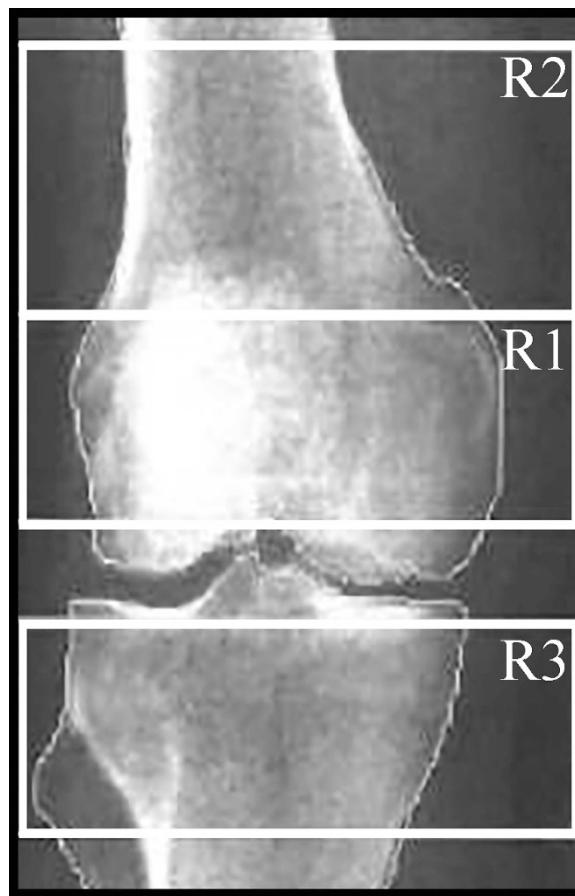


Figure 1 Anatomical regions of interest for DXA and QCT BMD analysis. R1: distal femoral epiphysis; R2: distal femoral metaphysis; R3: proximal tibial epiphysis.

calculation of vBMD. A single researcher performed all QCT analyses, using regions identical to those described for the DXA protocol; the reliability of this QCT analysis has been previously reported.³

Statistical analysis

Precision for each region of the DXA protocol was calculated using the short-term methodology recommended by International Society of Clinical Densitometry, defined as the root-mean-square standard deviation (RMS-SD), root-mean-square coefficient of variation (RMS-CV) and the least significant change.¹⁶ Inter-rater reliability for each region of the DXA protocol was determined using intra-class correlation coefficients (Model type: two-way random, absolute agreement). In total, 42 pairs of knee scans (84 unique images) were used for precision and reliability analyses. The relationship between DXA-based aBMD and QCT-derived vBMD was calculated using Pearson's product-moment correlation on knees that had both DXA and QCT scans; duplicate single-rater aBMD values from DXA scans were averaged and correlated with QCT vBMD measurements. In total, 46 DXA-QCT image pairs were used for correlational analyses. SPSS Statistics software was used for all statistical calculations (SPSS, Armonk, NY, USA). Unless reported otherwise, data are reported as mean \pm standard deviation, and considered significant at the $\alpha = 0.05$ level.

Statement of ethics. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research. All studies were approved by the Northwestern University Institutional Review Board and all subjects provided written informed consent before participation.

RESULTS

General

Demographics and clinical information of the participants are provided in Table 1. The average age of acute SCI participants at the time of initial scan was 28.2 ± 13.0 years; the chronic SCI cohort averaged 41.9 ± 12.2 years. The mean time post-injury was 2.1 ± 0.7 months for the acute population and 196.9 ± 111.4 months for participants with chronic SCI. Mean DXA-based aBMD for acute and chronic SCI is presented in Table 2, with results from each rater displayed separately. Expectedly, mean aBMD levels in the acute SCI cohort were significantly greater than those of the chronic SCI population at each ROI.

Precision of the knee DXA protocol

A total of 42 pairs of DXA knee images were available for evaluation. The RMS-SD (g cm^{-2}), RMS-CV (%) and least significant change (%) of aBMD estimates are displayed in Table 3; data are parsed by rater, and presented separately for the acute and chronic subgroups, as well as the overall cohort. In the acute SCI group, RMS-CV values averaged 1.70%, 1.39% and 1.66% for the distal femur epiphysis, distal femur metaphysis and proximal tibia epiphysis, respectively; corresponding values for the chronic SCI cohort are: 3.12, 4.70 and 3.40%.

Reliability and reproducibility of the knee DXA measurements

Intra-class correlation coefficients were used to quantify the intra- and inter-rater reliability of DXA-based BMD assessments at each knee

region. Reliability estimates were comparable in the acute and chronic SCI groups, with all intra-class correlation coefficients exceeding 0.97 (Table 4).

Correlation of QCT and DXA scans

Pearson product-moment correlations were used to quantify the strength of linear relationships between DXA-based aBMD and QCT-derived vBMD estimates for each knee region across the total cohort of study participants, and linear regression analysis was used to quantify the mapping between aBMD and vBMD at each site (Figure 2). Significant linear relationships between aBMD and vBMD were found at all ROIs.

DISCUSSION

This study quantified the precision and reliability of a DXA-based knee aBMD assessment protocol and the correlation between DXA-based aBMD and QCT-derived vBMD in both acute and chronic SCI populations. Across the knee ROIs analyzed in this investigation, the mean aBMD in individuals with acute SCI was approximately twice as high as the mean aBMD in individuals with chronic SCI (1.042 vs

Table 1 Demographic and clinical data of study participants

	Acute SCI	Chronic SCI
Time post injury (months)	2.1 ± 0.7	196.9 ± 111.4
Age at injury (years)	28.2 ± 13.0	41.9 ± 12.2
<i>Injury level distribution (%)</i>		
Cervical	66.7	26.5
Thoracic	33.3	70.6
Lumbar	0	2.9
<i>Gender distribution (%)</i>		
F	33.3	21.6
M	66.7	79.4
Body mass index	24.1 ± 4.99	24.1 ± 5.98

Abbreviations: F, female; M, male; SCI, spinal cord injury.

Table 2 DXA-based mean bone mineral density for each knee region

	Acute SCI (g cm^{-2})	Chronic SCI (g cm^{-2})
<i>Distal femur epiphysis</i>		
Rater 1	1.255 ± 0.133	0.605 ± 0.183
Rater 2	1.255 ± 0.133	0.607 ± 0.181
<i>Distal femur metaphysis</i>		
Rater 1	0.927 ± 0.098	0.458 ± 0.175
Rater 2	0.927 ± 0.098	0.462 ± 0.173
<i>Proximal tibia epiphysis</i>		
Rater 1	0.944 ± 0.144	0.458 ± 0.131
Rater 2	0.944 ± 0.144	0.457 ± 0.130

Abbreviations: DXA, dual energy X-ray absorptiometry; SCI, spinal cord injury.

Table 3 Estimates of precision for each knee region in acute, chronic and overall SCI cohorts

	Acute SCI	Chronic SCI	Overall cohort
<i>Distal femur epiphysis</i>			
<i>Rater 1</i>			
RMS-SD ^a	0.021	0.016	0.021
RMS-CV ^b	1.70	2.92	2.08
LSC ^c	4.70	8.08	5.80
<i>Rater 2</i>			
RMS-SD	0.021	0.019	0.023
RMS-CV	1.70	3.32	2.32
LSC	4.70	9.18	6.42
<i>Distal femur metaphysis</i>			
<i>Rater 1</i>			
RMS-SD	0.012	0.023	0.019
RMS-CV	1.39	5.53	2.61
LSC	3.85	15.31	7.22
<i>Rater 2</i>			
RMS-SD	0.0123	0.016	0.017
RMS-CV	1.39	3.86	2.25
LSC	3.85	10.70	6.24
<i>Proximal tibia epiphysis</i>			
<i>Rater 1</i>			
RMS-SD	0.016	0.018	0.021
RMS-CV	1.66	4.02	2.87
LSC	4.60	11.13	7.94
<i>Rater 2</i>			
RMS-SD	0.016	0.012	0.019
RMS-CV	1.66	2.77	2.63
LSC	4.60	7.67	7.28

Abbreviations: LSC, least significant change; RMS-CV, root-mean-square coefficient of variation; RMS-SD, root-mean-square standard deviation; SCI, spinal cord injury.

^aRMS-SD: g cm^{-2} .

^bRMS-CV: %.

^cLSC: %.

0.508 g cm⁻²). Measurements of aBMD also appeared to be more precise in the acute SCI cohort, with RMS-CV estimates of 1.70%, 1.39% and 1.66% for the distal femur epiphysis, distal femur metaphysis and proximal tibia epiphysis, respectively, compared with 3.12%, 4.70% and 3.40% in chronic SCI. However, the higher RMS-CV values in chronic SCI are largely attributable to this population's lower overall mean BMD rather than a systematic increase in RMS-SD. Indeed, for a similar absolute difference in aBMD, populations with lower mean aBMD will have higher RMS-CV estimates than those with higher mean aBMD, based on how RMS-CV is calculated. As such, if precision estimates—in particular, our estimates of least significant change—are expressed in units of aBMD (g cm⁻²) rather than as a percentage of mean aBMD, similar results are found for both the acute and chronic cohorts: 0.059, 0.036 and 0.043 g cm⁻² for

the acute subgroup and 0.049, 0.055 and 0.041 g cm⁻² in participants with chronic SCI.

Although few studies specifically designed to quantify the precision and reliability of DXA-based knee aBMD protocols exist in the literature, our estimates of these parameters are consistent with the available data. For example, Bakkum and colleagues have recently reported least significant knee BMD changes ranging from 0.047 to 0.077 g cm⁻² when using the existing Hologic DXA forearm acquisition algorithm.¹⁵ Given that these estimates were derived from able-bodied individuals—a population markedly less prone to heterotopic ossification and repositioning difficulties than the SCI population tested here—it is particularly noteworthy that our precision and reliability estimates were comparable. In another investigation, Morse *et al.* reported RMS-CV values that were lower at the distal femur (3.01%) than the proximal tibia (5.91%) in a cohort of individuals with chronic SCI,¹⁴ corresponding to least significant aBMD changes of 0.069 and 0.083 g cm⁻². Unlike the findings of Morse and colleagues, however, our estimates of precision and reliability were comparable at the distal femur and proximal tibia, potentially reflective of the different skeletal ROI used in the two studies and/or the consistency with which those ROI could be delineated. As a final comparison, estimates of least significant aBMD changes in postmenopausal women—another population where bone loss is prevalent—range from approximately 0.020 to 0.050 g cm⁻² at the traditional scanning sites of the hip and spine.^{17,18}

Because the anatomical ROIs used in our DXA protocol were derived from a previously described QCT protocol,³ we were able to quantify the strength and direction of a linear relationship between DXA-based aBMD measurements and their QCT-derived vBMD counterparts at each site (Figure 2). Importantly, the inclusion of individuals whose bone loss varied from negligible to severe (that is, acute SCI to chronic SCI) enabled these correlations to be examined over the full physiological range of knee BMDs, thus avoiding the well-known restriction of range problem in correlational analyses.¹⁹ Our results revealed a significant, positive correlation between DXA-based aBMD and QCT-derived vBMD at each ROI, although the

Table 4 Estimates of intra- and inter-rater reliability in acute, chronic and overall SCI cohorts

	Acute SCI	Chronic SCI	Overall
	ICC	ICC	ICC
<i>Distal femur epiphysis</i>			
Inter-rater	0.992	0.991	0.999
Intra-rater (R1)	0.988	0.990	0.998
Intra-rater (R2)	0.988	0.986	0.998
<i>Distal femur metaphysis</i>			
Inter-rater	0.994	0.983	0.999
Intra-rater (R1)	0.992	0.975	0.998
Intra-rater (R2)	0.992	0.987	0.996
<i>Proximal tibia epiphysis</i>			
Inter-rater	0.996	0.991	0.998
Intra-rater (R1)	0.994	0.985	0.997
Intra-rater (R2)	0.994	0.993	0.997

Abbreviations: ICC, intra-class correlation coefficient; SCI, spinal cord injury.

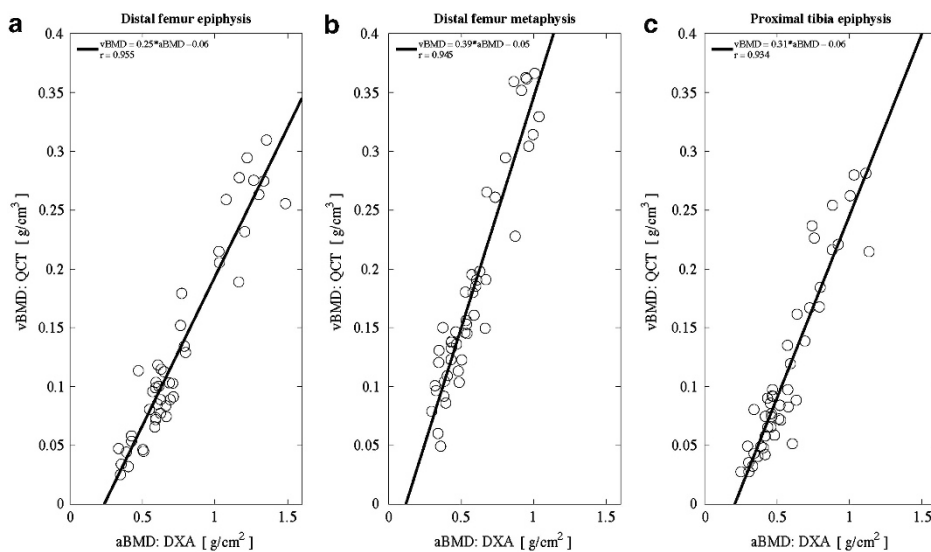


Figure 2 The relationship between QCT-derived vBMD vs DXA-based aBMD at each knee region. (a) Distal femur epiphysis; (b) distal femur metaphysis; (c) proximal tibia epiphysis. All panels: vertical axis reflects QCT-derived volumetric BMD (g cm⁻³); horizontal axis reflects DXA-based areal BMD (g cm⁻²); open circles: individual QCT-DXA pairs; bold line: linear regression fit of vBMD and aBMD.

slope of linear regression fits to these data varied slightly across sites. The difference in regression fits may be partly attributable to different proportions of cortical and trabecular bone at these sites. Nevertheless, the overall strength of each fit suggests that DXA-based aBMD and QCT-derived vBMD are linearly related and exhibit constant sensitivity over the relevant physiological operating range.

The primary limitation of this investigation is a potential underestimate of the effects of limb repositioning on precision and reliability. Although participants were repositioned between subsequent scans, a full dismount from the DXA table was not performed. Because changes in limb position and thus the imaging field can impact DXA-based aBMD estimates, it is possible that our performance metrics would have been lower had we more extensively repositioned each participant. In addition, although our estimates of short-term precision and reliability are highly clinically relevant, care should be taken when attempting to generalize these findings to situations in which long-term precision and reliability are more applicable. Finally, it should be reiterated that this study was performed using a Hologic Delphi DXA system, and consequently the absolute aBMD values reported herein will likely differ from aBMD measures computed using a GE Healthcare Lunar DXA system. Importantly, however, our protocol used Hologic Apex analysis software, which has comparable precision and reliability to GE Lunar Prodigy software.²⁰

Despite the potential clinical importance of monitoring knee BMD post SCI and the ubiquity of DXA-based aBMD measurements at the hip and spine, DXA-based assessments of knee aBMD have yet to become standard clinical practice. Given that this lag is driven in part by the lack of commercially available DXA knee acquisition algorithms, a critical first step is to validate knee aBMD assessment protocols that use existing DXA acquisition algorithms as their basis. We believe that the protocol described herein mirrors what would be encountered in a typical clinic visit, and adequately reflects the challenges inherent to DXA-based knee aBMD assessments, particularly in individuals with SCI. In light of these challenges, it is important to again note that our estimates of precision and reliability were comparable at all knee regions. This consistency may allow clinicians to selectively choose which region(s) to analyze for each patient, potentially mitigating the impact of some postural or bony obstruction artifacts.

In summary, our results indicate that DXA is sufficiently precise and reliable to be used as the basis for routine monitoring of knee BMD post SCI. However, future work that systematically characterizes the sensitivity of DXA-based knee aBMD measurements to changes in limb position, ROI definitions and ectopic bone formation over short- and long-time scales will be essential to the design and interpretation of bone health interventions post SCI. And finally, as has been done previously for the hip and spine, determining the ability of DXA-based knee aBMD to predict fractures and subsequent recovery will be essential to establishing the full clinical utility of the technique.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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- 1 Dudley-Javoroski S, Shields RK. Regional cortical and trabecular bone loss after spinal cord injury. *J Rehabil Res Dev* 2012; **49**: 1365–1376.
- 2 Battaglini RA, Lazzari AA, Garshick E, Morse LR. Spinal cord injury-induced osteoporosis: pathogenesis and emerging therapies. *Curr Osteoporosis Rep* 2012; **10**: 278–285.
- 3 Edwards WB, Schnitzer TJ, Troy KL, Edwards WB, Schnitzer TJ, Troy KL. Bone mineral and stiffness loss at the distal femur and proximal tibia in acute spinal cord injury. *Osteoporos Int* 2013; **25**: 1005–1015.
- 4 Edwards WB, Schnitzer TJ, Troy KL. Bone mineral loss at the proximal femur in acute spinal cord injury. *Osteoporos Int* 2013; **24**: 2461–2469.
- 5 Zehnder Y, Luthi M, Michel D, Knecht H, Perrelet R, Neto I *et al*. Long-term changes in bone metabolism, bone mineral density, quantitative ultrasound parameters, and fracture incidence after spinal cord injury: a cross-sectional observational study in 100 paraplegic men. *Osteoporos Int* 2004; **15**: 180–189.
- 6 Fattal C, Mariano-Goulart D, Thomas E, Rouays-Mabit H, Verollet C, Maimoun L. Osteoporosis in persons with spinal cord injury: the need for a targeted therapeutic education. *Arch Phys Med Rehabil* 2011; **92**: 59–67.
- 7 Biering-Sorensen F, Bohr HH, Schaadt OP. Longitudinal study of bone mineral content in the lumbar spine, the forearm and the lower extremities after spinal cord injury. *Eur J Clin Invest* 1990; **20**: 330–335.
- 8 Leslie WD, Nance PW. Dissociated hip and spine demineralization: a specific finding in spinal cord injury. *Arch Phys Med Rehabil* 1993; **74**: 960–964.
- 9 Ragnarsson KT, Sell GH. Lower extremity fractures after spinal cord injury: a retrospective study. *Arch Phys Med Rehabil* 1981; **62**: 418–423.
- 10 Comarr AE, Hutchinson RH, Bors E. Extremity fractures of patients with spinal cord injuries. *Am J Surg* 1962; **103**: 732–739.
- 11 Gaspar AP, Lazaretti-Castro M, Brandao CM. Bone mineral density in spinal cord injury: an evaluation of the distal femur. *J Osteoporos* 2012; **2012**: 519754.
- 12 Garland DE, Adkins RH, Kushwaha V, Stewart C. Risk factors for osteoporosis at the knee in the spinal cord injury population. *J Spinal Cord Med* 2004; **27**: 202–206.
- 13 Shields RK, Schlechte J, Dudley-Javoroski S, Zwart BD, Clark SD, Grant SA *et al*. Bone mineral density after spinal cord injury: a reliable method for knee measurement. *Arch Phys Med Rehabil* 2005; **86**: 1969–1973.
- 14 Morse LR, Lazzari AA, Battaglini R, Stolzmann KL, Matthes KR, Gagnon DR *et al*. Dual energy X-ray absorptiometry of the distal femur may be more reliable than the proximal tibia in spinal cord injury. *Arch Phys Med Rehabil* 2009; **90**: 827–831.
- 15 Bakkum AJ, Janssen TW, Rolf MP, Roos JC, Burcksen J, Knol DL *et al*. A reliable method for measuring proximal tibia and distal femur bone mineral density using dual-energy X-ray absorptiometry. *Med Engin Phys* 2013; **36**: 387–390.
- 16 Baim S, Wilson CR, Lewiecki EM, Luckey MM, Downs Jr RW, Lentle BC. Precision assessment and radiation safety for dual-energy X-ray absorptiometry: position paper of the International Society for Clinical Densitometry. *J Clin Densitom* 2005; **8**: 371–378.
- 17 Lodder MC, Lems WF, Ader HJ, Marthinsen AE, van Coeverden SC, Lips P *et al*. Reproducibility of bone mineral density measurement in daily practice. *Ann Rheumat Dis* 2004; **63**: 285–289.
- 18 Ravaut P, Reny JL, Giraudeau B, Porcher R, Dougados M, Roux C. Individual smallest detectable difference in bone mineral density measurements. *J Bone Miner Res* 1999; **14**: 1449–1456.
- 19 Cohen J, Cohen P, West S, Aiken L. *Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences*, 3rd edn. Mahwah, New Jersey, Lawrence Erlbaum Associates, 2003.
- 20 Fan B, Lewiecki EM, Sherman M, Lu Y, Miller PD, Genant HK *et al*. Improved precision with Hologic Apex software. *Osteoporos Int* 2008; **19**: 1597–1602.