Spinal Cord (2005) 43, 96–101

www.nature.com/sc

Original Article

Long-term changes in the tibia and radius bone mineral density following spinal cord injury

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Design: A prospective inception cohort study with an observational analytic design in a spinal cord injury (SCI) centre hospital.
Objective: To assess changes in trabecular and compact bone of the tibia and radius prospectively in subjects with SCI.
Subjects: In total, 10 individuals with an acute SCI.
Methods: Trabecular and compact bone density of the tibia and radius by peripheral quantitative computerised tomography.
Results: Analysis of the individual gradients of the curve coefficient showed changes in trabecular bone between −0.19 and −2.46 and in cortical bone between +0.07 and −0.93 in the tibia within 34 months after the SCI. Both trabecular and cortical bone showed a group mean loss of 99 mg/cm^3. No changes were observed in the radius.
Conclusion: There is a major decrease in tibia mineral density over 3 years; however, no change is observed for the radius mineral content. Large interindividual differences existed in the patterns of loss in the tibia bone substance after SCI. These patterns indicate that there is no steady state of bone mineral density following 3 years of spinal cord injury.
Spinal Cord (2005) **43,** 96–101. doi:10.1038/sj.sc.3101685; Published online 9 November 2004

Keywords: bone mineral density; spinal cord injury; bone mineral changes

Introduction

Spinal cord injury (SCI) is a condition known to be associated with osteopenia; a decrease in bone mass below the level of injury. Osteopenia leads in some individuals to osteoporosis with an increased risk of fractures.[1–7] Several authors report that approximately 2 years after the spinal cord injury, a new steady state between bone resorption and formation is re-established. However, this steady state is reached after the patient has lost a significant amount of bone minerals. At 16 months after SCI, bone mineral density (BMD) around the knee is comparable with the values seen in individuals at more than 5 years following SCI.[8] Biering-Sørensen *et al*[9] observed bone development longitudinally and report that the decrease in bone mineral content (BMC) of the lower extremities occurs rather uniformly. Another study of this group identified that SCI individuals with fractures of the lower extremities sustained after the injury show lower BMC compared to individuals without fractures.[10] One of our previous studies[11] observed a loss in trabecular and cortical bone, which was at first sight in line with previously reported results.[9,10] However, we found a large intersubject variability through qualitative analysis of the individual patterns of change. Finsen *et al*[12] report contradictory findings. They compared 19 SCI individuals with a median duration of SCI of 4 years with a control group. From this cross-sectional study design the authors derived considerable individual variations in BMD and in the degree of difference in BMD between SCI patients and controls. Furthermore, the degree of osteopenia in the affected limbs seemed to increase with the time of injury and no signs of steady state were corroborated.[12]

Whole bones are composed of cortical and trabecular bone tissue. This classification of bone tissue is based on relative density. Apparent bone density has a profound influence on the stress–strain behaviour of bone, which is markedly different between these two types of bone tissue. The major physical difference between trabecular and cortical bone is the increased porosity of trabecular bone.[13]

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One of the clinical effects of osteoporosis in paraplegia is spontaneous fracture of long bones.[14–16] The usual history of trauma and the classical signs of fracture are absent in these patients. Frequently, minor trauma is the cause of fracture.[17,18] Frisbie[19] attempted to quantify the risk of lower extremity fracture in paraplegia by retrospective analysis of medical records. In total, 33% of the patients in this study sustained 76 fracture events, resulting in 103 fractures (82% in the long bones of the lower extremity). Frisbie[19] concluded that there is a markedly increased risk of lower extremity fracture following SCI and that this risk seems to be raised further with ageing. A study of Vestergaard *et al*[20] included 438 SCI patients in which the overall fracture rate (2%/year) was higher than in the normal population (1%/year). Following the SCI the rate increased to a plateau from the third year onward. Before the SCI occurred in these subjects, however, their fracture rate was equal to that of the normal controls.[20]

Hence, the natural course of bone loss is not known with regard to SCI and injury duration. This prospective study was designed to elucidate the natural course of bone loss in individuals of the SCI population through a time-sequential assessment of the phenomena of bone loss associated with SCI. The aim of this study was to find an answer to the following two questions: First, do changes in BMD following an SCI reach a 'steady state' after more than 2 years postinjury? Second, are there high interindividual variations of change in BMD following an SCI? The bony organs chosen were the tibia and the radius.

Methods

Subjects and protocol

A total of 12 subjects with SCI were initially investigated within 5 weeks following the accident that resulted in SCI (t1). Approximately $3\frac{1}{2}$ years after the accident (42 ± 5.9 months), 10 subjects were measured again (t2). All participants signed a statement of informed consent as approved by the Review Board of the University Hospital Balgrist after receiving oral and written information about the research. All subjects had a traumatic SCI. At t2, two subjects were removed from the study because they had moved too far away from the Spinal Cord Injury Center, University Hospital Balgrist. A summary of the 10 subjects completing the study is given in Table 1.

The qualitative and quantitative analysis was performed with the 10 subjects who completed the study, nine males and one female. The subjects were aged 40.9 ± 19.7 years at t2.

Study design

Because of the expected heterogeneity of the population involved, a prospective cohort study with an observational analytic design was chosen.

Bone measurements

Bone density measurements were performed with a Densiscan 1000 (Scanco Medical, CH-8303 Bassersdorf, Switzerland) on the left tibia and on the left radius (unless these bones had been fractured). Two stacks of CT scans were analysed: (1) in the distal tibia epiphysis close to the ankle joint, and (2) in the distal radius epiphysis close to the wrist. To ensure that the CT scans were always made at the same angle relative to the bone axis the extremity involved was measured in an anatomically formed radiolucent cast.

The basic methodology employed in quantitative computed tomography (QCT) scanning involves the computation of the cross-sectional distribution of X-ray attenuation in a body by back-projecting the X-ray transmission measurements acquired at many angles

Table 1 Participating subjects specified by age, lesion level, Frankel classification, and individual bone parameter changes[a] of the left leg more than 3 years after SCI

Subject	*Age at t2 (years)*	*Lesion level*	*Frankel classification*	*Tibia %Δ trabecular bone (mg/cm^3)*	*Tibia %Δ cortical bone (mg/cm^3)*
1	62	Th-8	C	−83.5	−9.4
2	81	Th-1	C	−71	−40
3	25	Th-9	A	−56.6	−13.8
4	37	Th-11	D	−50.9	−17.1
5	54	Th-5	A	−57.5	−3.3
6	28	Th-11	D	−37	−0.8
7	24	L-5	C	−12.5	−22.7
8	45	Th-12	D	−13.7	+3
9	34	C-6	A	−9.8	−1.5
10	19	Th-11	A	−7.8	−7.3

[a]This change is expressed as percentage change of initial value (%Δ), and represents percentage change compared to the initial value measured

around the body until the spatial arrangement of the absorbing structures can be determined.[21] With the information available in QCT scans, it is possible to isolate BMD changes in both cortical and trabecular compartments.[13] A detailed description of the examination protocol has been described elsewhere.[22,23]

Two parameters were derived and calculated for a general characterisation of the measured bone:

Trabecular bone: to determine this bone parameter, the inner core of the bone was assessed. The core area contains only trabecular bone.

Compact bone (ie, cortical bone): this parameter represents the average bone density at the diaphyseal measuring site (bone mass divided by total cross-sectional area of the bone). Reproducibility in routine patient measurements was determined earlier to vary around 0.30% for the radius and tibia with pQCT.[22,24]

The first pQCT bone measurements were performed at week 5 after accident (t1), the last measurement 40.8 ± 5.9 months after the first measurement (t2). Four subjects who lived in the vicinity of the hospital had repeated measurements between these time points as well (Figure 2). For logistic reasons this was not possible for the other subjects.

Statistical analysis

Two-tailed paired *t*-tests ($P = 0.05$) were performed on BMD data (absolute values and percentage of initial values) to test for significant differences over the course of the study (average interval between paired BMD, 40.8 ± 5.9 months). Statistical analysis was performed with the SAS statistical package running on a PC. Results were considered significant at $P \leqslant 0.05$ except where stated otherwise. Data are presented as mean $\pm$ SD unless otherwise stated. As there was only one female, no division was made according to gender.

To be able to compare the individuals with each other, the bone density for each individual at t2 (40.8 ± 5.9 months) was calculated from the repeated measurements. Furthermore, the slope of the decrease in bone density between t1 and t2 was determined and compared between individuals (Table 1 and Figure 2).

Thus, both visual inspection and statistical analysis were used for the analysis of the data from each single case.[25] To estimate the amount of individual change in bone parameter development, results for each individual were calculated as percentage change of initial values. These percentages were compared qualitatively against each other.

Pearson's correlations were used to evaluate the relationships between tibia bone parameter development and age, level of lesion and initial BMD value respectively.

Results

Characteristics of the group are shown in Table 1.

Tibia trabecular bone

The group of 10 SCI individuals showed a significant decrease of trabecular tibia bone within 40.8 (± 5.9) months between first and last measurements following the SCI. This loss is apparent both in absolute values and in percentage of initial value ($P = 0.002$). Mean values $\pm$ SD at t1 and t2 are summarised in Figure 1.

Marked differences were observed when looking qualitatively at the individual patterns of loss of tibia trabecular bone, both in absolute values and in percentage change from the initial value. The largest loss measured amounted to 83%, the smallest was 7.8% (Table 1). The individual gradients of the trajectory for subjects with more than two time points indicate that in those subjects bone loss persist during the first 3 years after SCI (Figure 2).

All three subjects with multiple measurements show a continuous loss in tibia bone substance during the 3 years of measurement.

Tibia compact bone

A significant decrease in compact bone ($P = 0.015$). resulted between the first and last measurements (Figure 1). Individual patterns showed a large variability of bone mineral changes; a decrease of 40% was observed, however, a small increase of 3% was detected in one individual (Tables 1 and 2; Figure 2). The individual gradients of the trajectory for subjects with more than two time points indicate that in some subjects bone loss continued for more than 3 years (Figure 2).

Radius trabecular bone

There was no change in radius trabecular bone observable during the monitoring period for the whole group. Individual patterns of change vary between 10% loss and 14% increase of this bone parameter.

Radius compact bone

There was no change in radius compact bone observable during the monitoring period. Individual patterns of change vary between 3.5% loss and 4.5% increase of this bone parameter.

Individual volumetric bone densitometry values for trabecular and compact bone (in mg/cm^3) are summarised in Table 2. The parameter development in terms of percentage change from initial values (%IV) for the 4 years following the SCI is expressed in Table 1 for the tibia.

Correlations between tibia bone parameter development and age, level of lesion and bone curve coefficient

No significant correlation was found between tibia bone parameter development and age, level of lesion and initial BMD value, respectively.

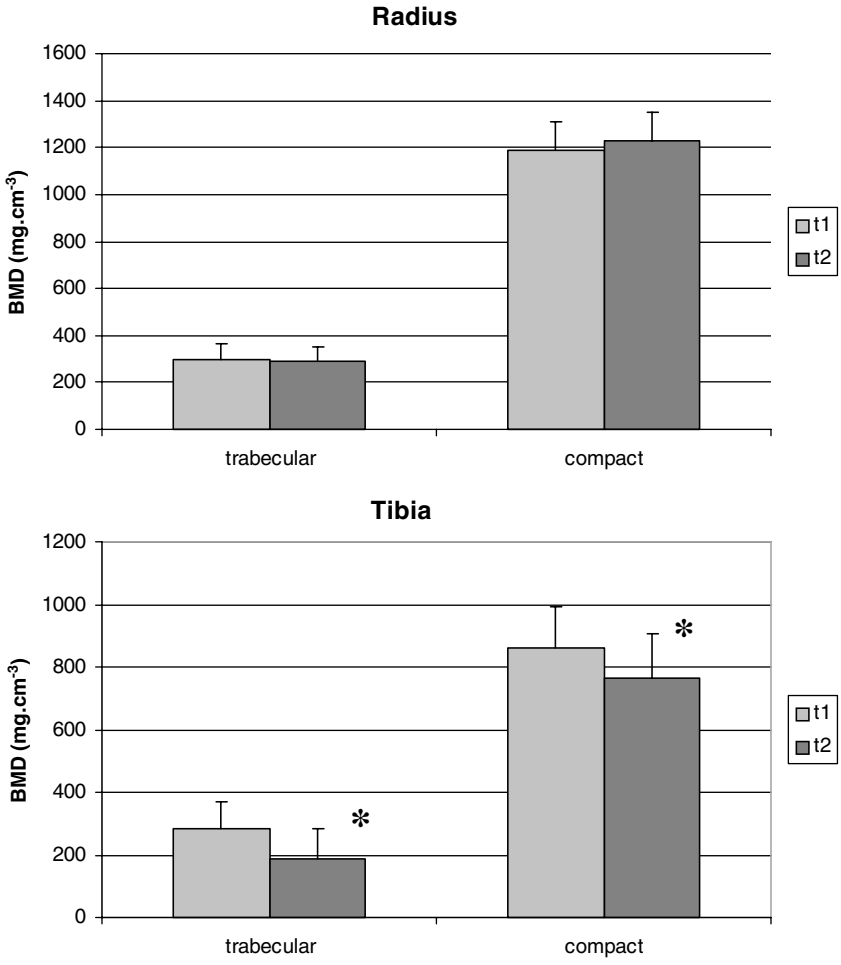

Figure 1 Radius trabecular and compact bone at time points t1 and t2 for the group of SCI subjects ($n = 10$). Tibia trabecular bone and compact bone at time points t1 and t2 for the group of SCI subjects ($n = 10$). *Signifies a significant difference ($P < 0.05$, paired t-test)

Discussion

The aim of this study was, firstly, to evaluate the changes in BMD following a SCI of more than 3 years duration using a pQCT scanner and, secondly, to explore individual differences in BMD changes following an SCI. To our knowledge, this is the first study that analyses the trabecular and compact bone parameters of a group of SCI individuals longitudinally for a period of more than 3 years.

Bone mass loss following the SCI may be expected to reduce bone strength. However, there seems to be a contradiction between the assumption that a steady state in bone formation is reached after 2 years following the SCI and the observation that fracture rate in SCI increases up to the third year onward after SCI. Within around $3\frac{1}{2}$ years following an SCI, a significant decrease of tibia trabecular bone and cortical bone was observed. There was no sign of a new steady state in bone formation in the lower extremity after 2 years following the SCI. The loss in trabecular and cortical bone within the first 2 years is in line with previously reported results.[9,10] However, the observed changes for the two bone parameters in this study reveal a large intersubject variability. Furthermore, some individuals showed BMD values during 4 years of SCI, which lie well above the initial values of other subjects. This finding infers the assumption that there might be a considerable individual variability in loss of bone substance following a traumatic SCI. Hence, it seems important to study responses in bone substance following an SCI in case study designs, since these designs may better reveal unusual or uncommon responses. In a mixed population of normal individuals and patients with osteopenia or osteoporosis, it has been possible to differentiate between fast and slow bone loser within a few months.[26] From the results of this study, it can be hypothesized that there are 'fast loser' and 'slow loser' individuals in a newly injured SCI population as well. Further research should substantiate this assumption and should determine the factors responsible for these differences in bone parameter development.

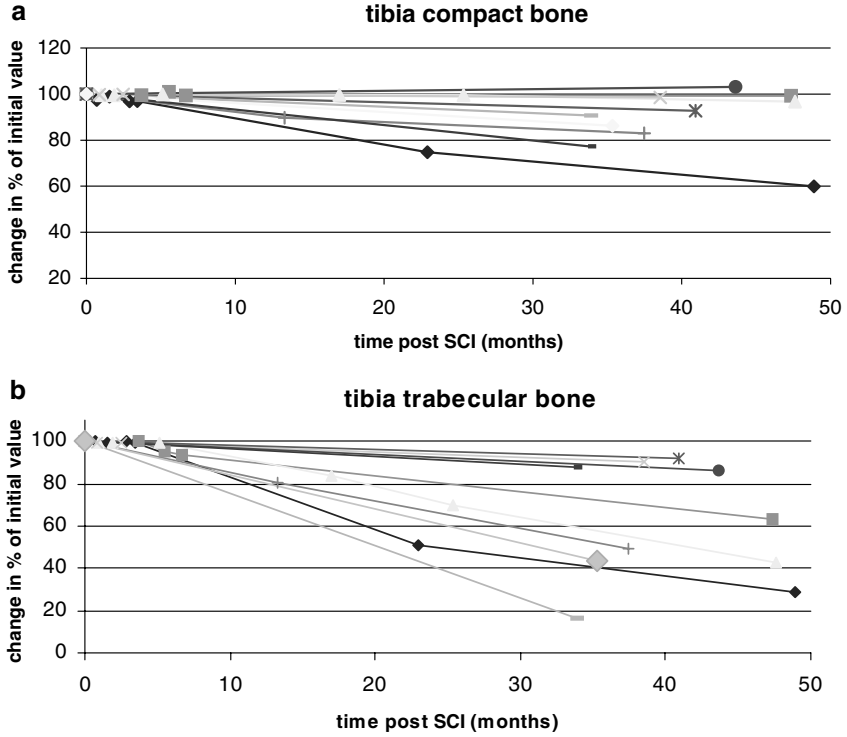

Figure 2 Tibia bone parameter development following SCI. (**a**) compact bone; (**b**) trabecular bone

Table 2 Absolute values for volumetric bone densitometry measurements (trabecular and compact bone; mg/cm^3) at time point t1 and t2

	Radius trabecular bone (mg/cm^3)		*Radius compact bone (mg/cm^3)*		*Tibia trabecular bone (mg/cm^3)*		*Tibia compact bone (mg/cm^3)*	
Subject	*t1*	*t2*	*t1*	*t2*	*t1*	*t2*	*t1*	*t2*
1	283	287	1332	1318	273	45	962	872
2	235	235	995	983	215	62	758	454
3	328	317	1171	1220	343	149	841	725
4	422	379	1392	1376	324	159	1113	923
5	277	282	1008	1025	347	147	771	746
6	265	268	1197	1206	238	150	789	783
7	316	311	1211	1168	296	259	882	682
8	155	177	1276	1335	154	133	654	674
9	359	365	1170	1190	347	313	957	943
10	325	323	1095	1063	372	343	893	828

The steepness of the loss of BMD does not correlate with the level of lesion, with the age or with the absolute initial BMD value of the subjects. This finding is at variance with previously reported results where moderate correlations between age and bone mineral density for three femoral sites were observed.[27] However, because of the large variance in the data for both ambulatory and SCI populations used in this cross-sectional study, it was difficult to discern with any certainty age or duration trends. Some prior cross-sectional studies have not demonstrated bone loss ongoing with chronic immobilization,[1,9,10] whereas several other studies suggest the opposite.[11,28–30] These results underpin the need for more longitudinal data, as in this study, for determination of true changes with time for individuals with a newly acquired SCI.

In our sample, we did not have a sufficient number of paraplegic and tetraplegic patients to statistically compare changes in BMD between these two groups. There was only one subject presenting with tetraplegia and we could, therefore, not expect a decrease of BMD with time after SCI at the radius. Some previous studies showed a fall in BMD of the upper extremity;[8,11] others did not observe any long-term changes in the upper

extremity bone substance.[5,9] A trabecular BMD loss following cervical SCI within 12 months of 28% and a cortical BMD loss of 3% following the SCI was reported for the radius. Subjects with paraplegia showed no loss in the upper extremity bone substance.[23] The results of the current study confirm these findings. Nine of the subjects under investigation in our study were paraplegic and did not show a loss in BMD in the upper extremity.

The relatively small sample size can be regarded as one of the limitations of this study. While we feel confident that the population is reasonably representative of the paraplegic SCI population at large, it might be necessary to recruit a broader population sample for more in depth investigation of the contributing factors that might influence bone mineral substance parameters following an SCI. These factors should additionally include gender, bodily conditions and body mass, habitual loading history, spasticity status and activity level.

In conclusion, we have longitudinally followed the changes in BMD in a cohort of patients with acute SCI, demonstrating large differences in change between subjects in the tibia. No changes in the radius were observed. Paired BMD measurements at the radius and tibia, performed on average 40 months apart, were sensitive in reflecting the changes in bone status.

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