Tibial bone density loss in spinal cord injured patients: Effects of FES exercise

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Abstract—A group of 37 spinal cord injured (SCI) patients underwent bone density measurements at the distal and proximal end of the tibia by a special computed tomography scanner, the OsteoQuant®. Fifteen of these patients had follow-up measurements while enrolled in a lower-limb exercise training program with functional electrical stimulation (FES). The pre-exercise measurements revealed a strong correlation (0.88 <r <0.90) of trabecular, subcortical, and cortical bone density between the distal and proximal ends of the tibia. The expected bone density loss during the first two years post injury (as calculated from the regression lines of bone density vs. time post injury) amounted to 51.5% for trabecular, 44.2% for subcortical, and 32.7% for cortical bone. No major bone density loss was calculated after 7 years post injury. Analysis of the bone density data during the FES exercise program revealed various degrees of loss. However, the rate of bone loss for this FES exercise group was less than expected from the regression lines. The reduction of bone loss was between 0.2 and 3.3% per year, and was significant (p<0.05) for all bone parameters at the distal end and for trabecular bone density at the proximal end of the tibia. These bone density measurements revealed a potentially positive effect of FES exercise intervention for the rehabilitation of SCI patients.

Key words: bone density, exercise, functional electrical stimulation, quantitative computed tomography, spinal cord injury.

INTRODUCTION

As early as the mid-1940s, clinical studies demonstrated that musculoskeletal disuse is associated with increased urinary calcium, and thus, a negative calcium balance (1). Subsequent bed rest studies investigating disuse identified the loss of bone density, assessed by direct bone measurements, as a major factor contributing to the negative calcium balance (2-4). The reduction of mechanical forces applied to the skeleton of spinal cord injured (SCI) patients and the resulting loss of bone mineral have been studied by several authors (5-9). Where bone measurements were part of the study (2-4,7,8), they included standard computed tomography (CT) applied to the cortical bone of the femur or dual-photon absorptiometry applied to the spine, the femoral neck, and the proximal end of the tibia. Whereas bone density in the lower extremities was consistently found to be lower as compared with normal controls, the mineral content of the spine was within normal range.

The effect of various types of exercises—functional electrical stimulation (FES) walking (7), weightbearing (8), tilt table (10), and FES knee extension and leg-cycle ergometry (11)—on bone in
SCI patients has been assessed in several studies with different outcomes. Two studies found a reduction in hypercalciuria (9) or increase in femoral cortical bone density (7) as a result of bone-loading exercise; two studies (8,11) found no effect of physical activity on the measured parameters, which included bone mineral content and density of the femur and tibia. These varied results may be due to differences in the bone density measurement techniques: CT (7) and dual-photon absorptiometry (8,11); the time since spinal cord injury; and the extent of bone loading by the particular exercise used. Thus, further study is needed to better understand the bone density loss in SCI patients and to determine how lower-limb FES exercise can alter this loss.

Therefore, the purpose of this study was to use a special CT scanner and SCI subjects to determine how bone density is lost in various compartments of the tibia (trabecular, subcompact, and compact bone) and to determine if bone loss can be reduced through lower-limb exercise induced by standardized FES. This article concentrates on reporting the results of the bone density measurements.

METHODS

Subjects

As part of the screening procedure for entry into FES exercise programs of the legs, 37 SCI patients underwent lower-limb bone density measurements. The subjects ranged between 19 and 64 years of age (median age, 32 years) and had sustained injury between 0.1 and 22.4 years ago (median, 4.3 years). Seven of the 37 subjects were females and ranged in age between 19 and 41 years. Five males were older than 40 years at the time of measurement. At the time of injury, the age range over the whole group was 17 to 49 years (median, 25 years) with 4 of the 5 males previously mentioned being older than 40 years.

Fifteen subjects entered the FES exercise program consisting of knee extension weight training and/or leg cycling. The selection criteria included appropriate muscle response to FES stimulation, no discomfort due to the stimulation, and availability for three stimulation sessions per week. These subjects had injury levels between C5 and T10. Six of these SCI subjects were classified as motor and sensory incomplete. At the time of injury, the age range was between 17.1 and 46.0 years, with only two subjects being older than 35 years (Table 1).

The medications taken by the subjects were mostly muscle relaxant and antispasmodic drugs, with some patients also taking urinary antibacterial agents, antidepressants, and stool softener, or medication to control hypertension or insomnia. None of the pharmaceutical agents is known to directly influence bone metabolism.

Protocol

Prior to participation, all 37 subjects signed a statement of informed consent as approved by the Institutional Review Board of Wright State University. Then, a special CT scanner (OsteoQuant®) was used to measure bone density in the tibia. The first 16 subjects had measurements at the distal end only, the subsequent 21 subjects also had bone density measured at the proximal end of the tibia. This measurement site was added in order to gain additional data close to the quadriceps muscle insertion points for those 15 subjects who were selected for the FES exercise programs.

Extensive medical screening was performed for each subject to identify any contraindications to participation in FES exercise. These medical evaluations included blood analysis, urinalysis, psychological and neurological testing, and X-rays of lower extremities and chest. In addition, a cardiologist conducted a detailed medical history and physical examination for each participant. Only those with medical clearance were allowed to participate in the study. Contraindications to participation in FES exercise included lower motoneuron involvement, previous lower extremity fracture, medical and/or psychological instability, and intolerance to electrical stimulation.

Two types of exercise programs were utilized: knee-extension resistance exercise (12) and leg cycle ergometry (13). A specially designed chair and electrical stimulator were utilized for FES-induced knee extension resistance exercise (KE). Surface electrodes were placed over motor points of the quadriceps muscles, and KE was alternated between legs at an average rate of 6 KE/min/leg. KE testing protocols were developed for pretraining and posttraining evaluations of performance using a progressive resistance load at ankle level (14).

The pretraining evaluation determined a “maximum” KE resistance load with which to begin
training. For this test, KE exercise was performed for five repetitions at each of several loads, starting with zero mass to be lifted and progressing in 0.5-kg increments to a maximum of 15 kg. The quadriceps muscles were considered fatigued when the KE failed to reach 50 percent of the 70° target angle. Since disuse osteoporosis that accompanies SCI may markedly decrease bone strength, the maximal mass was limited to 15 kg.

For the initial session a mass equal to one fourth of the maximal level achieved during pretesting was used for two sets of 30 repetitions of FES-KE exercise separated by a 5-minute rest. After another 5-minute rest, the mass was reduced by one half, and the exercise continued for 60 repetitions or to fatigue. When the subject was able to complete three consecutive sessions of this protocol, the mass to be lifted was increased by 0.5 kg for subsequent sessions. This progression was continued to a maximum 15-kg mass.

Leg cycle ergometry (LCE) took place on an ERGYS I (Therapeutic Technologies Inc., Tampa, FL) ergometer. Before FES-LCE exercise, surface electrodes were placed over motor points of the quadriceps, hamstring, and gluteal muscle groups. Electrical stimulation was provided by monophasic rectangular-wave pulses of 0.375-ms duration at a frequency of 35 Hz. Cyclic patterning of muscle contractions at a target pedaling cadence of 50 rpm was controlled by a microprocessor within the cycle ergometer. Maximal current was limited to 130 mA. Training session power output (PO) ranged from 0 W (no external resistance) to 30.6 W.

Each subject began training with no external flywheel resistance (0 W) on the LCE. During each
training session, the subjects were allowed three exercise bouts to achieve a total exercise duration of 30 minutes (10 minutes of rest were allowed between bouts). Training PO was increased by 6.1 W following completion of three consecutive training sessions consisting of 30 continuous minutes at the previous training PO. If 30 minutes had not been achieved after three exercise bouts, the PO was reduced by 6.1 W and a fourth exercise bout was performed to fatigue. If 5 minutes of continuous FES-LCE exercise could not be attained during the first exercise bout, the PO was immediately decreased by 6.1 W, and the previously described sequence was administered.

Both FES exercise programs were nominally 12 weeks in duration, and sessions were scheduled 3 times per week. If exercise sessions were missed due to illness, holidays, or other reasons, the duration of the program was extended until all 36 sessions were completed. The maximum time needed was 21 weeks; the median time was 14.5 weeks. In 90 percent of all cases the duration of the exercise programs was less than 16.5 weeks. After completing the initial exercise program, 9 of the 15 SCI individuals consented to remain active as research subjects and were started on additional 12-week exercise programs (see Table 1). KE was used exclusively for three subjects, LCE exclusively for nine subjects. The other three subjects started KE exercises for the first 12-week period and then switched to LCE exercises.

The physiological impact of the training was assessed by evaluation sessions scheduled before and after the training sessions. Most subjects underwent six evaluation sessions, also involving FES. The evaluation sessions were spread out over several weeks. The time interval between training sessions ranged from 2 to 8 weeks, the median being 5 weeks.

Bone density measurements in all subjects were performed before the start of the exercise program. Subjects who entered the exercise study had repeat bone measurements at the end of the exercise period. Four subjects underwent one additional measurement between exercise sessions; two subjects underwent two additional measurements. The measurement intervals were between 2.8 and 19.4 months. Half of the repeat measurements were performed at from 4.3- to 9.7-month intervals.

Bone Density Measurements

The bone density measurements were performed with an isotope-based (iodine-125) CT scanner, the OsteoQuant®. This scanner was specially designed and constructed in our laboratory to minimize the repeatability error associated with time-series measurements (15). Multiple slices were measured over the region of interest (ROI) 2 mm apart from each other. Each slice was evaluated separately by finding the outer contour of the bone. A certain number of pixel-wide shells were then removed until the boundary between cortical and trabecular bone was reached. The region between this boundary and the outer contour of the bone represents the area over which the averaged pixel values yielded the cortical bone density. From the intracortical boundary, a certain number of shells representing 20 percent of the cross-sectional bone area was removed and yielded the subcortical bone density. The remaining area represented trabecular bone density. The positioning of the slices at the very end of the tibia for the distal as well as for the proximal measurement site ensured that the trabecular bone represented about 60 to 70 percent of the total cross-sectional area of the bone. In the case of follow-up measurements at the same site, the ROIs remained constant for all sets of a given site. This was particularly important for the subcortical and cortical ROIs, where cortical thickness and bone density are subject to change. A change in measured density for these two compartments reflected the change in the amount of bone present, which is a combination of thickness and density. The typical volume of bone evaluated at the distal end of the tibia was $15 \text{ cm}^3$, whereas the volume at the proximal end was $30 \text{ cm}^3$.

Calibration data collected in house over the past 5 years in normal subjects of both sexes show a constant density for trabecular bone between ages 10 and 45, followed by a decline of about 1.4 percent per year. All subjects of the present study, with the exception of one (see Table 1), are below 40 years of age, well within the age range of constant bone density.

The in-vivo reproducibility of the scanner was tested by measuring six young nondisabled volunteers repeatedly over a 2-month period. Four sets of measurements were performed on each person at the distal end of the tibia. In addition, a water phantom was repeatedly measured over a 4-month period (82
occasions) to track the reliability of the scanner. This phantom reflects solely the performance of the scanner hardware without the influence of subject cooperation, diet and exercise, and operator interaction for the bone contour definition. A circular area in the center of the phantom served as the ROI for the evaluation of the water values.

Statistical Analysis

Pearson correlations were used to evaluate the relationships between bone parameters at distal and proximal measurement sites of the tibia. Least squares regression using the log of bone density versus the log of time post injury provided the best fit of the model $y = ax^b$.

To investigate the hypothesis that exercise reduces bone density loss, we converted bone density changes for each subject to percent change per year. Six subjects had additional bone measurements during the exercise period. The values calculated from these repeat measurements were examined and were similar to those calculated from the first measurements of all subjects. Thus, all of the data on percent changes per year were treated as independent and compared with zero using one-tailed, single-sample $t$-tests. For all tests, a 5 percent significance level was used.

RESULTS

Reproducibility of Bone Measurements

The measurements for each of the six nondisabled volunteers were expressed as a percentage change relative to the mean value of all four measurements for each bone parameter. The coefficients of variation (CV) for trabecular, subcortical, and cortical bone density in the distal end of the tibia are shown in Figure 1. The average CV for trabecular bone density was ±0.10 percent. For the subcortical bone density, the CV was ±0.37 percent; for the cortical bone density, it was ±0.58 percent. The water phantom values over a 90-day measurement period are shown in Figure 2. These measurements reflect the long-term stability and reliability for repeated measurements of the scanner and yielded a CV of ±0.033 percent. No trend of deviation from the calculated mean (at 0 percent) was visible.

Baseline Measurements

To obtain information about the bone density loss due to disuse for the SCI group as a whole, we first plotted the three bone parameters (cortical, subcortical, and trabecular bone density) for each of the two measurement sites (distal and proximal end of the tibia) against time since injury. (As an example, the subcortical bone density at the distal end of the tibia is shown in Figure 3.) A regression line of the form $y = ax^b$, with $x$ being the time since...
injury and y the bone density, was calculated for each bone parameter (Table 2). The p value in all cases is <0.001.

Based on the regression lines, we calculated the expected bone loss during the first 2 years and from 2 to 7 years post injury (Table 3). Due to the singularity of the regression lines at x = 0, the starting point was taken at 0.15 years post injury. Although the regression line shows a further slight reduction in bone density after 7 years post injury, this reduction is mainly induced by the mathematical form of the regression line. The actual data points appear to fit a horizontal line, indicating no further bone loss after 7 years postinjury.

There is a strong correlation of all bone density parameters between the distal and proximal measurement sites. Figure 4a shows the correlation of the subcortical density, and the correlation of the cross-sectional area is shown in Figure 4b. The results for regression and correlation of the bone density parameters are shown in Table 4. The bone densities at the proximal site are between 24 and 39 percent lower than at the distal site depending on ROI; conversely, the bone area at the proximal site is consistently almost twice as large as at the distal site.

### Table 2.
Change of bone density over time.

<table>
<thead>
<tr>
<th>Site/Region of Interest</th>
<th>a</th>
<th>b</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trabecular</td>
<td>0.273</td>
<td>-0.249</td>
<td>0.63</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subcortical</td>
<td>0.355</td>
<td>-0.190</td>
<td>0.67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cortical</td>
<td>0.574</td>
<td>-0.134</td>
<td>0.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proximal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trabecular</td>
<td>0.210</td>
<td>-0.249</td>
<td>0.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subcortical</td>
<td>0.304</td>
<td>-0.217</td>
<td>0.79</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cortical</td>
<td>0.472</td>
<td>-0.144</td>
<td>0.75</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Regression (a, b) and correlation (r, p) parameters for bone density (y) vs. time post injury (x) (y = ax^b) based on 37 measurements for the distal and 22 measurements for the proximal end of the tibia. All measurements were taken before the start of the FES exercise training. The r values are based on the log-transformed data.

### Table 3.
Expected bone loss in the tibia during the first 2 years and from 2 to 7 years postinjury.

<table>
<thead>
<tr>
<th>Bone Parameter</th>
<th>0-2 yr</th>
<th>2-7 yr</th>
<th>0-2 yr</th>
<th>2-7 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trabecular</td>
<td>51.5</td>
<td>14.1</td>
<td>51.4</td>
<td>14.1</td>
</tr>
<tr>
<td>Subcortical</td>
<td>41.9</td>
<td>12.9</td>
<td>46.4</td>
<td>13.6</td>
</tr>
<tr>
<td>Cortical</td>
<td>31.7</td>
<td>10.9</td>
<td>33.6</td>
<td>11.4</td>
</tr>
</tbody>
</table>

### Bone Density Changes During FES Exercise Training

The 15 subjects who entered the FES exercise training programs had from one to three follow-up bone measurements. To quantify the influence of the exercise frequency on the various bone parameters, we expressed the number of exercise and evaluation sessions between two successive bone measurements as an average number of exercise sessions per week. This allowed comparison of subjects with different measurement intervals. The difference in bone density between two measurement points, calculated as a percentage relative to the first of the two measurement points, was then plotted against the average exercise frequency. Because the measurement intervals varied considerably between subjects, all bone density changes were normalized to percent change per year. The various bone density parameters at both measurement sites show similar scatter plots as that for trabecular bone at the distal end of the tibia (Figure 5). Various degrees of loss
Figure 4.
Correlation of subcortical bone density (a) and cross-sectional area (b) between measurement sites at the distal and proximal end of the tibia before start of the FES exercise training for the subgroup (n = 21) who had measurements at distal and proximal end of the tibia.

Table 4.
Comparison of bone parameters.

<table>
<thead>
<tr>
<th>Region of Interest</th>
<th>Slope</th>
<th>Intercept</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trabecular</td>
<td>0.61</td>
<td>0.04</td>
<td>0.88</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subcortical</td>
<td>0.76</td>
<td>0.04</td>
<td>0.90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cortical</td>
<td>0.73</td>
<td>0.07</td>
<td>0.88</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Area</td>
<td>1.98</td>
<td>2.68</td>
<td>0.85</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Regression lines (slope, intercept) and correlations (r, p) for bone density parameters and cross-sectional area of proximal (y) vs. distal (x) measurement site in tibia.

Figure 5.
Change of trabecular bone density at the distal end of the tibia during the FES exercise programs. The data are normalized to percent change per year and are plotted against exercise frequency. Subjects who underwent more than one exercise program are represented with multiple data points.

are observed; however, they are not statistically significant with the exception of the loss in the trabecular bone at the distal end of the tibia. The measured bone density changes do not appear to depend on the exercise frequency.

Adjusted Bone Density Changes During FES Exercise Training

The previously described representation of bone density changes can potentially lead to erroneous conclusions. If long-term SCI patients (e.g., >7 years post injury) show stable bone density under exercise training conditions, they probably would have been stable also without exercise due to the long time since injury, particularly if age-dependent bone loss has not started yet. However, if a recently injured patient shows a decrease in bone density under the same exercise training conditions, the bone loss may be less than in the case where no exercise occurred (Figure 6). Therefore, a meaningful evaluation of the bone density data needs to compare the actual change in bone density with the expected change without exercise.

In the present FES exercise programs, it is not possible to obtain data with and without exercise in the same patient over the same time period. It appears that the next best estimate for bone density loss without exercise is available from the regression lines of the pre-exercise baseline measurements. The assumption is made that the bone loss without
Figure 6.
Actual (pairs of points connected with straight lines) and expected (exponential curve) bone density loss at two different time points post injury in a hypothetical patient. An SCI patient with some bone loss a short time after injury may show a positive difference (+d) between actual and expected loss and therefore a considerable effect of exercise. In contrast, a patient with very little change in bone density many years after injury will show no effect of exercise.

exercise can be estimated from these curves. Whereas the pre-exercise measurement, in most cases, will not coincide with the regression lines, the percentage loss over a given time interval removes the offset uncertainty of the regression line. The difference between expected bone density loss and actual change in bone density for the FES exercise group (see Figure 6) was calculated for all bone parameters at both measurement sites. As an example, Figure 7 shows this calculated change in bone density loss for the trabecular bone at the distal end of the tibia. (These are the same data points as previously shown in Figure 5.) Using this technique, there appears to be no dependence of change in bone density loss on exercise frequency for any of the bone density parameters. The average change of loss for each parameter is shown in Figure 8. The significance of these loss changes was evaluated with one-tailed t-tests and is significantly positive for all bone parameters at the distal end and for trabecular bone density at the proximal end of the tibia. For these significant parameters (Figure 8), the reduction in bone loss for the FES exercise group is between 1.7 percent per year for compact bone at the distal and 3.3 percent per year for trabecular bone at the proximal end of the tibia, with a tendency toward higher changes for trabecular bone density, less for subcortical, and least for cortical bone density.

Figure 7.
Change in loss of trabecular bone density at the distal end of the tibia as a function of FES exercise frequency. The change in loss is the difference between actual loss and expected loss as calculated from the group pre-exercise data. The same data points as in Figure 5 are represented here.

Figure 8.
Average change of bone density loss across the whole SCI group for each bone parameter measured. The significance levels are *p <0.05, **p <0.01, and ***p <0.005.

DISCUSSION

The in-vivo reproducibility measurements for trabecular bone density in the tibia measured by the OsteoQuant® show an error that is about one order of magnitude smaller than that achieved by trabecular bone density measurements in the spine measured by commercial CT scanners (16). CT is the only method currently available that can give separate information about trabecular, subcortical, and cortical bone densities. To date, commercial CT
scanners have been used successfully only for the spine but not for the extremities. The OsteoQuant® is able to measure bone density of the extremities at a high precision. Other methods for measuring bone density in the extremities (radiodensitometry, single- and dual-energy absorptiometry) are based on projections (16). This precludes the separation of the various bone compartments.

Bone density versus time since injury for our 37 SCI subjects, as graphically illustrated with the subcortical bone density of the distal end of the tibia (see Figure 3), show a fairly large scatter of the points about the regression line. This is indicative of the considerable heterogeneity within this SCI patient group. Although the expected bone density pre-injury is probably distributed in a normal fashion around the peak bone density (age range: 17-49 years with four males over 40 years), the actual loss post injury most likely depends greatly on the individual’s level of spasticity, activity, diet, and lifestyle. For the group as a whole, the correlation coefficients for the various regression lines of bone density versus time since injury are highly significant ($p<0.001$). This allowed us to calculate the expected loss of the bone density parameters over several time intervals post injury (see Table 3). The loss of trabecular bone density is about 70 percent by 7 years post injury. This has some far-reaching impact on bone strength. Based on measurements by Carter and Hayes (17), bone strength(s) is proportional to the density ($\rho$) squared: $s \propto \rho^2$. A loss of 70 percent of bone density will reduce the strength to $0.3^2 = 0.09$ of the original strength. As strain and stress are linearly related in the elastic range, and strength is the stress at failure, we can assume that the strain at failure is also reduced by a factor of 0.09. A reasonable estimate for strain at failure for normal trabecular bone is 0.025 (18). Normally occurring strains rarely exceed 0.002 (19). The strain at failure of trabecular bone with only 30 percent of material left would be reduced to $0.09 \times 0.0025 = 0.0023$. This figure comes close to the normally occurring strains of 0.002. It is likely, therefore, that 30 percent of bone is barely sufficient to support the weight of the body this many years after injury. Loading of the legs through standing, walking, or other forms of rehabilitation therapy at this time needs to proceed with utmost caution. It may be more realistic to prevent such a loss with FES or other weightbearing or resistance exercises introduced early in the rehabilitation process rather than to attempt reversal of the severe osteoporosis that tends to occur later.

The correlation of bone parameters between the distal and proximal measurement site (see Table 4) is quite striking. Not only are the correlation coefficients higher than those seen in nondisabled people between radius and spine [$r = 0.42 \ldots 0.70$ (20-25)], hip and spine [$r = 0.27 \ldots 0.72$ (23-25)], and hip and radius [$r = 0.40 \ldots 0.44$ (23-25)], but they are based on measurements performed at various times post injury. Therefore, it is clear that the bone loss at the distal site of the tibia closely tracks bone loss at the proximal site. This is also reflected by the density loss data (see Table 2) in which the three bone compartments show very similar losses at the distal and proximal sites.

The inverse relationship of bone density (higher at distal site) and cross-sectional bone area (lower at distal site) between the distal and proximal measurement sites highlights the biomechanical principle of “roughly constant strength” along a bone. According to the simplified assumption that the amount of bone in a certain cross-sectional area directly relates to bone strength, it can be understood that the bone density at the site with the larger cross-sectional area is smaller because the bone material is distributed over a larger area. Due to the thinness of the cortices at both ends of the tibia, the strength of the bone is mainly defined by the trabecular bone.

The evaluation of the effect of FES exercise on bone density depended on the assumption that the bone loss without exercise can be predicted based on the regression lines. Although this prediction may be associated with a considerable error for each individual subject, the group as a whole is likely to follow the regression line. It is for the same reason that the potentially beneficial effect of FES exercise on reducing bone loss can better be demonstrated for the group as a whole than for an individual subject.

Although the regression lines are the best estimates available to us about bone loss over time, it is legitimate to ask how well they reflect the actual bone loss. When the measurements of the first 14 subjects were analyzed for a preliminary evaluation (26), the regression coefficients for trabecular bone density at the distal end of the tibia were $a = 0.356$ and $b = -0.308$. Based on this regression curve, the bone loss over 6 months at 5 years post injury (the
The average bone density (0.0063 g/cm³) for our subject group is lower than that calculated with the regression coefficients of Table 2 (0.0043 g/cm³). The difference of 0.0020 g/cm³ represents only 1 percent relative to an average bone density of 0.20 g/cm³ as encountered in our subject group. Expressed as change over one year rather than 6 months, a 2 percent difference would be calculated. This is small relative to the changes shown in Figure 7. It appears, therefore, that the process of estimating bone loss from the regression lines is fairly robust. Nevertheless, the use of 37 subjects for calculation of the regression lines provides a considerably higher confidence level than using only 14 subjects.

The bone density data as plotted versus time since injury appear to level off after 7 years post injury. Based on the nature of the regression line, a small loss could still be calculated in that time frame. For practical purposes, all expected bone losses as presented here were based on the regression equation. It can be shown, however, that using 0.0 g/cm³ for the expected change after 7 years post injury reduces the change of loss (see Figure 7) in the relevant subjects by 0.01 to 0.03 percent. This is negligible compared with the actual changes calculated.

The variable time periods between bone measurements may appear to represent a problem for evaluating and interpreting the data. However, the representation of the data as bone density change per year normalizes the measured variable, whereas the expression of the exercise parameter as number of exercise sessions per week takes care of the variability in exercise frequency. The important aspect is that none of the subjects remained sedentary longer than one cycle of the bone remodeling system. In normal, nondisabled people, the time it takes for the skeleton to go through one remodeling cycle is approximately 90 days (27). None of the exercise periods were more than 8 weeks (55 days) apart from each other, and the 6 evaluation sessions involving FES took place during this period.

FES exercise training in this study did not increase bone density (see Figure 5); however, it does appear to reduce the rate of bone loss (see Figure 7) compared with the expected loss from the SCI group data. The amount of local bone stresses induced through the KE and LCE protocols used here were probably too small to generate a marked increase in bone density. However, they were apparently large enough to reduce the expected loss of bone. This is more evident at the distal site than at the proximal one. A possible explanation could be the different magnitude of stresses that acted on the two sites with the exercise modes used. If we take the simple case of weightbearing, approximately the same weight is borne by the proximal and distal end of the tibia. Through the difference in cross-sectional area of the bone, the force per unit of cross-sectional area (i.e., the stress) is larger at the distal than at the proximal end. This difference in local stresses could potentially have caused the difference in the observed bone density effects.

It is also notable that trabecular bone appeared to respond to FES exercise training to a larger extent than cortical bone. It is known that the two types of bone undergo turnover processes in distinctly different ways. Whereas cortical bone turns over by the tunneling process that leads to the creation of the Haversian system, trabecular bone turns over through minute remodeling sites created at the surface of the trabeculae (27). Since the trabecular surface is very large, many opportunities for trabecular turnover processes are available. This, in turn, may lead to a faster and more profound response of trabecular bone to metabolic or physical stimuli.

The lack of a relationship between bone density changes and FES exercise frequency can be interpreted in two different ways. Either there is indeed no dependence over the one to three exercise sessions per week, which would point to the possibility that even a small amount of exercise, such as 1 hour per week, is sufficient to reduce bone loss; or, the dependence upon the nature of the exercise used is so small that the limited number of data points cannot discern that dependence from the noise of the data.

The study by Biering-Sorensen, et al. (8) involving weightbearing exercises found the bone mineral content in the femoral shaft, as measured by dual-photon absorptiometry, to be less reduced compared with normal values than the mineral content at the proximal end of the tibia. The patient sample included 26 individuals who had sustained spinal cord lesions from 2 to 25 years prior to the measurements. These results are quite consistent with our own findings. The femoral shaft represents mostly cortical bone, whereas the proximal end of the tibia includes a considerable amount of...
trabecular bone. We found that trabecular bone was lost 1.5 times faster than cortical bone. Their findings concluded that trabecular bone was lost 2.0 times faster than compact bone. They also indicated that their patients who used long leg braces on a daily basis did not appear to have increased bone density. However, this conclusion was based on single measurements and not on multiple follow-ups.

Another study on SCI patients (7) involved cortical bone measurements at the midpoint of the femur by commercial CT. Comparisons were made among small groups of normal controls, SCI patients without exercise, and SCI patients in an FES-supported walking program. The cortical density of the FES exercise group was found to be between that of the nondisabled controls and the nonexercising SCI patients. Since no characterization of the patient groups regarding time since injury was given and since no follow-up measurements were performed, detailed comparison with our findings is difficult.

In summary, our SCI subjects demonstrated a strong correlation of trabecular, subcortical, and cortical bone density as well as cross-sectional bone area between the distal and proximal end of the tibia. Because the bone measurements were obtained at a wide range of times post injury, this correlation also supports a close similarity of the loss patterns at both sites. The pre-exercise measurements allowed the calculation of an expected bone loss curve. Both sites showed similar loss figures for the respective bone compartments, amounting to an average loss in the first two years post injury of 51.5 percent for trabecular, 44.2 percent for subcortical, and 32.7 percent for cortical bone density. The follow-up measurements during FES exercise training showed the importance of comparing the measured bone density changes with the expected changes during the same time interval. This analysis revealed the potentially positive influence of FES training on reducing the expected rate of bone loss.

REFERENCES


