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A validity study of phase velocity measurements in spinal cord injury

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Abstract—We measured a cross-section of able-bodied (AB) men (n = 175) and men with chronic spinal cord injury (SCI) (n = 33) residing in the community, 14 to 65 years old, to identify associations between dietary factors, physical activity, health status, and mechanical properties of long bones assessed by phase velocity measurement of flexural waves in the tibia during the second to seventh decades. This study (1) evaluated the influence of different types of osteoporosis risk factors on measured phase velocity of tibia bone as measured by Bone Stiffness Measurement Device (BSMD)-Swing in AB men and in men with long-standing SCI and (2) estimated the construct validity of phase velocity measurements by assessing the discriminatory capability of the BSMD-Swing. Linear regression analysis suggests a direct relationship between health status, tibia length, age, and phase velocity (R^2 = 23%). An analysis of variance results in significant differences in phase velocity values between AB controls and individuals with SCI with and without pathologic fracture history. Phase velocity measurements in the tibia shaft provide useful information about bone status in populations at risk for low-trauma fractures and seems well suited for assessing tibia bone status in SCI.

Key words: bone, flexural waves, phase velocity, physical activity, osteoporosis, spinal cord injury, validity.

INTRODUCTION

One of the possible clinical effects of changes in bone following spinal cord injury (SCI) is the occurrence of *pathologic* fractures of lower-limb long bones. These pathologic fractures occur in 2 to 6 percent of paraplegic patients [1–3]. A general perception exists that long bone fractures subsequent to SCI are becoming more common and that the management of these fractures will be increasingly important in rehabilitation medicine of the future [4]. Therefore, the mechanical properties of cortical bone are important for the maintenance of bone integrity, which has implications for the management of skeletal diseases such as osteoporosis in SCI. Osteoporosis is associated with a decrease in bone mass and deterioration in mechanical competence, a consequence of which is fracture from low-trauma falls [5]. In SCI, current diagnostic tests frequently fail to tell us what we want to know: does the tested person belong to the group of patients who will potentially develop a pathologic fracture?

Abbreviations: AB = able-bodied, AI = activity index, ANOVA = analysis of variance, BMC = bone mineral content, BMD = bone mineral density, BMI = body mass index, BSMD = Bone Stiffness Measurement Device, DEXA = dual-energy X-ray absorptiometry, PVT = phase velocity of the tibia, SCI = spinal cord injury, SD = standard deviation.

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Previous in vivo studies have mainly been concerned with bone density changes in relation to the time post-injury and the change in lifestyle rather than with changes in the mechanical properties of bone. Dual-energy X-ray absorptiometry (DEXA) has been used to establish the changes in bone mineral composition, allowing quantification of bone mineral density (BMD) (g/cm^2) and bone mineral content (BMC) (g) at specific sites of the body. However, the use of DEXA in following changes in bone mineral in SCI patients in their acute period of injury is limited since SCI patients have restricted mobility [6]. Furthermore, BMD explains only about 58 percent to 85 percent of the variance of strength (the ability to withstand an applied load [7]), which indicates that bone strength may depend on other parameters such as bone geometry and state of remodeling [8–9].

Wolff synthesized many of the prevalent ideas about bone physiology in 1870 with the formulation of Wolff's law: Bone remodels in response to the mechanical demands placed upon it; that is, bone is laid down when needed and resorbed where not needed [10]. Since specific forms of stress are not the only factor that determine bone growth, Nigg and Herzog suggested that Wolff's law of functional adaptation of bone should be adapted and could be worded as, "physical laws are a major factor influencing bone modeling and remodeling [11]." Mechanical loading determines growth, total bone mass, and functional capacity of the skeleton.

The functional capacity of bone is also expressed by the geometry, which relates to the distribution of the tissue composite in the bone [12]. Decline in skeletal mass makes the skeleton susceptible to fractures. In fact, the loss with age of the biomechanical strength of bone is more pronounced than the loss of bone mass, and at any given age, there is greater interindividual variation in the mechanical properties of bone than in the bone mass [13]. Hence, the development of clinically relevant testing methods for the mechanical properties of bone is important [14].

Wong et al. demonstrated that a relationship exists between bone loss and decrease in the velocity of elastic waves, which in turn is related to the osteoporosis index [15]. Flynn et al. assessed an at-risk group for tibia stress fractures and, for that reason, explored the associations between tibia bone quality as estimated by tibia flexural wave propagation velocity and subject characteristics [16]. The validity of the relationship between mechanical properties of human tibia bone and flexural wave velocity measurements in vitro was assessed by Bischof [17]. Bending stiffness for 21 tibias was measured with the use of three-point bending tests and was compared to calculated bending stiffness from phase velocity and area moment of inertia of tibia bone. The result was a very good correlation ($r = 0.93$) [17]. Results from an in vivo assessment of the bending stiffness of human tibias with a Bone Stiffness Measurement Device (BSMD)-Swing demonstrate dissociation in reaction between changes in mechanical properties of long bones and bone mineral development [18–19].

The physiologic background of the BSMD-Swing is based on the analysis of waves propagating in the tibia. Different types of waves can propagate along bars—e.g., longitudinal, torsional, and flexural waves and waves of higher order with changes in the cross-section of the bar [20]. The propagation of any wave type can be represented by the dispersion relation that describes the phase velocity of this wave as a function of the frequency or wave length. Flexural wave propagation velocity in the tibia bone estimates bending stiffness and ultimate fracture strength [21]. The measurement is based on elasticity theory, with the use of vibrational wave propagation to provide an in vivo measurement of the structural and mechanical properties of bone. Bischof showed that it is possible to measure the phase velocity of flexural waves in the shaft of tibia bone with accelerometers [17]. Together with information on the geometry of the measured structure, this capability leads to the possibility to calculate the properties of the structure in bending. The phase velocity of bending waves was calculated from signals derived from two accelerometers, with a defined distance between them, attached to the wave-conducting structure. With the use of a fast Fourier transform, the phase difference of the signals between the two accelerometers then was calculated [20].

We hypothesize that the BSMD-Swing, which at present is not commercially available, could potentially be clinically valuable in populations at risk for developing fractures in long bones.

Hence, with this study we investigated the validity of BSMD-Swing measurements in a clinical population. We followed previously published guidelines with recommendations for the design and statistical analysis of assessment studies of new diagnostic tests. The first phase of an assessment study should be performed in an easily accessible population, for instance, a population of diagnosed patients and healthy individuals [22].

The following research question guided the study: Do measurements of phase velocity propagation with the BSMD-Swing result in different values for able-bodied (AB) subjects and subjects with SCI with and without pathologic fracture history?

MATERIALS AND METHODS

Subjects and Experimental Procedure

We conducted measurements on 175 AB men without known orthopedic or neurological impairments, residents of the greater Zürich area between 14 and 60 years of age. In addition, 33 men with chronic SCI (injury for 2 or more years), registered at the Swiss Paraplegic Center Nottwil (Nottwil, Switzerland), were included in the study. None of the subjects were under medication or treatment for osteoporosis in either of the groups. All SCI subjects were wheelchair-dependent. The neurological level of the lesion ranged from C4 to L2. Five subjects with tetraplegia (C2–Th1) had neurologically incomplete lesions (modified American Spinal Injury Association [ASIA] impairment scale: A [n = 27], B [n = 4], and C [n = 2]). The number of SCI subjects specified by the neurological level of the lesion and the pathologic fracture history are given in **Tables 1** and **2**.

Before participating in the study, subjects received oral and written information about the research and were asked to sign an informed consent as approved by the institutional review board of the paraplegic center. After we received informed consent, we measured the right leg of each subject according to previously described methods [23]. The left leg was measured if a proximal or midshaft fracture in the right tibia had occurred previously.

Phase Velocity Measurements

The BSMD-Swing device comprises a handheld electromechanical hammer, a shin-mounted receiver assembly containing eight piezoelectric quartz accelerometers (Kistler Piezotron, Amherst, NY), and a personal computer containing the dedicated BSMD software on the hard disk. A prototype of the BSMD-Swing was used in this study. Menu-driven software (written in BORLAND C) presents test protocols to the measuring clinician and provides feedback about measurement conditions and measurement results on the computer screen. The phase velocity is calculated from eight accelerometers that are pressed against the tibia. The flexural wave is produced by a mechanical impact comparable to that of a patellar tendon reflex test. **Figure 1** shows the configuration of the hardware and a schematic operational configuration for a BSMD-Swing measurement. Resulting phase velocity values are expressed in $m \cdot s^{-1}$. A more detailed description of the device can be found elsewhere [17–19,21–24].

Background Information

Participating subjects completed a self-administered questionnaire in order to quantify the potential risk factors that might contribute to changes in mechanical bone properties. Several variables previously identified to be related to lower-limb fracture risk [25] were included in the questionnaire. Information regarding habitual physical activity, daily physical activity, diet, smoking and drinking habits, and medication was collected by interview before the measurement and checked at a second interview after the actual measurements. The variables include self-reported data on age at baseline (in years), previous lower-limb fractures (none/one or more), smoking status (according to a smoking index), alcohol and caffeine consumption in the past year (none or low/moderate/high), physical activity in relation to profession (none or low/moderate/high), recreational physical activity (none or

Table 1.
Characteristics of subjects with chronic spinal cord injury (SCI) specified by anatomical level of lesion and history of limb fracture. Mean time ± standard deviation since injury that caused SCI for those without fracture history is 13.6 ± 9.6 years and 20.1 ± 4.8 years for those with fracture history. Two SCI groups did not differ regarding mean duration of their SCI (p = 0.07).

Anatomical Level of Lesion	History of Limb Fracture	C5–C8	Th1–Th10	Th11–L2	Total
Neurologically Complete	No limb fracture history	3	12	3	18
	With limb fracture history	—	6	3	9
Neurologically Incomplete	No limb fracture history	3	1	—	4
	With limb fracture history	1	—	1	2
Total	—	7	19	7	33

Table 2.
Neurological level of lesion, Frankel classification, fracture site(s), and history for chronic SCI with pathological fracture history (SCI-Fx) group.

SCI-Fx Subject	Neurological Level of Lesion/Frankel Classification	Time Between Fx and SCI (yr)	Bone Fractured	Cause of Fx
1	T4/A	2	Left tibia; left & right femur	Fall out of wheelchair
		14	Left femur	Ranging exercise of left knee joint
2	T4/A	8	Left tibia	Unknown to patient
		12	Right femur	Transfer from wheelchair into bed
3	T12/A	4	Right femur	Fall out of wheelchair
		10	Distal femur (left & right)	Sliding forward out of wheelchair onto knees
4	T1/A	21	Left distal femur/Proximal tibia	Fall out of standing frame
		23	Left tibia	Fall out of wheelchair
		28	Left femur	Trying to change from lying to sitting while legs were crossed
5	C7/C	6	Right femur (distal)	Fall out of wheelchair
		8	Right femur	Transfer from car into wheelchair
		20	Left femur	Fall out of wheelchair
6	T8/A	5	Right femur	Unknown, discovered by PT during ranging exercises
7	T8/A	13	Right tibia (proximal)	Transfer into car
		14	Left tibia (distal)	Putting on a compression hose
8	L2/A	16	Right femur	Bending forward with the upper-body while legs were crossed
9	T10–11/A	10	Right tibia	Fall out of wheelchair
10	L1/A	8	Right femur	Transfer from car to wheelchair
		14	Left femur	Fall out of wheelchair
		14	Left femur/Right tibia	Fall out of wheelchair
11	T11/A	7	Right femur	Fall out of wheelchair

SCI = spinal cord injury Fx = fracture PT = physical therapist

low/moderate/high), chronic disease in family or disabling status prevalence (diabetes, osteoporosis, SCI; yes/no), and ratio of calcium-to-phosphorus intake (low/moderate/high).

A smoking index based on the number of years of habitual smoking × number of packs smoked per day × 365 was used as an indicator of a lifelong smoking habit [26]. Alcohol consumption was defined by the number of alcohol-containing beverages consumed: none/low = none or less than one beverage per week, moderate = one to six beverages per week, and high = one or more beverages per day. Caffeine consumption was defined by the number of caffeine-containing beverages (coffee, cola, tea) consumed: none/low = none or less than one beverage per day, moderate = fewer than five beverages per day, and high = five or more beverages per day. Physical activity in relation to profession was defined as low = mainly desk work, moderate = light physical activity, and high = physically demanding work. Recreational physical activity was defined as none/low = no physical demanding activities in leisure time, moderate = several hours of moderate physical activities (sports, housekeeping) per week, high = competitive sports activities or regular physical performance training. Individually initiated activities in SCI subjects, such as outdoor arm-crank training, were also included as sport activity. Physical activity history was defined in the same manner for all subjects and summarized to an overall physical activity index (AI). The chronic disease variable in relation to diabetes and osteoporosis prevalence was based on self-reported doctors' diagnoses.

For the SCI subjects, health status including use of medication, the neurological level of the lesion, and pathologic fracture history was assessed by a physician during an ambulatory visit to the paraplegic center. We studied the reliability and validity of the self-administered questionnaires of the SCI subjects by analyzing the level of agreement between the self reports and X-ray and medical records at the health center of the Swiss Paraplegic Center Nottwil.

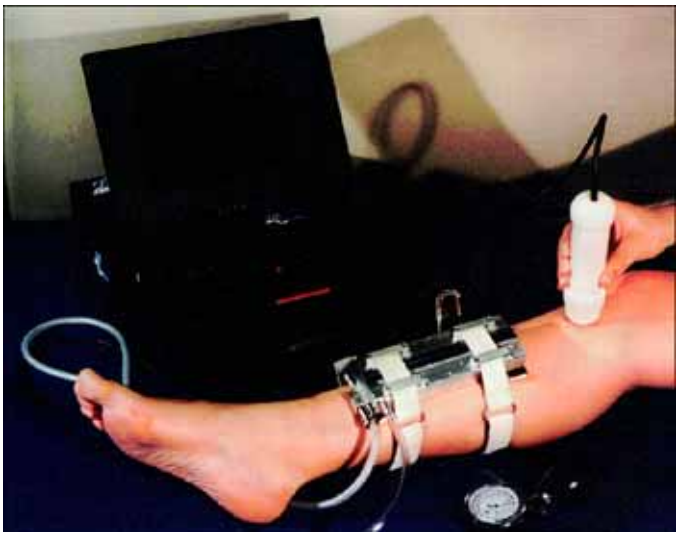

Figure 1.
Bone Stiffness Measurement Device-Swing. Support computer containing control unit is shown in background. Receiver assembly with eight accelerometers is mounted on shin of test subject. Test subject is holding hammer, which gives mechanical impact on head of tibial bone, which, in turn, produces flexural wave.

We used standard methods to measure body height and body weight. Body mass index (BMI) was calculated by equation: BMI = body weight (kg)/(body height (m))^2. Tibia length was measured as the distance between the medial knee joint cleft and the lower border of the medial malleolus. Tibia width at diaphysis was measured at the mid-point of tibia length with a vernier caliper. The amount of soft-tissue overlying the facies medialis at the mid-point of tibia was measured in millimeters with the caliper (Laboratory for Biomechanics, Swiss Federal Institute of Technology, Zurich, Switzerland). We deducted the mean of three soft-tissue measurements from the measured tibia width.

Validity and Statistical Analysis

We made statistical comparisons for lower-limb fracture risk factors between AB and SCI using Kruskal-Wallis-type χ^2 statistics (**Table 3**). The SYSTAT 7.0 program for personal computers (SSPS Inc., Chicago, IL) was used for all statistical procedures. For all tests, a significance level of $p \leq 0.05$ was chosen unless otherwise indicated.

In this study, we assessed in an easily accessible SCI population to determine the validity of phase velocity measurements in vivo. At this point, we are not concerned with the occurrence of selection bias [22]. In this

Table 3.
Descriptive statistics of study population for lower-limb risk factor characteristics in able-bodied (AB) and spinal cord injured (SCI) men aged 14 to 65 years.

Baseline Characteristic	AB (n = 175)	SCI (n = 33)	p-Value*
Phase Velocity (m•s^{-1})	463.9 ± 32.0	426.8 ± 50.0	<0.01
Age at Baseline (yr)	31.3 ± 12.2	38.2 ± 11.7	<0.01
Weight (kg)	74.4 ± 10.5	67.9 ± 10.6	0.01
Height (cm)	178.8 ± 6.4	176.6 ± 6.6	0.16
Body Mass Index (kg/m^2)	23.2 ± 3.5	21.8 ± 3.5	0.07
Smoking Index	910.3 ± 2588.3	2020.3 ± 3052.6	<0.01
Alcohol Consumption (mean of defined groups)	1.8 ± 0.7	2.9 ± 0.5	<0.01
Activity Index (mean of the sum of defined groups)	5.4 ± 1.4	6.2 ± 2.0	0.01
Diabetes (mean of defined groups)	1.2 ± 0.6	1.2 ± 0.5	0.92
Osteoporosis (mean of defined groups)	1.1 ± 0.6	1.0 ± 0.3	0.27
Caffeine (mean of defined groups)	3.3 ± 0.8	3.0 ± 0.7	0.09
Calcium-to-Phosphorus Ratio	3.0 ± 1.2	2.5 ± 0.8	0.06

Note: Values are given in mean ± standard deviation. *Kruskal-Wallis one-way analysis of variance ($p < 0.05$)

phase of diagnostic test assessment, we are interested in measurable differences between healthy controls and subjects with disease symptoms. The main purpose in developing the BSMD-Swing method was to diagnose "at-risk" groups for osteopenia following SCI. To investigate the influence of subject characteristics and behavioral factors on the measured phase velocity, we applied stepwise multiple regression analysis, using the model

Measured phase velocity of the tibia (PVT) = constant + HS + Age + BMI + CP + Diab + KO + Ost + SI + AI + Alk + TWR + TLR + *e*,

where PVT = the phase velocity measured and calculated from eight accelerometers that were pressed against the tibia ($m \cdot s^{-1}$), HS = health status (AB or SCI), BMI = body mass index, CP = calcium-to-phosphorus ratio, Diab = family history of diabetes, KO = caffeine consumption, Ost = family history of osteoporosis, SI = smoking index, AI = activity index, Alk = alcohol consumption, TWR = width of right leg tibia, and TLR = length of right leg tibia. The error term (*e*) consists of measurement errors, subject-specific effects such as genetics and BMD, and environmental factors not investigated in the present study. Using this model, we assumed that *e* was not correlated with any of the explanatory variables.

To determine whether men with SCI have lower values of PVT, we qualitatively compared the results with the data from the AB population. Three groups were defined: (1) AB controls, or "AB" (n = 175); (2) chronic SCI without pathologic fracture history, or "SCI" (n = 22); (3) chronic SCI with pathologic fracture history, or "SCI-Fx" (n = 11). We applied a one-way analysis of variance (ANOVA) to detect differences among AB, SCI, and SCI-Fx group means in measured PVT. We also estimated the ability of the test to measure differences between AB controls and the two groups of subjects with chronic SCI with an analysis of covariance, with age as the covariant. The effect of age needed to be considered, given the evidence in the literature that age might have an influence on bone mechanical properties [16]. In AB men, age-related changes in cross-sectional geometry appear to compensate for age reductions in bone strength [26]. We used Tukey's post hoc procedure for paired comparisons when the ANOVA yielded significant results.

RESULTS

Table 3 shows the distribution of baseline characteristics of the AB and SCI subjects. We found no significant differences between the two groups in body height, body mass index, family history of diabetes and osteoporosis, caffeine consumption, and calcium-to-phosphorus intake. Measured phase velocity and body weight were significantly lower in SCI, whereas age, smoking index, alcohol consumption, and AI were significantly higher in this group.

Results of the developed regression analysis model, investigating the influence of subject characteristics and behavioral factors (including sports activity) on the measured phase velocity, suggests a direct relationship between health status ($p < 0.0001$), tibia length ($p = 0.0001$), and age ($p = 0.0849$) and the measured phase velocity ($R^2 = 23\%$).

Mean time ± standard deviation (SD) since the injury that caused the SCI for the individuals without fracture history is 13.6 ± 9.6 years and 20.1 ± 4.8 years for those with fracture history. The two SCI groups did not differ regarding mean duration of their SCI ($p = 0.07$). We detected significant differences in measured phase velocity values (mean ± SD) between AB, SCI, and SCI-Fx group using an ANOVA. The results (**Figure 2**) remain similar after analysis of covariance with age as the covariant:

- AB (n = 175), 463.9 ± 32.0.
- SCI (n = 22), 438.4 ± 36.3.
- SCI-Fx (n = 11), 403.7 ± 66.1.

DISCUSSION

This study identified associations between subject characteristics, lifestyle factors, health status, and measured phase velocity of flexural waves propagating in tibia bone in a group of men in their 2nd to 7th decade. Phase velocity of flexural waves passing through the tibia is a mean to assess the mechanical properties of this bone [20]. In accordance with the Bernoulli-Euler model, the bending stiffness of a rotationally symmetrical long beam is proportional to the phase velocity of fourth-order flexural waves [17]. The validity of this relationship for the tibia has been confirmed in vitro. Others have suggested that a combination of biomechanical measurements and apparent density may improve bone strength prediction [28].

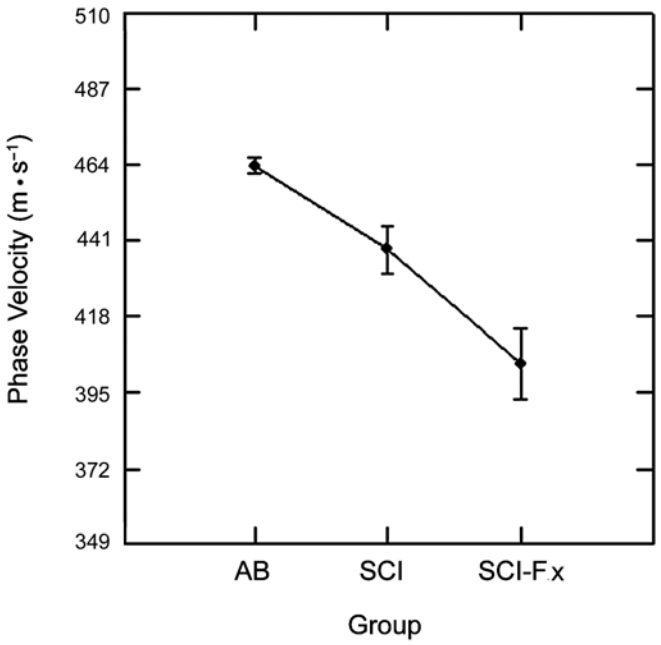

Figure 2.
Analysis of variance of measured phase velocity of tibia (PVT) for three examined groups. Mean ± standard deviation for able-bodied (AB) controls (n = 175), chronic spinal cord injury (SCI) (n = 22), and chronic SCI with pathological fracture history (SCI-Fx) (n = 11).

We assessed differences by measuring the phase velocity propagation in AB controls and subjects with chronic SCI with and without pathologic fracture history. The rationale behind the selection of SCI patients in this research stems from Wolff's law [11] and from several studies in which changes in mechanical properties of lower-limb bone following SCI were reported [29–30]. Furthermore, one can assume that environmental factors such as physical exercise, dietary calcium intake, and smoking and drinking habits interact with each other to determine bone status [31].

Health status, tibia length, and age were associated with phase velocity measurements in the present study. Bending of a bone causes tensile stress on the side of the bone being stretched and compressive stress on the side undergoing compression. The magnitude of the stresses increases with the distance from the neutral axis [12]. This might explain why individual differences in bone morphology might result in differences in stiffness values and consequently in measured values of phase velocity. However, further study is needed to gain more information on the relationship between phase velocity measurements and the influence of an anthropometric factor such as the tibia length. A relationship between age and tibia bone quality as estimated by tibia flexural wave propagation velocity has been reported previously by Flynn et al. [16].

The association between health status, tibia length, and age indicates the relevance of phase velocity propagation measurements in human long bones in SCI. When whole bones are subjected to physiological loading conditions, their mechanical behavior depends not only on the mass of the tissue and its material properties but also on the bones' geometry. Animal experiments show a reduction in weight of the bones in paralyzed limbs. Similar to the reduction in weight, the bending moment at breaking point reduces by 20 percent compared to controls [32]. In a cross-sectional study on the biomechanical properties of human tibias in long-term SCI, cortical thickness of SCI tibias were significantly thinner, suggesting structural adaptations following SCI that alter the mechanical properties [33].

Factors similar to the ones used in this study do not explain fracture risk in SCI and healthy reference populations [34]. Vestergaard et al. could not relate a specific daily life factor to fracture genesis in SCI—we concluded that this might be the consequence of bone biomechanical competence loss to such an extent that no factor by itself could modulate the fracture risk in SCI [34].

The present study shows that phase velocity values in subjects with chronic SCI are significantly lower than phase velocity values in an AB reference population. Also, there are significant measurable differences between SCI groups divided into individuals with and without pathologic fracture history. Clinical detection of these differences potentially allows the division of SCI patients into two groups with different mean phase velocity values: one group with and one without pathologic fracture history.

These results support the assertion that a relationship exists between bone mechanical properties and the presence of SCI. Furthermore, the data suggest that bone continues to modify its architecture after an SCI, and one can speculate that there are differences in the amount of changes in mechanical properties of bone for different groups of individuals; however, further (cross-sectional and prospective longitudinal) research is needed to substantiate this speculation.

Our study did not focus on the discrimination ability of the measurement device between SCI patients at risk of fractures and those not at risk. Prospective studies

should determine fracture risk in this population with the measurement device.

To obtain the diagnostic information of this new test alone, one should compare the outcomes of the test with other diagnostic tests in use. This necessitates the concurrent measurement of those tests in future research. Measurements of phase velocity of flexural waves obviously have an ability to provide information on the mechanical properties of the tibia. However, we need information on the geometry of the investigated parts of the bone to acquire more precise information on the bone bending stiffness. Some work in this area already has been undertaken [9]. Calculated bending stiffness derived from measured phase velocity correlates with the area moments of inertia in subjects with SCI. Bone strength is influenced by its geometrical properties such as the area moment of inertia that indicates the distribution of bone mineral around its bending axis [35–36]. However, bigger samples of subjects should be selected in the future, and with logistic regression analysis the contribution of this test to existing diagnostic tests should be estimated more precisely [22].

CONCLUSIONS

Phase velocity measurement of tibia bone evaluates bone mechanical characteristics that are influenced, at least partially, by health status, tibia length, and age. Values of phase velocity propagation in tibia bone are significantly lower in individuals with SCI with and without a pathologic fracture history compared to AB controls. Measurements of phase velocity in tibia bone of someone with SCI, therefore, are potentially of diagnostic value in the estimation of pathologic fracture risk in lower-limb bones in SCI. However, the relation of BSMD-Swing measurements and other existing measurement methods of bending stiffness (i.e., peripheral computed tomography) have yet to be fully determined on subjects with osteoporosis after SCI.

The BSMD-Swing, which is noninvasive, nonradiological, and dependable in handling, appears promising from clinical and research perspectives. Further research seems to be indicated in clinical populations into the relevance of the device in detecting persons with SCI who are at risk for pathologic bone breakage in time.

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