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Measurement of Modal Damping Factor to Monitor Bone Integrity and Osteoporosis on Female Tibiae *in vivo*

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Abstract

A non invasive method to assess bone structural integrity (osteoporosis) in female tibiae is presented, based on *in-vivo* measurement of bone dynamic characteristic (MDF) by applying vibration excitation in the range of acoustic frequencies, in the form of an acoustic sweep signal. The method has already been successfully applied on metallic structures and composites, including animal bones, and is supported by analytical and arithmetic tool based on model's theory. MDF experimental results are compared to data acquired with conventional method (pQCT). The comparison shows that changes in MDF correlate satisfactorily with all other measured characteristics. This research, in addition to authors' previous work strengthens the potential of the proposed method to consist a valuable assessment tool for *in-vivo* monitoring bone integrity and osteoporosis.

Keywords: Bone density; Damping; Osteoporosis; pQCT; Female tibiae

Abbreviations: MDF: Modal Damping Factor; BMD: Bone Mineral Density; pQCT: peripheral Quantitative Computer Tomography; vBMC: volumetric Bone Mineral Content; vBMD - volumetric Bone Mineral Density; DEXA: Dual Energy X-Ray Absorptiometry; vTotBMD: volumetric Total Bone Density; CSAtot: total Bone Area; vTrabBMD: Trabecular Bone Density; CTrab: Trabecular Content; CSATrab: Trabecular Area; vSubcrtBMD: Subcortical Bone Density; CSASubcrt: Subcortical Area; vCtBMD: volumetric Cortical Bone Density; CSAcrt: Cortical Area; peri: periosteal perimeter; endo: endosteal perimeter; THKcrt: Cortical shell thickness; SSIx, SSIy, SSIp: Stress/Strain Index in different axes; CMI: Cross Sectional Moment of Inertia; xCSMI: Equatorial Second Moment of Inertia; pCSMI: Polar Second Moment of Inertia; BSI: Bone Strength Index; SSI: Stress/Strain Index

Introduction

Bone mineral density is recognized as the most important single determinant of fracture risk in osteoporotic populations [1,2]. Accordingly, measurement of bone density is currently the mainstay for diagnosis and monitoring of osteoporosis. However, many other skeletal and extra skeletal factors and conditions may influence an individual's risk of developing a fracture, as in particular, a hip fracture [3]. Therefore, the ability of bone to withstand traumatic insults is the result of both the amount of mineralised tissue per unit of volume (density), and many other factors that are commonly referred to as bone quality. Loss of trabecular connectivity is considered one of the critical factors that weaken bone strength in osteoporosis [4]. Although data are still limited, this architectural abnormality may independently constitute an important factor for predicting fracture risk [5].

In vitro studies have shown that bone strength is correlated not only to mineral content, but also to the modulus of elasticity [6-8] and to the bone natural frequencies [9-13]. Thus, transmission techniques based on ultrasound attenuation or velocity have been developed as a clinical tool to screen patients at risk of osteoporosis [14]. The application of a new analytical-arithmetic and experimental method to assess bone integrity, based on sweeping sound excitation, which is equal or better predictor of bone strength than mineral density was presented by [15,16]. This method was also applied in materials with elastic behaviour [17-20], as well as in rats' tibiae [21], and gave excellent results. Moreover, ultrasound measures material's modulus of elasticity and uses high frequency sound, while the method reported here measures material damping using excitation in the acoustic range. The calculation and measurement of MDF can be applied in clinical settings to estimate the biomechanical competence of bone, and thus it may be used as a monitoring tool in metabolic bone diseases, especially osteoporosis. In this study, the promising application results of MDF method on women tibiae, in comparison to measurements acquired with conventional pQCT method for assessment of bone quality are reported.

Materials and Methods

Measurement of Damping

Natural frequency of any structural member is defined as the frequency at which the member vibrates if displaced from equilibrium. Usually, several frequencies coexist and signal analysis techniques are available for measurement of these frequencies. Material damping factor γ is defined as the energy dissipated throughout the medium in one cycle of deformation, normalized with respect to the elastic energy stored during that cycle, representing the fraction of strain energy lost in one full cycle [22].

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The vibration modal damping factor ζ (MDF) and Quality Factor (Q) are defined [22,23] as

$$\zeta = \sqrt{\frac{\gamma^2}{(4+\zeta^2)}} \tag{1}$$

$$Q = \frac{1}{2\zeta} \tag{2}$$

From [22], eq/on (3.74), page 146

$$\frac{2\zeta}{\sqrt{(1-\zeta^2)}} \cong 2\zeta = \left(\frac{\omega_n}{\omega}\right) \times \gamma \tag{3}$$

Hence, for
$$\binom{\omega}{\omega_n} = 1$$
 and $\binom{\delta}{\pi} = \gamma \cong 2\zeta$
 $\gamma = 2\zeta$ (4)

Then, raising to the second power both sides of equation (1) we get

$$\zeta^{2} = \frac{\gamma^{2}}{\left(4 + \zeta^{2}\right)} \Longrightarrow 4\zeta^{2} + \zeta^{4} = \gamma^{2}$$

$$\tag{5}$$

From equations (4) and (5) we get $\zeta^4 = 0$, which is true, given that ζ is too small. Hence equation (1) is valid.

Dedicated device capable for *in-vivo* MDF measurements was designed and constructed, consisting of a triggering unit which emits a sound transmitted to the bone through contact of a stem and of an accelerometer as output sensor. The device had the following technical characteristics:

Frequency sweep: 100Hz-10KHz 10Vpp at 1sec sweep time, Excitation: Electrodynamic Shaker, Gearing & Watson Type V2, with custom Power Amplifier Driver 100Hz-10Khz 20Watt Accelerometers: 2x PCB Piezotronics Model M353B17, sensitivity 9.33mV/g, Frequency Range: 1-10000Hz, Accelerometer Amplifier: PCB Piezotronics Model 482A16, 4 Channel, Gain x10 x100, Filters: Band Pass custom Software Filters 80Hz-12Khz KHZ, 2nd Order, Data Acquisition Hardware: National Instruments NI PCI-MIO-16E-1 16 Analog Input Channels with 1.25 Ms/s Sampling Rate at 12 Bit and 2 Analog Output Channels at 1MS/s 12 Bit), Connector Block: National Instruments NI BNC-2110 Noise Rejecting Shielded BNC Connector Block, Software: Custom Data Acquisition and Damping.

Analysis software

MDF was obtained *in vivo* by using equation (4) and applying the half-power bandwidth method [22,24]. Each bone (woman's tibia) was set with the aid of the triggering unit to free vibration from an initial displaced position and the signal of the accelerometer was then amplified and relayed to an analog-to-digital converter. The variation parameters were selectable through dedicated software developed for this purpose. The damping factor was calculated from the Fast Fourier Transform (FFT) analysis of time response data. It must be noted that the damping factor is proportional to the energy absorbed per cycle of vibration [23].

The triggering unit was applied on inner ankle. The bone response was acquired independently at different positions of tibia length through the accelerometer. This measured output was transferred, through signal conditioning electronics, to the computer and stored in memory. The response signal had frequency varying linearly between the thresholds set and variable amplitude.

Measurement of bone mineral density

Peripheral Quantitative Computed Tomography (pQCT) [25,26] was developed as a small-field, high-resolution extension of existing

QCT systems, to measure the peripheral skeleton with a substantial improvement of the image definition. Currently available pQCT machines perform transverse scans of a wide size-range of regions of interest, from large body segments such as the whole human head to tiny bones.

A basic pQCT machine consists of two major components: a scanner unit and a control/analysis computer system. The scanner unit contains: (a) a source that emits a very narrow X-ray beam, (b) a detector of the emitted radiation fixed at a short distance from the source, which can measure the radiation intensity and the attenuation produced by the tissues studied, and (c) a mechanical system allowing radial, transverse and axial displacements of the source-detector couple in order to achieve different scanning positions of the bone.

As a first step when the measurement is started, successive transverse displacements of the source-detector couple, repeated after small axial displacements, produce a computed radiograph or scoutview of the bone piece along its longitudinal axis, resembling a standard densitometric (DEXA) picture. Reference points on the screen allow selection of any convenient position along the bone axis. At that point, series of transverse measurements are performed after successive, partial rotation displacements of the couple until completion of a 180° excursion (translate/rotate mechanism).

pQCT measures only the attenuation of the radiation passing through the whole tomographic slice. The magnitude of the attenuation depends on both the mass and the number of electrons in the atoms of the elements present in the tomographic slice, so that bone minerals are most relevant for such measurements. The attenuation is expressed in cm⁻¹. By summing up the individual values assigned to each voxel, the machine can determine the mineral mass of vBMC and the vBMD of the whole bone slice or of a selected region of it. The vBMD represents the vBMC/bone volume relationship of the region and is usually expressed in mg/cm³.

Many bone variables can be measured by pQCT in different long bones. The available data can be classified according to their relevance as indicators of the different aspects of bone mechanical quality, architectural design, structural stiffness and strength. It has been demonstrated that pQCT-assessed vBMD is more representative of the actual bone material quality than the BMD expressed as a mass of mineral per square unit of projected bone area provided by DEXA. In addition, the information provided by the pQCT determinations can be processed by the machine in order to distinguish between trabecular and cortical bone in many instances, and calculate a number of variables which describe many aspects of bone architecture.

The machine used for the pQCT measurements was an XCT 2000 STRATEC. Measured variables were the cross-sectional diameters, endosteal and periosteal perimeters and average cortical thickness. These variables may help to evaluate the modeling-derived changes provoked by applied treatments. However, they do not affect the quality of the architectural design or the mechanical competence of long bones as much as the CSMIs do. The xCSMI and pCSMI of the cross-sectional bone area are relevant to long-bone stiffness and strength in bending and torsion, respectively. The software analysis of the XCT-960 Stratec machine calculates the CSMIs of the total or cortical bone areas as:

$$CSMI = \sum \left(A_i * d_i^2 \right) \tag{6}$$

where A_i is the area of an individual voxel within the bone section and d_i is the distance from the center of that area to the reference, bending (x,y) or torsion (z) axis. From equation (6) it is apparent that CSMI

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values increase linearly with (A) and proportionally to the distance (d^2) of the bone material from the reference axis. Therefore, the equatorial and polar CSMIs are true indicators of the bending or torsional stiffness/strength of the long bone, respectively, regardless of bone material quality.

The structural stiffness and strength of long hollow tubular structures are generally proportional to the product CSMI* E (E being the elastic modulus of the material of which the structure is made). The elastic modulus can only be assessed mechanically, but the apparent mineral density of the solid bone could reasonably estimate it. Hence, replacing E by the pQCT-assessed vBMD of the cortical bone in equation (6,7), the BSI was developed as the product:

$$BSI = xCSMI * corticalvBMD \tag{7}$$

The Norland/Stratec machines also provide another expression of BSI for long bones, the SSI, calculated as:

$$SSI = \frac{\left(pCSMI * corticalvBMDi\right)}{\left(dM_x * vBMDM_x\right)}$$
(8)

where dM_x is the maximal distance from a voxel to the polar (z) axis in the image and vBMDM_x is the maximal value for the cortical vBMD (i.e., 1200 mg/cm³).

Results

On the basis of the methods described above, MDF and BMD values were acquired experimentally on women's tibiae *in-vivo*, in order to verify the belief that damping change due to change in bone porosity is correlating with density and strength changes.

50 women 39-80 years old were scanned at the tibia for bone density and strength measurements with a pQCT XCT 2000 X-ray bone densitometer (Norland/Stratec) device, using software version 5.2 Research multiple measurements Mask. Tibia length measurements were performed, in order to extract accelerometer's positioning for MDF measurement. Each woman was placed in a special purpose device setting her tibia in the center of the tomographic Field of View (FOV). Three cross-sections were scanned. One distal scan was performed at 4% of tibia length (slice 1) apart from the articulate surface of the knee where trabecular bone structure is the dominant volume. A second proximal scan was performed at 38% of bone length (slice 2) apart from the above reference line, where cortical shell and density can accurately be assessed. Finally, a third scan was performed at 66% of tibia length (slice 3) in order to consider bone and muscle properties.

Analyses of these scans produced measurements of vTotBMD, CSAtot, vTrabBMD, CTrab, CSATrab, vSubcrtBMD, CSASubcrt, vCtBMD, CSAcrt, peri, endo, THKcrt, cross-sectional moments of inertia about anatomical axes (Ix, Iy), maximum (Imax) and minimum (Imin) moments of inertia, polar moment of inertia (Ip) and SSIx, SSIy, SSIp. Relatively high Iy values compared to Ix imply relatively greater resistance to bending in the medial-lateral direction than in the anterior-posterior one. For the analysis procedure the contour and peelmode modes were set at 1.

Damped natural frequency ω_d and damping factor ζ measurements were performed on each woman as described above. Each measurement occurred as the average value of at least ten measurements under the same conditions. Here must be stated that MDF, which is a material and system property, takes values varying in the interval (0,1), with low values corresponding to better bone quality, hence higher bone density, and high values corresponding to worse bone quality, hence lower bone density. Processing of acquired data lead to results presented in Figures 1-6. Namely, MDF values are presented against vTotBMD measured at slice 1 (4% of tibia length) (Figure 1) for two kinds of population: general population of all ages and the specific case of women over 60 years old, thus having already high fracture risk values and low bone density. Additionally, MDF vs vTrabBMD measured at slice 1 for the same populations as those of Figure 1 are presented in Figure 2. In Figure 3 MDF is plotted against CTrab measured at slice 1, for women of age above sixty years. All changes are statistically significant to 0.05 levels, whereas MDF and vTrabBMD are correlated at p<0.01 level (Table 1). From Figures 1-3 strong correlations of MDF to pQCT measured parameters are revealed. Namely, increase of density parameters







corresponding to better bone quality, correlates to decrease of MDF, expressing higher bone quality.

Next case referring to measurements acquired at slice 2 (38% of tibia length) is presented in Figures 4 and 5. Results are correlated for women with SSI values at slice 2 in the range of 1000-1300 mm³ (average range of measured values). MDF is strongly correlated at level p<0.01 to CSAtot and to vCtBMD at slice 2, as well as to other parameters measured with pQCT (Table 2).

The last case referring to measurements acquired at slice 3 (66% of tibia length) is presented in Figure 6. MDF values are correlated for women with SSI values at slice 3 in the range of 1000-1300 mm³ (average range of measured values).







| | MDF | TRAB_DEN | TOT_DEN | TRABV_CNT |
|-------------------------|-----|----------|---------|-----------|
| MDF Pearson Correlation | 1 | -0.766** | -0.590* | -0.538* |
| Sig. (2-tailed) | | 0.001 | 0.020 | 0.039 |
| Ν | 15 | 15 | 15 | 15 |

**Correlation is significant at the 0.01 level (2-tailed). *Correlation is significant at the 0.05 level (2-tailed).

Table 1: Correlation Factors for Age> 60 years.

| | MDF50 | TOT_A2 | CRT_DNS2 |
|---------------------------|-------|---------|----------|
| MDF50 Pearson Correlation | 1 | 0.745** | -0.681** |
| Sig. (2-tailed) | | 0.000 | 0.001 |
| Ν | 21 | 21 | 21 |

**Correlation is significant at the 0.01 level (2-tailed).

where,

TOT_A2 stands for Total Area in slice 2

CRT_DNS2 stands for Cortical Density in slice 2.

 Table 2: Correlation Coefficients for SSI2=1000-1300.

Discussion

The extracted from the data processed, indicative of the situation correlations, are presented in the above Figures 1-6. Specifically, observation of Figures 1 and 2 leads to an expected verification, namely, Total Density values (Figure 1) which correspond to Cortical and Trabecular volumes simultaneously, lie mainly in the interval (100-350), whereas Trabecular Density values (Figure 2) which correspond only to Trabecular Volumes lie in the interval (110-250), with MDF following accordingly. Hence, the Total Density values lie in an interval larger than that of Trabecular Density, and MDF behaves in the opposite way, as expected, because high MDF values express deteriorated bone quality and low MDF values express increased bone quality.

Additionally, from Figure 1 it is observed that the correlation Age>60, corresponding to population of age above 60 years, has smaller slope than the correlation All ages, corresponding to population of all ages, expressing something expected, because the population Age>60 is women over 60 years old, with already high fracture risk, hence, lower Total Bone Density and higher MDF in comparison to the All ages population. Similar remark can be derived by observing Figure 2, this time comparing MDF to Trabecular Bone Density.

Observation of Figures 2 and 5 reveals again expected points, namely, it is revealed that cortical density is much higher than trabecular, because cortical density values lie in the interval (975-1125) with relevant MDF values lying in the interval (0.45-0.14), whereas trabecular density values lie in the interval (110-270) with relevant MDF values lying in the interval (0.5-0.12).

Similar trend is observed in all Figures 1-6, namely, increase in bone density or any examined strength index corresponds to decrease in MDF and vice versa, something absolutely explainable and expected according to our previous research findings, no matter what is (cortical, trabecular and total including muscle) the bone volume tested.

It must be clarified that this methodology, used as a bone-conditionmonitoring tool, cannot give information for the distribution of the bone condition, i.e. distribution of porosity throughout the bone. Measuring the damping factor at one of the modes of vibration results in a weighted average of the material damping, the weight function being the corresponding natural vibration mode. Different modes can give information for the concentration of porosity at different places throughout the bone, but such attempt was not made in this work.

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This methodology might be further extended to stochastic analysis of inclusions of random size and location and be employed further to study the effects of bone morphology on its dynamic behavior and resistance to fracture.

The experiments performed in this work were monitoring the change in damping factor. It is estimated that changes due to loss of mineral in the bone are much more predominant in the trabecular than in the cortical bone or in the surrounding soft tissue. However, the correlations found with the conventional pQCT density measurements, without constituting a proof, are nevertheless in support of the assumptions made.

The studies conducted in this and previous authors' work show that MDF is directly related with stress concentration due to discontinuities in the bone material, such as the change in porosity accompanying osteoporosis [17-20]. In turn, stress concentration is known to cause fracture in materials with such discontinuities.

The conventional methods for bone quality assessment have the following disadvantages:

- Subjectivity
- High cost
- Patient radiation
- Invasiveness
- Non portability
- Require highly trained personnel
- Disease must have started in order to be identified.

On the contrary, MDF method has the following advantages:

- Objectivity
- High accuracy
- High sensitivity
- Repeatability
- Low cost
- Non invasiveness
- Absence of pain
- Portability
- No patient radiation
- Short measurement duration (2-3 min)
- Does not require highly trained personnel
- Detects osteoporosis much earlier than any other method [27]
- Method's results correlate with results acquired with all conventional methods, something that does not happen among them [21]
- Insensitive to variations in soft tissues composition
- Due to measuring data teletrasfer possibility, the test can be performed on patients living in remote areas and the diagnosis and therapy can be given from central medical units
- Test can be performed as often as wished due to non invasiveness, pain absence, no patient radiation characteristics
- Positive effect on labor and financial load from development of domestic use model, hence, patients will not visit diagnostic centers without reason
- Possibility for elderly care, with sensor on the patient, without obligatory travel of patient or nursing personnel

• Because highly qualified personnel for device use and precaution meters are not required (i.e. radiation), the diagnostic cost is relieved.

All above, as well as the fact that MDF is shown to be the most objective indicator and measure of the tendency of the osteoporotic bone to fracture, may render it an advantageous tool for diagnosis and monitoring of changes in bone architecture.

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