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Cepstrum method enables accurate assessment of thickness of cortical bone layers – Potential improvement for analysis of ultrasound backscatter from underlying trabecular matrix

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ABSTRACT

Osteoporosis is a major worldwide health concern causing growing amount of fractures annually. Backscatter parameters derived from the pulse-echo ultrasound measurements have been shown to relate with the bone microstructure and composition and may therefore be used for diagnostics of osteoporosis. To obtain reliable results, the effect of cortical bone must be taken into account prior the analyses of backscatter from trabecular matrix. At severe fracture locations, the cortical layer is often too thin to be measured with traditional peak detection methods. In this study, the cepstrum method was applied to determine thickness of thin cortical layer. Both numerical simulations and experimental measurements were utilized. Ultrasound propagation in a water-cortical bone-fat construct was simulated with the Wave 2000 software (finite difference time domain method). In simulations the transducer operated at 5 MHz, was 10 mm in diameter and had focal length at 30 mm. For *in vitro* experiments, 5 thin slices of bovine cortical bone (thickness 0.5 mm - 2.5 mm) were cut from a tibial shaft using a low-speed diamond saw. In addition, cortical-trabecular bone samples (n = 4) were sawn from the epiphysis of bovine tibia. The cortical thickness was calculated from simulated and experimentally measured signals with the cepstrum technique. The cortical-trabecular samples were scanned laterally to determine the mean cortical thickness. Acoustic measurements were conducted by using a focused transducer (centre frequency of 2.25 MHz, focal distance 50.4 mm, focal diameter 1.4 mm). Cortical bone thickness, determined with the cepstrum technique, showed good agreement with the thickness of the cortical bone in the simulation geometry ($r = 1.0$, $n = 11$, $p < 0.001$) and *in vitro* ($r = 0.94$, $n = 9$, $p < 0.001$). The accuracy of the cepstrum method, assessed as a mean absolute error, was 320 microns *in vitro* and 34 microns in simulations. In this study, the cepstrum analysis of ultrasound reflections from the cortical bone was found to provide a reasonable estimate of the thickness of thin cortical bone layers. This method may be applied for assessment of cortical thickness at the most severe fracture sites, such as the proximal femur where the thin cortical layer is covering the trabecular bone. Moreover, it may be used for compensation of the effect by cortical bone from the ultrasound backscatter measurements in trabecular bone. This could therefore provide more reliable diagnosis of osteoporosis with ultrasound techniques.

INTRODUCTION

In osteoporosis the total bone mass decreases, the trabecular structure deteriorates and the thickness of the cortical layer decreases. Quantitative ultrasound has been proposed to provide a low-cost and non-ionizing diagnostic method for osteoporosis. Backscatter parameters derived from the pulse-echo ultrasound measurements have been suggested to provide information not only on bone mineral density (BMD) but also on bone microstructure and composition [1,2,3,4]. Backscatter measurements may also be applied at the most critical fracture sites, the hip (proximal femur), by using the dual frequency ultrasound technique [5,6].

Different backscatter parameters have been introduced to characterize mechanical properties of trabecular bone. Clinically, the most suitable may be apparent integrated backscatter (AIB), which includes the attenuation within the trabecular matrix. The AIB has been shown to predict strongly the mechanical properties the trabecular matrix [7]. However, for reliable assessment of ultrasound backscatter from the trabecular bone the effect of the overlying cortical layer must be taken into account.

The cepstrum method has been previously applied for determination of the thickness of cortical layer in long bones [8,9]. However, at proximal femur the thickness of the cortical layer is often too thin to be detected with the traditional envelope detection methods. In this study, using numerical simulations and experiments, the cepstrum method was applied to determine the thickness of thin cortical layer. Specifically, the ability of cepstrum technique to assess the cortical thickness in realistic geometry, *i.e.* when the trabecular matrix is present directly under the cortex (*e.g.* in proximal femur), was evaluated. Reliable compensation of the attenuation in cortical bone could enable accurate determination of the backscatter coefficient from the trabecular matrix and enhanced diagnostics of osteoporosis with pulse-echo ultrasound.

MATERIALS AND METHODS

Numerical simulations

Ultrasound propagation in a water - cortical bone - fat construct (Figure 1.) was simulated using the finite difference time-domain method (Wave 2000 plus software, version 3.00

R3, CyberLogic inc., New York, NY, USA). In Wave 2000, the wave propagation is simulated in two-dimensions by

$$\rho\frac{\partial w}{\partial t}=\left[\mu+\eta\frac{\partial}{\partial t}\right]\nabla w+\left[\lambda+\mu+\phi\frac{\partial}{\partial t}+\frac{\eta}{3}\frac{\partial}{\partial t}\right]\nabla(\nabla\bullet w),\quad(1)$$

where ρ is the density of the material, λ is the first Lamé constant, μ is the second Lamé constant, η is the shear viscosity, φ is bulk viscosity, t is time, ∇ is the gradient operator, $\nabla\cdot$ is the divergence operator, and ∂ denotes the partial differential operator. $w(x, y, t)$ is a two-dimensional displacement vector.

A total of 11 simulation geometries were created, in which the thickness of the cortical bone varied from 0.5 to 1.5 mm. Fat tissue was placed under the cortical layer to mimic diaphyseal long bone geometry. In all simulations the properties of the transducer (in distilled water) were set as follows: transducer diameter 10 mm, center frequency 5 MHz (3.35 MHz - 6.66 MHz, -6 dB), focal length 30 mm. The simulated ultrasound pulse was defined to follow the shape of a sine Gaussian function

$$g(t)=A\cdot e^{\frac{-(t-D/2)^2}{a^2}}\cdot\sin(2\pi f t),\qquad(2)$$

where A is the amplitude, t is time, D is the duration of the pulse, f is the central frequency and a is the steepness of the function. The waveform parameters were set as follows: $A = 1$, $D = 2$ µs, $f = 5$ MHz and $a = 0.16$ µs. Infinite boundary conditions were set to prevent reflections from outer boundaries of the geometry.

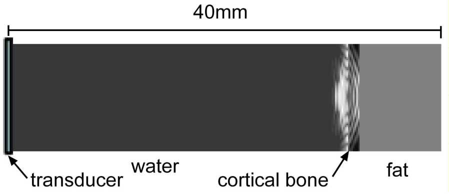

Figure 1. In the simulations the surface of the cortical bone was kept at the focal distance (30 mm) from the transducer and the amount of fat was adjusted to keep the total length of the geometry at 40 mm.

Cepstrum method

Theoretically, the received ultrasound echo signal $x(t)$ can be presented as a convolution of an impulse response $p(t)$, an attenuation function through the cortical layer $a(t)$ and a reflection function $r(t)$ [8]

$$x(t) = p(t) * a(t) * r(t)\qquad(3)$$

The function for reflections from the endosteal and periosteal surfaces of cortex separated by a distance d can be presented as

$$r(t)=R_1\delta(t-t_0)+R_2\delta\left(t-t_0-\frac{2d}{c}\right),\qquad(4)$$

where $\delta(t)$ is the Dirac delta function, c is the speed of sound and R_1 and $R_2$are the reflection coefficients of periosteal and endosteal surfaces, respectively. The spectrum of the signal can be found as

$$\left|X(f)\right|^2=\left|P(f)\right|^2\left|R_1+R_2e^{-2\beta f d}e^{-i2\pi f(2d/c)}\right|^2,\qquad(5)$$

and by taking the logarithm we get

$$2\log\left|X(f)\right|=2\log\left|P(f)\right|\cdot 2\log\left|R_1+R_2e^{-2\beta f d}e^{-i2\pi f(2d/c)}\right|,\quad(6)$$

where β is the slope of the attenuation vs. frequency in the cortical layer. The exponential factor in the last term $e^{-i2\pi f t}$ has an inverse Fourier transform of $\delta(s - t)$, where s is the transform variable and $t = 2d/c$. The cepstrum corresponding to $x(t)$ can be found as the inverse Fourier transformation of equation (6).

In practice, the procedure for calculation of cepstrum begins by windowing the two reflections out from the time domain signal. The region of interest is then transferred into frequency domain via FFT and the logarithm is taken to obtain the power spectrum. The background trend in the power spectrum, caused by the reflection from the periosteal surface, is removed by subtracting a smoothed spectrum from the original signal. The smoothed spectrum was obtained by low pass filtering the power spectrum. Then, the more rapid oscillation caused by the pulse reflected from the endosteal surface was restored. The inverse Fourier transformation for the transducer effective bandwidth resulted in a peak in time domain, indicating the time difference between the reflections from periosteum and endosteum. The algorithm for calculation of the cepstrum in this study can be simply presented as $|\mathrm{IFFT}(10*\log_{10}(|\mathrm{FFT}(x(n))|))|$, the magnitude of inverse FFT of the logarithmic magnitude spectrum.

In vitro measurements

For *in vitro* experiments, five thin slices of bovine cortical bone were cut from a tibial shaft with a low-speed diamond saw (Buehler Ltd., Lake Bluff, IL, USA). The thickness of the samples varied from 0.5 mm to 2.5 mm. For reference the thickness of the cortical bone slices was determined with a micrometer screw. In addition, cortical-trabecular bone samples ($n = 4$) were sawed from the epiphysis of bovine tibia. The cortical-trabecular samples were measured in lateral orientation using a mechanical ultrasound scanner with isotropic resolution of 700 µm (11x12 pixels or signals). The mean cortical thickness was determined from these signals with the cepstrum technique by using a constant value for sound speed (3550 m/s) in cortical bone [9]. For reference the thickness of the cortical bone layer was determined with a caliper.

Acoustic measurements were conducted using a focused transducer: 2.25 MHz centre frequency, 50.4 mm focal distance and beam diameter at focus 1.4 mm (Panametrics V307, Panametrics Inc., Waltham, MA, USA). The transducer was connected to an UltraPAC ultrasound pulser/receiver system (Physical Acoustics Corporation, Princeton, NJ, USA). The ultrasound measurement system was controlled with Labview 8.2 based software (National Instruments Corporation, Austin, TX, USA). Measured and simulated ultrasound signals were analyzed with Matlab (Matlab 7.3, The Mathworks Inc., Natick, MA, USA).

RESULTS

In simulation geometry and experimentally *in vitro*,cortical bone thickness, as determined with the cepstrum technique, showed good agreement with the thickness of the cortical bone (Figure 2.).

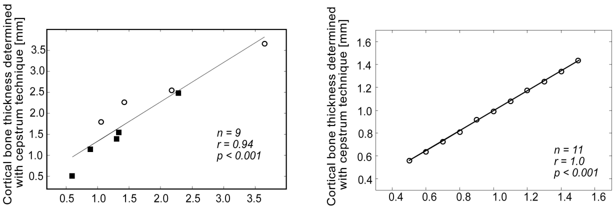

Figure 2. Measures of cortical thickness with cepstrum method correlated significantly with a) the micrometer screw

or caliper measurements *in vitro* (circles denote cortical-trabecular samples) and b) the actual geometry in numerical simulations.

The accuracy of the cepstrum method (mean absolute error) was 320 μm *in vitro* and 34 μm in simulations.

DISCUSSION AND CONCLUSIONS

In this study, the feasibility of cepstral analyses of pulse-echo ultrasound signals for determination of the thickness of thin cortical bone layers was evaluated. The absolute accuracy of measurements was similar to that reported previously for *in vivo* in measurements of long bones [9]. The present study applied cepstrum method for conditions where trabecular bone was present underneath the cortical layer. This has not been addressed previously and can be assumed to produce additional error sources for estimation of cortical bone thickness. The knowledge of cortical bone thickness potentially allows correction of the backscatter measurements from underlying trabecular bone. However, these analyses were discarded as they require prior knowledge of the frequency dependent attenuation and speed of sound in cortex. This is problematic as attenuation and sound speed may vary in ageing or diseased bone [10]. Whether constant values for these parameters can be used for the compensation of backscatter from the trabecular matrix remains unclear. These issues will be addressed in our future studies.

To conclude, the cepstrum analysis of ultrasound reflections from the endosteal and periosteal surfaces of the cortical bone was found to provide a reasonable estimate of the thickness of thin cortical bone layers. Thus, this method may be applied for assessment of cortical thickness at the most severe fracture sites, *e.g.* the proximal femur, where the cortical layer is thin and trabecular bone is present under the cortical layer. Moreover, it may be used for compensation of cortical bone effect from the ultrasound backscatter measurements in trabecular bone and could therefore provide more reliable diagnosis of osteoporosis with ultrasound techniques.

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