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● *Original Contribution*

USING THE GRADIENT OF HUMAN CORTICAL BONE PROPERTIES TO DETERMINE AGE-RELATED BONE CHANGES *VIA* ULTRASONIC GUIDED WAVES

CÉCILE BARON
Aix-Marseille Univ, Institute of Movement Sciences, Marseille, France

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Abstract—Bone fragility depends not only on bone mass but also on bone quality (structure and material). To accurately evaluate fracture risk or propose therapeutic treatment, clinicians need a criterion, which reflects the determinants of bone strength: geometry, structure and material. In human long bone, the changes due to aging, accentuated by osteoporosis are often revealed through the trabecularization of cortical bone, *i.e.*, increased porosity of endosteal bone inducing a thinning of the cortex. Consequently, the intracortical porosity gradient corresponding to the spatial variation in porosity across the cortical thickness is representative of loss of mass, changes in geometry (thinning) and variations in structure (porosity). This article examines the gradient of material properties and its age-related evolution as a relevant parameter to assess bone geometry, structure and material. By applying a homogenization process, cortical bone can be considered as an anisotropic functionally graded material with variations in material properties. A semi-analytical method based on the sextic Stroh formalism is proposed to solve the wave equation in an anisotropic functionally graded waveguide for two geometries, a plate and a tube, without using a multilayered model to represent the structure. This method provides an analytical solution called the matricant and explicitly expressed under the Peano series expansion form. Our findings indicate that ultrasonic guided waves are sensitive to the age-related evolution of realistic gradients in human bone properties across the cortical thickness and have their place in a multimodal clinical protocol. (E-mail: cecile.baron@univ-amu.fr)

Key Words: **Cortical bone, Porosity gradient, Elastic wave propagation, Stroh formalism, Waveguide.**

INTRODUCTION

It is now widely accepted that bone strength relies on two main factors: bone density and bone quality. Thus, accurate information is needed on the quantity of bone, the way it is organized and the mechanical quality of its constituent materials (elastic properties) to accurately evaluate fracture risk, to optimize treatment (time and dosage) and to reduce adverse effects. Nowadays, bone densitometry as determined by dual-energy X-ray absorptiometry (DXA) is the gold standard technique used to diagnose osteoporosis and to decide on treatment. It provides a value for bone mineral density (BMD), which is compared with that of a reference population to assess whether the patient is "normal," presents with osteopenia or presents with osteoporosis.

Address correspondence to: Cécile Baron, Institute of Movement Sciences UMR 7287 CNRS/AMU 163, Avenue de Luminy, 13288 Marseille Cedex 09, France. E-mail: cecile.baron@univ-amu.fr

One of the fundamental challenges in bone characterization is to identify the relevant parameters, which have to be correlated to the pathology and accessible through clinical measurements. Moreover, as with all technological developments for biomedical applications, it is essential to respect certain criteria: techniques should be nondestructive, noninvasive and nonradiating. Quantitative ultrasound techniques are good candidates on all these conditions. Yet, they continue to struggle for acceptance against the gold standard of DXA analysis, partly because no single physical parameter has been identified to represent the "structure, geometry, material" triangle. For a long time now, it has been recognized that bone mass alone (bone mineral density) is insufficient to predict risk of fracture (Faulkner 2000; Robbins et al. 2005). It has been reported that BMD alone explains less than half the risk of hip fractures (Marshall et al. 1996). Several studies have revealed cases where the effect of BMD on risk of fracture is atypical. Postmenopausal Chinese women, for example, have significantly

lower hip bone mineral density than white women and are classified at higher risk but in fact they have fewer fractures (Tobias et al. 1994; Xiaoge et al. 2000).

It would appear, then, that bone quantity alone is not sufficient to evaluate bone fragility and that bone geometry and quality are key factors which significantly affect bone strength (Augat et al. 1996; Ammann and Rizzoli, 2003; Moilanen et al. 2007; Gregory and Aspden 2008).

Moreover, even though BMD combines cortical and trabecular bone mass, the majority of what is measured by DXA is trabecular bone. As a consequence, osteoporosis treatments focus primarily on trabecular bone. Yet, while both bone compartments contribute to bone strength (Manske et al. 2009), several recent studies point out that cortical bone is a critical component in determining fracture resistance at the femoral neck (Augat and Schorlemmer, 2006; Holzer et al. 2009; Treece et al. 2010).

At the same time, as imaging techniques become more and more accurate, a newly visible characteristic of bone is emerging: intracortical porosity changes gradually across the thickness of long bones (Bousson et al. 2001; Tatarinov et al. 2005; Haïat et al. 2009; Grimal et al. 2011). When homogenization methods are applied to cortical bone, it can be viewed as a functionally graded material at mesoscopic scale.

Among the changes in cortical bone due to aging, there is a joint process accentuated by osteoporosis: trabecularization of the endosteal part leading to thinning of the cortex. Therefore, the gradient (spatial variation) of intracortical porosity is a parameter representative of increased variation in porosity across a reduced thickness and should be relevant to evaluate the combined effect of thinning and trabecularization. This gradient of intracortical porosity induces gradients of material properties (mass density and stiffness coefficients). Thus, characterizing the gradient of the bone properties across the cortical thickness, will provide information on structure (porosity), geometry (thickness) and material (stiffness).

In this study, we consider the diaphysis of long bone, in particular cortical bone. We model cortical bone as a one-phase material with varying mechanical properties (mass density and stiffness coefficients). Modeling how porosity changes across the cortical thickness and translating this variation in a microscopic property to mesoscopic level are complex tasks. We base ourselves on two studies (Bousson et al. 2000; Grimal et al. 2011) and define a mesoscopic functionally graded material (FGM) model. A semi-analytical method is proposed to solve the wave equation in an FGM waveguide. This method, based on the Stroh formalism, allows us to avoid a multilayered media approximation and to consider a cylindrical geometry in association with an anisotropic material. According to numerous experimental studies (Reilly and Burnstein 1974; Dong and Guo 2004; Lakshmanan et al. 2007), human cortical bone is assumed to be a transversely isotropic material. Here cortical bone is represented by a transversely isotropic plate or tube in vacuum. The dispersion curves of the guided waves are explored to evaluate the sensitivity of these waves to a realistic variation in intracortical porosity.

MATERIALS AND METHODS

Cortical bone as an anisotropic functionally graded material waveguide

The model takes into account the anisotropy and the heterogeneity of cortical bone: it is considered as transversely isotropic with linearly varying material properties. Moreover, two geometries are investigated for long bone modeled as a plate or as a tube with realistic dimensions.

Functionally graded material properties

Here, every attempt was made to model realistic variation in porosity across the cortical thickness. Based on previous work reported on femoral cortical bone samples from skeletons (Bousson et al. 2000, 2001), we focus on a solely female population (86 subjects) aged from 11 to 96. We use these authors' 3-point measurement of porosity (periosteal, midcortical and endosteal regions) to infer the evolution of porosity across the cortical thickness.

Then, the evolution of intracortical porosity (microscopic scale) is translated into a variation in the elastic properties of the bone at the mesoscopic level by using the regression models (size of the mesodomain $L = 0.5$ mm) proposed by Grimal and colleagues (Grimal et al. 2011). Thereby, the Young's and shear moduli and the Poisson ratios are expressed as a function of porosity.

Porosity varies with position across the thickness of the bone and, consequently, the Young's and shear moduli and Poisson ratios are also dependent on the spatial variable across the thickness (x - variable for the plate and r - variable for the tube), except for ν_{TL}, which is assumed to be constant at 0.3.

Then, we deduce the five independent stiffness coefficients as five spatially-dependent functions from the following equations:

$$\begin{aligned} c_{11} &= \frac{E_T(1-\nu_{TL}\nu_{LT})}{\Delta}; \quad c_{12} = \frac{E_T(\nu_{TT}+\nu_{TL}\nu_{LT})}{\Delta}; \\ c_{13} &= \frac{E_T(\nu_{LT}+\nu_{TT}\nu_{LT})}{\Delta}; \quad c_{33} = \frac{E_L(1-\nu_{TT}\nu_{TT})}{\Delta}; \\ c_{44} &= G_{LT}; \end{aligned} \tag{1}$$

with $\Delta = \nu_{TT}^2 + 2\nu_{LT}\nu_{TL} + 2\nu_{LT}\nu_{TL}\nu_{TT}$.