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● *Original Contribution*

ULTRASOUND CHARACTERIZATION OF BONE DEMINERALIZATION USING A SUPPORT VECTOR MACHINE

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Abstract—We propose an ultrasound-guided remote measurement technique, utilizing an acoustic radiation force beam as our excitation source and a receiving hydrophone, to assess non-invasively a bone's mechanical properties. Features, such as velocity, were extracted from the acoustic pressure received from the bone surface. The typical velocity of an intact bone (3540 m/s) was higher in comparison to that of a demineralized bone (2231 m/s). According to the receiver operating characteristic curve, the optimal velocity cutoff value of ≥3096 m/s yields 80% sensitivity and 82.61% specificity between intact and demineralized bone. Utilizing a support vector machine, the hours of bone demineralization were successfully classified with maximum accuracy >80% using 18% training data. The results indicate the potential application of our proposed technique and support vector machine for monitoring bone mechanical properties. (E-mail: denis.max@pnlsciences.com) © 2017 The Author(s). Published by Elsevier Inc. on behalf of World Federation for Ultrasound in Medicine & Biology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Key Words: **Bone, Demineralization, Support vector machines, Acoustic radiation force, Quantitative ultrasound.**

INTRODUCTION

Non-invasive techniques such as vibration analysis and quantitative ultrasound (QUS) have been used to assess long bone mechanical properties. Vibration analysis utilizes an impact hammer to generate vibrational waves and measure the resonant frequencies to assess the mechanical properties of long bones (Jurist 1970; Sonstegard and Matthews 1976; Steele et al. 1988; Van der Perre et al. 1983). In QUS analysis, guided waves from axial transmission measurement along the bone surface have been used to determine the material properties of long bones (Bossy et al. 2004a, 2004b; Gerlanc et al. 1975; Lee and Yoon 2004; Lowet and Van der Perre 1996; Moilanen 2008; Mole and Ganesan 2010; Rose 2004; Siegel et al. 1958; Ta et al. 2009; Vavva et al. 2008; Viktorov 1970). Recent progress in QUS, has focused on the extraction of the dispersion curves and exploitation of the multimodal waveguide of long bones to extract cortical thickness and stiffness (Vallet et al. 2016; Xu et al. 2016). However, the clinical utility of both vibrational analysis (Cornelissen et al. 1986; Saha and Lakes 1977; Van der Perre et al. 1983; Ziegert and Lewis 1979) and QUS (Bossy et al. 2004a, 2004b; Lee and Yoon 2004; Lowet and Van der Perre 1996; Moilanen 2008; Moilanen et al. 2006; Vavva et al. 2008) has been challenging because of the impact of soft tissue. The bone and overlying soft tissue layer guide wave modes overlap in time and frequency (Lee and Yoon 2004; Moilanen 2008). In a vibrational analysis, considerable differences in magnitude and temporal measurements occur when performed on the skin and directly on the bone (Ziegert and Lewis 1979). Bochud et al. (2017) summarized the effects of overlying soft tissue on QUS and obtained reliable bone strength estimates from calibrated bone phantoms using an inversion scheme based on the free-plate model, despite the presence of soft tissue. Thus, this study represents a step forward in quantifying the overlying soft tissue effects on QUS assessment of bone tissue.

Alizad et al. (2006) utilized acoustic radiation force excitation to study the change in resonant frequencies of a bone resulting from a change in its physical properties caused by a fracture. The method offered the advantage of applying a force remotely and directly to the bone under test, thus avoiding the interference of overlying muscle or

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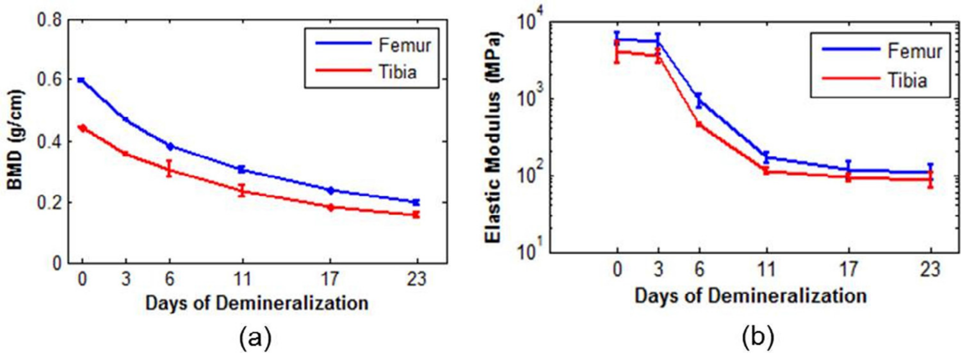

Fig. 1. Porcine femur and tibia bone (a) BMD and (b) elastic modulus results. The error bars represent ±1 standard deviation of the measurements in each bone group. BMD = bone mass density.

other tissues on force distribution. Similarly, Callé et al. (2003) utilized acoustic radiation force to generate vibrations along the bone tissue; however, in their study, the acoustic pressure radiating from the bone tissue was captured by a hydrophone. The captured signal was then used to produce an image of the bone tissue internal structure.

To improve the non-invasive assessment of bone mechanical properties, an ultrasound-guided remote measurement technique using acoustic radiation force (ARF) excitation in combination with machine learning is proposed. The ARF excitation exerts a localized transient force non-invasively on the bone surface, inducing vibrational waves along the bone surface. The radiated acoustic pressure from these vibrational waves is obtained for bone demineralization assessment. It should be noted that the acoustic radiation force does not propagate along the bone. The acoustic radiation force acts as a body force onto the bone surface generating the propagation of bending waves along the bone. The bending waves cause a deflection in the plane perpendicular to the bone surface. By coupling our receiver to the bone surface, we captured the radiated pressure from the deflection of the bone. Thereafter, a machine learning classification algorithm based on the support vector machine (SVM) (Vapnik 2000) is utilized for classifying the levels of bone demineralization.

In this article, features are extracted from the acoustic responses from the ultrasound-stimulated remote measurements. A SVM model is trained using the extracted features. Thereafter, the trained SVM model is used to classify the levels of demineralization of the bones.

CONTEXT: RELATING BONE DEMINERALIZATION AND BONE MECHANICS

To illustrate that bone mechanics directly reflect bone demineralization, *ex vivo* experiments comparing bone mineral density (the clinical gold standard for bone quality assessment) and elasticity measurements were conducted. Our goal with this experiment was to provide the pretext that although bone mineral density (BMD) is the gold standard for clinical bone assessment, it is unable to fully explain bone quality and strength. Bone specimens were demineralized to mimic the degradation of the bone mechanical properties. Thereafter, the relationship between the elasticity and BMD was examined. The bone demineralization and mechanics of porcine femurs (n = 2) and tibia (n = 2), obtained from a slaughterhouse, were examined. The *ex vivo* bone specimens' BMD was measured using a General Electric Lunar iDXA (GE Healthcare, Madison, WI, USA) dual-energy X-ray absorptiometry (DEXA) densitometer. Thereafter, the BMD and mechanical measurements were conducted at six time points. The first test was done on the intact (no demineralization) bone. The subsequent experiments were conducted in incremental demineralization events, where the bones were left in the 10% acid solution for 3, 6, 11, 17 and 23 d, respectively.

The BMD changes of the porcine femoral bone were observed from the intact (no demineralization) stage (day 0) to day 23 of demineralization. In parallel, bone elasticity was measured by a 4-point bending test using an MTS servo hydraulic 858 (MTS Corporation, Minneapolis, MN, USA) and 500-N load cell (Interface, Inc., Scottsdale, AZ, USA). The samples were tested to 100 N at the rate of 33.33 m/s. The elastic modulus (E) was obtained using the equation (Reed and Brown 2001)

$$E = \frac{5ml^3}{12I} \tag{1}$$

where m is the slope of the linear regime of the load-deflection curve, I the cross-sectional area moment of inertia and $l = 50$ mm the loading span distance.

Figure 1 illustrates the decrease in BMD and elasticity with demineralization. Figure 1a illustrates that the bone BMD decreases by approximately 33% from the intact state (day 0) to day 23 of demineralization. Similarly, the elasticity decreases by >80% from an intact state to the