Ultrasound in Med. & Biol., Vol. ■, No. ■, pp. 1–8, 2015

0301-5629/$ - see front matter

ELSEVIER

http://dx.doi.org/10.1016/j.ultrasmedbio.2015.06.005

● *Original Contribution*

SIGNAL OF INTEREST SELECTION STANDARD FOR ULTRASONIC BACKSCATTER IN CANCELLOUS BONE EVALUATION

Chengcheng Liu,* Tao Tang,* Feng Xu,* Dean Ta,*† Mami Matsukawa,‡ Bo Hu,* and Weiqi Wang*

*Department of Electronic Engineering, Fudan University, Shanghai, China; †Key Laboratory of Medical Imaging Computing and Computer Assisted Intervention (MICCAI) of Shanghai, Shanghai, China; and ‡Lab of Ultrasonic Electronics, Doshisha University, Kyoto, Japan

(*Received* 20 *February* 2015; *revised* 5 *June* 2015; *in final form* 5 *June* 2015)

Abstract—The aim of this study was to examine the effect of the backscattered signal of interest (SOI) on ultrasonic cancellous bone evaluation. *In vitro* backscatter measurements were performed using 16 bovine cancellous bone specimens and six different transducers with central frequencies of 0.5, 1, 2.25, 3.5, 5 and 10 MHz. The SOI for signal analysis was selected by a rectangular window. The delay (T1) and duration (T2) of the time window were varied, and the apparent integrated backscatter (AIB) and its correlation to bone volume fraction (BV/TV) were calculated. The results indicate that in addition to affecting the measured value of AIB, the SOI influences the observed correlation between AIB and BV/TV. Strong positive correlations were observed for short T1 (0.5 MHz: ≤6 μs, 1 MHz: ≤3 μs, 2.25 and 3.5 MHz: ≤2 μs, 5 and 10 MHz: ≤1 μs). However, strong negative correlations were observed when T1 was long (0.5 MHz: >9 μs, 1 MHz: >7 μs, 2.25 and 3.5 MHz: >3 μs, 5 and 10 MHz: >2 μs). The T2 value, especially low values (≤3 μs), also influenced the correlation coefficients. Positive correlations were more commonly observed at lower frequencies (*i.e.*, 0.5–1 MHz), whereas negative correlations were more common at higher frequencies (*i.e.*, 2.25–10 MHz). An explicit standard for *in vitro* SOI selection and cancellous bone assessment was proposed for a broad frequency range (0.5–10 MHz). Current conflicting findings are explained, and constructive suggestions for ultrasonic backscatter cancellous bone evaluation are provided. (E-mail: tda@fudan.edu.cn or tadean.fudan@gmail.com) © 2015 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Ultrasonic backscatter, Osteoporosis, Cancellous bone, Signal of interest, Bone volume fraction.**

INTRODUCTION

Osteoporosis is a metabolic bone disease characterized primarily by bone mass loss and microstructural deterioration, which increase the risk of a fragile fracture (Rachner et al. 2011). The most common method for diagnosing osteoporosis is based on an estimate of bone mineral density (BMD). However, BMD alone explains only 60% of fracture predictions (Harrar et al. 2013). Quantitative ultrasound (QUS) is an attractive, safe, inexpensive and portable alternative for bone assessment using non-ionizing radiation (Fujita et al. 2013; Haïat et al. 2005; Laugier and Haïat 2011; Le et al. 2010; Lin et al. 2014; Padilla et al. 2006; Roggen et al. 2015; Ta et al. 2009; Xu et al. 2014; Zhang et al. 2014).

Recently, ultrasonic backscattering has drawn significant attention as a non-invasive tool for assessment of cancellous bone (Bossy et al. 2005; Chaffaï et al. 2002; Conversano et al. 2015; Jiang et al. 2014; Liu et al. 2014a, 2014b; Ta et al. 2008; Wear 2008). Only one transducer in the pulse-echo mode is needed, and backscatter measurements can be conveniently performed on osteoporosis-sensitive bones, such as the hip and spine. The backscatter coefficient (BSC), broadband ultrasound backscatter (BUB) and apparent integrated backscatter (AIB) closely correlate with clinically relevant cancellous bone properties, including BMD, bone volume fraction (bone volume/total volume [BV/TV]), ultimate strength and Young's modulus (Hakulinen et al. 2004; Jenson et al. 2003; Riekkinen et al. 2006). BSC and BUB were compensated for frequency-dependent attenuation, which was assessed with the

Address correspondence to: Dean Ta, Department of Electronic Engineering, Fudan University, Shanghai 200433, China. E-mail: tda@fudan.edu.cn or tadean.fudan@gmail.com

Conflict of interest disclosure: The authors state that they have no conflicts of interest.

ultrasonic through-transmission measurement. So, the apparent backscatter coefficient (ABC) and AIB were preferred in the backscatter measurements, especially when considering the clinical applications, because they did not need to be compensated for the attenuation effect.

Thus far, however, studies have reported conflicting results. Although most research has indicated that backscatter is positively related to cancellous bone status (*i.e.*, BMD, BV/TV and ultimate strength) (Karjalainen et al. 2009, 2012; Litniewski et al. 2012; Moayyeri et al. 2012; Riekkinen et al. 2007; Wear et al. 2012; Zhang et al. 2013), some studies have reported a negative correlation (Hoffmeister 2011a; Hoffmeister et al. 2000, 2006, 2008, 2011). This contradiction has confused researchers and has obstructed clinical applications of ultrasonic backscatter for cancellous bone assessment. To date, no reasonable explanation has been given for these discrepant findings. Hoffmeister and colleagues suspect the discrepancy might be caused by the different attenuation of the specimens, the location and duration of the analysis gate and the frequency range used (Hoffmeister 2011a; Hoffmeister et al. 2006, 2011).

A reflected wave (RW) with relatively large amplitude is usually observed in front of the backscatter signal. The RW is a specular reflection resulting from the mismatch between the acoustic impedances of soft tissue (or water) and bone. In backscatter signal analysis, the RW is usually excluded and a time window is generally used to select the signal of interest (SOI) (Hakulinen et al. 2004; Riekkinen et al. 2006; Wear et al. 2012). The delay to the start of the backscatter signal (T1) and the length of the time window (T2) may directly influence backscatter parameters and cancellous bone evaluation. However, this issue has been neglected by most researchers. Researchers usually select the SOI on the basis of their individual preferences, and no explicit standard for SOI selection has been proposed. Our recent numerical simulations indicate that SOI selection significantly affects the backscatter parameters measured. As T1 increases, BSC and BUB decrease and AIB decreases more rapidly. BSC and BUB increase to a stable value with increasing T2. The increase in T2 causes AIB to increase at first and then decrease slightly (Liu et al. 2013).

The present work investigates the influence of the SOI on cancellous bone evaluation. *In vitro* backscatter experiments were performed using different transducers with central frequencies ranging from 0.5 to 10 MHz. Through changes in T1 and T2, the effect of SOI selection on AIB and its correlation with BV/TV were analyzed. An explicit SOI selection standard is proposed for cancellous bone evaluation in the range 0.5 to 10 MHz.

METHODS

Preparation of cancellous bone specimen

Sixteen cancellous bone specimens were prepared from the distal parts of bovine femurs, which were bought at a slaughterhouse in Kyoto. The specimens were cut along the principal anatomic orientations in a cuboid shape (approximately 3.0 × 3.0 × 1.5 cm). An oral irrigator was used to flush bone marrow out of the trabeculae. The specimens were stored in physiologic saline solution and degassed under vacuum to remove air bubbles before backscatter measurements.

Microstructure measurements

The specimens were scanned using a μ-CT (μ-CT80, SCANCO Medical, Switzerland) with a scanning resolution of 30 μm. The μ-CT microstructure measurements were performed by trained and certified technicians. The software suite for Micro-CT systems from SCANCO Medical was used to obtain microstructural information on the specimens, including BV/TV, mean trabecular thickness and mean trabecular separation, among other properties. The BV/TV of the specimens ranged from 0.074 to 0.475 with a mean ± standard deviation of 0.286 ± 0.128. BV/TV is an important index of cancellous bone status. The BV/TV of cancellous iliac crest bone was 0.228 ± 0.059 for healthy females and 0.142 ± 0.062 for osteoporotic females (Mullender et al. 2005). The BV/TV of the distal radius was 0.34 ± 0.10 for pre-menopausal normal women and 0.26 ± 0.09 for the post-menopausal women with fractures (Majumdar et al. 1997).

Ultrasonic backscatter measurements

Figure 1 is a schematic view of the backscatter measurement system. The bone specimen was placed in degassed water at room temperature (~21°C). The ultrasonic transducer was controlled using a three-axis motor controller (Ultrapac scanning, PK268-03B, NJ, USA). An ultrasonic pulser/receiver unit (Panametrics 5900PR, Olympus–Panametrics,Waltham, MA, USA) was used to transmit and receive ultrasonic signals. The ultrasound propagated along the medial-lateral direction of the specimens. To reduce random noise, 128 waveforms were measured and averaged in the time domain to obtain the backscatter signal for each specimen. Backscatter signal was recorded with a digitizing oscilloscope (HP 54642A, Hewlett-Packard, Palo Alto, CA, USA) and stored in a PC for further analysis. The reference signal was obtained by replacing the bone specimen with a polished steel plate, which was placed at the same distance of the middle of the bone specimen. Six unfocused transducers with central frequencies of 0.5, 1, 2.25, 3.5, 5