Feasibility of Applying MR Elastography to Measure Bone Stiffness in an Ex Vivo Model of Osteoporosis

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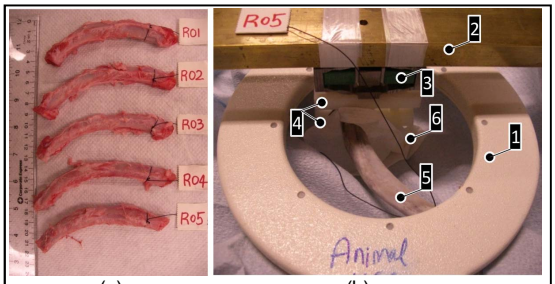
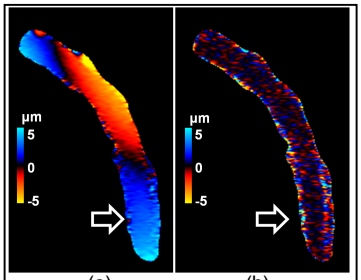
Introduction: Osteoporosis is a skeletal disorder characterized by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in the fragility of bone and hence susceptibility to fracture[1]. About 8% of the U.S. population suffer from osteoporosis, 80% of them are women. Pathologic fractures are the hallmark of osteoporosis and happen when the bone cannot sustain minimal trauma, such as falling from standing height, or the bone is so weak that even a normal load can exceed its strength. Fractures are more common than heart disease or cancer in women, affecting 1 in 2 women and 1 in 6 men older than 50 in North America [2], causing approximately 2.3 million fractures annually at a cost of more than 23 billion dollars per year in the USA and Europe [3]. Clinically, dual-energy X-ray absorptiometry (DEXA), quantitative ultrasound (QUS), quantitative CT (QCT) and MRI-based techniques are used to evaluate bone mineral density (BMD) for the diagnosis and management of the disease. However, BMD is not the only component contributing to bone strength, which depends on the combination of bone mineral mass and the bone microstructure/architecture[4]. It has been shown that a deterioration in collagen content or collagen cross-linking can increase fracture risk [5]. Therefore, assessing the overall biomechanical properties of bone could be more valuable than measuring BMD alone. We have shown that MR Elastography (MRE) is a promising noninvasive method of evaluating the biomechanical properties of ex vivo bone[6]. The purpose of this study was to create an ex vivo osteoporosis model of bone and test the feasibility of using MRE to detect changes in bone stiffness. We hypothesize that bone stiffness decreases in this osteoporosis model and this decrease can be detected by MRE.

Methods: (1) Osteoporosis model. Acetic acid exposure is known to soften bone by decreasing its calcium content. We used this method to create an ex vivo osteoporosis model. Five porcine ribs bought from a local grocery store were prepared with musculature removed (Fig. 1a). The weight of the five ribs ranged from 22.0 to 28.2 (mean = 24.4) grams, length ranged from 11.5 to 12.8 (mean = 12.1) cm and the thickness ranged from 1.2 to 1.7 (mean = 1.4) cm. The bones were soaked in a container with 1000 mL of distilled white vinegar (5% acidity, Supervalu, Inc. USA) and the container with the bones inside was kept in a constant 90°C water bath for 48 hours. MRE was performed on the five bones at room temperature (22°C) before the 48-hour acetic acid treatment for baseline measurements, and was then repeated after the treatment was finished and the bones were cooled down to room temperature. All of the bones were kept moist during the MRE exams using a wet paper tower wrapped around them. (2) Mechanical vibration. A piezoelectric stack mechanical driver was fabricated to apply mechanical vibrations to the bone at 1500 Hz. As seen in Fig. 1b, the driver was secured to a horizontal supporting bar, and was connected to the bone by a rigid clamp. The driver polarity was perpendicular to the supporting bar and the bone. The bone was inserted into the clamp and secured about 3 cm from one end of the bone. The bone sample was kept in a horizontal position oriented along the B0 direction. A single-channel receive-only surface coil (diameter = 17cm, GE, Milwaukee, Wisconsin, USA) was used in the exams. (3) MRE imaging sequence. A spin-echo MRE sequence was used to record the high-frequency motion in the bone as in an earlier study [6]. The parameters were as follows: 2.4 G/cm motion-encoding gradient train consisting of 60 total cycles at 1500Hz (30 cycles on each side of the refocusing pulse and synchronized with the motion), motion sensitivity = 13.8 μm/π rad, 8 phase offsets, FOV = 12 cm, TR/TE = 424/59 ms, BW = 31.25 kHz, coronal imaging plane, image matrix = 256X256, NEX = 1. A 1.5T MRI scanner (Signa, GE, Milwaukee, Wisconsin, USA) was used. (4) Inversion algorithm. A 2D phase gradient (PG) inversion was performed on the MRE wave data with 2D directional filters (cut-off frequencies of 0.1 and 128 cycles/FOV) to calculate stiffness images (elastograms) of the bones[7]. A large region of interest was drawn inside the bone, 3-7 pixels away from the edges and the driver location, to report the global stiffness.



(a) (b)

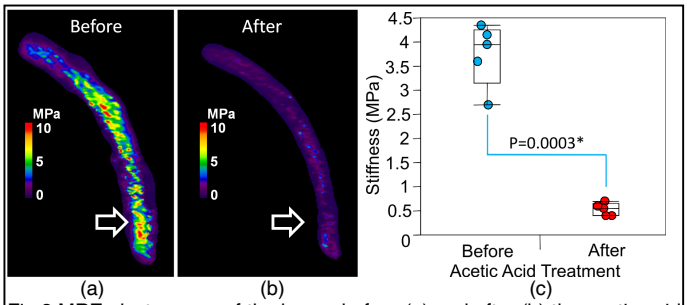
Fig.1 Ex vivo osteoporosis model and MR elastography setup. (a) Five porcine ribs. (b) MRE setup components: 1- surface coil, 2- support bar, 3- piezoelectric driver, 4- rigid clamp, 5- bone and 6- wet paper towel (uncovered to show the bone).



(a) (b)

Fig.2 MRE wave images with (a) the driver on and (b) the driver off. The arrow indicates the driver mounting location.

Results and Discussion: Fig. 2 shows that the piezoelectric driver and MRE motion sensitivity were sufficient to see wave motion in the bone, compared with the wave images collected with the driver off. Similar to what we observed in our previous study [6], the soft tissue in the marrow space was capable of transmitting the high-frequency cyclic motion in the bone. Fig. 3 shows the stiffness measurements of bones before and after the 48-hour acetic acid treatment. Before the treatment, global bone stiffness of the five ribs ranged from 2.7 to 4.4 (mean = 3.7) MPa. After the treatment, the global bone stiffness of the five ribs ranged from 0.4 to 0.7 (mean = 0.5) MPa. The paired T-test shows that the bones became statistically significantly softer after the treatment (p = 0.0003). This indicates that loss of bone minerals due to the acetic acid treatment deteriorated the bone mechanical properties. The MRE results were consistent with another study (data not shown here) in which a significant decrease of bone stiffness before and after a 48-hour acetic acid treatment were observed in porcine tibias using dynamic mechanic analysis (DMA). This ex vivo osteoporosis model allows for initial testing and validation of bone MRE techniques without the cost and time required to use an in vivo animal model. In the future, we will use the same methodology to examine ex vivo osteoporosis models of femurs and vertebrae where osteoporosis and pathologic fractures are common. We will also continue to develop bone MRE and investigate the feasibility of bone MRE in in vivo animal models.



(a) (b) (c)

Fig.3 MRE elastograms of the bones before (a) and after (b) the acetic acid treatment. The arrow indicates the driver mounting location.

Conclusion: In this study, MRE measured and detected the stiffness change in an ex vivo osteoporosis model of bone. Our next step is to further optimize the MRE technique by using a higher frequency (3-5 kHz) driver and a high-speed local gradient coil for improving the sensitivity, accuracy and spatial resolution of bone stiffness measurements. Our long term goal is to use MRE to noninvasively measure bone stiffness for risk assessment in patients with bone diseases, including osteoporosis.

References: 1. Consensus development conference: prophylaxis and treatment of osteoporosis. Osteoporos Int, 1991. 1(2). **2**. Cummings, S.R., Lancet, 2002. 359(9319). **3**. Genant, H., Current Orthopaedics, 1999. 13(2). **4**. Hodgskinson, R., Bone, 1997. 21(2). **5**. Burr, D.B., Bone, 2002. 31(1). **6**. Chen, J., ISMRM 848, 2009. **7**.Manduca, A., Med Image Anal, 2001. 5(4). **8**.Comelekoglu, U., Acta Orthop Traumatol Turc, 2007. 41(1).