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Short communication

Accuracy and reproducibility of bending stiffness measurements by mechanical response tissue analysis in artificial human ulnas

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ABSTRACT

Osteoporosis is characterized by reduced bone strength, but no FDA-approved medical device measures bone strength. Bone strength is strongly associated with bone stiffness, but no FDA-approved medical device measures bone stiffness either. Mechanical Response Tissue Analysis (MRTA) is a non-significant risk, non-invasive, radiation-free, vibration analysis technique for making immediate, direct functional measurements of the bending stiffness of long bones in humans *in vivo*. MRTA has been used for research purposes for more than 20 years, but little has been published about its accuracy. To begin to investigate its accuracy, we compared MRTA measurements of bending stiffness in 39 artificial human ulna bones to measurements made by Quasistatic Mechanical Testing (QMT). In the process, we also quantified the reproducibility (*i.e.*, precision and repeatability) of both methods. MRTA precision ($1.0 \pm 1.0\%$) and repeatability ($3.1 \pm 3.1\%$) were not as high as those of QMT ($0.2 \pm 0.2\%$ and $1.3 + 1.7\%$, respectively; both $p < 10^{-4}$). The relationship between MRTA and QMT measurements of ulna bending stiffness was indistinguishable from the identity line ($p = 0.44$) and paired measurements by the two methods agreed within a 95% confidence interval of $\pm 5\%$. If such accuracy can be achieved on real human ulnas *in situ*, and if the ulna is representative of the appendicular skeleton, MRTA may prove clinically useful.

1. Introduction

Osteoporosis is a skeletal disorder characterized by reduced bone strength and increased risk of fracture (National Institutes of Health, 2001), but no FDA-approved device measures bone strength. Consequently, osteoporosis is diagnosed by measuring bone mineral density (BMD) (Schousboe et al., 2013), even though BMD does not predict fractures well: among 200,000 postmenopausal women, 96% of those diagnosed with osteoporosis did not fracture, while 81% of fractures occurred in women who did not have osteoporosis (Siris et al., 2001). Bone strength is strongly associated ($r > 0.95$) with bone stiffness (Borders et al., 1977; Fyhrie and Vashishth, 2000; Jurist and Foltz, 1977; Roberts et al., 1996), but no FDA-approved device measures bone stiffness either. The reference method for measuring bone stiffness and strength, Quasistatic Mechanical Testing (QMT), can only be employed *in vitro*. Mechanical Response Tissue Analysis (MRTA) is a non-significant risk, non-invasive, radiation-free, vibration analysis technique for making direct functional measurements of the bending stiffness of long bones in humans *in vivo* (Steele et al., 1988). Because bending tests are especially sensitive to mid-span mechanical properties, MRTA may be useful for measuring the bending stiffness of cortical bone. About 80% of fractures after age 60 occur at cortical bone sites (Kanis et al., 2001).

MRTA has been used for research (Miller et al., 2013), but little has been published about its accuracy. To begin investigating this, we compared MRTA and QMT measurements of the bending stiffness of artificial human ulna bones. The ulna is convenient for MRTA testing *in vivo*, due to its superficiality and near-ideal biomechanics in bending. We began with artificial bones because they have dimensions and mechanical properties similar to real bones (Dunlap et al., 2008; Gardner et al., 2010; Heiner, 2008), and because they require no special handling, storage or disposal.

2. Methods

2.1. Specimens

Custom Sawbones® 4th generation composite human ulna bones ($N = 39$, Model #3426, Pacific Research Laboratories, Inc., Vashon, WA) were purchased. These artificial ulnas are comprised of a polyurethane foam core emulating cancellous bone covered by a glass-filled epoxy shell emulating cortical bone. Ulna geometry was standardized within manufacturing tolerances, while the percentage of glass fill in the epoxy was varied to achieve a range of bending stiffness across which to compare MRTA and QMT measurements. Four ulnas were manufactured at each of 9 levels of excess glass fill (−10%, −7.5%, −5%, −2.5%, 0%, +2.5%, +5%, +7.5%, and +10%), where 0% is the standard proprietary percentage. Two proof-of-concept ulnas with +6% excess glass fill

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and an anomalous ulna with 0% excess glass fill were also tested and included in the data analysis. Ulnas were received in four batches.

2.2. Data collection

For both methods, ulnas were supported and loaded in 3-point bending in a manner similar to that used in MRTA tests of human subjects *in vivo*. As illustrated in the Supplementary material, ulnas were oriented horizontally, posterior surface up, with the load applied downward at the midpoint of the span between supports. Proximally, the trochlear notch of the ulna was supported by the articulating trochlea at the distal end of a 4th generation composite Sawbones® humerus (Model #3404, Pacific Research Laboratories) that was held upright in a bone clamp (Model #1605, Pacific Research Laboratories). Distally, the anterior surface of the distal radioulnar joint was supported by the top of a vertical 50 mm × 75 mm × 300 mm steel block. To prevent confounding by variations in axial rotation of the ulna, axial rotation was standardized before each test by aligning a mark on the tubercle of the coronoid process on the medial side of the proximal end of each ulna with a mark on the medial side of the trochlea at the distal end of the humerus.

2.2.1. QMT data collection

QMT data were collected with a 10 kN load frame (QTest-Elite, MTS Systems Corporation, Eden Prairie, MN) using a 25 N load cell (Model 4501017B, MTS Systems Corporation) to measure applied force. To prevent viscous and inertial effects from confounding elastic force measurements, data (Fig. 1, Top) were collected at a crosshead speed of 0.1608 mm/min (*i.e.*, 1 step of the stepper motor driving the crosshead per data point at 10 Hz) for a strain rate $<0.0001/s$.

Loading cycles of 0–20 N were repeated until the coefficient of variation (CV=standard deviation/mean) of bending stiffness (K_B) in the last five cycles was $<1.0\%$. This CV was recorded as the index of QMT measurement precision. Ulnas were then dismounted. The mean of three such measurements was taken as the QMT measurement of K_B, and the CV of these measurements was recorded as the index of QMT measurement repeatability.

2.2.2. MRTA data collection

MRTA data were collected with a custom MRTA system comprised of an impedance head for measuring force and acceleration (Model 288D01, PCB Piezotronics, Inc., Depew, NY), an electromechanical shaker with integrated power amplifier (Model K2007E01, The Modal Shop, Inc., Cincinnati, OH), a dynamic signal analyzer (*Photon+*, Brüel & Kjær North America, Inc., Norcross, GA), and a laptop computer with signal processing and waveform source software (*RT Pro*, Brüel & Kjær North America, Inc.). Rubber tourniquets (x-tourn™ Cat 18679, Avcor Health Care Products, Ft Worth, TX) were used to prevent the coupling of extraneous vibrations of the mechanical structure into the ulna, and to emulate skin between the ulna and the force probe.

The applied load was comprised of a 1 N oscillating component randomly spanning a range of frequencies from 40 to 1200 Hz superimposed upon a manually adjusted static component of 10–20 N. While observing the imaginary part of the accelerance (*i.e.*, acceleration/force) frequency response function (FRF) (Fig. 1, Bottom), the static component was adjusted to increase the stiffness of the skin and thereby to raise and separate a higher frequency resonance determined primarily by the mechanical properties of the skin from the lower frequency resonance determined primarily by the mechanical properties of the ulna. Frequency response functions were recorded three times at 1 Hz intervals and the CV of the resulting K_B measurements was recorded as the index of MRTA measurement precision. Ulnas were then dismounted. The mean of three such measurements was taken as the MRTA measurement of K_B, and the CV of these measurements was recorded as the index of MRTA measurement repeatability.

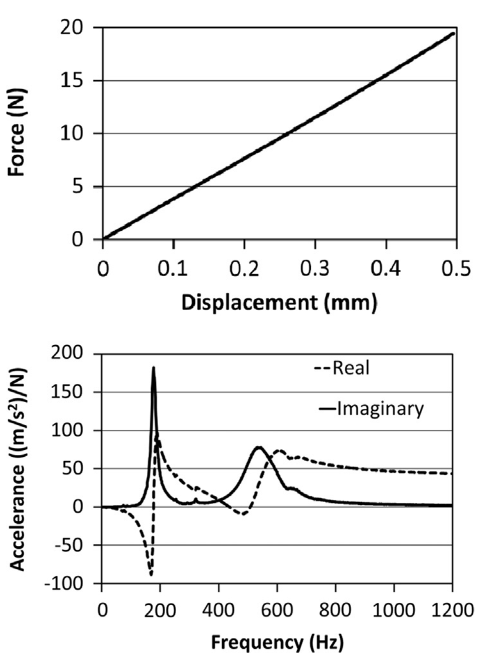

Fig. 1. Raw force *vs* displacement data collected by QMT (Top) and raw complex accelerance frequency response function data collected by MRTA (Bottom).

2.3. Data analysis

Because the slenderness ratio of the artificial ulna exceeded 20, shear forces were ignored and the ulna was modeled as a simply supported beam in bending with stiffness K_B. Then, even though the ulnas were the same length, ulna flexural rigidity (EI) was calculated from Euler beam theory for later comparison to real human ulnas of various lengths:

$$EI = K_B \times L^3/48 \tag{1}$$

where L=0.245 m was the span across which the ulna was supported.

2.3.1. QMT data analysis

In QMT bending tests, we derived K_B from the steepest slope of the force/displacement curve over half the 20 N range of applied force, in practice, always the upper half. Within the elastic range of the ulna, this measured stiffness K_M reflects the series combination of K_B and the stiffness of the test frame (K_F=83.44 N/mm in our case), which was dominated by the most compliant part, *i.e.*, the load cell (Fig. 2, Left)

$$K_M = K_B \times K_F/(K_B + K_F) \tag{2}$$

Rearrangement of Eq. (2) yielded K_B as

$$K_B = K_M \times K_F/(K_F - K_M) \tag{3}$$

2.3.2. MRTA data analysis

Like previous MRTA practitioners (Steele et al., 1988), we modeled the dynamic behavior of the ulna and overlying skin as a 7-parameter mechanical system (Fig. 2, Right), including the mass, stiffness and damping of the skin (M_S, K_S, B_S) and of the bone (M_B, K_B, B_B) together with an allowance for damping by surrounding soft tissue (B_p). The procedure by which optimum FRF data were selected for model fitting is described in the Supplementary material. Unlike previous practitioners, we fitted the complex, continuous-time transfer functions of both the stiffness and compliance of the skin-bone system to the corresponding FRFs derived from the accelerance FRF of each ulna. Invariably, the coefficient of determination (R^2) for fits to stiffness exceeded those for fits to compliance, the lowest of which was 0.977. Then we calculated EI from the average of the two estimates of K_B in the two fits.

2.4. Statistical analysis

The precision and repeatability of MRTA and QMT measurements were compared by paired Student's *t*-tests. The association of paired MRTA and QMT measurements was determined by regression analysis. Bland–Altman analysis (Bland and Altman, 1986) was used to quantify the bias and limits of agreement between them.

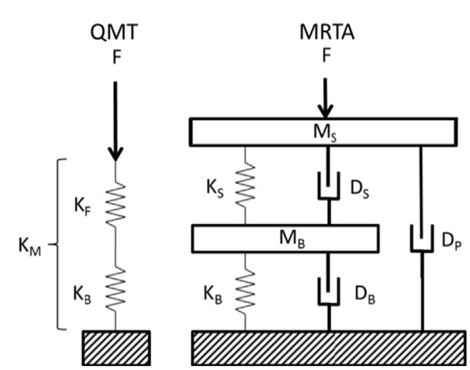

Fig. 2. Mechanical models assumed in the analysis of data from the 3-point bending tests by QMT (Left) and MRTA (Right). F=applied force. K_F=stiffness of QMT test frame. M_S, M_B=mass of skin, bone. K_S, K_B=stiffness of skin, bone. D_S, D_B, D_P=damping of skin, bone, peripheral tissue.