Validation of a dynamic MR elastography technique customized for in vitro biomechanical assessment of articular cartilage under high frequency cyclical shear

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Introduction

The purpose of this work was to validate a customized dynamic MR Elastography (MRE) technique designed to measure the dynamic shear properties of articular cartilage directly and nondestructively through its thickness. In contrast to conventional dynamic MRE techniques which have been mainly targeted to study soft tissue materials at low-frequencies (typically < 500 Hz) of mechanical excitation [5, 7], dynamic MRE of cartilage requires adequate generation and visualization of high-frequency (> 1 kHz) shear waves that propagate throughout the thickness of the cartilage with appropriate spatial and temporal sampling according to the small size (< 6 mm thick) and high dynamic shear modulus (> 200 kPa) of cartilage [2-4]. For this purpose, an application-specific z-axis gradient coil system and associated instrumentation were developed to bypass gradient amplitude and slew rate limitations (22 mT/m and ~200 mT/m/ms, respectively) of typical clinical MR scanners which prevent oscillatory gradients above 1360 Hz to reach adequate gradient strengths necessary for dynamic MRE of cartilage. Our ability to produce strong and fast-switching oscillatory gradients has enabled sensitive encoding of high-frequency (in the kilohertz) propagating shear waves to assess the internal distribution of mechanical properties of cartilage and other small-stiff materials [2-4].

The sensitivity and repeatability of the customized dynamic MRE technique to assess the biomechanical properties of cartilage through its thickness were validated using sets of homogeneous, cartilage-mimicking, small dual-layered phantoms (2.5 mm thick per layer x 10 mm^2) made of wirosil silicone (polyvinyl-siloxane). Shear stiffness (μ) measurements were obtained from each layer of the small-stiff dual-layered phantoms tested by customized dynamic MRE at 4- and 6-kHz of shear mechanical excitation and compared against μ values from large (15 mm thick x 19mm in diameter) reference phantoms of corresponding stiffness.

Given the correlation between changes in mechanical properties and degeneration by osteoarthritis of articular cartilage [6], dynamic MRE offers a sensitive tool for optimal study of cartilage mechanics in the context of structural changes to its matrix constituents [1-4, 6]. Application of the validated dynamic MRE technique was tested by assessing the difference in μ between superficial and deep layers in a plug of bovine articular cartilage about 5mm thick.

Methods

Wirosil silicone was identified as an appropriate cartilage-mimicking phantom material because of its good MRI signal, high stiffness, mechanical stability, and flexible preparation. Wirosil is a two-component (wirosil-1:wirosil-2) mixture, where a 1.0:1.0 mixing ratio by weight produces the stiffest cured form (μ ~ 300 kPa). We systematically evaluated large (20 mm thick x 25 mm in diameter) wirosil phantoms prepared at various mixing ratios (0.4:1.0 to 1.8:1.0) using conventional MRE at 1000 Hz to determine mixing ratios that would produce two stiff (μ > 200 kPa) wirosil phantoms with $\Delta\mu$ ~ 100 kPa. It was determined that wirosil preparations with mixing ratios of 1.8:1.0 and 0.9:1.0 produced phantoms with desired $\Delta\mu$ ~ 100 kPa, at ~200 kPa and ~300 kPa respectively, Figure 1.

Accordingly, small dual-layered (2.5 mm thick per layer x 10 mm^2) phantoms (n = 9) were constructed, Fig.1, to mimic the superficial (soft) and deep (stiff) layers of articular cartilage [1, 6]. Corresponding larger (15 mm thick x 19mm in diameter) single layer reference phantoms (soft, n = 7; and stiff, n = 7) were also constructed from the same wirosil preparations. Independent dynamic MRE testing of each small dual-layered and reference phantom was performed at 4- and 6-kHz. Typical acquisitions were made with a 1.5T clinical imager using a GRE MRE sequence with 50 motion-sensitizating gradients, TR = 500 ms, TE = 23 ms, flip angle = 40 deg., slice thickness = 4mm and FOV = 2x2 cm. Estimates of μ from phantoms were calculated using the gradient of the phase from the temporal harmonic of the collected wave images at the mechanical excitation frequency [5].

A two-sample t-test for independent samples with equal variances was used to determine agreement between mean μ values obtained from each layer of the small dual-layered phantoms and mean μ values from corresponding reference phantoms. T-tests were also used to determine the sensitivity of detecting a significant difference ($\Delta\mu$) between soft and stiff layers in the small dual-layered phantoms.

Additionally, dynamic MRE of a plug of bovine articular cartilage at 5 kHz was performed to test the ability of the technique to assess internal differences in μ between superficial and deep layers in the tissue.

Results

A photograph of the wirosil phantoms and results from dynamic MRE of a small dual-layered phantom at a mechanical excitation of 4 kHz are shown in Figure 2. The measured μ (mean ± SD) from soft and stiff small layers and corresponding reference wirosil phantoms are shown in the bar graph in Figure 1 as a function of mechanical excitation frequency. Wave images from dynamic MRE of a bovine articular cartilage plug tested at 5 kHz are shown in Figure 3. Measured μ (mean ± SD) values from surface- and deep- layers of the bovine articular cartilage plug were calculated to be 4578.08 ± 124.57kPa and 7714.76 ± 67.65kPa, respectively, which agree with the expected depth-dependent distribution of mechanical properties within articular cartilage tissue [1, 6].

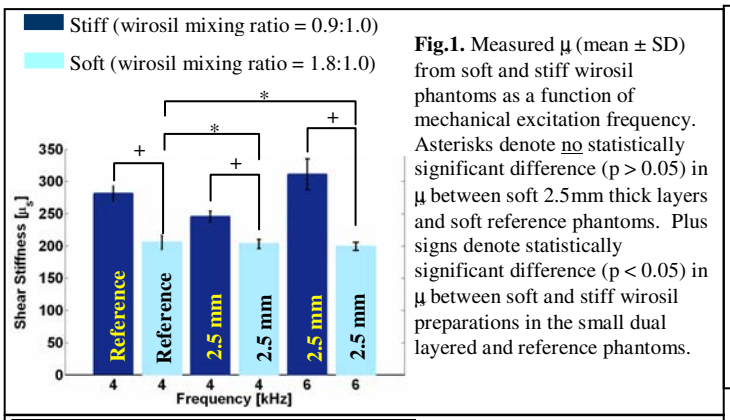

Fig.1. Measured μ (mean ± SD) from soft and stiff wirosil phantoms as a function of mechanical excitation frequency. Asterisks denote no statistically significant difference ($p > 0.05$) in μ between soft 2.5mm thick layers and soft reference phantoms. Plus signs denote statistically significant difference ($p < 0.05$) in μ between soft and stiff wirosil preparations in the small dual layered and reference phantoms.

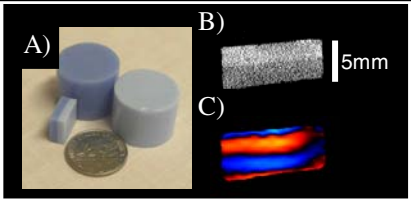

Fig.2. A) Photograph of small dual-layered and reference wirosil phantoms next to a US dime coin. B) GRE image of dual-layered phantom, and C) shear wave propagating at 4kHz through the dual-layered phantom.

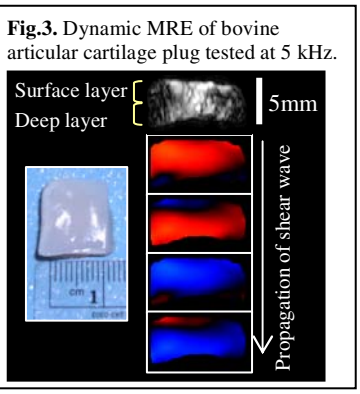

Fig.3. Dynamic MRE of bovine articular cartilage plug tested at 5 kHz.

References 1) Erne O, et al, J Biomech, 38(4): p667-672, 2004 **2)** Lopez O, et al, ISMRM, 2004 **3)** Lopez O, et al, ISMRM, 2003 **4)** Lopez O, SPIE Med Imag, 5369: p51-61, 2004 **5)** Manduca A, et al, Med Imag Anal, 5: p237-254, 2001 **6)** Mow VC, et al, Annual Rev. of Biomed. Eng, 4: p75-209, 2002 **7)** Muthupillai R, et al, Nat Med, 2(5): p601-603, 1996

Discussion

Results from our validation study demonstrated the sensitivity and repeatability of the customized dynamic MRE technique in detecting differences in mechanical properties within small-stiff, multilayered, cartilage mimicking materials. Despite small variations of measured μ values of the stiff layer in the small dual layered phantoms away from reference values, the technique performed well when detecting relative μ difference between layers. Variations could be attributed to noise levels and wave reflections which may hinder the phase gradient inversion of wave images. In conclusion, customized dynamic MRE is a sensitive tool for *in vitro* assessment of the internal biomechanical properties of articular cartilage.