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Characterization of the ultra-short echo time magnetic resonance (UTE MR) collagen signal associated with myocardial fibrosis

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Background

The homogeneous distribution of collagen in diffuse myocardial fibrosis renders the disease unsuitable for imaging using late gadolinium enhancement (LGE) [1]. More recently, the estimation of extracellular volume from T_1 maps involving gadolinium agents has shown promise; however, these methods are not specific to collagen and are governed by gadolinium kinetics [2]. The diagnosis of diffuse myocardial fibrosis would benefit from an imaging method that can directly detect collagen. Notably, ultra-short echo time magnetic resonance (UTE MR) is a technique that can be used to detect short T_2* species, including collagen [3]. Our objective is to characterize the UTE signal of protons in the collagen molecule, including their T_2* and chemical shift. Direct isolation of a collagen signal could aid in the diagnosis of myocardial fibrosis, especially for diffuse distributions, and the assessment of disease extent.

Methods

Collagen solutions of concentrations ranging from 0 % m/v to 50 % m/v were prepared by dissolving hydrolyzed type I and III collagen powder in 0.125 mM $MnCl_2$, where the signal decay of $MnCl_2$ mimicked that of cardiac muscle. Each solution was scanned using a 3D UTE pulse sequence at 7 T, acquiring TEs from 0.02 ms to 25 ms, at a resolution of 0.781 mm isotropic. Upon fitting with a model of bi-exponential T_2* with oscillation, the UTE collagen signal fraction was determined and calibrated against the collagen concentration. The T_2* and resonance frequency (arising from the chemical shift) of collagen were assessed in collagen solutions. Validation of the collagen signal properties was also performed in formalin-fixed canine heart tissue, imaged with TEs from 0.02 ms to 25 ms, at a resolution of 0.156 mm isotropic.

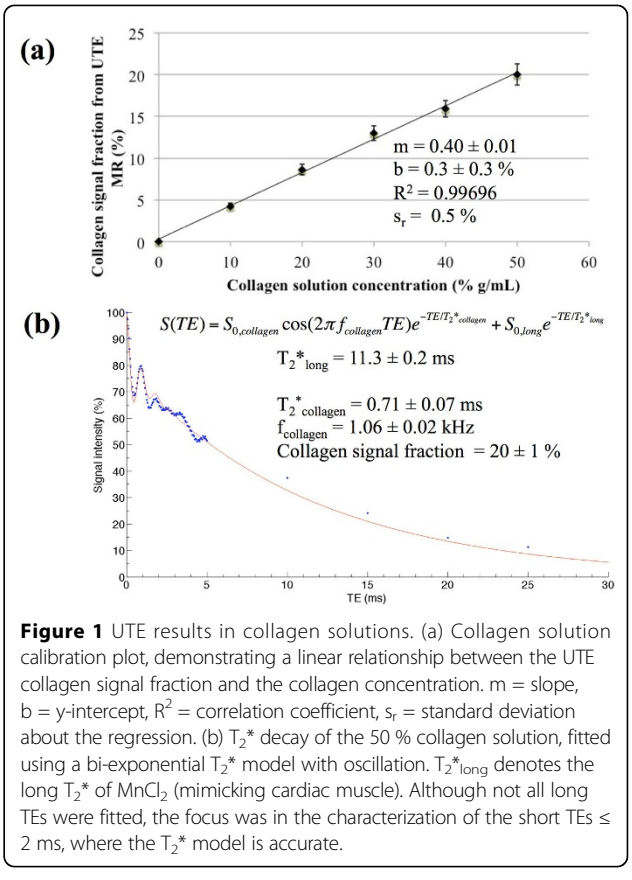

Figure 1 UTE results in collagen solutions. (a) Collagen solution calibration plot, demonstrating a linear relationship between the UTE collagen signal fraction and the collagen concentration. m = slope, b = y-intercept, R^2 = correlation coefficient, s_r = standard deviation about the regression. (b) T_2* decay of the 50 % collagen solution, fitted using a bi-exponential T_2* model with oscillation. T_2*$_{long}$ denotes the long T_2* of $MnCl_2$ (mimicking cardiac muscle). Although not all long TEs were fitted, the focus was in the characterization of the short TEs ≤ 2 ms, where the T_2* model is accurate.

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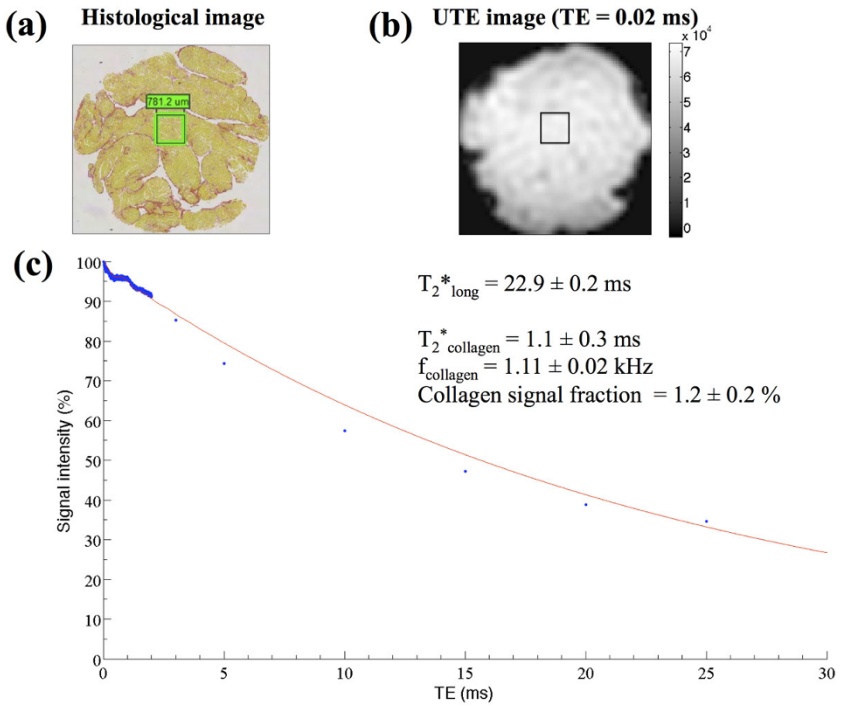

Figure 2 Histology and UTE results in canine heart tissue. (a) Histological slice of heart tissue, stained with Picrosirius Red. The 781.2 μm x 781.2 μm region-of-interest (ROI) used for analysis is delineated. The collagen area fraction in the ROI was determined to be 4 ± 2 %, based on a pixel threshold algorithm. (b) Corresponding UTE MR image at TE = 0.02 ms, with the ROI delineated. (c) T_2* decay within the ROI. T_2*$_{long}$ denotes the long T_2* of cardiac muscle. TEs ≤ 2 ms were finely sampled to determine the collagen T_2* and resonance frequency, where the T_2* model is accurate. Based on the calibration plot in Figure 1a, the collagen signal fraction of 1.2 ± 0.2 % was equivalent to a collagen concentration of 2.3 ± 0.9 %. Hence, there was agreement between the collagen area fraction determined from histology (4 ± 2 %) and the collagen concentration.

Results

For collagen concentrations of 10 % to 50 %, the mean collagen T_2* was 0.75 ± 0.05 ms, and the mean collagen frequency was 1.061 ± 0.004 kHz. A linear relationship (slope = 0.40 ± 0.01, R^2 = 0.99696) was determined between the UTE collagen signal fraction associated with these characteristics and the measured collagen concentration (Figure 1). Similarly in canine heart tissue, a signal with T_2* of 1.1 ± 0.3 ms and resonance frequency of 1.11 ± 0.02 kHz upfield of water was determined, consistent with collagen (Figure 2). The UTE collagen signal fraction of 1.2 ± 0.2 % in tissue corresponded to a collagen concentration of 2.3 ± 0.9 %, which was within the uncertainty of the collagen area fraction determined from histology (4 ± 2 %).

Conclusions

The results suggest that collagen associated with myocardial fibrosis can be endogenously detected and quantified using UTE MRI. This signal is specific to protons in collagen, characterized by a T_2* of ~ 0.8 ms and a resonance frequency of ~ 1.1 kHz upfield of water at 7 T. Such properties would be beneficial in the determination of collagen content due to disease.

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