

## Cardiac ECV is More Robust than Post-Contrast Cardiac T1 for Evaluating Temporal Changes in Left Ventricular Fibrosis

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**Introduction:** Cardiac magnetic resonance (CMR) is the only proven non-invasive modality for assessment of diffuse myocardial fibrosis. While post-contrast cardiac T1 has been shown to be inversely correlated with interstitial fibrosis, it can be influenced by various confounders, such as cardiac function, renal function, hematocrit, magnetic field strength, contrast agent type and dosage, and specific delayed imaging time. To compensate for these confounders, investigators have proposed to measure extracellular volume (ECV) derived from hematocrit and pre- and post-contrast myocardial and blood T1 values. Despite the advantages of ECV over post-contrast cardiac T1, systematic studies comparing the two measurements are lacking<sup>1</sup>. The purpose of this study was to compare the effectiveness of post-contrast cardiac T1 and ECV measurements for evaluating the temporal changes in left ventricular (LV) fibrosis in an established canine model with chronic atrial fibrillation (AF)<sup>2</sup>.

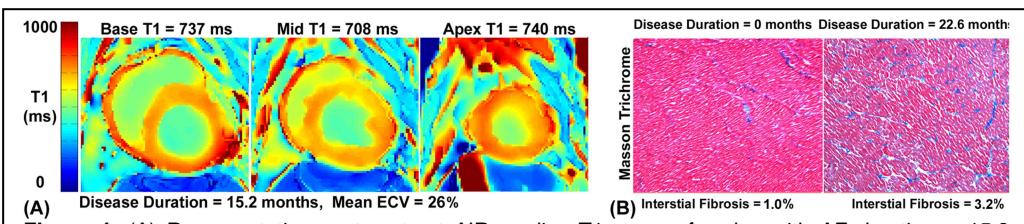
**Methods:** Seventeen mongrel dogs with different durations (0-22 months) of chronic AF were scanned multiple times for a total of 46 CMR scans at 3T (Verio, Siemens). Cardiac T1 maps were acquired in three short-axis planes (base, mid, and apex) using the arrhythmia-insensitive-rapid (AIR) cardiac T1 mapping pulse sequence<sup>3</sup> based on B1-insensitive saturation recovery of magnetization preparation, with the following relevant imaging parameters: spatial resolution = 1.4 mm x 1.4 mm x 7.0 mm, temporal resolution = 217 ms, and saturation recovery time (TD) = 600 ms. AIR pulse sequence acquired a proton density image,  $I_{PD}$ , and a saturation recovery T1 weighted image,  $I_{T1w}$ . A pixel-wise T1 map was calculated from the Bloch equation:  $T1 = -TD/\ln(1-I_{T1w}/I_{PD})$ . Cardiac T1 maps were acquired at pre-contrast and exactly 15 min after a bolus injection of Gd-BOPTA (MultiHance; 0.15 mmol/kg). Blood samples were drawn during MRI for hematocrit calculation. For image analysis, myocardial and left ventricular blood pool contours were manually segmented to calculate their mean T1 values. The resulting ECV was calculated as:  $ECV = 100(\%) \cdot (1 - \text{hematocrit}) \cdot \Delta R1(\text{myocardium}) / \Delta R1(\text{blood})$ , where  $R1 = 1/T1$  and  $\Delta$  is the difference between post-contrast and pre-contrast. Temporal changes in post-contrast LV T1, post-contrast blood T1, and ECV were modeled with linear mixed effect models to account for repeated measurements over disease duration. Six dogs were sacrificed at different durations of AF (0-22.6 months) for histologic quantification of LV fibrosis.

**Results:** Figure 1 shows post-contrast cardiac T1 maps of a dog with disease duration = 15.2 months, as well as LV tissue samples of different dogs with Masson's trichrome staining at baseline (interstitial fibrosis = 1.0%) and 22.6 months of AF duration (interstitial fibrosis = 3.2%). In Figure 2, LV and blood T1s changed significantly ( $p < 0.05$ ) with disease duration over 22 months. Note that the temporal trends in post-contrast LV and blood T1s are similar. In contrast, both ECV by CMR and interstitial fibrosis by histology did not change significantly with disease duration. Compared with histologic quantification of interstitial fibrosis, ECV agreed better than post-contrast LV T1.

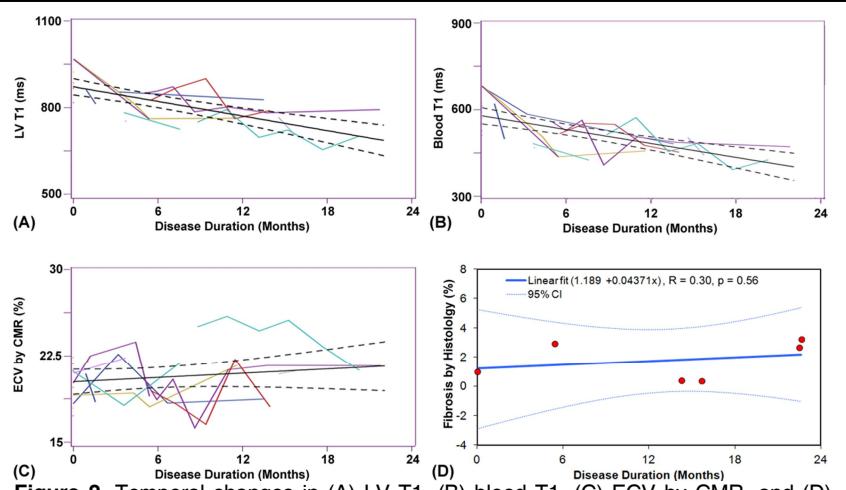
**Conclusion:** This study suggests that ECV is a more robust measure of extracellular space than post-contrast LV T1, especially for evaluating temporal changes in LV fibrosis.

### References:

1. Miller CA et al., *Circ Cardiovasc Imaging* 2013;6:373-383.
2. Dosdall DJ et al., *Am J Physiol Heart Circ Physiol* 2013;305(5):H725-31.
3. Fitts M et al., *MRM* 2013;70:1274-82.



**Figure 1.** (A) Representative post-contrast AIR cardiac T1 maps of a dog with AF duration = 15.2 months: (left) basal ( $T1 = 737$  ms), (middle) mid-ventricular ( $T1 = 708$  ms), and (right) apical ( $T1 = 740$  ms) planes, with mean ECV = 26%. (B) Histologic evaluation of LV tissues with Masson's trichrome staining. The LV tissue samples were from different dogs sacrificed at different durations of AF: (left) baseline and (right) 22.6 months. All specimens displayed with 10x magnification.



**Figure 2.** Temporal changes in (A) LV T1, (B) blood T1, (C) ECV by CMR, and (D) interstitial fibrosis by histology. Compared with histologic quantification of fibrosis, ECV agreed better than post-contrast LV T1.