# Myocardial Biopsy for the Validation of Cardiac Magnetic Resonance T1 Mapping for Quantification of Extracellular Matrix

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Disclosures: none

## Background

Diffuse myocardial fibrosis / extracellular matrix expansion is a landmark feature of various cardiac diseases and is associated with an unfavorable prognosis. Recently, cardiac magnetic resonance (CMR) T1-mapping has been proposed for the quantification of extracellular matrix.

Published series mainly used two T1 mapping sequences: 1. Modified Look-Locker Inversion recovery (MOLLI) T1 mapping, allowing the calculation of extracellular volume (ECV) [1], 2. Post-contrast multiple breath-hold T1 mapping [2]. In addition, native (pre-contrast) T1 mapping has gained increasing interest [3].

Although CMR T1 mapping is a very promising technique and has been advertised as the new “non-invasive myocardial biopsy”, validation data, particularly in heart failure patients, are sparse.

## Methods

**Patients**. 22 heart failure patients underwent CMR T1 mapping and left ventricular biopsy within 4 weeks. The population consisted of 16 HFpEF (heart failure with preserved ejection fraction) patients, 3 patients suffering from dilated cardiomyopathy and 3 amyloidosis patients. All patients gave written informed consent prior to study entry. The institutional review board approved the study protocol.

**CMR protocols**. All patients underwent a CMR study on a 1.5-T scanner (Avanto, Siemens Medical Solutions, Erlangen, Germany). Studies consisted of functional and LGE imaging, according to standard protocols. Additionally, 3 types of tissue characterization using T1-mapping techniques were performed:

1) A midventricular short-axis and a 4-chamber long-axis view were acquired using the modified look-locker inversion recovery (MOLLI) sequence. T1 times were derived by manually defining the region of interest, excluding areas in which late enhancement was present.
2) This was repeated 15-20 minutes after contrast agent application and hence we were able to calculate ECV (in %) using the formula:

$$ECV = (1 - hematocrit)\frac{\left(\frac{1}{T1_{myo\ post}} - \frac{1}{T1_{myo\ pre}}\right)}{\left(\frac{1}{T1_{blood\ post}} - \frac{1}{T1_{blood\ pre}}\right)}$$

3) Additionally, 15 minutes after intravenous Gadolinium injection, a multiple breath-hold ECG-triggered segmented inversion recovery spoiled gradient echo sequence with increasing inversion times was used to acquire a stack of 8 images in the middle short-axis slice over a range of inversion times from 115ms to 900ms.

**Left ventricular biopsies** taken during left heart catheterization were stained with modified Trichrome. Extracellular matrix was quantified with TissueFAXS and HistoQuest analysis and is given in % per $mm^2$.

## Results

Extracellular matrix by TissueFAXS was 43.8±20.8% of the myocardium, ECV as determined by MOLLI was 33.6±9.9%. The average post-contrast T1 time by the multiple breath-hold sequence was 407±85ms. Native MOLLI T1 times were 1000±61ms, T1 times 15 min after contrast agent application averaged at 393±40ms.

The amount of extracellular matrix by TissueFAXS correlated significantly with MOLLI ECV (r=0.583, p=0.011) and with multiple breath-hold post-contrast T1 times (r=-0.459, p=0.042), but not with native T1 times (r=0.375, p=0.114).

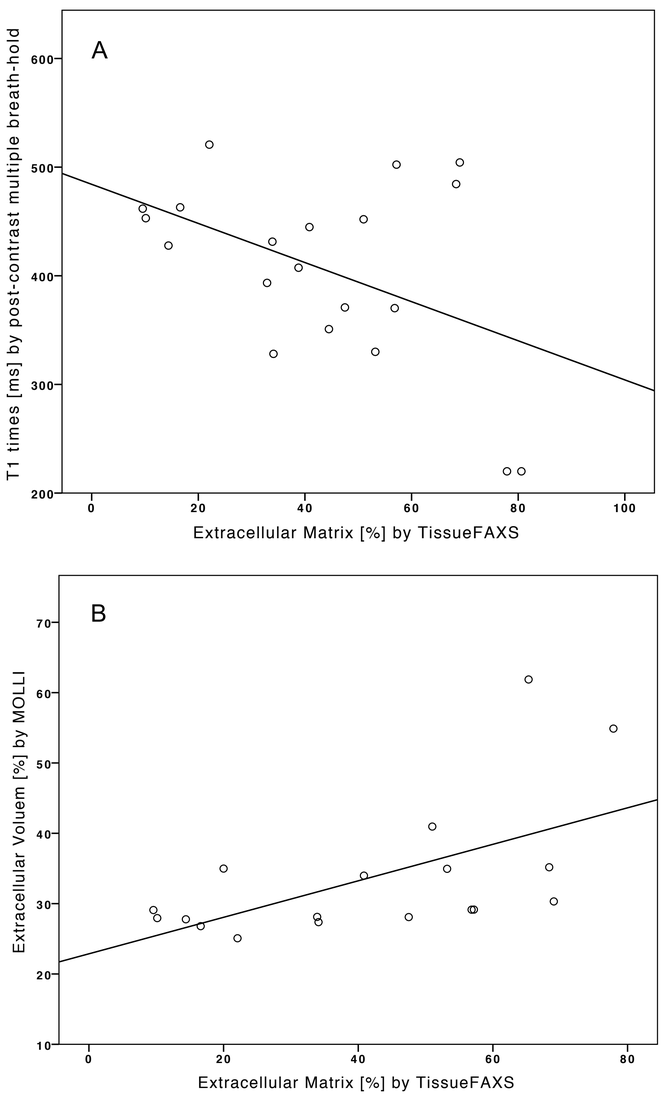


Figure 1: A. Correlation of extracellular matrix by TissueFAXS analysis with post-contrast multiple breath-hold T1-times; B. Correlation of extracellular matrix by TissueFAXS analysis with MOLLI ECV.

Multiple breath-hold T1 times correlated well with MOLLI ECV (r=-0.584, p=0.018) and with MOLLI post contrast T1 times (r=0.498, p=0.050).

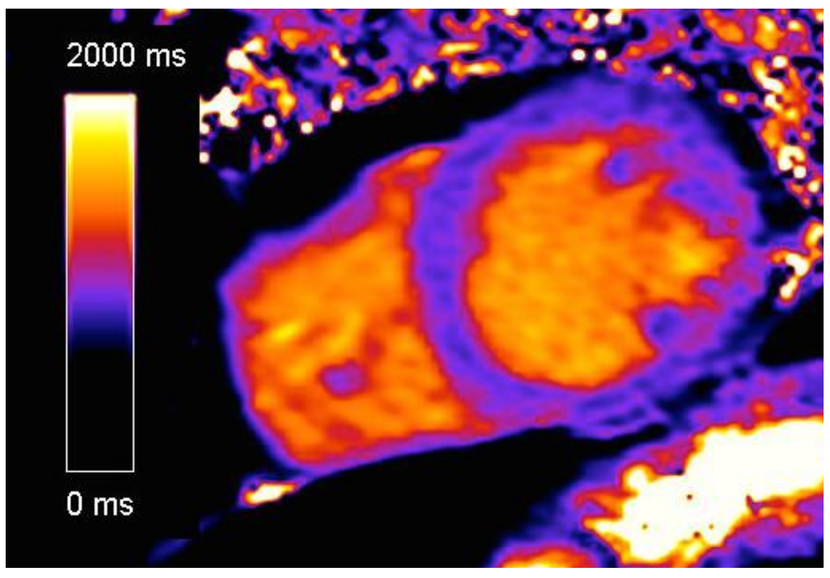


Figure 2: Color-encoded pre-contrast T1 map using MOLLI. In this HFpEF patient, native MOLLI T1 time was 956ms and ECV was 25%. T1 time by post-contrast multiple breath-hold was 521ms.

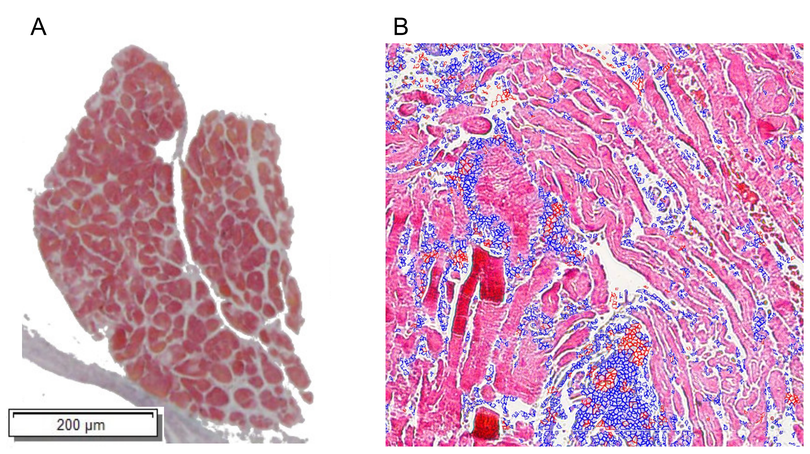


Figure 3: A. Myocardial specimen of the same patient as in Figure 2 with Trichrome staining. B. TissueFAXS and HistoQuest analysis were used to quantify exctracellular matrix expansion (marked blue) which was 22% in this individual.

## Conclusion

In the present series, MOLLI ECV appears to be the most accurate method for the quantification of extracellular matrix expansion when validated against myocardial biopsies. Although multiple breath-hold post-contrast T1 times may be influenced by renal function, heart rate, and time of image acquisition, it also appears useful for non-invasive measurement of extracellular matrix. Native T1 mapping showed the weakest correlation with extracellular matrix by TissueFAXS, but there was a tendency towards a significant relationship.

References.
1. White et al., JACC Cardiovasc Imaging. 2013 Sep;6(9):955-62.
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3. Bull et al., Heart. 2013 Jul;99(13):932-7.