Native T₁ Mapping for Myocardial Infarction
Time to Throw Out the Gadolinium?*

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Cardiac magnetic resonance (CMR) late gadolinium enhancement (LGE) (1) is the current clinical gold standard modality for evaluation of focal fibrosis and scar in patients with an ischemic or a nonischemic cardiomyopathy. LGE requires administration of an exogenous gadolinium-based contrast agent, which accumulates in the scar region. LGE imaging is commonly performed using an inversion recovery sequence 10 to 20 min after contrast injection to visualize myocardial scar. Patients are often referred for CMR examination for assessment of scar and myocardial perfusion, which both require gadolinium. As a result, over 80% of CMR examinations are performed with gadolinium.

Gadolinium contrast agents were considered very safe and were commonly used at double and even triple doses. In 2006, there were reports of nephrogenic systemic fibrosis, a systemic and potentially fatal scleroderma-like illness, in patients with moderate to severe renal dysfunction who had received gadolinium (2,3). However, with the new restriction for the use of gadolinium contrast in patients with compromised renal function, no recent cases of nephrogenic systemic fibrosis have been reported. Most patients now undergoing contrast CMR must undergo additional testing for kidney function. This testing adds another layer of cost and patient inconvenience. Despite normal renal function, there have been several recent reports of progressive increases in T₁-weighted magnetic resonance signal in various central nervous system structures following repeated gadolinium administration (4). Although the clinical significance of accumulation of the residual gadolinium in brain and bone is not yet understood, we should be more cautious in administering contrast agents and should try to avoid unnecessary contrast administration even in patients with normal renal function.

Myocardial T₁ mapping has emerged as a novel CMR sequence for evaluation of interstitial diffuse fibrosis. Initial T₁ mapping studies focused on shortened post-contrast myocardial T₁ values as a marker of fibrosis. However, there are many confounders of post-contrast T₁ measurements, such as contrast dose, timing, and type, diminishing the enthusiasm for post-contrast T₁ mapping. Instead, native T₁ mapping (i.e., T₁ imaging without a contrast agent) has emerged as the preferred approach to quantify myocardial T₁.

In this issue of JACC, Kali et al. (5) investigated the utility of native myocardial T₁ mapping at 3-T for detection of myocardial scar in a small cohort of patients with chronic ST-segment elevation and non-ST-segment elevation myocardial infarction. T₁ data were compared with LGE, which is considered the gold standard. Although the analysis was performed by blinded individuals, all subjects were known to have a chronic infarction. Infarct size and transmurality using a signal thresholding were similar for native T₁ maps and LGE images. The sensitivity and specificity for detecting chronic infarct quantitatively measured with thresholding were in the high 80s and 90s. However, sensitivity was only moderate (low 60%) for visual detection of infarct on native T₁ maps.

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The results of the study are encouraging and highlight the potential of native $T_1$ mapping for the detection of chronic infarction. However, the more modest sensitivity of visual assessment suggests that native $T_1$ mapping will not replace LGE imaging. With chronic infarction, LGE is usually readily appreciated and there is very little ambiguity in the clinical interpretation of LGE. Several quantitative scar delineation techniques for LGE, such as thresholding, have been proposed and used in research studies, but quantitative LGE scar delineation has not made it into clinical practice due to low reproducibility and lack of consensus on a standard method of segmentation. This challenge also applies to segmentation of native $T_1$. There are 2 factors that can affect these measurements: 1) identification of remote normal region; and 2) selection of thresholding value.

Over the past several decades, there have been sustained efforts by magnetic resonance scientists to accurately and reproducibly measure tissue relaxation parameters including $T_1$ and $T_2$. However, imaging and physiological confounders have limited our ability to accurately measure these tissue parameters. With recent advances in CMR, native $T_1$ mapping has re-emerged again as a “novel” imaging marker (6). There have been numerous $T_1$ mapping sequences, often with confusing acronyms, but fundamentally with a similar concept of sampling the recovery of magnetization to estimate native $T_1$ value. Despite technical challenges in robust measurement of $T_1$ values, the clinical significance of abnormal $T_1$ values remain unknown and under extensive investigation by many groups. But, are we simply adding another number to our long list of measures that CMR provides without truly affecting patient management? Despite many recent publications and sometimes contradictory data, it is still too early to judge how and in which disease native $T_1$ mapping will affect patient management. High variability in $T_1$ measurements often results in significant overlap in measurements between different myopathies, which make this technique of limited use in management of an individual patient. It also remains to be seen if technical innovation to simultaneously improve accuracy, reproducibility, and precision of $T_1$ measurements (7) can further push this field forward—enabling patient-specific diagnosis and prognosis.

The notion of replacing LGE with native $T_1$ mapping is enticing, but current data are limited to support this (5,8,9). First, although the native $T_1$ of infarcted myocardium differs from healthy myocardium, $T_1$ values are influenced by imaging and physiological confounders. Second, many of the current $T_1$ mapping sequences, including the MOLLI sequence (10) used by these investigators, are sensitive to myocardial $T_2$ as well; therefore, edema and inflammation could affect $T_1$ measurements (although not in the setting of chronic infarction). Third, similar to the challenges of LGE segmentation, determining a threshold value for abnormal native $T_1$ and a remote normal region will be difficult. Finally, despite the growth in installation of 3-T CMR scanners, the majority of clinical CMR scanners are 1.5-T.

In summary, for patients with renal dysfunction, there is an unmet clinical need for non–contrast-based scar imaging. With the emerging data on retention of gadolinium in the central nervous system as well as the additional cost of gadolinium, a noncontrast sequence for scar detection will be a great asset in our CMR imaging toolbox. Kali et al. (5) provide the proof-of-concept of potential of 3-T native $T_1$ mapping as a replacement for LGE. However, further technical challenges and larger multicenter, multivendor studies are needed to better understand the utility of native $T_1$ in detecting chronic infarction.

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