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EDITORIAL COMMENT

Absolute Quantification of Myocardial Tissue Composition

An Additional Level of Complexity or an Achievable Clinical Target?*

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The potential of cardiovascular magnetic resonance (CMR) as a noninvasive imaging tool for characterization of myocardial tissue has long been recognized. However, it was only with the introduction of late gadolinium enhancement (LGE) imaging in 1999 and 2000 that CMR became the established gold standard imaging technique for clinical assessment of myocardial necrosis and scarring (1). For the first time, CMR was able to provide an easily applicable method to assess irreversible myocardial tissue damage with exquisitely high resolution and to predict functional recovery (1). The pivotal role of CMR as a noninvasive imaging tool to assess tissue composition was underscored further with the advent of T_2-weighted (T2W) techniques for edema imaging in ischemic myocardium (2). The combination of T2W and LGE opened up the field of CMR to applications in the acute setting, by providing the imaging correlate of the underlying pathophysiological changes in acutely injured myocardium. As a result of the difference between area at risk by T2W and necrosis by LGE, the salvaged myocardial index (2) has been used as the main endpoint in clinical trials assessing the efficacy of invasive treatments for ST-segment elevation myocardial infarction (3,4). However, the validity of sequences for edema imaging has been extensively debated for various reasons, such as: the well-known limitations and artifacts of turbo-spin echo–based sequences, which hinder the accuracy and reliability of the sequences (5); the threshold-based post-processing methods (2 SD vs. 5 SD) (6) that are prone to errors; and the fact that the clinical meaning of the imaging features as a reflection of the underlying pathology is not entirely clear (7,8).

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In the continuous search for new techniques allowing for an even greater, detailed, and more accurate assessment of the myocardium, techniques such as T_1 and T_2 mapping have been explored. The great advantage of these modalities is thought to be the ability to provide a quantitative assessment of the tissue components on a voxel-by-voxel basis (9), and by doing so, potentially overcoming the limitations of the standard techniques that rely on threshold-based post-processing methods to define injury (6,7).

T_2-mapping techniques have been previously validated at 1.5-T in myocardial ischemia (9,10) and in inflammatory cardiomyopathies (11). The additional diagnostic value of T_2-mapping techniques compared with conventional turbo spin echo sequences was reflected in the increased accuracy in depicting myocardial edema (9) and in distinguishing normal from damaged myocardium by providing significantly different voxel-wise absolute T_2 values.

Edema imaging at 3-T has been performed mainly using T_2 preparation module steady-state free precession sequences (12) or pre-contrast T_1-mapping (13); in this issue of *iJACC,* for the first time, van Heeswijk et al. (14) validate a free-breathing radial gradient echo T_2-mapping technique at 3-T, demonstrating its accuracy and reproducibility in comparison to a breath-hold

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black-blood T2W fast spin echo technique. Their work represents a significant contribution to the technical developments in parameter-mapping techniques. Specifically, the investigators provide further improvement in the assessment of myocardial edema beyond conventional T2W fast spin echo sequences or bright-blood T_2 preparation module steady-state free precession techniques. The value of higher field strength for clinical imaging has previously been demonstrated for selected CMR applications and is mostly due to the higher signal-to-noise ratio and thus higher spatial and temporal resolution, which allow for improved sensitivity and specificity (15,16).

Although CMR techniques generally benefit from the higher field strength, this may not necessarily be the case for edema imaging. Techniques based on T2W–steady-state free precession are sensitive to susceptibility artifacts and larger radiofrequency inhomogeneities affecting image quality. The need for longer breath-hold times to enable T_1 recovery between T_2 preparation modules may also challenge the clinical applicability of 3-T CMR edema imaging. Although van Heeswijk et al. (14) do not report the prevalence of artifacts, the introduction of free-breathing T_2-mapping segmented k-space radial gradient echo may not only overcome some of the limitations described, but it also might provide a tool for accurate quantitative assessment of the change in tissue composition at 3-T and specifically to assess myocardial edema. A comparison study between 1.5-T and 3-T would be needed to establish the advantages of higher field strengths for imaging myocardial edema.

Although using mapping techniques for detailed quantitative tissue characterization is an attractive prospect, the aim of providing clinicians with absolute values to derive the exact composition of the myocardium is quite ambitious, especially in the current early stages of validation. At present, the scientific community is presented with different T_1- and T_2-mapping sequences resulting in different absolute normal tissue values depending on the field strength and the scanner manufacturer used. Although establishing absolute values for tissue characterization seems the natural conclusion to pursue when using a quantitative method, it might not be an achievable and deliverable target, given the variety of sequences available. Instead, we may need to rely on relative changes in signal with respect to established normal reference T_1-/T_2-values; in order to be able to have an objective quantification of the extent of LV damage, we will also need a better understanding of the pathophysiological modifications occurring in the normal myocardium due to the natural aging process. Until this is clarified, we are still dependent on threshold-based methods. Finally, pre-contrast T_1-mapping techniques have also been validated recently as methods to assess the area at risk (17), and a better understanding of how T_1 compares with T_2-mapping techniques will also be needed.

It is important to remember that for an imaging tool to be clinically useful, it has to be applicable in a wide range of conditions and easy to use and interpret. LGE has been a great example of this. However, the clinical applicability of mapping techniques is limited at present and a joint effort needs to be made to develop a standardized and established technique that is of clinical use. In conclusion, the scientific community has the opportunity to establish an accurate method for detailed tissue characterization of the myocardium. The key to success of mapping techniques will depend on the ability to make such detailed and complex information easily deliverable on a broad scale.

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REFERENCES

1. Kim R, Wu E, Rafael A. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med 2000;343:1445–53.
2. Friedrich MG, Abdel-Aty H, Taylor A, Schulz-Menger J, Messroghli D, Dietz R. The salvaged area at risk in reperfused acute myocardial infarction as visualized by cardiovascular magnetic resonance. J Am Coll Cardiol 2008;51:1581–7.
3. Thiele H, Hildebrand L, Schirdewahn C, et al. Impact of high-dose N-acetylcysteine versus placebo on contrast-induced nephropathy and myocardial reperfusion injury in unselected patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention: the LIPSIA-N-ACC (Prospective, Single-Blind, Placebo-Controlled, Randomized Leipzig Immediate Percutaneous Coronary Intervention Acute Myocardial Infarction N-ACC) trial. J Am Coll Cardiol 2010; 55:2201–9.
4. Lønborg J, Kelbæk H, Vejlstrup N, et al. Cardioprotective effects of ischemic postconditioning in patients treated with primary percutaneous coronary intervention, evaluated by magnetic resonance. Circ Cardiovasc Interv 2010;3:34–41.
5. Kellman P, Aletras AH, Mancini C, McVeigh ER, Arai AE. T2-prepared SSFP improves diagnostic confidence in edema imaging in acute myocardial

infarction compared to turbo spin echo. Magn Reson Med 2007;57:891–7.
6. Kwong RY, Farzaneh-Far A. Measuring myocardial scar by CMR. J Am Coll Cardiol Img 2011;4:157–60.
7. Wince WB, Kim RJ. Molecular imaging: T2-weighted CMR of the area at risk–a risky business? Nat Rev Cardiol 2010;7:547–9.
8. Friedrich MG, Kim HW, Kim RJ. T2-weighted imaging to assess post-infarct myocardium at risk. J Am Coll Cardiol Img 2011;4:1014–21.
9. Giri S, Chung YC, Merchant A, et al. T2 quantification for improved detection of myocardial edema. J Cardiovasc Magn Reson 2009;11:56.
10. Verhaert D, Thavendiranathan P, Giri S, et al. Direct T2 quantification of myocardial edema in acute ischemic injury. J Am Coll Cardiol Img 2011;4:269–78.
11. Thavendiranathan P, Walls M, Giri S, et al. Improved detection of myocardial involvement in acute inflammatory cardiomyopathies using T2 mapping. Circ Cardiovasc Imaging 2012;5:102–10.
12. Dall'Armellina E, Karia N, Lindsay AC, et al. Dynamic changes of edema and late gadolinium enhancement after acute myocardial infarction and their relationship to functional recovery and salvage index. Circ Cardiovasc Imaging 2011;4:228–36.
13. Dall'armellina E, Piechnik SK, Ferreira VM, et al. Cardiovascular magnetic resonance by non contrast T1-mapping allows assessment of severity of injury in acute myocardial infarction. J Cardiovasc Magn Reson 2012;14:15.
14. van Heeswijk RB, Feliciano H, Bongard C, et al. Free-breathing 3-T magnetic resonance T_2-mapping of the heart. J Am Coll Cardiol Img 2012;5:1231–9.
15. Lockie T, Ishida M, Perera D, et al. High-resolution magnetic resonance myocardial perfusion imaging at 3.0-Tesla to detect hemodynamically significant coronary stenoses as determined by fractional flow reserve. J Am Coll Cardiol 2011;57:70–5.
16. Arnold JR, Karamitsos TD, Bhamra-Ariza P, et al. Myocardial oxygenation in coronary artery disease: insights from blood oxygen level–dependent magnetic resonance imaging at 3 Tesla. J Am Coll Cardiol 2012;59:1954–64.
17. Ugander M, Bagi PS, Oki AJ, et al. Myocardial edema as detected by pre-contrast T1 and T2 CMR delineates area at risk associated with acute myocardial infarction. J Am Coll Cardiol Img 2012;5:596–603.

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