JACC: CARDIOVASCULAR IMAGING
VOL. 5, NO. 2, 2012
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ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC.
DOI:10.1016/j.jcmg.2011.08.022

EDITORIAL COMMENT

Do We Need a New Prescription to View Myocardial Perfusion?*

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The paper by Hsu et al. (1) in this issue of *iJACC* presents the results of a validation study on the use of cardiac magnetic resonance (CMR) imaging to map myocardial blood flow (MBF) at the spatial resolution of the underlying images ("pixel-wise"), acquired during the first pass of a gadolinium contrast bolus injection. This work raises 2 interesting questions: do we need pixel-level resolution for mapping MBF, despite the prevalent use of simpler and robust methods, which are exemplified by the bull's-eye plot, well known from nuclear cardiac imaging? And, what is to be gained by mapping, not just the relative distribution of blood flow, but also the absolute MBF in units of milliliters/minute/gram of tissue? Though the study by Hsu et al. (1) did not try to explicitly address these questions, the longer-term, clinical application, and significance of the reported technique depends on how these questions are answered.

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For the first question, which pertains to the spatial resolution of perfusion maps, one can draw on ample evidence from experimental and clinical studies that demonstrate the benefits depicting myocardial perfusion with at least a resolution that is adequate to resolve blood flow deficits limited to the subendocardial layer. Given that the in-plane resolution achieved with most CMR "first-pass" perfusion studies averages currently between 2 to 3 mm, a pixel-wise measurement is commensurate with the requirements for detecting subendocardial ischemia. But, imaging with higher spatial resolution also generally entails more noise, and this equally applies to noise levels in MBF maps that are generated from images. Nevertheless, it can be argued that the Achilles heel of CMR perfusion imaging is not the random noise, but rather the artifacts that can mimic perfusion defects (2). In this respect, the algorithms that are used to generate blood flow maps at the pixel level may help reduce the susceptibility to false-positive results. The algorithms, including the one used in the study by Hsu et al. (1), represent the myocardial contrast enhancement as a linear response to the contrast enhancement in the blood pool. Transitory, subendocardial dark rim artifacts seen during CMR first-pass imaging are therefore effectively suppressed from the blood flow maps. Though this aspect was not investigated in detail in the study by Hsu et al. (1), such benefits emerged from earlier studies of MBF quantification by CMR (3).

This last point already answers part of our second question: what is to be gained from pixel-wise measurements of absolute MBF, rather than assessing the level, or rate, of contrast enhancement? The latter only allows an assessment of regional differences within the same heart. A recent publication by Patel et al. (4) demonstrated that with multivessel coronary artery disease, one should look with CMR beyond the visual detection of regional, contrast-enhancement deficits, and also quantify the myocardial perfusion reserve to significantly improve the detection of flow limiting coronary disease. Quantifying MBF during maximal vasodilation, as was performed in the study by Hsu et al. (1), should at least provide equivalent benefits as the myocardial perfusion reserve quantification, and

*Editorials published in *JACC: Cardiovascular Imaging* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Imaging* or the American College of Cardiology.

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JACC: CARDIOVASCULAR IMAGING, VOL. 5, NO. 2, 2012
FEBRUARY 2012:167–8

eliminate the potentially confounding effects of an abnormal level of MBF at rest (5). Furthermore, for pixel-wise maps, the operation of calculating a perfusion reserve ratio is bound to amplify any noise in the resting perfusion measurements, which is the denominator in the perfusion reserve ratio. Arguably, 1 merit of the study by Hsu et al. (1) is, therefore, the effort to quantify absolute blood flow, rather than a quantity that approximates a perfusion reserve ratio. A further advantage is that a MBF map, in comparison to the underlying images, brings out differences in hyperemic flow more clearly. To appreciate this point, one should note that with a peripheral injection of contrast, equal increments in blood flow result in diminishing increases of contrast enhancement, as absolute MBF increases. Or stated differently, an increase of MBF from 2.5 ml/min/g to 3.0 ml/min/g produces a considerably smaller difference in peak contrast enhancement than an equal (0.5 ml/min/g) incremental change from 0.75 to 1.25 ml/min/g. With the blood flow maps, this "perfusion-myopia" is removed. A relatively open question is how the information derived from MBF values should be interpreted for the clinical diagnosis of myocardial ischemia and the determination of the extent of an ischemic zone, as MBF can at best only be a surrogate marker of ischemia. It is also still unclear whether or not this novel MBF assessment will significantly change patient prognosis. This can only be addressed by trials where MBF quantification is included in the outcome measures.

A further concern is the still widely prevalent need for manual image segmentation to generate the perfusion maps, though algorithms to automate the process, as exemplified by the methods described by Hsu et al. (1), have shown promise and are being adopted by at least 1 CMR equipment vendor for pre-clinical evaluation.

Despite the important benefits of MBF quantification, one has to take note of the sobering fact that, irrespective of imaging modality and of the considerable work invested in imaging-based MBF quantification, there is still relatively little demand in the clinical community for such quantitative tools in CAD diagnosis. The quantification of absolute MBF may in fact be more compelling for other etiologies that are characterized by microvascular coronary dysfunction, or subclinical, diffuse atherosclerosis (6), rather than focal ischemia caused by flow-limiting coronary disease in the epicardial arteries.

An important merit of the work by Hsu et al. (1) is to have developed a novel method that addresses simultaneously and effectively both MBF quantification and pixel-wise perfusion mapping. In the clinical realm, a new prescription to view CMR perfusion studies may not find immediate resonance, but for a further elucidation of coronary physiology in various cardiac diseases, any prescription that improves our perceptive powers to elucidate coronary physiology and disease, and avoids "perfusion myopia," will surely be welcomed quickly.

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Key Words: blood flow ■ coronary artery disease ■ ischemia ■ magnetic resonance ■ myocardial perfusion ■ quantification.