CMR-Based Quantitative Myocardial Perfusion
Pixel-Wise and Pound-Wise

Christopher M. Kramer, MD,* Y. Chandrashekhar, MD,† Jagat Narula, MD, PhD‡

Quantitative measurement of myocardial perfusion has been a goal of cardiovascular investigators for a number of years. Positron emission tomography (PET) has allowed assessment of myocardial blood flow in absolute value (milliliters per gram per minute) (1) and is accurate at identifying both flow-limiting epicardial coronary artery disease (CAD) as well as microvascular abnormalities. Qualitative cardiac magnetic resonance (CMR) stress perfusion has also made clinical inroads of late, demonstrating higher sensitivity and negative predictive value than single-photon emission computed tomography (SPECT) in a head-to-head comparison of symptomatic patients against x-ray coronary angiography employed as the reference standard (2). Although the feasibility is established the more important question is if we could do better with absolute quantitation of myocardial blood flow? A recent comparative study of qualitative versus quantitative analysis of myocardial blood flow reserve with CMR did not demonstrate any incremental value of quantitative assessment for the overall per patient accuracy, and this approach may be reasonable if the goal is to identify a patient with ischemia significant for justification of mechanical intervention (3). However, the quantitative approach was more accurate for the assessment of pathophysiology in more detail such as the delineation of the amount of myocardium at jeopardy.

Quantitative measures of myocardial blood flow have been validated over the years against microspheres in animal models (4), usually on a per segment or per sector level. In this issue of *JACC*, Hsu et al. (5) take this validation one step further, demonstrating accurate pixel level measurement of myocardial blood flow in both canines and humans with validation against microspheres in the former. A pixel comprising 32 µl of myocardium represented a remarkably small amount of tissue. They demonstrated an outstanding agreement between pixel-wise CMR myocardial blood flow estimates and microspheres as well as excellent sector-wise agreement. A substantial agreement was observed in the clinically relevant range of myocardial blood flow at rest and vasodilator stress and only began to fall off at extremely high flows usually not clinically attained. This study demonstrated remarkable spatial resolution of CMR blood flow measures and allowed straightforward resolution of transmural differences in blood flow; the resolution of CMR-verified blood flow gradient was superior to the spatial resolution of the microsphere measures. In fact, the clinical examples shown in the paper clearly demonstrated the ability to resolve the endocardial-to-epicardial blood flow differences during vasodilator stress, which were not surprisingly more profound in the setting of myocardial ischemia.

What are the limitations of this pixel-wise quantitative approach? The analysis is at present laborious and time-consuming, as each image has to be manually segmented. The noise ratio may be higher with pixel level measurements than those measuring and averaging a larger volume of tissue. This presents a problem with perfusion acquisitions, especially during vasodilator stress, as both cardiac and respiratory motion is often present. Nonrigid image registration is one potential fix for this problem. Further validation in a multitude of clinical settings will be necessary before this quantitative approach could become widely applicable.

In what clinical settings will an ability to measure pixel-wise myocardial blood flow become a difference-maker? In addition to better identifying the extent of myocardial ischemia, one could foresee using this approach to define microvascular dysfunction in condi-
tions such as the syndrome X. Whether subendocardial perfusion is truly reduced in the patients with chest pain and normal epicardial coronary arteries is still a controversial question. Pixel-wise quantitative blood flow measures could be just the ticket to resolve this controversy. Diabetes is yet another clinical scenario where the quantitation may allow better definition of diffuse small vessel disease, regardless of the extent of discrete epicardial stenoses. In the study by Patel et al. (3), although underpowered to be definitive, diabetic patients without epicardial CAD had equivalent blood flow reserve to patients without diabetes with epicardial CAD.

Research applications of such precise myocardial flow data are quite obvious and it is very easy to be overly enthusiastic about using pixel level CMR perfusion in many clinical conditions. However, the clinical utility of accurate myocardial blood flow quantitation still remains untested despite many years of availability in the PET arena. Right since the time of the early studies in PET, there has been the lingering question whether a precise (ml/min/mg of tissue) measurement of myocardial blood flow adds clinical utility compared to more global measurements in the territory of interest. This question became even more contentious when other measurements that were reasonably easy to acquire and analyze (e.g., coronary flow reserve which only need a ratio of before and after data), were shown to be clinically relevant and helpful for therapeutic decision-making. Thus, a pixel level CMR perfusion technique, even though it is able to distinguish perfusion abnormality in finite myocardial layers (e.g., sub-endocardium, mid-myocardium, or epicardium) needs to cross an even higher threshold of clinical relevance—showing it is better than what is currently available. At present, very few clinical conditions need or indeed benefit from such pixel level precision. Whether considered a curse or a boon, all emerging technologies are competing in a new era of scientific and economic scrutiny; they will face the challenge of a need to cross a higher standard for usefulness and show robustness in face of ever changing evaluation criteria (e.g., outcomes over feasibility). Until it is able show clinical utility, its current clinical role, pending more comparative outcome data, may be more suited to arbitrating deficiencies within current imaging techniques (e.g., identifying false positives or artifacts, etc.). Even though these newer and novel CMR techniques are a big advance and will prove themselves as an accurate tool, proving that ultra high resolution, pixel level perfusion measurements are clinically necessary will take a lot more study, despite their undoubted attractiveness. We continue to be amazed by what CMR technologies can achieve and thus chose to highlight this paper. However, as evident in this and other previous Editor’s Pages (6–12), we are also optimistically cautious about their clinical utility. To paraphrase Jefferson, it is better to wait till the “froth settles down on the cup of knowledge” before making optimistic judgments. Cardiovascular imagers will be easily given the gift of visualizing the myocardial flow with greater fidelity but will they be wiser for it should this come to a pass remains a question with poor spatial resolution.

REFERENCES