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EDITORIALS

Editor's Page

The Next Horizon in CMR: Spectroscopy

The present clinical applications of cardiovascular magnetic resonance (CMR) evaluate heart morphology and function, the aorta and the carotid, and vertebral and ileofemoral arteries. The next generation will generate diagnostic images of myocardial perfusion and the coronary arteries if CMR is to use all of its unique potential, something that is missing from present and planned clinical applications. The earliest application of magnetic resonance to the heart involved spectroscopy to evaluate myocardial metabolism using *in vitro* models (1). While spectroscopy is usually thought of as a research tool reserved for the basic science laboratory, a number of noteworthy studies have used spectroscopic methods for clinical investigation (2). Indeed, that is why magnetic resonance has become known as the technology that can go from the molecule to the man. This window through which we can peer into the metabolic function of the heart provides a unique means to evaluate clinically biochemical mechanisms of disease and their response to therapy. Thus, such important processes as ischemia and viability can be interrogated directly. The effect of therapeutic interventions on these processes can be evaluated. Such information is obtained without the use of contrast agents or radioactive tracers. Think of a future in which the clinical comprehensive cardiovascular examination would use CMR imaging to assess morphology, function and perfusion, CMR angiography to generate coronary arteriograms, and CMR spectroscopy to determine viability and detect ischemia. Thus, this Journal and the SCMR have excluded the word "imaging" in their inception, providing a means to acknowledge the importance of spectroscopy.

To review the topic of CMR spectroscopy is far beyond the scope of an editorial. That is a subject for future review articles. Nevertheless, it should be of interest to mention a few key points. First, several nuclei have already been clinically applied and several more have clinical potential. Clinical reports on spectroscopic studies have applied phosphorus-31 (^{31}P), hydrogen-1 (^{1}H) and sodium-23 (^{23}Na). Carbon-13 (^{13}C) (3) and fluorine-19 (^{19}F) are among nuclei that have clinical potential. None of these is radioactive. Second, ^{31}P has been the most widely applied clinically. From a ^{31}P spectrum, one can visualize myocardial high-energy phosphates and their products, which include ATP, phosphocreatine (PCr), and inorganic phosphate (Pi). The different spectral positions of the three peaks of ATP and the single peaks of PCr and Pi occur as a result of the phenomenon known as "chemical shift," which depends on the magnetic environment of the ^{31}P atomic nucleus. From the spectral position of the Pi peak, one can determine pH within the myocardium. Phosphocreatine is a labile high-energy phosphate that is depleted rapidly with an insult to the myocardium. On the other hand, ATP is depleted more slowly and with more advanced insults. The ratio of PCr to ATP provides some insight into the severity of an insult. For example, when myocardial ischemia is induced in a patient using handgrip exercise, PCr/ATP falls. At magnetic fields widely available for clinical use (i.e., up to 1.5 Tesla), myocardial Pi cannot yet be reproducibly visualized, as it is obscured by phosphates contained within the blood. At fields $\geq$3 Tesla, myocardial Pi is easily distinguished from other phosphates. The importance of visualizing Pi is well known from laboratory studies. The spectral position of Pi shifts in the acid pH direction with myocardial ischemia. This spectral shift provides a means for determining pH inside the myocardial cell. One recent and interesting observation is that PCr/ATP falls within handgrip exercise in some women with chest pain and normal coronary angiograms, suggesting ischemia due to microvascular disease. Other potential applications of PCr/ATP include detection of allo-

graft rejection, assessment of myocardial status in volume overload states like mitral regurgitation, and early detection of cardiotoxicity.

Third, with breakdown of the electrochemical mechanisms that maintain normal intra vs. extracellular sodium gradient, sodium concentration within the myocardial cell increases. It is possible to detect this increase using ^{23}Na CMR spectroscopic methods, and thereby provide yet another potential clinical means to detect myocardial ischemic insult and its severity. Fourth, it is possible to measure the concentration of intracellular creatine and myocardial lipids using ^{1}H spectroscopy. Creatine content is related to viable myocardial cell mass (4). Intracellular lipids which increase with ischemic insult have been observed in laboratory studies using ^{1}H spectroscopic approaches.

Many approaches are used to derive CMR spectra clinically. *In vitro* studies utilize an isolated heart in a laboratory spectrometer to generate spectra from the entire myocardium. Clinical studies typically use surface coils placed on the anterior chest wall. An approach known as ISIS (Image Selected *In-vivo* Spectroscopy) interrogates a three-dimensional volume which can be placed anywhere within the heart. This technique can sample the entire left ventricle or isolated interventricular septum. The ISIS method can also interrogate multiple volumes one at a time between the surface coil and the posterior myocardial wall analogous to m-mode echocardiography. Approaches that provide many spectra from various locations are known as "spectroscopic imaging." Another method, known as DRESS (Depth-REsolved Surface-coil Spectroscopy) provides spectra from a series of contiguous slices. A third approach, one-dimensional magnetic resonance spectroscopic imaging (1D-MRSI), generates spectra from a column of slices. In this case, the slices are similar in shape and volume. Finally, a more sophisticated approach, known as three-dimensional magnetic resonance spectroscopic imaging (3D-MRSI), generates spectra from a three-dimensional array of volumes.

To conclude, as you think about the future of clinical CMR, you can be assured that spectroscopy will play a very important role. It is already useful for clinical investigation. At this time it is clear that the ^{31}P CMR stress test provides important clinical insight that can be applied to patient care. Those involved in developing clinical systems should incorporate ^{31}P SI into their clinical instrumentation. Finally, we look forward to publishing abstracts and articles on CMR spectroscopic imaging. It is truly a unique aspect of CMR.

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