

## EDITORIALS

Editor's Page

# Magnetic Resonance Provides Insights into Pharmaceutical Effects

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The breadth of magnetic resonance (MR) methods provides an avenue for evaluation of the effects of cardiovascular pharmaceuticals both old and new. The impact of a given pharmaceutical agent can be examined clinically by:

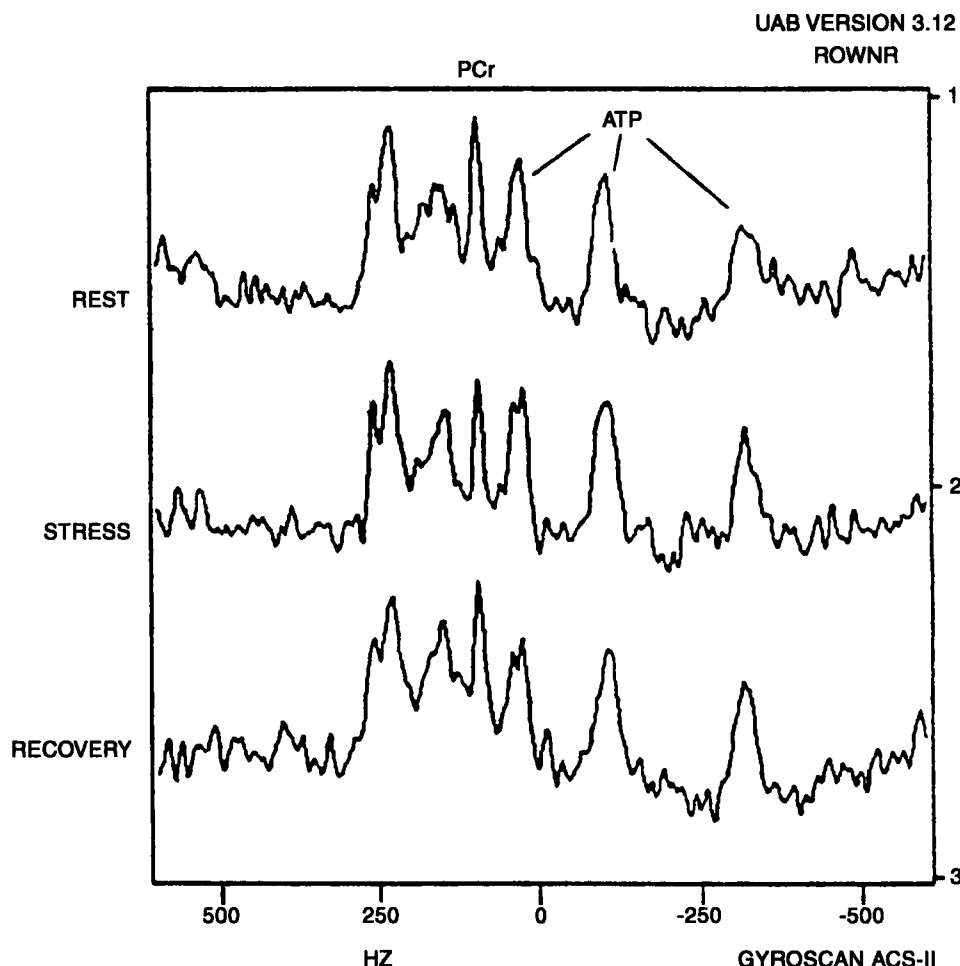
- using MRI to evaluate serial changes in myocardial contractile function (EDV, ESV, EF and regional thickness and thickening)
- using RF tagging to assess changes in myocardial stress and strain
- using magnetic resonance angiography to evaluate changes in the luminal size and in plaque morphology (and possibly character) in larger arteries such as the aorta, carotids and iliacs
- assessing regional myocardial perfusion (under development, but close)
- evaluation of change in myocardial energetics using PCr/ATP ratio at rest and with stress (see my editorial from last month; 1).

Magnetic resonance methods provide the ideal package for assessment of the effects of an intervention such as a pharmaceutical. Such assessment is useful to the practice of cardiovascular medicine, to the pharmaceutical industry and for research insights for NIH and grants from other funding agencies. One of the major goals of the SCMR is to make the pharmaceutical industry and governmental agencies (FDA, in the US) aware of the utility of cardiovascular magnetic resonance (CMR) in the evaluation of the effects of pharmaceuticals on heart and vascular function, pathology and metabolism.

The present issue of JCMR contains several manuscripts relevant to the area of pharmaceutical assessment. For example, the article by Nagel et al (2) describes “real-time” imaging as an expeditious approach for

evaluating left ventricular function. Hillenbrand et al (3) describes RF tagging to assess systolic function, an approach unique to CMR. The methods described are state-of-the-art for evaluating baseline and serial changes in myocardial function. Important advantages include the high-resolution and three-dimensional nature of magnetic resonance methods. The disturbing attenuation from lung, bone and soft tissue inherent in ultrasound studies and the regulatory (NRC) ionizing radiation and low resolution inherent in radionuclide methods are not problems with MR. Yet CMR does not only provide myocardial function information, it also generates metabolic insights for baseline and serial studies of the energy source for contractile function, the high-energy phosphates. While Evanochko and colleagues have applied phosphorus-31 spectroscopic imaging to assess transplant rejection at rest (4), that approach has been more successfully applied to the detection of myocardial ischemia induced by relatively low-level handgrip exercise stress. Consider the development of a class of new anti-ischemic drugs. What better approach is available than to document their beneficial effects by demonstrating protection of high-energy phosphate metabolism (e.g., PCr/ATP ratio) in patients who already have been shown to have significantly reduced PCr/ATP with handgrip exercise. Preliminary clinical studies using phosphorus-31 spectroscopy have already been performed in collaboration with an innovative pharmaceutical company (Figure 1).

It was reassuring to read the paper by Schroeder et al (5), which describes the safety of MR studies in the rapidly increasing volume of patients with intracoronary stents. It is unfortunate that these devices produce a small artifact in imaging studies. Nevertheless, the ability of magnetic resonance angiography (MRA) to perform cor-



**Figure 1.** Fifty-eight-year-old white male with 100% mid LAD occlusion but with excellent collaterals and only mild hypokinesis of the LV anterolateral wall. At baseline, the PCr/ATP ratio fell 23% between spectrum 1 and spectrum 2 during handgrip exercise stress. Spectrum 3 shows return of PCr/ATP to the "rest" level. With the addition of a new anti-ischemic pharmaceutical, the fall in PCr/ATP was eliminated. With withdrawal of the agent, the PCr/ATP response was the same as in the present set of spectra.

onary angiograms, while not yet perfect, promises to provide routine diagnostic studies in the near future (with further optimization of software and hardware). Nevertheless, applications of MRA to the larger vessels can depict intravascular plaque, and serial studies should provide an excellent approach to directly depicting plaque regression, if that does indeed occur, in patients on statins. Such noninvasive studies without ionizing radiation can be safely serially performed and would readily allow addressing the potentially beneficial effects of a new agent without having to wait for the inimitable "event." Studies using "events" take years. Studies using the angiographic surrogate would substantially reduce that time.

CMR not only has the great potential to detect and

assess the effects of pharmaceuticals, a fact that pharmaceutical companies and the FDA should know well (but generally do not), CMR is also useful for assessing the effects of surgical interventions. Friedrich (6) in this issue nicely reviews the role of CMR in the evaluation of the cardiomyopathies. Interventions for dilated cardiomyopathies including the cardiomyopathy associated with CAD consist of the Batista procedure, a surgical procedure to reduce LV size, which had been largely unsuccessful, and the newer Dor procedure, which does not resect the myocardium, but attempts to convert the LV from a spherical to an ellipsoidal configuration using a "left ventriculoplasty" and a patch, and cardiac transplantation.

Evanochko et al review the use of P-31 NMR spec-

troscopy to assess the status of the cardiac graft. While data acquired at rest have not been optimally informative, studies with stress might enhance the utility of spectroscopy. Regarding LV function assessment, volumetric accuracy is a hallmark of CMR and assessment of heart shape, and global and regional function have been used to assess the effectiveness of the Dor procedure. At present, the MR data suggest that in patients with CAD and myocardial scar, and when coupled with bypass graft surgery, the procedure reduces LV volumes, improves ejection fraction and improves stress and strain. Magnetic resonance data are limited to about 10 Dor patients at the present time and even the one with dilated cardiomyopathy has also improved clinically. CMR was an integral part of pre- and post-operative assessment in these patients.

To conclude, CMR has great potential to provide functional, perfusional, angiographic and metabolic insight into cardiovascular disease and into the impact of pharmaceutical and mechanical interventions.

*Gerald M. Pohost, MD, Editor*

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