Imaging Vulnerable Plaque

In the session "Imaging the Vulnerable Plaque," Chun Yuan, PhD, Vascular Imaging Laboratory, University of Washington, Seattle, WA, stated that MRI offers non-invasive *in vivo* characterization of human atherosclerosis. MRI's capabilities, he added, have been histologically validated, and its findings are quantitative and reproducible.

The valuable information that serial MRI imaging can provide includes insights into the natural history of atherosclerosis progression, and particularly into the role that lesion morphology, tissue composition, inflammation, hemodynamics and mechanical stress play in those lesions likely to cause future events.

Numerous studies of plaques in the carotid have shown MRI to accurately identify calcification, lipid rich/necrotic cores (LR/NC), intraplaque hemorrhage, and fibrous plaque caps. In the latter, it can distinguish intact thick caps from thin or ruptured caps. Yuan's own research has shown that thin caps are tenfold more likely to be associated with symptomotology than thick caps, while ruptured caps are 23-times as likely to be symptomatic.

Conversely, symptomatic patients were significantly more likely to have fibrous cap rupture, juxtaluminal hemorrhage or thrombus, type I hemorrhage or complicated AHA Type VI lesions. Other serial human carotid MRI imaging research has shown the presence of intraplaque hemorrhage to predict significant reductions in lumen volume, increases in vessel wall volume and LR/NC volume.

Links between these lesion features visualized with MRI carotid imaging and clinical events have also been documented. A Cox Regression Analysis by Takaya et al. (*Stroke* 2006; 37:818) showed significant increases in ipsilateral cerebrovascular events in the presence of intraplaque hemorrhage and thin/ruptured fibrous caps, and a strong trend (p=0.09) toward more events in the presence of LR/NC. Measures of LR/NC and IPH area also showed area increases to be associated with significantly more events. Other serial carotid imaging over 3 years revealed 13.0% increases in wall area in the presence of intraplaque hemorrhage as compared with 4.0% increases in wall area without intraplaque hemorrhage.

Highlights from the
American Heart Association 2006 Scientific Sessions

Summarizing, Yuan said, "MRI findings identify vulnerable plaques predictive of more rapid progression and increased likelihood of future ischemic events." He added, "Larger multicenter studies are needed to confirm these initial findings prior to the use of these techniques to guide clinical practice."

Cardiac Magnetic Resonance in the Diagnosis of Myocarditis

Myocarditis, an inflammation of the heart, is an uncommon condition with symptoms similar to those of heart failure. Late gadolinium enhancement (LGE) cardiac magnetic resonance (CMR) is a tool that is used to assess heart lesions and evaluate tissue viability. Gadolinium accumulates in abnormal tissue, causing the abnormal areas to become very bright and easy to see on the MRI.

Cardiac MRI was recently used in a study of 128 patients with suspected myocarditis. In order to be enrolled in the study, patients 1) had a history of respiratory and/or gastrointestinal symptoms within 8 weeks prior to the study, 2) were experiencing one of the following symptoms: fatigue/malaise, chest pain, dyspnea, or tachycardia and 3) exhibited one of the following ECG signs: conduction block, ST abnormalities, supraventricular tachycardia, or sustained or non-sustained ventricular tachycardia. LGE CMR was used to determine the affected area of the heart, and an endomyocardial biopsy was performed.

Of the 128 patients enrolled in the study, 87 were found to have actual myocarditis. The most common causes of the condition were parvovirus B19 (PVB19; n=49), human herpes virus 6 (HHV6; n=16), and a combined infection of PVB19/HHV6 (n=15). Fifteen patients were diagnosed with healing myocarditis, and 26 were found not to have myocarditis. Those infected with PVB19 had clinical presentations similar to a heart attack, had late gadolinium enhancement in the epicardial lateral wall of the heart, and eventually recovered. Patients with HHV6 or the combined PVB19/HHV6 infection had much more serious outcomes. These patients had MRIs that showed intramural anteroseptal LGE. Clinical presentation was similar to new onset heart failure, with some progressing to chronic heart failure. The presence of LGE in the septum at initial presentation, and the total amount of LGE (%LV) were the strongest independent predictors of impaired ventricular function and ventricular dilatation at follow-up.

"When you look at the outcomes of these patients, the data is really quite striking," said Dr. Dudley J. Pennell of The Royal Brompton Hospital, London. "This imaging is only possible using cardiovascular magnetic resonance to find this patchy, cellular, area of necrosis that occurs in tiny amounts, and this really makes cardiovascular MR the technique of choice for picking up this diagnosis. When you introduce this into clinical practice locally, you find there is a sudden epidemic of this diagnosis, which is clearly being missed normally." These findings were recently published by Mahrholdt et al, *Circulation* October 10, 2006; 114(15):1581-90.

Appropriate Uses of Noninvasive Imaging

Since their debut in 1974, computerized tomography (CT) scanners have been a core tool in non-invasive diagnostics. A combination of an x-ray and a computer, CT scans generate cross-sectional images of the body, enabling clinicians to see structures not otherwise visible with other non-invasive methods. In the past, these scans have had limitations in cardiology, and angiography has continued to be the gold standard. Advances in CT methodology, however, have expanded its potential in cardiology.

Stephan Achenbach, MD, University of Erlangen, Germany gave an overview of cardiac CT. These instruments have 0.4 mm spatial resolution and

~80 to 200 ms temporal resolution. The current state-of-the-art also includes a 16 (or more) slice CT, a rotation of less than 500 ms, the use of intravenous contrast and nitrates to improve image quality and can accommodate patients with heart rates less than 60 to 65 bpm. Dual source CT has a higher speed leading to higher resolution with good sensitivity and specificity. These machines have two x-ray sources and two detector arrays. Another advantage of dual source CT is that patients with a heart rate >65 bpm no longer need to be treated with beta blockers to slow the heart rate.

Multi-detector CT (MDCT) systems can take multiple x-rays simultaneously. Because of their speed, they are now being used for coronary artery imaging. Numerous publications have demonstrated that MDCT is comparable to cardiac catheterization in the detection of coronary stenosis with high sensitivity and specificity. There are, however, limitations associated with the technology. Severe calcification, for example, can make images difficult to interpret, and the motion of the heart causes some artifacts. Although cardiac CT can be utilized to visualize stent placement, the technology remains hindered by poor image quality in this applications. He also emphasized that this is a diagnostic tool only, and one cannot implement an intervention as in angiography.

Although limitations still exist, CT scans have their place in diagnosing certain classes of patients. The fact that CT scans have a high negative predictive value to rule out coronary stenosis means that cardiac catheterization can be avoided if a CT scan is negative. This is particularly helpful in patients that have a low probability of coronary blockages. "Do everything you can to have the highest quality imaging" in order to have reliable results, said Dr. Achenbach. He particularly stressed having adequate equipment, protocols, and staff training. Guidelines for the appropriate use of cardiac CT were recently published the *Journal of the American College of Cardiology* (Hendel et al. *JACC* 2006; 48(7):1475-1497).

CPR Guidelines and Hypothermia Improve Survival

Sudden cardiac arrest is a major public health concern, with more than 400,000 deaths annually in the United States alone. A patient's chance of survival drops by 7-10%/min when CPR is delayed after cardiac arrest. Widespread adherence to the new Advanced Cardiac Life Support/Emergency Cardiac Care guidelines for CPR and the increased use of therapeutic hypothermia may improve both of these statistics.

During cardiac arrest, spontaneous circulation ceases and the vital organs are not adequately perfused. If the patient is successfully resuscitated, circulation resumes, and reperfusion to the vital organs occurs. Reperfusion has been associated with free radical production which can lead to mitochondrial damage and programmed cell death. Mild hypothermia may suppress many of the chemical reactions associated with reperfusion injury.

In two prospective randomized trials comparing mild hypothermia (32-34°C) with normothermia in comatose survivors of out-of-hospital cardiac arrest favorable neurologic outcomes were observed. One study was conducted in five European countries and the other took place in four hospitals in Melbourne, Australia. The European study showed that cooling to 32-34°C for 24 hours decreased the chance of death (risk ratio, 0.74; 95% CI, 0.58-0.95) and increased the probability of good neurological outcome (risk ratio, 1.40; 95% CI, 1.08-1.81) (*NEJM* 2002; 346(8):549-556). The Australian study showed that cooling patients to 32-34°C for 12 hours increased the chance of good neurological recovery (risk ration 2.65; 95% CI,