Cardiovascular Molecular Imaging—State-of-the-Art 2008

Written by Lori Alexander

State-of-the-Art Cardiovascular Molecular Imaging

Multimodal imaging offers the advantage of noninvasive methods to visualize anatomy and tissue structure and measure physiologic function. A session that was developed jointly by the American Heart Association and the Society of Nuclear Medicine, "Molecular Imaging—State-of-the-Art 2008," provided an overview of the use of imaging techniques for assessing cardiovascular pathology, using biological imaging targets for the evaluation of myocardial viability, angiogenesis, inflammation, and vascular remodeling.

Myocardial Pathology and Cardiac Remodeling

Francis G. Spinale, MD, PhD, Medical University of South Carolina, Charleston, SC, defined the critical role of matrix metalloproteinase (MMP) activation in the pathophysiology of postmyocardial infarction (MI) remodeling and commented on the crucial role of imaging to evaluate post-MI remodeling. "[Such imaging] allows for continuous assessment of relationships between biological-structural-functional events following myocardial infarction and the impact of therapeutic interventions," he said.

Albert J. Sinusas, MD, Yale University School of Medicine, New Haven, CT, discussed the use of nuclear imaging with radiotracers to target myocardial pathology. This targeted imaging approach can be used to assess several characteristics of cardiac pathology, he said, including myocardial ischemia, damage or injury, inflammation, or denervation. The activation of MMPs plays an important role in vascular and myocardial remodeling, and single photon emission computed tomography (SPECT)/computed tomography (SPECT/CT) has been used with MMP-specific tracers to detect injury-induced MMP activation in the myocardium in animal studies. Such imaging can help researchers gain a better understanding of the pathophysiological processes that are associated with post-MI remodeling. As such, said Dr. Sinusas, "Targeted multimodality imaging may allow for risk stratification and evaluation of novel therapeutic interventions, like new MMP inhibitors or angiogenic therapy, directed at preventing post-myocardial infarction remodeling."

Christopher M. Kramer, MD, University of Virginia Health Sciences Center, Charlottesville, VA, discussed a number of magnetic resonance imaging (MRI) approaches for evaluation of myocardial injury and post-MI remodeling and for management of patients with heart failure.

Cardiovascular Pathophysiology

MRI can be used to evaluate cardiovascular pathophysiology at several levels, said David E. Sosnovik, MD, Massachusetts General Hospital, Boston, MA. Molecular imaging with MRI has the advantages of being tomographic and nonionizing and having the ability to generate images that have high spatial resolution and excellent soft-tissue contrast. Perhaps most importantly, MRI provides integrated anatomic, functional, and molecular information. Dr. Sosnovik said that molecular MRI of the myocardium can detect apoptosis, macrophage infiltration, myeloperoxidase secretion, and collagen type 1 (fibrosis).

Myocardial Viability

Antti Saraste, MD, PhD, Technische Universität, Munich, Germany, discussed advances in molecular imaging as a tool for evaluating myocardial viability. Observational studies have

suggested a survival benefit for patients who have a revascularization procedure done when myocardial viability is detected by imaging. Dr. Saraste noted that a meta-analysis of 24 studies (3088 patients) of myocardial viability testing (with F-18 fluorodeoxyglucose metabolic imaging or dobutamine echocardiography, or thallium perfusion imaging) demonstrated a strong association between myocardial viability on testing and improved survival; for patients with myocardial viability, revascularization was associated with a 79.6% reduction in annual mortality compared with medical treatment (16% vs 3.2%; p<0.0001) [Allman et al. *J Am Coll Cardiol* 2002].

Imaging parameters that are reflective of viability include residual perfusion/reserve, contractile reserve, oxidative metabolism, glucose utilization, membrane integrity, and gadolinium-DTPA enhancement. New perfusion tracers that have longer half-lives are expanding the clinical applicability of these agents.

Angiogenesis, Inflammatory Response, and Vascular Remodeling

Douglas W. Losordo, MD, Northwestern University Feinberg School of Medicine, Chicago, IL, provided a clinical perspective of the potential role of gene and cell therapy for the stimulation of angiogenesis in patients with ischemic cardiovascular disease. Angiogenesis helps maintain tissue viability through the development of collateral vessels in response to ischemic disease. Joseph C. Wu, MD, PhD, Stanford University, Stanford, CA, reviewed the current imaging approaches for tracking novel cell therapies in the management of ischemic heart disease, highlighting the strengths and limitations of these approaches in ongoing preclinical studies.

Angiogenesis is also related to atherosclerosis, which is a source of microhemorrhage, lipoprotein leakage, and immune cell recruitment and migration, and is associated with plaque in terms of inflammatory burden, rate of growth, and susceptibility to rupture. Jonathan R. Lindner, MD, Oregon Health & Science University, Portland, OR, discussed the use of molecular imaging with MRI, radionuclide imaging, and ultrasonography to evaluate atherosclerosis by examining macrophage content, plaque inflammation, and angiogenesis of the vessel wall. In addition, Dr. Lindner noted that imaging may also help identify individuals who are at risk for atherosclerosis by using biological markers of vulnerable plaque. Characteristics of vascular function also can be evaluated, through assessment of wall thickness, plaque composition (lipid core), flow dynamics, elasticity, and vasodilatory response.

Dr. Lindner also noted that molecular imaging of endothelial phenotype, inflammation, and matrix remodeling can be used to detect vascular remodeling in response to ischemia. As an example, Dr. Lindner described an animal study in which ultrasonographic molecular imaging of endothelial activation and leukocyte recruitment was used to assess the inflammatory response to severe peripheral vascular disease [Behm et al. *Circulation* 2008]. In the study, unilateral hindlimb ischemia was produced by arterial occlusion in mice, and molecular imaging was performed with microbubbles that were targeted to VCAM-1, α_5-integrin, or pan-leukocytes. Dr. Lindner said that targeted pan-leukocyte imaging with shell phosphatidylserine microbubbles primarily reflected an acute response, whereas molecular imaging of VCAM-1 or monocyte markers provided information on more chronic activation of the inflammatory response.

"Molecular imaging provides a promising method for studying vascular responses to ischemia and vasa vasorum proliferation in atherosclerosis and how they can be manipulated for therapeutic gain," added Dr. Lindner.