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MEETING HIGHLIGHTS

Meeting Highlights of the 9th Annual Scientific Sessions of the Society for Cardiovascular Magnetic Resonance

Miami, Florida, January 20–22, 2006

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Charlottesville, Virginia; Oxford, United Kingdom; Baltimore, Maryland; San Francisco, California; Philadelphia, Pennsylvania; Calgary, Canada; and Boston, Massachusetts

The 9th annual meeting of the Society for Cardiovascular Magnetic Resonance (SCMR) was held from January 20–22, 2006 under sunny skies in Miami, Florida. A well-attended introductory physician course was held prior to the start of the meeting with a concurrent 3-day technologists meeting. Over 800 physicians, scientists, trainees, nurses, and technologists attended the meeting which again featured parallel tracks for clinician scientists, basic scientists, and those interested in congenital applications. Nearly 400 abstracts were presented, including over 100 oral presentations. Seven abstract awards were chosen. A special lunchtime session on career development for trainees and students was offered. In addition, a concurrent technologist program updated technologists from around the world in the latest in cardiovascular magnetic resonance (CMR) technology and applications. New advances in imaging techniques, clinical applications, contrast agents, high field imaging, and molecular imaging were presented and debated. Complementary use of CMR and cardiac computed tomography (CCT) was also discussed.

CLINICAL SCIENCE

Best abstracts. A session was devoted to the best clinical oral abstracts and first prize went to Dr. Adrian Cheng of Oxford University (1). Dr. Cheng and colleagues demonstrated the feasibility of late gadolinium enhancement at 3-T using a longer inversion time. The delineation of hyperenhanced infarct regions in 16 patients with prior myocardial infarction (MI) was similar at 3- and 1.5-T. The utility of assessing myocardial perfusion at 3-T was highlighted in another study of healthy subjects and patients with suspected coronary artery disease. The higher field permitted improved spatial resolution and image quality (2).

Other top abstracts highlighted the use of CMR in acute MI. Cardiac magnetic resonance was used to follow patients with acute MI randomized to bone marrow-derived stem cell transfer or placebo (3). No improvements in left ventricular volumes or regional or global function were found with stem cell therapy. Cardiac magnetic resonance was shown to be more sensitive than single-photon emission computed tomography in detecting acute MI among 78 patients imaged with both modalities one week after primary stenting (4). Contrast-enhanced CMR evidence of microvascular obstruction in acute MI was the most important predictive parameter of cardiovascular events in a study of 122 patients followed for 3.5 years (5).

The second place clinical oral abstract was given by Dr. Ravi G. Assomull from the Royal Brompton Hospital. He presented data from 63 patients with dilated cardiomyopathy and ejection fraction ≤40% followed for nearly two years (6). The presence of mid-wall fibrosis as evidenced by late gadolinium enhancement was the only significant predictor of death and hospitalization on multivariate analysis. Other top abstracts included a demonstration that late gadolinium-enhanced CMR can be applied to identify scar from radiofrequency ablation of the pulmonary veins in the atrial fibrillation population (7). Stress perfusion CMR was shown to correlate well with fractional flow reserve measurements in the catheterization laboratory (8). Cardiac magnetic resonance measures of endothelial function demonstrated reduced endothelial-independent dilation in trained athletes compared with normal subjects (9).

CMR and sudden death. The opening plenary session on CMR and sudden cardiac death began with an illustrative pathologic review by Dr. Christina Basso from the University of Padua, Italy. Dr. Basso highlighted the underlying theme of fibrosis (an ideal target for contrast-enhanced CMR) as a substrate for sudden death in coronary artery disease, hypertrophic cardiomyopathy, myocarditis, and arrhythmogenic right ventricular (RV) cardiomyopathy. Dr. Katherine Wu of Johns Hopkins University reviewed the role of contrast-enhanced CMR methods for the identification of microvascular obstruction, necrosis, and cardiovas-

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Abbreviations and Acronyms

CCT = cardiac computed tomography
CHD = congenital heart disease
CMR = cardiac magnetic resonance
DTI = diffusion tensor imaging
ICD = implantable cardioverter-defibrillator
IRON = Inversion-Recovery ON-Resonant water suppression
MI = myocardial infarction
MRA = magnetic resonance angiography
RV = right ventricle/ventricular
SCMR = Society for Cardiovascular Magnetic Resonance
SPIO = superparamagnetic iron oxide particles
TOF = tetralogy of Fallot

cular risk in patients with prior MI. Subsequent talks detailed how late gadolinium-enhanced CMR may identify high-risk patients with hypertrophic cardiomyopathy and infiltrative cardiomyopathies. The session concluded with the presentation of Dr. Edward Martin (Oklahoma Heart Institute) on the clinical protocols to facilitate safe CMR scanning in patients with pacemakers and implantable cardioverter-defibrillators (ICDs). Over 200 non–pacemaker-dependent patients have now been safely scanned (cardiac and non-CMR scanning), generally in the presence of an electrophysiologist.

Guidelines and reimbursement. The session on "Guidelines and Reimbursement" highlighted the complex issue of CMR reimbursement. A common theme was relatively low reimbursement compared with physician effort in the U.S., Japan, and Europe. Dr. Nathaniel Reichek (St. Francis Hospital, New York) began reviewed currently available current procedural terminology codes in the U.S. and the lengthy process required to modify and update them. Dr. Martin discussed the likelihood that CMR reimbursement may be tied to laboratory accreditation. Dr. Eckart Fleck (German Heart Institute) reflected on the highly regulated situation in Europe where specific countries have laws restricting the practice of CMR to radiologists (Germany, Belgium) while others (England, France) allow cardiovascular specialists to practice CMR. Dr. Warren Manning presented new U.S. training recommendations published by the American College of Cardiology/American Heart Association for physicians out of training (10) and newly approved recommendations by the Society for Cardiovascular Magnetic Resonance (SCMR) for these physicians as well as cardiovascular trainees (11). Both documents allow for "out of laboratory" experiences to fulfill up to 50% of the three months required for level II training and are available at the SCMR website (12).

Imaging of myocardial perfusion. A spirited discussion of CMR myocardial perfusion imaging was held. Standardized protocols were reviewed including stress and rest imaging followed by late gadolinium enhancement. Limitations of first pass perfusion imaging were discussed, including imaging artifacts and the need for multicenter validation. Some argued for the superior accuracy of dobutamine stress function over vasodilator stress perfusion. A robust experience in private practice in Hong Kong was demonstrated. Pertinent abstracts included validation of perfusion imaging against fractional flow reserve measure at catheterization with a sensitivity and specificity of 94% and 83%, respectively, for significant stenoses in 42 patients (13). Over 400 patients with a negative adenosine stress perfusion study had an event-free survival of 99% over a period of at least 6 months (14). Quantitative measures of myocardial blood flow CMR in 27 patients undergoing percutaneous coronary intervention demonstrated that mean blood flow is lower in segments with scar and is related to scar transmurality (15).

Vascular/plaque imaging. An exciting session on the use of CMR angiography and plaque imaging for atherosclerotic vascular disease was kicked off by Dr. Sanjay Rajagopalan (Mt. Sinai, New York). Other speakers discussed new approaches to magnetic resonance angiography (MRA) in the peripheral and carotid arteries. Novel CMR spectroscopic (16) and perfusion methods (17) for assessing calf muscle physiology in peripheral arterial disease were reviewed. Finally, the role of carotid plaque imaging in clinical trials was discussed including the additive role of gadolinium contrast. Abstracts of particular interest in this arena included a demonstration that CMR could detect significant changes in aortic distensibility, brachial artery flow-mediated dilation, and aortic atherosclerosis within 3 months of starting statin therapy (18). In addition, a 32-channel 1.5-T magnetic resonance scanner using multicoil technology showed excellent results for lower extremity MRA with an extended field of view (19).

CMR and CCT. This session addressed the unresolved question of the relative importance of CMR and CCT in the evaluation of coronary artery disease. Dr. Hajime Sakuma discussed the benefit of CMR and effectively described the limitations and benefits compared with CCT. Both his group (20) and others (21) have published promising results with whole heart CMR imaging, akin to the three-dimensional computed tomography angiography approach but acquired using respiratory navigators. His group described a sensitivity of 82%, specificity of 90%, and diagnostic accuracy of 87% in 113 patients. In general, the quality of whole heart coronary MRA is more variable and less predictable than single breath-hold coronary computed tomography angiography.

Dr. Daniel Berman presented recent experiences with 64-detector CCT coronary imaging. Spatial resolution with CCT is better than for coronary magnetic resonance, and it has an acquisition time of seconds. In several published papers using 64-detector CCT, sensitivities and specificities compared with those of X-ray angiography have ranged from 90% to 100%. Coronary arterial calcification remains a significant limitation as does the need for iodinated contrast media in patients with renal insufficiency. Drs. Sakuma and Berman agreed that for now, CCT will likely be the

technique employed in most patients, while CMR will be used for patients with high calcium scores and renal insufficiency. Cardiac magnetic resonance may also be preferred when additional information, such as myocardial viability, is sought or repeated testing is anticipated.

Ventricular remodeling: insights from CMR. A session was devoted to the use of CMR as the window to the remodeling heart. Dr. Martin St. John Sutton (University of Pennsylvania) presented the development of this field using echocardiography. The CMR speakers discussed remodeling in the setting of MI and dilated cardiomyopathies. The CMR assessment of reverse remodeling with both medical and revascularization strategies was elucidated. Results in a total of more than 300 patients presented at the meeting showed a significant incremental prognostic value of infarct size quantification by CMR for predicting major adverse cardiac events after MI (5,22). Although larger infarcts are associated with adverse outcomes, a pilot trial indicates that patients, despite infarcts involving more than 40% of the left ventricular mass, may have a favorable outcome (23). Microvascular obstruction in acute MI was again shown to be a strong predictor of outcome (24).

BASIC SCIENCE

Best abstracts. Matthias Stuber, PhD, of Johns Hopkins University won first prize for a novel approach to creating positive contrast from supermagnetic nanoparticles called Inversion-Recovery ON-Resonant water suppression (IRON) (25). By suppressing the on-resonant protons within a certain bandwidth, signal enhancement was produced from the off-resonant protons in proximity to the iron nanoparticles. Second prize was presented to Khaled Z. Abd-Elmoniem, MSc, from the same institution for the improved accuracy of planar strain maps through correction of the false strain component generated by through-plane motion using a tagging methodology capable of tracking three-dimensional myocardial displacement in all points in an image plane (26).

Two other top basic abstracts focused on diffusion tensor imaging (DTI), a technique used to non-invasively characterize cardiac fiber orientation. In one study, three-dimensional deconstruction of cardiac tissue architecture was performed on an isolated canine heart (27) while another focused on improving in-vivo DTI, a challenge due to cardiac and respiratory motion and susceptibility gradients (28). Other top abstracts focused on spectroscopy. One demonstrated significant derangements in cardiac ^{31}phosphorous energy metabolism in patient with left ventricular noncompaction (29). Another used ultrashort echo time chemical shift imaging for the efficient quantitation of myocardial ^{23}Na concentrations (30). One group proposed a two-dimensional balanced steady state free precession technique for the detection of blood-oxygen level-dependent contrast in a model of coronary occlusion with excellent temporal and spatial resolution (31). The efficacy of P947, a short peptide ligand for matrix metalloproteinases, was established for the detection of atherosclerotic plaque in ApoE knockout mice (32). Real-time acquisition of black-blood cine cardiac images at 3-T was demonstrated using a real-time sequence with stimulated echos (33).

Cellular and molecular imaging/novel contrast agents. The cellular and molecular imaging session provided an overview of contrast ultrasound, bioluminescence, radionuclide, and CMR imaging approaches. While CMR techniques for stem cell tracking show promise for rapid transition to the clinical realm, methods for studying gene expression and molecular imaging of atherosclerotic progression are increasingly available. In a session devoted to novel contrast agents, an overview was presented of the mechanisms of gadolinium and iron oxide contrast as well as their use as targeted agents for plaque detection and cell tracking.

The advantages of high spatial resolution and targeted CMR contrast agents are being pursued. One such agent, an $\alpha_V\beta_3$-integrin–targeted paramagnetic nanoparticle containing the antiangiogenic agent fumagillin, was shown to monitor atherosclerotic progression and response to therapy in a rabbit model (34). Using a monoclonal antibody targeting platelet/endothelial cell adhesion molecule-1 bound to a superparamagnetic iron oxide particles (SPIO), selective uptake of the agent in mouse infarction was shown (35). In a preclinical MI model, SPIOs were used to exogenously label mesenchymal stem cells and study their migration after transmyocardial injection, suggesting that targeting of the peri-infarction zone is preferred (36). Intravenous ultrasmall and micrometer-sized SPIOs were used to track macrophage infiltration and transplant rejection in a heterotopic heart and lung rat transplantation model (37). The first in-vivo fluorescent tomography and CMR of a magnetofluoroscent nanoparticle uptake by macrophages in mouse infarction shows promise as a novel agent for targeting inflammation (38).

Parallel and other novel imaging techniques. One session was devoted to imaging methods to accelerate image acquisition in both the spatial and temporal domain (e.g., enhanced parallel imaging, spiral imaging, and k-t Blast techniques). These advances are providing faster CMR imaging and real-time image acquisition schemes. The usefulness of k-t Blast for accelerated image acquisition for first-pass contrast-enhanced CMR during rest and adenosine stress was demonstrated in patients with suspected coronary artery disease before catheterization (39). Using a prototype 32-receiver channel 1.5-T MR scanner, the feasibility of acquiring three-dimensional cine CMRs in a single breath-hold using parallel imaging for assessing cardiac structure and function was demonstrated (40). Several new imaging techniques for the visualization of iron oxide particles were presented. One technique, called GRadient Echo Acquisition for Superparamagnetic Particles (GRASP), uses a phasing/dephasing technique to render a bright signal

and was applied to the imaging of ferritin deposition in a rabbit carotid injury model (41). The IRON technique for positive enhancement of SPIOs was combined with fat suppression for iron-oxide-labeled stem cell detection in angiogenesis (42).

Interventional CMR. A session was devoted to advances in interventional CMR. Cardiac magnetic resonance shows promise for targeting of gene and stem cell therapy to specific areas of the heart such as the peri-infarction zone or atherosclerotic plaque. Electrophysiology applications are taking advantage of hybrid X-ray/magnetic resonance systems to obtain detailed anatomy of the pulmonary veins by CMR for guiding X-ray ablation therapy. Similarly, for pediatric applications, CMR can be used to obtain high-resolution anatomical details of congenital abnormalities that can be fused with X-ray images to guide therapy and concurrently decreasing the radiation dose. Safety of magnetic resonance delivery devices, ICDs, and pacemakers remains a concern. Recent studies suggest that more modern pacemakers and ICDs have been scanned without adverse events. However, more robust testing of pacemaker lead heating remains warranted especially as CMR moves to higher field strengths.

New developments in murine CMR. Given the enormous importance of transgenic mouse models, a full session was dedicated to this topic including an update on advanced tools for the assessment of left ventricular remodeling post-MI, spectroscopy to investigate myocardial metabolism, and molecular contrast agents for targeting atherosclerosis or transplant rejection. Interesting abstracts included the use of strain analysis by tagged CMR to quantify the progression of mechanical dyssynchrony during remodeling in a post-MI mouse model (43). Infarction alone leads to significant dyssynchrony, which does not change significantly over time. Mice with chronic pressure-overload from aortic constriction showed a reduced ejection fraction, increased left ventricular mass and end-diastolic volume, while cardiac phosphocreatine/adenosine triphosphate ratios were decreased (44). Murine molecular CMR is becoming increasingly important, and several abstracts reported on using different agents in mouse models including SPIOs (35), magnetofluoroscent nanoparticles (38), and gadolinium-based targeted contrast agents (45).

COMBINED CLINICAL AND BASIC SCIENCE

1.5- versus 3-T—complementary or competitive? 3-T cardiac imaging was well represented with its status as "promising but unproven" in 2005 advancing to "accepted and appropriate" in 2006. Cardiac magnetic resonance at 3-T can address most of the basic clinical questions that are routinely answered at 1.5-T (function, late enhancement), and that in certain situations CMR at 3-T may be superior (such as for coronary imaging and tagging) or vastly superior (qualitative perfusion and ^{31}P-MR spectroscopy) to 1.5-T. Nearly 10% of the abstracts reported on imaging at 3-T, clearly representing a growth area in CMR. Some were methods based in healthy subjects (46), but 12 abstracts presented data from over 100 patients, including children and patients with stents and sternal wires. Abstracts comparing 3- and 1.5-T described general increases in signal-to-noise ratio at 3-T (47,48), which are difficult to quantify precisely owing to differences between coil designs and other system characteristics. Specifically, it was shown that quantification of irreversible damage by late enhancement was similar for 1.5- and 3-T (1), and that perfusion imaging allows for higher resolution at 3-T (2). Electrocardiographic gating was not reported as being problematic, alleviating previous concerns over elevated magnetohydrodynamic signals.

Quantification in CMR. A session devoted to quantification in CMR reviewed state-of-the-art approaches to quantifying infarct size with late gadolinium enhancement as well as regional function with tagging, phase velocity mapping, and displacement encoding methods. In addition, flow quantification with phase velocity imaging and quantification of first-pass myocardial perfusion with deconvolution methods were discussed.

CONGENITAL HEART DISEASE (CHD)

A multiday program was dedicated to CMR in CHD. The "Controversies" session prompted vigorous discussions regarding whether CMR and CCT were competing or complementary, if single ventricle patients require routine catheterization during staged Fontan reconstruction or the merits of non-geometric echo-Doppler techniques when compared with CMR for ventricular function. The unique technical challenges facing the CMR imager in CHD were addressed. A session devoted to CMR in adult CHD discussed issues regarding coarctation of the aorta, the systemic RV, the Fontan circulation, and tetralogy of Fallot (TOF) in this aging patient population.

The top prize in the best abstract session in CHD compared perfusion imaging in 19 children with coronary angiography and found that it was feasible and concordant with angiographic findings (49). Tetralogy of Fallot was the subject of four reports in this session. One group reported that restrictive physiology was associated with worse exercise tolerance and that repair at a young age did not protect patients from RV diastolic dysfunction (50). Myocardial velocimetry was used to demonstrate decreased biventricular velocities of TOF patients when compared with patients with d-transposition of the great arteries (51). Myocardial scarring by late gadolinium enhancement in TOF correlates with life-threatening arrhythmias (52). A study of regional wall motion abnormalities of the RV in TOF found that the RV outflow tract is principally responsible for global RV dysfunction (53). Two reports championed the concept that general anesthesia is not necessary for keeping pediatric patients motionless in the scanner, using either deep sedation (54) or a modified video display system (55). A new technique utilizing parallel imaging and the "CENTRA-

keyhole" method was presented, which allowed for time-resolved, "cine," three-dimensional contrast-enhanced CMR angiography (56).

Conclusions. The 2006 meeting of the SCMR was highlighted by major advances in the field including the growth of applications at 3-T, important prognostic information in patients with MI and dilated cardiomyopathies, the use of CMR in major clinical trials of stem cell therapies, novel techniques for rapid imaging and targeting contrast agents, and new applications in murine models. The interaction of CMR and CCT will continue to be defined by advances in both fields. The 10th annual Scientific Sessions of the SCMR (February 2 to 4, 2007 in Rome, Italy) will be a combined meeting with the European CMR Working Group and promises to provide some answers and foster more debate as clinical and research applications of CMR continue to evolve.

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