Comparison of Velocity Vector Imaging Echocardiography With MRI in Mouse Models of Cardiomyopathy

Summary—Although 2-dimensional echocardiographic strain imaging cost-effectively and objectively quantifies ventricular wall motion, only 1 small study has directly compared strain measured with echocardiography against MRI (MRI) in mice. Using a different speckle-tracking algorithm (velocity vector imaging [VVI]), we compared circumferential (CS) and radial strain (RS) to displacement encoding with stimulated-echo MRI in 2 genetic mouse models of cardiomyopathy. CS and RS were measured in groups of wild-type mice and mice with gene targeted deficiency of cardiac myosin-binding protein-C or muscle LIM protein. There was modest correlation between VVI and MRI measured strains, with global CS yielding a stronger correlation compared with global RS (CS $R^2=0.4452$ versus RS $R^2=0.2794$, both $p<0.05$). Overall, strain measured by VVI was more variable than MRI and the limits of agreement were slightly, but not significantly, closer for global CS than RS. Both VVI and MRI strain measurements showed significantly lower global CS strain in the knockout groups compared with the wild-type, but only the VVI CS strain measurements were different between the 2 knockout groups. These data demonstrate that measurements of LV CS and RS are feasible in mice using VVI, although correlations and agreement were modest. VVI may complement conventional methods that objectively assess global and regional LV function and be particularly useful for high through-put phenotyping of murine models.

Conclusions—Measurements of left ventricular CS and RS are feasible in small animals using 2-dimensional echocardiography. VVI and MRI strain measurements correlated modestly and the agreement between the modalities tended to be greater for CS than RS. Although VVI and MRI strains were able to differentiate between wild-type and knockout mice, only global CS VVI differentiated between the 2 models of cardiomyopathy.

In Situ Confocal Imaging in Intact Heart Reveals Stress-Induced Ca2+ Release Variability in a Murine Catecholaminergic Polymorphic Ventricular Tachycardia Model of Type 2 Ryanodine ReceptorR4496C+/− Mutation

Summary—Ca2+ handling abnormalities play important roles in the pathophysiology of heart failure, arrhythmias, and sudden cardiac death. Patients with a specific mutation (R4496C) in the cardiac Ca2+ release channel, type 2 ryanodine receptor, suffer from exercise/stress-induced catecholaminergic polymorphic ventricular tachycardia (CPVT) and sudden cardiac death but are typically healthy at rest. The reason that the resting defect in Ca2+ dynamics in vitro in isolated myocytes does not correspond to the clinical manifestations of CPVT patients with the same mutation is unexplained. In a genetically modified mouse model of CPVT (type 2 ryanodine receptorR4496C+/−), we applied in situ confocal imaging techniques to study Ca2+ handling in undisrupted myocardium of intact hearts. This approach allows investigation under near-physiological conditions. Type 2 ryanodine receptorR4496C+/− mutants were found to be functionally normal in situ under resting conditions but had a high degree of Ca2+ release variability on intense adrenergic stimulation. This new pattern of Ca2+ handling abnormality is an integrated, tissue-level response of mutated myocytes to adrenergic stress, closely correlated with CPVT. Our data reveal that Ca2+ release variability results from electric defects, likely originating from Purkinje fibers, rather than the failure of Ca2+ release response to action potentials in mutated ventricular myocytes. The present study provides insights into Ca2+ release and electric dysfunction in CPVT.

Conclusions—Our studies using an in situ confocal imaging approach suggest that mutated RyR2s are functionally normal at rest but display a high degree of Ca2+ release variability on intense adrenergic stimulation. Ca2+ release variability is a Ca2+ release abnormality resulting from electric defects rather than the failure of the Ca2+ release response to action potentials in mutated ventricular myocytes. Our data provide important insights into Ca2+ release and electric dysfunction in an established model of catecholaminergic polymorphic ventricular tachycardia.

Pulmonary Venous Anatomy Imaging With Low-Dose, Prospectively ECG-Triggered, High-Pitch 128-Slice Dual-Source Computed Tomography

Summary—Cardiac computed tomography (CT) is often used to noninvasively define left atrial and pulmonary venous anatomy before atrial fibrillation ablation procedures. Exposure to ionizing radiation from CT is of concern, and efforts to reduce radiation dose, while maintaining excellent image quality, are imperative. Second-generation 128-slice dual-source CT scanners enable ECG-triggered, single heart beat image acquisition. In the present study, use of a high-pitch protocol with dual-source CT is shown to obtain excellent quality scans with a minimal radiation dose of 1.4 mSv and scan acquisition time of only 6 seconds during sinus rhythm or atrial fibrillation. Radiation dose was markedly lower than prior non–high-pitch retrospective or prospectively triggered CT pulmonary vein scans.
Cardiac Magnetic Resonance Imaging Study of Ventricular Scar in Arrhythmogenic Right Ventricular Cardiomyopathy: Comparison of 3D Standard Electroanatomical Voltage Mapping and Contrast-Enhanced Cardiac Magnetic Resonance

Summary—The hallmark pathological lesion of arrhythmogenic right ventricular cardiomyopathy (ARVC) is myocardial loss with replacement by fibrofatty tissue. RV lesions are assessed as mechanical wall dysfunction by traditional imaging techniques, such as echocardiography and angiography. Emerging tools offer the possibility to directly visualize a fibrofatty ventricular scar. Endocardial voltage mapping (EVM) by the CARTO system has been demonstrated to identify “low-voltage” myocardial areas (“electroanatomical scar”) invasively, whereas contrast-enhanced cardiac magnetic resonance (CE-CMR) has the potential to detect regions of delayed contrast enhancement (DCE) noninvasively. The potential utility of such imaging approaches is still under evaluation, and their role for detection of ventricular scar has not been included among the recently revised task force diagnostic criteria for ARVC. Our study was designed to evaluate the diagnostic accuracy of direct visualization of a ventricular scar and to compare the ability of EVM and CE-CMR for imaging scar lesions in ARVC. The study demonstrates that EVM allows accurate identification of RV electroanatomical scars in ARVC patients and supports its clinical use for substrate-based mapping and catheter ablation of RV tachycardias, as well as for imaging-guided endomyocardial biopsy. On the contrary, available DCE-CMR appears less sensitive in visualizing RV scars, limiting its usefulness for clinical diagnosis and for guiding interventional RV procedures. Of interest, the high prevalence of left ventricular DCE in our study patients is in keeping with the perspective of biventricular disease involvement and indicates the diagnostic relevance of left ventricular scar detection by CE-CMR resonance in ARVC patients.

Conclusions—EVM and CE-CMR allow identification of RV scar lesions in most ARVC patients. CE-CMR is less sensitive than EVM in identifying RV scar lesions. The high prevalence of LV DCE confirms the frequent biventricular involvement and indicates the diagnostic relevance of LV scar detection by CE-CMR.

Molecular Imaging of Mesenchymal Stem Cell: Mechanistic Insight Into Cardiac Repair After Experimental Myocardial Infarction

Summary—Adult stem cells have been used to treat heart diseases for over a decade. Preclinical studies have demonstrated that mesenchymal stem cells (MSCs) facilitate both myocardial repair and neovascularization in animal models of cardiac injury. Human clinical trials have also validated the safety of MSC therapy in patients with acute myocardial infarction and heart failure. However, the mechanisms whereby MSCs exert their beneficial effect in improving cardiac function is not precisely known. Here, we used molecular imaging to track the fate of MSCs following their injection into the peri-infarct regions of the heart. We showed that human MSCs can develop into endothelial-like cells, but not cardiomyocytes. However, these injected cells disappeared completely from the heart in two months. Interestingly, the improvement in cardiac function as measured by changes in ejection fraction persisted for up to 6 months. We also found that injection of MSCs into the heart enhanced the development of new blood vessels and decreased cardiac fibrosis following myocardial infarction. In conclusion, the beneficial effects extended by the MSCs are mediated by a paracrine effect, through factors secreted by the MSCs. Thus, our animal model provided insights into the potential mechanisms whereby MSCs help to repair the heart after myocardial infarction.

Conclusions—hMSCs differentiated into endothelial cells and integrated into blood vessels after experimental myocardial infarction. The differentiated hMSCs only lasted for up to 50 days in vivo, but improvement in cardiac function persisted for up to 6 months. Increased angiogenesis and decreased fibrosis were associated with cardiac functional improvement after hMSC transplantation.

Mapping and Ablation of the Pulmonary Veins and Cavo-Tricuspid Isthmus With a MRI-Compatible Externally Irrigated Ablation Catheter and Integrated Electrophysiology System

Summary—Conventional x-ray–guided fluoroscopy remains the foundation of catheter navigation in the majority of contemporary clinical electrophysiology procedures. In the past decade, MRI–guided ablation has steadily emerged as a promising alternative in interventional electrophysiology, offering potential advantages.
over traditional fluoroscopic guidance, including: (1) improved anatomic visualization of the heart and surrounding structures; (2) avoidance of ionizing radiation; and (3) intraprocedural visualization of lesion formation. The current study represents the development of a MRI-compatible irrigated ablation catheter and electrophysiological pacing and recording system, which will be a platform for clinical applications in MRI-guided interventional electrophysiology.

Conclusions—These data demonstrate the feasibility of using multiple catheters, an integrated EP pacing and recording system, and externally irrigated ablation with cardiovascular magnetic resonance guidance to undertake clinically relevant biatrial mapping and ablation.5

Provider-Directed Imaging Stress Testing Reduces Health Care Expenditures in Lower-Risk Chest Pain Patients Presenting to the Emergency Department

Summary—In an effort to define a more efficient and efficacious care pathway for patients with chest pain treated in an observation unit, we examined the role of a mandatory cardiac magnetic resonance (CMR) stress imaging pathway in lower-risk emergency department patients with symptoms of acute coronary syndrome. In comparison to a mandatory CMR pathway, participants in a care pathway in which care providers chose the stress imaging modality (with an option for CMR) had decreased cost, similar lengths of stay, and similar clinical outcomes. The results of this randomized trial suggest that preserving the physician choice in selecting a stress modality is an important component to efficient care delivery in patients with lower-risk symptoms of acute coronary syndrome being treated in an emergency department–directed observation unit. These findings are in contrast to prior findings in patients at intermediate to high risk, in whom an observation unit strategy with stress CMR is a cost-effective alternative to inpatient care. The health policy implication of this research is that before instituting a mandate for a particular imaging modality, prospective studies to evaluate the impact on efficiency and cost should be performed.

Conclusions—In patients with lower-risk chest pain receiving emergency department–directed OU care, the ability of a physician to select a cardiac stress imaging modality (including echocardiography, CMR, or radionuclide testing) was more cost-effective than a pathway that mandates a CMR stress test. Contrary to prior observations in individuals with intermediate- to high-risk chest pain, in those with lower-risk chest pain, these results highlight the importance of physician-related choices during acute coronary syndrome diagnostic protocols.8

Computed Tomography Myocardial Perfusion Imaging With 320-Row Detector

Computed Tomography Accurately Detects Myocardial Ischemia in Patients With Obstructive Coronary Artery Disease

Summary—Coronary computed tomography angiography (CTA) provides high sensitivity and negative predictive value for the detection of obstructive coronary artery disease (CAD). Its primary strengths are the ability to quantify atherosclerosis and accurately exclude the presence of obstructive CAD. However, the degree of coronary obstruction measured by CTA or conventional angiography remains a poor predictor of reversible ischemia caused by atherosclerosis. Recent advances in cardiac computed tomography (CT) technology have enabled the assessment of the physiological significance of coronary stenoses using myocardial CT perfusion imaging (CTP).

This promising technology, when combined with coronary CTA, has the capability of evaluating CAD in comprehensive fashion and is likely to be most useful in the evaluation of lesions detected by CT angiography. This study demonstrates that myocardial CTP imaging, performed with a 320-row detector CT scanner, can accurately detect obstructive atherosclerosis causing myocardial ischemia in symptomatic patients with suspected CAD.

Conclusions—Computed tomography perfusion imaging with rest and adenosine stress 320-row CT is accurate in detecting obstructive atherosclerosis causing myocardial ischemia.9

Spin-Labeling MRI Detects Increased Myocardial Blood Flow After Endothelial Cell Transplantation in the Infarcted Heart

Summary—Endothelial cells (ECs) and endothelial progenitor cells (EPCs) have been isolated or derived from various sources including blood, bone marrow, embryonic stem cells and induced pluripotent stem cells. ECs and EPCs have been postulated to form new vasculature, preserve cardiac function, and inhibit apoptosis in the infarcted heart. However, mechanisms underlying the salutary effects of these cells are not well understood: in fact, whether neovascularization leads to improved regional myocardial blood flow (MBF) has yet to be clearly demonstrated. To evaluate EC- or EPC-mediated cardiovascular repair over time and to improve clinical translation for cell-based therapies, noninvasive imaging methods for estimating MBF are desirable. At present, positron emission tomography is the clinical standard for MBF measurement. However, radioactive perfusion tracers such as N-13 ammonia, O-15 water, or Rb-82 have short half-lives and hence require an on-site cyclotron or Rubidium generator. Optimally, a method that permits serial MBF evaluations without accruing radiation exposure/risk is most useful. In the present report, we first validate a spin-labeling MRI (SL-MRI) technique for quantification of MBF; we then demonstrate that this technique is highly reproducible and sensitive for detecting regional MBF changes in response to EC grafting in a rat model of myocardial infarction. Because SL-MRI utilizes endogenous blood (water) as a perfusion tracer, it eliminates the need to inject exogenous tracers. The clinical feasibility of SL-MRI–based MBF measurement has recently been demonstrated in humans. Our study provides evidence that MBF is a unique and sensitive index to evaluate the impact of EC-mediated therapy on regional microvascular function after infarction.

Conclusions—MBF in free-breathing rats measured by SL-MRI is validated by the standard color microsphere technique. SL-MRI allows quantification of temporal changes of regional MBF in response to EC treatment. The proof-of-principle study indicates that MBF is a unique and sensitive index to evaluate EC-mediated therapy for the infarcted heart.10

Combined Cardiac MRI and C-Reactive Protein Levels Identify a Cohort at Low Risk for Defibrillator Firings and Death

Summary—The prevention of sudden cardiac death remains an imprecise science. Current clinical practice for selecting patients for primary prevention implantable cardioverter-defibrillators (ICDs) predominantly relies on demonstrating reduced left ventricular ejection fraction. However, this criterion lacks sensitivity and specificity. Although 80,000 Americans annually receive devices based on low left ventricular ejection fraction, only a minority (5% per year) will have appropriate ICD therapy, and a significantly larger number of patients will be subjected to the adverse effects of procedural
complications, inappropriate discharges, infections, and device malfunctions. Prior studies have supported the role of the myocardial substrate in ventricular arrhythmogenesis. In the current study, we examined whether a combined index of myocardial tissue heterogeneity (gray zone) assessed by cardiac magnetic resonance could differentiate between low- and high-risk patients independently or in combination with serum biomarkers, such as high-sensitivity C-reactive protein. We prospectively enrolled 235 patients with ischemic and nonischemic cardiomyopathy. Patients who had the lowest levels of both gray zone and high-sensitivity C-reactive protein had the lowest risk of appropriate ICD discharges and cardiac death, with an annual incidence of 0.7% per year, which is below reported ICD-complication rates. These results are unique in identifying a low-risk cohort using combined risk indices that may reflect the underlying substrate and a proinflammatory environment that adversely modifies the myocardial substrate. Future prospective studies will be needed to determine whether such a strategy can be used to safely and cost-effectively reduce unnecessary ICD implantations.

Conclusions—In a cohort of primary prevention ICD candidates, combining a myocardial heterogeneity index with an inflammatory biomarker identified a subgroup with a very low risk for adverse cardiac events, including ventricular arrhythmias. This novel approach warrants further investigation to confirm its value as a clinical risk stratification tool.11

Identification and Acute Targeting of Gaps in Atrial Ablation Lesion Sets Using a Real-Time MRI System

Summary—The goal in most ablation procedures is to electrically isolate one region from another by creating a set of contiguous and transmural ablation lesions. Yet, despite the best effort of electrophysiologists, gaps remain in ablation lesion sets. This stems from the fact that when ablating there is no direct visualization of ablation-related tissue changes and ablation is inferred based on numerous indirect parameters. MRI (MRI) has excellent soft tissue visualization characteristics, and in this study, this property of MRI was used to acutely identify ablation lesions and in turn identify the gaps between ablation lesions. A challenge in using MRI for ablation is that the currently used ablation catheters are not MRI compatible. For this study, MRI-compatible electrophysiology mapping and ablation catheters were developed. A complete real-time MRI-based electrophysiology system was also developed by integrating the use of MRI-compatible catheters with real-time imaging. This system was used to acutely identify the ablation lesions, the gaps in between the lesions, and then target the gaps acutely. An MRI-based electrophysiology system not only does away with exposure of ionizing radiation to the patient and the operator but also allows direct visualization of tissue changes, with ablation potentially leading to significant improvement in ablation procedure outcomes.

Conclusions—Real-time-MRI system can be used to identify and acutely target gaps in atrial ablation lesion sets. Acute targeting of gaps in ablation lesion sets can potentially lead to significant improvement in clinical outcomes.12

Demonstration of Blood Pressure-Independent Noninfarct Myocardial Fibrosis in Primary Aldosteronism: A Cardiac MRI Study

Summary—It was previously thought that primary aldosteronism represented a rare and fairly benign form of hypertension. However, it is now clear that primary aldosteronism is a common cause of hypertension and associates with excess cardiac morbidity, independent of blood pressure effects. Until recently, imaging modalities to demonstrate aldosterone-mediated cardiac fibrosis have been inferred by using 2-dimensional echocardiography and videodensitometry, as well as measuring plasma markers of collagen turnover. The current study is the first to use contrast-enhanced cardiac MRI, the gold standard imaging technique for myocardial fibrosis, to demonstrate the effects of aldosterone excess in subjects with no evidence of coronary artery disease. Our data provide further evidence that myocardial fibrosis can occur due to aldosterone-mediated cardiac damage that is independent of blood pressure. These results highlight the importance of early diagnosis of this condition in subjects with high blood pressure. They suggest that treatment strategies should be aimed at ameliorating the effects of aldosterone excess as well as lowering blood pressure. Whether aldosterone-mediated cardiac fibrosis is reversible with treatment of aldosterone excess remains to be seen.

Conclusions—These data illustrate that patients with primary aldosteronism (PA) exhibit frequent myocardial fibrosis as demonstrated by late gadolinium enhancement using cardiac MRI; this finding is independent of blood pressure. This may be mediated partly through inflammation and oxidative stress. This study highlights the importance of specific targeting of aldosterone excess as well as blood pressure reduction to minimize cardiac morbidity in PA.13

Differentiation Between Fresh and Old Left Ventricular Thrombi by Deformation Imaging

Summary—Left ventricular thrombi after myocardial infarction are linked with a risk of systemic embolization. The majority of these events occur within the initial 4 months after myocardial infarction. Thus, the ability to differentiate between old and fresh left ventricular thrombosis is of clinical importance. This study applied the technique of echocardiographic myocardial deformation imaging to the analysis of left ventricular thrombi. The 2-part study proposes an echocardiographic method to reliably differentiate fresh from old intracavitary thrombi, easy to implement in everyday routine. In this prospective study, sufficient anticoagulation not only diminished the risk of systemic embolization—a well-known fact—but also resulted in fresh thrombus resolution, whereas in patients with old thrombi, anticoagulation had no effect on thrombus resolution. This study has potentially significant clinical implications that should be explored in a larger, prospective study. Such a study might provide new insights concerning the identification of patients with fresh left ventricular thrombus in whom unfavorable consequences might be more likely and who therefore might benefit from anticoagulation.

Conclusions—Fresh and old intracavitary thrombi can be reliably differentiated by deformation imaging. In fresh thrombi, anticoagulation with phenprocoumon results in thrombus resolution in most patients.14

Early Stem Cell Engraftment Predicts Late Cardiac Functional Recovery: Preclinical Insights From Molecular Imaging

Summary—Human cardiac progenitor cell transplantation is an exciting new therapy to ameliorate cardiac dysfunction after myocardial infarction. However, much remains to be understood regarding the parameters for successful cell therapy, including the optimal cell dose, engraftment rate, long-term survival, and delivery route. Molecular imaging techniques can be used to monitor the retention, engraftment, and delivery of stem cells after their delivery in vivo. In this study, we stably modified human cardiac progenitor cells...
to express variants of the thymidine kinase reporter gene, thereby enabling use of positron emission tomography to monitor cellular engraftment and survival after intramyocardial delivery. We found that human cardiac progenitor cell transplantation resulted in a modest improvement in myocardial contractility and that this improvement in contractility correlated with the number of engrafted cells at early time points. Importantly, we showed that cellular engraftment at early time points can provide valuable prognostic information regarding the ultimate success of human cardiac progenitor cell transplant at later time points. In light of the variable response to cell transplantation seen in recent clinical cell therapy trials, molecular imaging techniques may prove pivotal to ensuring adequate cellular delivery and optimizing patient outcomes.

Conclusions—PET reporter gene imaging can provide important diagnostic and prognostic information regarding the ultimate success of hCPC treatment for myocardial infarction.

Systemic-to-Pulmonary Collateral Flow, as Measured by Cardiac MRI, Is Associated With Acute Post-Fontan Clinical Outcomes

Summary—Systemic-pulmonary collateral (SPC) flow is a well-recognized phenomenon in single ventricle patients after superior cavo-pulmonary connection. The clinical impact of these vessels following Fontan completion is not clear. We have recently described a novel method of quantifying SPC flow by cardiac magnetic resonance (CMR) imaging using phase-contrast velocity mapping techniques. We retrospectively reviewed the acute post-Fontan clinical course of 44 patients who had their burden of SPC flow quantified by CMR imaging prior to Fontan completion. Overall, these patients had a mean SPC flow volume of 1.5±0.9 L/min/m², which comprised 31±11% of total aortic flow and 44±15% of total pulmonary venous flow. We found significant linear associations between increasing amounts of SPC flow and duration of chest tube and hospitalization after Fontan. After adjusting for Fontan type and the presence of a fenestration, there was an increased odds of both prolonged chest tube duration and prolonged hospitalization, based on increasing amounts of all measures of SPC flow. It is unclear from these data whether the presence of SPC flow is the primary driver of a more complicated post-Fontan course, or whether the presence of SPC flow is a marker of underlying unfavorable anatomy or physiology. Future prospective study is needed to better understand the “natural” history of SPC flow in single ventricle patients through the staged surgical pathway, and to examine the efficacy and durability of catheter-based embolization on SPC flow and its effects on longer-term clinical outcomes.

Conclusions—Increasing SPC flow before Fontan, as measured by CMR imaging, is associated with increased duration of hospitalization and chest tube following Fontan completion.

Subclinical Left Ventricular Dysfunction in Preeclamptic Women With Preserved Left Ventricular Ejection Fraction: A 2D Speckle-Tracking Imaging Study

Summary—Patients with preeclampsia are at an increased risk of cardiovascular disease, which has been associated with long-term postpartum morbidity and mortality. Ejection fraction remains relatively preserved until late in the course of the disease. Measurement of strain using speckle echocardiography is being increasingly used to detect subclinical myocardial dysfunction. In this study, we show that women with preeclampsia have subclinical myocardial dysfunction as demonstrated by a decreased global longitudinal, radial, and circumferential strain in the setting of preserved ejection fraction. Our data are a step toward early detection of myocardial dysfunction in preeclampsia.

Conclusions—Myocardial strain imaging using speckle tracking is more sensitive than left ventricular ejection fraction to detect differences in left ventricular systolic function in women with and without preeclampsia.

Repolarization Changes Underlying Long-Term Cardiac Memory Due to Right Ventricular Pacing: Noninvasive Mapping With Electrocardiographic Imaging

Summary—Recent studies have drawn attention to the potentially deleterious effects of long-term right ventricular (RV) pacing on cardiac mechanical function. In addition, RV pacing is known to result in electric changes (as manifested by an altered T-wave axis), a phenomenon described as cardiac memory, although a detailed understanding of the spatial pattern of repolarization changes resulting from RV pacing has remained lacking. Using noninvasive electrocardiographic imaging, the present study provides novel insights into the pattern of electric remodeling induced by RV pacing. Two new insights emerged from the present study. First, the region close to the site of pacing exhibits a local action potential prolongation, resulting in a potentially arrhythmogenic dispersion of repolarization. Second, this dispersion of repolarization is only partially evident during continuous RV pacing, raising the intriguing possibility that the potentially arrhythmogenic substrate induced by RV pacing is only fully present after cessation of pacing. The clinical implications of these findings require further study, but the results offer mechanistic insights into the potential clinical sequelae of RV pacing.

Conclusions—These results demonstrate that electric remodeling in response to ventricular pacing in human subjects results in action potential prolongation near the site of abnormal activation and a marked dispersion of repolarization. This dispersion of repolarization is potentially arrhythmogenic and, intriguingly, was less evident during continuous right ventricular pacing, suggesting the novel possibility that continuous right ventricular pacing at least partially suppresses pacemaker-induced cardiac memory.

High-Resolution Versus Standard-Resolution Cardiovascular MR Myocardial Perfusion Imaging for the Detection of Coronary Artery Disease

Summary—Coronary artery disease is the leading cause of death worldwide and accurate methods of detection are therefore important. Furthermore, the detection of ischemia in patients with known coronary artery disease is increasingly used to guide revascularization decisions, particularly in complex cases. Myocardial perfusion cardiovascular MR (CMR) has emerged as a highly accurate modality to detect ischemia, and the recent CE-MARC study demonstrated a higher diagnostic accuracy compared with single photon emission CT. Myocardial perfusion CMR offers significantly greater spatial resolution than single photon emission CT without any ionizing radiation exposure. In this study of 100 patients, we used a new technique to increase the spatial resolution of myocardial perfusion CMR even further (<2 mm in-plane). The results showed that overall diagnostic accuracy as measured by the area under the receiver operator curve was better with the high spatial resolution technique. In addition,
Effects of Hemodynamics on Global and Regional Lung Perfusion: A Quantitative Lung Perfusion Study by MRI

Summary—Using lung perfusion quantification by MRI, we demonstrated the complex association of lung perfusion with cardiac output and hemodynamics. Although absolute global and regional lung perfusion were determined mainly by cardiac output, regional perfusion distribution was affected by hemodynamic abnormalities, predominantly elevated left ventricular end-diastolic pressure and resultant increases in mean pulmonary artery pressure. Among those with significantly elevated left ventricular end-diastolic pressure, there was near equalization of lung perfusion from anterior to posterior lung fields in the supine position, abolishing the normal gravitational lung perfusion gradient. Multivariate regression analysis suggested that mean pulmonary artery pressure was the most important determinant of altered perfusion distribution among all the hemodynamic indices, underscoring the importance of the pulmonary arterial response to left ventricular end-diastolic pressure and not simply left ventricular end-diastolic pressure alone in the pathophysiology of left heart failure. Our findings underscore the complexity of heart-lung interactions in determining pulmonary hemodynamics in left heart failure.

Conclusions—Increased left ventricular filling pressure and the resultant increase in pulmonary arterial pressure are associated with disruption of the normal gravitational lung perfusion gradient. Our findings underscore the complexity of heart-lung interaction in determining pulmonary hemodynamics in left heart failure.

First Serial Assessment at 6 Months and 2 Years of the Second Generation of Absorb Everolimus-Eluting Bioresorbable Vascular Scaffold: A Multi-Imaging Modality Study

Summary—The first generation of fully bioresorbable everolimus-eluting scaffold exhibited late recoil at 6 months, with a late lumen loss intermediate between bare-metal stent and drug-eluting stent. The second generation of everolimus-eluting bioresorbable vascular scaffold, with changes in the design platform and manufacturing process, fully remediated this mechanical deficiency, and the scaffold area was found to be unchanged at 6 months by optical coherence tomography (OCT). At 12 month follow-up, analysis by OCT and ultrasound confirmed the persistence of an unchanged scaffold area without substantial loss in lumen area, whereas vasomotion became again detectable. From 6 to 24 months, late luminal loss increased from 0.16±0.18 to 0.27±0.20 mm on quantitative coronary angiography, with an increase in neointima of 0.68±0.43 mm² on OCT and 0.17±0.26 mm² on intravascular ultrasound. Struts still recognizable on OCT at 2 years showed 99% of neointimal coverage with optical and ultrasonic signs of bioresorption accompanied by increase in mean scaffold area compared with baseline (0.54±1.09 mm² on intravascular ultrasound, P=0.003 and 0.77±1.33 mm² on OCT, P=0.016). The increase in scaffold area may be a prelude to the late lumen enlargement seen with the first generation. Two-year major adverse cardiac event rate was 6.8% without any scaffold thrombosis.

Conclusions—This serial analysis of the second generation of the everolimus-eluting bioresorbable vascular scaffold confirmed, at medium term, the safety and efficacy of the new device.

Quantifying Pulmonary Regurgitation and Right Ventricular Function in Surgically Repaired Tetralogy of Fallot: A Comparative Analysis of Echocardiography and MRI

Summary—Patients with tetralogy of Fallot represent a growing population of congenital heart disease. Clinicians seek to quantify pulmonary regurgitation and right ventricular function over successive appointments in patients with TOF to identify those in need of intervention or pulmonary valve replacement. To date, although echocardiography is the most valuable tool, it has fallen short in consistent quantification of pulmonary regurgitation and right ventricular function. In this study, we describe an echocardiographic tool with which to assess pulmonary regurgitation in tetralogy of Fallot that only modestly correlates with measurements made by cardiac magnetic resonance. In addition, echocardiographic measures of right ventricular function showed limited performance when compared with those derived from cardiac magnetic resonance. Although these echo measures still fall short of the reliability set by CMR for decision making, these results help motivate ongoing investigative efforts to improve echocardiographic assessment of the postoperative patient with tetralogy of Fallot.

Conclusions—This study suggests that the diastolic and systolic time-velocity integrals ratio may make a modest contribution to the overall assessment of pulmonary regurgitation (PR) in patients with repaired tetralogy of Fallot and warrants further investigation. However, echocardiography continues to have a limited ability to quantify PR and RV function as compared with CMR.

Prognostic Impact of Hyperglycemia in Nondiabetic and Diabetic Patients With ST-Elevation Myocardial Infarction: Insights From Contrast-Enhanced MRI

Summary—Previous studies have suggested that hyperglycemia on admission is a risk factor for increased mortality in patients with acute ST-elevation myocardial infarction (STEMI). However, data regarding the relationship between hyperglycemia and myocardial damage in STEMI are scarce. This largest cardiac magnetic resonance study to date evaluating the relationship of diabetes mellitus status and elevated glucose levels on admission on myocardial damage in STEMI patients reperfused by primary percutaneous coronary intervention has 2 essential findings: (1) STEMI patients with preexisting diabetes mellitus are at greater risk for major adverse cardiovascular events despite having similar infarct sizes and extent of reperfusion injury than patients without known diabetes mellitus. (2) Elevated glucose levels on admission are associated with greater myocardial damage (larger infarcts, more pronounced reperfusion injury, left ventricular dysfunction) and an increased risk of clinical events at long-term
Myocardial Perfusion Reserve Assessed by T2-Prepared Steady-State Free Precession Blood Oxygen Level–Dependent MRI in Comparison to Fractional Flow Reserve

Summary—T2-prepared steady-state free precession blood oxygen level–dependent cardiac MRI is based on different magnetic properties of oxyhemoglobin and deoxyhemoglobin. This results in a relative decrease of T2* and T2 relaxation time in ischemic and thus lower oxygenated myocardium. In our study, we demonstrate that this effect correlates to invasively measured fractional flow reserve in the respective coronary artery. Our described approach warrants consideration as an alternative to contrast–enhanced perfusion studies, especially in patients with severe renal failure in which the use of exogenous contrast agents should be avoided.

Conclusions—Blood oxygen level–dependent imaging reliably detects hemodynamic significant coronary artery disease and is, thus, an alternative to contrast–enhanced perfusion studies.

Acute Pulmonary Vein Isolation Is Achieved by a Combination of Reversible and Irreversible Atrial Injury After Catheter Ablation: Evidence From MRI

Summary—Single ablative therapy for paroxysmal atrial fibrillation has moderate success, and many patients present with recurrent arrhythmia. We proposed that the structure of the radiofrequency lesion applied during ablation is important in determining recurrences. The nature of the radiofrequency lesion was studied using MRI with gadolinium-enhanced imaging and high-signal T2-weighted imaging. Twenty-five patients underwent MRI scans for delayed enhancement (DE) and T2 at 3 time points: before ablation, within 24 hours, and 6 months after ablation. Patients were divided into those with (n=11) and without (n=14) recurrent arrhythmia. Levels of DE+T2 were low in preprocedural scans but rose dramatically immediately after the procedure. Acute DE was greater in patients without recurrences compared with those with recurrences. Conversely, T2 levels were lower in patients without recurrences and higher in those with recurrences. On the late scans, T2 reduced to baseline. DE, however, remained and was greater in patients without recurrences. We, therefore, propose that acute radiofrequency ablation injury is composed of 2 types of tissue damage. DE infers largely necrotic tissue injury, which lasts longer and causes persistent conduction block. T2 is a transitory phenomenon coexisting with DE, causing acute conduction block. We propose that resolution of the T2 signal is associated with recurrences of pulmonary vein connection and, therefore, arrhythmia recurrences. Modifications in our ablative techniques to achieve more DE at the acute ablation would potentially be important in conferring a better ablation outcome. These data potentially provide a mechanistic explanation as to why pulmonary veins reconnect after wide area circumferential ablation.

Conclusions—The higher T2 signal on acute scans and greater decline in DE on chronic imaging in patients with recurrences suggest that they have more reversible tissue injury, providing a potential mechanism for pulmonary vein reconnection, resulting in arrhythmia recurrence.

Patients With Syndrome X Have Normal Transmural Myocardial Perfusion and Oxygenation: A 3-T Cardiovascular MRI Study

Summary—The pathophysiology of chest pain in patients with syndrome X (chest pain, abnormal exercise treadmill test, normal coronary angiogram) remains controversial. Previous studies using nuclear techniques or cardiovascular magnetic resonance to assess myocardial perfusion have shown conflicting results. Other studies suggest that abnormal pain perception is a central component of the pathophysiology of this enigmatic syndrome. We used cardiovascular magnetic resonance to quantitatively assess regional myocardial blood flow and oxygenation during vasodilatory stress (adenosine) in patients with syndrome X and healthy controls. The findings indicate that patients with syndrome X have no evidence of transmural hyperperfusion or deoxygenation but a greater incidence of chest pain during vasodilatory stress compared with controls. Studies using high-resolution perfusion cardiovascular magnetic resonance (<1-mm in-plane resolution) are needed to further investigate subendocardial and subepicardial perfusion in these patients.

Conclusions—Patients with syndrome X show greater sensitivity to chest pain compared with controls but no evidence of deoxygenation or hyperperfusion during vasodilatory stress.

Sex Differences in Myocardial Salvage and Clinical Outcome in Patients With Acute Reperfused ST-Elevation Myocardial Infarction: Advances in Cardiovascular Imaging

Summary—Studies have highlighted important sex differences in the pathophysiology, presentation, treatment, and outcome of ischemic heart disease. It has been also speculated that the efficacy (myocardial salvage) of primary percutaneous coronary intervention (PCI) in high-risk patients with ST-elevation myocardial infarction (STEMI) appears to be sex-dependent. Whether sex disparities in clinical care and death after STEMI are still present in the current PCI era remains a matter of constant debate and has important clinical implications. In this study, we analyzed the relationship between sex and outcomes as well as sex and myocardial salvage in an unselected and consecutive population of patients with STEMI exclusively reperfused by primary PCI. Our study is the first using cardiac MRI for assessment of sex-specific reperfusion therapy efficacy. We observed no sex-associated differences in myocardial salvage and reperfusion injury. Although women STEMI patients had higher unadjusted in-hospital and 30-day mortality rates than did men, multivariate analysis revealed that these differences were likely because of disparities in baseline risk. Thus, our data highlight that sex by itself, in the current PCI era, does not independently predict....
Prediction of Arrhythmic Events in Ischemic and Dilated Cardiomyopathy Patients Referred for Implantable Cardiac Defibrillator: Evaluation of Multiple Scar Quantification Measures for Late Gadolinium Enhancement MRI

Summary—Scar signal quantification on late gadolinium enhancement cardiac magnetic resonance has been proposed to have use for the prediction of arrhythmic events in patients with ischemic cardiomyopathy eligible for implantable cardiac defibrillators (ICD). For this noninvasive tool to have widespread clinical value it would ideally be applicable to ischemic and nonischemic referral populations, predict highly relevant clinical outcomes (such as appropriate ICD therapy, resuscitated cardiac arrest, and sudden cardiac death), and demonstrate associations independent of other validated risk markers, such as ejection fraction. In the current study of 124 consecutively referred patients, we demonstrate that total scar burden by signal quantification is a reproducible imaging biomarker that appears to meet these desired criteria. While being sensitive to distinct thresholds for ischemic and nonischemic subcohorts, the quantification of total scar burden identifies patients at an elevated risk of future arrhythmic events. These findings support a need for the expanded investigation of this imaging modality to identify patients most likely to benefit from ICD implantation.

Conclusions—Myocardial scar quantification by Late Gadolinium Enhancement (LGE)-CMR predicts arrhythmic events in patients being evaluated for ICD eligibility irrespective of cardiomyopathy etiology.26

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