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iREVIEWS

STATE-OF-THE-ART PAPER

Interventional Cardiovascular Magnetic Resonance Imaging

A New Opportunity for Image-Guided Interventions

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Cardiovascular magnetic resonance (CMR) combines excellent soft-tissue contrast, multiplanar views, and dynamic imaging of cardiac function without ionizing radiation exposure. Interventional cardiovascular magnetic resonance (iCMR) leverages these features to enhance conventional interventional procedures or to enable novel ones. Although still awaiting clinical deployment, this young field has tremendous potential. We survey promising clinical applications for iCMR. Next, we discuss the technologies that allow CMR-guided interventions and, finally, what still needs to be done to bring them to the clinic. (J Am Coll Cardiol Img 2009;2:1321–31) © 2009 by the American College of Cardiology Foundation

Minimally invasive and catheter-based therapies are targeting increasingly complex pathologies. This agenda requires better procedural image guidance (Table 1). Interventional cardiovascular magnetic resonance (iCMR) proposes to use the superb tissue imaging afforded by cardiovascular magnetic resonance (CMR) as a surrogate for direct surgical visualization. By providing multiple views and real-time functional imaging without ionizing radiation exposure, CMR could guide traditional interventional procedures and enable novel ones. We provide a brief overview of cardiovascular procedures that could benefit from real-time CMR guidance, followed by technical advances helping to move toward clinical testing.

Clinical Targets

Catheter-based endovascular interventions. CMR visualizes vessel wall and lumen without exogenous contrast. Interest in atherosclerosis imaging fueled much of the early work in intravascular CMR. Building on internal receiver coils for high-resolution intracardiac ^{31}P nuclear magnetic resonance (1), local endovascular coils were developed to characterize arterial wall composition with improved signal-to-noise ratio and resolution (2,3). Flow and motion, however, remain significant challenges to high-resolution magnetic resonance (MR) vessel images with realistic scan times in vivo.

Vascular interventions such as angioplasty and stenting under CMR could reduce radiation and iodinated contrast exposure compared with X-ray procedures. The use of CMR may also allow image-based monitoring for serious complications such as vessel wall dissection or perforation (4,5). Newer stent alloys (including Nitinol and nickel-cobalt-chromium) are more compatible with CMR than older stainless-steel materials. Despite a dearth of other commercial devices suitable for interventional CMR, numerous endovascular procedures have been demonstrated in pre-clinical and early clinical studies. Although coronary catheteriza-

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tion and stenting have been performed under CMR guidance in healthy animals (6–8), we caution that clinical CMR lacks sufficient spatial or temporal resolution to guide meaningful clinical coronary interventional procedures.

Larger peripheral vessels such as aorta and iliac arteries are more attractive targets for CMR-guided procedures. Simple iliac angioplasty and stenting was performed in human feasibility studies by Manke et al. (9), albeit with limited imaging guidance. Renal artery stenting has been conducted solely under CMR in an animal renal artery stenosis (10). CMR-directed tube endografts repaired porcine abdominal aortic aneurysms (11) and thoracic aortic dissection after distinguishing true and false lumens (12). Aortic coarctation stenting with CMR guidance also has been explored (5). The authors of a clinical pilot study (13) successfully demonstrated CMR-assisted angioplasty for aortic coarctation in combination with X-ray.

ABBREVIATIONS AND ACRONYMS

3D = 3-dimensional

CMR = cardiovascular magnetic resonance

EP = electrophysiology

iCMR = interventional cardiovascular magnetic resonance

RF = radiofrequency

VSD = ventricular septal defect

XFM = X-ray–fused with magnetic resonance imaging

Completely blocked vessel segments (chronic total occlusions) are virtually invisible in X-ray angiography where contrast cannot enter the obstructed lumen. The use of CMR can help to depict the mural contour of the occluded vessel and can help avoid perforation. Recanalization of an animal model carotid chronic total occlusion with the use of a custom active CMR device was significantly more successful than X-ray-guided alternatives (14). Newer devices are being developed that clearly indicate the device position during recanalization (15).

Moving beyond the vessels: extra-anatomic bypass, structural heart, and biological therapies. The use of CMR could allow catheter-based procedures to escape the traditional confines of vascular lumens. Extra-anatomic bypass, directly connecting two otherwise-unconnected vascular structures, might be enabled without surgery because of CMR guidance. In transjugular intrahepatic portosystemic shunt procedures, CMR helped reduce the number of needle passes needed to connect the hepatic to portal vein within the liver (16). Mesocaval puncture is an alternative portocaval trajectory enabled by CMR and custom-designed needle devices (17). A nonsurgical Blalock-Taussig subclavian-pulmonary shunt is a tantalizing potential application of this technology.

Structural heart disease interventions may benefit from the use of CMR in visualizing critical anatomy. CMR has guided-needle (18) and laser (19) atrial septal puncture and delivery of Nitinol closure devices for atrial septal defects (20–22) in swine. The use of CMR has enhanced positioning (with regard to myocardial fibrous skeleton and coronary arteries) and monitoring of transcatheter (23) and surgical transapical (24) (Fig. 1) aortic valve implants in swine with immediate evaluation of valve performance and flow. Hybrid imaging guidance for valve placement is also under development with the use of an adjacent "CMR-friendly" X-ray fluoroscope at the edge of the magnet (25).

With the development of novel biologic treatments, including local small molecule, gene, or cellular agents, CMR could play an important role in testing, delivering, and monitoring these therapies. The use of CMR provides enhanced catheter-based endomyocardial targeting and interactive imaging of local cell or drug accumulation and dispersion compared with X-ray or electroanatomic imaging (26,27). Several groups (28–31) have demonstrated successful delivery or tracking of cell and gene products to myocardial targets in animals by using CMR.

Pediatrics. Pediatric patients stand to gain much from CMR-guided interventional procedures. Children with congenital heart disease often require multiple catheterizations to assess physiological parameters and for treatment that might avoid or delay open-heart surgery. Each interventional procedure, however, is offset by the risk for mechanical complications and possible long-term consequences from X-ray exposure. Children are especially susceptible to radiation injury, and pediatric interventions often are protracted, contributing further to the risk of chromosomal damage and malignancy (32). For medical staff, occupational X-ray exposure risks cancer and cataracts (33), whereas protective lead garments risk chronic orthopedic injury (34).

Razavi et al. (35) brought real-time CMR into the clinic. They guided diagnostic catheterizations and electrophysiological procedures in children and adults with congenital heart disease by using a combined MR/X-ray suite. The use of CMR-guided catheterization has also enhanced the assessment of total or split pulmonary vascular resistance in patients (36,37). Beyond invasive diagnostics, CMR might enhance treatment of structural pathology in children and adults with congenital heart disease. Interventions for structural abnormalities such as ventricular septal defect could benefit from improved visualization of the septal defect and close procedural monitoring. Pre-clinical CMR-guided pulmonary artery and valve stenting (38) suggests

Table 1. Comparison of Imaging Modalities for Real-Time Procedural Guidance

	Real-Time CMR	X-Ray	Echocardiography (Surface or Intracavitary)	Computed Tomography
Ionizing radiation	No	Yes	No	Yes
Structures depicted	Hydrogen (or other magnetic nuclei) containing-tissues	X-ray attenuating (iodinated contrast-filled structures, bone)	Echo dense and echo reflective	Bone and soft tissue
Typical spatial resolution	1.5 × 2 × 5 mm*	<0.4 mm	0.6–1 mm	1–2 mm isotropic
Typical frame rate	5–10 frames/s*	15–30 frames/s	20–30 frames/s	2–4 frames/s
Advantages	No ionizing radiation Multiplanar views Soft-tissue contrast Novel contrast mechanisms	Widely deployed Numerous devices available High temporal and spatial resolution	Portable Lower cost High SNR Flow and motion measurements	Multislice
Disadvantages	High magnetic field limits devices Low SNR Potential RF heating Gadolinium contrast	Radiation exposure Limited soft tissue discrimination Projection-only (2D) views Iodinated radiocontrast	Limited acoustic windows Air and device shadowing Limited "context" (field of view)	Excessive radiation doses Iodinated contrast

*Note the frame rate and spatial resolution given for CMR are arbitrary and represent a typical compromise between spatial and temporal resolution at 1.5-T using parallel imaging with an acceleration factor of 2.
CMR = cardiovascular magnetic resonance; RF = radiofrequency; SNR = signal-to-noise ratio.

percutaneous pulmonary valve replacement (39) might be feasible under CMR. As mentioned previously, CMR may enable percutaneous creation and closure of pulmonary-systemic shunts.

Electrophysiology (EP). Interventional CMR proposes one-stop visualization of cardiac surfaces being mapped, monitoring of ablation, and assessment of ablation lesions. Compared with ablation under direct surgical exposure, conventional catheter ablations of atrial fibrillation or ventricular-tachycardia are lengthy and complex, in part because of inadequate targeting and visualization of ablation lesions. The use of CMR offers value beyond creating baseline roadmaps now widely imported into electroanatomic mapping systems (40). Investigators have begun to correlate ablation lesions to successful rhythm therapy (41,42). MR-compatible cardiac monitoring and ablation systems have enabled simple CMR-guided EP procedures (4,43–45). Figure 2 displays a sample CMR-guided EP mapping and recording study (45). Recently, Nazarian et al. (46) at Johns Hopkins demonstrated

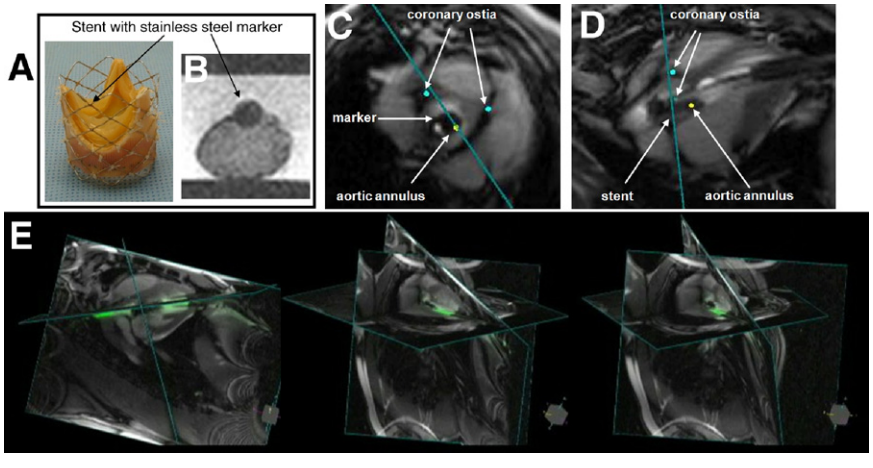

Figure 1. CMR-Guided Transapical Aortic Valve Replacement

(A) Bioprosthesis mounted on a platinum iridium stent with a stainless-steel marker welded on the side of the stent between the commissures. **(B)** The marker is visible as a dark signal in the cardiovascular magnetic resonance (CMR) and indicates the orientation of the prosthesis. Short-axis view and long-axis view of the implanted prosthesis in a pig under real-time CMR are shown in **C** and **D**, respectively. **Blue dots** are digital markers indicating the coronary ostia whereas the **yellow dot** shows aortic annulus location. **(E)** Three-dimensional rendering snapshots show multiple image planes displayed at their relative 3-dimensional position. Images courtesy of Ming Li, PhD, and Keith A. Horvath, MD, Cardiothoracic Surgery Research Program, National Heart, Lung, and Blood Institute.

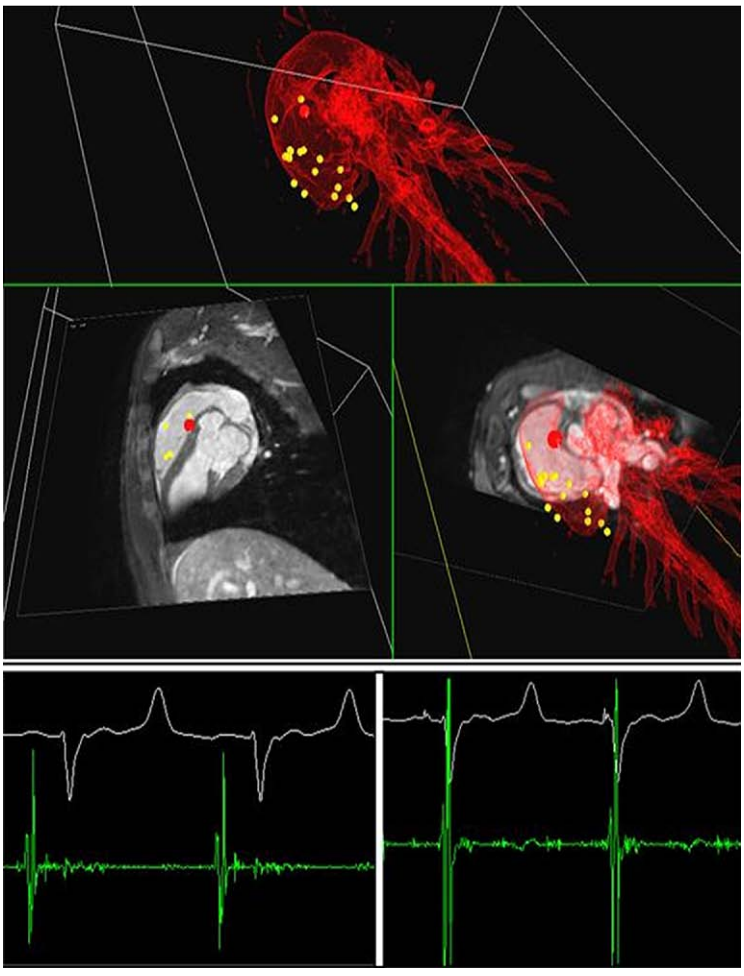

Figure 2. Electrophysiological Cardiac Mapping Under Real-Time CMR Guidance

(Top) Roadmap-based real-time 3-dimensional visualization of the catheter position during recording (**red dot**) on the magnetic resonance-electrophysiological workstation. The **yellow dots** in the 3-dimensional rendering of the heart indicate previous mapping positions. **(Bottom)** In-bore electrophysiological recordings at 2 selected positions showing an atrial signal **(left)** and a ventricular signal **(right)**. Graphic courtesy of Steffen Weiss, PhD, Philips Healthcare.

the feasibility of real-time CMR-guided EP mapping in 2 patients.

Multimodality image guidance. X-ray combined with magnetic resonance imaging, referred to as coregistration or XFM (X-ray fused with magnetic resonance imaging), overlays previously acquired MR images to enhance otherwise-difficult X-ray fluoroscopy procedures. These XFM procedures can benefit from the wide armamentarium of X-ray-compatible catheter equipment, along with additional 3-dimensional (3D) information about target vascular structures afforded by previous CMR. This multimodality approach has been used clinically in complex X-ray procedures such as biopsy of the myocardial free wall (47). The use of XFM also enabled precise endomyocardial injections (48) and a complex repair of membranous ventricular septal defects with significantly decreased fluoroscopy times in animal studies (49). Clinical EP studies already combine CMR roadmaps in commercial electroanatomic mapping systems (40).

In XFM, 3D contours of cardiovascular structures from CMR are overlaid on live X-ray (Fig. 3). Views update as the C-arm or table position changes. X-ray and CMR can be coregistered by the use of a shared table space (50), but patient movement causes misregistration. External fiducial marker beads on the patient can align MR and X-ray acquisitions even after patients move (47,51). Static roadmaps also become inaccurate from respiratory and cardiac motion, which can be corrected by the use of more sophisticated techniques (52). Cath-

eter position can be computed from 2 X-ray projections and back-displayed on a 3D MR roadmap.

Interventional MRI in other clinical disciplines. Several other clinical disciplines have embraced interventional MRI to guide critical procedures. Most enjoy targets that are relatively accessible, immobile, or require short, straight-needle devices. Neurosurgeons routinely use pre-procedural MRI with stereotactic frames for biopsies and resections; many conduct intraoperative MRI to guide, for example, tumor resection margins (53) or placement of deep-brain stimulation electrodes (54). Biopsy is also conducted under MRI for suspected liver, breast, and prostate malignancies (55). Tumor cryo- and radiofrequency ablation benefit from MRI guidance, which creates real-time temperature maps of target tissue (56). The use of MRI enhances orthopedic biopsies, injections, and other therapies as well (57). Many of these applications have fueled development of local imaging coils and MR-compatible manipulators and robotics (58).

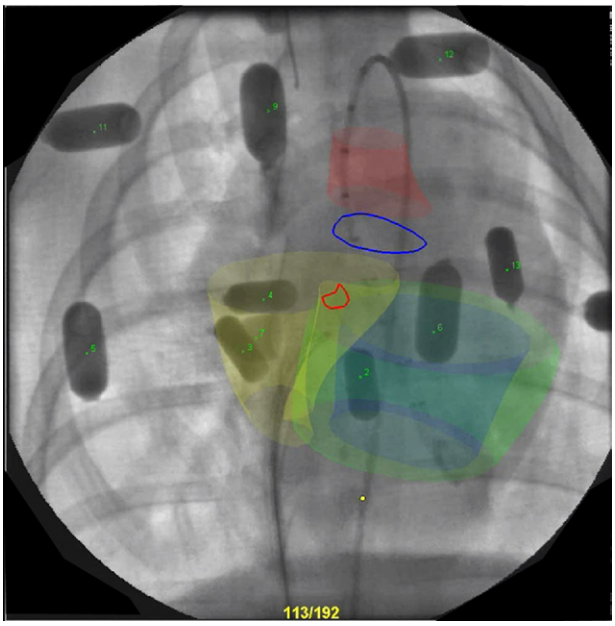

Figure 3. X-Ray Fused With MRI

Representative X-ray fused with magnetic resonance imaging (MRI) display with contours from cardiovascular magnetic resonance (CMR) overlaid on live X-ray. Aorta **(red)**, right ventricle **(yellow)**, left endocardial **(blue)**, and epicardial **(green)** surfaces from CMR shown in 3 dimensions with aortic annulus and ventricular septal defect locations outlined in **blue** and **red**, respectively. Multimodality external fiducial markers also are seen numbered.

Technology Behind iCMR

In this section we review advances in scanner design, imaging, and catheter devices that enable iCMR. We also discuss the remaining hurdles to clinical use.

Interventional suite and scanner selection. Short, wide, closed-bore 1.5- and 3.0-T scanners are now available. These systems provide superior image quality than earlier lower-field open magnets. Wide-bore scanners also allow satisfactory transfemoral access to patients for interventional procedures compared with earlier closed-bore machines. The use of 3.0-T offers the potential to increase resolution and signal-to-noise ratio, but 3.0-T has been challenging to use with workhorse imaging techniques considered essential at 1.5-T.

Most research sites colocalize or combine MRI and X-ray angiography equipment to allow combined procedures and angiographic bailout (Fig. 4). Transfer tables or mobile MRI units (59) permit elective intermodality transfer or emergency evacuation. In a properly shielded room, both systems also run independently as MRI scanner and X-ray interventional labs. Fiberoptic or pneumatic headset systems with noise cancellation allow staff and patients to communicate despite loud acoustic MRI noise.

Real-time CMR. Steady-state free precession (often referred to as TrueFISP, FIESTA, or FFE) provides excellent blood and myocardial contrast in electrocardiogram-gated (nonreal-time) acquisitions. Steady-state free precession is now widely available in real time and has become the "workhorse" pulse sequence for interventional procedures. That said, it is no simple feat to acquire, reconstruct via computer, and display CMR images in less than a quarter second. Newer parallel techniques that use large receiver coil arrays and advanced computational techniques (60–62) allow even-faster scanning. Coupled with high-performance computing multiple-processor systems, real-time CMR is now available with image updates at 10 frames/s. Other phenomena, such as blood flow and myocardial tags, also can be imaged in real time. Although these MR images have a relatively small pixel matrix compared with X-ray (192 × 128 vs. 1,024 × 1,024), they are comparably rich in information because of extra soft-tissue detail (See Table 1).

Real-time MRI interfaces reconstruct and display images geared for interventional procedure guidance (63,64). Multiple concurrent slices can be displayed in 3D to indicate their relative location and orientation (Fig. 5A). Where real-time MRI resolution is inadequate, high-resolution previous

Figure 4. Interventional CMR Suite

An interventional cardiovascular magnetic resonance (CMR) suite showing adjacent and interoperable magnetic resonance imaging scanner and X-ray angiography labs. A docking gurney allows rapid intermodality transfer. Courtesy of Alexander J. Dick, MD, Sunnybrook Health Sciences Centre, Toronto.

cine or MR angiography roadmaps can also be incorporated to complement the live imaging (Figs. 5B and 5C). Real-time user interfaces (Fig. 6) are now available from commercial system vendors (65). Foot pedals and related remote controls afford the in-room operator some control over scan planes, but interventional MRI usually requires a dedicated scan operator in addition to the interventionist.

When using 2-dimensional imaging techniques, it can be difficult to locate a structure or device that moves out of the selected scan plane. X-ray operators are accustomed to projection views where the entire anatomy or device is visible in the field of view despite its position in the ("through-plane") third dimension. Independent coloring of multiple active device channels and device-only projection views help overcome this problem (63). Alternatively, computer algorithms can locate and even automatically reposition the scan plane to show the entire active MR device in 3 dimensions (66–68). Comparable techniques have been developed to track the position of passive devices (69).

Interventional devices. The same mechanisms that provide unique image contrast during CMR also make most X-ray catheters either invisible or unacceptable for use during iCMR procedures. Metallic cores or braiding that impart catheter pushability and torquability cause imaging artifacts and obscure entire organs. Polymer-only catheters are not visible unless modified and often lack requisite mechanical performance. Conspicuous and safe CMR catheter devices are not generally commercially available but represent an active area of research and development. Interventional CMR devices typically are classified by the mechanism they are visualized in imaging and connection to scanner hardware: passive, semiactive, and active.

Passive devices rely on material properties for visibility during CMR. Material magnetic susceptibility, or how it responds to a magnetic field, can cause inhomogeneities in the main magnetic field that result in signal voids (negative contrast or dark spots) on images. Positive contrast (bright spots) can be generated by the use of paramagnetic T1 shortening contrast agents. Many early passive devices used polymer catheters with ferromagnetic (70) or paramagnetic coatings or rings (71,72). Other approaches include filling catheter balloons with CO_2 (Fig. 7A) (73) or more novel contrast agents such as ^{19}F (74) and hyperpolarized ^{13}C (75) detected with multispectral CMR. Off-resonance imaging techniques (76,77) improve the specificity of the device-related signal but usually sacrifice visibility of surrounding anatomy. Recently, several groups (78,79) have developed sophisticated nonmetallic guidewires that mimic the mechanical properties of metallic X-ray guidewires. They are conspicuous because of small metal (susceptibility) markers. An example of a passive device visualized through magnetic susceptibility effects is shown in Figure 8, where a passive guidewire navigates an iliac artery. Passive devices avoid many of the radiofrequency (RF) safety concerns discussed in the "Ensuring iCMR Safety" section and often are simpler to manufacture. However, they remain difficult to discern from background tissue in vivo, especially within curved vascular structures.

Active devices for interventional CMR incorporate small coils or antennae on independent channels connected to the scanner to track (80) or display the device. "Tracking" requires special CMR pulse sequences to

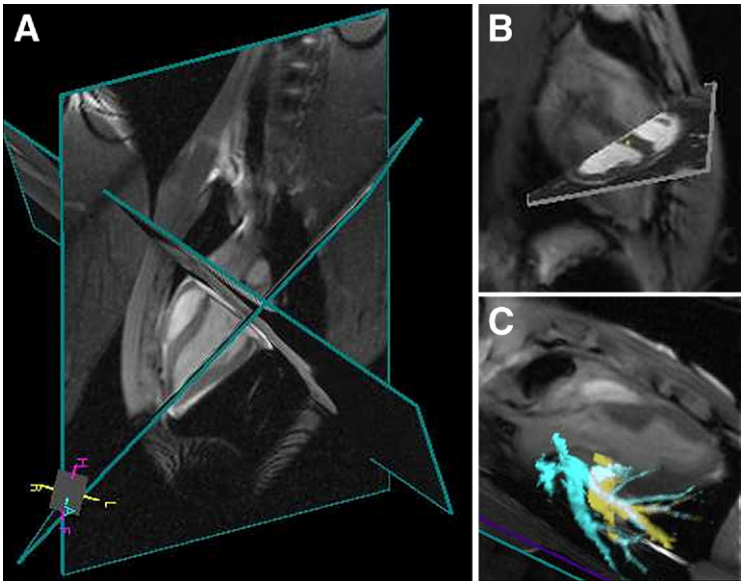

Figure 5. Real-Time Cardiac MR

Multiplanar real-time cardiac imaging at 4 to 5 frames/s **(A)** with pre-acquired static cardiac magnetic resonance (MR) image **(B)** and pulmonary vessel 3-dimensional MR angiography **(C)** roadmaps.

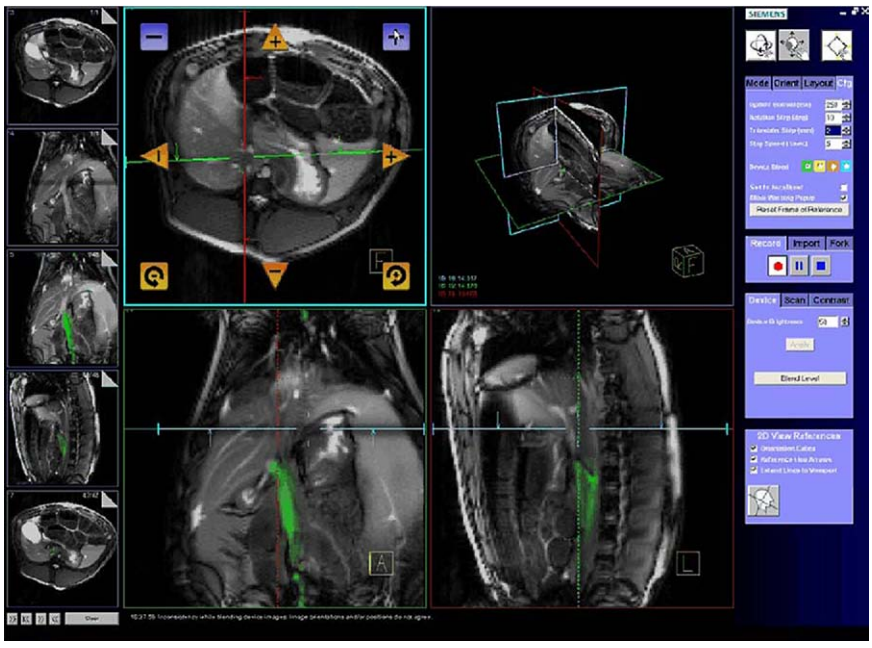

Figure 6. Real-Time MRI User Interface Showing MR-Guided Delivery and Biopsy of Encapsulated Human Islet Cells in a Pig

Example of a real-time magnetic resonance imaging (MRI) user interface from Siemens. Similar interfaces are available for Philips and GE systems. Features include scan plane manipulation, independent device channel coloring, 3-dimensional viewing window, static image roadmaps, and quick access to select slice orientations. Figure courtesy of Christine H. Lorenz, PhD, Siemens Corporate Research, Inc., and Aravind Arepally, MD, Johns Hopkins Medical Institutions, Baltimore, Maryland.

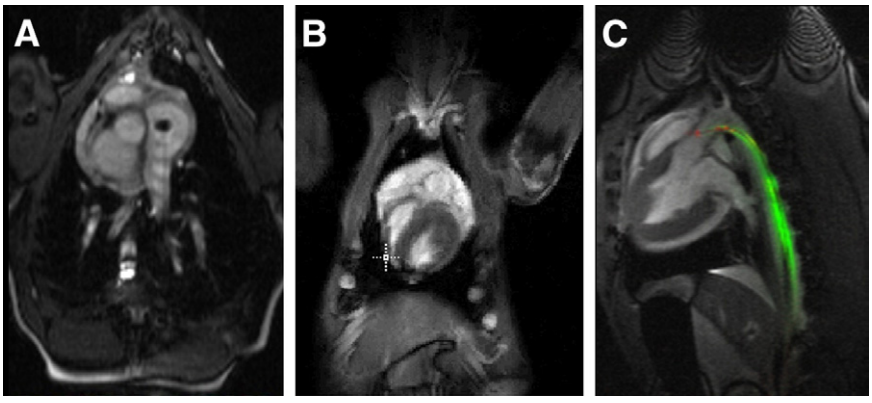

Figure 7. Interventional CMR Devices

Three representative approaches to catheters designed to be tracked using cardiovascular magnetic resonance (CMR). **(A)** Passive nonbraided balloon catheter filled with CO_2 in a right atrium. **(B)** Active tracking catheter in the right heart. Image courtesy of Michael Bock, PhD, German Cancer Research Center (DKFZ), Heidelberg, Germany. **(C)** Two-channel active guidewire in the aorta approaching the left heart.

locate the tracking coil in 3D space with the computer-synthesized device position overlaid onto images (Fig. 7B). Active device "imaging" or "profiling" allows a device to be depicted uniquely (for example, based on color) on CMR images acquired in real time. An example is the active guidewire in Figure 7C. Many of the early coil designs for atheroimaging evolved into active catheters and guidewires devices having loop and loopless (81) antenna configurations. It is challenging to incorporate requisite electrical and mechanical components in appropriately sized designs that simultaneously satisfy operators' functional expectations. Clinical-grade active guidewires and catheters are nearing clinical reality (82), but thorough performance and safety evaluation remains an important step.

Semiactive devices typically contain circuit elements such as inductively coupled markers. These do not require long transmission lines (connecting electrical cables) and need not be connected directly to the scanner but may be more visible than passive devices. Through mutual inductance the signal around the inductively coupled coil can be detected by surface

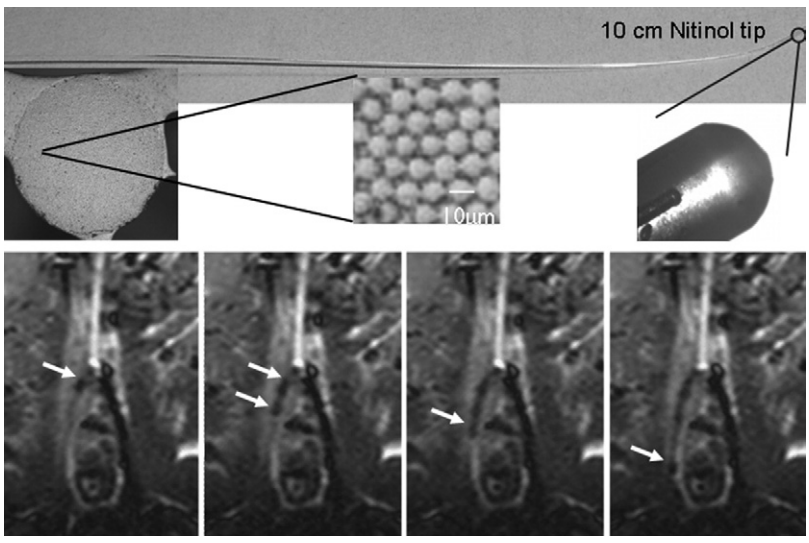

Figure 8. Iliac Artery Navigation Using a Passive Guidewire

(Top) Polymer guidewire with a Nitinol tip. **(Bottom)** Magnetic resonance-guided probing of the contralateral iliac artery with the guidewire **(arrows)** and a catheter. Susceptibility artifacts in cardiovascular magnetic resonance (CMR) images arise from the iron doped guidewire, which is also visible under fluoroscopy. These artifacts partially obscure the target tissue. Images courtesy of Gabriele A. Krombach, MD, Department of Diagnostic Radiology, University Hospital Aachen, Aachen, Germany.

receiver coils. Inductively coupled markers can be incorporated on the end of catheters (83,84), but device visualization is then limited to this segment. Further optical tuning (85,86) or signal separation (87) techniques may be required to clearly distinguish these devices from background imaging.

Ensuring iCMR safety. MRI uses 3 significant electromagnetic fields. The static, permanent magnetic field, B0, can exert tremendous force and torque on ferromagnetic objects, drawing them into the bore. Consequently, instruments, monitoring equipment, and other implements used near MRI scanners must be nonmagnetic or properly labeled and secured to avoid creating dangerous projectiles in the room. Time-varying magnetic field gradients used to create images may cause peripheral nerve stimulation, which limits the slew rate and therefore imaging speed. The vibration of these gradient coils creates the acoustic noise that can be mitigated by the use of hearing protection and MR-compatible communication systems. Finally, the pulsed electromagnetic RF field, B1, used to energize hydrogen spins during imaging, produces a significant heating risk. Long conductors such as cables connecting local receiver coils, electrocardiogram leads, and active CMR devices, when exposed to the changing magnetic fields, can develop induced currents and heat due to resistive losses. More important, coupling with the electrical field component of B1 can store electrical energy along the device that creates heat near the device tips (88). Several approaches have been explored to minimize active device heating, including detuning devices during transmission when RF energy is highest, and the use of RF chokes (89) or transformers (90) in transmission lines to alter their electrical length. Newer optical transmission lines (91) or wireless coils may provide safer alternatives in the future to relay device MR signals to the scanner.

Conclusions: The Future of iCMR

Pre-clinical demonstrations of iCMR have been enticing. The question remains how to bring this technology into the clinic. The requisite imaging capabilities for iCMR are available on commercial MRI systems. Compatible clinical-grade catheter devices remain largely unavailable absent much commercial investment. Academic centers are now independently developing clinical-grade active and passive catheter tools. Although the pace of development has been slow, future opportunities remain rich.

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