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EDITORIAL COMMENT

Cardiac Electrophysiology Procedures, Known Unknowns, and Unknown Unknowns

The Potential of Magnetic Resonance Guidance*

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Surgeons have the benefit of tactile and visual information for identification of diseased substrates and for measurement of the effect of their procedures. In contrast, cardiac electrophysiologists must use indirect measures for directing catheters to tissues of interest and for measurement of tissue modification. Fluoroscopy provides familiar landmarks and is readily available in all electrophysiology laboratories. It also provides projection imaging of the entire catheter, highlighting such features as coplanarity of sheaths and catheters, and catheter buckling, which are invaluable for optimizing tissue contact and preventing complications. However, fluoroscopy lacks soft tissue resolution and provides no information regarding tissue characteristics before or after ablation. Additionally, fluoroscopy produces ionizing radiation with potential health effects for patients and laboratory staff.

Analysis of electrograms is an important adjunct of even the simplest anatomic procedures, providing substantial information regarding tissue characteristics and modification after ablation. However, although electrogram features combined with pacing maneuvers are and will remain the cornerstone of electrophysiology, they have limitations for substrate identification. Electrogram features are highly dependent on variables including filtering schemes, electrode size, interelectrode distance, angle of contact, adjacent tissue characteristics, and direction of impulse propagation relative to the electrodes. Contact force and catheter stability can also affect electrogram features. Although force and stability can be quantified with force and position sensing catheters, we are currently unaware of many aspects of the interaction of the catheter tip with its 3-dimensional (3D) environment. Additionally, the depth of substrate and thickness of the intervening and/or adjacent viable myocardium can inhibit the identification of arrhythmia substrates based on electrograms.

Electroanatomic mapping systems have enabled the visualization of electrogram information in the context of 3D anatomy displayed from pre-procedural magnetic resonance (MR), computed tomography, or even positron emission tomography images. The ability to integrate anatomic images with electrogram-based tissue characteristics has provided new avenues for substrate identification. However, registration inaccuracies, and lack of real-time feedback regarding tissue changes during ablation, have limited the generalizability and utility of image integration. The only current imaging modality that can provide limited 2D, but real-time soft tissue information during the procedure is intracardiac echocardiography. The ability to register intracardiac echocardiography images with electroanatomic mapping systems and to track catheter movement relative to the image plane has vastly improved catheter ablation success in the

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setting of complex anatomic substrates. However, intracardiac echocardiography is ultimately limited by the resolution of ultrasound for distinguishing anatomic changes beyond thickness and echodensity.

MR guidance of electrophysiology procedures would eliminate radiation exposure and enhance catheter maneuvering to anatomic regions, such as the pyramidal space, left ventricular summit, and papillary muscles. Real-time MR would allow direct monitoring of surrounding structures, such as the esophagus, pericardial space, and coronary vasculature, thus providing real-time feedback to reduce the chance of complications. Additionally, MR images have been shown to be useful for arrhythmic substrate identification (1–4) and lesion visualization (5–7). However, the use of real-time MR in the complex electrophysiology environment has been hindered by concerns including catheter heating (8), current induction (9), image distortion (10), and electromagnetic interference (11). In a prior study, we demonstrated the feasibility of performing electrophysiology studies via real-time MR guidance in patients (12). Recently, Hilbert et al. (13) published their experience of using real-time MR-guided cavotricuspid isthmus (CTI) ablation in a series of 6 patients.

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In this issue of *JACC: Clinical Electrophysiology*, Chubb et al. (14) present their collaborative progress in developing and testing an MR electrophysiology system for clinical ablation procedures. The studies were performed using a standard 1.5-T clinical MR scanner. To reject electromagnetic interference noise, display intracardiac electrograms, and enable pacing, ablation, and tip temperature monitoring, an electrophysiological recording system specifically manufactured for MR was used (Horizon, Imricor Medical Systems, Burnsville, Minnesota) and coupled to a standard clinical radiofrequency generator (IBI 1500, St. Jude Medical, St. Paul, Minnesota). An ablation catheter developed by the same manufacturer (Vision Ablation Catheter, Imricor Medical Systems) was used to mitigate electromagnetic interference and unwanted heating, catheter movement, and current induction caused by the radiofrequency, static, and gradient magnetic fields of the MR scanner. Importantly, the Imricor catheter incorporates active MR tracking, which enables continuous monitoring of the catheter tip position. The inability to track the catheter tip would significantly diminish procedural safety because of the lack of projection imaging with MR guidance. Finally, an MR-compatible guidance platform for mapping and ablation (Interventional MRI Suite [iSuite], Philips Research, Hamburg, Germany) was incorporated to visualize 3D anatomy and electroanatomic maps.

Ex vivo testing of the ablation catheter revealed minimal MR-induced force and torque, heating, and discrepancy between tip tracking and actual tip locations. The authors then performed preclinical testing in 5 pigs. Using active MR tracking, catheters were successfully placed in the coronary sinus and maneuvered in the right atrium. Irrigated radiofrequency lesions were applied from the superior to the inferior vena cava. Lesion formation was confirmed by baseline and post-ablation activation mapping, MR imaging, and histology. Following the completion of the preclinical testing, the setup was evaluated in 10 clinical participants with typical atrial flutter. All participants completed the protocol without safety issues. Ablation was performed in all but 1 participant where a persistent impedance error prevented radiofrequency power delivery. Of the remaining 9 participants, 7 had CTI ablation completed under MR guidance, whereas 2 required fluoroscopy for completion of the procedure. Of the 7 patients with CTI ablation completed under MR guidance 2 had flutter recurrences. It is important to note that the relatively high rate of flutter recurrence in this study is likely attributable to the anatomic shape of the CTI and the maneuvering range of this early investigational catheter.

The results from Chubb et al. (14), along with those from Hilbert et al, (13), which were also achieved using the Imricor system, demonstrate the feasibility of safe tracking and positioning of catheters and ablation using real-time MR guidance. This represents significant progress toward the realization of real-time MR guidance for electrophysiology procedures. Before this technology becomes generalizable to the entire electrophysiology community, however, several issues must be resolved. First, electrophysiologists must become comfortable with interpretation of multiplanar images obtained in unconventional views, because segmented 3D images that extract other image features would forego the ability to view adjacent structures, one of the greatest attributes of MR guidance. Second, electrophysiologists must become adept at interpreting various MR sequences optimized for evaluation of different features. Third, steerable sheaths, needles, and other electrophysiology equipment must be developed to be MR compatible. Fourth, artifact suppression methodologies must mature. Despite the image improvement with wideband (15) and ultrashort echo time sequences (16), visualization of the anteroapical left ventricle in left pectoral defibrillator recipients is currently suboptimal for procedural guidance.

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This is not only a challenge to MR physicists and radiologists. Device manufacturer efforts to develop MR conditional devices are applauded and will certainly improve the safety of MR-guided electrophysiology procedures. However, device manufacturers should also focus on strategies to mitigate the susceptibility artifact produced by the ferromagnetic material in the high-voltage transformer of defibrillator systems.

There are many known unknowns that will likely be revealed once these challenges are overcome and real-time MR-guided electrophysiology can be used. These include: 1) the catheter tip interaction with its 3D endocardial, epicardial, or intravascular environment and adjacent myocardium; 2) accurate catheter guidance to scar substrates deep to the surface; 3) real-time assessment of lesion depth versus tissue thickness; 4) real-time assessment of tissue edema versus destruction; 5) real-time assessment of lesion proximity to vascular structures of interest, the phrenic nerve, or esophagus; 6) real-time assessment of tissue temperature in the target and nearby tissues; and 7) small sentinel pericardial effusions before hemodynamic instability. The ability to directly visualize these important variables, which are currently recognized, but monitored only through imperfect surrogates, is exciting. But the most stimulating promise of real-time MR guidance is the potential to uncover the unknown unknowns. Will new assays for tissue characterization uncover new arrhythmia substrates for "idiopathic" arrhythmias? Will T_1-relaxation time signatures that associate with critical isthmus sites in fixed reentry be found? Or tissue signals that promote functional reentry? Will 4-dimensional flow, and tissue characteristic or thickness-specific power settings that minimize edema and maximize durable lesions be found? Will new myocardial/vascular features be recognized as critical determinants of immediate or long-term post procedural complications? As electrophysiologists we can start looking forward to the day when we can leave the lead shield on the hanger and use the incredible array of MR sequences for optimal treatment of our patients.

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