Exposing Gaps in Linear Radiofrequency Lesions
Form Before Function

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The termination of atrial fibrillation (AF) by radiofrequency ablation in the left atrium is undeniable evidence that the pathophysiology underlying AF can be ameliorated. The cornerstone of this therapy, pulmonary vein isolation, can be achieved acutely in virtually 100% of patients. Recurrent AF is the bane of this procedure, however, and is most commonly attributed to recovery of pulmonary vein conduction through the ablation lines. Return of conduction across ablation lines to the mitral isthmus and the left atrial roof contribute to postablation arrhythmias as well. Intensive investigation of sophisticated ablation systems has failed to yield consistently durable ablation lines. Efforts to map and eliminate conductive gaps at the time of ablation have not resolved this problem. Gaps in linear ablation lines for AF ablation are a reality of current clinical practice. As a result, the single procedure success rate for AF ablation is constrained. It appears that a major advance in ablation and/or mapping technologies is needed to improve the state of catheter ablation for AF.

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Despite the clinical problems they produce, gaps within ablation lines represent fascinating examples of myocardial electrophysiology. A brief review is relevant to placing new studies in perspective. The animal model of the myocardial gap was introduced almost 100 years ago by Garrey to study fibrillatory conduction patterns over an isthmus of myocardial tissue. With the advent of linear surgical and catheter-based ablation for AF, the model has been used extensively to reveal the complex conduction behavior associated with discontinuous linear lesions. Direct experimentation has benefited from computer modeling to provide deeper insights into gap conduction.

A description of gap conduction involves all 3 determinants of myocardial impulse propagation: (1) passive tissue electric properties, (2) excitable membrane properties, and (3) excitation wave front geometry. Although sometimes overlooked, propagation wave front geometry may be the defining feature of gap physiology. As a propagating wave front emerges from a gap within a line of conduction block, the depolarizing current generated by the small gap is abruptly dispersed over a larger area, resulting in a slowing of conduction. This effect is most marked at the edges of the gap resulting in a convex wave front beyond the gap. Notably, when the wave front curvature reaches a critical value, such as imposed by a small gap, propagation ceases at a site distal to the gap itself because the current generated by the depolarized tissue becomes inadequate to activate the tissue ahead of it. The role of wave front curvature in myocardial impulse propagation is elegantly presented by Cabo et al and by Fast et al. Factors that reduce the ability of myocardium to generate depolarizing current will enhance conduction block through the gap. Thus, passive and active tissue properties modify wave front propagation through the gap. Factors that reduce membrane excitability or cell-to-cell coupling, such as tissue injury, rapid stimulation rates, fiber orientation, gap geometry, elevated resting membrane potential, and sodium channel blockade increase the propensity to conduction block. Under these conditions, conduction may fail through a gap that would conduct in presence of normal physiology. These effects of reduced membrane excitability may be the basis for recovery of conduction through ablation lines.

Because myocardial tissue is not regenerative, the return of pulmonary vein conduction after acute electric isolation represents a transient electrophysiological effect. It is known that action potential duration, dV/dt, and maximal action potential amplitude are decreased up to 8 mm from the edge of a newly created radiofrequency lesion. These effects recover over time and may be due to thermal injury, electroperoration, microvascular vascular damage, reduced connexin content, or direct electric effects on cellular structures. Therefore, a perimeter of tissue with compromised electrophysiological properties is present around radiofrequency lesions and may encompass the tissue within and around gaps in ablation lines. Conceivably, within this perimeter, tissue excitability may be impaired through depressed membrane dV/dt and action potential amplitude. Also, conceivably, as these effects recede over time, a nonconductive gap becomes conductive.

Into this background, the article by Ranjan et al appears in this issue of Circulation Arrhythmias and Electrophysiology. The article proposes to study the effects of altered tissue conductivity on propagation through ablation gaps and to visualize gaps using MRI. This study has 3 parts, with the unifying concept that recovery of reduced tissue conductivity in gaps may allow for late recovery of gap conduction. As described above, this hypothesis has been previously proposed but requires verification. First, the authors used an

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established computational model to study gap conduction behavior in the setting of normal and reduced tissue conductivities. As anticipated, reducing the tissue conductivity (increasing cell-to-cell resistance) predisposed to conduction block at gap widths that allow propagation at normal conductivity. Second, the authors created discontinuous linear radiofrequency ablation lesions in the right ventricular free wall of open-chest dogs. The gap was narrowed by incremental ablation until conduction block was documented using a plaque electrode array. The epicardial gap widths were 1.85 to 5.5 mm at loss of conduction. Histological findings showed a graded tissue injury about the ablation lesion from dense coagulation necrosis deep within the lesion progressing to less severe injury before reaching uninjured tissue. The protocol did not assess the electric properties of the tissue about the gap to demonstrate the relevance of their computer modeling, however. Recovery of conduction across the actual gaps was not demonstrated. As such, the proposed mechanism for delayed return of conduction is not directly supported by this work. Third, Ranjan et al demonstrated the ability of high-resolution MRI to visualize the nonconductive ablation gaps acutely in the intact animal. There was significant correlation between the gap widths measured visually and by MRI. Consistent with the graded histological injury pattern, areas of differing signal intensities were noted about the lesions. The ability to visualize nonconductive gaps is the most significant aspect of this work and is an example of the type of advance needed to improve outcomes for AF ablation.

Discontinuities in linear ablation lines that conduct can be mapped and ablated. The problem lies with anatomic gaps that are temporarily nonfunctional after ablation despite efforts to unmask them with adenosine, isoproterenol, pacing along the ablation line, and extended waiting periods. In the case of electric quiescence, exposure by gap function will fail, and some form of anatomic visualization is required. In this situation, the appreciation of gap form (anatomy) is required before gap function (conduction) returns. Intraprocedural methods to image ablation lesions in development include endoscopic visualization, intracardiac ultrasound, and MRI. Direct endocardial optical visualization systems can confirm endocardial lesion continuity but do not assess lesion depth. High-frequency intracardiac ultrasound incorporated into the ablation catheter can image lesion depth in real time. A major problem with this technology is a highly directional imaging beam and complete dependence on the ablation catheter orientation to the tissue. In addition, the ultrasound catheter cannot image where it does not go. Thus, gaps between catheter positions cannot be recognized. In contrast, MRI provides transmural lesion assessment independent of any catheter restrictions.

The technology used by Ranjan et al demonstrates promise, but many issues remain. Residual conduction has been demonstrated in gaps as little as 0.3 mm in cross-sectional area. Conduction may persist as the result of thin sleeves of surviving myocardium about vasculature crossing ablation lines. Such fine structures may be below the resolution of the imaging technology. It is evident that pulmonary vein to atrium connections can be lengthy and circuitous. It is unknown if MRI will be able to recognize anatomically convoluted connections. The true anatomy of gaps in pulmonary vein ablation lines in humans is not described. Assumptions about the gap dimension that will support conduction in canine ventricular tissue may not be representative of the behavior of gaps in human atria. Although the authors theorize that any gap > 1.4 mm may allow reconnection, not all gaps, even of adequate width, will conduct. In animal models, ablation lesion sets producing bifurcated or angled conduction paths may fail to conduct despite containing cross-sectional areas of viable myocardium that conduct over a straight propagation path. Even gaps that conduct at physiological heart rates may fail to conduct at rapid rates limiting their ability to participate in fibrillatory processes. Thus, nonfunctioning gaps may be targeted for ablation with imaging guidance. During real-time MRI of radiofrequency ablation, imaging within the first 20 seconds of ablation has shown the highest discrimination of tissue injury from tissue edema. Real-time imaging poses its own problems of ablation outside the imaging plane. Because of tissue edema, imaging after lesion delivery may overestimate lesion size and continuity for some MRI sequences. Relevant to this, our group has examined atrial biopsies taken from pulmonary vein ablation lines at the time of full surgical maze procedure in patients with recurrent AF after previous complete catheter-based pulmonary vein isolation (unpublished data). From this data, reconnected pulmonary veins often show nontransmural ablation lesions with intermixed scar and surviving myocardium. Discrete sections of normal tissue are less common. It is unknown if tissue characterization by MRI can recognize the potentially indistinct tissue precursors that lead to this partially devitalized substrate. Finally, despite the pioneering work of the authors, the technology for intraprocedural real-time MRI is far from widespread commercial use.

Ultimately, the problems with discontinuous linear ablation for AF will be resolved in 1 of 3 ways. A safe energy source will emerge for consistent linear lesion formation or our understanding of AF pathophysiology evolves to circumvent the need for linear ablation. These 2 means are being actively pursued but represent quantum shifts in our abilities. The third method is to remedy the current shortcomings of linear ablation by imaging recoverable gaps at the time of ablation. The tools to implement this strategy may be within reach. It is premature to conclude which technology will provide the solution to gap reconnection. Ranjan et al have demonstrated that magnetic resonance has many attributes relevant to this need but its challenges are apparent as well.

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