Unipolar Electrogram Morphology to Assess Lesion Formation During Catheter Ablation of Atrial Fibrillation
Successful Translation Into Clinical Practice

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The past decade has seen a significant increase in catheter ablation procedures for atrial fibrillation (AF); however, data on the efficacy of pulmonary vein (PV) isolation (PVI) are soberingly modest, with single and multiple procedure success rates of 54% and 79% for paroxysmal AF, respectively, during long-term follow-up (>3 years). The main mechanism of AF recurrence after catheter ablation is resumption of PV-left atrial (LA) conduction.3 The time-dependent inevitability of recovery of PV conduction has been consistently demonstrated in acute studies showing PV conduction in ≤93% of patients during an intraprocedural waiting period of 60 minutes after PVI.4 Furthermore, late recurrence of AF is associated with conduction recovery in ≥1 PV in >97% of patients who are having a redo procedure.5 Thus, durable PVI is critical if we are to make inroads toward enhancing procedural efficacy.

Gaps in the ablation line6 and failure to produce transmural lesions6 are implicated in recovery of PV conduction. PVI can be achieved after partial completion of a circumferential ring of lesions around the PVs, irrespective of intervening gaps. This is thought to result from a combination of irreversible and reversible atrial injury.7 Reversible atrial injury may stem from incomplete lesion formation that causes temporary electric uncoupling but not cell death ≤3.5 mm away from the lesion boundary, dependent on tissue temperature and tissue geometry.8 With time, tissue at the boundary of the transmural lesion recovers normal conduction during the course of 1 to 4 weeks.6 Thus, lesion gaps that exhibit conduction block frequently go undetected during the index procedure, and block persists for up to several weeks or months thereafter until tissue injury heals. Conduction block may occur in tissue with normal conductivity despite a gap of ≤1.4 mm and in abnormal tissue with a gap as large as 4 mm.9 Complex gap geometry may produce transient unidirectional and rate-dependent block.10

The opinions expressed in this editorial are not necessarily those of the editors or of the American Heart Association.

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(Circ Arrhythm Electrophysiol. 2013;6:1050-1052.)
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Circ Arrhythm Electrophysiol is available at http://circcep.ahajournals.org
DOI: 10.1161/CIRCEP.113.001145

After PVI during the initial procedure, gap detection may be facilitated by a visual log of the central portion of lesions placed on an electroanatomic mapping system and via residual electric signals detected by a multipolar mapping catheter placed at the PV-LA junction. Fundamentally, this will miss electrically silent gaps that persist as a result of aforementioned tissue stunning. Dormant conduction can be identified by use of intravenous adenosine that hyperpolarizes atrial cell membranes, permitting transient conduction at sites with incomplete cell destruction.11 Although further ablation at these sites may improve AF-free survival,12 paradoxically it also identifies those patients with a greater likelihood of AF recurrence despite additional ablation, possibly reflecting a higher likelihood of other incomplete lesions.13 A unifying message from these studies is that acute electric isolation does not reliably predict permanent electric isolation.

Permanent conduction block across linear lesions requires transmural lesions. There are a limited number of reliable, easily reproducible methods for assessing intraprocedural lesion completeness. Loss of electric excitability along a circumferential PVI line markedly enhances single-procedure success of AF ablation compared with bidirectional PV-LA conduction block alone.14 Use of contact force technology can improve lesion efficacy, reduce recovery of PV conduction,15,16 and improve single-procedure efficacy17 but is not universally available at present. High-resolution MRI scanning, near-field ultrasound, and lesion thermography hold promise for lesion completeness and gap detection but are not widely available.5,7,9

With this in mind, the findings reported by Bortone et al18 in this issue of Circulation: Arrhythmia and Electrophysiology provide a welcome contribution to the goal of improving durable PVI and procedural success for catheter ablation. The authors used unipolar electrogram morphology criteria that are previously validated in a porcine model19 to guide transmural lesion formation. In the Otomo study,19 loss of the negative component of the unipolar atrial electrogram (RS morphology to R morphology) differentiated transmural from nontransmural lesions (characterized by persistence of an S wave) with 100% sensitivity and specificity.18 It is important to note that unipolar, but not bipolar, signals show morphology characteristics that are independent of catheter orientation and direction of atrial activation wave front.

In the present study, authors compared 2 groups of patients with paroxysmal AF undergoing PVI facilitated by an electroanatomic mapping system, merged preprocedural LA computed tomographic scan, and a circular mapping catheter. In the first group, 50 patients underwent PVI, with radiofrequency
application continued at each site until the development of a completely positive unipolar signal at that site. The second group of 50 patients was a historical control group who underwent PVI with 30 seconds of ablation at each site. In both groups, continuous and wide circular lesions around the PVs were created and the veins isolated 2-by-2 at the antra. The end point was bidirectional block across the PV-LA junction with a 30-minute waiting period to detect dormant conduction. Patient follow-up was standard with a 12-lead ECG and continuous 24-hour Holter monitor at 1, 3, 6, 9, and 12 months after ablation and every 6 months thereafter.

The pertinent findings of the study were that the unipolar ablation group compared with the controls had a statistically significant (1) reduction in procedural time, x-ray exposure, and total ablation time by 25, 6, and 37 minutes, respectively; (2) reduction in total energy required to achieve PVI by 66 kJ; and (3) 18% absolute reduction in the risk of recurrent AF at a mean follow-up of ≥2 years after the first ablation procedure off antiarrhythmic drugs (88% versus 70%). A mean of only 15±1 seconds of radiofrequency ablation was required to achieve a unipolar R morphology (considered a transmural lesion). Intriguingly, there was a high incidence of recovery of PV conduction (38%) in the unipolar ablation group, which was lower than the control group (53%) but did not reach statistical significance. A similarly high proportion of patients required carina ablation to achieve PVI (30% versus 32%). Of note, patients did not undergo adenosine testing nor pace capture along the line during the index procedure.

Of the 6 patients who had AF recurrence in unipolar RF group, all had evidence of recovery of PV conduction during the index procedure. Interestingly, at the redo procedure, gaps in the ablation line had recovered RS unipolar morphology, and ablation at these sites resulted in PV reisolation.

Bortone et al18 are the first to use intraprocedural electrogram morphology as a measure of lesion effectiveness in an attempt to achieve durable PVI. The authors ought to be congratulated in successfully translating findings from an animal study into human practice and for achieving excellent midterm AF-free survival for their patients. The attractiveness of the technique is clearly the shortened procedural time, radiation exposure, and superiority in outcomes, with the implementation of a reproducible, readily available intraprocedural tool that can be applied universally.

However, as with any new methodology, there are some limitations that need to be stressed. For one, loss of the negative deflection on the unipolar RS morphology is observed with reversible tissue injury, which is true of any of the indirect measurements of lesion transmurality. Additional evidence for the imperfect positive predictive value of the morphology change is the unexpectedly high rate of PV conduction recovery in the study group. We have found that rendering the ablation line unexcitable14,20 has reduced the intraprocedural rate of PV conduction recovery to <5%, although conduction recovery should be nil for a perfect lesion set.

These observations also highlight limitations of the ovine model on which the electrogram-based criteria for transmurality for this study are fundamentally based. In the Otomo study,19 only thin atrial tissue was tested, which makes the method particularly relevant to ablation at the thin posterior wall of the LA adjacent to the esophagus, where limiting RF energy is critical. However, it is not clear that unipolar electrogram morphology criteria apply to lesions in thicker tissue.

We have shown, from independent studies at 2 centers, that median impedance decrease nearly doubles with an average contact force >20 g at the ablation catheter tip compared with poor contact and is consistent across different force-sensing platforms.21,22 In the study by Bortone et al18 the control group had RF ablation performed for an empirical 30 seconds at each site without any feedback on electrogram abatement or impedance changes, presumably without adjustment of the catheter to improve contact. In fact mean impedance change was identical in the unipolar ablation and the control group, which is hard to explain because catheter adjustments made in the study group should have resulted in better contact and a higher average impedance decrease. Finally, the study was not randomized, and the use of a historical control introduces considerable selection bias; thus, results can only be interpreted as hypothesis generating.

We welcome the findings of Bortone et al18 because they represent an important step forward in la quête ultime for permanent PV isolation during catheter ablation for AF. More than any technique or technology or combination thereof, it is more important to appreciate that during and after RF application, if one pays meticulous attention to closing gaps and to scrutinizing the available lesion-specific information at your fingertips, more patients will have persistent PVI that will result in fewer recurrences of AF.

Disclosures

Dr Kumar is a recipient of the Neil-Hamilton Fairley Overseas Fellowship co-funded by the National Health and Medical Research Council and the National Heart Foundation of Australia and a recipient of the Bushell Travelling Fellowship funded by the Royal Australasian College of Physicians. Dr Michaud has received honoraria from St Jude Medical, Boston Scientific, and Medtronic as well as research support from Boston Scientific and Biosense Webster.

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**Key Words:** Editorials ■ atrial fibrillation ■ catheter ablation ■ catheter contact force, radiofrequency
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_Circ Arrhythm Electrophysiol_. 2013;6:1050-1052
doi: 10.1161/CIRCEP.113.001145

_Circulation: Arrhythmia and Electrophysiology_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3149. Online ISSN: 1941-3084

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circep.ahajournals.org/content/6/6/1050

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