The treatment of atrial fibrillation (AF) using pulmonary vein isolation (PVI) to eliminate pulmonary vein (PV) triggers improves long-term outcomes and slows disease progression, yet remains less effective for individuals with persistent AF than for those with paroxysmal AF. Although this likely reflects the fact that patients with persistent AF have AF-maintaining substrates beyond the PVs, anatomical isolation of the posterior left atrial wall, left atrial appendage, empirical left atrial linear ablation, and better ablation energy delivery have not improved their outcomes.

One developing strategy is to personalize AF ablation to target regions that are functionally important yet may vary in location for each individual. Optical mapping reveals localized organized sites (known as drivers) in animal models and, recently in ex vivo human hearts during AF, with varying locations where ablation can be effective. Several groups have shown that including AF propagation patterns in machine learning models improves prediction of long-term ablation outcomes. Nevertheless, targeting AF drivers remains difficult, in large part, because of technical challenges in mapping AF in patients. Although optical mapping visualizes the propagation of action potentials in ex vivo preparations of AF, several technical factors preclude its use in patients. Clinical mapping is, therefore, limited to marking the surrogate of electrogram activation times, which are challenging to interpret in disorganized and rapid rhythms. Accordingly, although they are promising in smaller studies, no AF map-guided ablation strategy has yet improved upon PVI in broad patient cohorts in randomized multicenter trials.

Lin et al studied a novel mapping approach to personalize AF ablation in 170 patients with persistent AF, who were randomized 1:1 to map-guided ablation plus PVI or PVI alone in 3 centers in Taiwan and Japan. Exclusion criteria were a prior maze surgical ablation for AF, left atrial clot, or arriving in sinus rhythm. Mapped periodic or repetitive (PRISM) sites near the PVs were first targeted by encompassing them within wide-area circumferential PVI with radiofrequency ablation (approximately one-half of patients) or by extending the PVI ablation from cryoablation. If AF did not terminate, the investigators targeted PRISM sites further from the PVs. Operators also ablated non-PV triggers and were given discretion to also ablate a roof or mitral line. Conventional ablation included PVI with radiofrequency or cryoballoon catheters. The authors report that PRISM-guided ablation was associated with less recurrence of all atrial arrhythmias at 1-year follow-up compared with PVI alone (32.9% vs 57.6%; \( P = .002 \)). Procedurally, patients had 2 to 3 left atrial PRISM sites, in line with the presence of AF drivers by other mapping methods, that were targeted near PVs only (type I) in one-third and throughout the left atrium (type II) in two-thirds of patients. AF was terminated by ablation in 23.5% of patients receiving PRISM-guided ablation and in 12.9% of those receiving PVI alone. In the PRISM group, mapped sites were not ablated in 18 patients for safety or if AF had already terminated. No major adverse events were reported.

The authors should be congratulated for completing this multicenter randomized clinical trial that demonstrates the value of mapping fibrillatory conduction to guide ablation to potential drivers sites, which improved outcomes in patients with persistent AF. Some technical aspects are worthy of discussion. The authors described PRISM in 2021 to assess electrogram periodicity (repeated patterns of activation waves) and similarity (the degree to which waveforms resemble each other). This elegant approach is highly practical, enabling widely used high-density catheters to identify sites proposed by the authors to be focal or rotational AF drivers. PRISM sites were recorded for periods as short as 10 seconds, and next steps should include defining their temporal and spatial stability and reproducibility. Using differing AF mapping approaches, we and several other groups showed that...
organized AF sites may fluctuate spatially yet return to conserved locations, which would explain how spatially targeted therapy (ablation) may be effective. It would be useful also to compare PRISM to other AF mapping strategies for further mechanistic insights.

The study by Lin et al,7 although elegant, presents some limitations. First, mapping was performed only in the left atrium, leaving PRISM sites in the right atrium unstudied. A growing body of literature6,6,10 shows that anatomical right atrial ablation may improve outcomes from current AF ablation strategies, which are predominantly in the left atrium, which is consistent with several mapping studies that revealed a third of potential AF drivers in the right atrium. Second, the authors included patients with prior AF ablation, which may modify the durability of PVI or alter PRISM sites. Only 20% of enrolled patients were women,7 which is a common feature of AF trials but must be improved in future studies. Third, heterogeneity between ablation groups, such as allowing additional roof or mitral lines, ablation of non-PV triggers, and continuing the use of antiarrhythmic medications, confuses the interpretation of PRISM-based ablation.

In conclusion, the important trial by Lin et al7 adds AF mapping of PRISM sites to the very short list of strategies proven in randomized multicenter trials of patients with persistent AF to improve ablation outcomes beyond PVI. Next steps should include testing this approach in larger patient cohorts and correlating repetitive AF sites to pathophysiological processes, such as atrial fibrosis, abnormal repolarization, or conduction dynamics. The goal of such studies would be to address the fundamental question: which individuals with persistent AF would most benefit from additional ablation, and in whom would PVI alone be optimal?

ARTICLE INFORMATION
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