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Mapping Ripples or Waves in Atrial Fibrillation?

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Therapy for persistent atrial fibrillation (AF) is limited by uncertainty in its mechanisms yet, unlike in organized rhythms, mechanisms for AF may vary dramatically with mapping technique. The traditional approach of drawing contour maps of AF by assigning an onset time to each electrogram reveals disordered activity in patients with permanent AF at non-arrhythmia surgery^{1, 2}. This accounts for AF complexity, but does not explain some clinical observations. Recent studies^{3, 4} using signal processing to filter far-field and assist mapping reveal rotational or focal drivers of persistent AF where local ablation can terminate AF, with promising long-term outcomes in many^{5–10} but not all^{11–13} studies. It is unclear if divergent results reflect different mapping methods, epicardial versus endocardial^{1, 2} mapping, patient selection or inter-center variations in AF ablation success¹⁴. Advances in AF mapping will require comparisons between methods, ideally referenced to clinical endpoints to facilitate interpretation.

In this issue of the *Journal*, Takahashi et al.¹⁵ use ‘Ripple Mapping’, a novel electrogram analysis previously applied to organized supraventricular¹⁶ and ventricular arrhythmias¹⁷, to identify potential focal drivers of persistent AF associated with AF termination by ablation. The authors identified 45 patients in whom persistent AF continued after pulmonary vein isolation (PVI), in whom point-by-point left atrial mapping was performed using a high-density catheter, followed by stepwise ablation. Ripple mapping was applied retrospectively for 3 AF cycles at 13±3 sites per patient, compared to manually annotated bipolar electrogram timings in 7 patients. AF propagation maps from ripple-annotated timings showed organized, mostly focal activation at 14% of sites in persistent AF. During stepwise ablation, lesions determined *post-hoc* to pass through these sites were more likely to terminate AF than lesions through non-organized regions (22% vs. 7%, p=0.015). The authors conclude that ripple mapping may help future prospective mapping to identify ablation targets in persistent AF.

The authors should be commended for applying ripple analyses in this novel way. Ripple mapping displays activation via ‘columns’ with height proportional to voltage at each

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location over time, rather than depicting each electrogram by a single onset time and voltage. Thus, a ripple map of macro-reentry may show multiple small ripples indicating a site of fractionated signals, or single tall 'up and down' columns indicating non-complex signals.

There are some limitations worthy of discussion. First, the method may be time consuming, since it requires moving a multipolar catheter to scores of atrial locations for analysis. Second, since AF sources 'wobble' in nearly all descriptions^{3–10}, this small sampling approach may lead to underdetection. Third, the accuracy of ripple analysis for AF depends on how bipolar electrograms are handled, which poses some challenges in AF. The amplitude and polarity of bipolar electrograms depends on wavefront direction, which varies rapidly in AF and is unknown *a priori*. In addition, each pole of a bipolar electrode in AF may detect these different waves of unknown directionality and integrate far-field activity, as the authors acknowledge.

Comparative mapping studies reveal that conventional marking of bipolar electrograms in AF may not indicate local activation time. The figure shows juxtaposed catheters (see fluoroscopy) to compare bipolar AF electrograms¹⁸ with monophasic action potentials (MAP) that indicate local activation¹⁹. While some bipolar electrograms (red tracings) clearly reflect local activity (blue arrows on MAP), many do not – indeed some better match far field notches on the MAP. Moreover, many local activations were not reflected in bipolar electrograms – indicated either by very small or no deflections. Traditional (or ripple) analysis of this channel may show disorganized activity, yet MAPs show regularity with far-field notches. In other studies, optical recordings of human AF may show regular activations yet simultaneous electrograms show many additional deflections²⁰, which lie within repolarization and thus indicate far-field activity or noise. Thus, while these maps of optical action potentials revealed sites of rotational activation where ablation terminated AF²⁰, rotational activation may be missed on electrogram maps. Finally, as discussed, activation mapping may miss rotational elements which move, and is challenging at sites of fractionated activity.

Further studies should thus compare the results of Takahashi et al¹⁵ to other approaches to map AF. The authors use ripple mapping to support increasing numbers of studies which confirm localized sources in persistent AF. However, while drivers were predominantly focal by ripple analysis, they are often rotational by optical mapping²⁰, analyses of endocardial baskets²¹, epicardial mapping by ECGI⁴ and recent work using novel computational electrogram analyses to guide ablation which terminated AF before PVI²². Comparative AF mapping in patients at sites where ablation terminates persistent AF may help to reconcile divergence between mapping approaches. Using this approach, recent studies have revealed rotational as well as focal drivers at sites of AF termination using mapping methods²³ previously reported not to show rotational activity in different patients (or animal models) mapped epicardially²⁴. After such validation, techniques can be used to address questions such as why acute AF termination often does not predict long-term outcome.

In conclusion, Takahashi et al should be congratulated on using ripple mapping to identify potential drivers of persistent AF. The prevalence of AF drivers between patients, and

whether they indicate focal, rotational or other activation patterns will be assisted by studies that compare AF mapping modalities in the same patients, referenced to acute termination by map-guided ablation. This approach is analogous to methods widely used to validate mapping for other rhythms. Novel and potentially complementary AF mapping approaches validated in this way will offer a real opportunity to improve ablation outcomes.

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Figure. Bipolar electrograms may not detect local activity in Human Atrial Fibrillation

Compared to local activity (blue arrows) from a monophasic action potential catheter (MAP) in a patient undergoing AF ablation, electrograms from 2 mm spaced bipoles (in red, SP9,10; SP19,20) on a physically juxtaposed catheter (see fluoroscopic inset) show (a) *false positives*: deflections that do not reflect local activity (MAP upstroke), of which 2 are highlighted in boxes; (b) *false negatives*: where local activity are poorly represented by bipolar electrograms, of which 2 are highlighted by ‘?’ (from reference¹⁸, with permission from Heart Rhythm).