

Terminating atrial fibrillation by cooling the heart



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Disappointing results of pharmacological therapy in many patients with atrial fibrillation (AF)¹ have motivated efforts to develop device therapy for this complex electrical disorder. Such devices have focused on mechanisms including ablation of tissue harboring triggers or substrates, mechanical devitalization of the left atrial appendage to provide antiarrhythmic² as well as antithrombotic effects, and the application of low energy electrical fields to defibrillate AF.³ However, there are other mechanisms to modulate cardiac fibrillation that have rarely been translated into therapy, including hyperpolarizing myocytes,⁴ or stretching,⁵ or cooling the heart^{6,7} to cause defibrillation.

In this issue of *HeartRhythm*, Naksuk et al⁸ describe an innovative and creative prototype device to defibrillate AF by direct cooling. The authors developed a device that exploits the Peltier effect by using electrical energy (8.6–14 V, 3.6 A) to create a cold surface placed on the epicardium and a hot surface that is cooled by a copper mesh and saline irrigation. The authors calibrated 4 × 4 or 2 × 2 cm² devices in 2 ex vivo swine hearts to identify settings to achieve a <5°C target temperature. They then measured the physiological impact of this calibrated device in a proof-of-concept in vivo canine study, applying the device repeatedly to distinct atrial regions through a sternotomy. From a technical perspective, target temperature was achieved in two-thirds of the trials in 3–4 minutes. Physiologically, the authors studied the impact of cooling on atrial pacing capture, conduction time, and AF. During atrial pacing, cooling produced a progressive increase in capture threshold cooling, ultimately leading to loss of capture. During atrial capture, conduction time prolonged substantially in two-thirds of the trials when lower epicardial and endocardial temperatures were achieved. AF was then induced and studied during rapid pacing. Epicardial cooling to –0.5°C caused AF to terminate into sinus rhythm, and AF

was no longer inducible. Mild ecchymosis and histological inflammation were observed where cooling was applied.

The authors should be congratulated on this creative approach to modulate atrial substrates and potentially treat AF. While described as a prototype, the device demonstrates feasibility for a number of mechanistic interventions that could form the basis of future therapy. To develop such therapy, several of the authors' observations merit further study. First, studies are needed to confirm that this device terminates self-sustained AF, since one could argue that termination of AF maintained by burst pacing may represent loss of pacing capture by cooling. Second, while cooling may well terminate AF, studies are needed to define the relative efficacy of cooling different regions given the spatially nonuniform nature of triggers and substrates in human AF. Third, it should be defined to what extent uniform cooling fields produce spatially nonuniform physiological effects because, for instance, creating islands of slow conduction could potentially be proarrhythmic. Such studies could use multipolar catheters or optical imaging within the cooled field to map contours (isochrones) of activation and recovery, which should be done at fast rates (restitution) that reveal conduction slowing⁹ and repolarization abnormalities¹⁰ for AF that are obscure at slow rates. Fourth, “designed” cooling matched to tissue thickness, anisotropy, warming effects from perfusion or mediastinal structures, or the presence of scar¹¹ could be tested for its ability to modulate fibrillatory disorganization or reorient the trajectory of AF drivers.¹⁰ Finally, other cooling technologies may be more effective. The authors use Peltier elements as a starting point, but such devices are rigid and may constrain cardiac motion. This may pose a challenge if longer duration applications are needed or if implanted devices are considered. Flexible Peltier elements are under development,¹² but currently provide lower cooling efficiency. It is also important to establish that such devices and their cooling range of –1.4°C to 16.2°C can be applied under near-clinical conditions without producing mechanical dysfunction, thrombosis, or noncardiac sequelae.

In conclusion, Naksuk et al are to be congratulated for their innovative therapy to treat cardiac fibrillation, which builds on several relatively unexplored yet plausible mechanistic avenues. The authors successfully demonstrate that this approach is feasible with real potential for future therapy. We look forward to future exciting developments in this direction.

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