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EDITORIAL COMMENT

After the Fire and Ice Age, Are We Entering the Metal Age?*

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In the early 1980s, the early age of catheter ablation, thermal lesions were achieved within the myocardium using direct current (1). Typically, 300 to 400 J were applied via the 2-mm distal electrode of a nondeflectable catheter. However, these shocks led to a spark (arcing), an explosion, and a pressure wave. These phenomena created large but uncontrolled myocardial lesions with potential hazardous effects. In the early 1990s, radiofrequency (RF) catheter ablation was introduced and rapidly adopted by the community. Because the method allows for high efficacy and safety profiles by inducing well-controlled thermal lesions through resistive heating of myocardial tissue, it has become the standard of care for the treatment of arrhythmias refractory to medical therapy. However, there remain some limitations that affect the efficacy and safety of this procedure. One such limitation is the inability to achieve durable/large/transmural lesions with the safe delivery of low power to myocardial tissue. In addition, there are risks of "steam pops" and cardiac perforation when higher levels of energy are used. Yokoyama et al. (2) showed that on thigh muscle preparation, using 50 W and a contact force of 40*g*, could result in a lesion depth and volume of 10 mm and 1,500 mm^2. However, on a beating heart using 30 W and 40*g* of contact force in average, Sacher et al. (3) showed that the mean lesion depth and volume were 5 mm and around 250 mm^2. These experiments were performed on viable myocardium as in the study of Nguyen et al. (4), but what happens in scar myocardium, the targeted area for ventricular tachycardia ablation, remains largely unexplored.

Over the past 15 years, a series of innovations have emerged to overcome these issues, such as the use of irrigated-tip or porous-tip catheters to obtain a larger lesion with less risk of charring, contact force to maximize catheter and tissue contact, bipolar and epicardial ablation to maximize lesion transmurality, or needle ablation catheters to deliver RF within the myocardial wall (5). In addition to these innovations in RF catheter approach and technology, other energy sources have been proposed such as microwave, laser, high-intensity focused ultrasound, cryoenergy, and more recently electroporation. Despite the fact that most of these energy sources may create large lesion ex vivo, their application to the clinical field has been disappointed or limited so far. For example, the EPICOR system (St. Jude Medical, Minneapolis, Minnesota) using high-intensity focused ultrasound indicated for epicardial beating heart surgical atrial fibrillation ablation required a perfect contact with the absence of air to create a good lesion (6). On top of the generator able to produce these different types of energy, the other limitation was often the device to deliver the energy (balloon that limited the indication to pulmonary vein isolation for example). Cryoenergy, the second most developed energy source, is quite effective for pulmonary vein isolation and junctional tachycardia ablation; however, it does not create a larger lesion than RF ablation does. Therefore, RF remains the gold standard for cardiac ablation, and any improvement of the method would be welcome to overcome its limitations, particularly for the management of intramural scar (7–9).

In oncology, various types of nanoparticles have been proposed to increase the efficiency of RF for the treatment of solid tumors. A number of studies have reported higher RF-induced heating when the tissue is loaded with gold nanoparticles or carbon (10,11).

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Nguyen et al. (12) showed that when myocardial tissue was pre-treated with carbon nanotubes, it resulted in significantly larger lesions at both low and high power settings. Unfortunately carbon nanotubes are not easy to deliver in vivo within the myocardial tissue.

Gadolinium chelates are commonly used as nonspecific extracellular contrast media using magnetic resonance imaging, thanks to their paramagnetic properties. The tolerance of these molecules is excellent and their use in clinical practice has been approved by regulatory agencies for decades. In cardiology, gadolinium chelates are known to accumulate within myocardial scar, because these areas show interstitial expansion and altered washout kinetics. This contrast has been the cornerstone of viability imaging on magnetic resonance imaging for years. In

SEE PAGE 177

this issue of *JACC: Clinical Electrophysiology*, Nguyen et al. (4) establish a proof of concept using gadolinium chelates for their ability to improve RF-induced heating. They used an ex vivo model of bovine myocardium pre-treated with infiltrations of 1 ml of gadolinium via direct needle injection to a depth of 5 mm. The investigators report a marked increase of lesion volume at both 20 W and 50 W when the myocardium is locally loaded with gadolinium versus saline. In a second step, they tested their hypothesis, in vivo, in the beating hearts of pigs. RF applications were performed on the endocardium after local direct gadolinium or saline injection. Despite a very small number of lesions (6 vs. 6), they found a dramatic difference in lesion volume when comparing sites with gadolinium (592 ml) versus sites with saline infusion (102 ml). Thus, these results are promising as they indicate a potential use of gadolinium chelates to increase the efficiency of cardiac RF ablation. The advantages of the approach are that these molecules are already approved for clinical use and available on the market at limited costs. However, the optimal intratissular concentration and method for gadolinium administration remain to be established. In the present study, the investigators have used needle catheters to deliver the drug within the myocardium and obtain locally a high concentration of gadolinium. However, an easier method to accumulate enough gadolinium in the myocardium would be required before performing any clinical study. In an attempt to assess the feasibility of a systemic gadolinium administration, the investigators have designed thermo-sensitive liposomal gadolinium preparations for intravenous administration. However, this last method failed to improve lesion size as assessed on a series of epicardial RF applications, which indicates that the proposed method cannot reach sufficient gadolinium concentration within the myocardium. Thus, additional research is desirable to define the minimal amount of gadolinium necessary to observe a thermal effect and to assess whether this concentration can be reached using systemic administration. If feasible, the method would be ideally suited to the management of post-infarction ventricular tachycardia. Indeed, one could imagine infusing a high concentration of gadolinium 10 to 15 min before performing RF ablation at the border zone of the scar, an area often responsible for ventricular tachycardia isthmuses and known to accumulate gadolinium chelates.

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