Nanoparticles Yield Big Results

David E. Haines, MD

The efficacy of catheter ablation has improved dramatically over the past 3 decades as our understanding of ablation lesion formation has led to technological advances that have resulted in the ability to reliably create large and deep lesions. In the early years, operators were constrained during radiofrequency (RF) ablation with 2-mm nonirrigated electrodes by the tendency for the electrode–tissue interface temperatures to exceed 100°C resulting in boiling of blood and the formation of coagulum and char.1,2 Adherent coagulum reduces available electrode surface area resulting in a progressive and rapid rise in impedance and requires cessation of energy delivery. Thus, the magnitude of power that can be delivered to the tissue is limited. Because larger ablation electrode tips and irrigated electrode tips were introduced, electrode–tissue interface temperatures were lower, allowing the operator to ablate with higher powers and create much larger lesions.3,4 Presently, large ablative lesions can be created with a variety of technologies including irrigated RF ablation with force sensing,3 ultrasound ablation,4 and laser ablation.5 But despite these advances in lesion science, there are still some ablation targets such as the critical substrates for the propagation of reentrant ventricular tachycardia that are sometimes beyond our reach.6,9

See Article by Nguyen et al

In this issue of Circulation Arrhythmias and Electrophysiology, Nguyen et al10 describe a novel technique for increasing lesion size with RF ablation while simultaneously providing a secondary method to improve ablation targeting. By delivering a low dose of metallic nanoparticles to tissue, the authors demonstrated greater depth of tissue heating and larger lesion formation. The mechanisms proposed for this phenomenon are both electric and thermal. RF energy creates lesions by conversion of electric energy to thermal energy through resistive (ohmic) heating of tissue which decreases proportionally with distance from the RF source in an isotropic medium.11,12 In a medium with higher tissue electric conductivity, there should be greater tissue heating.13 Deep tissue heating from the core of resistive tissue heating from RF energy delivery is dependent on thermal conduction. At steady state, the temperature gradient from a constant temperature source should be identical whether the thermal conductivity of the medium is high or low. But if thermal conductivity is increased by tissue infusion with metallic nanoparticles, then the rate of tissue temperature rise should be faster, and steady-state temperatures should be achieved faster. The authors demonstrated this phenomenon nicely by the faster rate of tissue temperature rise at 3- and 5-mm depth in preparations infused with ferrous oxide compared with controls. Thus, it was predicted, then confirmed experimentally, that tissue infusion with metallic nanoparticles could yield larger RF ablation lesions.

But power without control is a dangerous combination. With increasing capability to create deep lesions, we have observed an increasing prevalence of collateral injury outside the targeted ablation zone. In particular, the often-fatal complication of atrial esophageal fistula is a consequence of excess ablation on the posterior left atrial wall during atrial fibrillation ablation.14 Thermally mediated necrosis of the muscularis and epithelial layers of the esophagus can lead to subsequent atrial esophageal fistula formation with disastrous results. Advances like infusion of metallic nanoparticles will not necessarily improve patient outcomes if it results in an increase in complications, or if the operator reduces amplitude of power delivery to avoid collateral injury and as a result creates ineffective lesions. Presently, we are lacking commercially available technologies to allow us to monitor lesion growth real time. Instead, we depend on surrogate metrics of lesion formation, such as power, electrode–tissue interface temperature, impedance drop, or force-time integral. Although these parameters help the operator determine whether or not a lesion is being created, they cannot be reliably used to limit ablation so as to prevent collateral injury. The challenge of catheter ablation in the modern era, therefore, is not only to be able to create large lesions when required but also to have the control to limit ablation to the targeted substrate and only the targeted substrate.

One approach to localize lesion formation and prevent unwanted heating in contiguous tissue would be to infuse a substance into the tissue that modulates its heating properties. Nguyen et al have demonstrated this proof of concept with metallic nanoparticles, although their infusion into thin walled myocardium might result in increased heating outside of the heart and increase the risk of collateral injury to nontargeted tissue. But perhaps the desired effect of localizing heating to the tissue without heating to the tissues beyond could be achieved with infusion of nanoparticles with other electric and thermal properties that would enhance this targeted heating. The concept of combining tissue selectivity and localized catheter energy delivery has been used successfully with photodynamic therapy and laser ablation,15 and now may have utility using RF energy for ablation.
The ongoing objective of maximizing ablation lesion size when deep substrates need to be targeted, but limiting lesion formation only to that targeted tissue and no other, remains the elusive goal, but one that is worthy of our efforts. Priming the ablation target with metallic nanoparticles demonstrates unique proof of concept that brings us one step closer to this goal.

Disclosures
None.

References
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