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EDITORIAL COMMENT

Eliminating Coagulum Formation With Charge Delivery During Radiofrequency Ablation

Negative May Be a Positive!*

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Since its introduction into clinical practice in the 1980s, radiofrequency (RF) catheter ablation has seen a meteoric rise in the treatment of cardiac arrhythmias owing to its safety and efficacy profile and ability to precisely target arrhythmogenic tissue. Driven by seminal observations by Haines (1), Wittkampf et al. (2), and Nakagawa et al. (3), among many others, the past 3 decades have seen remarkable evolution in catheter design allowing more effective and reliable energy delivery to target tissue. Permanent tissue destruction is a fundamental goal of RF ablation and reliably occurs when tissue temperature of >50°C can be achieved (4). There are a plethora of factors that influence lesion formation; however, lesion size is fundamentally governed by extent of tissue heating, which occurs via resistive and conductive means (5).

When comparing solid-tip versus irrigated catheters, there are key biophysical differences that must be appreciated (**Figure 1A**) (3). First, with solid-tip catheters lesion width and depth increase linearly with electrode-tissue interface temperature up to 90°C (6). With electrode-tip interface temperature of 80°C to 100°C, coagulum forms on the catheter tip due to the boiling of plasma and adherence of denatured plasma proteins. This results in a reduction in the surface area at the catheter tip, a larger local current density, thrombus formation, and progression of the coagulum, followed by a sudden rise in the impedance (6). This phenomenon frequently limits the duration of RF delivery and thus extent of energy delivery to target tissue (3). Without irrigation, tissue temperature is highest just beneath the endocardial surface with a steady gradient to lower temperatures in the deeper layers. If power or lesion duration is limited to avoid high temperatures at the catheter tip-tissue interface, smaller, superficial lesions will result (3). In contrast, irrigation cools the tip-tissue interface, thus avoiding coagulum formation and allowing higher power settings for longer duration. Importantly, surface cooling changes lesion geometry so that a smaller surface area is exposed to tissue temperatures exceeding 50°C and maximal lesion width is found 1 mm to 3.5 mm beneath the endocardial surface (**Figure 1A**) (3,7,8). Contrary to common belief, irrigated lesions are smaller than nonirrigated lesions at the same power setting and duration (3).

Given the need to create deeper, transmural lesions and the risk of thrombus formation at higher power settings, nonirrigated ablation catheters have been supplanted largely by open-irrigated catheters. However, the risk of clinical thromboembolic events such as stroke or transient ischemic attacks has not been entirely eliminated with the use of open-irrigated catheters despite systemic anticoagulation periprocedurally and additional heparinization intraprocedurally: for example, stroke is reported to occur with a frequency of ~0.6% to 2.5% in atrial fibrillation ablation literature (9,10). Even more compelling are data that asymptomatic thromboembolic events detected by brain magnetic resonance imaging can

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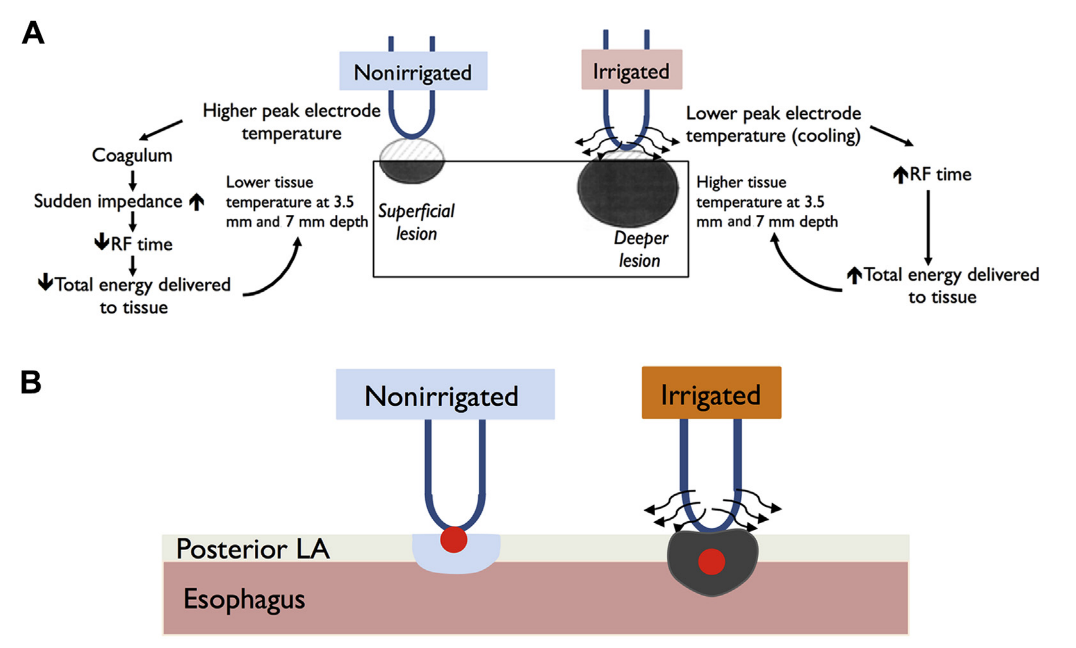
FIGURE 1 Impact of Irrigated Versus Nonirrigated Ablation on Lesion Size, Geometry, and Potential Collateral Injury



(A) Ablation lesions delivered under power control with nonirrigated catheter **(left)** and irrigated catheter **(right)**. Nonirrigated power controlled lesions are smaller and more superficial due to shorter ablation duration and smaller amount of energy delivered to tissue due to the high peak electrode temperature with sudden rise in impedance prohibiting ablation (3). In contrast, irrigated lesions are deeper with peak tissue temperatures between 3.5 mm and 7.5 mm depths (3). **(B)** Schematic hypothesizing that nonirrigated ablation in the posterior left atrial wall would produce lesions mainly limited to the endocardium with less collateral esophageal injury than with irrigated lesions, which would produce maximal tissue temperatures **(red dot)** near the epicardial surface and possibly within esophageal tissue. LA = left atrium; RF = radiofrequency.

occur in a substantial proportion of patients (14%) undergoing catheter ablation for atrial fibrillation (11), some of whom may experience subtle neurocognitive dysfunction (12). It is entirely possible that many such events may be a result of “soft thrombus” formation, which can develop as a result of denaturation and aggregation of plasma proteins at blood temperatures between 50°C and 80°C. Soft thrombus is poorly adherent to the ablation electrode and is not associated with an impedance increase. In contradistinction, “char formation” can be detected by impedance increase (13). Clearly, thrombus formation remains a significant contemporary challenge during catheter ablation of cardiac arrhythmias.

Within the context of this discussion, the contribution by Lim et al. (14), in this issue of *JACC: Clinical Electrophysiology*, unveils an important novel method of reducing thrombus formation via continuously delivering a negative charge at the catheter tip. The premise for this design is that fibrinogen, which is a fundamental building block for thrombus, is negatively charged and preferentially binds to positively charged surfaces, which then induces conformational changes in its molecular structure that further invokes a prothrombotic cascade (15).

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The investigators designed a system wherein high-impedance, negative direct current is delivered from a 9-V battery to the ablation catheter in parallel to the signal-processing pathway in a canine model. After identifying that a minimum negative current of 100 μA was required to eliminate coagulum, the investigators performed ablation using 2 solid-tip catheters and 1 closed-loop irrigation catheter to assess the extent of thrombus formation on the catheter tip using direct inspection, intracardiac echo, and scanning electron microscopy. One-half of the 110 lesions were delivered using negative charge and the other one-half without charge in a nonrandom fashion. Remarkably, negative charge application showed an “all or none” response with negatively charged applications being completely devoid of any coagulum macroscopically, whereas ~91% of the uncharged catheter tip surface was coated with coagulum; these findings were confirmed on scanning electron microscopy. Importantly, negative charge did not affect electrogram signal amplitude or quality or the ability of the ablation unit to deliver energy. Lesion volume was similar between negative-charge and no-charge catheters. The study is an important step forward in potentially reducing thromboembolic risk in the future.

However, there are a number of caveats worthy of attention. Seventy of 110 lesions were delivered with power settings of 50 W with temperature settings of 65°C to 95°C for ablation duration of 120 s, 30 of 110 lesions with 12 W to 15 W, 80°C for 120 s and 10 of 110 at 80 W, 75°C. These settings are rarely used in clinical practice, and hence conclusions about applicability of the results to human practice presently can be reserved until the experiments are repeated with clinically relevant settings. Also, systemic anticoagulation was not given, which may have overestimated the difference between the groups. Next, the potential proarrhythmic risk of this setup in the human lab remains unknown. Further work is needed to validate the logistics of voltage source and amount of charge required in the human setting, grounding, safety, and interference with electromagnetic or impedance-based mapping systems, and other circuitry in the electrophysiology lab that provide veritable challenges in signal recording and filtering. Although tested with a closed-loop irrigation system, the effect of negative charge on commonly used catheters, for example, an open-irrigated, force-sensing catheter, remains unknown. No information is available about lesion geometry. Lastly, whether this technology translates to meaningful reduction in thromboembolic events will prove challenging due to low event rates. It is very likely that the embolic events attributed solely to thrombus formation on the catheter are even lower, thus posing a greater challenge to demonstrate clinical efficacy of this technology.

There are, however some potential advantages to this system that are not well studied. In thin-walled tissue (e.g., the posterior left atrium) lying in close proximity to structures vulnerable to collateral damage (e.g., esophagus), the lesion geometry associated with nonirrigated catheter tips may offer an advantage. In this case, the maximal hotspot occurs within 1 mm of the endocardial surface and a decreasing thermal gradient occurs in the direction of the epicardium and esophagus, in which case, the maximum diameter of the lesion is at the endocardial surface. Theoretically, with effective cooling by irrigation and power settings being equal, the esophagus would be exposed to much higher temperatures to achieve the same endocardial lesion surface area (**Figure 1B**). It is thus plausible that nonirrigated lesion delivery may allow one to achieve a thin transmural lesion more quickly with relative sparing of the esophagus. Adding negative charge delivery to the catheter may reduce or eliminate the risk of thrombus formation associated with nonirrigated lesions, allowing more controlled applications to the desired level of tissue penetration. In addition, decreasing irrigant flow may save the patient significant fluid volume during the procedure, which has been associated with complications (16). The method could be combined with other novel technologies such as thermal strain imaging (which may allow assessment of depth of lesions) (15) or catheters that allow real-time visualization of lesion formation (17).

In summary, Lim et al. (14) ought to be congratulated for a truly innovative method for reducing or eliminating thrombus formation on catheter tips that is ingenious in its simplicity. This technology has the potential for rapid application to the human lab, possibly at a minimal cost. Most importantly, it has the potential to reduce embolic events, both clinical and silent.

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