Discrepancies Between Catheter Tip and Tissue Temperature in Cooled-Tip Ablation
Relevance to Guiding Left Atrial Ablation

G. Keith Bruce, MD; T. Jared Bunch, MD; Mark A. Milton, MD; Alvaro Sarabanda, MD, PhD; Susan B. Johnson, BS; Douglas L. Packer, MD

Background—It is not known whether catheter tip temperatures with a cooled-tip ablation can be reliably extrapolated to estimate actual tissue temperatures. The relationship between catheter tip temperatures, tissue temperatures, power, and microbubble formation is not known.

Methods and Results—Nine dogs underwent 111 radiofrequency energy deliveries at the pulmonary vein ostia with a cooled-tip catheter. Catheter tip and tissue temperatures were markedly discrepant. Catheter tip temperature plateaus at 36°C to 39°C with increasing power, whereas tissue temperature increases to a mean of 75°C to 110°C at 45 W (maximum temperature >100°C). Seventy-two energy deliveries were performed, titrating power to microbubble formation guided by intracardiac echocardiography. Type I and II microbubble formation occurred in 45 (63%) and 19 (26%) ablations, respectively. Type I microbubble emergence occurred at lower powers (21 ± 8 versus 26 ± 4 W; \(P = 0.05\)), catheter tip temperatures (38 ± 5°C versus 48 ± 10°C; \(P = 0.02\)), and tissue temperatures (65 ± 19°C versus 81 ± 9°C; \(P < 0.001\)) than type II microbubble formation. Maximum impedance decreases during ablation before microbubble formation were less with type I microbubble (20 ± 9 versus 37 ± 11 Ω; \(P < 0.001\)) compared with type II microbubbles. One quarter of type I microbubbles abruptly transitioned to type II microbubbles with significant changes in power or catheter tip temperature. No microbubbles were seen in 19 ablations (26%) despite powers up to 26 ± 9 W and tissue temperatures up to 81 ± 17°C.

Conclusions—Catheter tip and tissue temperatures are markedly discrepant during cooled-tip ablation. Type I and II microbubble formation occurs at overlapping power and catheter tip and tissue temperature ranges. Neither the absence of microbubbles nor the presence of type I microbubble formation ensures against excessive tissue heating. The appearance of microbubbles may indicate possible tissue overheating and signal a need to decrease energy. (Circulation. 2005;112:954-960.)

Key Words: ablation • arrhythmia • atrium • catheter ablation • echocardiography

Advances in radiofrequency catheter ablation have revolutionized the treatment of atrial fibrillation. However, energy delivery can lead to development of pulmonary vein (PV) stenosis, clot, char, and crater formation or to stroke or other peripheral thromboembolic events.1–3 Atrio-esophageal fistulas precipitating air embolus and death have also been reported.4 These adverse events are believed to result from excessive thermal injury5,6 to the PV or atrial wall not reflected by catheter tip temperatures.5,5

Guidance of energy delivery with a cooled-tip, irrigated catheter is difficult because catheter tip temperatures are reduced by continuous tip solution flow.7,8 It is not known whether catheter tip temperatures in this setting can be extrapolated reliably to estimate actual tissue temperatures. In many cases, energy delivery becomes power controlled, and the relationship between power, tip temperature, and tissue temperature has not been established.

Microbubble formation, often observed during a radiofrequency ablation, alternatively has been forwarded as a means of guiding energy delivery.9,10 It has been proposed that power adjustment, guided by direct visualization of this phenomenon, might reduce the risk of PV stenosis and improve long-term cure.9 Intracardiac echocardiography (ICE) has the potential of monitoring lesion formation by direct observation of tissue changes and such microbubble formation during energy delivery.11 Nevertheless, before advocating the guidance of radiofrequency energy delivery by microbubble formation, we must address the precise relationship between catheter tip temperatures, tissue temperatures, power, and microbubble formation. This study was...
undertaken in an in vivo canine model to explore these relationships during cooled-tip, radiofrequency ablation at the PV ostium.

Methods

Animal Preparation and Catheterization

The protocol was approved by the Mayo Foundation Animal Care and Use Committee, and the study followed guidelines from The Biomedical Investigator’s Handbook of Research Using Animal Models. Nine dogs (weight, 30 to 40 kg) were anesthetized with ketamine (10 mg/kg) and diazepam (0.5 mg/kg), intubated, ventilated, and maintained on 1% to 3% isoflurane in room air. Continuous ECG monitoring was established via 5 surface leads. Percutaneous sheaths were placed in the right and left jugular and femoral veins for access and in the left femoral artery for continuous blood pressure monitoring. Transeptal catheterization was performed in a standard fashion under ICE guidance.

ICE Study

ICE was performed to guide transeptal catheterization and ablation catheter placement and to monitor microbubble formation. The 10F, 5.5- to 10-MHz ultrasound catheter with a 4-way, steerable tip was interfaced with an Acuson Sequoia imaging platform. Ultrasound gain settings ranged from −4 to 4 dB. Monitoring during ablation was at 5.5 to 7.5 MHz to best disclose microbubbles. The entire left atrium was examined to allow classification of microbubbles as either type I (scattered) or type II (dense showers). An analysis using a sample volume placed over or near the catheter tip was performed to quantify what was previously qualitatively classified as type I or type II microbubbles. Real-time monitoring was performed during ablation, and the ICE images were analyzed offline to correlate microbubble formation with ablation parameters.

Tissue Temperature Monitoring and Thermocouple Placement

Left- and right-sided thoracotomies were performed with incisions at the fourth or fifth intercostal space. The PVs were dissected to their junction with the left atrium, and thermocouples with radiopaque markers were implanted at the superior and inferior aspects of the orifices of the left superior, left inferior, and right superior PVs. Four to six thermocouples were implanted on the epicardial surface of each PV, typically resulting in 12 to 18 thermocouples implanted per dog. Tissue temperatures were measured during each second of radiofrequency energy application with an accuracy of ±0.42°C using T-type thermocouples (NI4350, National Instruments Corp). The temperature measurement system was calibrated before each ablation by correlation with the animal’s core temperature.

Energy Delivery

Two indifferent ablation electrodes (100 cm²) were placed on the animal’s shaved back. The 4-mm cooled-tip electrode catheter (EP Technologies Inc) was positioned at the ostium of the left superior, left inferior, and right superior PVs immediately overlying the thermocouples, as targeted by biplane fluoroscopy. The tip was flushed with D5W at a flow rate of 36 ± 4 cm/min during energy delivery from a 500-kHz radiofrequency output of a radiofrequency generator (EP Technologies Inc). Energy delivery via this cooled-tip system was power controlled, with up titration from 5 to 45 W. Titration to microbubble formation was performed in a stepwise approach by increasing power in 5-W increments after the tissue temperature measured by the thermocouples reached a plateau. Energy delivery was terminated at 120 seconds regardless of microbubble appearance unless the generator automatically terminated delivery secondary to a sudden, dramatic increase in impedance (ie, an impedance rise).

Results

Power Dependence of Ablation Parameters

Twenty-four PVs were ablated with 111 energy deliveries. The left superior PV orifice was ablated in 9, the left inferior PV orifice in 9, and the right superior PV orifice in 6. Figure 1 shows the typical paradigm used for energy titration with cooled-tip ablation from which data were obtained. Table 1 shows the ablation parameters at specified power levels. Impedance declined modestly to 90 to 95 Ω with increasing powers to 35 W but then increased to >100 Ω with higher powers. Tissue temperatures rose with increasing power delivery up to a mean temperature of 75.3°C at 45 W. However, the catheter tip temperatures increased and then plateaued in the range of 35°C to 39°C over the same increasing power levels. This relationship between tissue and tip temperatures for all animals is shown in Figure 2.

Outcome of Titrating Energy Delivery to Microbubble Formation

Seventy-two radiofrequency energy deliveries were performed via the cooled-tip catheter while specifically titrating energy delivery to microbubble formation. Results are shown in Figure 3. Microbubbles were classified according to a previously described clinical format: type I, limited, scattered microbubbles, and type II, a dense shower of microbubbles. Nineteen ablations (26%) resulted in no microbubble forma-
tion. Type I microbubble formation was seen in 45 (63%) of 72 energy deliveries. Type II microbubble formation occurred with 19 energy deliveries (26%), with 11 of these developing in the setting of preexisting type I microbubble formation and 8 developing de novo without intervening type I microbubbles.

### Ablation Parameters at the Emergence of Type I and II Microbubbles

Table 2 shows the ablation parameters at the initial emergence of microbubbles as shown schematically in Figure 3. Type I microbubble onset occurred earlier in the ablation (44±55 versus 63±30 seconds; \(P=0.03\)), at slightly lower power settings (21±8 versus 26±4 W; \(P=0.05\)), at lower tissue temperatures (65±19°C versus 81±9°C; \(P<0.001\)), and with lower catheter tip temperatures (48±12°C versus 52±3°C; \(P=0.02\)) than type II microbubble onset. The impedance was similar at the initial emergence of both type I and type II microbubbles. During ablation producing either type I or type II microbubbles, the impedance typically decreased to a nadir, then rose immediately before microbubble formation. The maximum impedance decrease from baseline before microbubble formation for ablations resulting in type I microbubbles was 20±9 versus 37±11 Ω seen in those that resulted in type II microbubbles (\(P<0.001\)).

During 11 of the 45 energy deliveries (24%) with successful energy titration to the formation of type I microbubbles, a subsequent abrupt transition to type II microbubble formation was seen. Table 3 shows the ablation parameters associated with this transition. The transition occurred with no significant change in power delivery (20±7 versus 22±2 W; \(P=0.56\)) or catheter tip temperatures (41±7°C versus 42±9°C; \(P=0.50\)). Tissue temperatures trended higher (72±6°C versus 80±10°C; \(P=0.08\)). Impedance significantly increased with the transition (101±17 versus 160±53 Ω; \(P<0.001\)). Marked changes in impedance, either significant decreases before microbubble formation or large increases during type I microbubble formation, appeared predictive of impeding type II microbubble formation.

### Distribution of Temperatures and Power at Microbubble Onset

Figure 4 shows the distribution of microbubble occurrence according to 3 different ablation parameters. Figure 4A shows the appearance of microbubbles according to tissue temperatures. Type II microbubbles did not occur at tissue temperatures <60°C. However, type I microbubble onset occurred over a wide range of tissue temperatures from <40°C to >80°C. Figure 4B shows that type I and II microbubble onset occurred over the entire range of catheter tip temperatures, with a clustering of type I at the lower range (30°C to 45°C) and type II at a higher range (35°C to 50°C). Figure 4C shows the onset of microbubble formation as a function of power. As seen in the relationship between microbubble occurrence and type of microbubble formation during 72 energy deliveries. Type II microbubbles followed formation of type I microbubbles in 11 of 45 ablations (24%). During 8 ablations (11%), type II microbubbles formed spontaneously without precedent type I microbubble formation.
Microbubble Formation

and tip temperatures, type I and II microbubble onset occurred over wide and overlapping power ranges.

Tissue Temperatures in the Absence of Microbubble Formation

In 19 of 72 energy titrations, no microbubble formation occurred despite powers up to 26 ± 9 W (range, 15 to 45 W) and maximum tissue temperatures up to 81 ± 17°C (range, 49°C to 104°C). Maximum power was not reached in all ablations because some titrations took >120 seconds to reach steady state at each power level. Figure 5 illustrates the maximum tissue temperatures obtained in the absence of microbubble formation. During 10 deliveries, maximum tissue temperature was <80°C; during 7 energy deliveries, tissue temperatures were 80°C to 100°C; and during 2 energy deliveries, tissue temperatures were >100°C. The mean power in the absence of microbubble formation was 19 ± 8 W; the mean tissue temperature was 65 ± 16°C; and the mean catheter tip temperature was 37 ± 7°C. The distribution of tissue temperatures during each ablation-second in the absence of microbubble formation was as follows: <60°C in 37% of ablation-seconds, 61°C to 80°C in 42% of ablation-seconds, and >80°C in 21% of ablation-seconds.

Microbubble Patterns and Venographic and Pathological Data

Three of the dogs survived 1 week after single energy deliveries per vein segment. No significant stenosis was seen at 1 week on venographic and pathological analyses in the 3 veins in which type I microbubbles were seen during ablation (tissue temperature at microbubble onset, 35°C to 74°C). Type II microbubbles (without intervening type I microbubbles) were seen in 3 veins during ablation (tissue temperature at microbubble onset, 87°C to 89°C). All 3 veins had either significant stenosis (>70%) or total occlusion at 1-week venography, with marked fibrotic changes of the vein seen at necropsy. Postmortem assessment of the PV ostia revealed good correlation between thermocouple placement and lesions generated in both the acute and chronic animals. Type II microbubbles were associated with adverse PV effects.

Discussion

Key Findings

This study discloses several important findings. First, during cooled-tip ablation, catheter tip temperatures are markedly

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MB indicates microbubble. Values in parentheses are ranges.

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discrepant from tissue temperatures. Although catheter tip temperatures should be lower with “cooled” ablation, the extent of the variance is impressive. Second, type I and type II microbubble formation occurs over wide and overlapping ranges of power and catheter tip temperatures. Third, it is difficult to consistently obtain type I microbubble formation with energy delivery without type II microbubble occurrence before or during type I microbubble formation. Fourth, neither the presence of type I microbubble formation nor the absence of microbubble formation ensures against excessive tissue heating. Fifth, PV stenosis may be heralded by type II microbubble formation.

**Limitations of Standard Ablation**

The success of ablation using radiofrequency energy delivered via standard catheter tips has been limited in part by achievable lesion size. This may be due to limited resistive heating of underlying tissue at the catheter tip–tissue interface related to deliverable power, electrode size, or tissue contact. Resulting conductive heating to achieve a definitive temperature in surrounding myocardium is thereby constrained and further limited by the characteristics of the tissue being ablated. The scar accompanying a myocardial infarction, for example, may limit both contributors to tissue ablation.14,15 Driving conventional delivery systems to higher powers to enhance lesion size is limited by the occurrence of coagulum formation or the impedance rise, with a resulting decrease in power delivery to the myocardium16–18 and the potential for thromboembolic events.

**Cooled-Tip Ablation**

These risks have been tempered by the development and application of larger ablative electrodes and active electrode cooling through internal or external irrigation measures. The ability to create lesions of greater volume and depth with larger-tipped electrodes has been documented in a variety of studies.19–21 It is due to greater tissue contact19 and enhanced convective cooling accompanying the greater electrode–blood pool interface.21 However, larger electrodes have significant variability in their electrode-tissue interface, depending on catheter tip orientation.20,21 In contrast, active cooling has been shown to produce equivalent lesions with energy delivery via smaller electrodes, with less dependence on catheter tip orientation and extrinsic cooling.22

This study confirmed a potential disadvantage of any active ablation tip cooling process. Because electrodes are “cooled” by convective heat loss into the blood pool or cooling solution, catheter tip temperatures as measured at the electrode-myocardial interface were consistently 36°C to 39°C at all power levels. These data further extend available literature to demonstrate and quantify the magnitude of the discrepancy between actual 70°C to 100°C atrial and PV tissue temperatures and catheter tip temperatures at various power levels. This has been demonstrated in thigh muscle preparations23 but not in atrial tissue relevant to the ablation of atrial fibrillation. Although catheter tip temperatures and tissue temperatures are expected to be discrepant with cooled-tip ablation, we found the differences to be marked.

Variation in the time to reach steady-state tissue temperatures at a given power was qualitatively noted and was a function of the amount of tissue heating, as countered by the heat loss to the “system.” This involves a combination of factors such as resistive and conductive heating to the point at

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**Figure 4.**

A. Distribution of microbubble onset according to tissue temperature. Both type I and II microbubbles increased with elevated catheter tip temperatures. B. Distribution of microbubble onset according to catheter tip temperature. Both type I and II microbubbles increased with elevated tissue temperatures. C. Distribution of microbubble onset according to power. Both type I and II microbubbles increased with increased power, but ceiling was reached at 30 W.

**Figure 5.** Tissue temperatures in absence of microbubble (MB) formation.
which temperature is measured, as counterbalanced by such factors as convective heat loss. With robust convective cooling at the catheter tip or into lung tissue on the other side of the ablation, additional time may be required to reach steady state.

**Microbubbles and Ablation**

In this study, microbubble imaging was optimized with 5.5- to 7.5-MHz range phased-array ultrasound visualization. This range matched the characteristics of the ultrasound beam to the microbubble size. Imaging at higher frequencies occasionally missed microbubble formation. This study also exposes the difficulty in reliably titrating power to produce a favorable type of microbubbles. We found it difficult to obtain type I microbubble formation without type II microbubble occurrence. This difficulty was demonstrated by (1) occasional extreme tissue temperature generation during type I microbubble appearance, (2) inadvertent type II microbubble formation during 24% of energy deliveries with type I microbubbles at similar instantaneous levels of power, (3) the appearance of type I and type II microbubble formation over wide and overlapping ranges of power and catheter tip temperatures, and (4) the absence of microbubbles in 26% of energy deliveries. Maximum tissue temperatures $>80^\circ$C were documented in almost half of the energy titrations when no microbubble formation occurred.

These findings indicate that microbubble formation is not a straightforward surrogate for tissue heating. The absence of microbubble formation clearly does not indicate that tissue heating is inadequate or that the power level should be increased, nor does the presence of type I microbubbles indicate safe tissue heating. This marker is fairly specific for tissue heating as judged by tissue temperatures but is not a routinely sensitive one. These data suggest that type I and type II microbubbles represent different phenomena. Specifically, type I microbubbles are noted to occur over the entire spectrum of tissue temperatures, whereas type II microbubbles occurred only at tissue temperatures $>60^\circ$C. Type I microbubbles may represent an electrolytic phenomenon, whereas type II microbubbles suggest steam formation with associated tissue disruption and impedance rises. Further elucidation of the mechanisms of microbubble formation requires additional studies.

**Study Limitations**

Several limitations should be kept in mind when these data are interpreted. This study was performed in an animal model of ablation at the venoatrial junction. Different catheter tip–tissue temperature relationships could prevail at other atrial ablation sites outside brisk PV blood flow. This study also tested a specific closed-loop, cooled-tip catheter, which may or may not reflect tissue heating with other open irrigation systems. Additional studies are required to establish the relationship between delivered power, tip temperature, and tissue temperature with those systems. Those studies will be difficult, however, because true microbubble formation can be obscured by the tip irrigation into the left atrium.

The thickness of the LA wall and the distance between the thermocouples and catheter tip are other possible issues affecting the accuracy with which the temperature, as measured by thermocouples, reflects the tissue temperatures at the electrode tip–endocardial tissue interface. However, these study characteristics would result, if anything, in an underestimation of actual tissue temperatures. Despite this potential limitation, there were marked tissue and catheter tip temperature discrepancies. In addition, an underestimation of actual tissue temperature does not affect the underlying study conclusion that tissue overheating can occur without reflection in the catheter tip temperature. This study also was not designed to control for varying mechanical pressures at the catheter tip–endocardial interface and other factors that might influence both tissue temperatures and microbubble formation.

Each ablation was directed at different thermocouples within a single vein ostium. We therefore cannot exclude the possibility of lesion overlap. However, if an impedance rise and/or type II microbubble formation occurred, additional energy deliveries were not made at that site secondary to concern of possible altered thermodynamics related to heat-mediated tissue changes. The study fails to produce exact recommendations for optimal power settings for cooled-tip catheter radiofrequency ablation but does strike a cautionary note against driving ablation to excessive tissue temperatures.

At this point, the extent to which microbubbles and/or excessive tissue temperatures may translate into clinically relevant complications such as PV stenosis, atro-esophageal fistulas, and thromboembolic events is unclear. However, the occurrence of PV stenosis at 1 week in these animals supports a relationship between type II microbubbles and complications related to ablation. Additional studies are required to match these findings with the actual occurrence of untoward sequelae of high-temperature ablation.

**Clinical Implications**

These findings of markedly discrepant catheter tip and tissue temperatures and the variability of type I and II microbubble occurrence are of importance in the clinical ablation arena. Titrating radiofrequency energy delivery in the left atrium or at the PV ostium to produce type I microbubble formation with a cooled-tip catheter is difficult to accomplish reproducibly, and type II microbubbles may occur without ICE warning. Wide swings in impedance may be a better predictor of this process. Microbubble formation is also a more complicated phenomenon than simply a function of tissue heating. Therefore, instead of being a goal of energy delivery, type I microbubble formation should be considered an indication of possible tissue overheating, which should prompt a rapid decrease in or discontinuation of energy delivery. The appearance of type I microbubbles or the absence of this phenomenon may give a false sense of assurance that significant tissue overheating is not occurring. Obviously, additional studies are required to produce a clearer understanding of the mechanisms of microbubble formation and to develop alternative means of assessing tissue temperature and to guide ablation.

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Disclosure

Dr Packer has received significant unrestricted research grant support from several catheter manufacturers, but has no equity interest in these companies.

References

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