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Continuous ablation improves lesion maturation compared with intermittent ablation strategies

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Abstract

Background: Interrupted ablation is increasingly proposed as part of high-power short-duration radiofrequency ablation (RFA) strategies and may also result from loss of contact from respiratory patterns or cardiac motion. To study the extent that ablation interruption affects lesions.

Methods: In ex vivo and in vivo experiments, lesion characteristics and tissue temperatures were compared between continuous (group 1) and interrupted (groups 2 and 3) RFA with equal total ablation duration and contact force. Extended duration ablation lesions were also characterized from 1 to 5 minutes.

Results: In the ex vivo study, continuous RFA (group 1) produced larger total lesion volumes compared with each interrupted ablation lesion group (273.8 ± 36.5 vs 205.1 ± 34.2 vs 174.3 ± 32.3 mm³, all $P < .001$). Peak temperatures for group 1 were higher at 3 and 5 mm than groups 2 and 3. In vivo, continuous ablation resulted in larger lesions, greater lesion depths, and higher tissue temperatures. Longer ablation durations created larger lesion volumes and increased lesion depths. However, after 3 minutes of ablation, the rate of lesion volume, and depth formation decreased.

Conclusions: Continuous RFA delivery resulted in larger and deeper lesions with higher tissue temperatures compared with interrupted ablation. This study may have implications for high-power short duration ablation strategies, motivates strategies to reduce variations in ablation delivery, and provides an upper limit for ablation duration beyond which power delivery has diminishing returns.

Keywords

ablation biophysics; arrhythmia; catheter ablation; contact; interrupted; lesion formation

1 | INTRODUCTION

Effective ablation for cardiac arrhythmias requires the durable achievement of myocardial cell death at specific sites originating or enabling conduction of abnormal electrical activity while avoiding damage to extracardiac structures. Interrupted radiofrequency ablation (RFA) has been increasingly proposed for high-power short duration ablation strategies,¹ and may occur due to cardiac or respiratory motion.² However, it is unstudied how the interruption of RFA might affect lesion characteristics and tissue temperatures, which directly impact efficacy and procedural risk due to the impact on noncardiac structures.

Technologies have been developed to control and enhance energy delivery such as contact-sensing technology,³ irrigation with saline⁴ or hypotonic solutions,⁵ and algorithms aimed at estimating lesion size.⁶ However, RFA lesion characteristics may change when delivered to the myocardium that has been previously ablated due to tissue edema,⁷ such as when RFA is interrupted and reinitiated or with intermittent contact due to respiratory or cardiac motion.² Variability in lesion characteristics may decrease efficacy via inadequate tissue penetration or by leaving discontinuities in lesion sets and may increase procedural risk by delivering energy to non-pathological structures. We set out to evaluate the hypothesis that ablation lesion characteristics will significantly differ based on continuity of ablation despite equal cumulative ablation duration and contact force and that lesion creation quickly asymptotes with extended duration ablation.

We tested our hypothesis in controlled ex vivo and in vivo studies by applying ablation continuously or with varying levels of interruption to evaluate the resulting lesion characteristics on pathologic evaluation.

2 | METHODS

2.1 | Ex vivo model

Experimental protocols were approved by IACUC at the University of Colorado. An ex vivo model was used, as previously described in detail.^{8,9} Viable bovine myocardium was placed on a submersible load cell in a circulating saline bath at 37°C. The fluid was circulated in the saline bath at a rate of 5 L/min using a perfusion pump designed for cardiac bypass. Energy application and contact force were standardized by ensuring equal force (10 g) applied to the myocardial tissue as measured by the submersible load cell. An open-irrigated (4 mm) ablation catheter (Biosense Webster, Diamond Bar, CA) was oriented perpendicular to myocardium using a deflectable sheath (Abbott, Minneapolis, MN) during ablation in all cases. All ablation applications were performed on the endocardial surface of the bovine myocardial preparation with 10 g of force and 50 W power.

2.2 | Intermittent RFA

In the ex vivo bovine model, three groups (N = 30 each) were created using continuous and intermittent RF energy application (Figure 1). Sixty seconds of total RF energy application was applied in all groups. In group 1, RF was applied for 60 seconds continuously. In group 2, RF was applied for 30 seconds twice with a 30 seconds intervening pause. In group 3, RF was applied for 15 seconds four times with 15 seconds intervening pauses.

2.3 | Extended duration RFA

In the ex vivo bovine model, 50 W RFA was delivered to bovine myocardial tissue under 10 g of force for durations of 1, 2, 3, and 5 minutes. Lesion characteristics of volume and depth were analyzed by sectioning tissue and measurement with electronic calipers. Absolute measurements and rates of change for volume and depth were calculated (see Section 2.5 below).

2.4 | In vivo model

An open-chest murine model was used as previously described.¹⁰ In short, the animal is anesthetized, and sternotomy is created. The pericardium is opened to expose the heart and a customized clamp is used for exposure and grounding electrode. One RF lesion was delivered in a unipolar configuration to the epicardial free wall of the left ventricle using a custom-made, nonirrigated 2-mm tip catheter. The energy was applied at 10 W in all cases. Three groups (total N = 35) were created using continuous and intermittent RF energy application in an equivalent fashion to the ex vivo model (Figure 1).

2.5 | Ablation lesion volume measurement

Tissues were analyzed using a digital micrometer after sectioning. For each lesion, volumes were calculated using the equation for an oblate ellipsoid as described and validated in previous studies.^{8,9} Measurements required for this calculation included (a) maximum depth, (b) maximum diameter, (c) depth at maximum diameter, and (d) lesion surface diameter. The volume of an ellipsoid ablation lesion was calculated as:

$$\text{Lesion volume} = \left[0.75\pi \left(\frac{B}{2} \right)^2 (A - C) \right] - \left[0.25\pi \left(\frac{D}{2} \right)^2 (A - 2C) \right].$$

2.6 | Tissue temperature analysis

T-type thermocouple wires were inserted horizontally into the myocardium at 3 and 5 mm depths perpendicularly to the ablation surface. Continuous thermocouple analog inputs were converted to digital signals using LabView software (version 7.0). Temperature and temperature rise over time were sampled during RF application at a rate of 5 Hz. Peak tissue temperature was defined as the maximum temperature reading during RF application. The area under the temperature curve was calculated as a temperature-time integral for all lesions. RF applications that generated steam pops were excluded from temperature curve analysis. Steam pops were defined by visual steam bubble formation with associated tactile and audible cavitation and collapse.

2.7 | Statistical analysis

Statistical analyses were performed using IBM SPSS version 24.0 (IBM SPSS Statistics; IBM Corporation, Armonk, NY). χ^2 Test used for dichotomous comparisons in lesion characteristics from groups 1 through 3. *t* Tests were used to compare continuous variables (lesion characteristics, impedances, and temperatures) between different groups with equal variances within the groups not assumed. *P* values are from paired comparisons within each group vs each other group. Statistical significance was defined as a *P* value less than .05.

3 | RESULTS

3.1 | Ex vivo intermittent ablation

Table 1 describes the ex vivo myocardial ablation lesion characteristics after energy was applied at 50 W and 10 g among the three groups. Continuous RFA (group 1) produced larger total lesion volumes compared with each interrupted ablation lesion group (273.8 ± 36.5 vs 205.1 ± 34.2 vs 174.3 ± 32.3 mm³, all $P < .001$). In addition, ablation lesions in group 1 had larger average maximum depths compared with each of group 2 and group 3 (5.7 ± 0.4 vs 5.4 ± 0.4 , $P = .003$ and 5.7 ± 0.4 vs 5.1 ± 0.3 , $P < .001$). There were four steam pops in the continuous group and none in groups 2 or 3 ($P = \text{NS}$). Peak temperatures for lesions in group 1 were significantly higher at 3- and 5-mm depth compared with groups 2 and 3. Rate of temperature rise from 50°C to 53°C during the final ablation application at 5-mm depth was 0.52, 0.48, and 0.32 degrees per second in groups 1, 2, and 3, respectively. Temperature trends over time are displayed in Figure 2.

3.2 | Ex vivo extended ablation duration

Open irrigated RFA had significantly greater lesion depth and volumes at increasing ablation duration (Figure 3A). The rate of lesion volume formation was greatest for the first minute and was then maintained nearly constant at approximately 28% of the volume from the initial minute for the next 4 minutes (256.1 vs 70.75 mm³/min) (Figure 3B). The rate of lesion depth formation was greatest for the first minute and decreased to 12.5% of the initial minute between minute 1 and 3 and further decreased to 6.25% of the first minute in the fifth minute of energy delivery (6.5 vs. 0.7 mm/min vs 0.35 mm/min) (Figure 3C). There were no steam pops during energy delivery for any of the lesions. Full characteristics for extended ablation duration are provided in Table 3.

3.3 | In vivo intermittent ablation

The total RF duration was the same across the three groups (60 seconds). Continuous ablation resulted in larger lesion volumes compared with interrupted ablation (Table 2). Similarly, lesion depth was greater in continuous vs interrupted ablation with 15-second ablations (group 3) but not for 30-second lesions (group 2). No steam pops were observed during ablation in any group. Interrupted ablation resulted in 48% of the lesion volume between group 1 and group 3 with a reduction of 32% in depth (Figure 4).

4 | DISCUSSION

This study revealed that continuous RFA delivery resulted in larger and deeper lesions with higher tissue temperatures compared with interrupted delivery of ablation. Multiple factors may influence the lesion characteristics between continuous and interrupted delivery of ablation including conductive heat diffusion, electrode-tissue interface changes, and changes in tissue characteristics such as edema. This has implications for clinical practice, particularly when deeper lesions are required, such as midmyocardial substrates in the ventricle or when safety for surrounding noncardiac structures is desired such as in the posterior left atrium. Tissue edema has previously been shown by near field ultrasound to develop with short latency during ablation and would be expected to have fully developed

within the pause of groups 2 and 3.⁷ Our results show that interruption of ablation decreases the volume of ablation more significantly than it decreases depth. Furthermore, the decreasing rate of temperature rise in the final ablation lesion application in groups 1 to 3 suggests that changes in tissue due to prior ablation (such as edema) may limit subsequent ablation lesions. Interrupted ablation due to factors such as esophageal heating in the posterior left atrium may impact lesion maturation and/or durability, due to this effect on lesion characteristics.

Acute reconnection of the pulmonary veins after PVI may be more common during significant respiratory ventilation and at sites with greater contact force variability,² suggesting that strategies such as apnea, jet ventilation,¹¹ or reduced tidal volumes¹² may improve ablation success. Similarly, adherence of the catheter to tissue (for cryotherapy)¹³ or catheter control techniques such as robotic guide catheters¹⁴ and magnetic catheter manipulation¹⁵ may be used to avoid interruption of ablation. Finally, in-line contact force controllers may be used to fine-tune contact force with manual catheter manipulation.¹⁶ Our results support the investigation of such strategies to maintain continuous energy delivery during RFA.

Extended duration ablation achieved lesions of larger volume and greater depth; however, the rate of lesion volume and depth formation decreased with times extending beyond 1 minute. Lesion volume creation after 1 minute was roughly linear and occurred at a much lower rate than the first minute. Lesion depth creation plateaued much more quickly. The reduced rate of lesion volume and depth creation suggests that the efficacy of additional energy applications is low while increasing the risk of steam pops. This was especially pronounced for depth creation, which would be relevant in the ablation of ventricular arrhythmia sites of origin in thicker regions such as the LV crux or summit. Although not statistically significant in our study, the risk of steam pops is expected to increase with longer durations and higher tissue temperatures. Desired lesion volume and depth should be counterbalanced with safety based on anatomy and arrhythmia substrate. When ablating at high powers, regardless of duration, it is important to monitor lesion formation to prevent steam pops.¹⁷

The effect of intermittent ablation due to respiratory or cardiac motion may be less pronounced with high-power short duration ablation since volume creation is more rapid at higher power, although this may affect lesion dimensions.¹ In situations where interruption of RF energy delivery is likely and wide-based, shallow lesions are desired, this technique may be considered. Previously, we showed that drag lesions were significantly larger than point-by-point linear lesions with controlled RF time and power.⁸ This study supports that difference in lesions characteristics is largely due to intermittent RF energy delivery.

4.1 | Limitations

Limitations of this study include models with a lack of significant fibrosis, which may alter lesion geometry and limit the applicability of these findings to atrial tissue and idiopathic ventricular arrhythmias. The study assessed a range of intermittent ablation application frequencies (from continuous to 15 seconds intervals), which is in the range of respiratory mechanics; however, we did not assess high-frequency interruptions such as that due to

cardiac motion. Finally, the data is limited by immediate lesion assessment rather than long term lesion assessment in which the recovery of tissue or conduction may occur. Epicardial ablation in the in vivo model and endocardial ablation in the ex vivo model does not fully recapitulate in vivo endocardial ablation; however, the in vivo model is designed to represent the influence of edema or ventricular perfusion on lesion characteristics and the ex vivo model represents the effect of convective heat loss and ambient fluid circulation. Future clinical data in a survival porcine model may be required to evaluate long term recovery of conduction with intermittent and continuous endocardial ablation.

5 | CONCLUSIONS

Continuous RF energy delivery resulted in larger and deeper lesions with higher tissue temperatures compared with interrupted delivery of ablation. This study supports strategies that are aimed at reducing the variability of contact to deliver effective ablative therapy and further suggests that extended duration ablation lesions may have diminishing returns. Longer ablation durations created larger lesion volumes and increased lesion depths. However, after 3 minutes of ablation, the rate of lesion volume and depth formation decreased. This has implications for clinical practice, particularly when targeting deep, midmyocardial circuits in the ventricle.

Disclosures:

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FIGURE 1.

Intermittent RF ablation groups. In group 1, continuous ablation (black) was applied for 60 seconds without interruption. In group 2, ablation was applied for 30 seconds two times, interrupted by a 30-second pause (white). In group 3, the energy was applied for 15 seconds four times with three intervening pauses. RF, radiofrequency

FIGURE 2.

Peak tissue temperatures at 3 and 5 mm with continuous vs interrupted energy delivery. Continuous temperature recording was conducted in bovine myocardium at 3 mm (solid lines) and 5 mm (dashed lines) from the ablation electrode. Group 1 (red) had the fastest rise and greatest maximum temperature at 3 and 5 mm. Groups 2 (yellow) and 3 (blue) showed decreased rates of temperature rise with continued ablation as well as reduced maximum tissue temperatures at 3 and 5 mm

FIGURE 3.

Lesion characteristics with extended ablation. A, Representative gross pathologic sections of ex vivo bovine ablation lesions are shown for extended ablation at 1, 2, 3, and 5 minutes. B, Lesion volume increases rapidly for the first 1 minute and then rises linearly with extended duration of ablation. C, Lesion depth creation quickly plateaus after 1 minute of ablation despite linearly increasing volume

FIGURE 4.

In vivo myocardial ablation lesions. Representative images are shown for in vivo murine epicardial ablation lesions. Continuous ablation (group 1, left) resulted in larger ablation lesions compared with interrupted ablation (groups 2 and 3, middle and right)

TABLE 1
Ex vivo myocardial ablation lesion characteristics after energy applied at 50 W and 10 g of force

	Group 1 (N = 30)	Group 2 (N = 30)	Group 3 (N = 30)	1 vs2 P value	2 vs3 P value	1 vs3 P value
Maximum depth, mm	5.7 ± 0.4	5.4 ± 0.4	5.1 ± 0.3	.003	<.001	<.001
Maximum diameter, mm	11.0 ± 0.6	10.3 ± 0.8	10.0 ± 0.8	<.001	...	<.001
Max surface diameter, mm	7.8 ± 0.8	7.3 ± 0.9	6.4 ± 0.5	<.001	<.001	<.001
Volume, mm ³	273.8 ± 36.5	205.1 ± 34.2	174.3 ± 32.3	<.001	<.001	<.001
Initial impedance	102 ± 14	106 ± 16	102 ± 6	...	...	...
Final impedance, Ω	88 ± 16	89 ± 17	86 ± 5	...	...	...
Impedance reduction, Ω	14 ± 7	16 ± 3	16 ± 3	...	...	...
Peak temperature 3 mm, °C	73.0 ± 5.1	66.4 ± 7.0	59.7 ± 7.2	.007	.016	<.001
Peak temperature 5 mm, °C	64.0 ± 4.5	58.2 ± 5.2	53.0 ± 5.4	.003	.012	<.001

TABLE 2

In vivo myocardial ablation lesion characteristics after energy applied at 10 W

	Group 1 (N=11)	Group 2 (N=12)	Group 3 (N=12)	1 vs 2 P value	1 vs 3 P value
Maximum depth, mm	2.2 ± 0.7	1.8 ± 0.6	1.5 ± 0.5	...	<.05
Surface diameter, mm	6.2 ± 0.4	5.9 ± 0.4	5.3 ± 0.6	...	<.05
Volume, mm ³	36.9 ± 13.6	26.7 ± 8.3	19.1 ± 10.0	<.05	<.05
Initial impedance	214 ± 117	244 ± 100	291 ± 138	...	...
Final impedance, Ω	185 ± 116	210 ± 101	241 ± 129	...	...
Impedance reduction, Ω	29 ± 2	34 ± 6	50 ± 30	...	...
Peak temperature, °C	51 ± 4	50 ± 4	47 ± 4	...	<.05

TABLE 3
Ex vivo myocardial ablation lesion characteristics after extended duration radiofrequency application

	1 min	2 min	3 min	5 min	1 vs2 P value	2 vs3 P value	3 vs5 P value
Maximum depth, mm	5.6 ± 0.4	6.3 ± 0.9	7.0 ± 0.6	7.7 ± 0.5	<0.001	<0.001	<0.001
Maximum diameter, mm	10.8 ± 0.8	11.1 ± 1.6	11.8 ± 1.1	13.2 ± 1.0	...	...	<0.001
Max surface diameter, mm	7.1 ± 0.6	8.0 ± 0.5	7.6 ± 0.7	7.6 ± 0.7	<0.001	0.016	0.955
Volume, mm ³	256.1 ± 49.7	330.7 ± 143.8	406.4 ± 119.5	539.1 ± 100.2	0.011	0.031	<0.001
Initial impedance	138 ± 21	137 ± 6	139 ± 10	138 ± 6	...	...	...
Final impedance, Ω	122 ± 23	122 ± 8	127 ± 11	125 ± 5	...	0.04	...
Impedance reduction, Ω	17 ± 5	15 ± 7	13 ± 5	13 ± 5	...	...	...
Peak temperature (tip), °C	41 ± 2	42 ± 2	43 ± 1	43 ± 2	0.011	...	...
Steam pops	0	0	0	0	...	...	...