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BASIC SCIENCE

Bipolar ablation for deep intra-myocardial circuits: human *ex vivo* development and *in vivo* experience

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Aims Current conventional ablation strategies for ventricular tachycardia (VT) aim to interrupt reentrant circuits by creating ablation lesions. However, the critical components of reentrant VT circuits may be located at deep intramural sites. We hypothesized that bipolar ablations would create deeper lesions than unipolar ablation in human hearts.

Methods and results Ablation was performed on nine explanted human hearts at the time of transplantation. Following explant, the hearts were perfused by using a Langendorff perfusion setup. For bipolar ablation, the endocardial catheter was connected to the generator as the active electrode and the epicardial catheter as the return electrode. Unipolar ablation was performed at 50 W with irrigation of 25 mL/min, with temperature limit of 50°C. Bipolar ablation was performed with the same settings. Subsequently, in a patient with an incessant septal VT, catheters were positioned on the septum from both the ventricles and radiofrequency was delivered with 40 W. In the explanted hearts, there were a total of nine unipolar ablations and four bipolar ablations. The lesion depth was greater with bipolar ablation, 14.8 vs. 6.1 mm ($P < 0.01$), but the width was not different (9.8 vs. 7.8 mm). All bipolar lesions achieved transmurality in contrast to the unipolar ablations. In the patient with a septal focus, bipolar ablation resulted in termination of VT with no inducible VTs.

Conclusion By using a bipolar ablation technique, we have demonstrated the creation of significantly deeper lesions without increasing the lesion width, compared with standard ablation. Further clinical trials are warranted to detail the risks of this technique.

Keywords Bipolar ablation • Ventricular tachycardia • Langendorff perfusion

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Background

Catheter ablation of post-infarction ventricular tachycardia (VT) relies on the interruption of one or more critical reentry circuits, most frequently by radiofrequency (RF) ablation. Irrigated RF catheter ablation has allowed for greater power delivery without coagulum formation and increased lesion depth.[1] However, procedural failure to eliminate all inducible VT, as well as recurrent VT after RF ablation continue to be a significant limitation and obstacle to the advancement of this therapy.[2,3] Ventricular tachycardia involving the interventricular septum (IVS) is relatively frequent in post-infarction myocardial ischaemia[4] as well as in non-ischaemic dilated cardiomyopathy.[5] Tachycardias involving the IVS have special anatomical considerations, including dual blood supply (left anterior descending branch of the left coronary artery and right coronary artery), the location of the conduction system, and the possibility of true mid-myocardial septal scars. This combination of factors may influence the outcome of ablation and may account for a significant number of ablation failures and recurrences. For example, the risk of damaging the conduction system may impose constraints on the delivery of therapy for some VT originating from the IVS. Furthermore, the inability to create truly transmural lesions across the IVS (hence not reaching critical intramural areas), even with the use of irrigated catheters, has been identified as a cause of ablation failure.[4–7] Sivagangabalan *et al.*,[8] using a chronic

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What's new?

- First study of the lesion morphology during human bipolar ablation.
- Bipolar radiofrequency ablation lesions in human myopathic hearts are deeper, but not wider than standard unipolar lesions.
- Bipolar ablation may be suited for deep intra-myocardial circuits, not accessible with unipolar ablation.
- Bipolar ablation may be an essential part of the toolkit for ablation of septal and mid-myocardial ventricular tachycardia circuits.

ovine infarct model, have previously demonstrated that septal VTs typically have a common intramural isthmus capable of exit on either side of the septum, and ablation was frequently necessary on both sides of the septum to render the tachycardia non-inducible.

Experimental models have demonstrated that IVS lesion transmurality can be achieved more readily with dual catheter bipolar ablation than with sequential unipolar ablation.[9,10] Despite the success of bipolar ablation both *in vitro* and *in vivo* animal studies, there has been limited demonstration of its application in humans.[11] In addition, there has been limited clinical evaluation of the morphology and depth of the lesions in human hearts. In the clinical setting, it would be expected that the septal substrate involved various degrees of fibrosis and hypertrophy, not encountered in the animal studies, thus, it is crucial to demonstrate lesion depth in hearts with cardiac disease that would be the targets for this technique. Thus, we evaluated whether transmural ablation lesions could be created with a two catheter bipolar ablation configuration in hypertrophied and fibrosed human hearts *ex vivo* in a human Langendorff model. We sequentially translated this expertise to a case of a patient with previous failed standard single catheter ablation for a septal VT; this was successfully targeted with bipolar ablation.

Methods

In vitro experiments

The experimental protocol was approved by the University Health Network ethics committee and the informed consent was obtained from each patient. Nine human hearts were obtained at the time of cardiac transplantation. Following explant, the coronary arteries were selectively cannulated and the hearts perfused by using a modified Langendorff perfusion setup. The hearts were placed in circulating Tyrode's solution to mimic chamber blood flow and were paced by epicardial electrodes at a cycle length (CL) of 800 ms. Unipolar and bipolar ablation was performed at the basal left ventricular (LV) free wall at sites of maximal thickness. Catheters were aligned endocardially and epicardially. The endocardial catheter was connected to the RF generator as the active electrode with the epicardial catheter as the return electrode. A custom switch box allowed measurement from the distal thermocouple from each catheter, allowing the temperatures from the tip of both catheters, as well as bipolar impedance and power to be logged for each ablation. Both catheters were positioned parallel to the myocardium and stabilized by a single operator. Irrigated (25 mL/min) bipolar ablation was performed at 50 W with temperature control from both LV and right ventricular (RV) catheters, power limiting if either temperature exceeded 50°C. The unipolar ablations were performed in a similar manner, except the return electrode was an indifferent electrode. The power and temperature control settings were identical. Each ablation was performed for 60 s. A bipolar ablation was performed on each of the four hearts assigned to the bipolar ablation, whereas a total of nine unipolar ablations were performed on the five hearts assigned to the unipolar group.

Statistical analysis

Values are presented as means ± standard deviation, except for ablation parameters; temperature, power, and impedance are presented with the range. The maximal lesion depth and width was estimated for each lesion by direct measurements on the tissue (*Figure 1*). An independent sample *t*-test was used for comparison between the unipolar and the bipolar ablation groups. A $P < 0.05$ was considered statistically significant.

Results

In vitro study results

In the explanted hearts, there were a total of nine unipolar ablations and four bipolar ablations. The lesion depth was greater with bipolar

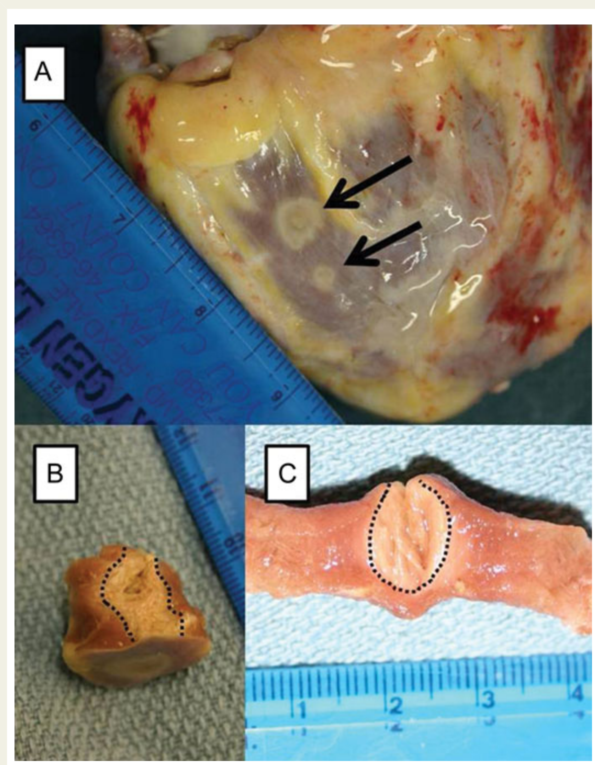

Figure 1 (*A*) An example of two unipolar ablation lesions can be clearly seen on the epicardial surface (arrows). (*B*) A cylinder containing a bipolar ablation lesion has been cut out to demonstrate the transmural nature of the lesion. For comparison, (*C*) shows a not quite transmural lesion from a unipolar ablation in a thinner portion of myocardium. The lesion has been circled with a dotted line for clarity.

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ablation, 14.8 ± 0.5 vs. 6.1 ± 1.7 mm ($P < 0.01$), but the width was not different (9.8 ± 1.9 vs. 7.8 ± 3.4 mm, P = ns). All bipolar lesions achieved transmurality in contrast to the unipolar ablations (*Figure 1*). For the bipolar ablations, the average temperature of the active catheter was 41°C (37–46°C) and the temperature of the return catheter electrode was 40°C (37–49°C). The average power was 41 W (36–45 W) and the impedance 97 Ω (81–115 Ω).

Clinical case presentation and procedural details

The patient is a 56-year-old male with ischaemic cardiomyopathy in the setting of peripheral vascular disease, hypertension, hyperlipidaemia, and hypothyroidism.

His medical history was significant for myocardial infarction in 1989 with subsequent bypass surgery in 1990. A prophylactic implantable cardioverter-defibrillator (ICD) was implanted in 2002. His first presentation with ventricular arrhythmia was in November 2009 when he presented with two appropriate shocks for ventricular fibrillation, and then another shock for VT in 2010. In July 2011, he developed increasing angina, and underwent coronary angiography which was complicated by VT and another ICD discharge, despite treatment with mexiletine and amiodarone. The patient was not deemed suitable for revascularization. The possibility of performing ethanol ablation was abandoned due to the poor LV function and unsuitable anatomy.

There were two clinical tachycardia morphologies, both with left bundle branch block morphology. Due to the extensive coronary artery disease, the arrhythmia was poorly tolerated.

Ventricular tachycardia ablation was attempted initially in August 2011. During the electrophysiological (EP) study, four VTs with CL of 269–446 ms were readily induced. Activation mapping of the LV endocardium during the slowest VT morphology revealed an extensive area of mid-diastolic and pre-systolic potentials in addition to fractionated electrocardiograms between the mitral annulus and the inferior wall close to the IVS. Concealed entrainment was demonstrated in this region, with long stimulus to QRS intervals, suggestive of an entry site. After several ablations were performed from both sides of the IVS, the patient was still inducible in tachycardia and the procedure was abandoned. During the following 3 months, the patient presented with frequent episodes of tachycardia necessitating antitachycardia pacing and defibrillation from the device. However, as the rate was substantially slower, the device frequently did not detect the arrhythmia. Despite the slower rate, the patient experienced angina and hypotension during VT.

The patient was taken to the EP lab for a second procedure while in incessant slow VT. Activation mapping of the stable VT from the RV endocardium revealed signals that preceded the surface QRS electrocardiograms by as much as 48 ms, with concealed entrainment with optimal post-pacing intervals. Multiple ablations in the RV IVS resulted only in slowing in the CL to 682 ms, but not termination. At this point, the decision was made to attempt overdrive suppression in atrial demand mode (AAI), by using his ICD. This was successful, with a conducted QRS width of 95 ms. Unfortunately, the VT accelerated to over 90 per minute, requiring aggressive pace termination.

Because of intolerable symptoms, presumably due to ischaemia, the haemodynamic alteration associated with this slow VT, and the loss of atrioventricular synchrony, the patient was brought back 2 weeks later for a third ablation. This was planned a priori as a biventricular endocardial ablation. Prior to the procedure, the thickness of the IVS was measured at 11 mm by an echocardiogram. Ventricular tachycardia with a CL of 684 ms was induced with programmed ventricular stimulation and the morphology was identical to the one left during the previous procedure. Two ablation catheters (St Jude IBI Cool-Path Irrigated) were positioned on both sides of the IVS (*Figure 2*) and the post-pacing intervals following entrainment were optimal from both LV and RV septal endocardium. The RV signals preceded the left-sided signals by 40 ms (*Figure 3*). Ablation was initiated at 20 W and titrated up to 40 W, with a temperature limit of 65°C and the flow rate was maintained at 30 cc/min during ablation. The VT terminated when the power was increased to 40 W, during the fifth RF application (*Figure 3*). A total of nine bipolar ablation lesions were delivered across the septum. The clinical VT could not be re-induced during programmed stimulation after the ablation. However, a much faster and haemodynamically unstable VT (CL = 337 ms) was induced, but not targeted for ablation, hence no further ablation was performed. The patient had some recurrences of VT during the first months after ablation, but at 1-year follow-up he is without symptomatic or sustained arrhythmias and is currently doing well on the same antiarrhythmic medications as pre-ablation (amiodarone and mexiletine).

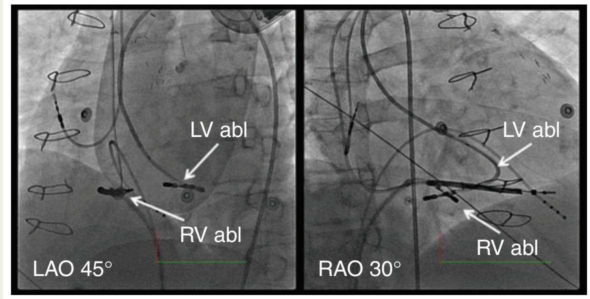

Figure 2 Fluoroscopic image of the catheter setup in left anterior oblique 45° and right anterior oblique 30° projections which shows the close approximation of the ablation catheters on the intraventricular septum. RV abl, right ventricular ablation catheter; LV abl, left ventricular ablation catheter; LAO, left anterior oblique; RAO, right anterior oblique.

Discussion

In diseased human hearts that often have thickened ventricular myocardium, we have demonstrated here, that a single RF generator, two catheter bipolar ablation technique is feasible and produces greater lesion depth than standard unipolar ablation. Most importantly, this is the initial pathological description in humans that transmural ablation lesions can be achieved across areas of thick and scarred myocardium with a *two catheter, single RF generator* bipolar ablation. Such a strategy warrants consideration as it presents an option for greater lesion depth by using currently existing technology available to electrophysiologists.

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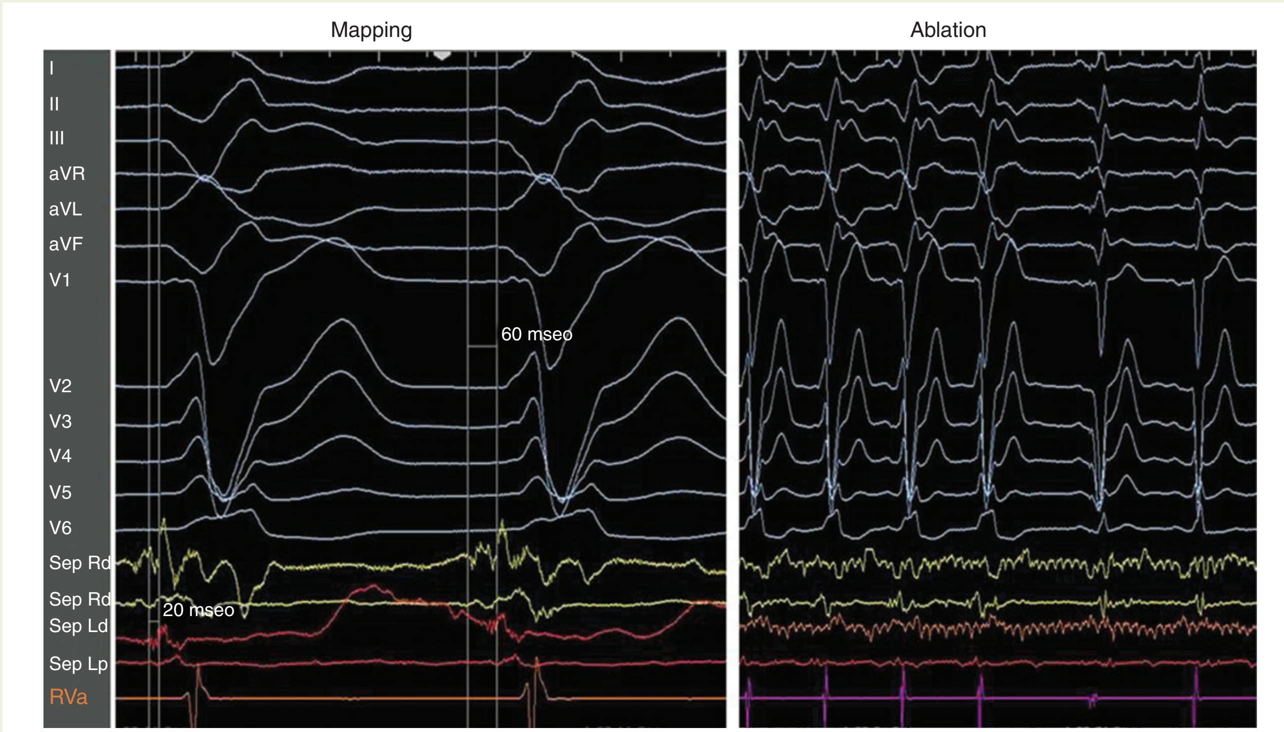

Figure 3 The electrocardiograms (EGMs) from the successful site during mapping. The right ventricular signal is much earlier (EGM-QRS = 60 ms) than the left ventricular signals (EGM-QRS = 20 ms), which is in line with the left bundle morphology of the tachycardia. Also note the intense fractionation and low amplitude of the local EGMs. During ablation the tachycardia terminates after 16 s, when the power had been increased to 40 W.

One important limitation of VT ablation is the depth of penetration of the lesions. Even though improved by the use of irrigated catheters, this remains a challenge in scarred and hypertrophied hearts with intramural and critical mid-myocardial or epicardial circuits. Although epicardial ablation has been useful in the treatment of truly epicardial circuits, deep intramural circuits have proven to be difficult targets.[5]

Traditionally, RF ablation current is deployed in a unipolar fashion between the tip of the mapping/ablation catheter and an indifferent electrode placed on the patient surface (often on the thigh). Recently, multipolar catheters have been introduced that provide the possibility to ablate in a bipolar fashion between individual electrodes on a single catheter.[12–14] With two separate standard ablation catheters inside the heart on either side of the target substrate (IVS or free wall), it is possible to allow for the flow of the RF current between the two intracardiac electrodes. Recently, Koruth *et al.*[11] presented their initial experience from nine patients, including four patients with septal VTs. Their result were promising, as they could successfully ablate five of six VTs; however, there were some late recurrences in their case series.

Sivagangabalan *et al.*, using a chronic ovine infarct model, showed that septal VTs typically have a common intramural isthmus capable of exit on either side of the septum with a very short delay between the earliest LV and RV activations. In that study, septal RF energy was delivered in the ventricle with the earliest tachycardia breakout. Failure to create a transmural septal ablation lesion at the scar border resulted in persistent inducibility of septal VT and shifted the earlier activation to the opposite ventricle, while ablation from both sides of the septum resulted in transmural ablation that rendered septal VT non-inducible. Further experimental work in phantom agar models[9] and porcine ventricular tissue[11] has revealed that bipolar ablation is not as sensitive to contact and catheter alignment as unipolar ablation. This may be an advantage of the bipolar ablation technique in positioning catheters in beating human hearts in the clinical setting and obtaining successful termination of tachycardia without the need for added expertise.

Various strategies have been attempted to deal with deep intramural arrhythmia targets including 'needle' ablation and transcoronary ethanol ablation. Both these techniques will require in addition to adapting to new technology, training of catheter deployment. Needle ablation involves a specially designed catheter for mapping and ablation that is currently in development and trials. Sapp *et al.*[15] described pre-clinical work with a catheter developed for intra-myocardial drug delivery. They were able to produce very large and deep lesions with this catheter in animal models. This technique has some prerequisites such as catheter having to be directed perpendicular in order for the needle to engage the myocardium and the catheter design that needs to be verified in human experience.

Another alternative, especially for intramural septal VT is ethanol ablation. This method has been employed in patients with some success.[6,7] This technique is largely limited by the complexity of the procedure and the fact that the area of interest has to be nourished by an accessible coronary artery branch that is of suitable size. The size of the scar created is not easily controlled and this method

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may be best suited as a last resort, especially in patients with very poor LV function as was the case in our patient.

It is increasingly recognized that the successful ablation of septal VT circuits may require RF application on both endocardial surfaces of the IVS. Our study has demonstrated that IVS lesion transmurality can be achieved more readily with bipolar ablation than with unipolar ablation. For patients with therapy-resistant ventricular arrhythmia, bipolar ablation may be an important part of a toolkit for the ablating electrophysiologist.

Conflict of interest: Dr. Nanthakumar is a consultant to St. Jude Medical, Biosense Webster and Boston Scientific.

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