Novel case of linear ultra-low cryoablation catheter for treatment of ventricular tachycardia

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Introduction

Despite ongoing advances in the field, the ablation of ventricular tachycardia (VT) remains challenging and recurrences reported by studies in ischemic patients range between 28% and 46% during long term follow-up.[1,2]

Several factors contribute to these results, but the complexity of transmural substrates and the inability to deliver deep and durable lesions to effectively reach this substrate represents an important challenge. In this context, efforts have been focused on the development of different techniques that allow creation of deeper lesions, such as the use of low-ionic irrigants instead of normal saline, impedance modulation, bipolar ablation, or needle radiofrequency ablation.[1,3–5]

Recently, ultra-low-temperature cryoablation has been developed that uses near-critical nitrogen that exists in the state between liquid and gaseous form. Compared to traditional cryoablation, which uses gaseous nitrous oxide, near-critical nitrogen has a much more favorable cryogenic properties and is able to generate temperatures as low as $-196°C$.[6] Clinical implementation of this novel technology, called ultra-low-temperature cryoablation (ULTC), consists of a console with an integrated user interface and an ablation catheter. The near-critical nitrogen circulates through a cooling system from the console to the catheter to achieve ultra-low temperatures.

KEYWORDS Ablation; Ventricular tachycardia; Ventricular arrhythmias; Cryoablation; Ultra-low temperature
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KEY TEACHING POINTS

- Understand how new technologies can increase efficacy of ventricular tachycardia (VT) ablation. Novel technologies are focused on achieving the increased tissue depth required for VT ablation.
- Lesion depth matters. Ultra-low-temperature cryoablation has the advantage of being able to titrate lesion depth according to tissue thickness in a given region.
- In the near future, we will be able to choose between different technologies for VT ablation. Ultra-low-temperature cryoablation could be a useful ablation tool, creating deeper ventricular lesions compared to conventional radiofrequency. Studies assessing its safety and feasibility are ongoing.

Current preclinical data have already demonstrated that ULTC is effective and capable of creating durable, deep, and contiguous atrial and ventricular lesions in an vivo model in sheep and swine (up to 1.96 ± 0.8 mm depth in the atrium and 5.61 ± 2.2 mm depth in the ventricle, limited by the thickness of the tissue).[7] However, more recent preclinical data have demonstrated that depths approaching 15 mm can be achieved with ULTC in ventricular tissue.[8]

The first-in-human cavotricuspid isthmus ablation using ULTC demonstrated its capability as an effective energy source for typical flutter ablation.[7] Data from Cryocure-2 reported 85% freedom from atrial fibrillation at 12 months in patients with persistent atrial fibrillation after a single ULTC procedure.[9] In this case report, we present a first-in-human case of successful endocardial VT ablation using an ultra-low-temperature cryoablation system.

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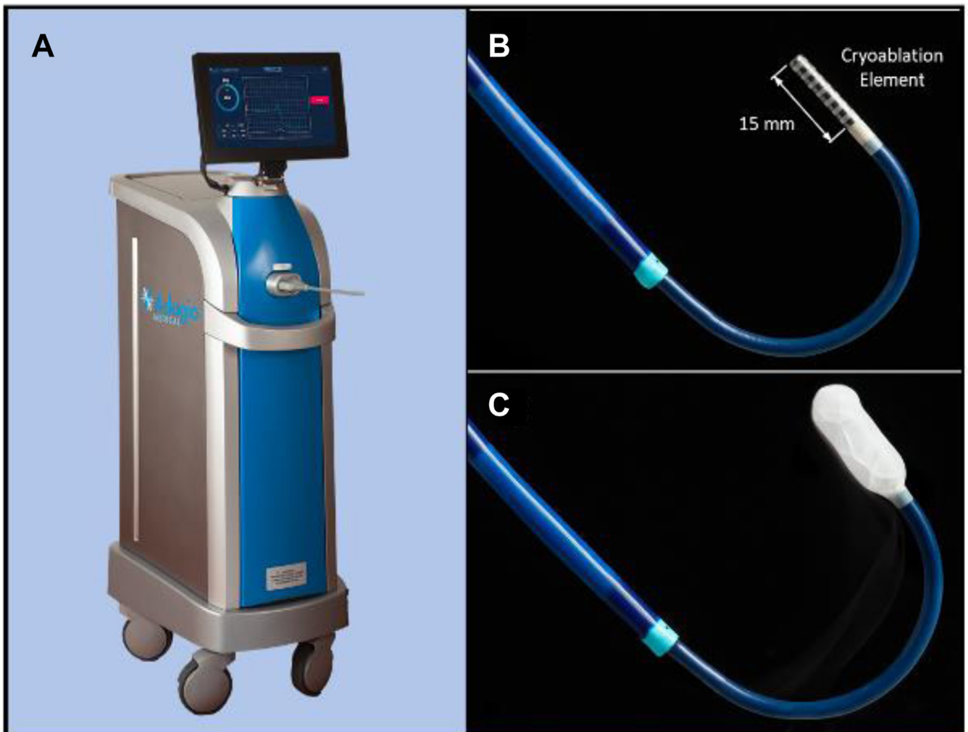

D

Freeze Time (minutes)	Lesion Depth (mm)
1	4.5
2	7.5
3	10.0
4	11.7
5	13.5

Figure 1 The ultra-low-temperature cryoablation system (Adagio Medical, Laguna Hills, CA). **A:** Cryoablation console. **B:** Ventricular tachycardia (VT) catheter, before freezing. **C:** VT catheter with the ice ball forming on cryoablation element. **D:** Ventricular lesion depth as a function of freeze time using first freeze—1-minute thaw—second freeze cryoablation cycle. (Courtesy Adagio Medical, Inc. CS-098.)

Case report

This is a case of a 79-year-old man with a history of diabetes, hypertension, dyslipidemia, ischemic cardiomyopathy, anterior myocardial infarction in 1993, and an implantable cardioverter-defibrillator implanted for secondary prevention in 2018. The patient was admitted to our hospital after having frequent episodes of well-tolerated, slow VT (136–140 beats per minute [bpm]) despite therapy with oral amiodarone and beta blockers that required many deliveries of antitachycardia pacing and shocks.

After hospital admission, the patient was treated with intravenous amiodarone but this did not eliminate the episodes of VT. Repeat transthoracic echocardiography showed mildly reduced left ventricular ejection fraction of 41% and a left ventricular end-diastolic diameter of 63 mm. Because of ongoing VT, the patient was scheduled for a VT ablation using a novel ULTC linear catheter (Adagio Medical Inc, Laguna Hills, CA) as a part of CryoCure VT clinical study (NCT #04893317).

The procedure was performed under general anesthesia.

Through the left femoral access, an intracardiac echocardiography (ICE) was advanced toward the right atrium (home view) and into the right ventricular septum sequentially. The ICE catheter was rotated in a clockwise fashion to visualize the different left ventricle structures and the ablation catheter. A standard quadripolar catheter was placed into the right ventricular apex. Transseptal access to the left ventricle was established at the beginning of the procedure as well using a 10F Mullins sheath, and a 10F braided SL-1 sheath (Abbott Inc, Minneapolis, MN) was placed in the aorta. Arterial access was also obtained for retroaortic approach. An electroanatomic mapping system was also

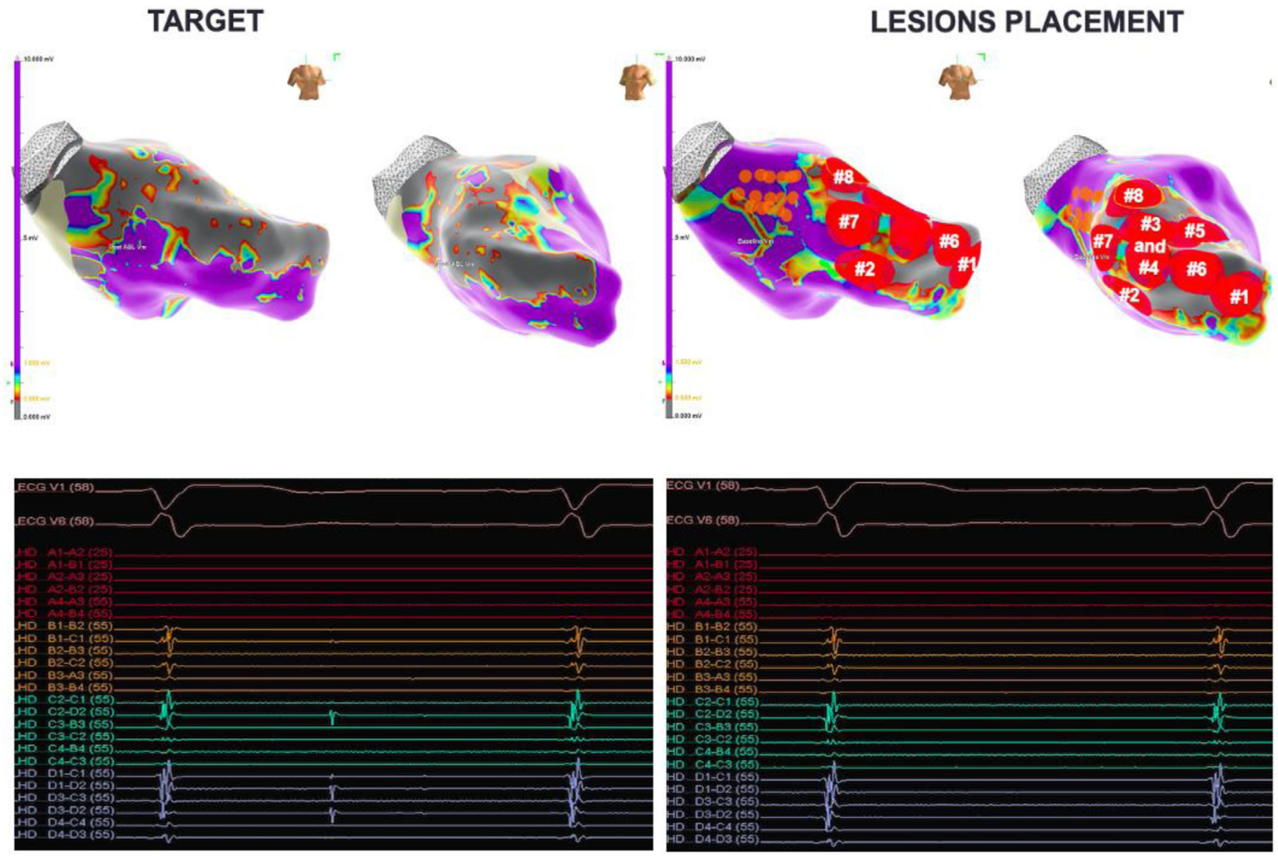

Figure 2 Bipolar voltage maps performed in sinus rhythm using a multipolar mapping catheter and electroanatomic mapping system (HD Grid, EnSite Precision; Abbott, Minneapolis, MN). Baseline voltage maps are shown on the left side where gray regions represent dense scar with voltage <0.5 mV, purple regions represent voltage >1.5 mV, and other color regions represent scar border zones (0.5–1.5 mV). The right-side images show the cryoablation lesions applied. The size of the lesions depicted is based on the calculated size shown in preclinical models. The lower panel shows the abolition of signals from the targeted region.

used (EnSite Precision, Abbott) with a multipolar mapping catheter (Advisor HD Grid SE; Abbott).

The ULTC catheter (Adagio Medical) is a bidirectional, deflectable catheter with a 15 mm distal cryoablation element. The cryothermal energy is delivered to the tissue using near-critical nitrogen (T ~ -196°C) along the entire length of the cryoablation element, creating a large ball of ice (Figure 1). All ULTC lesions are applied over a fixed duration of time (60–300 s), followed by at least a 60-second thaw and another application at the original duration (freeze-thaw-freeze). Depending on the duration of the application, tissue depths of 4.5–13.5 mm can be achieved using durations of 60–300 seconds, respectively (Figure 1).

Using a retrograde aortic approach, a baseline sinus rhythm bipolar voltage map was performed. Dense scar was defined as <0.5 mV, normal tissue as >1.5 mV, and scar border zone between 0.5 and 1.5 mV, as previously published.[10] The voltage map identified a large scar in the anterior wall that extended to the apex with a large number of late potentials that were labeled on the map (Figure 2).

During mapping, a slow VT at 130 bpm was spontaneously induced, which was successfully cardioverted to sinus rhythm with a synchronized biphasic shock (200 J). The VT morphology suggested an apical origin, with a superior axis and negative concordance in the precordial leads. Once the voltage map was complete, programmed ventricular stimulation was performed at drive cycle lengths of 600 and 450 ms with up to 3 extrastimuli down to ventricular effective refractory period. Another monomorphic VT was induced, also with an apical origin, superior axis, and negative concordance, but this VT was faster than the first one (193 bpm). Given the 2 different VTs induced, we opted to perform a substrate-guided ablation during sinus rhythm.

Using the Adagio Medical ULTC system, cryoablations were delivered in the targeted area (anterior and anteroapical wall) (Figure 2). Given the tissue thickness in the target region on ICE, we opted to deliver 5 lesions with 180-second duration (freeze-thaw-freeze) and 1 lesion for 120 seconds. After a total of 6 ablations, programmed stimulation was performed and a new VT was induced, this time with an inferior axis and transition in V_3–V_4 coming from a more anterobasal position. At this point, 2 more applications (freeze-thaw-freeze) were delivered in the anterobasal wall with 120-second durations. The ICE catheter was used to monitor the catheter contact and the lesion size (Figure 3). The total cryoablation time for the case was 42 minutes.

Once the ablation set was considered completed and after a 20-minute waiting period, programmed ventricular

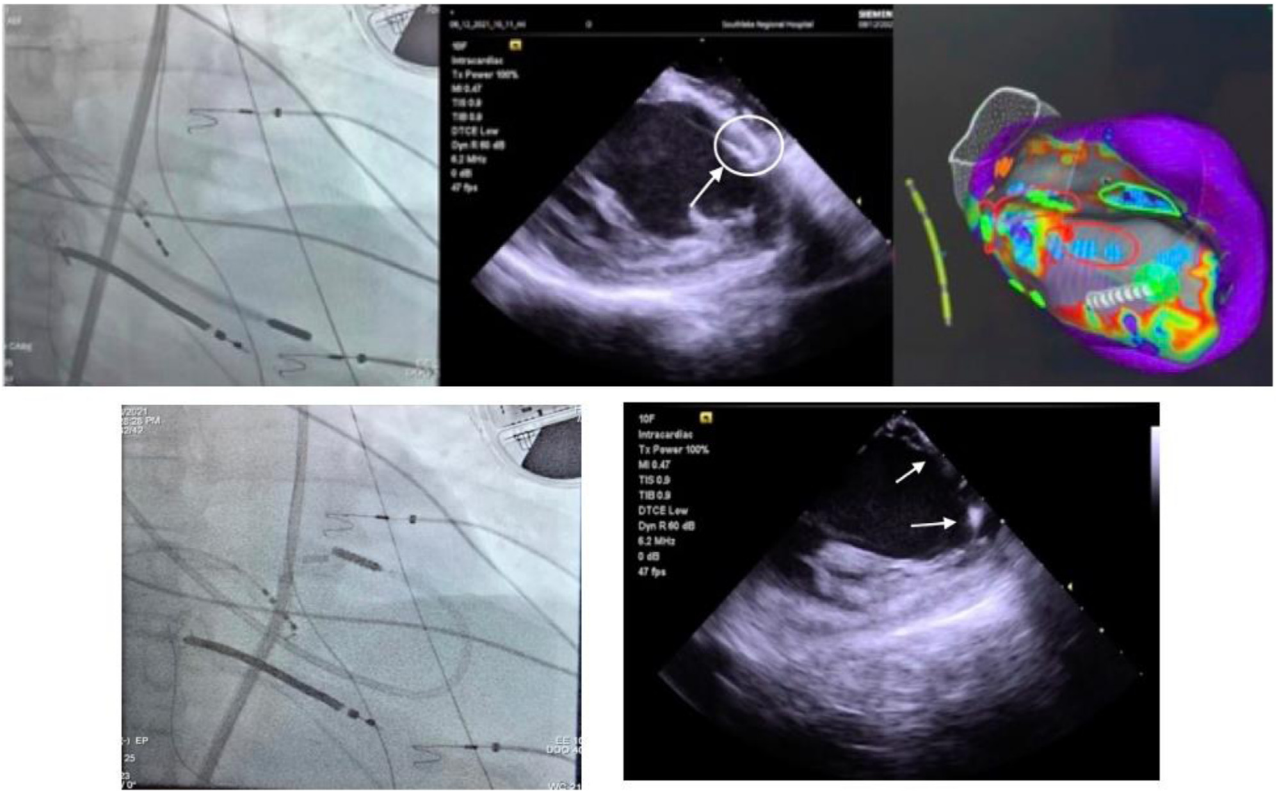

Figure 3 Fluoroscopic, intracardiac echocardiographic (ICE), and electroanatomic depictions of the ultra-low-temperature cryoablation catheter (Adagio Medical, Laguna Hills, CA). On the left side of the upper images, fluoroscopy shows the dark 15 mm tip of the ablation catheter. In the middle upper panel, the tip of the catheter is seen on ICE (*arrow*). The lesion has a ring-enhancing border with low echogenicity in the center (*circle*). Ice formation on the catheter tip is not easily seen on ICE. On the right upper panel, the catheter is shown on the mapping system. In the lower left panel, the catheter is flexed into a semicircular shape to get good contact with the anterobasal wall. The curved catheter is seen on the ICE image to the right. The ICE images are inverted vertically since the imaging catheter is retroflexed in the right ventricle.

stimulation was performed again with no induction of VT. There were no acute complications and the patient was discharged the morning after the procedure. During the first 2 months of follow-up, the patient did not present with further VTs.

Discussion

The present case report demonstrates the ability of ULTC to perform a successful endocardial VT ablation in a patient with recurrent drug-refractory VT.

At the beginning of the procedure, 3 different VTs were easily induced and after 8 freezes covering an extensive anteroapical scar, the patient had no further inducible VT. Consistent with preclinical data, this case suggests that ULTC is capable of creating ventricular lesions deep enough to reach an extensive myocardial ventricular substrate.

When using novel forms of energy delivery for achieving the increased tissue depth required for VT ablation, there is a balance between efficacy and risk.[8] Use of low-ionic irrigants may increase tissue depth but has been associated with steam pops.[4] Bipolar ablation between 2 catheters has been used but is also reported to be associated with steam pop, perforation, and clot formation.[11] Finally, needle-tip catheter ablation technologies have also been used but have either been terminated in development or have also resulted in complications.[12]

ULTC has the advantage of being able to titrate lesion depth according to tissue thickness in a given region (which could be assessed on preoperative computed tomography or magnetic resonance imaging or intraoperative ICE). Although the lesion durations can be 2–3 minutes long, the 15 mm cryoablation element and achievable transmurality in preclinical work through pure endocardial ablation mean that fewer lesions need to be applied. In this case, for example, only 8 lesions were required to cover a very large region with total energy application time of 42 minutes. For context, in the VISTA trial of VT ablations in patients with ischemic cardiomyopathy,[13] the total energy application time was 68 $\pm$ 21 minutes in the substrate ablation group vs 35 $\pm$ 27 minutes in the mapped hemodynamically stable VT ablation group. Consistent energy delivery is also facilitated by the cryoadhesion with minimum input from the operator after the first 15–20 seconds of the freeze.

Like other energy sources, ULTC delivered in the excess of tissue depth carries the risk of potential complications, such as perforation or injury to epicardial structures (such as the coronary arteries). From the 30 patients that underwent cavotricuspid isthmus ablation in the study conducted by Klaver and colleagues,[7] 1 patient had a transient ST elevation in the inferolateral leads associated with temporary AV conduction block, which resolved spontaneously within a minute. The event was attributed to vasospasm of the right coronary artery owing to lateral placement of the cryoablation catheter.

In our case, the patient, who was a high-risk patient, did not suffer any acute complication and was discharged in stable condition the morning after the ablation. Certainly, this case report suggests that ULTC could be a useful ablation tool for the treatment of ventricular arrhythmias, creating deeper ventricular lesions compared to conventional radiofrequency. However, only ongoing and future clinical trials will ultimately answer whether ULTC can be used safely and efficiently for the long-term treatment of VT.

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