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ATRIAL FIBRILLATION

A Lattice-Tip Temperature-Controlled Radiofrequency Ablation Catheter for Wide Thermal Lesions

First-in-Human Experience With Atrial Fibrillation

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ABSTRACT

OBJECTIVES This study sought to evaluate the safety and acute performance of the lattice tip for the treatment of atrial flutter and fibrillation (AF).

BACKGROUND A novel catheter using an expandable lattice structure with a wide thermal footprint incorporating multiple surface thermocouples/mini-electrodes has been designed for high-resolution mapping and high-current, temperature-controlled radiofrequency ablation (RFA).

METHODS Patients with typical right atrial flutter or AF were prospectively enrolled in a single-arm study at 3 centers. Patients with atrial flutter underwent cavotricuspid isthmus (CTI) ablation. Patients with paroxysmal AF underwent pulmonary vein isolation (PVI) and CTI if desired, and for patients with persistent AF, mitral isthmus and left atrial roof lines were also permitted. Mapping was performed with the lattice (Sphere-9) catheter and a novel compatible electroanatomic mapping system (Prism-1). RFA was performed in a point-by-point fashion (T_{max}, 73°C to 80°C; range 2 to 7 s). Patients were followed for 3 months.

RESULTS A total of 71 patients underwent ablation: 65 PVI (38% with persistent AF) and 22 mitral isthmus, 24 roof, and 48 CTI lines. PVI was achieved in 64 of 65 (98.5%) by using the lattice alone and required a mean of 2.7 ± 0.70 RFA min. Mitral block was achieved in 100% by using 11.5 ± 10.7 applications and 1.0 ± 0.92 RFA min; only 1 patient required adjunctive epicardial coronary sinus ablation. Roof line and CTI block were achieved in 95.8% and 100% of patients, using 4.9 ± 1.9 and 5.9 ± 3.1 applications for 0.4 ± 0.16 and 0.5 ± 0.24 RFA min, respectively. At 3 months, there were no deaths, strokes, tamponade, or atrioesophageal fistula.

CONCLUSIONS This first-in-human study demonstrated clinical feasibility and safety for rapid high-current, temperature-controlled point-by-point PVI and linear ablation. (J Am Coll Cardiol EP 2020;6:507–19) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

AFL = atrial flutter

CTI = cavotricuspid isthmus

EAM = electroanatomic map

LA = left atrium

PAF = paroxysmal atrial fibrillation

PerAF = persistent atrial fibrillation

PV = pulmonary vein

PVI = pulmonary vein isolation

RF = radiofrequency

RFA = radiofrequency ablation

Catheter ablation of atrial fibrillation (AF) is one of the most commonly performed procedures in cardiac electrophysiology. However, AF ablation is a complex procedure, with outcomes that are highly dependent on the operator level of expertise (1). Over the past decade, there have been extensive efforts to improve ablation technology to facilitate procedural safety and efficacy. Some of these technological advances, such as catheters with contact feedback, objective annotation of ablation applications based on biophysical ablation parameters, and temperature-guided irrigated ablation, have improved the efficacy of point-by-point radiofrequency (RF) ablation (RFA) catheters, but they have only modestly improved the ease of the procedure (2–7). Instead, the largest strides in improving the technical ease of the procedure have resulted from the advent of single-shot pulmonary vein isolation (PVI) technologies—first cryoballoons, then laser balloons, and most recently, RF balloons (8–10).

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Despite their success, one-shot technologies still have substantial limitations. First, they are designed to isolate only the pulmonary veins (PVs). This may be clinically effective in most patients with paroxysmal AF (PAF), but there are still a substantial minority of patients that require ablation at non-PV trigger sites and for other concurrent rhythms, such as atrial flutter (AFL). Most importantly, PVI alone appears insufficient to treat many, if not most, patients with persistent AF (PerAF). Electrophysiologists have deployed a number of extra-PV lesion sets including mitral isthmus lines, roof lines, posterior lines, cavotricuspid isthmus (CTI) lines, posterior box isolation, left atrial appendage isolation, and ablation at putative AF sources/rotors using a variety of AF electrogram mapping approaches. Although there is no consensus as to the optimal additional lesion set(s) for PerAF, one-shot technologies are not suitable for a tailored ablation strategy. It is therefore not surprising that these constitute only approximately 25% of all AF ablation procedures being performed worldwide, with the remainder employing point-by-point ablation catheters.

Thus, there is a strong desire for an ablation tool that: 1) provides operators the flexibility to tailor the lesion set to each patient's individual anatomy and physiology; 2) can be quickly maneuvered and positioned at the requisite locations with an ease-of-use profile reminiscent of one-shot technologies; 3) can create lesions rapidly to potentiate short procedure times; 4) delivers lesions with enough redundancy so as to maximize overlap of adjacent lesions; 5) can titrate the amount of ablative energy to accommodate not only the thin tissue along the posterior wall, but also the thicker tissue along the anterior left atrium (LA) and mitral isthmus; and yet 6) consists of only a single catheter for mapping and ablation, reducing both workflow complexity and procedure cost.

To this end, a novel catheter incorporating an expandable spheroid-shaped lattice tip with a large thermal footprint has been designed for high-current RF ablation at low current density (11). This lattice tip allows delivery of higher energy but at a lower risk for

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Clinical Electrophysiology* author instructions page.

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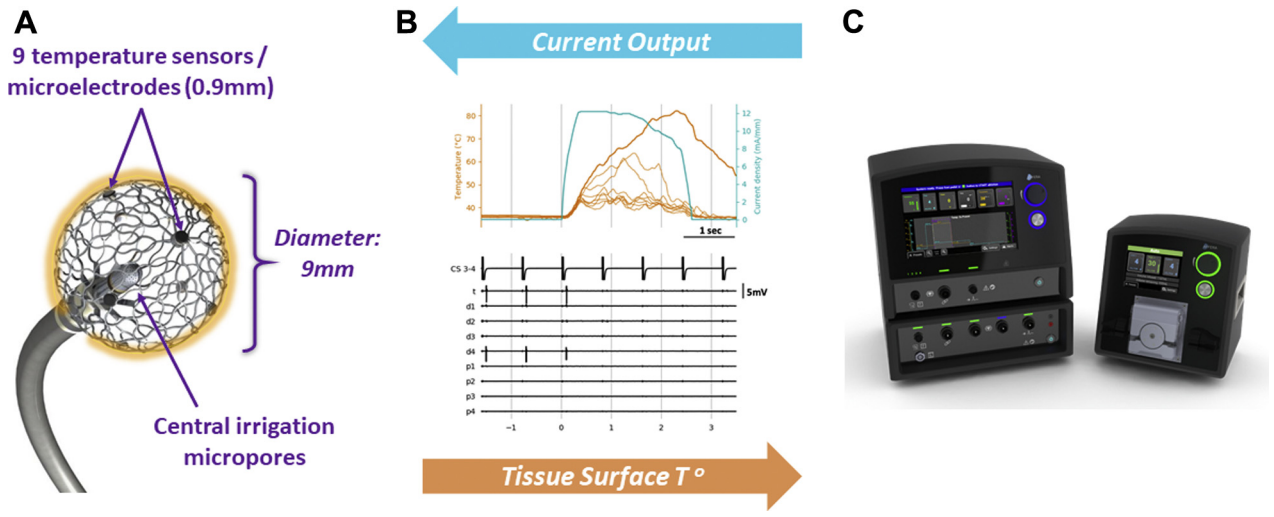
FIGURE 1 **Lattice Catheter and Mapping/Ablation System**



The system includes an integrated mapping system, high-current radiofrequency generator, and irrigation pump. **(A)** The expanded lattice electrode has a diameter of 9 mm and contains 9 thermocouples/mini-electrodes (Video 1). **(B)** Radiofrequency energy is emitted from the entire lattice framework to create a uniform current cloud. **(C)** The generator operates in a temperature-controlled mode: modulating current output to avoid heating the surface beyond a pre-set temperature limit. In the example shown **(B)**, ablation starts at maximal current output **(cyan scale)** and is titrated down to maintain a maximum surface temperature of 80°C **(orange graphs)**. Note the immediate reduction in electrogram amplitude recorded from the microelectrodes during ablation.

tissue overheating. The 7.5-F catheter is saline irrigated and incorporates 9 thermocouples that provide real-time tissue surface temperature monitoring to a proprietary high-current RF generator. A temperature-control algorithm modulates the current to maximize output without tissue overheating. It also has 9 mini-electrodes with a central noncontact electrode for 9 close unipolar electrograms and a magnetic localization sensor to allow electroanatomic mapping (EAM), including anatomic rendering and multielectrode voltage and activation mapping. Accordingly, in a multicenter, first-in-human clinical trial of this lattice-tip catheter system, we evaluated its feasibility, acute performance, and safety in treating patients with AFL and AF.

METHODS

This study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committees at all participating sites and by local health authorities in the participating countries. All participants gave informed consent. Prospective data collection included reporting of all clinical outcomes and adverse events.

STUDY DESIGN. This was a first-in-human, prospective, multicenter, single-arm, clinical study of the Affera system (Affera, Inc., Watertown, Massachusetts) conducted at 3 centers in 2 European countries (2 centers in the Czech Republic and 1 in Lithuania).

STUDY POPULATION. Eligible patients were 18 years or older with symptomatic PAF (defined as AF terminating spontaneously or with intervention within 7 days), PerAF (defined as AF sustained beyond 7 days), or typical right AFL. This analysis included patients who planned to have a first-ever ablation procedure for the target arrhythmia; patients undergoing either redo procedures or ablation of ventricular arrhythmias were not included. Key exclusion criteria included left ventricular ejection fraction of <40%, presence of intracardiac thrombus, previous cardiac ablation, or stroke within 6 months.

RFA SYSTEM. This proprietary technology includes an ablation catheter (Sphere-9, the lattice), a high-current RF generator (HexaGen) with a peristaltic pump, and an EAM system (Prism-1). At its core is the lattice-tip catheter (Figure 1), a 7.5-F bidirectional deflectable catheter with an expandable conductive lattice electrode. The lattice is inserted into the sheath in a collapsed form, but once exiting the sheath, the electrode expands to a 9-mm-diameter spherical configuration (Video 1). The lattice contains 9 mini-electrodes (0.7-mm diameter), each containing a temperature sensor, with uniform

surface distribution to allow tissue contact of at least 1 electrode at any catheter-tissue angle. The lattice also contains an electrode at its center contacting only blood, which is used as a local indifferent electrode. Two additional ring electrodes are located just proximal on the shaft. The center of the lattice contains a protected irrigation nozzle with micropores to provide homogeneous cooling unaffected by catheter-tissue pressure or the angle of tissue engagement. Despite their small diameter, the lattice struts act as a solid electrode, and RF current is distributed uniformly around the sphere (11,12). Bipolar electrograms can be configured between any of the electrodes on the ablation catheter. In particular, bipolar electrograms between each mini-electrode and the center electrode (to provide close unipolar electrograms) were typically used to assess the local response to ablation without contamination of far-field activity. The system provides an indication of catheter-tissue contact by continuously evaluating the impedance between each mini-electrode and center electrode.

The proprietary high-current generator (HexaGen) operates in temperature-controlled mode. The small mass and direct tissue engagement of the temperature sensors allow rapid response to temperature changes for dynamic modulation of current output. Ablation starts at the maximal pre-set current output and is titrated to maintain the surface temperature limit on the sensor recording the highest temperature. Although energy delivery is primarily controlled by this temperature limit, a current limit is also applied to constrain maximum energy delivery. This is specified as a percentage of the maximum current squared because resistive heating is proportional to current-squared density and therefore to current squared. For example, a current limit of 100% represents the maximum RF generator current of 3.7 A, whereas a current limit of 50% represents a current of 2.6 A. Furthermore, RF current through the lattice does not produce noise on the mini-electrodes, allowing monitoring of real-time electrogram changes during ablation. The high- and low-pass filters for unipolar and bipolar electrograms were 1 to 300 Hz and 30 to 300 Hz, respectively.

The EAM system (Prism-1) uses a magnetic sensor within the lattice catheter tip for tracking and building 3-dimensional maps. Anatomy acquisition is performed at a pre-defined respiratory phase (respiratory gating).

PROCEDURAL WORKFLOW. Pre-procedural computed tomography or magnetic resonance imaging was not required but was performed in some patients according to center practices. Procedures were performed with either uninterrupted warfarin or by holding a single direct thrombin inhibitor dose. Unfractionated heparin was administered to achieve an activated clotting time target of 300 to 400 s.

Most of the AF procedures (58 of 65, 89.2%) were performed under general anesthesia. Monitoring of esophageal temperature was performed according to each center's normal practice and included 1 of 3 techniques: 1) single thermocouple esophageal probe (Tuner Medical, Orange, California); 2) multi-thermocouple esophageal probes (CIRCA-S-CATH; Circa Scientific, Englewood, Colorado); or 3) mechanical esophageal deviation (DV8, Manual Surgical Sciences, Minneapolis, Minnesota) without temperature monitoring (13–15). Esophageal endoscopy was performed 1 to 2 days post-ablation in selected patients with esophageal temperature increases or in other cases according to physician preference.

MAPPING PROTOCOL. A decapolar catheter was placed in the coronary sinus. An intracardiac echocardiography catheter (8-F AcuNav, Siemens Healthcare, Mountain View, California) helped guide transseptal punctures, monitor lesion formation, and evaluate for complications. The lattice catheter was advanced into the right or LA through a fixed-curve or a steerable sheath (SL or Agilis NxT, Abbott, St. Paul, Minnesota). A single transseptal puncture was performed in patients with PAF undergoing PVI alone. Dual transseptal punctures were performed in a subset of patients (17 of 65, 26.2%) as per center preference. In these patients, a circular mapping catheter was used to confirm PVI, differential pacing, and evaluation of block.

The lattice catheter was first used to create a 3-dimensional EAM of the right atrium in patients with typical right AFL or the LA in patients with AF. EAM construction was performed by moving the lattice catheter within the chamber, including caval veins, pulmonary veins, and atrial appendage, to delineate these structures and the relationships between them (i.e., left PV-LA appendage ridge). Voltage and activation maps were often created simultaneously during anatomy acquisition. Normal electrogram amplitude with the lattice catheter was typically defined as ≥1.0 mV.

ABLATION PROTOCOL. Ablation around the pulmonary veins was performed using 2 energy settings designed for the thinner posterior wall and the thicker anterior/septal walls based on pre-clinical experiments (11). In the thicker anterior and septal walls, each application was typically 5 s in duration, with a target temperature of 75°C. For the posterior

TABLE 1 Baseline Patient Characteristics

Age, yrs (n = 71)	62.2 ± 9.3
Male	50/71 (70)
Medical history	
Paroxysmal AF	40/65 (62)
Persistent AF	25/65 (38)
Right atrial flutter or empiric CTI	48/71 (68)
Body mass index, kg/m^2 (n = 71)	29.8 ± 4.9
Hypertension	48/71 (68)
Diabetes	4/71 (6)
Left ventricular ejection fraction, % (n = 64)	59.5 ± 7.3
Left atrial dimension, mm (n = 64)	42.7 ± 5.9
Warfarin	25/71 (35)
DOAC	41/71 (58)
Antiarrhythmic medication	53/71 (75)

Values are mean ± SD or n/N (%).
AF = atrial fibrillation; CTI = cavotricuspid isthmus; DOAC = direct oral anticoagulant.

TABLE 2 Procedural Details (N = 71)

Cavotricuspid isthmus line	
Successful linear lesion	48/48 (100)
Success using lattice catheter only	48/48 (100)
Number of RF applications	5.9 ± 3.1
Total RF time, min	0.5 ± 0.24
Transpired ablation time, min*	2.3 ± 1.6
Fluoroscopy time, min†	4.8 ± 2.2
Pulmonary vein isolation	
Successful lesion set	130/130 (100)
Success using lattice catheter only	129/130 (99.2)
Number of RF applications	39.5 ± 8.9
Total RF time, min	2.7 ± 0.70
Transpired ablation time, min*	21.8 ± 12.1
Total left atrial dwell time, min‡	43.0 ± 18.4
Fluoroscopy time, min§	7.0 ± 6.7
Mitral isthmus line	
Successful linear lesion	22/22 (100)
Success using lattice catheter only	21/22 (95.5)
Number of RF applications	11.5 ± 10.7
Total RF time, min	1.0 ± 0.92
Transpired ablation time, min	5.8 ± 6.4
Roof line	
Successful linear lesion	23/24 (95.8)
Success using lattice catheter only	23/24 (95.8)
Number of RF applications	4.9 ± 1.9
Total RF time, min	0.4 ± 0.16
Transpired ablation time, min	3.0 ± 4.4

Values are n/N (%) or mean ± SD. *Defined as the time transpiring from the start of the first application to the end of the last application in the lesion set. †In most cases, ablation was performed with ICE guidance alone, so data shown here includes only the 6 cases in whom fluoroscopy was used to guide CTI ablation. ‡Defined as the time transpiring from catheter entry to exit from the body. §Includes the fluoroscopy time for mapping and ablation, including linear lesions beyond PVI.
CTI = cavotricuspid isthmus; ICE = intracardiac echocardiography catheter; PVI = pulmonary vein isolation; RF = radiofrequency.

wall, applications were typically 2.5 s duration, with a temperature limit of 80°C; however, when the esophagus was mechanically displaced, 3- to 5-s applications were used. CTI ablation was typically performed with the settings designed for the anterior/septal walls (5 s, temperature limit of 75°C). The posterior mitral isthmus line was performed with 5- to 7-s applications, with a temperature limit of 75°C. The current limit for RF energy delivery was not specified in the protocol and varied between 80% and 100% as investigators adjusted dosing.

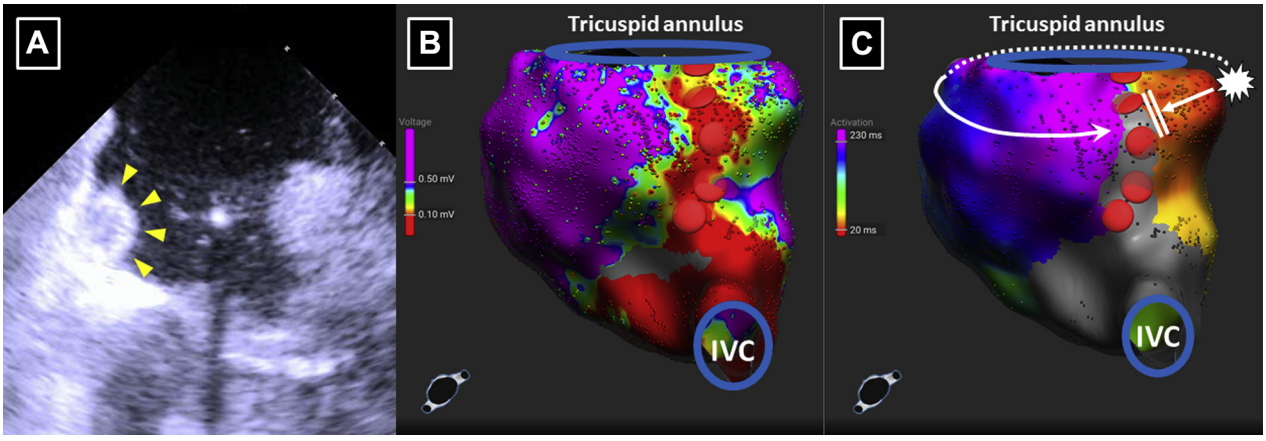
The irrigation solution was normal saline, and the nominal irrigation rates during mapping and during energy delivery were 4 and 15 ml/min, respectively. Ablation data recorded during RFA included current output, surface temperature, impedance, and electrogram attenuation.

PVI was performed with a wide antral approach, isolating the left and right ipsilateral veins en bloc. The target distance between lesions was 6 to 8 mm. This was based on the catheter's larger footprint and lesion diameter, and allowing approximately 25% overlap between ablation lesions (11). Ablation of the anterior right superior PV was performed after pacing from the lattice catheter at 15 mA to assess phrenic nerve capture. In instances of nerve capture, the line of ablation was moved proximally, away from the phrenic nerve. In patients in whom the esophagus was not deviated (2 out of 3 centers), the esophageal temperature was monitored during each application. If esophageal temperature increased by ≥1°C, subsequent applications were held until the temperature decreased to within 1°C of baseline temperature.

PVI was determined by entrance block to each PV defined by elimination of all local electrograms or the appearance of dissociated PV potentials. At the beginning, this was performed using a circular multielectrode catheter placed in each PV after ablation. Because this maneuver showed concordance with electrograms recorded by the lattice catheter, the latter was used in the majority of patients for determination of entrance block. Evaluation for acute reconnection using a pre-specified waiting period or adenosine was performed by some but not all operators according to each center's clinical practice. Additional touch-up applications were permitted if acute PV reconnection was observed.

Patients with PerAF were treated with PVI plus posterior mitral isthmus and/or LA roof lines as indicated for arrhythmia or created empirically according to the operator practice. Posterior mitral isthmus lines were applied between the mitral annulus and the left inferior PV. Roof lines were placed superiorly between the contralateral PVI lesion sets. A CTI line was created in patients with

FIGURE 2 Ablation of the Cavotricuspid Isthmus



(A) The lattice tip **(arrowheads)** is shown on the cavotricuspid isthmus during ablation (corresponding videos in Videos 2 and 3). Also shown in inferior views are post-ablation **(B)** voltage and **(C)** activation maps during proximal coronary sinus pacing. Medial-to-lateral block is evident with a trans-isthmus time of 210 ms. IVC = inferior vena cava.

documented typical right AFL, or empirically per operator practice. The presence of block across each line was evaluated by differential pacing maneuvers and/or activation mapping. The lattice catheter was used only for endocardial ablation. In case of failure to achieve PVI or line of block, a standard irrigated RF catheter was permitted to complete the procedure.

FOLLOW-UP. To evaluate safety and acute efficacy, patients were followed for a minimum of 3 months, including a phone call at 10 days and a clinic visit at 3 months that included a 12-lead electrocardiogram, review of medications, and review of adverse events. Patients underwent a 48-h Holter monitoring during follow-up. Additional monitoring was performed based on symptoms.

STUDY OUTCOMES. Safety endpoints include the occurrence of major adverse events, including atrioesophageal fistula, cardiac tamponade or perforation, death, severe pericarditis (defined as requiring hospitalization or resulting in a pericardial effusion requiring drainage), valvular damage, major vascular complication or bleeding, intraprocedural device complications requiring open-chest or heart surgery, myocardial infarction, phrenic nerve paralysis, PV stenosis, thromboembolism, stroke, or transient ischemic attack.

Acute efficacy was defined as confirmation of PVI and bidirectional block across ablation lines. The mapping times, RF application times, and transpired ablation times were determined by using time stamps from the mapping system; the LA dwell time was calculated as the combined mapping plus transpired ablation time with the lattice catheter in the LA.

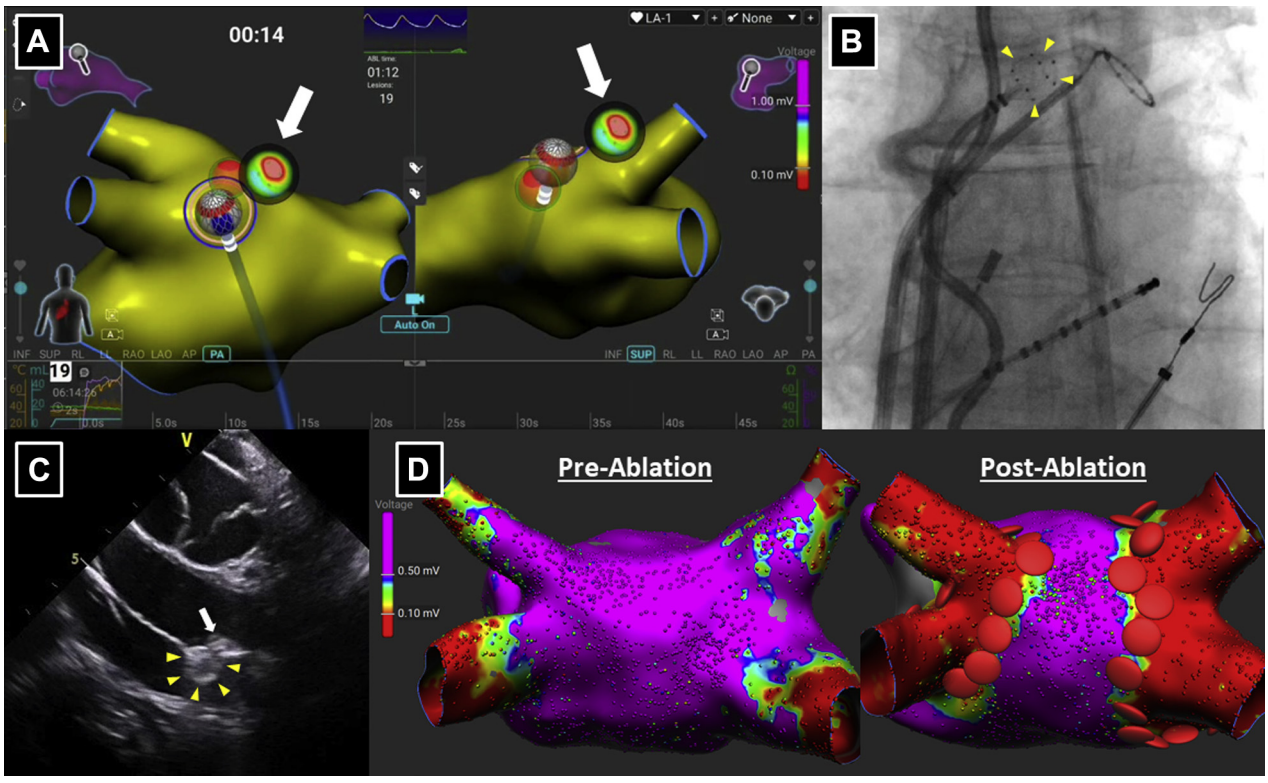
STATISTICAL ANALYSIS. Because this was a feasibility study for a new technology, descriptive statistics were used to characterize study outcomes and safety parameters, and there was no formal hypothesis testing or power calculation. Continuous variables are reported as mean ± SD or median (range) as appropriate, and categorical variables are reported as number (percentage).

RESULTS

PATIENT CHARACTERISTICS. Between May 2018 and May 2019, 71 patients were enrolled at 3 sites (8 operators) for this first-in-human study. The target clinical rhythm was typical right atrial flutter in 6 patients and AF in 65 patients: 40 (61.5%) and 25 (38.5%) with PAF and PerAF, respectively. The cohort was 62.2 ± 9.3 years old; was moderately overweight, with a body mass index of 29.8 ± 4.9 kg/m^2; and had a moderately enlarged LA diameter of 42.7 ± 5.9 mm. Approximately two thirds were men, and 68% had hypertension (Table 1).

MAPPING. The lattice catheter could successfully map all relevant atrial structures, including the pulmonary veins and LA appendage, and EAMs were constructed in all cases pre-ablation. The baseline LA mapping time was 9.9 ± 5.6 min, containing 6,818 ± 1,927 points/map, with an electrogram noise level of 0.009 ± 0.003 mV.

FIGURE 3 **Pulmonary Vein Isolation**

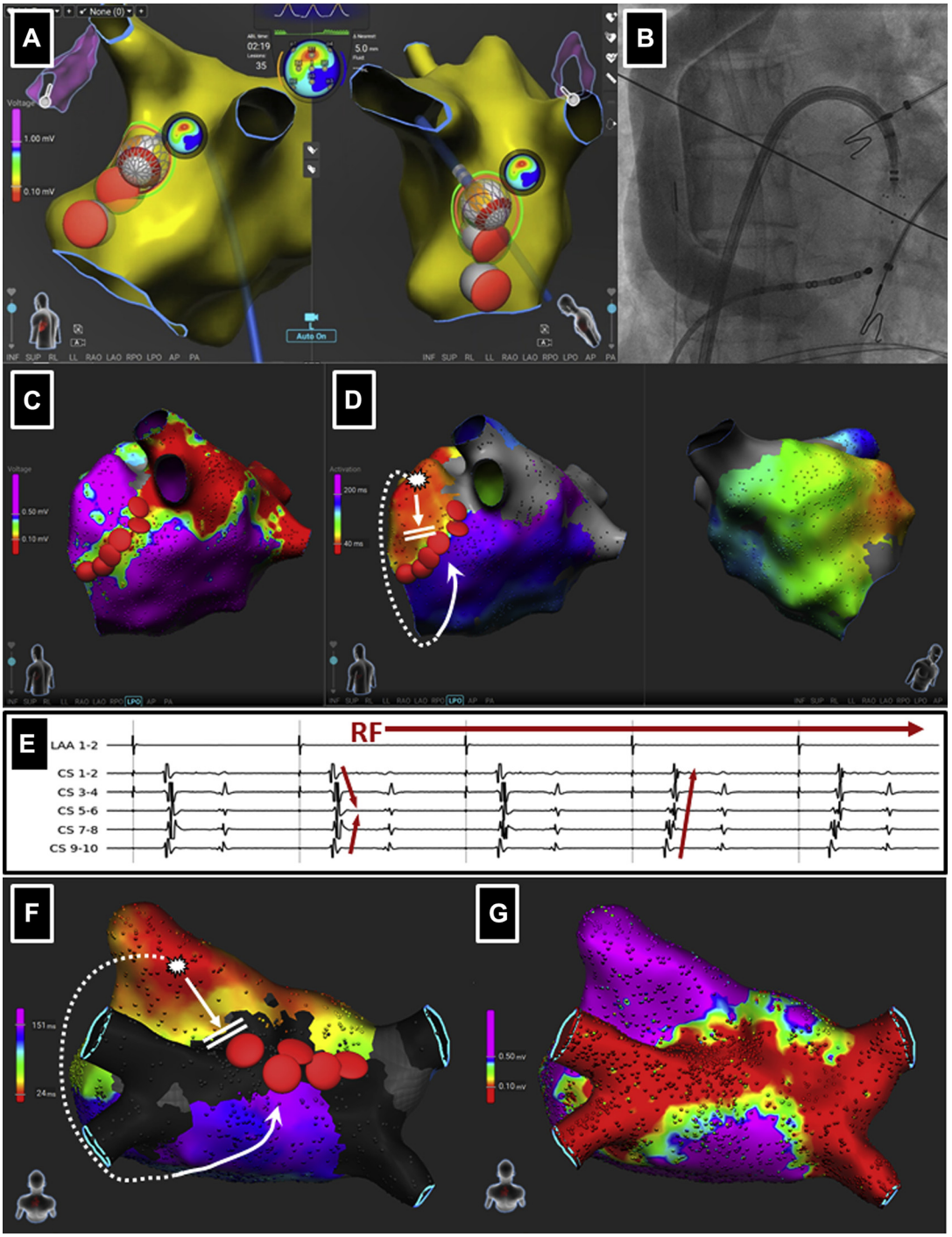


(A) During ablation, the heat detected by the surface thermocouples is represented on a pop-up bullseye map **(arrow)** that hovers near the ablation tip icon (corresponding video in Video 4). **(B)** On this anteroposterior fluoroscopic image view, the lattice tip **(arrowheads)** is shown near the S-shaped esophageal temperature probe; in other patients, esophageal displacement was performed. **(C)** The lattice tip **(arrowheads)** is shown touching the ridge between the left pulmonary veins and left atrial appendage (corresponding video in Video 5). **(D)** An example of pre- and post-ablation voltage maps are shown.

CTI LINE. Bidirectional CTI block was achieved with the lattice catheter in 48 of 48 patients (**Table 2**) with 5.9 ± 3.1 RF applications and a total RF time of 0.5 ± 0.24 min. RF applications were 5.0 ± 0.9 s in duration, with a target temperature of 75 ± 3°C. The transpired ablation time, defined as time transpiring from the beginning of the first CTI lesion to the end of the last CTI lesion, was 2.3 ± 1.6 min (see example in **Figure 2** and Video 2). By intracardiac echocardiography (Video 3), one can appreciate both: 1) the ease of ultrasonic tip visualization; and 2) the large footprint of the lattice tip on the CTI enabling block with a limited number of applications. Ablation along the CTI's inferior vena cava edge also highlighted the advantage of the lattice as being able to easily negotiate this often-complex topography by simply overhanging, with tissue contact along its proximal edge. Finally, in most cases, ablation was performed with intracardiac echocardiography catheter guidance alone. When fluoroscopy was used for CTI ablation (n = 6), fluoroscopy time was 4.8 ± 2.2 min.

PVI. Electrical isolation was achieved in 129 of 130 (99.2%) ipsilateral PV pairs with the lattice catheter alone (**Table 2**); in 1 case early in the study experience, a conventional irrigated RF catheter was used to complete isolation. PVI required 39.5 ± 8.9 RF applications/patient, total RF time of 2.7 ± 0.70 min, and total transpired ablation time of 21.8 ± 12.1 min: 10.8 ± 5.0 and 11.0 ± 8.3 min for the right and left PVs encircling lesion sets, respectively. RF applications were 4.2 ± 1.2 s in duration, with a target temperature of 77 ± 3°C (see example in **Figure 3** and Videos 4 and 5). The LA catheter dwell time was 43.0 ± 18.4 min. Acute PV reconnections were observed in 7 of 130 (5.4%) PV pairs. The total fluoroscopy time during mapping and ablation (including linear lesions beyond PVI) was 7.0 ± 6.7 min. The cumulative volume of irrigation was 432 ± 147 ml.

FIGURE 4 Left Atrial Linear Lesions: Mitral Annulus and Roof Lines



(A) A still image during ablation of the posterior mitral annulus (corresponding video in Video 6). **(B)** A fluoroscopy image of the lattice tip during mitral ablation; in this example, the esophagus was displaced rightward away from the ablation sites. Post-ablation **(C)** voltage and **(D)** activation maps are shown during left atrial appendage pacing. There is low voltage along the ablation line with medial-to-lateral block and a trans-isthmus time of 160 ms. **(E)** Reversal of coronary sinus (CS) activation during the last application. After placing left atrial roof line, **(F)** voltage and **(G)** activation mapping during left atrial appendage pacing shows block across the linear lesion. LAA = left atrial appendage; RF = radiofrequency.

LA LINEAR ABLATION: MITRAL ISTHMUS AND ROOF LINES. Mitral isthmus bidirectional block was achieved in 22 of 22 patients (Table 2). The number of RF applications was 11.5 ± 10.7, the total RF time was 1.0 ± 0.92 min, and the total transpired ablation time was 5.8 ± 6.4 min (examples in Figure 4 and Video 6). RF applications were 5.3 ± 0.8 s in duration, with target temperature 75 ± 1°C. Block was achieved in 21 of 22 (95.5%) patients with the lattice tip alone. One patient required coronary sinus lesions with a conventional irrigated RF catheter. In this case, the RF generator current limit was set to a lower value during mitral isthmus ablation: ≤85% of maximum current squared, as opposed to that used in the remaining cases, >85% of maximum current squared. Interestingly, in a retrospective analysis, the higher current settings (>85%, n = 11) were associated with bidirectional block using fewer RFA applications (8.5 ± 3.8 vs. 14.5 ± 14.3; p = 0.10) and shorter ablation time (46.2 ± 19.8 s vs. 76.3 ± 74.1 s; p = 0.11) than with the lower current settings (≤85%, n = 11 patients). However, these comparisons did not reach statistical significance, likely due to the small number of patients.

Bidirectional block across roof lines was achieved in 23 of 24 (95.8%) patients using the lattice-tip catheter (Table 2). The number of RF applications required for roof line block was 4.9 ± 1.9, the total RF time was 0.4 ± 0.16 min, and the total transpired ablation time was 3.0 ± 4.4 min (example in Figure 4). RF applications were 4.7 ± 0.7 s in duration, with a target temperature of 75 ± 2°C.

SAFETY. Over 3 months of follow-up, there were no primary adverse events. Specifically, there was no instance of atrioesophageal fistula, cardiac tamponade, death, severe pericarditis, valvular damage, major vascular access complication or bleeding, intraprocedural device complications requiring cardiac surgery, myocardial infarction, phrenic nerve paralysis, PV stenosis, stroke, thromboembolism, or transient ischemic attack (Table 3).

One patient with PerAF exhibited sinoatrial blockade after cardioversion following PVI, mitral isthmus line, and CTI ablation and subsequently underwent pacemaker implantation. However, this patient had documented sinus node dysfunction before the procedure; accordingly, this was not a complication of the device. Other minor complications included pericarditis treated with anti-inflammatory medications, an asymptomatic pericardial effusion not requiring intervention, 3 vascular complications treated conservatively, and 1 acute pharyngitis related to esophageal temperature probe placement (Table 3). Two additional adverse events were unrelated to the procedure: a common cold and acute nasopharyngitis.

TABLE 3 Procedure Complications (N = 71)

Major complications	
Stroke	0 (0)
Pericardial tamponade	0 (0)
Phrenic nerve paralysis	0 (0)
Pulmonary vein stenosis	0 (0)
Atrioesophageal fistula	0 (0)
Vascular-major complications	0 (0)
Death	0 (0)
Minor complications	
Sinoatrial blockade requiring pacemaker implantation*	1 (1.7)
Transient ischemic attack	0 (0)
Vascular-minor complications†	3 (5.0)
Pericarditis§	1 (1.7)
Pericardial effusion-no hemodynamic compromise‡	1 (1.7)
Pharyngitis‖	1 (1.7)
Esophageal observations	
Any esophageal abnormality¶	6/20 (30)
Minor erythema	4/20 (20)
Moderate erosion	2/20 (10)
Ulceration	0 (0)
Esophageal abnormality as function of posterior left atrium dosing	
Lesion duration = 4–5 s	3/8 (37.5)
Lesion duration ≤ 3.5 s	3/12 (25.0)

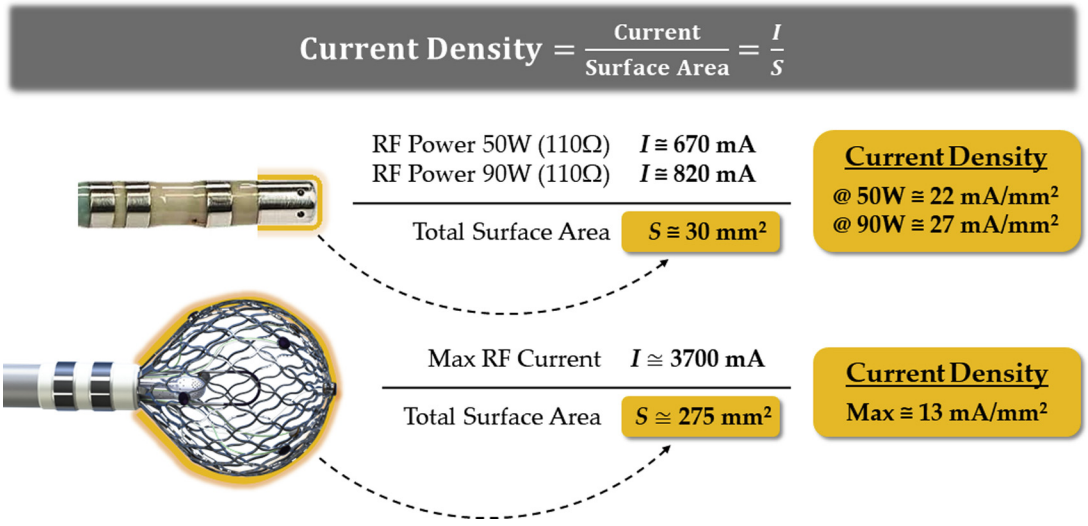
Values are n, n (%) or n/N (%). *This was noted in a patient with persistent AF after cardioversion following PVI, mitral isthmus line, and CTI ablation. This patient had documented sinus node dysfunction before the procedure, and no ablation lesions were near the sinus node. Accordingly, this was not related to the catheter but, rather, the underlying physiology. †1 patient each with groin abscess, hematoma, and arteriovenous fistula. All were confirmed with ultrasonography and treated conservatively. ‡Noted in 1 patient and treated with anti-inflammatory medications. §An asymptomatic minimal pericardial effusion not requiring intervention. ‖Related to placement of a temperature probe into the esophagus. ¶Identified by endoscopy in patients ablated with temperature monitoring. (Patients with esophageal deviation are not included.) All abnormalities resolved upon repeat endoscopy 1 to 2 weeks later.

In 20 of 29 patients with AF (69%) in whom the esophagus was not mechanically deviated, esophageal endoscopy was performed. Six patients (30%) had esophageal injury: 4 minor erythema, 2 moderate erosion, and no frank ulcers. Esophageal lesions were numerically less frequent when posterior LA energy delivery was limited: 38% with 4 to 5 s versus 25% with ≤3.5 s (p = NS) (Table 3). Upon repeat endoscopy 1 to 2 weeks later, all lesions showed complete resolution.

DISCUSSION

This is a first-in-human clinical study assessing the feasibility, acute effectiveness, and safety of a novel mapping and ablation technology using an expandable RF lattice-tip catheter. This technology was able

FIGURE 5 Biophysical Differences Between the Lattice Tip and a Standard Irrigated Radiofrequency Ablation Catheter



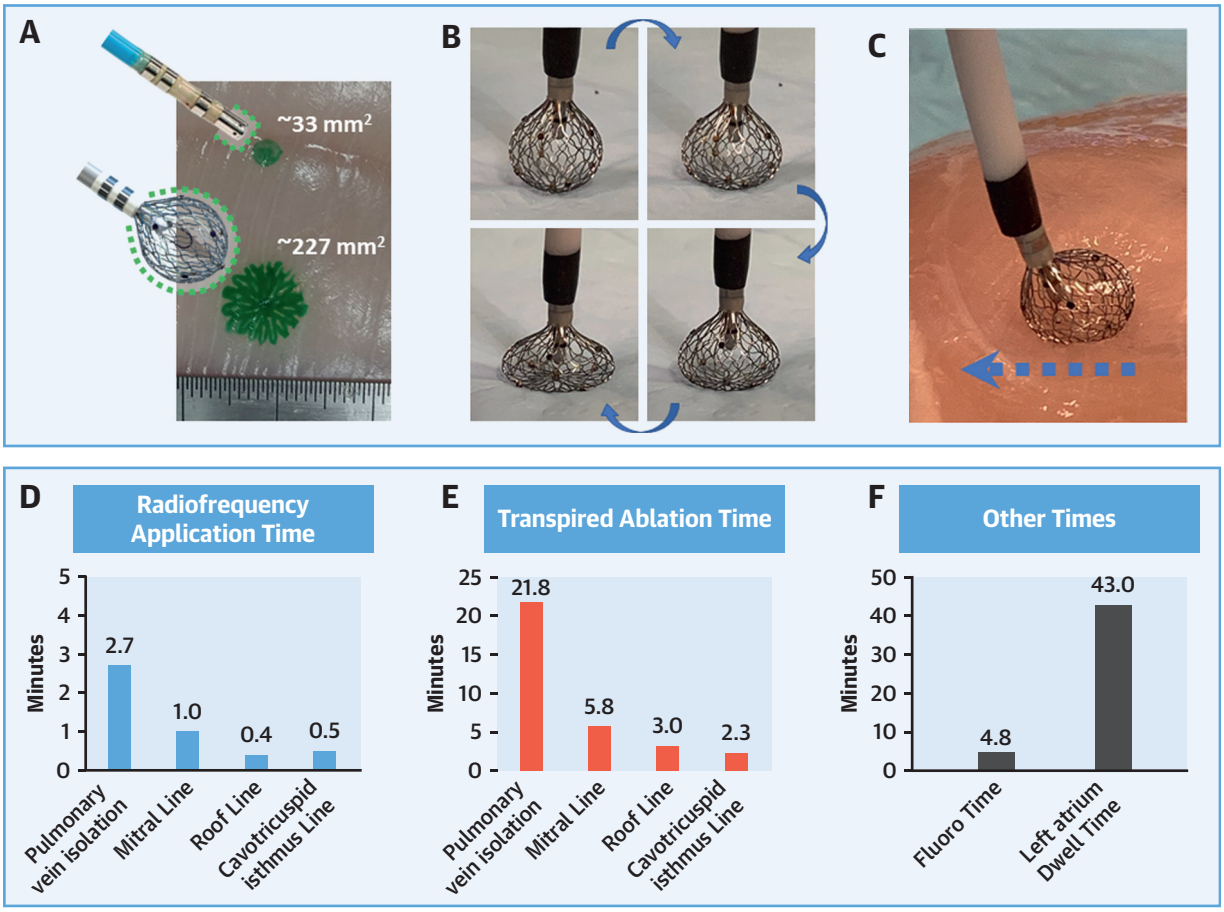
The maximal current delivered to the lattice tip is 4- to 6-fold greater than standard 3.5-mm/8-F-tip catheters, but the surface area over which this energy is distributed over the lattice tip is nearly 10-fold greater (275 mm^2 vs. 30 mm^2). Accordingly, the maximal average current density during ablation with the lattice-tip is approximately 40% to 50% less than with standard tips, thereby minimizing the probability of the tissue overheating. RF = radiofrequency.

to guide the rapid deployment of the AF/AFL ablation lesion sets most commonly used in clinical practice—electrical isolation of the pulmonary veins and linear block across the CTI, mitral isthmus, and LA roof. The rate of safety events was low, without evidence of major complications related to AF ablation, including cardiac perforation/tamponade, atrioesophageal fistula, cerebrovascular events, or PV stenosis.

THE LATTICE-TIP CATHETER. This technology could create lesions that, on one hand, are suitable for the thin posterior LA wall and, on the other hand, are able to ablate transmurally along the thicker anterior LA and the mitral annulus (despite epicardial cooling from the coronary sinus blood flow). This ability to create a titratable range of lesion dimensions is related to the larger surface area of the lattice structure. The lattice tip has a 10-fold larger effective area compared with a conventional 8-F/3.5-mm electrode (275 vs. approximately 28 mm^2) and therefore delivers significantly higher currents at a lower current density (Figure 5). The lattice-tip couples to the target myocardium with a greater surface area than the standard tip, and the consequent region of tissue heating, the thermal footprint, is larger—in turn, leading to wider lesions (Central Illustration). The lower current density also results in more homogeneous heating with reduced risk for hot spots and steam pops from tissue overheating. In addition, the use of a high-current generator permits energy delivery for short durations, limiting collateral damage from passive conductive heating (11).

The lattice provided the flexibility to tailor the ablation lesions to each patient's individual anatomy, ensuring sufficient lesion overlap and redundancy. Another advantage of this technology is the integration of high-resolution mapping and ablation in a single catheter. The multielectrode lattice with its small and closely spaced electrodes creates dense maps sufficient for defining the anatomy and for voltage and activation mapping. Although we did not routinely pace from the lattice tip, this can also be used for the evaluation of exit block after PVI, differential pacing, and entrainment of macro-reentrant circuits. It also reduces the need for 2 transseptal punctures during PVI; indeed, over one-half of the AF ablations in this series were performed by using a single transseptal sheath. Although not assessed quantitatively, the lattice mesh structure provided a gentle engagement of the tissue that improved tissue stability and prevented sliding of the catheter during application (Central Illustration). This was particularly noticeable during ablation at the posterior right PVs, anterior left PVs, and mitral isthmus.

CENTRAL ILLUSTRATION **The Lattice-Tip Radiofrequency Ablation Catheter**



Anter, E. et al. J Am Coll Cardiol EP. 2020;6(5):507–19.

(A) The thermal footprint potentials of the lattice-tip and standard-tip catheters are depicted by dipping each in **green ink** and blotting onto the surface of meat; the former is approximately 7-fold larger. The lattice-tip's **(B)** compressibility and **(C)** tendency to not slide across tissue with lateral force facilitate catheter stability during ablation (corresponding videos in Videos 7 and 8). Below are **(D)** the radiofrequency application and **(E)** transpired ablation times for various atrial linear lesions with the lattice tip, as well as **(F)** the overall fluoroscopy and left atrium dwell times.

LATTICE-TIP CATHETER ABLATION PERFORMANCE. In all patients, except 1 patient during the initial experience phase, PVI was achieved with the lattice catheter alone. Most striking, however, was the favorable performance of this large thermal footprint catheter: the mean RF application time with the lattice tip was only 2.75 min, and the mean transpired ablation time (from the first to the last PVI lesion), which is the most relevant parameter from a workflow perspective, was only 21.8 min. Furthermore, mitral isthmus ablation with the lattice was 100% successful, requiring epicardial CS ablation in only 4.5% of cases. Furthermore, for mitral isthmus ablation: 1) the mean RF application time was only 1.0 min; and 2) the lattice-tip transpired time was only 5.8 ± 6.4 min.

Finally, we assessed the LA dwell time, defined as the time transpiring from when the lattice catheter was first introduced into the chamber to when it was removed. The observed LA catheter dwell time of 43.0 min is all the more remarkable when considering that this time encapsulates not only atrial mapping and PVI but also mitral isthmus and roof ablation in approximately 40% of the AF cohort. These results are favorable not only as a point-by-point ablation solution, but even for one-shot catheters, such as

balloon ablation catheters and the recently introduced pulsed field ablation basket catheter (10,16) (see Supplemental Tables 1 and 2 and Supplemental Figure 1, for comparative data). Thus, the lattice catheter not only retains the flexibility of point-by-point ablation but has a workflow reminiscent of one-shot technologies.

CLINICAL EFFICACY. The focus of this report is the safety and acute efficacy of this novel technology, so clinical follow-up primarily addressed safety considerations. The only short-term efficacy data available is that during the first 3 months of follow-up, a single patient with AF presented with clinical recurrence. Data from long-term follow-up will be necessary to evaluate the true clinical efficacy of this technology; continued follow-up of this cohort, as well as future cohorts from additional studies, will help clarify this. On the other hand, the observed ability to achieve linear block of the various lesion sets with limited numbers of applications may hint toward its long-term effectiveness. In the CTI, the catheter footprint covers roughly 20% to 25% of the linear length of the ablation line, consistent with the small number of applications required to achieve block. This was similarly observed for the often-challenging mitral line—a limited number of endocardial-only applications were frequently sufficient for block. Ultimately, however, it will be important to assess the durability of all of these lesion sets by conducting dedicated invasive remapping studies.

SAFETY. There were no major complications such as atrioesophageal fistula, cardiac tamponade, phrenic nerve paralysis, PV stenosis, or stroke/transient ischemic attack. However, endoscopy identified esophageal erythema/erosions in 30% of patients in whom esophageal temperature monitoring had been employed. This incidence is within the range of previously reported post-ablation esophageal injury rates (from 10% to 40%), with a recent systematic review indicating an average esophageal injury rate of 15% (1,17). On the other hand, that review also reported an average deep esophageal ulcer rate of approximately 4%, but none were observed in our experience. Of course, these observations are derived from a modest number of patients in whom endoscopy was performed in only 69% of those with temperature monitoring; future studies should evaluate this more systematically and in a larger patient cohort. Also, the safety profile we observed is predicated on the use of either esophageal temperature monitoring or mechanical esophageal deviation; in their absence, little from the present report should be extrapolated regarding the safety of lattice-tip ablation.

STUDY LIMITATIONS. The small sample size, short follow-up, and observational design of this first-in-human study precludes robust direct comparison to other ablation technologies, thereby limiting our ability to draw definitive conclusions about its relative safety and efficacy. A multicenter study with pre-specified settings, long-term follow-up, and comparison to conventional technologies should be conducted in the future. This technology's safety should also be investigated in larger multicenter studies. Indeed, although no patient presented with symptoms of PV stenosis, routine follow-up computed tomography/magnetic resonance imaging was not performed; accordingly, we cannot rule out the possibility of subclinical PV stenosis. Similarly, only routine brain magnetic resonance imaging can determine the presence and frequency of silent cerebral ischemic events.

CONCLUSIONS

This first-in-human study demonstrates the workflow advantages of integrating high-resolution mapping with high-power ablation into a single catheter. Most importantly, however, this novel lattice-tip catheter highlights the advantages of RFA with a large thermal footprint: one retains both the flexibility of point-by-point catheters and the ease of use of one-shot technologies to create PVI, CTI, mitral isthmus, and LA roof lines.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: A novel technology based on a lattice electrode with a large thermal footprint demonstrated clinical feasibility and safety for rapid point-by-point PVI and linear ablation.

TRANSLATIONAL OUTLOOK: Larger, multicenter trials are needed to compare the safety and long-term durability of this technology versus standard technologies in treating patients with atrial fibrillation.

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KEY WORDS atrial fibrillation, catheter ablation, mitral line, multielectrode, pulmonary vein isolation

APPENDIX For a supplemental figure, tables, and videos, please see the online version of this paper.