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A Lattice-Tip Temperature-Controlled Radiofrequency Ablation Catheter

Durability of Pulmonary Vein Isolation and Linear Lesion Block

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ABSTRACT

OBJECTIVES This study was designed to evaluate lesion durability on invasive electrophysiologic remapping.

BACKGROUND The lattice-tip catheter generates a large thermal footprint during temperature-controlled irrigated radiofrequency ablation. In a first-in-human study, this catheter performed rapid point-by-point pulmonary vein isolation (PVI) and other linear atrial ablations.

METHODS In a prospective 3-center single-arm study, paroxysmal or persistent atrial fibrillation patients underwent PVI and, as needed, linear ablation at the cavotricuspid isthmus (CTI), mitral isthmus (MI), and/or left atrial roof; no other atrial substrate was ablated. Using the lattice catheter and a custom electroanatomic mapping system, temperature-controlled (Tmax 73° to 80°C; 2 to 7 s) point-by-point ablation was performed. Patients were followed for 12 months.

RESULTS A total of 65 patients (61.5% paroxysmal/38.5% persistent) underwent ablation: PVI in 65, MI in 22, left atrial roof in 24, and CTI in 48 patients. At a median of 108 days after the index procedure, protocol-mandated remapping was performed in 27 patients. The pulmonary veins (PVs) remained durably isolated in all but 1 reconnected PV—translating to durable isolation in 99.1% of PVs, or 96.3% of patients with all PVs isolated. Of 47 linear atrial lesions initially placed during the index procedure, durability was observed in 10 of 11 (90.9%) MI lines, all 11 (100%) roof lines, and all 25 (100%) CTI lines. After a median follow-up of 270 days, the 12-month Kaplan-Meier estimate for freedom from atrial arrhythmias was 94.4 ± 3.2%.

CONCLUSIONS Temperature-controlled lattice-tip point-by-point ablation showed not only highly durable PVI lesion sets, but also durable contiguity of linear atrial lesions. (J Am Coll Cardiol EP 2020;6:623–35) © 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
AT = atrial tachycardia
CTI = cavotricuspid isthmus
EAM = electroanatomical map
LA = left atrium
LPV = left pulmonary vein
PAF = paroxysmal atrial fibrillation
PerAF = persistent atrial fibrillation
PVI = pulmonary vein isolation
RF = radiofrequency
RFA = radiofrequency ablation

The technical complexity of catheter ablation of atrial fibrillation (AF) has prompted development of numerous technologies to facilitate the procedure. Most advances have focused on facilitating pulmonary vein isolation (PVI)—in particular, "one-shot" ablation catheters such as the cryoballoon (1). Their ease-of-use has popularized them such that balloon ablation now represents ~25% of all AF ablation procedures performed worldwide.

On the other hand, point-by-point radiofrequency ablation (RFA) remains the most common catheter approach to treating AF because of its flexibility—both in tailoring energy to varying tissue thickness/safety concerns, and in creating lesion sets beyond PVI. However, the advances in point RFA that have occurred over the past 2 decades—saline irrigation, contact force sensing, and more recently, surface thermocouples—have largely focused on improving the quality of individual lesions (2–6). Although important, these features have less impact on the technical ease of creating contiguous, electrically durable point-by-point linear lesions.

Recently, a point RFA technology was designed to both maintain the rapid workflow characteristic of one-shot ablation technologies, and facilitate the contiguity of adjacent spot lesions (7). This catheter is comprised of a 7.5-F shaft, with a compressible spheroid-shaped ~9-mm diameter lattice electrode tip that delivers temperature-controlled saline-irrigated radiofrequency energy. The broad area of surface interaction between the deformable lattice-tip and target tissue creates a large thermal footprint, and consequently a uniform, wide ablation lesion. In addition, the stability of catheter positioning at any location is enhanced by the combination of: 1) compressibility of the lattice mesh with a spring-like interaction with tissue; and 2) a complex tip surface topography that attenuates catheter sliding along tissue.

In a first-in-human multicenter clinical study of first-time ablation for paroxysmal or persistent AF, this lattice catheter potentiated extremely rapid procedural times for PVI and bidirectional block across linear lesions—the mitral isthmus (MI), cavotricuspid isthmus (CTI), and left atrial (LA) roof (8). Although this acute performance was promising, little is known about the durability of these lesion sets. Accordingly, we now report on the outcomes of protocol-driven invasive remapping procedures—on the integrity of both the PVI lesion sets, and the linear atrial lesions.

METHODS

This study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committees and local health authorities at all participating sites/countries. Informed consent was obtained from all subjects.

STUDY DESIGN. As previously described, 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 Union countries (2 centers in the Czech Republic and 1 in Lithuania; NCT04210622) (8). The initial ablation procedures were performed at all 3 centers, and the remap procedures were conducted at the 2 Czech centers.

Briefly, eligible patients were adults with symptomatic paroxysmal atrial fibrillation (PAF) or persistent atrial fibrillation (PerAF). This analysis included patients who underwent 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 $< 40\%$, previous cardiac ablation, or stroke within 6 months.

ELECTROANATOMICAL MAPPING AND ABLATION SYSTEM. The ablation technology includes a lattice-tip ablation catheter (Sphere-9, Affera, Inc.), a high-current radiofrequency (RF) generator (HexaGen;

Liva Nova (MicroPort CRM) and St. Jude Medical (Abbott) for participation in scientific advisory boards; and has received speaker honoraria from Bayer, Biosense Webster, Biotronik, Boehringer Ingelheim, Boston Scientific, Daiichi-Sankyo, Medtronic, Merck Sharp & Dohme, Mylan, Pfizer, ProMed sro, and St. Jude Medical (Abbott). Drs. Reddy, Anter and Nakagawa have received research grants from Affera, Inc. Drs. Reddy, Anter, and Jackman also hold stock options in Affera, Inc. Dr. Nakagawa is also a consultant to Affera, Inc. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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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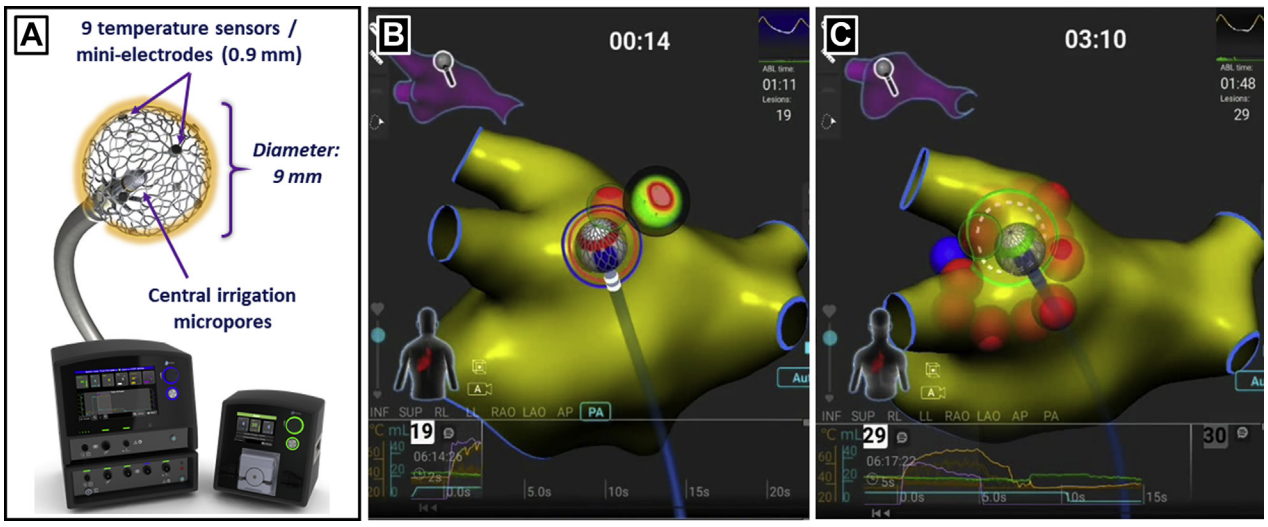
FIGURE 1 Lattice Catheter and Mapping/Ablation System



(A) The system includes the lattice-tip catheter, an integrated mapping system, high-current radiofrequency generator, and irrigation pump. The expanded lattice electrode (diameter, 9 mm) contains 9 mini-electrodes with embedded thermocouples. Radiofrequency energy emanates from the entire lattice framework to create a uniform current cloud, and the generator modulates current output in a temperature-controlled mode. **(B)** During ablation, heat detected by the surface thermocouples is represented on a pop-up bullseye map that hovers near the ablation tip icon. **(C)** After circumferential pulmonary vein ablation, electrical isolation is verified using the mini-electrodes on the lattice-tip.

Affera, Inc.) with a peristaltic saline infusion pump, and an electroanatomical mapping (EAM) system (Prism-1, Affera, Inc.). As previously described, the 7.5-F bidirectional deflectable catheter has at its tip an expandable 9-mm diameter lattice electrode (**Figure 1**) (7,8). This lattice contains 9 mini-electrodes (0.7-mm diameter) on the spherical surface, as well as a central indifferent electrode that cannot contact tissue. Each mini-electrode also incorporates a temperature sensor to enable temperature-controlled saline-irrigated RFA from the entire conductive spherical lattice tip; saline is homogeneously sprayed from the center of the lattice from a protected irrigation nozzle with micropores at 4 or 15 ml/min during mapping or during energy delivery, respectively. Although bipolar electrograms can be configured between any of the electrodes, the typical configuration we have chosen is bipolar between each mini-electrode and the center electrode. The system also provides an indication of catheter-tissue contact by continuously evaluating the impedance between each mini- and center electrode. A magnetic sensor situated within the lattice catheter tip allows the EAM system to track and build 3-dimensional maps.

PROCEDURAL WORKFLOW. As previously described, the initial ablation procedures were performed under either general anesthesia (56 of 65, 86.2%) or sedation, either using esophageal temperature monitoring or mechanical esophageal deviation (DV8; Manual Surgical Sciences, Minneapolis, Minnesota) without temperature monitoring (8). A decapolar catheter was placed in the coronary sinus, an intracardiac echocardiography catheter (8-F AcuNav, Siemens, Mountain View, California) helped guide transseptal punctures, and the lattice catheter was advanced through a fixed-curve or a steerable sheath (SL or Agilis NxT, Abbott, St. Paul, Minnesota). A single transseptal puncture was performed in most patients (48 of 65, 73.8%); dual transseptal punctures were performed in the remaining.

The pulmonary veins (PVs) were circumferentially isolated using the lattice catheter with each ipsilateral PV pair isolated together (**Figure 1**). According to operator preference, selected PerAF patients additionally underwent ablation of the posterior mitral isthmus, CTI, and/or LA roof. Energy was delivered using 2 settings designed for the thinner posterior wall (typically 2.5-s duration, target temperature 80°C) or the thicker anterior/septal walls (typically 5-s duration, target temperature 75°C) (7). When the esophagus was mechanically displaced, 3- to 5-s applications were used along the posterior wall. CTI ablation was typically performed at 5-s duration and

TABLE 1 Baseline Patient Characteristics

	Full AF Cohort (N = 65)	Remap Cohort (N = 27)	p Value
Age, yrs	62.4 ± 9.2	64.8 ± 9.5	0.271
Male	44 (68)	19 (70)	0.801
Body mass index, kg/m^2	29.5 ± 4.3	30.2 ± 3.9	0.450
Medical history			
Paroxysmal AF	40 (62)	15 (56)	0.594
Persistent AF	25 (38)	12 (44)	0.594
Hypertension	43 (66)	16 (59)	0.530
Diabetes	4 (6)	1 (4)	0.637
LVEF %	59.6 ± 7.3 (63)	58.9 ± 9.3	0.729
Left atrial dimension mm	42.5 ± 5.8 (63)	43.6 ± 6.6	0.455
Medications			
Warfarin	21 (32)	11 (41)	0.439
DOAC	39 (60)	14 (52)	0.471
Antiarrhythmic medication	50 (77)	23 (85)	0.372

Values are n (%) or mean ± SD.
DOAC = direct oral anticoagulants; LVEF = left ventricular ejection fraction.

TABLE 2 Index Procedure Details

	Full AF Cohort (N = 65)	Remap Cohort (n = 27)
Pulmonary vein isolation		
Successful PV lesion sets	130/130 (100)	54/54 (100)
Success using lattice catheter only	129/130 (99.2)	53/54 (98.1)
Number of RF applications	39.5 ± 8.9	39.5 ± 6.2
Total RF time, min	2.7 ± 0.7	2.7 ± 0.5
Transpired ablation time, min*	21.8 ± 12.1	18.6 ± 8.2
Total atrial dwell time, min†	43.0 ± 18.4	37.3 ± 15.7
Mitral isthmus line		
Successful linear lesion	22/22 (100)	11/11 (100)
Success using lattice catheter only	21/22 (95.5)	10/11 (90.9)
Number of RF applications	11.5 ± 10.7	14.2 ± 14.2
Total RF time, min	1.0 ± 0.9	1.2 ± 1.2
Transpired ablation time, min*	5.8 ± 6.4	6.5 ± 8.1
Roof line		
Successful linear lesion	23/24 (95.8)	11/11 (100.0)
Success using lattice catheter only	23/24 (95.8)	11/11 (100.0)
Number of RF applications	4.9 ± 1.9	5.7 ± 1.6
Total RF time, min	0.4 ± 0.2	0.5 ± 0.1
Transpired ablation time, min*	3.0 ± 4.4	4.2 ± 6.2
Cavotricuspid isthmus line		
Successful linear lesion	42/42 (100)	25/25 (100)
Success using lattice catheter only	42/42 (100)	25/25 (100)
Number of RF applications	6.1 ± 3.2	5.6 ± 1.9
Total RF time, min	0.5 ± 0.3	0.4 ± 0.1
Transpired ablation time, min*	2.1 ± 1.3	1.9 ± 1.0

Values are n/total (%)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. †Defined as the time transpiring from catheter entry to exit from the body, including linear lesions beyond PVI.
PV = pulmonary vein; RF = radiofrequency; other abbreviation as in Table 1.

a temperature of 75°C. The MI line was typically placed with 5- to 7-s applications, and a temperature of 75°C. The RF current limit was not specified in the protocol and varied between 80% and 100% as investigators adjusted dosing. As described in the Supplemental Appendix (and Supplemental Table 1), despite overall more energy being delivered by the lattice-tip, the current density (10.1 to 11.0 mA/mm^2) is less than delivered by standard irrigated catheters (18.8 to 30.2 mA/mm^2).

Based on the lattice electrode's large footprint, lesion diameter, and allowing ~25% overlap, the target distance between lesions was 6 to 8 mm. 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. Transpired ablation time reflects the time elapsing from the start of the first application to the end of the last application.

REMAPPING PROCEDURE AND FOLLOW-UP. At participating sites, per the clinical protocol, patients were requested to undergo a repeat invasive electrophysiologic procedure at ~3 months after the initial procedure to assess lesion durability, irrespective of arrhythmia recurrence. Voltage and activation mapping were performed using a standard EAM system (CARTO, Biosense-Webster Inc., Irvine, California), and multielectrode catheters. Lesion gaps received additional RFA using a standard irrigated catheter.

Patients were followed for up to 12 months, including 48-h Holter monitoring at 3, 6, and 12 months after the index ablation procedure. Additional monitoring was performed based on symptoms.

METHODOLOGY FOR ANALYZING THE INDEX ABLATION LESIONS. Adjacent RFA deliveries during the index procedure were identified by the EAM system. Spatial connectivity was used to analyze the geometry of each lesion set. This analysis included spacing between adjacent RFA deliveries, spacing between adjacent sites of heating, and lesion set length.

The distances between adjacent deliveries were measured from the center of the lattice tip at each RFA site to the centers of adjacent sites in the same lesion set. Sites of heating were also identified for each lesion, and gap lengths were measured between heating sites in adjacent RFA deliveries (see Supplemental Figure 1). The length of each lesion set was measured as the cumulative distance between the centers of the sites of heating in adjacent RFA deliveries.

STATISTICAL ANALYSIS. Being a feasibility study for a new technology, descriptive statistics were used to characterize study outcomes and safety parameters; there was no formal hypothesis testing or power calculation. The Kaplan-Meier estimator was used to calculate event-free survival outcomes. Continuous variables are reported as mean ± SD, or median (range), and categorical variables are reported as number (percentage).

RESULTS

PATIENT CHARACTERISTICS. Between May 2018 and May 2019, 65 AF patients (40 PAF [61.5%] and 25 PerAF [38.5%]) underwent ablation at 3 sites (8 operators) in this first-in-human study. At a median of 108 days (interquartile range = 84 days) after the index ablation procedure, 27 of 55 (49.1%) potential patients available for remapping at the 2 centers agreed to undergo this second procedure. The baseline clinical characteristics of the full ablation cohort and the remap cohort are shown in Table 1. The 27-patient remap cohort was relatively evenly split between those initially presenting with PAF (n = 15, 56%) or PerAF (n = 12, 44%). The clinical characteristics of the remap cohort were similar to the full AF cohort.

INDEX PROCEDURE. The acute procedural performance parameters during the index ablation procedure have been previously reported (8). Table 2 shows a comparison of the various procedural parameters of the initial AF ablation lesion set in both the full 65-patient cohort and the 27-patient remap cohort. All ipsilateral PV pairs of the remap cohort had been successfully electrically isolated during the index procedure with the lattice catheter using 39.5 ± 6.2 RF applications/patient, for a total RF time of 2.7 ± 0.5 min and total transpired ablation time of 18.6 ± 8.2 min.

Using the lattice catheter, bidirectional block across the posterior MI (in 11 patients), CTI (in 25 patients), and LA roof (in 11 patients) had been achieved during the index procedure in all remap cohort patients with attempts (Table 2). In 1 patient, MI block required an additional lesion from within the coronary sinus using a conventional 3.5-mm tip ablation catheter. The number of RF applications/patient required were 14.2 ± 14.2, 5.6 ± 1.9, and 5.7 ± 1.6 for the MI, CTI, and LA roof lines, respectively. The total RF times were 1.2 ± 1.2, 0.4 ± 0.1, and 0.5 ± 0.1 min, respectively. The total transpired ablation times were 6.5 ± 8.1, 1.9 ± 1.0, and 4.2 ± 6.2 min, respectively.

TABLE 3 Remap Procedure Details

	Full Cohort (N = 27)	PAF Cohort (n = 15)	PerAF Cohort (n = 12)
Timing of remap procedure, days	133 ± 76	154 ± 92	106 ± 41
Durability of pulmonary vein isolation			
Patients with all PVs isolated	26/27 (96.3)	14/15 (93.3)	12/12 (100.0)
Ipsilateral PV pairs isolated	53/54 (98.1)	29/30 (96.7)	24/24 (100.0)
PVs isolated	108/109 (99.1)	59/60 (98.3)	49/49 (100.0)
Durability of the linear atrial lesions			
Mitral isthmus line blocked	10/11 (90.9)	2/2 (100.0)	8/9 (88.9)
LA roof line blocked	11/11 (100)	3/3 (100)	8/8 (100)
CT isthmus line blocked	25/25 (100)	13/13 (100)	12/12 (100)

Values are mean +/− SD or n/N (%).

CT = cavotricuspid; LA = left atrial; PAF = paroxysmal atrial fibrillation; PerAF = persistent atrial fibrillation; other abbreviation as in Table 2.

REMAP PROCEDURE. Of the 27 patients who underwent remapping, the PVs remained durably isolated in all but 1 instance of a reconnected right superior PV—translating to durability in 99.1% of PVs, 98.1% of ipsilateral PV pairs, and 96.3% of patients with all PVs isolated (Table 3). An example of the voltage map during the remap procedure is shown in Figure 2.

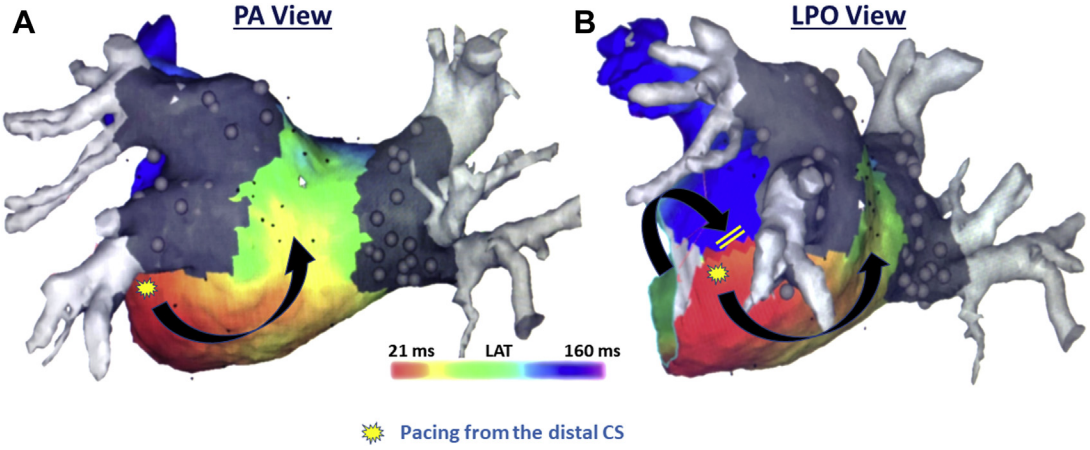
A total of 47 atrial linear lesions had been placed during the index ablation procedure in these patients—11 posterior MI lines, 11 LA roof lines, and 25 CTI lines. Of these, durable bidirectional block was shown in all LA roof and CTI lines, and in all but 1 MI line (Table 3). An example of durable mitral isthmus block is shown by activation mapping in Figure 2.

For the patient with a PV reconnection, using a conventional 3.5-mm tip saline-irrigated RFA catheter, 8 RF lesions were placed at a single location near the LA roof to re-isolate the right superior PV. Similarly, for the patient with unidirectional block in the MI line, bidirectional block was achieved with 2 epicardial lesions placed from the coronary sinus using a conventional 3.5-mm tip irrigated RFA catheter (Figure 3).

Five other patients underwent additional ablation using a conventional irrigated RF catheter. The first, a PAF patient who presented with an LA roof-dependent atypical flutter before the remapping procedure, was found to have intact lesion sets, and required LA roof ablation (Figure 4; see details below). Ablation in the remaining 4 patients was performed not for patient symptoms, arrhythmia recurrence, or gaps in lesion sets, but rather because of physician preference.

ANALYSIS OF THE INDEX ABLATION LESION SET. The ablation lesion sets created by the lattice-tip catheter during the index ablation procedure were

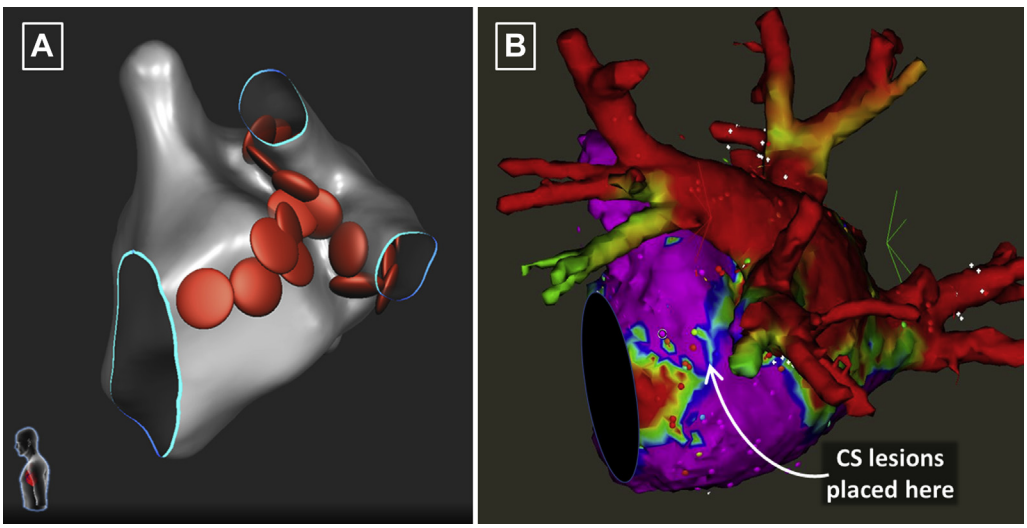
FIGURE 2 Durability of Pulmonary Vein Isolation and Mitral Isthmus Block



During remapping, the pulmonary veins were electrically isolated, and the mitral isthmus was bi-directionally blocked—this was confirmed with multielectrode mapping catheters. In these posterior (PA) **(A)** and left-posterior oblique (LPO) **(B)** views of conventional electroanatomical activation mapping, conduction block is observed along the mitral isthmus line during distal coronary sinus pacing. The scar threshold **(grey color)** was set to ≤0.1 mV (fill threshold = 15 mm). CS = coronary sinus; LAT = local activation time.

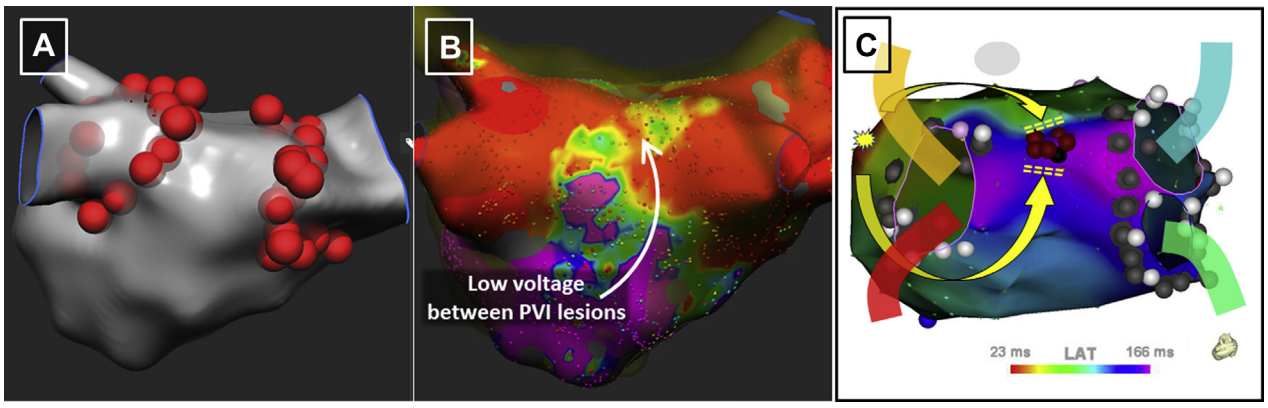
characterized in detail by evaluating both the distances between adjacent lesion tags and the distances between adjacent heat signatures. Whereas the former is self-explanatory, the latter refers to heat detected by the lattice-tip thermocouples (Supplemental Figure 1). As shown in **Table 4**, the overall lengths of the ipsilateral PVI lesion sets were 122 ± 30.8 mm; the lengths of the various linear lesions—MI, LA roof, and CTI lines—were 37.8 ± 11.2, 25.4 ± 11.2, and 30.3 ± 13.8 mm, respectively. For all

FIGURE 3 An Incomplete Mitral Isthmus Line



(A) In this left-posterior oblique view, the left pulmonary vein and mitral isthmus lesions placed during the index procedure by the lattice-tip are shown. **(B)** Shown is a bipolar voltage map (color range, 0.1 to 0.5 mV) during the remap procedure using a conventional mapping system. The pulmonary veins remained isolated, but the mitral isthmus line was only unidirectionally blocked—conduction from medial to lateral was evident upon coronary sinus pacing (not shown). Bidirectional mitral isthmus block was reconstituted using a conventional irrigated catheter to place 2 coronary sinus lesions.

FIGURE 4 Atypical Left Atrial Flutter After Durable Pulmonary Vein Isolation



The baseline anatomical shell shows the pulmonary vein isolation lesions created with the lattice-tip catheter **(A).** The immediate post-ablation voltage map reveals a low voltage area between the pulmonary vein isolation lesion sets **(B),** thereby potentiating an atypical flutter. This was eliminated during the remapping procedure—within 10 s of radiofrequency energy delivery along the posterior left atrial roof with a standard irrigated catheter. After ablation, activation mapping during left atrial appendage pacing showed roof line block **(C).** LAT = local activation time; PVI = pulmonary vein isolation.

of these lesion sets, the average spacing between the centers of adjacent lesions was ~6.6 mm, with 1 SD being ~2 mm; thus, the centers of the majority of lesions were < 9 mm from each adjacent lesion. Similarly, the heat signatures of adjacent lesions had an average gap distance of ~3.7 mm.

CLINICAL FOLLOW-UP. The majority of patients (57 of 65, 88%) had stopped taking class I or III antiarrhythmic drugs (AADs) by the time of the last follow-up; those who continued were on previously failed drugs at the same or reduced doses. For the 8 patients who continued medications, the reason was symptoms in 4 patients (50%), whereas the remaining 4 patients (50%) simply continued the medications as they reported not being instructed to stop them.

We previously reported that the short-term safety of lattice ablation was favorable, including no pericardial tamponade, atrioesophageal fistula, stroke, phrenic nerve injury, or PV stenosis. Over the full of follow-up (median = 270 days; interquartile range = 192 days), there were no additional long-term safety events such as PV stenosis or atrioesophageal fistula, including minor complications.

Compliance with 48-h Holter monitoring was 66% overall, including 95% for the final scheduled Holter. The 12-month Kaplan-Meier estimates for freedom from AF/atrial flutter (AFL)/atrial tachycardia (AT) and AF for the full AF cohort were 94.4 ± 3.2% and 98.5 ± 1.5%, respectively (**Figures 5A and 5B**). The 12-month Kaplan-Meier estimates for freedom from AF/AFL/AT for the PAF and PerAF cohorts were 97.2 ± 2.7% and 89.6 ± 7.2%, respectively (**Figures 5C and 5D**). As sensitivity analyses, 12-month Kaplan-Meier estimates for freedom from AF/AFL/AT were calculated after excluding either: 1) the 5 patients receiving additional ablation during the remap procedure (97.3 ± 2.7%) (Supplemental Figure 2); or 2) the 8 patients who continued AADs (98.2 ± 1.7%) (Supplemental Figure 3). Finally, there were no recurrences after including 1.12 ablation procedures/patient (Supplemental Figure 4).

Overall, there were three patients with clinical recurrences. The first was the PAF patient who initially underwent PVI and CTI, but then presented with an atypical atrial flutter at 169 days on Holter monitoring. The redo procedure at 210 days revealed intact PVI and CTI lesion sets. However, there was an LA roof-dependent atypical flutter coursing through an

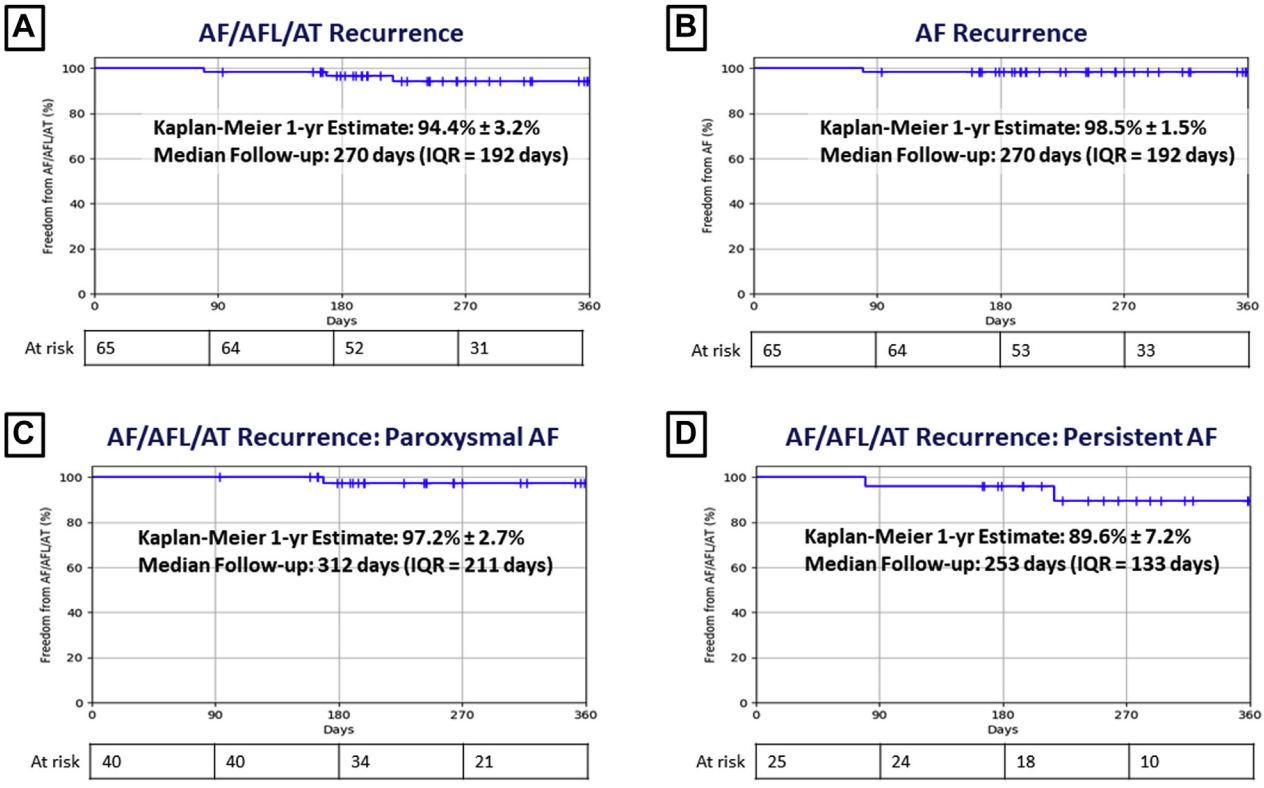
TABLE 4 Lattice-Tip Lesion Characteristics

Lesion Type	Lesion Length (mm)	Lesion Center Spacing (mm)	"Hot" Sensor Spacing (mm)*
PVI lesion set (n = 126)†	122.0 ± 30.8	6.6 ± 2.2	3.9 ± 2.0
Left PVs (n = 63)	106.7 ± 24.6	6.6 ± 2.3	4.1 ± 2.1
Right PVs (n = 63)	137.4 ± 28.7	6.6 ± 2.0	3.7 ± 1.9
Linear atrial lesions			
Mitral isthmus line (n = 22)	37.8 ± 11.2	6.4 ± 2.4	3.5 ± 1.8
LA roof line (n = 23)‡	25.4 ± 11.2	7.0 ± 2.2	4.1 ± 1.9
CT isthmus line (n = 39)§	30.3 ± 13.8	7.0 ± 2.2	3.5 ± 1.8

*"Hot" is defined as a thermocouple that achieves a temperature ≥ 52°C for ≥0.5 s. †Excluded 2 patients because 1 dataset was not saved, and another was corrupted. ‡Excluded 1 LA roof line because only 1 lesion was delivered. §Excluded 1 CT isthmus line due to missing data.

PVI = pulmonary vein isolation; other abbreviations as in Table 3.

FIGURE 5 Arrhythmia Recurrence Over Follow-Up



Kaplan-Meier curves of 1-year freedom from atrial fibrillation (AF)/atrial flutter (AFL)/atrial tachycardia (AT) recurrence **(A)** and AF recurrence **(B)** is shown for the full 65-patient cohort, and freedom from AF/AFL/AT recurrence in the paroxysmal **(C)** and persistent **(D)** AF subgroups.

area of low-voltage substrate over the posterior LA and roof between the two PV lesion sets (Figure 4). This was treated with ablation along the LA roof using a conventional irrigated RFA catheter. Subsequent Holter monitoring at 273 and 346 days revealed no further recurrence.

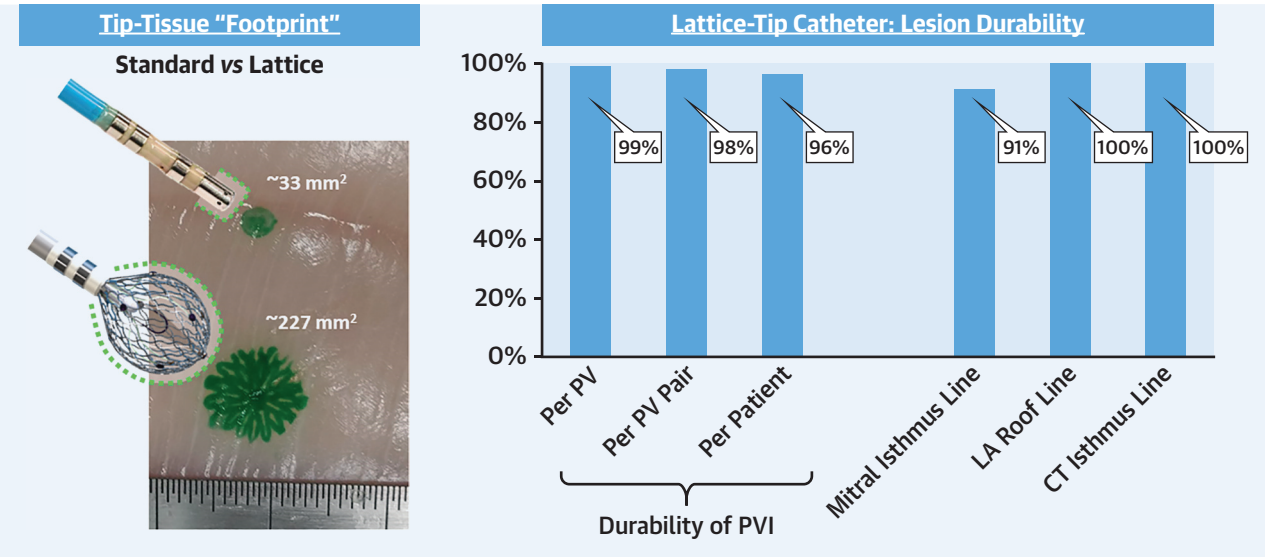
The second recurrence was a PerAF patient (weight, 115 kg; LA diameter, 60 mm) who initially underwent both PVI and linear ablation of the mitral isthmus, LA roof, and CTI. He was noted to be in AF by Holter at 80 days, during an office visit at ~90 days, and when he arrived for a redo procedure at 176 days. This procedure revealed that all of the initial lesion sets were intact, so a standard irrigated RFA catheter was used to create additional ablation lesions, including a posterior-inferior line to complete a posterior box and anterior LA ablation. The patient was discharged off AADs and remained in sinus rhythm at 3-months follow-up.

The third recurrence was in a persistent patient who initially received PVI and CTI. Remapping at 112 days revealed intact PVI and CTI lesion sets, so no ablation was performed. At 217 days, the patient presented with symptomatic atrial flutter confirmed on a 12-lead electrocardiogram. The patient was prescribed amiodarone and scheduled for electrical cardioversion, but converted spontaneously. Subsequent Holter monitoring revealed sinus rhythm.

DISCUSSION

The Achilles heel of AF ablation has long been the difficulty in creating durable linear lesions—the archetype being PV encirclement. Although conduction block is typically achieved acutely, the mechanism is often a combination of both tissue necrosis (which is desirable) and reversible injury such as tissue edema or hemorrhage (9). And, because the contribution of the latter is transient, the subsequent resumption of electrical conduction culminates in clinical recurrence. In this context, the remapping results of the lattice-tip RF catheter are striking: high rates of lesion durability (>90%) were observed for

CENTRAL ILLUSTRATION **The Lattice-Tip Catheter Achieves High Lesion Durability**



Reddy, V.Y. et al. J Am Coll Cardiol EP. 2020;6(6):623–35.

(Left) The lattice-tip and a standard-tip catheter are dipped into green ink and blotted onto tissue: the lattice-tip catheter-tissue interaction is ~7-fold greater, and during ablation, results in a substantially larger thermal footprint. **(Right)** The durability of the lattice-tip lesions is shown, as assessed by protocol-mandated invasive remapping in 27 patients. Pulmonary vein isolation durability is expressed for: 1) individual veins; 2) ipsilateral pulmonary vein pairs; and 3) on a per patient basis (that is, percent of patients with all veins isolated). Also shown is the persistence of bidirectional block across the various linear lesions. CT = cavotricuspid; LA = left atrial; PV = pulmonary vein.

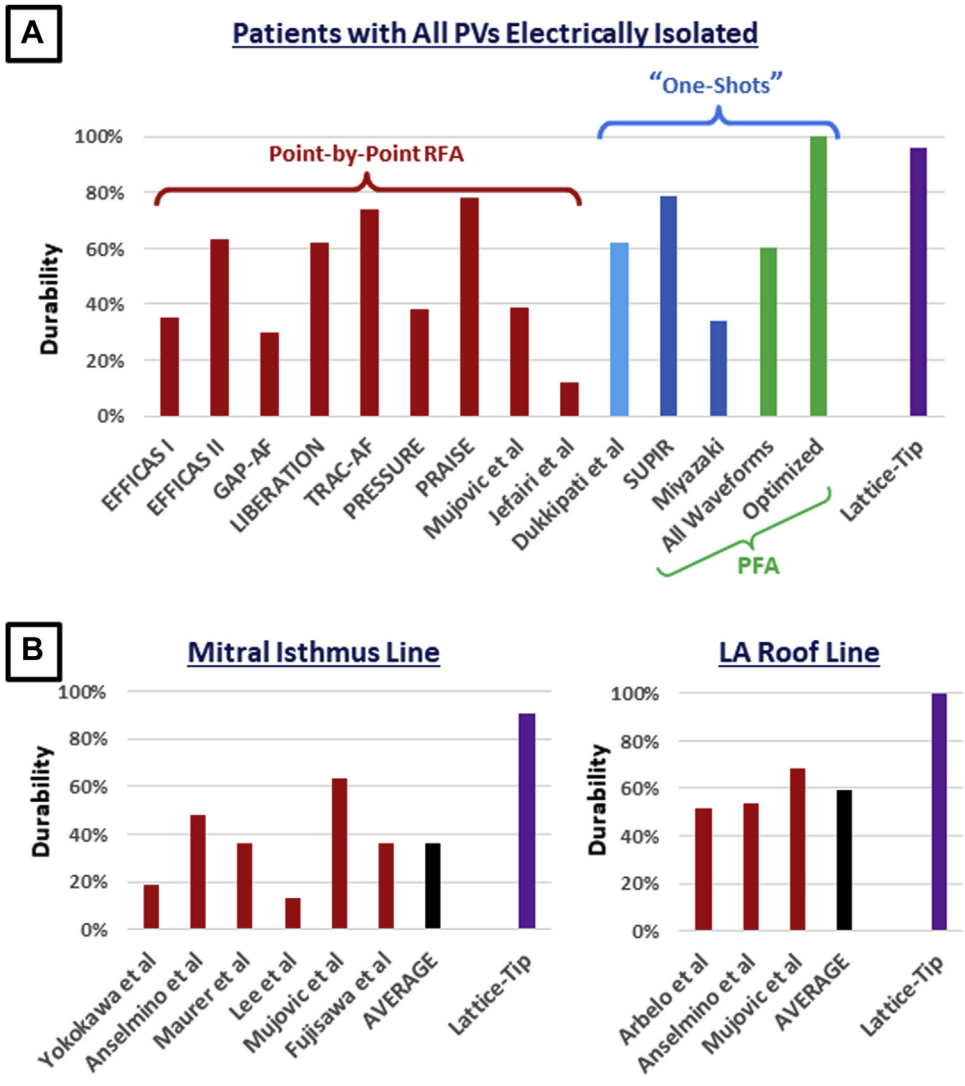
not only PV isolation, but also the linear atrial lesion sets most commonly used in clinical practice—the posterior MI, LA roof, and CTI (Central Illustration). After a median follow-up of 270 days, the 12-month Kaplan-Meier estimate for freedom from all atrial arrhythmias (AF/AFL/AT) was 94.4%.

DURABILITY OF PV ISOLATION. Although PVI has been the cornerstone of ablative therapy for AF, be it paroxysmal or persistent, determining the actual success of achieving durable PVI is problematic. Because it is currently not possible to noninvasively determine whether PVs are electrically isolated, the only accurate assessment is by a repeat catheter procedure several months after the index procedure to directly measure electrical PV activity—an approach that asymptomatic patients are largely unwilling to undergo. However, there have been a few studies of protocol-mandated invasive re-looks; typically ~3 months after the index procedure (see Figure 6).

For point-by-point RF ablation, one of the first and largest is the GAP-AF (Gap-Atrial Fibrillation-German Atrial Fibrillation Competence Network 1) trial, a multicenter trial in which 93 patients underwent re-look procedures after initial RF ablation (10). Whereas all PVs were acutely isolated, only 30% of patients had sustained/durable PVI at the 3-month re-look procedure. Other studies have reported somewhat better durability rates; but despite being predominantly single-center studies with highly experienced operators, none have reported PVI durability rates on a per-patient basis exceeding 80% after point-by-point RF ablation (Figure 6A).

One-shot ablation technologies, such as the laser- and cryoballoon, have rendered PVI an easier, more accessible procedure for many operators. The durability rates for these procedures have also approached 80% (Figure 6A). But the real-world multicenter experience seems to be considerably worse: while not easily assessable, one approach to estimating PVI durability in large datasets is to examine patients undergoing redo procedures for symptom recurrence. In the recent large RF versus cryoballoon trial, FIRE and ICE, patients undergoing clinically driven redo procedures showed only a 22% durability rate for cryoballoon ablation (and a 17% durability rate for RF ablation) (11). There were 1.4 ± 1.1 and 2.1 ± 1.4 reconnected PVs per patient, respectively.

FIGURE 6 Comparing Lesion Durability for the Lattice-Tip to Other Ablation Catheters



(A) The percentage of patients with all pulmonary veins durably isolated is shown for various standard irrigated radiofrequency ablation (RFA) catheters **(red),** one-shot ablation technologies (laser balloon **[light blue],** cryoballoon **[dark blue],** and the pulsed-field ablation [PFA] basket catheter **[green]),** and the lattice-tip catheter **(purple).** Lattice-tip durability (96%) was substantially better than both other point-by-point RFA catheters (average, 48%; range, 12% to 78%), and the one-shot balloons (average, 58%; range, 34% to 79%), and even comparable to PFA using the optimized biphasic waveform (100%). **(B)** Lattice-tip mitral isthmus line durability (90%) exceeds the outcomes using standard-tip RFA catheters (average, 36%; range, 13% to 63%). Similarly, left atrial (LA) roof line durability with the lattice-tip (100%) again exceeded that observed with standard-tip catheters (average, 60%; range, 53% to 68%). Not all values are shown for all studies because they were not reported. The outcomes and references for these studies are detailed in the Supplemental Appendix (Supplemental Refs. 2,3,7,13,14,16, and 20).

Durable PVI has only been observed recently with pulsed-field ablation (12). Because this modality nonthermally preferentially ablates myocardium, multiple redundant lesions may safely be placed at each PV to improve lesion durability. In a 2-center study of a one-shot basket/flower catheter technology using pulsed-field energy, PVI durability upon protocol-mandated remapping was 100% in the 18 patients treated with the final refined pulse field waveform (in the full patient cohort using all waveforms, PVI durability was observed in 60% of patients). Against this comparator, the remapping outcomes of lattice-tip ablation are favorable: 96% of the 27 remap patients had durably isolated PVs, with

99% of all PVs being durably isolated. Furthermore, point-by-point ablation retains the ability to tailor the location of the PV encircling lesions to achieve both a proximal level of PVI, and to rather seamlessly negotiate variations in PV anatomy—common PV ostia, extranumerary PVs such as right middle or roof PVs, and common inferior PVs.

Overall, PVI durability with the lattice tip exceeds that observed with other point-by-point technologies, and compares favorably with the best one-shot technologies. However, the perfect time to assess lesion durability is unknown—perhaps 1-year would be a better timepoint than 3-months. Also, there may be other determinants to clinical success beyond electrical PVI (such as ablation of the peri-atrial atrial ganglia) that were not assessed in this study.

DURABILITY OF LINEAR ATRIAL LESIONS. The one-shot technologies, particularly pulsed-field ablation, are promising, but by definition, are largely limited to only ablating PVs. However, there is increasing awareness that other LA ablation lesions, such as MI and LA roof lines, may be important to improving the success of PerAF ablation (13). Even PAF patients sometimes require right atrial CTI ablation to eliminate typical atrial flutter.

There is limited historic data on the durability of linear lesions with point-by-point ablation catheters. Beyond the fact that even acute bidirectional MI block can be challenging, the durability of this line using conventional 3.5-mm tip irrigated catheters is poor: MI line durability has been reported to be 36%, ranging from as low as 13% to the highest being 63% (**Figure 6B**). Similarly, LA roof line durability has been reported to be moderately better at 60% (range, 52% to 68%), but even this is far from acceptable (**Figure 6B**). In contrast, after lattice-tip ablation, both of these linear lesions were durable in more than 90% of patients. CTI ablation was also durable in 100% of cases, although admittedly, durability using even conventional point-by-point catheters is likely to be high for this linear lesion.

THE LATTICE-TIP CATHETER. There are several features of the lattice catheter that may account for the high rates of lesion durability. Foremost is a tendency of the catheter tip to remain in stable contact with the target tissue during ablation. This seems related to both the compressibility of the spherical mesh, and the fact that the surface topography of this tip may mitigate sliding/dislodgement of the catheter away from the target site. From a biophysical perspective, the interaction of the 9-mm lattice with the myocardium creates a large thermal footprint able to generate wide ablation lesions, which facilitates overlap with adjacent lesions. The surface thermocouples arrayed on the spherical-tip potentiates closed-loop temperate feedback to optimize current delivery.

These expectations of catheter efficiency and ease-of-use were realized in the acute performance of the lattice catheter: delivering 2.7 ± 0.70 min of RF energy, bilateral PVI was achieved in 21.8 ± 12.1 min of transpired ablation time (time transpiring from the beginning of the first lesion to end of the last) (8). Similarly, for the MI and LA roof lines, block required 1.0 ± 0.92 and 0.4 ± 0.16 min of RF energy delivery and transpired ablation times of 5.8 ± 6.4 and 3.0 ± 4.4 min, respectively. Based on these performance parameters, it is less surprising that these lesions were largely durable.

When we characterized the relative spacing of adjacent ablation points, the centers of most lesions were < 9 mm from each adjacent lesion. The small number of electrically incomplete lesion sets precluded any reasonable comparative statistical analysis of complete versus incomplete linear lesion sets. But minimally, these analyses indicate that high rates of lesion durability are achieved with this spacing strategy.

Finally, 2 other temperature-controlled saline-irrigated RFA catheters (both ~7.5-F with 3.5- to 4-mm solid tips) have recently been introduced (5,6). Future studies should directly compare their performance to the lattice-tip's larger thermal footprint.

CLINICAL OUTCOME. This durability of lesion sets translated to a 94.4% rate of freedom from any recurrent atrial arrhythmias (AF/AFL/AT) over 1-year follow-up. This clinical outcome is better than previous reported outcomes of AF ablation; for example, in CABANA (Catheter Ablation vs Antiarrhythmic Drug Therapy for Atrial Fibrillation), the largest clinical trial of AF ablation ever performed, the 1-year success rate of AF ablation was ~65% (1,14). The success rate we observed was preserved over sensitivity analyses taking into account either those patients who received additional ablation during the remap procedure or those patients who continued AADs. Furthermore, the 1-year freedom from AF alone was 98.5%. Not surprisingly, AF/AFL/AT-free survival after ablation of PAF (97.2%) was higher than that observed for PerAF (89.6%). However, even the latter was better than previous reports of ablation outcomes of persistent AF: for example, in STAR-AF 2 (Substrate and Trigger Ablation for Reduction of Atrial Fibrillation Trial Part II) trial, the largest published clinical trial of catheter ablation of PerAF, the 1-year success was ~50% (15).

These lattice-tip outcomes suggest that durable ablation lesion sets—PVI for PAF and PVI plus linear lesions for PerAF—are crucial missing variables to achieving high success of AF ablation. While compelling, there are some important caveats to these data: 1) the overall size of the cohort is not large; 2) there were only 3 centers in this study; 3) the intermittent nature of the Holter monitoring follow-up can miss recurrences; and 4) overall compliance with Holter monitoring was suboptimal (66%), although compliance with the final Holter was 95%—recurrence rates might increase with use of implantable loop recorders. Ultimately, these clinical AF recurrence data should be viewed as intriguing and hypothesis-generating, and must be re-assessed in larger definitive clinical studies.

STUDY LIMITATIONS. Whereas the number of patients undergoing remapping (n = 27) is robust, the number of patients ultimately contributing to clinical follow-up (n = 65) is still relatively modest; accordingly, the favorable AF recurrence data should be corroborated with larger, ideally randomized, clinical trials. Similarly, there were a reasonable number of operators performing the procedures in the remap and full cohorts (8 operators at 3 sites, respectively), but again, a large clinical outcome trial would ideally include more operators. Remapping procedures were not performed at 1 center, but clinical outcomes did not vary (Supplemental Figure 5).

Because there were so few nondurable linear lesion sets, the lesion spacing analyses were not able to determine the tolerances of acceptability: additional studies with more varied, greater adjacent spacing are required to comprehensively determine if the ablation points can be placed even further apart and still maintain durability. Finally, despite no identified major safety events, the overall number of patients studied herein remains small; larger studies are required to establish the safety of this technology.

CONCLUSIONS

This first-in-human study shows that the novel lattice-tip catheter, by virtue of its large thermal footprint, creates contiguous point-by-point temperature-controlled RFA lesions with high rates of linear lesion durability—for PVI, for LA linear lesions at the MI and roof, and for CTI ablation.

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PERSPECTIVES

COMPETENCY INMEDICAL KNOWLEDGE: A novel technology based on a lattice electrode with a large thermal footprint showed very high rates of lesion durability upon invasive electrophysiologic remapping, including PVI, and linear atrial lesions along the MI, LA roof, and CTI.

TRANSLATIONAL OUTLOOK: Larger, multicenter trials are needed to fully define the clinical outcomes and safety of this technology versus standard technologies in treating patients with AF.

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KEY WORDS atrial fibrillation, catheter ablation, cavotricuspid isthmus, lattice-tip, lesion durability, temperature-controlled, mitral isthmus, pulmonary vein isolation, roof line

APPENDIX For additional disclosures and supplemental text, tables, figures, and references, please see the online version of this paper.