# First-in-human demonstration of 18-month spatiotemporal stability of active atrial fibrillation source detected by electrographic flow mapping in persistent atrial fibrillation

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## Introduction

Advanced mapping methods for atrial fibrillation (AF) have previously suffered from poor spatiotemporal stability. Electrographic flow (EGF) mapping is a novel technique using computer vision and optical flow smoothing algorithms to avoid this issue.

The aim of this first-in-human case report is to demonstrate the spatiotemporal stability and long-term reproducibility of a putative AF source in a patient suffering from long-standing persistent AF associated with hypertrophic cardiomyopathy by comparing EGF maps recorded 18 months apart.

## Case report

A 66-year-old woman with a past medical history of hypertrophic cardiomyopathy, essential hypertension, hypothyroidism, and pulmonary hypertension was referred for pulmonary vein isolation (PVI). She was first diagnosed with AF in 2016 with increasingly frequent, highly symptomatic AF recurrences requiring sotalol for rhythm control. By late 2018, sotalol was no longer effective and she was switched to amiodarone. However, in 2019, she developed even more disabling symptoms associated with her persistent AF despite medical treatment with amiodarone. She was referred for PVI in July 2019. Upon presentation, the patient had a severely dilated left atrium with high left atrial volume index (66 mL/m$^2$) and a $CHA_2DS_2$-VASc = 3. Under general anesthesia, a preprocedural transesophageal

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## KEY TEACHING POINTS

- Persistent atrial fibrillation (AF) may be maintained by leading drivers located outside the pulmonary veins and represent adjunctive ablation targets beyond pulmonary vein isolation.
- Prior advanced mapping methods have notoriously suffered from poor spatiotemporal stability and map reproducibility.
- Electrographic flow is a novel technique with a processing pipeline designed to account for spatially incoherent arrhythmias like AF.

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echocardiogram was performed and demonstrated slow flow in the left atrial appendage (LAA) at 20 cm/s with spontaneous contrast throughout the left atrium but without any visible thrombus in the LAA. After access was obtained via the right (8.5F × 2) and the left (6F and 10F) femoral veins, a decapolar coronary sinus catheter was inserted and double transseptal puncture was performed under intracardiac echocardiographic guidance. Intracardiac echocardiography was further used to provide precise, real-time visualization of both intracardiac anatomy and devices positioned within the heart. A circular mapping catheter (Lasso® NAV catheter; Biosense Webster, Irvine, CA) was advanced through an SL1 sheath for electroanatomic mapping of the left atrium (CARTO®; Biosense Webster, Irvine, CA) and the 4 pulmonary veins (PVs). Via a steerable introducer sheath (Agilis™ NxT; Abbott, Abbott Park, IL) an ablation catheter (Navistar® RMT ThermoCool®; Biosense Webster, Irvine, CA) was inserted into the left atrium. Throughout the procedure, activated clotting time was monitored at regular intervals to maintain activated clotting time > 300 seconds. Ablation was performed using a power setting of 40–45 W and temperature limit set to 43°C with flow rate of 17 mL/min using a

remote magnetic navigation system (Stereotaxis, St. Louis, MO).

After PVI was complete and confirmed to be intact with entrance block, the patient remained in AF. At this point in the procedure, the circular mapping catheter was exchanged for a 60 mm, 64-electrode basket catheter (FIRMap™; Abbott, Abbott Park, IL) to perform EGF mapping to look for extra-PV sources of AF. The Summary EGF map (Figure 1A) showed a highly dominant source at GH2 located near the anterior roof insertion of the LAA with activity level (percentage of time a source is on or active) of 67.7% that emanates flow in a centrifugal pattern (Figure 1B). In addition to the summary EGF map, the corresponding Streamline plot (Figure 1D) clearly showed the origin of flow (origins depicted in red and ending in blue) from the focus at GH2 emanating outward in a centrifugal pattern. Targeted, focal radiofrequency (RF) ablation was performed at this location, as shown on the 3-D electroanatomic map (Figure 1C). During ablation at this location, the patient's AF organized into a 2:1 atrial tachycardia with tachycardia cycle length of 300 ms.

It should be noted that because the patient's AF organized to an atrial tachycardia after focal ablation of the EGF-identified active source, repeat EGF mapping was considered superfluous and not performed. Further diagnostics confirmed typical cavotricuspid isthmus–dependent right atrial flutter. Linear ablation of the cavotricuspid isthmus was performed that restored sinus rhythm.

During the 3-month blanking period, the patient remained off antiarrhythmic drugs and maintained sinus rhythm. She continued to do well for the next 7 months after the blanking period until May 2020, when she started experiencing paroxysms of AF and was restarted on amiodarone. However, by June 2020, 11 months after the index procedure, the patient developed an amiodarone-induced hyperthyroidism and amiodarone treatment had to be discontinued. Shortly after stopping amiodarone, the patient developed highly symptomatic, persistent AF requiring repeated electrical cardioversions over the span of several months. In February 2021, the patient finally underwent a redo ablation procedure for recurrent persistent AF. It should be noted that a rhythm-control strategy was pursued, given her relatively young age and as she had done quite well with rhythm-control while on amiodarone. Although she had a history of hypertrophic cardiomyopathy, she did not have strong indications for a primary prevention implantable cardioverter-defibrillator and a pace-and-ablate strategy was not considered. She had no prior history of documented cardiac arrest, ventricular fibrillation, or hemodynamically significant ventricular tachycardia. There was also no first-degree relative with a history of hypertrophic cardiomyopathy–related sudden cardiac death, massive left ventricular (LV) wall thickness, or unexplained syncope. Her transthoracic echocardiograms showed intact LV systolic function with ejection fraction (EF) 60% and no LV apical aneurysm. There was no significant change in her LVEF or left atrial size between or after her ablation procedures.

The same procedural setup including catheters and mapping system was applied as in the first procedure. Interrogation of the PVs revealed reconnection of the right inferior PV, which was reisolated with RF ablation. After confirming intact PVI with entrance block, EGF mapping was performed. Based on her left atrial size, a 60 mm basket catheter was again selected for mapping. Careful review was made of the 2019 EGF maps and corresponding 3-D electroanatomic maps showing the basket position within the anatomy. Using the 3-D electroanatomic map, the basket was positioned in approximately the same position as during the first procedure in 2019 (Figure 2C). EGF mapping revealed a focal source at EF3 with activity 31.4%, again localized to the anterior roof insertion of the LAA (Figure 2A), and the EGF Segment map (Figure 2B) shows the EGF patterns during the 2-second segment with the highest source prevalence. Likewise, the corresponding Streamline plot also confirmed origin of flow emanating in a divergent pattern from a focus at EF3 (Figure 2D). Source activity was diminished compared with the EGF maps from July 2019 and targeted ablation was performed at this location. The final RF lesion set performed in this redo procedure, shown by the RF lesion tags on the electroanatomic map (Visitag™, CARTO; Biosense Webster), included reisolation of the right inferior PV and ablation of the EGF-identified focal source localized to the anterior roof insertion of the LAA (Figure 3C). Postablation EGF mapping confirmed elimination of the focal source, with the EGF Summary map showing the ablated area as a region that no longer drives flow, but instead is now a region of passive flow (white cloud in Figure 3A). In the absence of any active source, the EGF Segment map reveals only chaotic flow (Figure 3B), and the accompanying Streamline plot likewise showed that flow was no longer originating from the ablated focal source at EF3 (Figure 3D). No other active sources were detected in either of the atria or in the superior vena cava.

The final ablation lesion set performed during this patient's redo-ablation procedure was reisolation of the right inferior PV and focal ablation performed at the EGF-identified focal source at EF3 located at the anterior roof insertion of the LAA (Figure 3C). Postablation, the patient was successfully externally cardioverted to sinus rhythm. She recovered from the procedure without complications. At the time of this writing, the patient is in the last few weeks of her 3-month blanking period, but remains in sinus rhythm in the absence of any antiarrhythmic drugs.

## Discussion

Catheter ablation including PVI is the most effective treatment option in symptomatic paroxysmal and persistent, drug-refractory AF; however, catheter ablation success rates for persistent AF remain poor.[1] Although debate surrounds the mechanisms of AF initiation and maintenance, there is growing evidence supporting the presence of self-sustaining extra-PV drivers and/or triggers that maintain AF, and these localized AF sources may represent adjunctive ablation targets beyond PVI.[2–6] Attempts to map AF and reveal localized
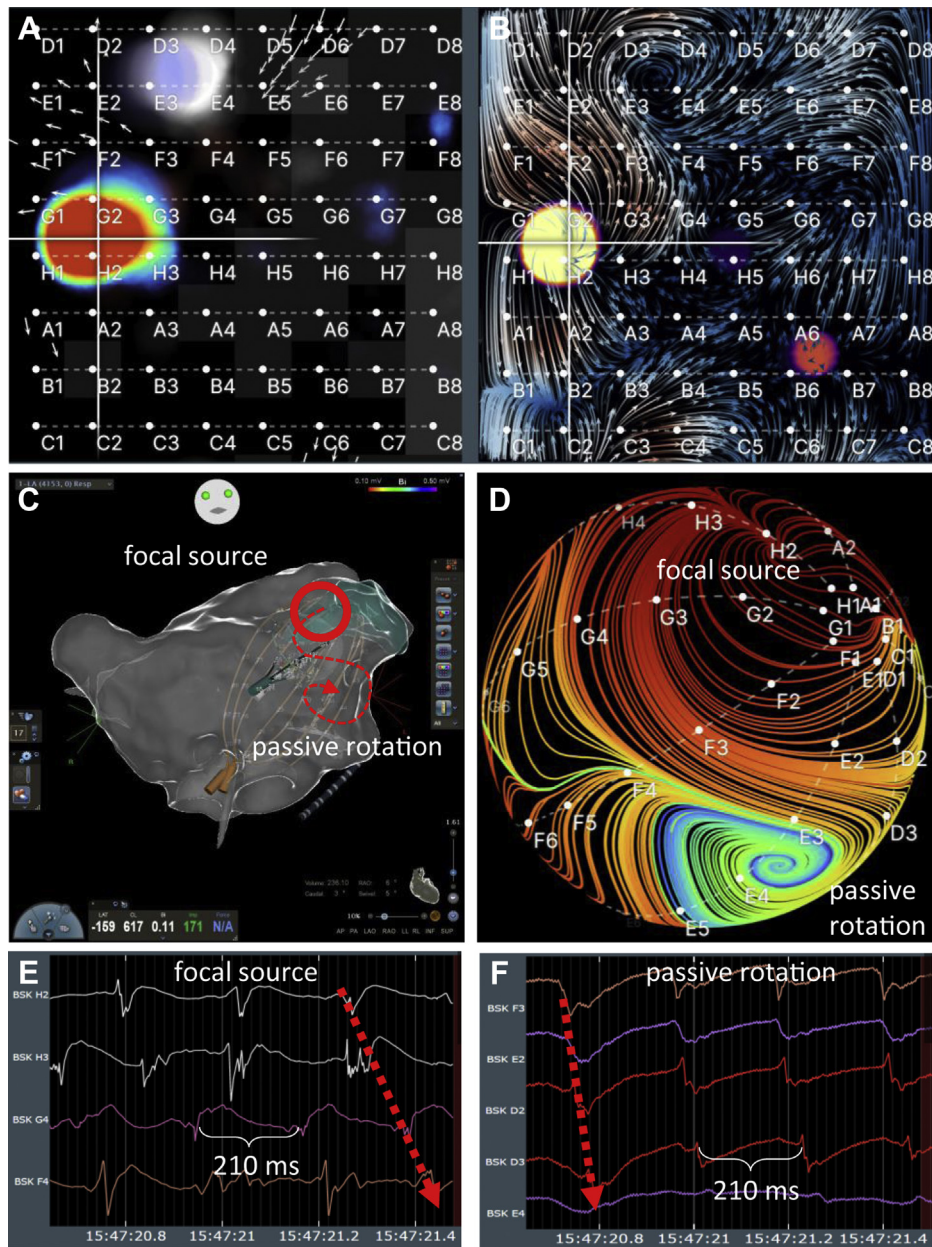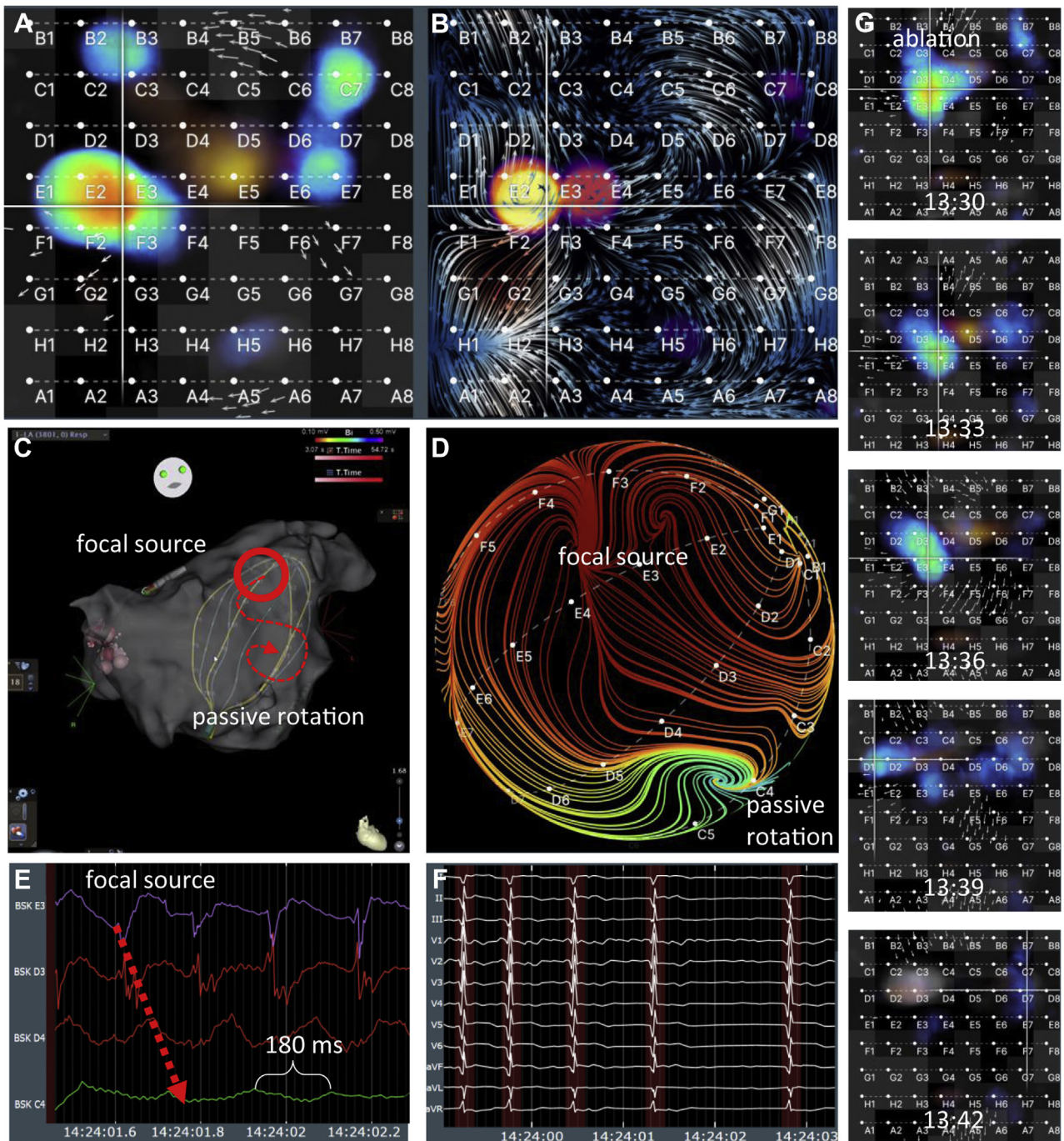
**Figure 1**   **A:** Initial electrographic flow (EGF) Summary map over 1 minute of recording detects an active source at GH2 (*red spot with cross-hairs*). Ablation at that location led to organization into a 2:1 atrial tachycardia. Note the white cloud at DE34 indicating a passive rotational phenomenon. **B:** EGF Segment map displays flow patterns over 2 seconds and shows divergent action potential flow emanating from the source at GH2. The passive rotational flow is also visible at DE34 as accepting flow, but not generating flow. **C:** Electroanatomic map indicates that the active source at GH2 is located near the anterior roof insertion of the left atrial appendage (LAA) while the passive rotational phenomenon at DE34 is located inferior to the base of the LAA in the lateral left atrium above the mitral annulus. **D:** Streamline plot shows main source of flow emanating from H2 and flowing down and around the dome of the basket around the mitral valve. **E:** Unipolar electrograms (EGMs) around active source at H2 showing atrial fibrillation cycle length of 210 ms. **F:** Unipolar EGMs around passive rotational phenomenon at DE34 are characteristically different than those corresponding to the active source at GH2.

drivers continue to increase, though with varying clinical results.[7–12] These mapping methods have previously suffered from technical limitations such as lack of beat-by-beat mapping, sensitivity to errors of timing and morphology correlation, susceptibility to signal artifact and noise, and poor spatiotemporal stability, as well as the inability to distinguish active from passive electrical phenomena.[13]

EGF mapping (Ablamap® software; Ablacon, Wheat Ridge, CO) is an innovative method used to approximate

cardiac action potential flow through the atrium that can detect AF sources in patients with persistent AF.[14,15] Unipolar EGMs recorded from a 64-electrode basket catheter over 1 minute are processed using the Ablamap software. The electrical potential profile between the electrode positions at a given point in time (ie, snapshots of the electrical field for every sampled point in time) is estimated by a Green's function biharmonic spline fit assuming that the charge in the system is passively distributing according to minimal

**Figure 2**    **A:** Eighteen months after the first procedure, the electrographic flow (EGF) Summary map over 1 minute of recording shows an active source at EF3. Activity is lower than in Figure 1A (source spot is less red). **B:** Two-second EGF Segment maps show divergent action potential flow originating from EF3. **C:** Electroanatomic map again shows that the active source at EF34 is located near the anterior roof insertion of the left atrial appendage (LAA). **D:** Streamline plot shows main source of electrographic flow at EF3 with flow going downward and around the mitral valve, just as was seen during the first procedure. Note also the presence of the same passive rotational phenomenon located inferior to the base of the LAA in the lateral left atrium above the mitral annulus. **E:** Unipolar electrograms around active source at EF3 showing atrial fibrillation (AF) cycle length of 180 ms and activation from E3 to D3 to C4, consistent with the streamline plot of electrographic flow in panel D. **F:** Corresponding 12-lead electrocardiogram shows AF. **G:** Serial EGF Summary maps acquired during radiofrequency application document progressive elimination of source activity at EF3.

energy. Using a Horn-Schunk flow estimation, these snapshots taken every 19 ms are then assembled to determine the spatial voltage gradients compared with the temporal voltage gradients derived from each 2 subsequent frames. By assuming that all voltage points at a certain point in

time are parts of traveling action potential waves with a corresponding spatial gradient, if each voltage point with its gradient moves to a different location in the next frame, their original location will see a changed voltage that can be estimated from its gradient and the vector by which the point
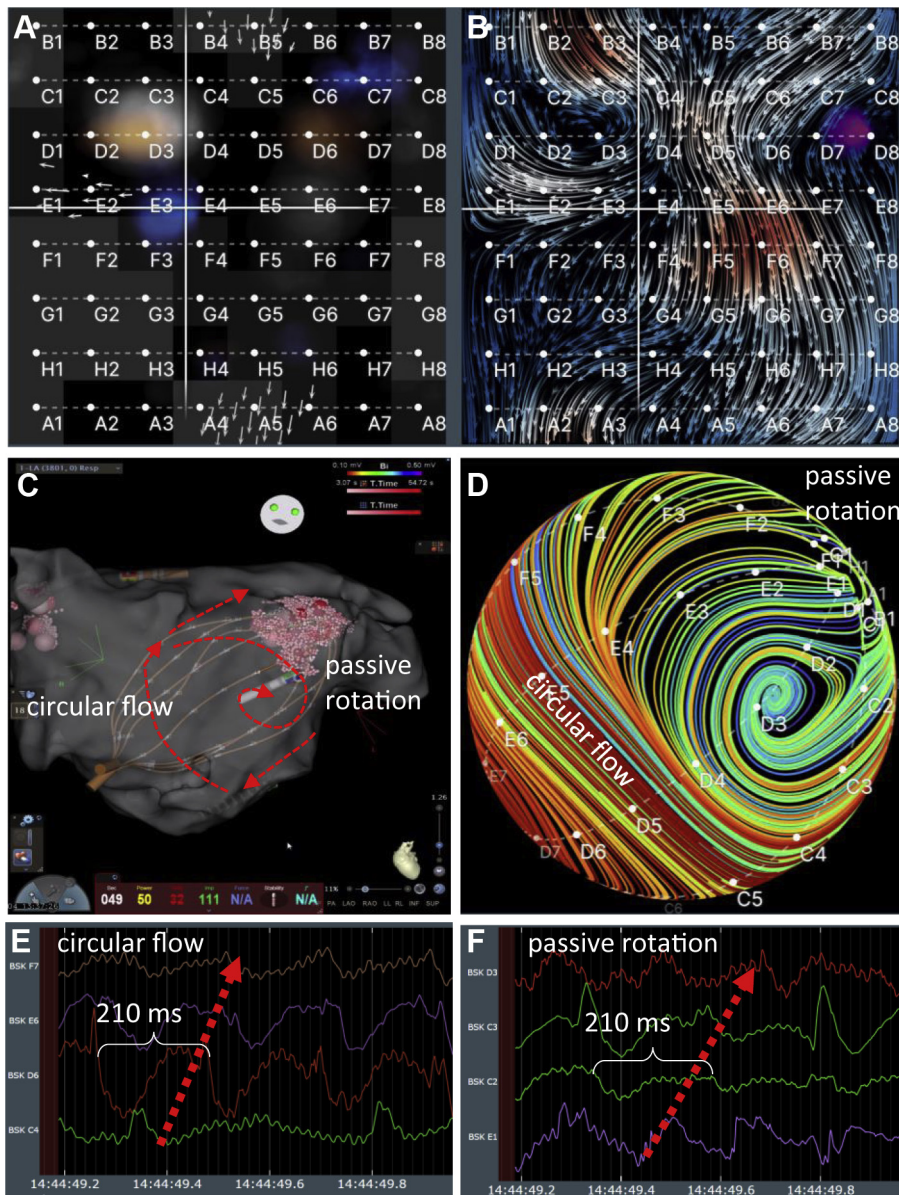
**Figure 3**    **A:** After ablation of EF3 the patient remained in persistent atrial fibrillation (AF) and the electrographic flow (EGF) Summary map shows no active source remaining (no red spot). A passive phenomenon is now present at D3. **B:** EGF Segment maps show chaotic action potential flow with no driving source emanating flow remaining. **C:** Electroanatomic map shows the location of all radiofrequency ablation applications to reisolate the right inferior pulmonary vein and to eliminate the focal source detected and localized to the anterior roof insertion of the left atrial appendage (LAA). **D:** Likewise, the Streamline plot no longer shows origination of electrographic flow from the LAA and postablation the direction of flow has reversed—starting from the proximal portion of the basket near the interatrial septum and flowing upward toward the left atrial roof. **E:** Unipolar electrograms (EGMs) in the region around the previously active source at EF3 now shows AF cycle length of 210 ms and reversal of activation from C4 toward F7. **F:** The passive rotation previously noted at the time of the first procedure 18 months prior still remains inferior to the base of the LAA in the lateral left atrium above the mitral annulus with the corresponding unipolar EGMs showing activation from E1 to D3, corresponding to the Streamline plot of electrographic flow in panel D.

has moved, thus creating a "film" of the excitation waves' behavior and propagation over time. EGF mapping displays the dominant patterns of the excitation wave propagation film in the resulting flow vector maps and can measure their consistency over time, allowing the visualization of EGF and statistical singularities with divergent flow, called sources. The EGF Summary map displays all active sources and passive rotations detected over the course of 1 minute of recording. Active sources appear redder the higher their prevalence and bluer the lower their prevalence. Similarly, passive rotations appear whiter the higher their prevalence and grayer the lower their prevalence. The size (radius) of the source representation depends on the velocity detected around the singularity. The percentage of time a source can be detected at its highest intensity in a 2-second segment is called activity—eg, 25% activity means that the source is detected for one-quarter of the segments at its highest detection rate. If a segment shows lower than maximum detection rate it counts correspondingly less to the total activity.

In AF, there is inherently high variability of the electrical flow fields; however, the origins of EGF, which are defined as sources, often appear in the same locations. Because EGF maps are generated to show the dominant patterns of excitation wave propagation from the resulting flow vector maps over each 2-second interval, the EGF Summary maps can organize the seemingly chaotic flow fields during AF by integrating this repetitive behavior of source activity over time. Increasing evidence in both animal models and humans supports the existence of spatially localized, extra-PV triggers that maintain AF with a hierarchical spatiotemporal organization;[2] however, detailed characterization of these triggers remains sparse because currently available mapping systems and algorithms are unable to reproducibly detect and localize these extra-PV triggers intraprocedurally and thus, their spatiotemporal stability has never previously been characterized. This case report serves to document the clinical novelty of a first-in-human demonstration of interprocedural spatiotemporal stability of an active AF source over a period of 18 months.

The limitations of using a basket catheter to record high-quality intracardiac signal with low signal-to-noise ratios owing to nonuniform contact with the atrial endocardial surface, catheter deformation with spline bunching/splaying, and suboptimal atrial coverage have been well documented. Source detection with EGF mapping employs an optical flow algorithm that triangulates between electrodes, assuming that excitation wavelength is less than the electrode distance, and thus provides better spatial resolution than the grid constant of the multielectrode basket catheter used to record the signals. While the robustness of the EGF mapping signal processing pipeline mitigates some of these characteristic pitfalls of panoramic mapping, with careful basket positioning and attention to spline distribution and atrial coverage, the interprocedural reproducibility and spatiotemporal stability of EGF mapping suggests that signal acquisition using a basket catheter is sufficient to detect and localize AF sources. EGF mapping is a promising new technology that creates full, near real-time temporospatial visualizations of atrial electrical wavefront propagation to identify putative AF sources. The *FLOW-AF* randomized controlled clinical trial (NCT04473963) is underway to evaluate the reliability of EGF mapping to identify AF sources and guide ablation therapy in persistent AF patients.

## Conclusion

This is the first in-human report of an AF mapping technology that demonstrates interprocedural map reproducibility with spatiotemporal stability of EGF-identified sources of AF in the same patient during procedures performed 18 months apart. Additional prospective EGF mapping reproducibility studies are in progress.

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