Noninvasive electrocardiographic imaging–guided targeting of drivers of persistent atrial fibrillation: The TARGET-AF1 trial

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BACKGROUND  Mechanisms sustaining persistent atrial fibrillation (AF) remain uncertain.

OBJECTIVES  The purpose of this study was to use electrocardiographic imaging (ECGI) mapping to guide localized driver ablation in patients with persistent AF.

METHODS  Patients undergoing catheter ablation for persistent AF <2 years were included. Patients were enrolled consecutively between 2018 and 2020. ECGI mapping was used to identify focal and rotational potential drivers (PDs). PDs were ablated after pulmonary vein isolation (PVI). The ablation response and freedom from AF/atrial tachycardia (AT) at 1 year were assessed.

RESULTS  Forty patients were enrolled. AF terminated with PVI in 8 patients, and 32 underwent ECGI-guided driver ablation. Average procedural duration was 228.8 ± 66.7 minutes, with a total radiofrequency delivery time of 38.9 ± 14.1 minutes. During 1 year of follow-up, the primary endpoint of freedom from AF/AT was achieved in 26 patients (65%). The secondary endpoint of freedom from AF was achieved in 30 patients (75%). AF termination was achieved in 20 of 40 patients (50%). The composite endpoint of an ablation response (AF termination or cycle length slowing ≥10%) occurred in 37 of 40 patients (92.5%). In total, 181 drivers (48 focal and 133 rotational) were ablated, with an ablation response achieved in 59 (32.6%). Focal drivers and drivers with a higher recurrence rate and greater temporal stability were more likely to be associated with an ablation response including AF termination (P ≤.001).

CONCLUSION  ECGI-guided ablation plus PVI results in high freedom from AF during follow-up and an ablation response in a large proportion of patients. Using driver type and characteristics may facilitate a hierarchical ablation approach.

KEYWORDS  Atrial fibrillation; Atrial mapping; Catheter ablation; Mapping system; Rotor

Electrocardiographic imaging (ECGI) mapping is one such methodology. The CardioInsight mapping system (Medtronic, Minneapolis, MN) noninvasively reconstructs the electrical activity of the heart from body surface potential recordings obtained from a 252-electrode vest and geometric information of heart from noncontrast computed tomography (CT) imaging. ECGI mapping using the CardioInsight system utilizes phase analysis to identify circulating wavefronts and focal activations that may act as a potential driver (PD) of AF.

An early single-center experience utilizing ECGI mapping in guiding PD ablation in AF showed promising results, with a high AF termination rate and freedom from AF during follow-up in patients with persistent AF. The multicenter AFACART (Noninvasive Mapping of Atrial Fibrillation) study demonstrated high rates of AF termination during PD ablation, which was a promising proof of concept, but rates...
of atrial tachycardia (AT) recurrence were high. Whether this was a result of localized driver ablation before pulmonary vein isolation (PVI) is unclear, as studies have shown that PVI organizes AF and improves driver identification. The average total ablation duration in the AFACART study was also significantly higher than that reported in other studies in which localized drivers were targeted post-PVI.

It is well recognized that extensive ablation increases the risk of reentry formation and AT recurrence, and this outcome may have related to the workflow in AFACART. Both AFACART and the preceding Bordeaux experience used ECGI mapping to guide ablation but did not rely only on this, and results may have been impacted by their previous experience ablating patients to sinus rhythm.

This prospective, single-arm study aimed to utilize the ECGI mapping system to rigorously guide localized PD ablation post-PVI in patients with persistent AF. The response to ablation at driver sites was monitored, and freedom from AF/AT was assessed during follow-up.

Methods

Patients undergoing catheter ablation for persistent AF (<24 months and no previous AF ablation) were prospectively included in the study. Patients were enrolled consecutively between 2018 and 2020. Exclusion criteria included left atrial (LA) diameter >5 cm, left ventricular ejection fraction <40%, New York Heart Association functional class III or IV heart failure, age <18 or >80 years, hypertrophic cardiomyopathy, or greater than moderate valve disease. All procedures were performed with uninterrupted anticoagulation therapy and intravenous heparin administration to achieve an activated clotting time >300 ms. The procedures were performed with patients under either conscious sedation or general anesthesia. Patients provided informed consent for their involvement in this study. The study was approved by the UK National Research Ethics Service (17/EM/0333) and complied with the Declaration of Helsinki. It was prospectively registered on ClinicalTrials.gov (NCT04632680).

CT scan

All study subjects were fitted with the ECGI 252 multielectrode vest and underwent a noncontrast CT scan. A 3-dimensional biatrial geometry was segmented from the CT scan in a semi-automated fashion on the ECGI mapping system (CardioInsight, Medtronic), and the relationship to each of the 252 vest electrodes to the atrial anatomy was determined (Supplemental Figure 1).

Electrophysiological procedure

All procedures were performed using the CARTO mapping system (Biosense Webster, Inc, Diamond Bar, CA). Right atrial (RA) and LA geometries were created using 2.6–2–mm spacing PentaRay NAV catheter (Biosense Webster). A high-density bipolar voltage map was created in all patients to establish the relationship between drivers and low-voltage zones (LVZs). Neither this nor any data from contact electrogram mapping in terms of activation were used to guide ablation. Bipolar voltage <0.5 mV were defined as a site of LVZs. A decapolar catheter (Biosense Webster) was positioned in the coronary sinus. A quadripolar catheter (Biosense Webster) was positioned in the RA appendage. A ThermCool SmartTouch catheter (Biosense Webster) was used for ablation. LabSystem Pro (Boston Scientific, Marlborough, MA) was used to record and display electrogram data.

If patients were in sinus rhythm, then AF was induced through burst atrial pacing and left to stabilize for at least 10 minutes before mapping and PVI. If patients terminated to sinus rhythm with PVI, no further ablation was performed. If patients remained in AF post-PVI, only ECGI maps post-PVI were used to guide ablation at sites identified as PDs. Fifteen seconds of cumulated atrial intervals, each of minimum duration ≥850 ms, were collected to generate a biatrial map of PDs. The minimum 850-ms recording was chosen because it has been used previously with the ECGI system and has been shown to produce results consistent with longer recording segments. The cumulative period of 15 seconds was chosen because the driver regions and characteristics are consistent after this duration. Intravenous beta-blockers and/or calcium channel blockers were administered if the ventricular rate required slowing. If this failed to slow the rate adequately, then adenosine was administered. ECGI maps were reviewed to identify PDs. Focal drivers were defined as centrifugal activation originating from a point. Rotational drivers were defined as ≥1.5 revolutions around a spatially stable core (in an area <2 cm²) on phase maps. Drivers occurring in the same region of an 18-segment model of the atria were assumed to be occurrence of the same driver. Drivers were targeted strictly guided by only ECGI mapping in order of those with the most frequent occurrence during the 15-second mapping period.

AF cycle length (CL) was documented after each PD ablation. AF CL was measured over 30 cycles using the PentaRay NAV catheter positioned in the LA appendage, quadripolar catheter positioned in the RA appendage, and decapolar catheter in the coronary sinus. The average of the CL change at the 3 measurement sites was used as the change in CL.

Following PVI, a 20-minute waiting period was observed before ablation of PDs was commenced in the LA and RA body. This was to avoid any delayed effect potentially attributable to PVI, which might influence AF CL during ablation at the sites of PDs. To monitor the effect of ablation at the PD sites as identified on the post-PVI maps, AF CL was again monitored as described earlier. Although small changes in CL (usually 5–6 ms) have been used to determine a response to ablation, it was thought that ablation of a clear driver ought to have a more substantial effect. Therefore, confirmed drivers were defined as sites where ablation resulted in ≥10% slowing of the CL, organization of the rhythm to an AT, or termination to sinus rhythm. If AF persisted despite ablation of all localized drivers identified on the post-PVI maps, an
additional ECGI map was created. Any new localized drivers identified were ablated. If patients remained in AF after ablation of the localized drivers identified on the second ECGI maps post-PVI, an additional ECGI map was created. Any localized drivers identified on this ECGI map were not targeted with ablation, and patients were cardioverted with a DC shock.

Ablation strategy
PVI was achieved with bilateral wide area circumferential ablation aiming for isolation as ipsilateral pulmonary vein pairs. Ablation at driver sites was delivered with a contact force of 5–40g, with power of 30–40 W. Ablation at sites with either focal or rotational activation was delivered as discrete focal points, aiming for the center of the focal or rotational activation. Further ablation was delivered in a cluster of lesions surrounding the first point. Ablation in any region was stopped if the endpoint was met (ie, AF terminated or CL slowed) or once no signal remained in the area of the focal/rotational activation. Care was taken not to form a linear lesion with clusters so as not to impact any AF mechanisms in this way. Beyond isolating PVs and targeting PDs, no additional ablation was performed in AF. If the AF organized into an AT, this was mapped using local activation times and entrainment and ablated. The ECGI mapping system was not used to map AT.

Follow-up
Patients underwent follow-up at 3, 6, 9, and 12 months. Clinical evaluation included 12-lead electrocardiography and assessment of patient symptoms. In addition, patients underwent follow-up at 3, 6, 9, and 12 months. Clinical variables are given as mean ± SD or median (interquartile range). Categorical variables are given as number (percentage). The Fisher exact test was used for comparison of nominal variables. The Student t test or its nonparametric equivalent Mann-Whitney test was used for comparison of continuous variables. Odds ratios (ORs) were calculated to determine the predictive value of the driver type on the ablation response achieved. Sensitivity and specificity were determined for PD temporal stability and recurrence rate in view of predicting an ablation response. P < .05 was considered significant.

Results
Forty patients were included in this study (Figure 1). Baseline characteristics are listed in Table 1. Of the 40 patients, 30 (75%) were in AF at the start of the procedure; the remaining were in sinus rhythm. AF was induced with burst atrial pacing at the start of the procedure in those who were in sinus rhythm at the start of the procedure. All procedures were performed successfully without any complications. Average procedural duration was 228.8 ± 66.7 minutes, and average fluoroscopy time was 1.0 ± 1.1 minutes. Average total radiofrequency delivery time was 38.9 ± 14.1 minutes. Average total localized driver radiofrequency delivery time was 10.1 ± 2.9 minutes, with an average radiofrequency delivery time per driver of 2.5 ± 0.5 minutes.

Localized driver mapping
On the initial ECGI maps post-PVI, a total of 213 PDs were identified in the 32 patients, with all patients having at least 1 PD (6.5 ± 1.5 drivers per patient; range 2–14 drivers per patient). All of the PDs identified pre-PVI outside of the pulmonary vein ostia were also seen on the first post-PVI ECGI maps. The PDs were predominantly rotational in nature (157 rotational drivers [73.7%] and 56 focal drivers [26.3%]). Of the 213 PDs, 154 (72.3%) were mapped to the LA and 59 (27.7%) to the RA. Across the RA and LA, PDs were mapped predominantly to the posterior wall (21.1%), followed by the lateral wall (20.2%), roof (13.2%), and anterior wall (9.7%). In the LA, PDs were predominantly mapped to the posterior wall (19.5%), followed by the lateral wall (16.9%), anterior wall (13.6%), and roof (11.0%). In the RA, PDs were predominantly mapped to the lateral wall (28.8%), RAA (22.0%), and roof (18.6%). Figure 2 shows the proportion of identified PDs in each segment of the 18-segment model. The proportion of focal and rotational drivers identified (P = .46) and their anatomic distribution (P = .56) were not significantly different in patients with AF at the start of the case compared to those who were in sinus rhythm and had AF induced. Rotational drivers demonstrated an average recurrence rate of 2.8 ± 2.1 and average temporal stability of 3.3 ± 2.1. Focal drivers demonstrated an average recurrence rate of 3.3 ± 2.0 and
average temporal stability of 4.4 ± 2.0. The anatomic locations of the drivers are given in Supplemental Table 1.

Of the 213 PDs identified post-PVI, 32 were not targeted because the AF either terminated to AT or sinus rhythm on ablation of another driver. The remaining 181 drivers were targeted with ablation (133 rotational and 48 focal), with an average of 5.7 ± 1.7 targeted per patient (range 1–10). Of the 32 patients, 20 (62.5%) remained in AF after localized driver ablation and had additional ECGI maps created to identify additional drivers. In these 20 patients, 7 (35.0%) had additional drivers identified on their second ECGI maps post-PVI.

Response to ablation of PDs

Response on a per-patient basis

Of the 40 patients, AF terminated in 8 (20%) with PVI alone, terminating to sinus rhythm in 5 or AT in 3. The remaining 32 patients (80%) remained in AF post-PVI and underwent ECGI-guided localized driver mapping and ablation.

The secondary composite endpoint of an ablation response (AF termination and/or SCL) was achieved in 37 of the 40 patients (92.5%) comprising the whole cohort. An ablation response was seen in 29 of the 32 patients (90.6%) who underwent ECGI-guided ablation. This included SCL in 17 patients (58.6%) and AF termination in 12 patients (41.4%; 9 AT and 3 SR). The secondary endpoint of AF termination was achieved in 20 of 40 patients (50%) of the whole cohort. Figure 1 and Supplemental Table 1 summarize the ablation response on a per-driver and per-patient basis.

Response on a per-driver basis

Of the 181 drivers targeted with ablation, 122 PDs (67.4%) resulted in no discernible effect. A study-defined ablation response (SCL of ≥10% increase in CL or AF termination including to SR and AT) was achieved with the remaining 59 drivers (32.6%; 47 SCL; AF termination to AT 9; AF termination to SR 3). Figures 3, 4, and 5 and Supplemental Figure 2 show examples of drivers for which ablation resulted in a study-defined response.

According to driver type, an ablation response was more often seen with focal drivers compared to rotational drivers.
(26/48 [54.2%] focal drivers vs 33/133 (24.8%) rotational drivers; \( P < .001 \)). Therefore, a focal driver was more likely to result in an ablation response compared to a rotational driver (OR 3.6; 95% confidence interval [CI] 1.8–7.1; \( P < .001 \)).

Rotational PDs with higher recurrence rate were more likely to demonstrate a study-defined ablation response (5.4 ± 2.2 PD occurrences with an ablation response vs 1.9 ± 1.2 PD occurrences without an ablation response; \( P < .001 \)). An optimal cutoff for rotational PD recurrence rate and achieving an ablation response was 4.4 ± 1.9 (sensitivity 85.4%, 95% CI 68.8%–92.4%; specificity 86.4%, 95% CI 71.2%–85.4%). Rotational PDs with greater temporal

![Figure 2](image)

Figure 2  The 18 biatrial segment model used to determine the anatomic location and distribution of the potential drivers identified. Percentages of potential drivers identified in each segment of the 18-biatrial segment model are given. LA = left atrium; LAA = left atrial appendage; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RA = right atrium; RAA = right atrial appendage; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein; SVC = superior vena cava.

![Figure 3](image)

Figure 3  A: Electrocardiographic (ECG) imaging map in the left anterior oblique (LAO) view showing an atrial fibrillation driver with rotational activity at the lateral wall of the RA/RAA. B: CARTO map of the RA in the LAO view showing ablation at the site of the driver, which resulted in atrial tachycardia on the electrograms (C), including surface ECG, coronary sinus (CS), and pulmonary vein (PV) signals. This was mapped to a mitral isthmus–dependent flutter that changed to a cavo-tricuspid (CTI)-dependent flutter, with a mitral line. The CTI-dependent flutter was effectively ablated with a CTI line. LAA = left atrial appendage; LUPV = left upper pulmonary vein; RA = right atrium; RAA = right atrial appendage; SVC = superior vena cava.
stability were more likely to demonstrate a study-defined ablation response (5.9 ± 2.1 rotations in PD with an ablation response vs 2.3 ± 1.2 rotations in PD without an ablation response; \( P < .001 \)). An optimal cutoff for rotational PD temporal stability and achieving an ablation response was 4.2 ± 1.7 (sensitivity 87.2\%, 95\% CI 70.1–92.4\%; specificity 88.3\%, 95\% CI 71.2–88.4\%).

Focal drivers with higher recurrence rate were also more likely to demonstrate a study-defined ablation response (4.7 ± 1.3 occurrences in PD with an ablation response vs 1.3 ± 0.5 occurrences in PD without an ablation response; \( P < .001 \)). An optimal cutoff for focal PD recurrence rate and achieving an ablation response was 4.0 ± 1.3 (sensitivity 86.2\%, 95\% CI 70.2–93.4\%; specificity 86.3\%, 95\% CI 71.2–87.4\%). Focal PDs with greater temporal stability were more likely to demonstrate a study-defined ablation response (6.6 ± 2.4 consecutive focal discharges in PD with an ablation response vs 3.1 ± 1.5 focal discharges in PD without an ablation response; \( P < .001 \)). An optimal cutoff for focal PD temporal stability and achieving an ablation response was 4.7 ± 1.8 (sensitivity 89.1\%, 95\% CI 72.2–94.4\%; specificity 88.3\%, 95\% CI 71.2–88.4\%).

AF termination on ablation

Table 2 lists differences in driver characteristics in patients in whom AF termination was achieved on driver ablation. Focal drivers were more likely to demonstrate AF termination on ablation compared to rotational drivers (64/48 [12.5\%] focal drivers vs 6/133 [4.5\%] rotational drivers; \( P = .02 \)). Ablation of a focal driver was more predictive of AF termination than ablation of a rotational driver (OR 4.6; 95\% CI 1.2–17.1; \( P = .02 \)).

Rotational drivers with higher recurrence rate were more likely to demonstrate AF termination on ablation (5.7 ± 1.9 occurrences in PD with AF termination on ablation vs 2.6 ± 1.9 occurrences in PD without AF termination on ablation; \( P < .001 \)). Rotational drivers with higher consecutive rotations (ie, temporal stability) were more likely to demonstrate AF termination on ablation (5.8 ± 2.1 rotations in PD with AF termination on ablation vs 2.1 ± 1.5 rotations in PD without AF termination on ablation; \( P < .001 \)). Focal drivers with higher recurrence rate were also more likely to demonstrate AF termination on ablation (4.9 ± 1.3 drivers with an ablation response vs 1.5 ± 0.6 drivers without AF termination on ablation; \( P < .008 \)). Focal drivers with higher consecutive focal discharges (ie, temporal stability) were more likely to demonstrate AF termination on ablation (6.5 ± 2.4 consecutive focal discharges in PD with AF termination on ablation vs 2.8 ± 1.5 focal discharges in PD without AF termination on ablation; \( P < .001 \)).

Relationship of confirmed drivers to LVZs

Of the 33 rotational drivers that resulted in a study-defined ablation response, 28 (84.8\%) were mapped to sites of

Figure 4  **A:** ECG imaging map in the LAO view showing an atrial fibrillation driver with rotational activity along the anterior wall of the left atrium (LA). **B:** CARTO map of the LA in the anteroposterior view showing ablation at the site of driver, which resulted in sinus rhythm on the electrograms (C), including surface ECG, CS, and PV signals. Abbreviations as in Figure 3.
LVZs, whereas only 5 of the 26 confirmed focal drivers (19.2%) were mapped to sites of LVZs. Rotational drivers showed a predilection to LVZs ($P < .001$).

**Clinical outcomes**

Of the 40 patients included in the study, the primary outcome was achieved in 26 (65%), who remained free from AF/AT at 1 year off antiarrhythmic drugs after a single procedure. Of the 14 patients who had AF/AT recurrence, 10 had AF recurrence and 4 had AT recurrence. The secondary endpoint of freedom from AF at 1-year follow-up off antiarrhythmic drugs was therefore achieved in 30 of 40 patients (75%).

Of the 14 patients who had AF/AT recurrence, 6 (42.9%) underwent an additional catheter ablation procedure using conventional techniques. When assessing only the 32 patients who underwent ECGI-guided localized driver ablation, 22 (68.8%) were free from AF/AT at 1-year follow-up. Of the 10 patients who had AF/AT recurrence, 7 had AF recurrence and 3 had AT recurrence. The rate of freedom from AF at 1-year follow-up was 78.1%. When comparing patients with AF who underwent ECGI-guided ablation and those who terminated to SR with PVI, there was no significant difference in AF/AT recurrence during follow-up ($n = 10 \ [31.3\%] \ vs \ n = 4 \ [50\%]$, respectively; $P = .42$). When comparing recurrence of AF only during follow-up, there was no significant difference between these groups ($n = 7 \ [21.9\%] \ vs \ n = 3 \ [37.5\%]$, respectively; $P = .39$). The number of PDs ablated did not predict freedom from AF/AT during 1-year follow-up ($5.6 \pm 2.2$ drivers ablated in patients free from AF/AT vs $5.7 \pm 1.3$ drivers ablated in patients not free from AF/AT; $P = .48$). AF termination did predict freedom from AF/AT during 1-year follow-up (OR $3.4; 95\% \ CI 1.4–8.6; P = .008$).

**Table 2** Differences in characteristics of drivers for which ablation that did vs ablation that did not result in AF termination

<table>
<thead>
<tr>
<th></th>
<th>AF termination on ablation ($n = 12$)</th>
<th>No AF termination on ablation ($n = 169$)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of focal drivers</td>
<td>50.0</td>
<td>31.1</td>
<td>.03</td>
</tr>
<tr>
<td>Recurrence rate</td>
<td>$5.7 \pm 1.6$</td>
<td>$2.7 \pm 2.0$</td>
<td>$&lt;.001$</td>
</tr>
<tr>
<td>Temporal stability</td>
<td>$6.5 \pm 2.3$</td>
<td>$2.6 \pm 1.8$</td>
<td>$&lt;.001$</td>
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Values are given as percent or mean ± SD unless otherwise indicated. AF = atrial fibrillation.

**Discussion**

ECGI mapping was used to guide localized driver ablation in patients with persistent AF. Of the 40 patients included in the
study, the primary outcome was achieved in 65% of patients, who remained free from AF/AT at 1 year off antiarrhythmic drugs after a single procedure. The secondary endpoint of freedom from AF at 1-year follow-up off antiarrhythmic drugs was achieved in 75% of patients. An ablation response that met the study criteria was seen in 92.5% of patients, with AF termination achieved in half of the cohort. An ablation response was seen with only 33% of localized drivers. However, driver characteristics had an impact on the ablation response achieved whereby focal drivers and drivers with higher recurrence rate and greater temporal stability were more likely to achieve an ablation response, including AF termination.

Clinical outcomes
In total, using this workflow of PVI followed by targeting of drivers guided by ECGI mapping, 65% remained free from atrial arrhythmia off antiarrhythmic drugs. This is similar to the single-center experience reported by the Bordeaux group (64%) but considerably more than the multicenter experience in AFACART (34%). There were 2 important differences tested in this study. (1) PVI was performed first in this study and ECGI-guided ablation was performed only in those who remained in AF. (2) ECGI mapping was used not just to guide the operator in an attempt to ablate to sinus rhythm, which might be impacted by other information from intracardiac electrogroms and operator experience, but ablation was targeted specifically as dictated by the finding of drivers on the CardioInsight system regardless of operator opinion or findings on endocardial signals.

In the current study, freedom from AF (ie, allowing for AT) at 1 year off antiarrhythmic drugs after a single procedure was 75%, which is comparable to that reported in the Bordeaux experience (80%) and AFACART (77%), albeit with the use of antiarrhythmic drugs accepted in the other studies.1,3 AT occurrence during follow-up in this study was therefore remarkably lower than that reported in the AFACART study.3 Extensive atrial ablation may predispose to reentry formation, and the greater ablation duration in AFACART compared to that in this study may explain the lower rate of AT recurrence during follow-up seen in this study.

STAR AF II (Substrate and Trigger Ablation for Reduction of Atrial Fibrillation Trial) and a recent meta-analysis suggest that approximately 50%–60% of patients remain free from arrhythmia in the medium term after persistent AF ablation.15,16 The 65% success rate with this approach is arguably at the upper end of that reported in other studies. AF termination predicted freedom from AF/AT. This association has been demonstrated in some studies but not others.17–22 It is plausible that AF termination using localized driver ablation should predict freedom from AF/AT. The data provided on drivers that are important and worth targeting may therefore improve outcomes further. Large-scale randomized studies are needed to determine an impact of this or similar ablation strategies compared to PVI alone.

Response to ablation
A majority of patients in this study responded to ablation acutely. Considering the overall strategy, 37 of 40 patients (93%) responded to ablation. Considering the 32 patients who remained in AF post-PVI, 29 (91%) responded to ablation, with AF termination in 12 (41%) and SCL in 17 (59%). This is less than the AF termination rate achieved in the Bordeaux experience (80%) or in AFACART3 (72%) but is comparable to the AFACART composite endpoint of AF termination or SCL achieved in 94%.

Why there is such a discrepancy seen in terms of AF termination rates remains unclear. In AFACART, the average total driver only ablation duration was 46 minutes, whereas in this study the average total driver ablation duration was only approximately 10 minutes. In addition, in AFACART, ablation was performed pre-PVI. However, this unlikely is a contributing factor to the higher rate of AF termination because previous studies have shown that PVI organizes AF and makes driver identification easier.2,6,7,25 One possibility is that this study was heavily protocol based and involved ablation of drivers strictly guided by the CardioInsight system. The Bordeaux experience and the AFACART study may not have been as strict and may have used the system as a guide to help highly experienced operators in ablating to sinus rhythm. This difference may be the difference expected between highly experienced AF ablators and what less experienced operators might achieve when simply ablating guided by CardioInsight maps.

Although previous studies reported the proportion of patients who responded to ablation guided by ECGI mapping,1,3 this study also reported the response to ablation on a per-driver basis. In contrast to previous studies using different AF mapping technologies, a lower proportion of localized drivers identified on ECGI maps were associated with an ablation response or AF termination.2,6,7,25 This may be due to the technical challenges of noninvasive mapping. Drivers were also identified using previously published arbitrary definitions7 (focal activations with radial spread or rotational activations completing ≥1.5 revolutions). It is possible that not all such “drivers” are real or mechanistically important. Whether refinements to the technology and the definitions of drivers and what is targeted can improve the sensitivity and specificity of true driver detection and ablation response remain to be seen. The mapping data acquired by the ECGI system are fairly consistent in terms of driver detection, distribution, and characteristics provided a minimum of 850-ms intervals are used and a minimum of 10–15 seconds of cumulative data is analyzed.11 Recordings pre- and post-PVI or before and after adenosine administration have shown consistent findings.5,10

Driver characteristics associated with an ablation response
Despite a lower rate of AF termination achieved with ablation of the localized drivers, certain driver characteristics were more likely to be associated with AF termination. Focal
and rotational PDs with a higher recurrence rate and greater temporal stability were more likely to result in AF termination on ablation. These findings are consistent with those of previous studies.\textsuperscript{5,6} These findings suggest that a hierarchal approach should be adopted when targeting localized drivers mapped with the CardioInsight system whereby drivers with greater stability in terms of their recurrence rate and temporal stability should be targeted first. Not only should this result in an ablation response quicker but it also should minimize the amount of (perhaps unnecessary and potentially harmful) ablation required.

With this study demonstrating that drivers with certain characteristics are more likely to result in an ablation response, particularly AF termination, it raises interesting questions about the order in which drivers should be ablated, whether one should be selective in terms of which drivers to ablate, whether one should aim for termination or only ablate the more important drivers, and whether some drivers ought to be targeted regardless of AF termination. The results of the AFACART study suggest that a more selective approach targeting fewer drivers may predispose less to subsequent ATs.

Drivers with rotational activation were predominantly located in LVZs, suggesting that they may be anchored to areas of structural remodeling or scar. It is also recognized that the focal discharges seen on endocardial mapping may not have been truly focal and could well represent endocardial breakthrough due to dissociation of the endocardial and epicardial layers.\textsuperscript{26} There was no significant predilection of drivers for any particular LA anatomic site.

Ablation of focal drivers was more likely to result in an ablation response compared to rotational drivers of any particular LA anatomic site. Previous studies have shown that ECGI maps can inappropriately identify rotational drivers, particularly at sites of conduction block.\textsuperscript{27} The findings of this study further support these findings whereby a larger proportion of rotational drivers did not demonstrate an ablation response compared to focal drivers. This suggests either that focal drivers are more important in maintaining AF or that rotational PDs are prone to erroneous identification. In either case, logical conclusions would be that consideration should be given to ablation of focal PDs first, and that rotational PDs should be scrutinized carefully.

Study limitations
One study limitation is the small patient numbers. Outcome data for a cohort of this size, although very encouraging, should be viewed as feasibility data. The patient numbers are comparable to that of other proof-of-concept studies evaluating novel methods and technologies,\textsuperscript{6,28–30} and it is hoped that this work will inform future strategies and ultimately large-scale randomized controlled trials to define outcomes relative to other strategies.

To determine the mechanistic significance of PDs, we necessarily focused on electrophysiological endpoints because there is arguably no other way to verify that a driver has been mapped. Although termination of AF is clear, the importance of CL prolongation is less certain. Others have used termination of AF or CL prolongation as a surrogate for the interruption of mechanisms important for the maintenance of AF.\textsuperscript{2,5,6,12,13}

It is possible that the rate-slowing medications required for ECGI mapping could have an impact on AF mechanisms. We previously showed that adenosine does not have an impact on AF mechanisms as determined by ECGI mapping,\textsuperscript{10} but other drugs have not been investigated.

A minority of patients were in sinus rhythm at the start of the procedure following cardioversion. Although these data suggest that the mechanisms of induced AF seem no different from those of established AF, uncertainty about this remains.

Conclusion
ECGI mapping was used to map and ablate localized drivers in AF post-PVI. Localized drivers in the form of focal and rotational drivers were identified in all patients. An ablation response occurred in nearly all patients, although AF terminated in only half. PVI followed by ECGI-guided localized driver ablation was associated with an acceptable rate of freedom from AF at 1-year follow-up. The drivers that demonstrated an ablation response were more likely focal in nature and demonstrated greater stability. These data enhance our understanding of AF mechanisms and may help to refine targeting of PDs.

Appendix
Supplementary data
Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2022.01.042.

References