

Characterization of Electrograms Associated With Termination of Chronic Atrial Fibrillation by Catheter Ablation

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Objectives	This study sought to determine the characteristics of atrial electrograms predictive of slowing or termination of atrial fibrillation (AF) during ablation of chronic AF.
Background	There is growing recognition of a role for electrogram-based ablation.
Methods	Forty consecutive patients (34 male, 59 ± 10 years) undergoing ablation for chronic AF persisting for a median of 12 months (range 1 to 84 months) were included. After pulmonary vein isolation and roof line ablation, electrogram-based ablation was performed in the left atrium and coronary sinus. Targeted electrograms were acquired in a 4-s window and characterized by: 1) percentage of continuous electrical activity; 2) bipolar voltage; 3) dominant frequency; 4) fractionation index; 5) mean absolute value of derivatives of electrograms; 6) local cycle length; and 7) presence of a temporal gradient of activation. Electrogram characteristics at favorable ablation regions, defined as those associated with slowing (a ≥6-ms increase in AF cycle length) or termination of AF were compared with those at unfavorable regions.
Results	The AF was terminated by electrogram-based ablation in 29 patients (73%) after targeting a total of 171 regions. Ablation at 37 (22%) of these regions was followed by AF slowing, and at 29 (17%) by AF termination. The percentage of continuous electrical activity and the presence of a temporal gradient of activation were independent predictors of favorable ablation regions (p = 0.016 and p = 0.038, respectively). Other electrogram characteristics at favorable ablation regions were not significantly different from those at unfavorable ablation regions.
Conclusions	Catheter ablation at sites displaying a greater percentage of continuous activity or a temporal activation gradient is associated with slowing or termination of chronic AF. (J Am Coll Cardiol 2008;51:1003-10) © 2008 by the American College of Cardiology Foundation

Ablation targeting complex atrial electrical activities (electrogram-based ablation) with or without pulmonary vein (PV) isolation and left atrial (LA) linear ablation has

been shown to be effective in chronic atrial fibrillation (AF) (1-4). Although the techniques of PV isolation and linear ablation have been well described (5-10), there is less knowledge about electrogram-based ablation. In particular, characteristics of atrial electrogram associated with modifi-

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cation of AF substrate have not been investigated. Complex fractionated and rapid electrograms may be related to various mechanisms, including slow anisotropic conduction, high-frequency activities, or autonomic ganglionated plexi (11-13), and ablation targeting such electrograms results in a dramatic increase in AF cycle length (AFCL) and/or

Abbreviations and Acronyms

AF	= atrial fibrillation
CL	= cycle length
CS	= coronary sinus
DF	= dominant frequency
LA	= left atrium
LAA	= left atrial appendage
PV	= pulmonary vein
RF	= radiofrequency

termination of AF. On the other hand, ablation at some of such sites leads to little effect on the AF process (4). This prospective clinical study therefore sought to evaluate the characteristics of complex atrial electrograms in relation to their effects on the AF process.

Methods

Study population. The study consisted of 40 consecutive patients (34 male, 59 ± 10 years) with symptomatic drug-refractory chronic AF undergoing ablation. Patients had their first episode of AF a median of 67 months before ablation (range 1 to 300 months) and had persistent AF for 12 months (range 1 to 84 months). Three patients underwent ablation 1 month after they presented with persistent AF associated with heart failure. Of 17 patients who had undergone electrical cardioversion before ablation, 12 had failed to convert to sinus rhythm and the other 5 had failed to stay in sinus rhythm for >7 days.

Structural heart disease was present in 20 patients (idiopathic dilated cardiomyopathy in 6 patients, hypertensive heart in 5 patients, valve disease in 5 patients, hypertrophic cardiomyopathy in 2 patients, and ischemic heart disease in 2 patients). The mean left ventricular ejection fraction was $58 \pm 12\%$, and 5 patients (13%) had an ejection fraction of <45%. Parasternal, longitudinal, and transverse LA diameters were 48 ± 7 mm, 60 ± 7 mm, and 45 ± 6 mm, respectively.

3.2 ± 1.5 antiarrhythmic drugs had failed, and 10 patients (25%) were taking amiodarone at the time of the procedure. Antiarrhythmic drugs were discontinued ≥ 5 half-lives before ablation. All patients gave written informed consent to the ablation protocol.

Electrophysiological study. All patients underwent anticoagulation for at least 1 month as well as transesophageal echocardiography to exclude atrial thrombus before the procedure. Electrophysiological study was performed with midazolam sedation and morphine analgesia. The LA was accessed trans-septally, and a single bolus of 50 IU/kg heparin was administered immediately after trans-septal puncture. A deflectable quadripolar catheter (Xtrem, ELA Medical, Montrouge, France) was deployed in the coronary sinus (CS) from the femoral vein. A circumferential decapolar catheter (Lasso, Biosense-Webster, Diamond Bar, California) was used to guide PV isolation and, once complete, the lasso was positioned in the right atrial appendage for continuous monitoring of the right atrial cycle length (CL). A 3.5-mm irrigated-tip catheter (ThermoCool, Biosense-Webster) was used for ablation and mapping, and to record AFCL in the left atrial appendage (LAA) before and after each step of the ablation protocol.

Surface electrocardiogram and bipolar intracardiac electrograms were monitored on a computer-based digital amplifier/recorder system (Labsystem Pro, Bard Electrophysiology, Lowell, Massachusetts). Intracardiac electrograms were filtered from 30 to 250 Hz and measured with online calipers at a sweep speed of 100 mm/s.

AFCL measurement. The AFCL was determined by averaging the consecutive cycles in a 10-s recording at the left and right atrial appendage using automated monitoring software (Labsystem Pro, Bard Electrophysiology). The apex of both appendages was selected for accurate measurement of AFCL because of unambiguous high-voltage electrograms in contrast to the usually chaotic activity in the remaining atrium. Measurements of AFCL were obtained before and immediately after ablation of each targeted region. The difference in mean CL in 2 serial measurements at the LAA during 1-min window was 2.5 ± 1.6 ms in the present patients. Thus, a 6-ms (mean + 2 standard deviations) change in LAA CL after ablation was defined as a significant change in AFCL.

Catheter ablation protocol. Technical parameters during PV isolation, electrogram-based ablation, and linear ablation have been previously described (2,9,10). Briefly, catheter ablation of AF was performed in the following sequence until termination of AF: 1) PV isolation; 2) roof line ablation; 3) electrogram-based ablation targeting the LA or CS tissue; and 4) mitral isthmus linear ablation. Termination of AF was defined as conversion into persistent atrial tachycardia or direct restoration of sinus rhythm from AF; transient change from AF into atrial tachycardia (and return to AF) was not considered as termination of AF. Atrial tachycardia was defined as an organized atrial rhythm with stable CL, morphology, and activation sequence in both atria. If AF was converted into atrial tachycardia, mapping and catheter ablation were continued until restoration of sinus rhythm. A cavotricuspid isthmus line was performed at the end of the procedure in all patients.

During electrogram-based ablation, 6 pre-determined regions were ablated in a randomized sequence: the anterior LA, posterior LA, inferior LA, septal LA, base of LAA, and CS. The lateral LA was ablated in the step of mitral isthmus linear ablation. Electrograms were targeted visually on the base of complexity and fractionation as reported previously (1,2). Each atrial region was anatomically defined as follows: the posterior LA consisted of a square with the boundaries of the 4 PV orifices, the anterior LA extended from the LA roof line connecting both superior PVs to the superior mitral annulus, the inferior LA extended from the lower aspect of the 2 inferior PV ostia to the inferior mitral annulus, the base of LAA was circumferentially explored, and the CS was mapped from the distal to proximal segment. Radiofrequency (RF) ablation was performed point by point or during continuous dragging motion. The RF energy power was limited to 30 W in the LA and 25 W in the CS and delivered at each point for 20 to 60 s.

The end point of ablation in each region was transformation of complex fractionated electrograms into discrete electrograms and slowing of local CL compared with LAA CL or elimination of electrograms. The RF delivery was also stopped after 60 s of application. Finally, when atrial activity followed a consistent sequence temporally with varying CL, focal sources shown by a site with radial spread of activation to the surrounding tissue (centrifugal activation) were targeted (14).

Analysis of electrogram characteristics. In electrogram-based ablation, electrograms were acquired for 4 s in several sites in each targeted atrial region prior to ablation: 3 sites in the anterior LA (lateral, septal, and high [close to the roof line]), 3 sites in the inferior LA (a septal site facing the ostium of the CS, intermediate site, and lateral site [4 o'clock at the mitral annulus]), 4 sites in the posterior LA (near the right and left PV, superior, and inferior), 4 sites in the LA septum (anterior, inferior, posterior, and superior to the fossa ovalis), 4 sites in the LAA (anterior, superior, posterior, and inferior junction to the LA body), and 3 sites within the CS (distal at 3 o'clock, midportion at 4 to 5 o'clock [2 to 3 cm inside], and proximal portion [from the ostium to 1 cm inside] of the CS).

Complex electrical activities were evaluated by: 1) percentage of continuous electrical activity during 4 s (Fig. 1); 2) maximal bipolar voltage during continuous activity (Fig. 2); 3) determination of dominant frequency (DF) by a fast Fourier transform, and difference in this local DF compared with that in the LAA; 4) determination of a fractionation index defined as the number of deflections with an absolute value of >0.05 mV from the baseline using specially designed software (Fig. 3); and 5) mean absolute value of derivatives of electrograms (dV/dt); thus, a larger value represents a steeper slope.

When only discrete electrograms were present in a region, they were assessed by: 1) mean local CL and CL difference between local and the LAA; and 2) presence of a temporal gradient of activation, defined as a temporal difference of ≥ 70 ms between the proximal and distal bipoles of the mapping catheter (Fig. 4). Such an activation gradient may indicate either local conduction block (11) or sequential

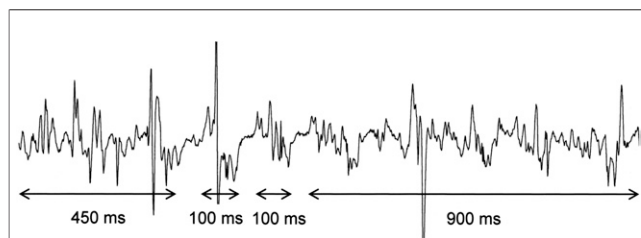


Figure 1 Evaluation of Continuous Activity Percentage

Continuous activities with duration of 450 ms, 100 ms, and 900 ms are interrupted by an isoelectric line of >50 ms. Duration of continuous activity in this observation window is 90%.

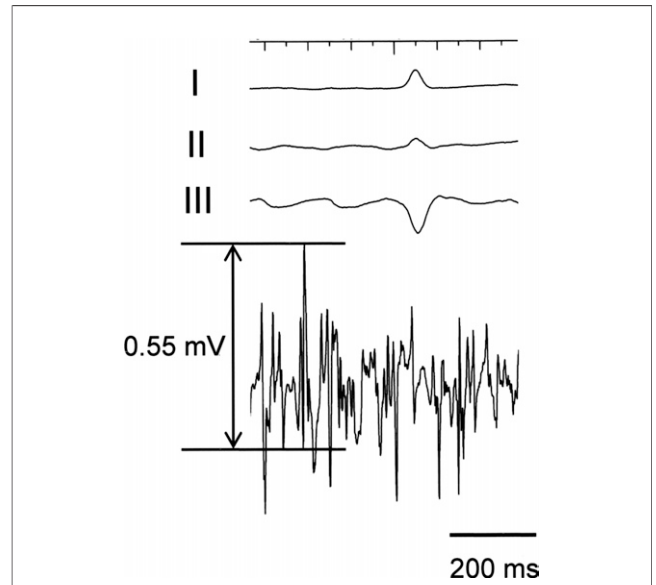


Figure 2 Evaluation of Maximal Bipolar Voltage

Maximal bipolar voltage in this observation window is 0.55 mV.

activation of proximal and distal bipoles by a rotating wave (14,15).

The above parameters were calculated by a single investigator (Y.T.) who was blinded to ablation results. The parameters were then compared among ablation sites associated with: 1) no significant change in LAA CL; 2) LAA CL slowing ≥ 6 ms; and 3) AF termination during or just after ablation.

Follow-up. Patients were hospitalized for 1 day at 1 month, 3 months, 6 months, and 12 months after the procedure for clinical review and ambulatory monitoring. Antiarrhythmic drugs were administered for 2 months after the procedure, and recurrences were not assessed during this period (blanking period). If tachyarrhythmia was not observed during this period, these antiarrhythmic drugs were discontinued. Patients were followed up for at least 3 months after the last procedure.

Statistical analysis. Data are presented as mean \pm standard deviation unless stated otherwise. Continuous variables were compared with one-way analysis of variance (or Kruskal-Wallis test when the data were not normally distributed). Comparison of proportions was performed by chi-square test (or Fisher exact test when a value was <5 in one of the cells). A value of $p < 0.05$ was considered as statistically significant. Multiple logistic regression analysis was performed to assess independent predictors for significant impact of ablation. For continuous variables associated with impacts of ablation, receiver-operator characteristic curves were used to determine a cutoff value with best sensitivity and specificity. Because data were acquired at several recording sites in a given region, statistical comparisons were made using variables representing the most complex or rapid activity, that is the maximal values for a DF, percentage of

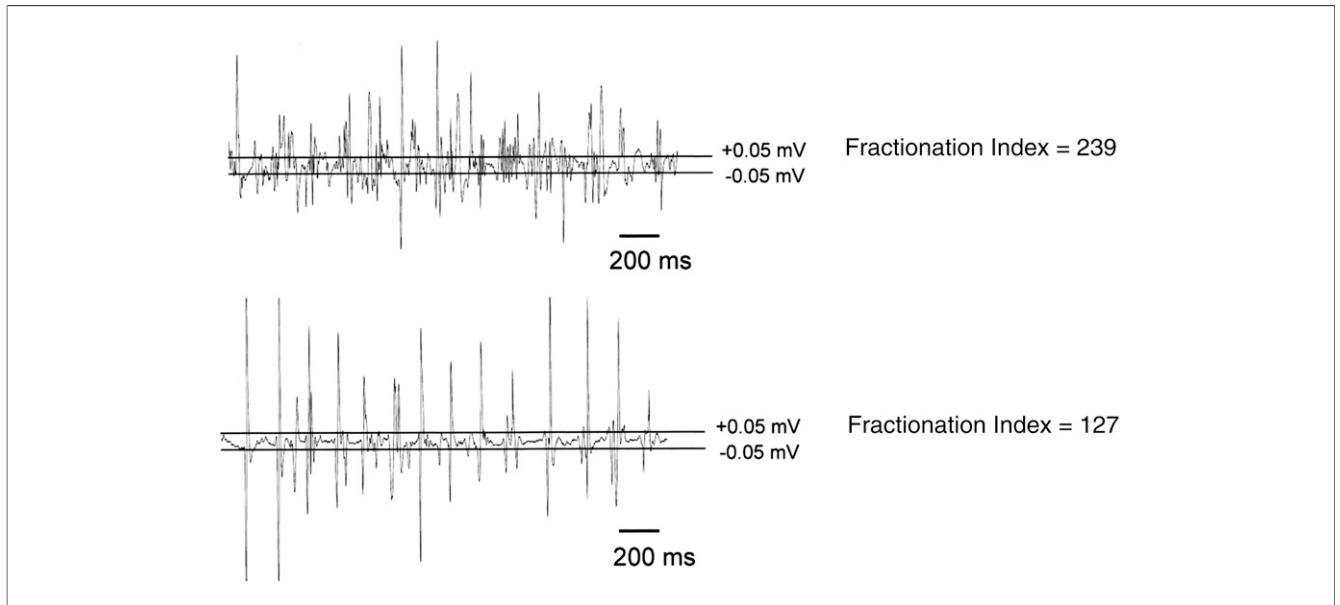


Figure 3 Fractionation Index

Fractionation index in the upper panel is greater than that in the lower panel, representing a greater number of deflections.

continuous electrical activity, fractionation index, and mean absolute value of dV/dt and the minimal values for local CL.

Results

Procedural results. During ablation, AF was terminated in 39 of 40 patients (98%) with conversion to atrial tachycardia in 25 patients (63%) and direct restoration of sinus rhythm in 14 patients (35%). In the remaining patient, infusion of 300 mg of amiodarone converted AF into atrial tachycardia after completion of the ablation protocol. Termination of AF was not seen

in any patient during PV isolation, 3 patients (8%) during roof line ablation, 29 patients (73%) during electrogram-based ablation in the LA/CS, and 7 patients (18%) after mitral isthmus linear ablation. The procedural, fluoroscopic, and total RF delivery duration were 227 ± 71 min, 84 ± 30 min, and 82 ± 27 min, respectively. There was a single procedure-related complication: cardiac tamponade after a steam pop during mitral isthmus ablation despite the fact that RF power was limited to 30 W. The patient was treated by pericardiocentesis without long-term sequela.

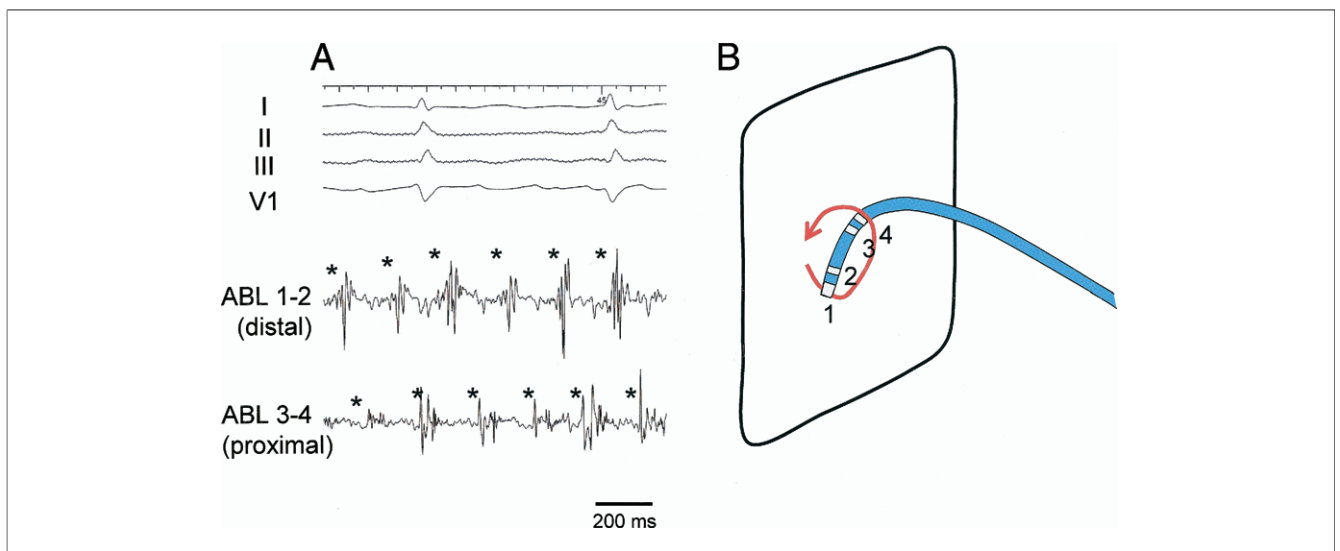


Figure 4 Activation Gradient

(A) A temporal gradient of at least 70 ms between the distal and proximal bipoles on the map electrode is observed. (B) Possible mechanism underlying activation gradient between the distal and proximal bipoles. A mapping catheter lies across a small re-entry circuit, which plays a driving role.

Table 1 Electrogram Characteristics of Targeted Regions

	Anterior LA (n = 27)	Posterior LA (n = 28)	Septal LA (n = 29)	LAA (n = 27)	Inferior LA (n = 31)	CS (n = 29)	p Value
Percentage of continuous activity (%; median [1st, 3rd quartile])	65 (45, 80)	38 (18, 68)	80 (54, 91)	80 (45, 95)	70 (51, 85)	45 (25, 85)	0.01*
Voltage of continuous activity (mV)	0.22 ± 0.16	0.17 ± 0.08	0.16 ± 0.11	0.21 ± 0.08	0.20 ± 0.10	0.18 ± 0.07	0.3†
Local DF (Hz)	6.90 ± 2.50	7.05 ± 3.00	7.96 ± 2.91	8.36 ± 3.46	7.10 ± 2.24	7.54 ± 2.24	0.3†
DF difference with LAA (Hz)‡	0.57 ± 2.36	0.81 ± 2.95	1.87 ± 2.87	—	0.75 ± 2.43	1.16 ± 2.52	0.4†
Fractionation index	149 ± 61	133 ± 49	161 ± 58	189 ± 67	145 ± 45	159 ± 46	0.01†
Mean absolute value of dV/dt (V/s ²)	0.013 ± 0.007	0.011 ± 0.004	0.013 ± 0.006	0.022 ± 0.009	0.015 ± 0.006	0.015 ± 0.005	<0.0001†
Local mean cycle length (ms)	174 ± 17	180 ± 28	172 ± 27	163 ± 21	167 ± 21	171 ± 23	0.6†
Cycle length difference with LAA (ms)§	12 ± 7	18 ± 19	9 ± 25	—	8 ± 14	13 ± 16	0.6†
Activation gradient (patients)	2	3	9	5	4	3	0.2¶

*Kruskal-Wallis test was used. †One-way analysis of variance was used. ‡Positive value represents that local DF is greater than DF at the LAA. §Positive value represents that local cycle length is greater than cycle length at the LAA. ¶Fisher exact test was used.

CS = coronary sinus; DF = dominant frequency; LA = left atrium; LAA = left atrial appendage.

Electrogram characteristics in relation to anatomical location and amiodarone use. The electrogram characteristics by anatomical location are shown in Table 1. The percentage of continuous activity, fractionation index, and mean absolute value of dV/dt differed significantly among regions. In addition, electrogram characteristics were compared between patients taking and not taking amiodarone at the time of the study, showing a longer CL in patients on amiodarone (Table 2).

Impact of ablation and anatomical location. In the 29 patients in whom AF was terminated during electrogram-based ablation, a median of 4 regions per patient (in addition to the PV isolation and roof line) were targeted, for a total of 171 regions. During ablation in these 171 regions, no prolongation of AFCL ≥6 ms was observed in 105 regions (61%), an increase in AFCL of ≥6 ms occurred in 37 regions (22%), and termination of AF occurred in 29 regions (17%). The incidence of a ≥6 ms increase in AFCL or termination of AF at each targeted region is indicated in Table 3. Mean duration of RF delivery in the anterior LA, posterior LA, septal LA, LAA, inferior LA, and CS were 3 ± 1 min, 5 ± 2 min, 4 ± 2 min, 4 ± 2 min, 5 ± 3 min, and 7 ± 2 min, respectively. Mean duration of RF delivery

in the regions with AF termination, a ≥6 ms increase in AFCL, and a <6 ms increase in AFCL were 5 ± 4 min, 4 ± 2 min, and 4 ± 2 min, respectively (p = 0.4).

Impact of ablation in relation to electrogram characteristics. Comparisons of electrogram characteristics showed significant difference in the percentage of continuous electrical activity and presence of a temporal gradient of activation (Table 4). Continuous activity was present for a median of 80% of time during a 4-s recording window at regions with AF termination, 70% at those with a ≥6 ms increase in AFCL, and 50% at those without ablation impact. A temporal activation gradient was observed in 24% of regions with ablation impact versus 10% of those without. Bipolar voltage, local CL, fractionation index, DF and mean absolute value of dV/dt were not different at regions with or without ablation impacts. Multiple logistic regression analysis demonstrated that percentage of continuous electrical activity (p = 0.016, odds ratio 1.013, 95% confidence interval 1.003 to 1.023) and the presence of a temporal gradient of activation (p = 0.038, odds ratio 2.526, 95% confidence interval 1.052 to 6.069) were independent predictors of favorable ablation regions, where AF termination or a ≥6-ms increase in AFCL occurred.

Table 2 Electrogram Characteristics in Patients Taking and Not Taking Amiodarone

	Ablation Regions in Patients Not Taking Amiodarone (n = 128)	Ablation Regions in Patients Taking Amiodarone (n = 43)	p Value
Percentage of continuous activity (%; median [1st, 3rd quartile])	65 (30, 90)	70 (41, 85)	0.84*
Voltage of continuous activity (mV)	0.20 ± 0.11	0.18 ± 0.09	0.34†
Local DF (Hz)	7.30 ± 2.48	8.02 ± 3.44	0.14†
DF difference with LAA (Hz)‡	0.88 ± 2.48	2.14 ± 3.31	0.01†
Fractionation index	158 ± 59	153 ± 49	0.66†
Mean absolute value of dV/dt (V/s ²)	0.015 ± 0.007	0.015 ± 0.006	0.70†
Local mean cycle length (ms)	166 ± 22	182 ± 23	0.004†
Cycle length difference with LAA (ms)§	8 ± 17	11 ± 19	0.40†
Activation gradient (n, [%])	19 (15%)	7 (16%)	0.81

*Kruskal-Wallis test was used. †One-way analysis of variance was used. ‡Positive value represents that local DF is greater than DF at the LAA. §Positive value represents that local cycle length is greater than cycle length at the LAA. ||Chi-square test was used.

Abbreviations as in Table 1.

Table 3 Impact of Ablation of Targeted Regions

	Anterior LA (n = 27)	Posterior LA (n = 28)	Septal LA (n = 29)	LAA (n = 27)	Inferior LA (n = 31)	CS (n = 29)	p Value
Termination of AF or a ≥ 6 -ms increase in AFCL (patients [%])	10 (37%)	5 (18%)	16 (55%)	16 (59%)	11 (35%)	8 (28%)	0.01*
Termination of AF (patients [%])	3 (11%)	3 (11%)	7 (24%)	8 (30%)	5 (16%)	3 (10%)	
A ≥ 6 -ms increase in AFCL (patients [%])	7 (26%)	2 (7%)	9 (31%)	8 (30%)	6 (19%)	5 (17%)	

*Chi-square test was used.

AF = atrial fibrillation; AFCL = atrial fibrillation cycle length; other abbreviations as in Table 1.

Using a receiver-operator characteristic analysis, continuous activity present for $\geq 70\%$ of time was associated with a sensitivity and specificity of 64% and 62% and a positive and negative predictive value of 51% and 73% for favorable ablation regions. The presence of temporal gradient of activation was predictive of favorable ablation regions with a sensitivity, specificity, positive predictive value, and negative predictive value of 24%, 90%, 62%, and 66%, respectively. Lastly, excluding the 10 patients taking amiodarone, there was still a significant difference in the percentage of continuous activity ($p = 0.0027$), but not in the presence of a temporal gradient of activation ($p = 0.64$).

Ablation of source of activity. A source showing centrifugal activation was found in 10 regions (6%) after ablation of a median of 5 regions (1 to 6) in electrogram-based LA/CS ablation; the CS in 2 patients, anterior LA in 3 patients, inferior LA in 1 patient, and base of the LAA in 4 patients. Local ablation abruptly terminated AF in 7 patients and resulted in a significant increase in AFCL (8 ms, 12 ms, and 24 ms, respectively) in the remaining 3 patients.

Follow-up. Beyond 2 months after ablation, 18 patients (45%) had recurrent arrhythmias at 1.5 ± 2.9 months, and 16 of these underwent a repeat procedure at 3.7 ± 2.9 months after the index procedure. All repeat procedures were performed for recurrent atrial tachycardia. Fifteen patients had 1 atrial tachycardia (macro-re-entry around the mitral annulus in 7 patients, macro-re-entry through the LA roof in 1 patient, common atrial flutter in 1 patient,

focal tachycardia in 6 patients [PV in 2, LA septum in 2, posterior LA in 1, and CS in 1]), and 1 patient had 2 atrial tachycardias (macro-re-entry around the mitral annulus and focal tachycardia from the LA septum).

During a follow-up of 13.9 ± 2.8 months after the last procedure, 36 patients (90%) were in stable sinus rhythm (33 without antiarrhythmic drugs), 1 with ischemic heart disease died of heart failure, 1 is in persistent atrial tachycardia, and 2 are in persistent AF.

Discussion

The present prospective study showed that various patterns of complex electrograms were ubiquitously distributed in the LA and CS region in patients with chronic AF, and that the percentage of continuous activity and a temporal gradient of activation at the ablation area were associated with slowing or termination of AF.

Electrogram-based ablation. In the present study, termination of AF occurred in 73% of cases during electrogram-based ablation (after PV isolation and roof line), confirming the importance of electrogram analysis in the ablation process, as already described (1-4). Favorable ablation regions were distributed over a broad area, indicating that the entire atria and all of the thoracic veins need to be screened for ablation targets.

Complex fractionated electrograms are thought to be caused by slow or anisotropic conduction, temporal overlapping of different wave fronts entering the mapping area,

Table 4 Characteristics of Electrograms and Impact of Ablation

	Ablation Regions With AF Termination (n = 29)	Ablation Regions With a ≥ 6 -ms Increase in AFCL (n = 37)	Ablation Regions With a < 6 -ms Increase in AFCL (n = 105)	p Value
Percentage of continuous activity (%; median [1st, 3rd quartile])	80 (60, 90)	70 (43, 86)	50 (25, 85)	0.0018*
Voltage of continuous activity (mV)	0.20 ± 0.11	0.16 ± 0.09	0.20 ± 0.11	0.12†
Local DF (Hz)	7.87 ± 3.38	7.71 ± 3.10	7.29 ± 2.43	0.52†
DF difference with LAA (Hz)§	1.79 ± 3.22	1.51 ± 3.12	0.91 ± 2.45	0.23†
Fractionation index	164 ± 63	150 ± 66	157 ± 50	1.0†
Mean absolute value of dV/dt (V/s^2)	0.015 ± 0.006	0.015 ± 0.009	0.015 ± 0.007	0.91†
Local mean cycle length (ms)	166 ± 21	178 ± 26	169 ± 23	0.21†
Cycle length difference with LAA (ms)	-8 ± 22	-5 ± 10	-9 ± 17	0.58†
Activation gradient (patients [%])	7 (24%)	9 (24%)	10 (10%)	0.03‡

*Kruskal-Wallis test was used. †One-way analysis of variance was used. ‡Chi-square test was used. §Positive value represents that local DF is greater than DF at the LAA. ||Positive value represents that local cycle length is greater than cycle length at the LAA.

Abbreviations as in Tables 1 and 3.

or shortening of the CL (11,12,16). They may represent a focus actively driving the atria or critical zone for maintenance of AF. Alternatively, complex fractionated electrograms may simply result from passive conduction because of a decrease in AFCL. Thus, it is important to distinguish active from passive patterns, and criteria defining electrograms more optimal for ablation targets are required.

Electrogram characteristics and impacts of ablation. The percentage of continuous activity was a specific variable indicating critical fibrillatory substrate, whereas the fractionation index was not associated with impacts of ablation. This may suggest that fractionated electrograms separated by an isoelectric segment are more likely to reflect passive propagation. Surprisingly, local CL was not associated with impacts of ablation, which may be explained by the inability to measure CL accurately at the site displaying fractionated continuous electrograms. On the other hand, predictive values of the percentage of continuous activity for favorable ablation regions are modest, which is attributed to a limitation to distinguish underlying mechanisms by the morphology of local atrial electrograms.

The presence of an activation gradient from the proximal to the distal electrode was the other electrogram characteristic associated with slowing or termination of AF. This pattern has already been described in previous studies using high-resolution mapping (14,15). Those studies showed that a sequential activation of rotating waves with centrifugal activation to the surrounding tissue suggests localized re-entry maintaining atrial tachycardia or AF. Although a temporal gradient can also occur because of slow conduction, we favor the notion that it more likely suggests the presence of localized re-entry (Fig. 4B).

Low-voltage electrograms did not seem specific, although they have been associated with areas of interest in other studies (1).

Lastly, a DF was not a useful variable for predicting favorable ablation sites. Frequency spectral analysis has been advocated for analysis of complex electrograms (17–19). This technique may reveal hidden organization and identify rotor or source of activity from DF differences in high-resolution optical mapping data (20). In humans, it has been shown that sites of AF termination had higher DFs in paroxysmal AF, but its usefulness was not shown in chronic AF as in the present study (18,19). Failure to differentiate sites of interest using DFs can be attributed to the fact that more complex electrogram patterns displaying high variability of activation results in multiple peaks in frequency spectra. Slight changes in the signal can influence a DF regardless of the real activation rate.

Clinical relevance. Our study makes 2 useful points for clinicians. First, catheter ablation can maintain sinus rhythm in 90% of patients with chronic AF during 14 ± 3 months of follow-up (including a repeat procedure), when a combined approach of PV isolation, linear lesions, and electrogram-based ablation is used. Second, of atrial elec-

trograms analyzed herein, electrograms with temporal gradients or a high percentage of continuous activity were the only electrogram characteristics independently associated with AF termination during ablation.

Study limitations. First, we only analyzed 3 or 4 complex electrograms in each of the 6 regions targeted for ablation. This is because evaluation of electrogram characteristics and AFCL before and after ablation is time-consuming and we tried to limit procedural duration in the LA. If we had evaluated all sites targeted for ablation in each region, however, we may have had different results. Second, electrogram-based ablation was performed after PV isolation and roof line ablation; thus, a high percentage of continuous activity and electrograms with temporal gradients may not be predictive if electrogram-based ablation is applied alone or a different ablation sequence is chosen. Third, the AFCL was the only tool available to us for monitoring the effects of ablation during ongoing AF. Lastly, this study was not designed to evaluate the risks and benefits of achieving AF termination versus other ablation approaches. However, our prior study showed that this approach was well tolerated and was associated with an acceptable risk–benefit ratio despite the large amount of RF energy delivery (21).

Conclusions

Catheter ablation at sites displaying a greater percentage of continuous activity or a temporal activation gradient is associated with slowing or termination of AF. Further refinement in electrogram analysis may be needed to improve the accuracy of identifying favorable ablation regions in electrogram-based ablation of chronic AF.

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