# Epicardial adipose tissue-based defragmentation approach to persistent atrial fibrillation: Its impact on complex fractionated electrograms and ablation outcome

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**BACKGROUND** Increased epicardial adipose tissue (EAT) volume is associated with atrial fibrillation (AF). However, the efficacy of EAT-based left atrial (LA) ablation for persistent AF (PsAF) is unclear.

**OBJECTIVE** The purpose of this study was to assess whether EAT-based LA ablation is effective for PsAF.

**METHODS** In 60 PsAF patients (group I), 3-dimensional reconstructed computed tomography images depicting EAT were merged with NavX-based dominant-frequency (DF) and complex fractionated electrogram (CFE) maps obtained during AF. Pulmonary vein antrum isolation (PVAI) was followed by map-guided EAT-based ablation. Results were compared to those in a historical control group (group II, case-matched patients who underwent generalized stepwise ablation including linear plus CFE-targeted ablation).

**RESULTS** In 70% (n = 42) of group I patients, the LA-EAT was located at the pulmonary vein antra; anterior and inferior surfaces, roof, septum, and mitral annulus; and left atrial appendage. EAT was at or near (<3 mm) 71% (390/550) of high-DF (> −8 Hz) sites. In 41 patients with persistent AF despite EAT-targeted ablation, CFE burden decreased significantly (from 96% to 13%, $P < .0001$), and DF decreased within the coronary sinus (6.9 ± 0.7 Hz vs 5.9 ± 0.7 Hz, $P < .0001$). Radiofrequency energy duration was significantly less in group I than in group II (25 ± 6 minutes vs 31 ± 12 minutes, $P < .05$). During 16-month follow-up, freedom from AF on antiarrhythmic drugs was 78% vs 60% ($P < .05$).

**CONCLUSION** PVAI plus EAT-based ablation efficiently eliminates high-frequency sources and yields relatively high success. EAT-based LA ablation is a simple, clinically feasible PsAF ablation strategy.

**KEYWORDS** Epicardial adipose tissue; Atrial fibrillation; Dominant frequency; Complex fractionated electrogram; EAT-based left atrial ablation

**ABBREVIATIONS 3D** = 3-dimensional; **AAD** = antiarrhythmic drug; **AF** = atrial fibrillation; **ANOVA** = one-way analysis of variance; **AT** = atrial tachyarrhythmia; **CFE** = complex fractionated electrogram; **CI** = confidence interval; **CS** = coronary sinus; **DF** = dominant frequency; **EAT** = epicardial adipose tissue; **GP** = ganglionated plexus; **IQR** = interquartile range; **LA** = left atrium; **LAA** = left atrial appendage; **MA** = mitral annulus; **PsAF** = persistent atrial fibrillation; **PV** = pulmonary vein; **PVAI** = pulmonary vein antrum isolation; **RF** = radiofrequency

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## Introduction

Pulmonary vein antrum isolation (PVAI) has become a widely accepted strategy for paroxysmal atrial fibrillation (AF).[1–4] An ablation strategy for persistent atrial fibrillation (PsAF) has not been established; however, various ablation strategies, such as those targeting complex fractionated atrial electrograms (CFEs)[1] and high dominant frequency (DF) sites,[2] linear ablation,[3,4] rotor modulation,[5] and combination strategies,[6–9] have been proposed.

A recent study showed increased epicardial adipose tissue (EAT) volume to be associated with PsAF, and high-DF sites were located adjacent to the EAT sites.[10] EAT contains abundant ganglionated plexuses (GPs) and secretes several activated proinflammatory cytokines.[11] If EAT plays a mechanistic role in PsAF, ablation of EAT sites may yield a favorable clinical outcome. Nevertheless, the efficacy of EAT-targeted left atrial (LA) ablation in patients with PsAF is unclear. We conducted a clinical study to evaluate the feasibility of an EAT-based linear defragmentation approach to PsAF and electrophysiologic and clinical outcomes, and we compared these outcomes with those of linear LA plus complex fractionated electrogram (CFE)-targeted ablation in a historical control group.

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## Methods

### Treatment group

Sixty patients with symptomatic, drug-refractory PsAF (AF lasting $<1$ year, n = 21) or long-standing PsAF (AF lasting $>1$ year, n = 39)[12] were enrolled in the study and named group I. After providing written informed consent, all 60 patients underwent electrophysiologic study and catheter ablation under approval of our institutional review board. No patients were treated with amiodarone, and all other antiarrhythmic drugs (AADs) were discontinued for at least 5 half-lives by the day before the procedure. Patients who had previously undergone ablation were excluded from the study.

### Electrophysiologic study

The AF radiofrequency (RF) catheter ablation procedures were performed with a NavX system (Ensite, NavX, St. Jude Medical, St. Paul, MN, USA). Transseptal puncture was performed by reliance on fluoroscopic landmarks, and 2 8Fr SL0 sheaths were advanced into the LA. A circular mapping catheter (20-pole, 15-25-mm Lasso catheter with 6-mm bipole spacing, Biosense Webster, Diamond Bar, CA) and 4-mm irrigated-tip catheter (Safire, St. Jude Medical) were introduced into the LA via a single transseptal puncture site. All patients presented to the electrophysiology laboratory in AF. After creation of detailed LA geometry with a circular catheter and ablation catheter, high-density electrograms were acquired with a double-loop multipolar catheter (20-pole, 20-mm AFocus II catheter with 4-mm bipole spacing, St. Jude Medical) registered at multiple LA sites.

### CFE and fast Fourier transform analyses

Bipolar signals from the mapping catheter were acquired during AF and filtered between 30 and 500 Hz. The NavX mapping parameters were set to the CFE mean, by which an interval-analysis algorithm was used to measure the average fractionation index at each site, and a color map of fractionation intervals (CFE map) was constructed. The fractionation interval was defined as the average time between consecutive deflections during a 5-second recording period. The settings included a refractory period of 40 ms, peak-to-peak sensitivity between 0.05 and 0.1 mV, and duration of 10 ms. Continuous CFEs (con-CFEs) were defined as having a mean fractionation interval $<50$ ms and variable CFEs as having a fractionation interval of 50 to 120 ms.[13,14] For fast Fourier transform analysis, DF distribution was analyzed, and a DF map was constructed using DF software installed in the NavX mapping system (sampling rate 1200 Hz, resolution 0.14 Hz, with Hamming window function).[13,14] The bipolar signals obtained from the 5-second recording were analyzed, and the highest peak frequency of the resulting spectrum was identified as the DF. A high-DF site was defined as a site with a frequency $>8$ Hz and colored bright purple on the DF map from the NavX system.[2]

### Multidetector computed tomography and EAT measurements

Details of EAT detection have been described previously.[15] In brief, the EAT volume was calculated from contrast images obtained with a 3-dimensional (3D) spiral computed tomography (CT) scanner (64-channel Somatom-Definition, Siemens-Medical Solutions, Forchheim, Germany) within 1 week before the procedure. During the end-expiratory phase, volume image acquisitions were gated with the R wave. To minimize motion artifacts, each patient was given beta-blocker and underwent CT scanning only if the heart rate was $>80$ bpm. On a workstation (EnSite-Verismo, St. Jude Medical), the total EAT was detected by assigning Hounsfield units ranging from $-50$ to $-200$ to fat, and the total EAT volume was semi-automatically reconstructed from contiguous 0.5-mm axial image slices from the pulmonary artery bifurcation to the diaphragm. Thereafter, the volume of EAT surrounding the LA (LA-EAT) was manually segmented from the total EAT, that is, the EAT volume was deleted from the left ventricular side anterior to the mitral annulus (MA) and the right atrial side anterior to the right superior pulmonary vein (PV) and then from the lower side of the coronary sinus (CS), leaving the LA-EAT.[13]

In addition, axial CT images were transferred to the NavX mapping system equipped with NavX system image integration software (EnSite-Verismo, St. Jude Medical).[16] Surface reconstruction of the LA plus the PV volume was segmented from each chamber of interest. The LA-EAT was also segmented and reconstructed after detection by assignment of Hounsfield units from $-200$ to $-50$, as described earlier.

### Quantitative assessment of the distribution of EAT, high-DF sites, and CFEs before PVAI

The 3D LA and LA-EAT CT images were merged with NavX-based DF and CFE maps obtained during AF.[16] Thereafter, we divided the PVs and LA into 9 segments: PV antra; septal, posterior, inferior, lateral, and anterior surfaces and roof of the LA; MA; and left atrial appendage (LAA). The presence of EAT, high-DF sites, and CFE sites in the LA segments was assessed, and association between the EAT sites and high-DF and CFE sites was quantified. The respiratory compensation was collected just before mapping to filter the low-frequency cardiac shift associated with the breathing cycle. The reported navigation error of NavX fusion is 3.4 mm[17]; therefore, overlap between the EAT and CFE/high DF sites was defined as location of a CFE/high-DF site $<3$ mm from the EAT periphery. When high-DF/CFE sites overlapped with an EAT site, the definitions were mutually exclusive; thus, we chose the one with the shortest distance to the EAT. The overlap between an EAT site and high-frequency sources was calculated per segment as follows: total sites with spatial proximity between high-frequency sources and LA-EAT/total sites with high-frequency sources in each LA segment (expressed as a percentage).