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CASE REPORT
Cardiovascular imaging

Long-term atrial arrhythmia characterization and treatment efficacy evaluation using non-invasive echocardiography-based electromechanical cycle length mapping: a case series

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Background Atrial fibrillation (AF) is a prevalent cardiac condition characterized by irregular heart rhythm. Conventional non-invasive diagnostic techniques, while useful, have limitations in providing comprehensive information for treatment planning. To address this gap, electromechanical cycle length mapping (ECLM), a non-invasive echocardiography-based technique, has emerged as a promising approach. Electromechanical cycle length mapping offers quantitative and spatially specific insights into atrial electromechanical activation rate mapping, thereby enhancing our understanding of arrhythmia disease progression in AF patients.

Case summary In this case series, we present two patient cases demonstrating the potential utility of ECLM in monitoring and evaluating treatment responses in atrial arrhythmia. The 1st case involved a 61-year-old male with persistent AF who underwent multiple procedures, including direct current cardioversion (DCCV) and radiofrequency ablation. Over three different DCCV encounters, pre- and post-procedure ECLM scans were performed, and the results showed the localization and incomplete elimination of arrhythmic triggers post-DCCV, which were used as early indicators of AF recurrence. The 2nd case involved a 71-year-old male with paroxysmal AF who also underwent cardioversion and ablation procedures. Electromechanical cycle length mapping imaging demonstrated a progressive reduction and elimination of arrhythmia triggers after each encounter, resulting in long-term maintenance of sinus rhythm.

Discussion The findings from this case series highlight the potential of ECLM as a non-invasive imaging tool for long-term monitoring and evaluating immediate and long-term treatment responses in AF patients. The integration of ECLM with standard echocardiograms holds promise in guiding clinical decisions and improving patient outcomes in managing atrial fibrillation.

Keywords Case report • Echocardiography • Atrial fibrillation • Cardioversion • Electromechanical activation • Atrial cycle length

ESC curriculum 2.1 Imaging modalities • 2.2 Echocardiography • 5.3 Atrial fibrillation • 5.4 Atrial flutter

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Learning points

- Electromechanical cycle length mapping (ECLM) is a novel, non-invasive bi-atrial localization imaging tool of electromechanical activation rates with echocardiography.
- Electromechanical cycle length mapping metrics can quantify the presence and variability of cardiac arrhythmic triggers.
- Longitudinal tracking of the atrial fibrillation (AF) burden presence through ECLM may inform on AF disease progression.

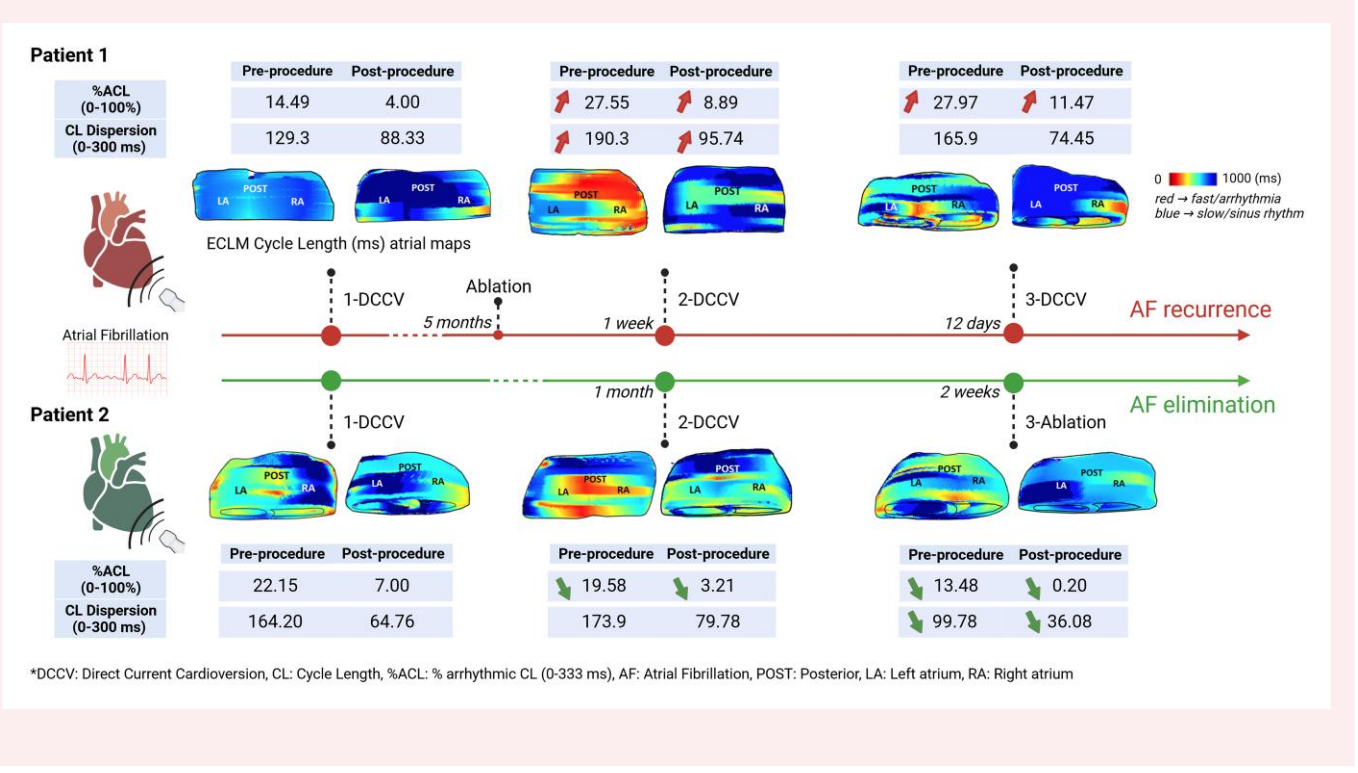
Introduction

Atrial fibrillation (AF) treatment options range from antiarrhythmic medication to cardioversion (direct current cardioversion, DCCV) and cardiac ablation procedures for rhythm control.[1,2] These solutions can be tailored to suit arrhythmia persistence and other patient characteristics. Yet, traditional non-invasive diagnostic tools such as the 12-lead electrocardiogram (EKG) lack spatial specificity and offer limited information on AF disease progression to guide treatment planning more effectively.[3,4] Intracardiac dominant frequency (DF) mapping is a technique that helps identify high-frequency sites[5] found typically near the pulmonary veins yet may be present anywhere in the atria. Localizing and eliminating these DF gradients through radiofrequency ablation may predict long-term freedom from AF.[6,7] When non-invasive treatment options are followed, alternative methods for characterizing the presence of high-frequency sites may prove effective in predicting treatment efficacy.

Electromechanical cycle length mapping (ECLM) is a non-invasive echocardiography-based technique that characterizes the electromechanical activation rates fast and accurately. Electromechanical cycle length mapping was shown capable of successfully mapping and quantifying atrial electromechanical cycle lengths (CLs) in paced canines[8] and healthy sinus rhythm (SR) subjects,[9] as well as identifying arrhythmic CLs in AF[9] and atrial flutter (AFL) subjects.[10] In AF subjects, same-day pre-DCCV ECLM metrics successfully distinguished active atrial arrhythmia and, most importantly, independently predicted 1-month AF DCCV response.[9]

In the presented cases, we report ECLM scans from two patients undergoing multiple AF treatment procedures.

Summary figure



Methods

The study was approved by Columbia University's Institutional Review Board. Atrial fibrillation diagnosis was confirmed by the attending physician for both patients. Transthoracic ECLM ultrasound scans were performed at each encounter within 1-h pre-procedure and 2-h post-procedure. Electromechanical cycle length mapping is implemented on a research ultrasound system (Verasonics Vantage, Seattle, WA) with a high–frame rate (2000 frames/s) single diverging wave acquisition. Four standard apical echocardiographic views[11,12] (4-, 2-, 3-, and 3.5-chamber, *Figure 1*, *Step 1*) are acquired. During each scan, 2 s of

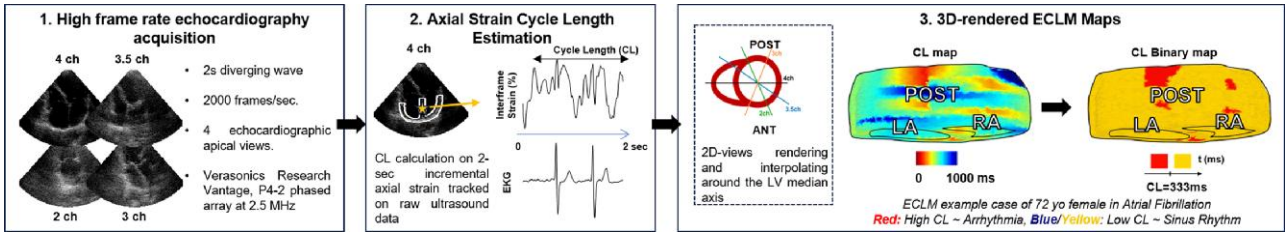


Figure 1 Electromechanical cycle length mapping pipeline steps: 1. High–frame rate ultrasound acquisition with a single diverging wave at four apical views of the heart for 2 s. 2. Axial interframe strain of the atrial myocardium is imaged over time, and a frequency analysis algorithm is applied to calculate the electromechanical activation frequency of each part of the myocardium over at least two cardiac cycles. 3. 3D-rendered electromechanical cycle length mappings generated from the co-registration of the multi–2D ultrasound views and interpolated in space visualize the electromechanical cycle lengths localized across the atrial myocardium (0–1000 ms). A threshold at cycle length = 333 ms, corresponding to an activation frequency of 3 Hz and above, is applied, and areas with arrhythmic cycle length are computed and visualized in red, while normal regions are in orange (cycle length binary map). Based on literature review, the 3 Hz threshold is selected, corresponding to the upper-bound threshold of sinus rhythm activation rates and the lower-bound threshold of atrial fibrillation activation rates.[7,13] POST, posterior wall; LA, left Atrium; RA, right atrium.

raw ultrasound data encompassing at least two complete cardiac cycles were collected. Electromechanical cycle length mapping involves tracking the axial displacement of the manually segmented atrial myocardium over time to derive the interframe axial strain of the muscle. The dominant frequency of the 2-s strain signal was calculated for each point to determine the electromechanical activation rate[8] (*Figure 1*, *Step 2*). Subsequently, 2D- and 3D-rendered atrial ECLM CL maps are generated (*Figure 1*, *Step 3*), illustrating the electromechanical activation rates found across the myocardium, with red showcasing low-CL regions (high-frequency rates of potential arrhythmic triggers) and blue areas of high CL (low-frequency rates of physiological sinus rhythm). Electromechanical cycle length mapping quantification metrics[9] may assess the arrhythmia extent by calculating (i) the percentage of atrial arrhythmic CLs (%ACL ≤ 333 ms), i.e. the proportion of the atrial myocardium that activates with CLs below 333 ms[7,13] and corresponds to potential arrhythmia triggers and (ii) the CL dispersion, i.e. the standard deviation of CLs throughout the atrial chambers.[14]

Patient 1

A 61-year-old male with a history of persistent AF and no prior ablation procedures presented in 2020 for a DCCV following a symptomatic atrial arrhythmia recurrence 2 weeks after his 1st DCCV. At that time, he was treated with therapeutic anticoagulation, flecainide 100 mg p.o. b.i.d., and metoprolol. Electromechanical cycle length mapping ultrasound data were collected pre-DCCV, with spontaneous AFL reported in the 12-lead EKG. Representative B-mode videos of the four apical views acquired are included as Supplementary material. Electromechanical cycle length mapping pre-DCCV localized an AFL CL of 194 ms in the right atrium (RA) anterior wall, with only a 2% divergence from the 12-lead EKG atrial CL of 190 ms (*Figure 2A*). Post-successful DCCV ECLM maps showed minimal remaining arrhythmia triggers in the RA free wall (4% of the atrial wall, *Figure 2B*). Electromechanical cycle length mapping CL dispersion is reduced but still displays variability across the RA (*Figure* 4A, 1-DCCV). After a week of maintaining SR, the subject experienced AF recurrence, confirmed with an at-home 1-lead personal EKG device. The patient underwent RF ablation ~5 months post-DCCV, during which right and left pulmonary vein isolation (PVI) was achieved, along with Cavotricuspid Isthmus (CTI) line ablation for CTI-dependent AFL termination (AFL CL 210 ms). The left atrium (LA) exhibited grossly normal voltage. Electromechanical cycle length mapping data were not collected during this procedure. The subject maintained SR for 1 week, after which he reverted to AF and underwent a follow-up DCCV while still on flecainide 100 mg p.o. b.i.d. and metoprolol, during which we encountered the subject for the second time. Pre-DCCV ECLM maps noted widespread and variable trigger sites throughout the atrium, with multiple CL rates present in the LA mid-wall and roof corresponding to AF, and a single AFL CL localized across the RA free wall and posterior roof, corresponding to 167.2 ms (28% of the atrial wall), a 0.4% divergence from 12-lead EKG atrial AFL CL of 168 ms (*Figure 2C*). Despite SR presence post-DCCV, ECLM maps show a high percentage of remaining arrhythmia triggers in the RA anterior wall (9% of the atrial wall; *Figures 2D*,and 4A, 2-DCCV), suggesting increased potential for atrial arrhythmia recurrence. This was confirmed as the patient reverted to AF within the first 24 h, during at-home recovery.

Our 3rd and final encounter occurred 12 days later for a follow-up DCCV of persistent AF. At that point, flecainide had been changed to propafenone 225 mg p.o. b.i.d. Pre-DCCV ECLM showcased irregular AF triggers spread across the entire atrial myocardium (*Figure 2E*), while the AFL rates were no longer present, aligning with the clinical diagnosis from the 12-lead EKG. Post-DCCV, ECLM maps showcased a reduced yet significant percentage of remaining arrhythmia triggers primarily in the RA free wall (11% of the atrial myocardium), with a relatively reduced yet present CL variability in the RA anterior base (*Figures 2F* and, 4A, 3-DCCV). Sinus rhythm was maintained for 2 days, after which the patient was referred for a 2nd ablation procedure. The patient decided to defer future study participation. *Table 1* summarizes the measurements for ECLM %ACL and CL dispersion during each encounter.

Patient 2

Patient 2 is a 71-year-old male with a history of CAD, paroxysmal AF s/p RFA, and DCCV, who recorded AF rhythm with HR up to 135 b.p.m. In 2020, he underwent PVI and CTI ablation. Atrial fibrillation recurred, and he was treated with metoprolol for rate control and referred for DCCV in 2021 (17 months later), in which written informed consent for the ECLM study was obtained. The spontaneous rhythm was noted to be AF, and pre-DCCV ECLM results showcased extended AF arrhythmic triggers (19.58% of the atrial myocardium) mainly localized in the RA anterior wall (*Figure 3A*), the presence and variability of which were greatly reduced post-successful DCCV (*Figures 3B* and *4B*, 1-DCCV). The subject remained in SR for 1 month, after which he was brought back upon AF recurrence for a repeat DCCV during our 2nd encounter.

Table 1 Electromechanical cycle length mapping %ACL and CL dispersion values at each procedure encounter for Patients 1 and 2

	Patient 1					Patient 2
Age (years old)	61					71
Gender	Male					Male
LVEF	55–60%					60–65%
LA size	Severe LA enlargement					Moderate LA enlargement
Encounter Procedure type	**July 2020 DCCV**	**Late April 2021 DCCV**	**Early May 2021 DCCV**	**June 2021 DCCV**	**Early July 2021 DCCV**	**Late July 2021 RF ablation**
	%ACL (%)					
Pre-procedure	14.49 ± 8.23	27.55 ± 15.73	27.97 ± 25.55	22.15 ± 21.55	19.58 ± 16.94	13.48 ± 6.93
Post-procedure	4.00 ± 2.90	8.89 ± 6.31	11.47 ± 7.74	7.00 ± 6.273	3.21 ± 2.89	0.20 ± 0.39
	CL dispersion (ms)					
Pre-procedure	129.3 ± 33.01	190.3 ± 49.92	165.9 ± 74.45	164.2 ± 43.27	173.9 ± 75.61	99.78 ± 12.63
Post-procedure	88.33 ± 28.47	95.74 ± 35.46	113.9 ± 15.89	64.76 ± 15.36	79.78 ± 15.40	36.08 ± 14.67

%ACL values range from 0 to 100% and CL dispersion may vary from 0 to 250 ms.

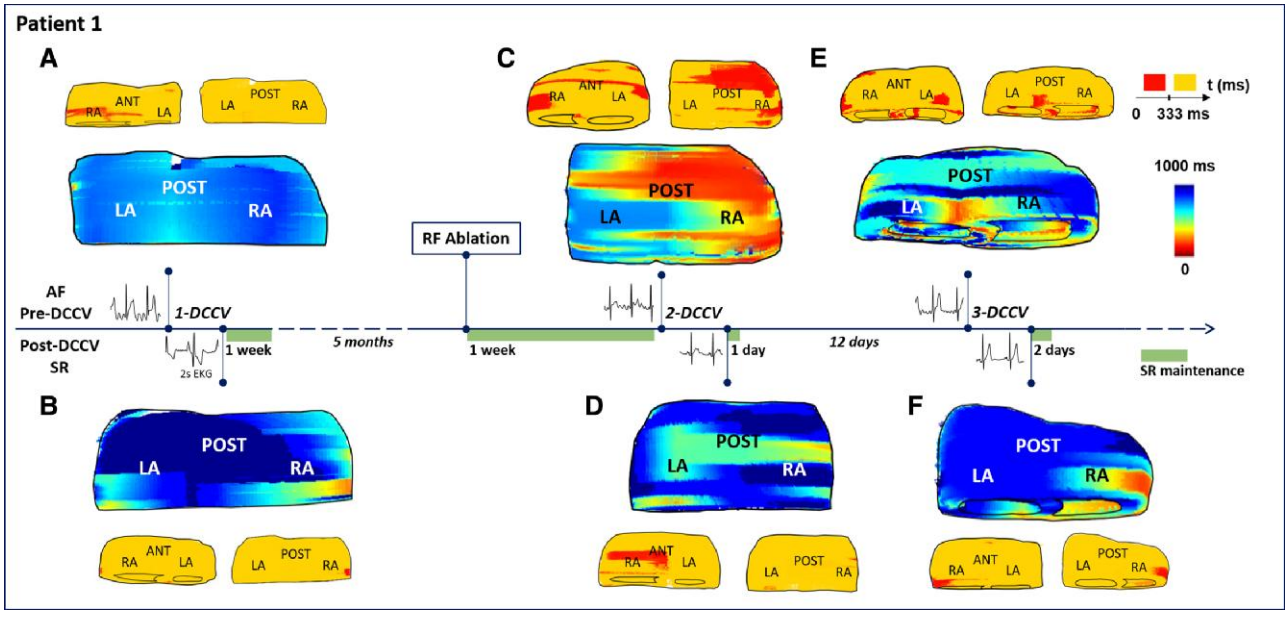


Figure 2 Case 1. 3D-rendered ECLM cycle length and binary atrial maps, collected and generated over three different encounters: 1st encounter, 1-DCCV *A*) pre- and *B*) post-DCCV; 2nd encounter, 2-DCCV *C*) pre- and *D*) post-DCCV; 3rd encounter, 3-DCCV *E*) pre- and *F*) post-DCCV. In the ECLM continuous cycle length maps, red and blue denote faster and slower activation rates (ms), respectively. In the ECLM binary maps, red connotes areas of arrhythmic CL. Ultrasound data were acquired using a Verasonics Vantage 256 ultrasound scanner. POST, posterior wall; ANT, anterior wall; LA, left atrium; RA, right atrium.

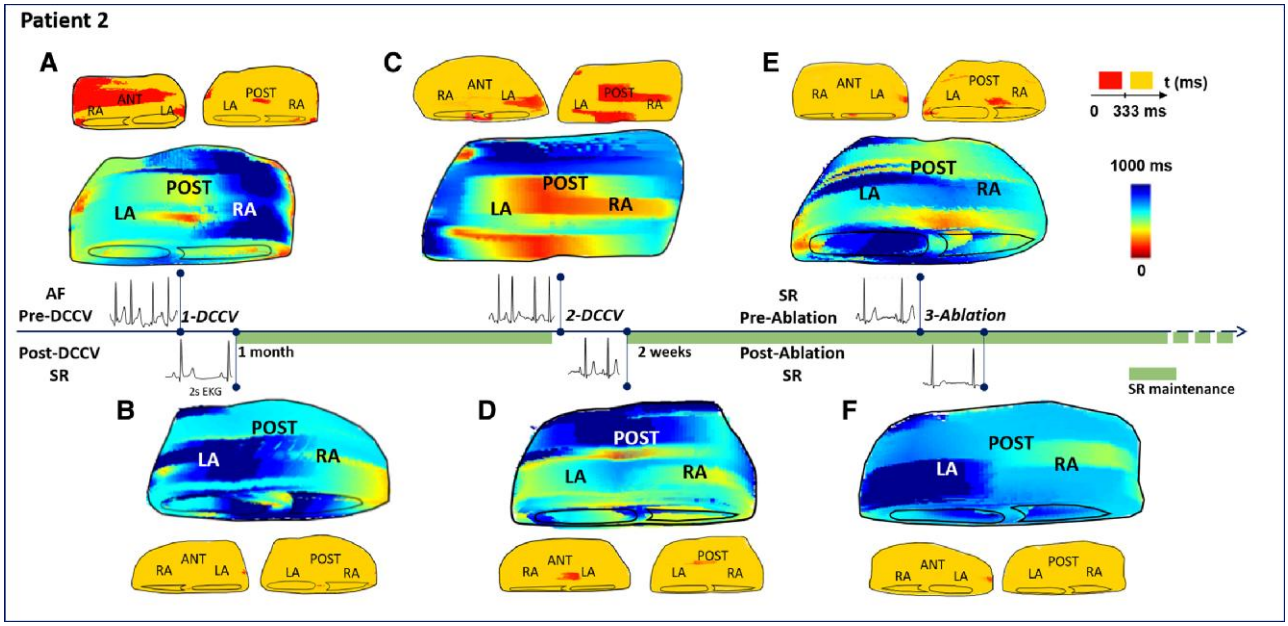


Figure 3 Case 2. 3D-rendered ECLM CL and binary maps, collected and generated over three different encounters: 1st encounter, 1-DCCV *A*) pre- and *B*) post-DCCV; 2nd encounter, 2-DCCV *C*) pre- and *D*) post-DCCV; 3rd encounter, 3-Ablation *E*) pre- and *F*) post-radiofrequency ablation. In the ECLM continuous cycle length maps, red and blue denote faster and slower activation rates (ms), respectively. In the ECLM binary maps, red connotes areas of arrhythmic CLs. Ultrasound data were acquired using a Verasonics Vantage 256 ultrasound scanner. POST, posterior wall; ANT, anterior wall; LA, left atrium; RA, right atrium.

Pre-repeat DCCV ECLM results highlighted elevated %ACL and CL dispersion values compared with post-1st DCCV values, indicating AF recurrence (*Figure 4B*, 2-DCCV). Primary ECLM arrhythmic trigger sources were localized in the posterior basal septal walls (*Figure 3C*). These triggers were eliminated post-successful DCCV (*Figure 3D*), and post-DCCV ECLM metrics were reduced (*Table 1*). However, a follow-up radiofrequency (RF) ablation was scheduled to enhance the likelihood of long-term AF termination.

The subject presented two weeks later for his 2nd AF ablation, and pre-and post-ablation ECLM data were collected. Despite maintaining SR, ECLM %ACL and CL dispersion values were found to be higher than post-repeat DCCV (*Figures* 3E and 4B, 3-Ablation, *Table 1*) and localized particularly in the LA posterior and septal walls, indicating potential arrhythmia triggers for future AF episodes. During ablation, intracardiac voltage mapping revealed an overall low voltage in the LA, particularly in the posterior wall. Entrance and exit blocks from the previous ablation were confirmed in all pulmonary veins and a CTI block. Ablation lesions were applied to the left atrial roof, connecting the right superior to the left superior pulmonary vein and mitral isthmus. These post-ablation ECLM results depict the best improvement thus far, with 0.2% remaining arrhythmic triggers and the minimum 36.08 ms CL dispersion value, corresponding to a most synchronous activation rate across the entire atrial myocardium. Notably, the patient remained in SR through 1-year of follow-up.

Discussion

The current standard technique in the clinic for arrhythmia detection remains the 12-lead EKG, which reliably detects the presence of an arrhythmia but may not capture the full complexity of the disease. In addition, although echocardiography is the go-to modality for fast, bedside cardiac imaging, it often fails to inform on the cardiac conduction abnormalities and is currently underutilized by electrophysiologists for arrhythmia characterization.[15] Echocardiography-based ECLM provides quantitative, otherwise unavailable, information on electromechanical mapping that maps the location and extent of potential arrhythmia triggers in 2D and pseudo-3D. The clinical cases presented herein highlight the potential utility of long-term ECLM echocardiography imaging in monitoring the evolution of atrial arrhythmia.

In the first case study, the ECLM echocardiography exam was capable of distinguishing between AFL and AF, localizing AFL triggers in the RA, tracking the elimination of AFL after two DCCVs and one AF/AFL ablation procedure, and mapping the emergence of erratic AF triggers during the 3rd encounter. The progressive severity of the arrhythmia is evident, with increasing ECLM %ACL and CL dispersion values over time, pre- and post-DCCV, along with progressively shorter AF recurrence times. The 2nd patient presented with recurring AF and underwent two cardioversions and one follow-up ablation. The subject received 10-min ECLM scans, before and after each procedure at bedside. Notably, ECLM mapping demonstrated a consistent improvement in the distribution and amplitude of AF signals over time, ultimately resulting in the complete elimination of AF and no recurrence during the 1-year follow-up.

In both cases, conventional echocardiography views- bedside ECLM provided quantitative maps and thus informed on the effectiveness of the applied treatment, mapping arrhythmia trigger sites and their possible prognostic value with regard to the future recurrence of AF. By comparing imaging results at different time points, ECLM can visualize and quantify intra-subject atrial arrhythmic presence, introducing disease classification stages, and providing valuable insights into disease progression and treatment efficacy. More

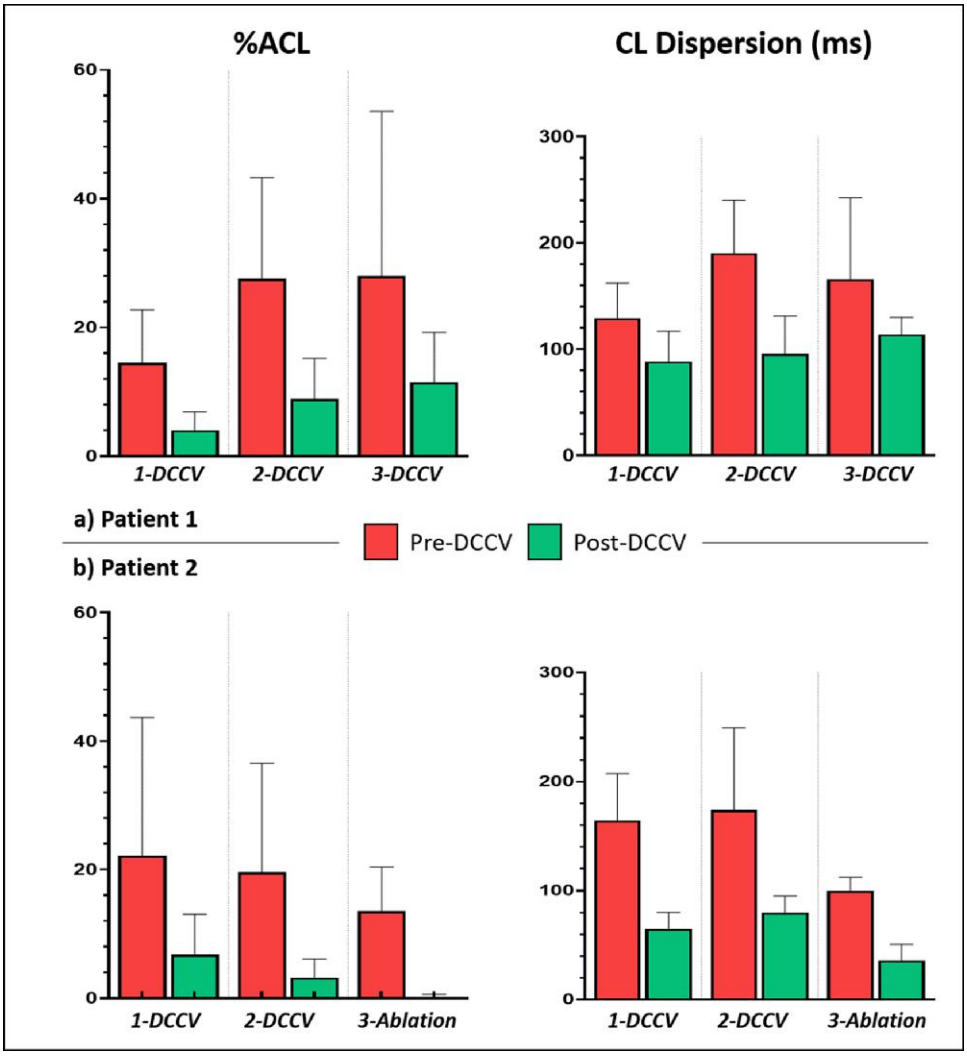


Figure 4 Electromechanical cycle length mapping evaluation metrics. Percentage of atrial myocardium with activation rate within the arrhythmic range (%ACL or %CL ≤ 333 ms) and CL dispersion for *A*) Patient 1 and *B*) Patient 2 at each encounter. Each data point corresponds to an individual view. *N* too low to perform statistical analysis.

particularly, the preliminary results of ECLM performed pre- and post-ablation during Patient 2's last encounter introduce the potential use of ECLM as an AF mapping technique complementary to the intracardiac voltage mapping performed during the procedure. As part of a future study, it is therefore interesting to investigate the correlation of low-CL areas identified in ECLM maps to endocardial low-voltage areas identified on the intracardiac electroanatomic maps and selected ablation targets. Moreover, post-ablation ECLM maps could be used to indicate areas with remaining arrhythmic triggers that were not targeted during ablation and may become sources of AF recurrence and future ablation prime targets. The predictive value of ECLM metrics in informing the potential of successful DCCV[9] is also expected to apply in informing AF ablation outcomes.

The advantage of bedside longitudinal ECLM was demonstrated in AF and AFL subjects, yet its application for fast, non-invasive visualization of various cardiac arrhythmias and electromechanical synchronization abnormalities is self-evident. Particularly in subjects receiving compulsory transoesophageal echocardiogram (TEE) pre-DCCV, TEE-integrated ECLM imaging may be implemented as part of this process, visualizing and informing on the arrhythmia extent and determining whether DCCV is the appropriate course of action or if proceeding with ablation therapy is more advisable. Implementing ECLM on clinically relevant lower framerates is imperative for its clinical integration and is currently in progress. To this purpose, our group has reported on machine learning techniques that have been shown to effectively reduce the frame rate down to clinically relevant levels of 125 frames/s.[16,17]

These findings are particularly exciting when we compare ECLM against other non-invasive arrhythmia mapping techniques, such as surface electrocardiographic imaging, for which similar metrics exhibited weak long-term AF termination prediction capabilities.[18] Electrocardiographic imaging relies on pre-existing non-contrast computed tomography scans, not allowing for fast, point-of-care diagnosis. In contrast, transmural ECLM results can be generated within a 5–10-min apical echocardiography exam, followed by ∼10 min of operator-independent processing. Therefore, all scans were performed during each subject's procedure preparation or recovery idle time with

a portable ultrasound system with attached post-processing hardware, causing no disturbance of the clinical schedule flow. The non-ionizing and clinically ubiquitous cardiac ultrasound technology renders it a well-suited platform for integrating the ECLM algorithm that clinicians may frequently use to provide a visual insight into the cardiac rhythm, currently available with intracardiac electroanatomic mapping.

Some limitations include the need for larger patient populations and longer follow-ups. In addition, the possible confounding effects of membrane-stabilizing antiarrhythmic medications need to be explored further. Nevertheless, ECLM represents a promising approach to enhance our understanding of the complex AF pathophysiology and optimize treatment strategies. Future research is expected to establish the optimal use of ECLM in clinical practice as a fast, non-invasive, non-ionizing imaging tool integrated with standard echocardiograms for accurate AF mapping, disease staging, and assessment of treatment, response, and prediction.

Conclusion

This case study highlights the benefits of longitudinal ECLM quantitative imaging for monitoring atrial arrhythmia progress in determining immediate and long-term treatment responses. Electromechanical cycle length mapping's capability to quantify the presence of arrhythmia and capture longitudinal changes render it a valuable tool in evaluating treatment response and guiding clinical decisions with a simple, non-invasive echocardiography-based technique.

Lead author biography

Melina was born in Athens, Greece. She holds an integrated bachelor's and master's diploma in electrical and computer engineering from the National Technical University of Athens, Greece, with a major in computer science. She is currently a PhD candidate in biomedical engineering at Columbia University and part of the Ultrasound and Elasticity Imaging Laboratory (UEIL). Her research interests include the development of non-invasive ultrasound imaging techniques for the electrical and mechanical activation mapping of the heart and further development of electromechanical wave imaging for improved arrhythmia characterization and clinical diagnosis.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

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Consent: The authors confirm that written consent for the submission and publication of this case report, including images and associated text, has been obtained from the patient in line with the COPE guidelines.

Conflict of interest: Dr Angelo Biviano is a Medical Advisory Board Member of Boston Scientific and GE Healthcare. The other authors had no conflicts of interest.

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Data availability

The data underlying this article will be shared upon reasonable request to the corresponding author.

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