# ORIGINAL ARTICLE

# Left atrial functional changes associated with repeated

catheter ablations for atrial fibrillation

Revised: 10 October 2024

Ravi Ranjan MD, PhD<sup>1,2,3</sup> 💿

Jiawei Dong MS<sup>1,2,3</sup> | Eugene Kwan MS<sup>1,2,3</sup> | Jake A. Bergquist PhD<sup>1,2,4</sup> | Derek J. Dosdall PhD<sup>1,2,5</sup> | Edward V. DiBella PhD<sup>6</sup> | Rob S. MacLeod PhD<sup>1,2,4</sup> Gregory J. Stoddard MBA, MPH<sup>7</sup> Klitos Konstantidinis MD<sup>3</sup> | Benjamin A. Steinberg MD<sup>3</sup> | T. Jared Bunch MD<sup>3</sup> |

<sup>1</sup>Department of Biomedical Engineering, University of Utah, Salt Lake City, Utah, USA

<sup>2</sup>Nora Eccles Harrison Cardiovascular Research and Training Institute, University of Utah, Salt Lake City, Utah, USA

<sup>3</sup>Department of Internal Medicine, Division of Cardiovascular Medicine, University of Utah, Salt Lake City, Utah, USA

<sup>4</sup>Scientific Computing and Imaging Institute, University of Utah, Salt Lake City, Utah, USA

<sup>5</sup>Department of Surgery, Division of Cardiothoracic Surgery, University of Utah, Salt Lake City, Utah, USA

<sup>6</sup>Radiology and Imaging Sciences, University of Utah, Salt Lake City, Utah, USA

<sup>7</sup>Department of Internal Medicine, Division of Epidemiology, University of Utah, Salt Lake City, Utah, USA

#### Correspondence

Ravi Ranjan, MD, PhD, Cardiovascular Medicine, University of Utah, Salt Lake City, UT. USA. Email: ravi.ranjan@hsc.utah.edu

Disclosures: Ravi Ranjan is supported by NIH R01 grant HL142913. He is a consultant to Abbott and has a research grant from Biosense Webster. Jake A. Bergquist is supported by NIH/HNLBI T32HL00757. Benjamin Steinberg is supported by NIH/NHLBI K23HL143156. Other authors: No disclosures.

#### Funding information

Nora Eccles Treadwell Foundation

## Abstract

Introduction: The impact of repeated atrial fibrillation (AF) ablations on left atrial (LA) mechanical function remains uncertain, with limited long-term follow-up data. Methods: This retrospective study involved 108 AF patients who underwent two catheter ablations with cardiac magnetic resonance imaging (MRI) done before and 3 months after each of the ablations from 2010 to 2021. The rate of change in peak longitudinal atrial strain (PLAS) assessed LA function. Additionally, a sub-study of 36 patients who underwent an extra MRI before the second ablation, gave us an additional time segment to evaluate the basis of change in PLAS.

Results: In the two-ablation, three MRI sub-study 1, the PLAS percent change rate was similar before and after the first ablation ( $r_{11} = -0.9 \pm 3.1\%$ /year, p = 0.771). However, the strain change rate from postablation 1 to postablation 2 was significantly worse ( $r_{12} = -23.7 \pm 4.8\%$ /year, p < 0.001). In the sub-study 2 with four MRIs, all three rates were negative, with reductions from postablation 1 to pre-ablation 2  $(r_{22} = -13.3 \pm 2.6\%/\text{year}, p < 0.001)$  and from pre-ablation 2 to postablation 2  $(r_{23} = -8.9 \pm 3.9\%/\text{year}, p = 0.028)$  being significant.

**Conclusion:** The present study suggests that the more ablations performed, the more significant the decrease in the postablation mechanical function of the LA. The natural progression of AF (strain change from postablation 1 to pre-ablation 2) had a greater negative influence on LA mechanical function compared to the second ablation itself suggesting that second ablation in patients with recurrence after first ablation is an effective strategy even from the LA mechanical function aspect.

#### KEYWORDS

AF progression, atrial fibrillation, LA function, MRI, repeated ablations, strain

\_\_\_\_\_ This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. © 2024 The Author(s). Journal of Cardiovascular Electrophysiology published by Wiley Periodicals LLC.



# 1 | INTRODUCTION

Catheter ablation, a key intervention for atrial fibrillation (AF), aims to restore sinus rhythm by isolating the pulmonary veins and creating scar tissue to disrupt the abnormal electrical pathways responsible for arrhythmias.<sup>1</sup> While effective, this procedure can inadvertently impact normal cardiac electrical signaling and left atrial (LA) conduit and contractile function due to scar tissue formation and fibrosis.<sup>2</sup> An immediate consequence of catheter ablation is a temporary reduction in LA function, typically followed by a period of restoration.<sup>3</sup> However, the cumulative effects of repeated ablations and the resulting scar formation on LA mechanical function are not well-understood. Research indicates that scar tissue and fibrosis postablation can significantly impair LA function and reduce its contractile capacity.4,5 Given the prevalence of AF recurrence, especially in persistent AF cases, repeated ablations are often necessary to improve outcomes.<sup>6</sup> Despite restoring sinus rhythm, the creation of extensive scar tissue in the LA wall through multiple ablations has shown an inverse relationship with LA function.<sup>5,7</sup>

The natural history of AF can simultaneously negatively impact LA function with intrinsic scar and fibrosis formation over time that is both dependent and independent of treatment approach. For example, over time, a gradual shift from paroxysmal to chronic AF is observed in more than 50% of patients with high HATCH scores (hypertension, age > 75 years, transient ischemic attack or stroke, chronic obstructive pulmonary disorder, heart failure), within a decade of diagnosis.<sup>8–10</sup> Additional factors such as obesity and metabolic syndrome further contribute to the progression of AF.<sup>11–13</sup> As ablation adds "therapeutic" scar to the left atrium, this scar can be a positive if it offsets and is less than the scar related to the natural history of AF and exposure of the atrium to AF.

This study investigates the interplay between disease progression and the effects of catheter ablation on atrial mechanical performance. Cardiac magnetic resonance imaging (MRI) is employed here as a robust tool for evaluating LA volume and function.<sup>14</sup> Notably, feature-tracking MRI has proven effective in assessing peak longitudinal atrial strain (PLAS), a vital measure of atrial mechanical performance.<sup>15,16</sup> This study aims to monitor changes in LA function using PLAS analysis in MRI examinations conducted before and after AF ablation procedures. We hypothesize that an increase in number of ablation procedure correlates with a decline in LA mechanical performance. Additionally, this research seeks to compare the impact of catheter ablation with the natural progression of AF, examining patient cases spanning nearly a decade postdiagnosis.

# 2 | METHODS

The study was conducted at the University of Utah Hospital and involved a retrospective analysis of patients who underwent multiple catheter ablations for AF between 2010 and 2021. By analyzing MRI data from the University of Utah database, the

study aims to elucidate the long-term outcomes of repeated catheter ablations and their progression in AF management. Inclusion criteria were as follows: patients needed to be diagnosed with AF; have undergone two catheter ablations for AF; possess cine MRI studies conducted during sinus rhythm at least 1-month postablation; and have at least one MRI before any ablation, one after each ablation, and in certain instances, an additional MRI before the second ablation. Patients who met these criteria were excluded if they had undergone cryo-ablation, had atrial thrombosis, or had a prosthetic valve replacement. These criteria aimed to ensure a homogeneous and specific patient population for the study. Each patient's medical notes were checked for cardioversion records, and MRI studies done within 4 weeks after cardioversion were not included, as suggested by the guideline.<sup>17</sup> The ablation day was defined as day zero and time interval to MRI was measured from that reference. The University of Utah Institutional Review Board (IRB) approved this study.

## 2.1 | Study population

Figure 1 illustrates the study design and the process of selecting patients. Initially, from a cohort of 1548 patients, 360 were identified who had undergone two or more catheter ablations. Of these, an additional 252 did not meet the inclusion or exclusion criteria, and 29 patients were excluded due to undergoing a cryo-ablation procedure. The study ultimately included 108 patients who underwent two catheter ablations and had between three and four MRI scans.

When comparing the selected and nonselected patients, significant differences were found only in the type of AF. In the study cohort, 81 out of 108 patients had paroxysmal AF, while in the excluded group, 142 out of 252 patients had paroxysmal AF. No significant differences were observed in the other demographic variables shown in Table 1.

Table 1 details the demographic data for the included 108 patients. In sub-study 1, each patient had one MRI before and one after each ablation, totaling three MRIs. This part of the study was segmented into two phases (assess the incremental impact of the first and second ablation independently on left atrial function): the first phase between the first and second MRI (from PRE1 to POST1), and the second phase between the second and third MRI (from PRE2 to POST2, Figure 1). We calculated the percentage change in strain and rate of change during each phase, denoted as  $r_{11}$  for the first ablation and  $r_{12}$  for the second ablation.

Next, we sought to also study the impact of the natural history of AF on the ablated substrate of the LA. Sub-study 2 focused on the 36 patients who underwent an additional MRI between their two ablations. This further examination into LA mechanical function entailed assessing the strain changes between the two ablations using four MRIs. This sub-study was divided into three temporal segments, with rate of change calculations for each:  $r_{21}$  and  $r_{23}$  for the changes around the ablations, and  $r_{22}$  for the inter-ablation period without any catheter ablations (from POST1 to PRE2, Figure 1).

3



**FIGURE 1** Flow chart describing study design and patient selection process. One group of patients with two ablations and three MRIs (*n* = 108) and a group of patients (*n* = 36) in the cohort had one additional MRI before the second ablation. MRI, magnetic resonance imaging.

**TABLE 1** Patient characteristics of the cohort (*n* = 108).

| Male                                   | 72 (66.7%)  |
|--|-------------|
| Female                                 | 36 (33.3%)  |
| Age (Years)                            | 64.3 ± 10.3 |
| Left ventricular ejection fraction (%) | 57.0 ± 11.2 |
| Body mass index (kg/m²)                | 31.0 ± 6.7  |
| Paroxysmal AF                          | 81 (75.0%)  |
| Persistent AF                          | 27 (25.0%)  |
| Hypertension (%)                       | 68.5        |
| Diabetes mellitus (%)                  | 27.8        |
| Obstructive sleep apnea (%)            | 44.4        |
| Coronary artery disease (%)            | 26.9        |
| Congestive heart failure (%)           | 40.7        |
| Cerebrovascular accident (%)           | 11.1        |

*Note.* Values are given as a count (%) or mean ± SD. Abbreviation: AF, Atrial Fibrillation.

#### 2.2 | Cardiac MRI

The study employed a standardized cardiac cine MRI protocol in patients with sinus rhythm, as described before.<sup>18</sup> Utilizing 3-Tesla MR imaging units, long-axis 2-chamber views were acquired with ECG-gated steady-state free precession (SSFP) sequences. Imaging parameters included a 260 by 192 matrix, a repetition time (TR) of 3.7 ms, an echo time (TE) of 1.5 ms, a flip angle of 50 degrees, a pixel size of 1.48 mm, 8 mm slice thickness, and 12 views per segment. Temporal resolution varied (20–30 ms). Diastolic LA phase views were obtained. Standardization ensured consistent evaluation of cardiac parameters across participants.

#### 2.3 | Feature tracking strain analysis

The study employed magnetic resonance feature tracking (MRFT) to quantitatively evaluate myocardial motion and deformation, encompassing strain, strain rate, torsion, and dyssynchrony.<sup>19,20</sup>

-WILEY

We utilized the Ncorr algorithm, a 2D digital image correlation method developed by Blaber et al., known for its flexibility and high quality, adapted specifically for MR cine images.<sup>15</sup> The investigation focused on the left atrium, where a region of interest (ROI) larger than the targeted area was drawn on the reference image and applied to all frames across the cardiac cycle. The longitudinal direction was defined from the left ventricular apex to the mid-mitral valve, with a longitudinal axis drawn in a 2-chamber view. Eight evenly distributed points of interest (POI) along the LA wall's middle line were tracked for myocardial strain curves throughout the cardiac cycle. The resulting average global longitudinal strain curve offered a comprehensive overview, and the peak of the mean global longitudinal strain was reported as a crucial metric, providing insights into myocardial performance during the cardiac cycle. This approach allowed for a detailed and dynamic assessment of cardiac function.

Each sub-study had *n* number of MRI studies, and as a result, the time can be divided into (n-1) temporal segments as shown in Figure 1. For the *i*th segment (*i* = 1, 2,..., *n*-1), we defined the percent change of strain according to Equation 1 and Equation 2.

$$\Delta \varepsilon_i = \frac{\varepsilon_{i+1} - \varepsilon_i}{\varepsilon_i} \times 100\%$$
 (1)

$$r_{ji} = \frac{\Delta \varepsilon_{ji}}{t_{ji}}$$
(2)

Where *j* represents sub-study number (*j* = 1, 2),  $\Delta \varepsilon_i$  was the percent change of strain from the *ith* to the (*i* + 1)*th* MRI study,  $\varepsilon_i$  was the PLAS measurement in the *ith* MRI study,  $t_i$  was the time from the *ith* to the (*i* + 1)*th* MRI study in years, and  $r_{ji}$  was the rate of change in percent per year for sub-study *j*.

#### 2.4 Statistical analysis

When describing the sample, continuous variables, including MRI study days, age, and time intervals, were reported as mean ± standard deviation (SD). When describing outcomes, including the parameter PLAS, continuous variables were presented as mean ± standard error (SE). Categorical variables, such as the presence of paroxysmal AF in patients, were expressed as percentages. Pairwise comparisons of the rates of change in strain were performed using paired t-tests. A one-sample t-test was employed to assess the significance of changes in strain rates. Statistical significance was set at a p-value of less than 0.05. We evaluated differences in LA strain before and after the two catheter ablations, as well as between the first and second ablations. Strain changes can be influenced by individual factors like age, gender, and underlying substrate. To account for this variability, we used a simple linear model to capture strain changes over time, avoiding unnecessary assumptions that could complicate the analysis. All statistical analyses were conducted using the RStudio statistics package, version 4.3.1.<sup>21</sup>

# 3 | RESULTS

# 3.1 | Effects of multiple ablations on LA function

Sub-study 1 included 108 patients with AF who underwent two catheter ablations. Each patient underwent an MRI before and after the first ablation and another MRI following the second ablation, resulting in three MRIs for each patient in this sub-study. At the time of the initial MRI (PRE1), the mean age of the patients was  $64.3 \pm 10.3$  years.

Patients underwent two catheter ablations for AF using varying lesion sets. Data on lesion sets were collected for all patients who received ablation since 2010. In the first ablation, 13 patients (12.0%) received a cavo-tricuspid isthmus (CTI) line, 39 patients (36.1%) had only pulmonary vein isolation (PVI), and 69 patients (63.9%) underwent PVI with additional lines (PVI-plus), including an LA roof line (43.5%), fibrosis homogenization (79.7%), posterior wall isolation (2.9%), and other lesion sets. During the second ablation, 51 patients (47.2%) received a CTI line, 8 patients (7.4%) underwent only PVI, and 100 patients (92.6%) had PVI with additional lines, including an LA roof line (63.0%), fibrosis homogenization (65.0%), posterior wall isolation (15.0%), and other lesion sets.

For PVI-only and PVI-plus comparison during the first ablation, we compared their PLAS in POST1: PVI-only (39 patients) versus PVIplus (69 patients), and there was no significant difference in PLAS between PVI-only and PVI-plus in the POST1 ( $15.6 \pm 3.3\%$  vs  $16.2 \pm 3.9\%$ , p = 0.355). For PVI-only and PVI-plus comparison during the second ablation, we compared their PLAS in POST2: PVI-only (eight patients) versus PVI-plus (100 patients), and there was a significant difference between PVI-only and PVI-plus in the PLAS ( $15.5 \pm 3.5\%$  vs  $13.1 \pm 3.1\%$ , p = 0.044). PVI plus strategies resulted in lower PLAS and the difference was statistically significant.

In our database, we reviewed the usage of antiarrhythmic medications at the time of these MRIs. The antiarrhythmics included amiodarone, sotalol, tikosyn, flecainide, and propafenone. In the entire cohort (n = 108), the percentages of patients on antiarrhythmics were 20.4% at PRE1, 39.8% at POST1, and 47.2% at POST2. There have been no reports indicating that antiarrhythmics impact left atrial strain.

The LA strain was analyzed using feature tracking strain measurements from each MRI study. The LA strain results are depicted in Figure 2. The mean and SE of the rates of change in strain are summarized in Table 2. Both rates demonstrated a negative mean, indicating a reduction in LA strain, with  $r_{12}$  showing a larger absolute reduction than  $r_{11}$  ( $|r_{11}| < |r_{12}|$ ).

A one-sample t-test was applied to each rate of change, revealing significant differences for  $r_{12}$  (-23.7 ± 4.8%/year, p < 0.001), as indicated in Table 3. This result suggests a significant decrease in LA function after the second ablation. In contrast, the rate change around the first ablation was not significant ( $r_{11} = -0.9 \pm 3.1\%$ /year, p = 0.771), indicating that the first ablation did not significantly alter LA function. Additionally, a paired *t*-test confirmed a significant



**FIGURE 2** The strain of AF patients (*n* = 108) with two catheter ablations with one MRI before all and one MRI after each ablation. Error bars represent standard error (SE).AF, Atrial Fibrillation; MRI, magnetic resonance imaging.

**TABLE 2** Description of the rate of strain change (%/year) in patients with two catheter ablations and three MRIs.

|                                     | r <sub>11</sub> | r <sub>12</sub> |
|-------------------------------------|-----------------|-----------------|
| Mean                                | -0.9            | -23.7           |
| SE                                  | 3.1             | 4.8             |
| Time interval, mean $\pm$ SD, years | $0.4 \pm 0.1$   | $1.8 \pm 1.7$   |
|                                     |                 |                 |

Note. rate r<sub>1i</sub> = rate of change per year, i = 1, 2

Abbreviations: MRI, magnetic resonance imaging; SD, standard deviation; SE, standard error.

**TABLE 3** Statistical tests of the rate of change (%/year) in patients with two ablations and three MRI studies.

| No. | Test                      | Study Question   | Comparison                             | P-value |
|-----|---------------------------|------------------|--|---------|
| 1   | One sample <i>t</i> -test | Did change occur | $r_{11} = 0$                           | 0.771   |
| 2   | One sample <i>t</i> -test | Did change occur | $r_{12} = 0$                           | <0.001  |
| 3   | Paired t-test             | Did rates differ | r <sub>11</sub> versus r <sub>12</sub> | <0.001  |

Abbreviation: MRI, magnetic resonance imaging.

difference between the two rates of change ( $-0.9 \pm 3.1\%$ /year vs.  $-23.7 \pm 4.8\%$ /year, *p* < 0.001).

# 3.2 | Strain assessment between two sequential ablations with four MRIs

In sub-study 2, we evaluated 36 AF patients (23 male, 13 female) who underwent two catheter ablations. Each patient received four MRIs: one before and after each ablation. This sub-study aimed to determine whether changes in LA strain post-ablations were attributable 5

to disease progression or the effects of the repeat ablations. At the initial pre-ablation MRI (PRE1), the mean age was  $63.8 \pm 9.0$  years.

Patients underwent two catheter ablations for AF using varying lesion sets. Data on lesion sets were collected for all patients who received ablation since 2010. In the first ablation, five patients (13.9%) received a CTI line, nine patients (25.0%) had only PVI, and 27 patients (75.0%) underwent PVI with additional lines (PVI-plus), including an LA roof line (37.0%), fibrosis homogenization (96.3%), posterior wall isolation (0.0%), and other lesion sets. During the second ablation, 18 patients (50.0%) received a CTI line, two patients (5.6%) underwent PVI-only, and 34 patients (94.4%) had PVI-plus with additional lines, including an LA roof line (70.6%), fibrosis homogenization (20.6%), and other lesion sets.

For PVI-only and PVI-plus comparison during the first ablation, we compared their PLAS in POST1: PVI-only (9 patients) versus PVI-plus (27 patients). In POST1, there was no significant difference between PVI-only and PVI-plus in the PLAS ( $15.8 \pm 4.2\%$  vs  $14.6 \pm 3.0\%$ , p = 0.367). For PVI-only and PVI-plus comparison during the second ablation, we compared their PLAS in POST2: PVI-only (two patients) versus PVI-plus (33 patients), and there was no significant difference in PLAS between PVI-only and PVI-plus ( $14.3 \pm 5.2\%$  vs  $12.4 \pm 2.6\%$ , p = 0.339).

The LA strain assessments from these four MRIs are compared in Figure 3. This set of data serves as the best available approximation of the natural disease progression, representing the closest analogue to data that would have been collected from an untreated control group, had it been ethical to do so. The rates of change are summarized in Table 4, where all three have negative mean values, indicating reductions in LA strain. The magnitudes of these average rates are ordered as follows:  $|r_{21}| < |r_{23}| < |r_{22}|$ .

One-sample t-tests were conducted for each rate of change, showing significant reductions in LA strain for  $r_{22}$  (-13.3 ± 2.6%/year, p < 0.001) and  $r_{23}$  (-8.9 ± 3.9%/year, p = 0.028), as detailed in Table 5. The rate of change associated with the first ablation (-2.5 ± 2.6%/ year, p = 0.349) was not significant, suggesting no substantial change in LA function post-first ablation or possibly a deceleration in the disease progression. However, the lack of statistical significance does not necessarily imply no change.

Furthermore, a paired t-test comparing the rates of change between  $r_{21}$  (-2.5 ± 2.6%/year) and  $r_{22}$  (-13.3 ± 2.6%/year) demonstrated a significant difference (p = 0.008). Although  $r_{23}$  is more than three times larger in magnitude than  $r_{21}$ , there is no statistical difference between them (-8.9 ± 3.9%/year vs. -2.5 ± 2.6%/year, p = 0.248).

# 4 | DISCUSSION

This study explored the impact of repeated catheter ablations on the LA mechanical function in patients with atrial fibrillation. Our key findings include: (1) The first ablation did not significantly alter the PLAS compared to pre-ablation levels. (2) There was a



**FIGURE 3** Mean strain (%) of AF patients measured in four MRI studies (same *n* = 36 at each time point). Error bars represent standard error (SE).AF, Atrial Fibrillation; MRI, magnetic resonance imaging.

**TABLE 4** Description of the rate of change (%/year) in patients with two catheter ablations and four MRIs.

|                                     | r <sub>21</sub> | r <sub>22</sub> | r <sub>23</sub> |
|-------------------------------------|-----------------|-----------------|-----------------|
| Mean                                | -2.5            | -13.3           | -8.9            |
| SE                                  | 2.6             | 2.6             | 3.9             |
| Time interval, mean $\pm$ SD, years | $0.4 \pm 0.2$   | 2.0 ± 1.7       | 0.6 ± 0.3       |

Note: r<sub>2i</sub> = rate of change per year, i = 1, 2, 3

Abbreviations: MRI, magnetic resonance imaging; SD, standard deviation; SE, standard error.

**TABLE 5** Statistical tests of the rate of change (%/year) in patients with two ablations and four MRIs (n = 36).

| No. | Test                      | Study Question   | Comparison                             | P-value |
|-----|---------------------------|------------------|--|---------|
| 1   | One sample <i>t</i> -test | Did change occur | $r_{21} = 0$                           | 0.349   |
| 2   | One sample <i>t</i> -test | Did change occur | $r_{22} = 0$                           | < 0.001 |
| 3   | One sample <i>t</i> -test | Did change occur | $r_{23} = 0$                           | 0.028   |
| 4   | Paired <i>t</i> -test     | Did rates differ | r <sub>21</sub> versus r <sub>22</sub> | 0.008   |
| 5   | Paired <i>t</i> -test     | Did rates differ | r <sub>21</sub> versus r <sub>23</sub> | 0.248   |
| 6   | Paired <i>t</i> -test     | Did rates differ | r <sub>22</sub> versus r <sub>23</sub> | 0.407   |

Abbreviation: MRI, magnetic resonance imaging.

noticeable decline in PLAS between the first and second ablations. (3) The rate of strain reduction was mitigated by the second ablation. In our first sub-study, which included 108 patients (66.7% male) undergoing a two-ablation, three-MRI sequence, we observed no significant change in PLAS after the first ablation. However, the rate of strain reduction accelerated significantly after the first ablation and continued to decrease after the second, suggesting a progressive impairment of LA mechanical function. In the second ablation procedure compared to the first, the number of patients with a CTI line increased from 13 to 51. Conversely, the number of patients undergoing PVI-only decreased from 39 to 8, while those requiring PVI-plus procedures rose from 69 to 100. This implies that there was an increase in the number of patients treated with a more comprehensive approach, requiring additional ablations beyond just the pulmonary veins.

Following ablation, some patients may continue to experience symptoms due to persistent poor left atrial mechanical function, which can pose significant clinical challenges. Common symptoms include palpitations, fatigue, and dyspnea, which may indicate incomplete restoration of atrial function or recurrent arrhythmias. Complications arising from this unresolved condition can be substantial, ranging from thromboembolic events due to atrial stasis to heart failure exacerbations driven by ineffective atrial contraction. Such outcomes necessitate careful post-procedural monitoring and may require additional interventions to manage the ongoing risk factors and symptoms. Addressing these complications promptly is crucial, as they carry significant implications for long-term patient outcomes and quality of life. This highlights the importance of a thorough evaluation of atrial mechanical function and patient symptoms during follow-up visits, ensuring that any residual effects of the ablation are adequately managed.

As the number of ablations increased, the rate of change in LA strain became more pronounced and predominantly negative. This may reflect a worsening in LA contractility or diminishing returns from subsequent ablations. Although catheter ablation can initially restore sinus rhythm and prevent further LA functional deterioration, repeated ablations may adversely affect LA contractility. It is crucial to weigh the potential benefits of multiple ablations against their possible negative impacts on atrial strain.

The progressive decline in LA mechanical function observed during long-term follow-up could be due to both the natural progression of atrial fibrillation and adverse effects from catheter-induced tissue scarring. Prolonged atrial fibrillation is known to cause progressive atrial dilation and functional impairments, including reduced atrial compliance and contractility.<sup>5</sup>

Tops et al. and Habibi et al. both examined the change in strain from pre-ablation to shortly after the ablation and followed up at 1 to 1.5 years postablation.<sup>7,22</sup> Tops et al. assessed the predictive value of pre-ablation baseline strain in predicting AF recurrence.<sup>22</sup> Habibi et al. revealed an acute reduction in LA function after ablation and an inverse correlation between LA Late Gadolinium Enhancement (LGE) and LA function.<sup>7</sup> Habibi et al. also reported that the long-term changes of LA function were associated positively with sinus rhythm restoration and inversely with increased LA LGE.<sup>23</sup> In our study, all patients underwent two catheter ablations for AF, with three MRIs, and some had four MRIs. We found that LA strain did not change significantly after the first ablation compared to the pre-ablation baseline, and the second ablation was effective in slowing the reduction of LA strain form AF itself.

Sub-study 2 focused on a subset of 36 patients (63.9% male), analyzing the pre- and post- ablation PLAS across two ablations. We found that while the first ablation did not significantly impact LA function, the second ablation, resulted in a larger reduction in strain but that reduction was still lower than the reduction in LA strain from AF disease progression.

Like sub-study 1, in the second ablation procedure relative to the first, there was an increase in patients receiving a CTI line, from 5 to 18, indicating more treatments for atrial flutter. Meanwhile, the number of patients undergoing PVI-only decreased from 9 to 2. Additionally, those needing PVI-plus procedures, which involve more extensive ablations beyond just the pulmonary veins, rose from 27 to 34. This suggests a shift towards more comprehensive treatment strategies for individuals with complex or persistent AF.

Based on our data, we show for the first time that the rate of PLAS declines due to the disease itself  $(r_{22})$  is much more detrimental than the effect of the second ablation ( $r_{23}$ ) on PLAS. So, if patient continues to have AF after the first ablation, the second ablations seem to be an effective strategy to pursue without worrying about the additional scarring from ablation and its effect of lowering the PLAS. It is important to note that the absence of statistical significance does not imply no change, this may be a power issue, and larger studies would perhaps show a significant change. Future management of atrial fibrillation could benefit from a longitudinal assessment of LA function and structure, which would help in tailoring optimal treatment strategies that balance electrical restoration with mechanical integrity. The potential risks of mechanical disruption should be carefully weighed against the benefits of ablation. Further research is needed to examine the relationship between LA mechanical function, the extent of LA scarring, and underlying structural changes affecting LA strain.

# 5 | LIMITATIONS

Our study has several limitations. It is a single-center study with an observational and retrospective design. Furthermore, our patient sample is restricted to individuals who underwent catheter ablations and had MRIs that met our specific criteria. All patients included had recurrent AF after the first ablation and underwent repeated ablations. The MRIs were obtained using various machines operated by different technicians, which introduced considerable variability in the data. This variation, both among patients and in image quality, contributed to significant inconsistencies in our findings. We acknowledge that the lack of LGE data in our study is a limitation, as this imaging modality could provide valuable insights into atrial fibrosis and scar burden. Future prospective studies with access to comprehensive LGE data would be needed to explore this aspect in more detail.

# 6 | CONCLUSIONS

In conclusion, this study revealed that the LA mechanical function remained consistent with pre- ablation levels after the first ablation procedure. However, a subsequent ablation was found to negatively impact the LA function, but it was less detrimental that the role of decline in mechanical function from AF itself.

### ACKNOWLEDGMENTS

The Nora Eccles Harrison Foundation for Cardiovascular Research funded this research. The National Institutes of Health under Ruth L. Kirschstein National Research Service Award T32HL007576 from the National Heart, Lung, and Blood Institute. The National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number UM1TR004409. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

### DATA AVAILABILITY STATEMENT

The datasets from the corresponding author during the current study are available upon reasonable request.

#### ETHICS STATEMENT

This is a retrospective data collection from procedures performed at our center. The University of Utah Institutional Review Board (IRB) approved this study. Informed consent was not obtained from patients for this retrospective study. Data was obtained from a deidentified database.

# ORCID

Jiawei Dong D http://orcid.org/0000-0003-3167-166X Derek J. Dosdall D http://orcid.org/0000-0001-5059-6824 Edward V. DiBella D http://orcid.org/0000-0001-9196-3731 Rob S. MacLeod D http://orcid.org/0000-0002-0000-0356 Gregory J. Stoddard D http://orcid.org/0000-0002-6292-276X Benjamin A. Steinberg D http://orcid.org/0000-0002-4729-7820 Ravi Ranjan D http://orcid.org/0000-0002-3321-2435

#### REFERENCES

- Haïssaguerre M, Jaïs P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med.* 1998;339(10):659-666.
- Stoppel WL, Kaplan DL, Black LD. Electrical and mechanical stimulation of cardiac cells and tissue constructs. Adv Drug Deliv Rev. 2016;96:135-155.
- Dong J, Kwan E, Bergquist JA, et al. Ablation-induced left atrial mechanical dysfunction recovers in weeks after ablation. *J Interv Card Electrophysiol.* 2024:1-10. https://doi.org/10.1007/s10840-024-01795-x
- Akoum N, Daccarett M, McGann C, et al. Atrial fibrosis helps select the appropriate patient and strategy in catheter ablation of atrial fibrillation: a DE-MRI guided approach. J Cardiovasc Electrophysiol. 2011;22(1):16-22.
- Kuppahally SS, Akoum N, Burgon NS, et al. Left atrial strain and strain rate in patients with paroxysmal and persistent atrial fibrillation: relationship to left atrial structural remodeling detected by delayed-enhancement MRI. *Circ Cardiovasc Imaging.* 2010;3(3): 231-239.
- Takigawa M, Takahashi A, Kuwahara T, et al. Long-term follow-up after catheter ablation of paroxysmal atrial fibrillation: the incidence of recurrence and progression of atrial fibrillation. *Circ Arrhythm Electrophysiol.* 2014;7(2):267-273.

- Habibi M, Lima JAC, Khurram IM, et al. Association of left atrial function and left atrial enhancement in patients with atrial fibrillation: cardiac magnetic resonance study. *Circ Cardiovasc Imaging*. 2015;8(2):e002769.
- Kerr CR, Humphries KH, Talajic M, et al. Progression to chronic atrial fibrillation after the initial diagnosis of paroxysmal atrial fibrillation: results from the Canadian registry of atrial fibrillation. *Am Heart J*. 2005;149(3):489-496.
- Padfield GJ, Steinberg C, Swampillai J, et al. Progression of paroxysmal to persistent atrial fibrillation: 10-year follow-up in the Canadian registry of atrial fibrillation. *Heart Rhythm.* 2017;14(6): 801-807.
- de Vos CB, Pisters R, Nieuwlaat R, et al. Progression from paroxysmal to persistent atrial fibrillation. J Am Coll Cardiol. 2010;55(8): 725-731.
- Pathak RK, Middeldorp ME, Meredith M, et al. Long-term effect of goal-directed weight management in an atrial fibrillation cohort. J Am Coll Cardiol. 2015;65(20):2159-2169.
- Middeldorp ME, Pathak RK, Meredith M, et al. PREVEntion and regReSsive effect of weight-loss and risk factor modification on atrial fibrillation: the REVERSE-AF study. *EP Europace*. 2018;20(12): 1929-1935.
- Xia Y, Li XF, Liu J, Yu M, Fang PH, Zhang S. The influence of metabolic syndrome on atrial fibrillation recurrence: five-year outcomes after a single cryoballoon ablation procedure. J Geriatr Cardiol. 2021 18(12):1019-1028.
- Kühl JT, Lønborg J, Fuchs A, et al. Assessment of left atrial volume and function: a comparative study between echocardiography, magnetic resonance imaging and multi slice computed tomography. *Int J Cardiovasc Imaging*. 2012;28(5):1061-1071.
- 15. Blaber J, Adair B, Antoniou A. Ncorr: open-source 2D digital image correlation matlab software. *Exp Mech.* 2015;55(6):1105-1122.
- Kowallick JT, Kutty S, Edelmann F, et al. Quantification of left atrial strain and strain rate using cardiovascular magnetic resonance

myocardial feature tracking: a feasibility study. J Cardiovasc Magn Reson. 2014;16(1):60.

- 17. Calkins H, Hindricks G, Cappato R, et al. 2017 HRS/EHRA/ECAS/ APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Heart Rhythm*. 2017;14(10): e275-e444.
- Parmar BR, Jarrett TR, Burgon NS, et al. Comparison of left atrial area marked ablated in electroanatomical maps with scar in MRI. J Cardiovasc Electrophysiol. 2014;25(5):457-463.
- Xu J, Yang W, Zhao S, Lu M. State-of-the-art myocardial strain by CMR feature tracking: clinical applications and future perspectives. *Eur Radiol.* 2022;32(8):5424-5435.
- Yang W, Li H, He J, et al. Left ventricular strain measurements derived from MR feature tracking: a head-to-head comparison of a higher temporal resolution method with a conventional method. *J Magn Reson Imaging*. 2022 56(3):801-811.
- 21. R Core TeamR: A Language and Environment for Statistical Computing. R Core Team; 2023.
- 22. Tops LF, Delgado V, Bertini M, et al. Left atrial strain predicts reverse remodeling after catheter ablation for atrial fibrillation. *J Am Coll Cardiol.* 2011;57(3):324-331.
- 23. Habibi M, Lima JAC, Gucuk Ipek E, et al. Short-and long-term associations of atrial fibrillation catheter ablation with left atrial structure and function: a cardiac magnetic resonance study. *J Cardiovasc Electrophysiol.* 2021;32(2):316-324.

**How to cite this article:** Dong J, Kwan E, Bergquist JA, et al. Left atrial functional changes associated with repeated catheter ablations for atrial fibrillation. *J Cardiovasc Electrophysiol.* 2024;1-8. doi:10.1111/jce.16484