Atrial fibrillation (AF) is associated with extensive abnormalities in atrial structure and function. It is well-established that structural atrial changes precede the development of AF and progress with increased duration of sustained AF. The changes in atrial function impair not only the booster pump function but also the atrial reservoir and conduit functions during ventricular systole and early diastole. Progressive atrial remodeling includes fibrotic changes that promote AF maintenance. This idea is supported by observations of increased left atrial (LA) fibrosis in patients with long-standing persistent AF. LA structural and functional remodeling is associated with increased incidence of AF, as well as AF recurrence after cardioversion or ablation.

**Background**—Atrial fibrillation (AF) is associated with left atrial (LA) structural and functional changes. Cardiac magnetic resonance late gadolinium enhancement (LGE) and feature-tracking are capable of noninvasive quantification of LA fibrosis and myocardial motion, respectively. We sought to examine the association of phasic LA function with LA enhancement in patients with AF.

**Methods and Results**—LA structure and function was measured in 90 patients with AF (age 61±10 years; 76% men) referred for ablation and 14 healthy volunteers. Peak global longitudinal LA strain, LA systolic strain rate, and early and late diastolic strain rates were measured using cine–cardiac magnetic resonance images acquired during sinus rhythm. The degree of LGE was quantified. Compared with patients with paroxysmal AF (60% of cohort), those with persistent AF had larger maximum LA volume index (56±17 versus 49±13 mL/m²; \( P=0.036 \)), and increased LGE (27.1±11.7% versus 36.8±14.8%; \( P<0.001 \)). Aside from LA active emptying fraction, all LA parameters (passive emptying fraction, peak global longitudinal LA strain, systolic strain rate, early diastolic strain rate, and late diastolic strain rate) were lower in patients with persistent AF (\( P<0.05 \) for all). Healthy volunteers had less LGE and higher LA functional parameters compared with patients with AF (\( P<0.05 \) for all). In multivariable analysis, increased LGE was associated with lower LA passive emptying fraction, peak global longitudinal LA strain, systolic strain rate, early diastolic strain rate, and late diastolic strain rate (\( P<0.05 \) for all).

**Conclusions**—Increased LA enhancement is associated with decreased LA reservoir, conduit, and booster pump functions. Phasic measurement of LA function using feature-tracking cardiac magnetic resonance may add important information about the physiological importance of LA fibrosis. (Circ Cardiovasc Imaging. 2015;8:e002769. DOI: 10.1161/CIRCIMAGING.114.002769.)

**Key Words:** atrial fibrillation ■ atrial function, left ■ gadolinium ■ magnetic resonance imaging

**Atrial Structure and Function**

**Association of Left Atrial Function and Left Atrial Enhancement in Patients With Atrial Fibrillation**

**Cardiac Magnetic Resonance Study**

Mohammadali Habibi, MD; Joao A.C. Lima, MD; Irfan M. Khurram, MD; Stefan L. Zimmerman, MD; Vadim Zipunnikov, PhD; Kotaro Fukumoto, MD, PhD; David Spragg, MD; Hiroshi Ashikaga, MD, PhD; John Rickard, MD; Joseph E. Marine, MD; Hugh Calkins, MD; Saman Nazarian, MD, PhD

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**Conclusions**—Increased LA enhancement is associated with decreased LA reservoir, conduit, and booster pump functions. Phasic measurement of LA function using feature-tracking cardiac magnetic resonance may add important information about the physiological importance of LA fibrosis. (Circ Cardiovasc Imaging. 2015;8:e002769. DOI: 10.1161/CIRCIMAGING.114.002769.)

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**Atrial fibrillation** (AF) is associated with extensive abnormalities in atrial structure and function. It is well-established that structural atrial changes precede the development of AF and progress with increased duration of sustained AF. The changes in atrial function impair not only the booster pump function but also the atrial reservoir and conduit functions during ventricular systole and early diastole. Progressive atrial remodeling includes fibrotic changes that promote AF maintenance. This idea is supported by observations of increased left atrial (LA) fibrosis in patients with long-standing persistent AF. LA structural and functional remodeling is associated with increased incidence of AF, as well as AF recurrence after cardioversion or ablation.

**See Clinical Perspective**

Late gadolinium enhanced (LGE) cardiac magnetic resonance (CMR) can noninvasively quantify the extent of LA fibrosis. Atrial function is commonly evaluated by speckle-tracking echocardiography; however, the technique is limited for resolution of the thin and asymmetrical LA myocardium and for the analysis of the posterior LA, where most of the fibrosis are located. In contrast, myocardial motion can be accurately tracked with CMR because of its ability to accurately define endocardial and epicardial borders. CMR feature-tracking, a novel post-processing technique which tracks myocardial motion using cine CMR images, has recently been developed. In this study, we sought to examine the
association of LA fibrosis measured with LGE-CMR with phasic LA remodeling measured with feature-tracking CMR in patients with AF. We hypothesized that increased atrial LGE is associated with reduced LA function as assessed by feature-tracking CMR.

Methods
The Johns Hopkins Institutional Review Board approved the study, and all patients provided written informed consent. Between December 2011 and May 2013, 142 consecutive patients with drug refractory AF were referred for CMR before catheter ablation of AF. Of the total 142 patients, 49 were in AF at the time of CMR and were excluded. In 3 patients, the cine images were not analyzable because of poor quality, leaving a final study cohort of 90 patients.

LA structure and function were also assessed in 14 volunteers free of cardiovascular disease.

CMR Protocol
Images were acquired using 1.5-Tesla scanners (Avanto and Aera, Siemens, Erlangen, Germany) and a 6-channel–phased array body coil in combination with a 6-channel spine matrix coil. Cine-CMR images were acquired using a steady-state free precession sequence with the following parameters: minimal TR/TE, slice thickness 8 mm, spacing 2 mm, flip angle 78°, field of view 36 to 40 cm, and typical in-plane resolution 1.5x1.5 mm. LGE-CMR images were acquired within a range of 15 to 25 minutes (mean 18.8±2.4 minutes) after a gadolinium injection (0.2 mmol/kg; gadopentetate dimeglumine; Bayer Healthcare Pharmaceuticals, Montville, NJ), using a fat-saturated 3D inversion recovery–prepared fast spoiled gradient recalled echo sequence with respiratory navigation and ECG gating, echo time of 1.52 ms, repetition time of 3.8 ms, in-plane resolution of 1.3×1.3 mm, slice thickness of 2.0 mm, and flip angle of 10°. Trigger time for 3D LGE-CMR images was optimized to acquire imaging data during diastole of LA as observed from the cine images. The optimal inversion time was identified with an inversion time scout scan (median 270 ms; range 240–290 ms) to maximize nulling of the LA myocardium.

Quantification of LA Enhancement
The method we used for the measurement of LA enhancement has been previously described in detail.20 In brief, an operator blinded to the measured LA functional parameters processed images offline by using QMass MR software (version 7.2, Leiden University Medical Center, Leiden, The Netherlands). Multiplarar reformatted axial images with 3.5-mm slice thickness were reconstructed from 3D axial image data. Epicardial and endocardial contours were manually drawn around the LA myocardium (Figure 1). LA wall thickness was measured by averaging the distance between LA endocardium and epicardium in all segments. For measurement of LA enhancement, we used the image intensity ratio (IIR), defined as the mean pixel intensity of each sector divided by the mean pixel intensity of the entire LA blood pool. A threshold of 0.97 and 1.61 for IIR, which previously was shown to be to a bipolar voltage of <0.5 and <0.1 mV, respectively, was used for mild LA enhancement and dense enhancement determination, respectively.20 Inter- and intraobserver variability of IIR have been previously assessed in the same study with inter- and intraclass correlation coefficients of 0.97 and 0.98, respectively.20

LA Functional Analysis
Multimodality Tissue Tracking software (MTT; version 6.0, Toshiba, Japan) was used to measure phasic LA volumes, strain, and strain rate from a 4-chamber and 2-chamber cine CMR images.18,19 An experienced operator contoured endocardial and epicardial LA borders in a 2- and 4- chamber cine CMR images, taking care to exclude the pulmonary veins and the LA appendage. Once contouring is complete in 1 phase, the software automatically tracks on screen pixels during the cardiac cycle (Movie I in the Data Supplement). The operator then reviewed all contours generated by the software for quality control. On the basis of the biplane area–length method, the software generates LA volume curves during the cardiac cycle (Figure 2). Using the volume/time curve measurements for maximum LA volume (LAV max), LA volume before LA contraction (LAV pre-a) and minimum LA volume (LAV min) were extracted. All volume measurements were indexed to body surface area. LA passive and active emptying fractions were then calculated as follows:
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- LA passive emptying fraction (LAPEF): \(100 \times \frac{LAV_{\text{max}} - LAV_{\text{pre-a}}}{LAV_{\text{max}}}\)
- LA active emptying fraction (LAAEF): \(100 \times \frac{LAV_{\text{pre-a}} - LAV_{\text{min}}}{LAV_{\text{pre-a}}}\)

Strain Measurement

Global longitudinal strain and strain rate curves were generated by averaging longitudinal strain and strain rate measurements in all LA segments, as shown in Figure 2. Global peak LA longitudinal strain (PLAS) was measured from the global longitudinal strain curve. Using longitudinal strain rate curves, peak systolic LA strain rate (SR-s), absolute values of peak early and late diastolic strain rates (SR-ed and SR-ld, respectively) were measured (Figure 2).

To assess the inter- and intraobserver reproducibility of measured LA functional parameters, 2 readers blinded to other measurements remeasured LA parameters using the same technique in 20 patients randomly selected from the whole cohort. In addition, LA functional parameters were remeasured by the original reader blinded to the first measurement.

Statistical Analysis

Continuous variables are presented as mean ± SD. Categorical variables are presented as frequencies and percentages. Differences between group means were evaluated with \(t\) tests (continuous variables) or \(\chi^2\) analysis (categorical variables) as appropriate. The association of fibrosis with measured LA parameters was assessed using Pearson correlation in all patients and also in patients with paroxysmal and persistent AF, separately. Multivariable linear regression was performed with LA fibrosis as the dependent variable and each LA functional and structural parameters as an independent variable. For each LA functional and structural parameter, a separate model was analyzed. To avoid collinearity, correlations between continuous variables were tested using the Spearman correlation coefficient and variables with \(r>0.50\) were not included in the same multivariable model. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for history of hypertension, heart failure, left ventricular ejection fraction, type of AF (paroxysmal or persistent), LA volume index (LAVI), and LA wall thickness. Intraclass correlation coefficient analysis was performed to evaluate inter- and intraobserver agreement. Statistical analyses were performed using Stata software (Version 11.2, Stata Corp, TX).

Results

Of 90 patients in the cohort, 68 were men (76%), 36 (40%) had persistent AF, and 20 (22%) had prior AF ablation. The average age was 61±10 years (range 36–83 years). Heart failure was more prevalent among patients with persistent AF (22% versus 6%; \(P=0.018\), respectively). None of the patients had significant valvular disease. Healthy volunteers included 4 women and 10 men with an average age of 43±9 years (range 25–57 years). The baseline demographic and

Table 1. Baseline Characteristics of Patients

<table>
<thead>
<tr>
<th></th>
<th>Total (n=90)</th>
<th>Paroxysmal (n=54)</th>
<th>Persistent (n=36)</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>61±10</td>
<td>61±10</td>
<td>60±9</td>
<td>0.416</td>
</tr>
<tr>
<td>Sex (men), %</td>
<td>76</td>
<td>72</td>
<td>81</td>
<td>0.367</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>29±5</td>
<td>28±5</td>
<td>29±5</td>
<td>0.256</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>48</td>
<td>48</td>
<td>47</td>
<td>0.931</td>
</tr>
<tr>
<td>History of heart failure, %</td>
<td>12</td>
<td>6</td>
<td>22</td>
<td>0.018</td>
</tr>
<tr>
<td>Coronary artery disease, %</td>
<td>12</td>
<td>13</td>
<td>11</td>
<td>0.768</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>7</td>
<td>6</td>
<td>8</td>
<td>0.605</td>
</tr>
<tr>
<td>Obstructive sleep apnea, %</td>
<td>24</td>
<td>24</td>
<td>25</td>
<td>0.920</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>58±6</td>
<td>59±5</td>
<td>56±5</td>
<td>0.104</td>
</tr>
</tbody>
</table>
clinical characteristics of patients have been summarized in Table 1.

**LA Structure and Function in Persistent and Paroxysmal AF**

Structural and functional LA parameters in patients with paroxysmal and persistent AF have been summarized in Table 2. Patients with persistent AF had more extensive LGE using both thresholds (36.8±14.8% versus 27.1±11.7%, for mild LA enhancement and 5.8±4.4% versus 9.2±7.3% for dense LA enhancement; \( P <0.01 \)). At the same time, patients with persistent AF had larger LAVI (LA\(_{\text{max}}\): 56±17 versus 49±13 mL/m\(^2\); \( P =0.036 \) and LA\(_{\text{min}}\): 36±14 versus 28±11 mL/m\(^2\); \( P =0.008 \)). LA conduit phase function determined by LAPEF was significantly lower in patients with persistent AF (17±6% versus 23±8%; \( P =0.008 \)). Patients with persistent AF also had lower measurements of LA function (LAPEF: 16±5% versus 20±7%; \( P <0.05 \) for both). All patients with AF had at least mild LA enhancement (IIR >0.97, range 7% to 69%); however, in the healthy volunteer group, 12 (85%) had mild LA enhancement (range 2% to 18%). Only 1 healthy volunteer had 2% of dense LA enhancement; however, in patients with AF, 89 (99%) had dense LA enhancement (IIR >1.61, range 1% to 29%). Mean LA wall thickness was comparable among 2 groups (2.06±0.32 versus 2.15±0.30 mm in patients with AF and healthy volunteers, respectively; \( P =0.308 \)). All measures of LA function were significantly higher in healthy volunteers compared with patients with AF (\( P <0.01 \) for all).

**LA Structure and Function in Patients With Prior Ablation**

Our study cohort consists of 20 patients with prior ablation who were undergoing a repeat ablation because of the failure of the first procedure. Although the amount of mild enhancement was comparable in these patients with those with no history of ablation (34.6±12.1% versus 30±14.1%; \( P =0.193 \)), they had lower measures of LA function (LAPEF: 16±5% versus 19±7%; \( P =0.028 \); PLAS: 17±5% versus 24±8%; \( P <0.001 \)). All measures of the phasic LA strain rate were also lower in patients with prior ablation (\( P <0.05 \) for all).

**LA Structure and Function in Healthy Volunteers**

Structural and functional LA parameters in patients with AF and healthy volunteers have been summarized in Table 3. Healthy volunteers had smaller LA size (LA\(_{\text{max}}\): 36±10 versus 52±15 mL/m\(^2\) and LA\(_{\text{min}}\): 18±6 versus 31±13 mL/m\(^2\); \( P <0.001 \) for both). All patients with AF had at least mild LA enhancement (IIR >0.97, range 7% to 69%); however, in the healthy volunteer group, 12 (85%) had mild LA enhancement (range 2% to 18%). Only 1 healthy volunteer had 2% of dense LA enhancement; however, in patients with AF, 89 (99%) had dense LA enhancement (IIR >1.61, range 1% to 29%). Mean LA wall thickness was comparable among 2 groups (2.06±0.32 versus 2.15±0.30 mm in patients with AF and healthy volunteers, respectively; \( P =0.308 \)). All measures of LA function were significantly higher in healthy volunteers compared with patients with AF (\( P <0.01 \) for all).

### Table 2. Left Atrial Structure and Function in Patients Stratified by Type of Atrial Fibrillation

<table>
<thead>
<tr>
<th>LA Parameters</th>
<th>Total Patients With AF (n=90)</th>
<th>Paroxysmal (n=54)</th>
<th>Persistent (n=36)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA mild enhancement, %</td>
<td>31±13.8</td>
<td>27.1±11.7</td>
<td>36.8±14.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LA dense enhancement, %</td>
<td>7.2±5.9</td>
<td>5.8±4.4</td>
<td>9.1±7.3</td>
<td>0.009</td>
</tr>
<tr>
<td>LA wall thickness</td>
<td>2.06±0.31</td>
<td>2.00±0.31</td>
<td>2.00±0.28</td>
<td>0.150</td>
</tr>
<tr>
<td>LA(_{\text{max}}), mL/m(^2)</td>
<td>52±15</td>
<td>49±13</td>
<td>56±17</td>
<td>0.036</td>
</tr>
<tr>
<td>LA(_{\text{min}}), mL/m(^2)</td>
<td>31±13</td>
<td>28±11</td>
<td>36±14</td>
<td>0.008</td>
</tr>
<tr>
<td>LAPEF, %</td>
<td>19±7</td>
<td>20±6</td>
<td>17±6</td>
<td>0.019</td>
</tr>
<tr>
<td>LAAEF, %</td>
<td>23±8</td>
<td>23±8</td>
<td>22±8</td>
<td>0.294</td>
</tr>
<tr>
<td>PLAS, %</td>
<td>22±8</td>
<td>24±8</td>
<td>20±7</td>
<td>0.012</td>
</tr>
<tr>
<td>SR-s, s(^{-1})</td>
<td>0.93±0.36</td>
<td>1±0.39</td>
<td>0.83±0.28</td>
<td>0.024</td>
</tr>
<tr>
<td>SR-ed, s(^{-1})</td>
<td>0.82±0.39</td>
<td>0.89±0.42</td>
<td>0.72±0.33</td>
<td>0.049</td>
</tr>
<tr>
<td>SR-ld, s(^{-1})</td>
<td>1.07±0.57</td>
<td>1.17±0.62</td>
<td>0.91±0.47</td>
<td>0.030</td>
</tr>
</tbody>
</table>

LA indicates left atrial; LAAEF, LA active emptying fraction; LAPEF, LA passive emptying fraction; LA\(_{\text{max}}\), maximum LA volume index; LA\(_{\text{min}}\), minimum LA volume index; PLAS, peak global LA longitudinal strain; SR-ed, early diastolic strain rate; SR-ld, late diastolic strain rate; and SR-s, systolic strain rate.
Discussion
To the best of our knowledge, this is the first study to examine the association of phasic LA function with LA enhancement using feature-tracking CMR. In this study, we note an inverse association between the extent of LA enhancement and passive LA emptying fraction, peak global LA strain and LA strain rate during systole, early diastole, and late diastole as surrogates of reservoir, conduit, and booster pump functions of LA, respectively. This association was independent of age, sex, hypertension, heart failure, left ventricular ejection fraction, type of AF, LA size, and wall thickness. The study also shows that patients with AF have more structural and functional changes in LA compared with healthy volunteers. Moreover, persistent AF is associated with greater reduction in all phases of LA function and more advanced LA structural changes.

Challenges in the Assessment of LA Structure and Function
LA anatomic, contractile, and electric remodeling promotes the maintenance of AF and further structural and functional deterioration. Therefore, assessment of LA structure and function has both predictive and prognostic values. LA velocity measured with tissue Doppler imaging has been traditionally used in the assessment of LA function. However, because of the translation and tethering effect of mitral valve and left ventricle on LA velocity and angle dependency, tissue Doppler imaging is unable to differentiate between true atrial contraction and mitral annular and ventricular motion. More recently, speckle-tracking echocardiography has been used to assess LA function and to measure strain and strain rate. However, given the posterior location and thin wall of the LA, and the presence of pulmonary veins and appendage, assessment of LA wall motion might be challenging, despite having a higher temporal resolution compared with CMR. On the contrary, CMR is not only the gold standard imaging modality in the assessment of cardiac motion but also the only modality capable of quantification of LA fibrosis as the hallmark of structural changes in patients with AF using both LGE or T1 mapping. Feature-tracking MRI has been recently proposed as a novel method in the assessment and quantification of LA function using cine CMR images. One limiting factor in the assessment of LA function is the quality of images. Given the high image quality and spatial resolution of CMR images compared with echocardiography, LA function can be assessed using the volumetric method (by measuring LA volumes in different phases of cardiac cycle and calculating the emptying fractions) and also by strain and strain rate analyses in all segments of the LA. In our study, of 107 participants in sinus rhythm, the images were analyzable in 104 subjects (97.2%). However, the feasibility of speckle-tracking echocardiography in measurement of LA strain and strain rate ranges between 76% and 94%. Qualitative factors that influenced the reliability of feature-tracking observations included significant arrhythmia and inability to breath hold.

LA Structure and Function in Patient With AF
In our study, the IIR was used to detect differences in LA wall enhancement between healthy volunteers and patients with AF. All patients with AF had at least mild LA enhancement; however, healthy subjects had much less mild LA enhancement and almost no dense enhancement. These findings are comparable with the study of Oakes et al in which 6 healthy volunteers had only minimal LA wall enhancement (1.7±0.3%) compared with the average LA enhancement of 8.0%, 21%, and 50% in patients with AF with mild, moderate, and extensive enhancement, respectively. As it has been shown, previously patients with persistent AF have more extensive atrial structural changes and deterioration of atrial function. In a study of 74 paroxysmal and 44 patients with persistent AF, those with persistent AF had lower absolute values for both strain and strain rate measurements and also lower total LA emptying fraction. Kuppahally et al also reported lower LA midseptal strain and SR-s, and lower midlateral strain but not SR-s in 31 patients with persistent AF compared with 24 patients with paroxysmal AF. In the same study, patients with persistent AF

Table 3. Left Atrial Structure and Function in Healthy Volunteers and in Patients With Atrial Fibrillation

<table>
<thead>
<tr>
<th>LA Parameters</th>
<th>Total Patients With AF (n=90)</th>
<th>Healthy Volunteers (n=14)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA mild enhancement, %</td>
<td>31±13.8</td>
<td>8.9±6.0 *</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LA dense enhancement, %</td>
<td>7.1±5.9</td>
<td>0.1±0.5 †</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LA wall thickness</td>
<td>2.06±0.32</td>
<td>2.15±0.30</td>
<td>0.308</td>
</tr>
<tr>
<td>LAVI max, mL/m²</td>
<td>52±15</td>
<td>36±10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LAVI min, mL/m²</td>
<td>31±13</td>
<td>18±6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LAPEF, %</td>
<td>19±7</td>
<td>24±6</td>
<td>0.002</td>
</tr>
<tr>
<td>LA AEF, %</td>
<td>23±8</td>
<td>34±10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PLAS, %</td>
<td>22±8</td>
<td>33±9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SR-s, s⁻¹</td>
<td>0.93±0.36</td>
<td>1.39±0.48</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SR-ld, s⁻¹</td>
<td>0.82±0.39</td>
<td>1.1±0.40</td>
<td>0.01</td>
</tr>
<tr>
<td>SR-ed, s⁻¹</td>
<td>1.07±0.57</td>
<td>1.75±0.89</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* LA mild enhancement was present in 12 of the healthy volunteers.
† Only 1 healthy volunteer had dense enhancement.
Figure 3. Correlation of left atrial (LA) enhancement and (A) maximum LA volume index, (B) minimum LA volume index, (C) LA passive emptying fraction, (D) LA active emptying fraction, (E) LA peak global longitudinal strain, (F) systolic LA strain rate, (G) early diastolic atrial strain rate (absolute value), and (H) late diastolic LA strain rate (absolute values).
also had more fibrosis, larger LA size, and lower LA emptying fraction. Similar results were presented in another study of 971 individuals with AF, where LA size increased across AF types (paroxysmal, persistent, and permanent, respectively), whereas LA function measured by total and passive emptying fraction deteriorated. In this study, LAAEF was not significantly different among AF subtypes. Our study is in agreement with these findings because we also found that patients with persistent AF had larger LA size and lower LAPEF but not LAAEF. In addition, we found that patients with persistent AF had a higher percentage of LA fibrosis and lower global strain and strain rate measurements in all phases of LA function. These findings support the hypothesis of progressive atrial remodeling with the maintenance of AF.

**Association of LA Fibrosis and LA Function**

Deposition of extracellular matrix and fibrosis are hallmarks of LA structural changes in AF. Several experimental models have demonstrated that LA fibrosis is a substrate for promotion and maintenance of AF. Despite several studies

| Table 4. Association of Left Atrial Functional and Structural Parameters With Left Atrial Fibrosis |
|---------------------------------|---------------------------------|--|--|
| **LA Parameters**               | **Model 1 (n=90)**               | **Model 2 (n=90)**               |
| LAVI<sub>max</sub>, mL/m<sup>2</sup> | 3.6                             | 9.0                             |
| LAVI<sub>min</sub>, mL/m<sup>2</sup> | –5.3                            | –4.1                            |
| LAPEF, %                         | –3.25                           | –3.2                           |
| LAAEF, %                         | –5.9                            | –4.9                            |
| PLAS, %                          | –6.1                            | –5.2                            |
| SR-s, %/ms                       | –6.4                            | –5.3                            |
| SR-ed, %/ms                      | –4.7                            | –3.9                            |
| SR-ld, %/ms                      | –4.7                            | –3.9                            |

The table illustrates multivariable regression analyses of the association of left atrial (LA) parameters with LA fibrosis. Six different regression models were analyzed. Each row represents a separate multivariable model with LA fibrosis as the dependent variable and the LA parameter as the independent variable. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for history of hypertension, heart failure, left ventricular ejection fraction, type of atrial fibrillation (persistent or paroxysmal), maximum LA volume index, and LA wall thickness.

LA indicates left atrial; LAAEF, LA active emptying fraction; LAPEF, LA passive emptying fraction; LAVI<sub>max</sub>, maximum LA volume index; LAVI<sub>min</sub>, minimum LA volume index; PLAS, peak global LA longitudinal strain; SR-ed, early diastolic strain rate; SR-ld, late diastolic strain rate; and SR-s, systolic strain rate.

*All β coefficient values are per SD.*
investigating the progressive nature of LA remodeling and fibrosis in the setting of AF, the association between LA LGE as a measure of LA fibrosis and phasic LA dysfunction has not been extensively studied. To our knowledge, the only previous study examining this association has been performed by Kuppahally et al\textsuperscript{7} on 55 patients with AF. The authors reported an inverse association between LA midseptal and midlateral strain and strain rate measured with speckle-tracking echocardiography and the percentage of LA fibrosis detected with LGE-CMR. This association was more prominent in patients with persistent AF than in patients with paroxysmal AF. Our findings complement the results of this study because we found an inverse association between LAPEF (representing conduit function), peak global LA strain (representing conduit function), and SR-s, SR-ed, and SR-id (representing reservoir, conduit and booster pump functions) with the extent of LA enhancement.

Compared with the study of Kuppahally et al, we examined this association with global strain as well as phasic LA rate measurements of the entire LA, including measurements from the posterior segments where most of the fibrosis is located. Importantly, all of our study population was in sinus rhythm at the time of CMR enabling measurement of both passive and active emptying fractions. In addition, both LA enhancement and strain/strain rate measurements were performed using the same CMR images, thus minimizing bias caused by temporal changes in LA function/fibrosis between different modalities.

The extent of fibrosis and LA function in patients with prior ablation should be interpreted cautiously because some LA remodeling is likely because of the prior procedure,\textsuperscript{13,32} whereas some differences in these parameters are likely because of the selection of patients with more advanced structural disease in the subset with repeat ablation.\textsuperscript{11,21–23}

Limitations
This is a relatively small study with 90 participants; however, on the basis of another study using feature-tracking CMR, a sample size of 29 has 90% power and α error of 0.05 to detect a change of 5% in strain measurements.\textsuperscript{17} The LGE-MRI sequence used in this study provided a 1.3×1.3 mm in-plane resolution and was obtained during ventricular diastole/atrial systole, thus maximizing atrial myocardial thickness for measurement. Nevertheless, atrial myocardial thickness may be near the limit of image resolution in some cases. Because of volume averaging, the analyzed LA myocardial sector may have included blood pool or epicardial fat in some cases. The cohort included patients with paroxysmal and persistent AF, as well as patients with and without prior ablations. The resulting increased variability in the extent of fibrosis and LA myocardial function and also likely increased the standard error for the magnitudes of associations. On the contrary, the heterogeneity of the cohort improves the generalizability of our results. In addition, adjusted and stratified analyses were performed to minimize the possibility of confounding. The objective of the present study was to examine the association of LA enhancement and function using LGE-MRI and feature-tracking MRI. The association of clinical end points with LA enhancement or atrial transport function was not examined and will be the subject of future articles, once appropriate clinical follow-up has been performed. Because of time constraints, and to obtain functional image data, T1 mapping sequences were not obtained in this cohort of patients. Therefore, the analysis of fibrosis has been performed using LGE sequences. Future studies to examine the association of LA T1 mapping with LA function are warranted.

Conclusions
LA LGE was inversely correlated with passive LA emptying fraction, peak global LA strain, and strain rate in all phases of LA function. Patients with persistent AF had worse LA function throughout the entire cardiac cycle compared with those with paroxysmal AF. Feature-tracking CMR, a novel tool in the analysis of LA function, enables detailed assessment of phasic LA volume, strain, and strain rate. Quantification of LA function using feature-tracking CMR may provide additional insight for procedural outcomes and stroke risk stratification in patients with AF.
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Disclosures
Dr Nazarian is on the MRI advisory panel for Medtronic, and is a scientific advisor to and principal investigator for research funding to Norbert and Louise Grunwald Cardiac Arrhythmia Research Fund, The Roz and Marvin W Weiner Family Foundation. The content is provided by guest on November 12, 2017 http://circimaging.ahajournals.org/ Downloaded from

References
CLINICAL PERSPECTIVE

Atrial fibrillation is associated with functional, structural, and electric changes in the left atrium. Fibrosis is the hallmark of structural changes in the left atrium, which promote atrial fibrillation, and can be noninvasively measured using late gadolinium enhancement MRI. Functional left atrial (LA) measures include passive and active emptying fractions, strain, and strain rate, which are traditionally assessed using speckle tracking echocardiography. However, echocardiographic assessment of LA function is challenging because of the posterior location and thin wall of the left atrium. In this study, we examined the association of LA enhancement with phasic LA function using the novel method of feature-tracking MRI. We found an inverse association between LA fibrosis and LA functional parameters in all phases, independent of the LA size and the common clinical risk factors for atrial fibrillation. Measurement of LA function using MRI may be useful as a surrogate of LA fibrosis for atrial fibrillation procedural candidate selection and risk stratification with regard to anticoagulation strategies.
Association of Left Atrial Function and Left Atrial Enhancement in Patients With Atrial Fibrillation: Cardiac Magnetic Resonance Study

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Legend of the video:

**Video 1.** Feature-tracking CMR was used to track LA myocardial motion in 2 and 4-chamber cine images.