Title

Magnetic Resonance Contrast-enhanced T_1 Mapping in the Human Atrium: Validation and Impact on Clinical Outcome Following Catheter Ablation for Atrial Fibrillation

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Abstract

Objective: To validate and assess the impact of cardiac magnetic resonance imaging (CMR) atrial T_1 mapping on the clinical outcome following catheter ablation for atrial fibrillation(AF).

Background: Atrial fibrosis is a pathologic correlate of atrial fibrillation (AF) and is accompanied by electrophysiologic remodeling.

Methods: CMR was performed in 3 groups using a clinical 1.5-T scanner: controls, paroxysmal AF (PAF) patients and persistent AF (PeAF) patients. A T_1 mapping sequence was used to calculate the post-contrast T_1 relaxation time (T_1 time) at the interatrial septum as an index of diffuse fibrosis. A subset of 23 AF subjects underwent left atrial endocardial bipolar voltage mapping for electrophysiologic correlation. Following AF ablation, patients underwent clinical assessment and 7-day holter monitoring at 6-monthly intervals for freedom from recurrent arrhythmia.

Results: 20 controls, 71 PAF patients, and 41 PeAF patients underwent CMR. Atrial T_1 time progressively shortened across groups (controls: 307±39 ms, PAF patients 260±41 ms, PeAF patients: 240±31 ms, $p<0.001$). Atrial T_1 time correlated with mean septal voltage ($R^2=0.47$, $p<0.001$) and global LA voltage ($R^2=0.48$, $p<0.001$). Advancing age, a diagnosis of AF, and AF duration independently predicted shortened atrial T_1 time ($F=9.69$, $p<0.001$). The single procedure success rate was 74% at 12±5 months post-ablation. Atrial T_1 time and AF category independently predicted arrhythmia recurrence (adjusted $R^2=0.29$, $p<0.01$).

Conclusion: Atrial T_1 time as measured using CMR provides an index of atrial fibrosis that correlates with tissue voltage, AF type and clinical outcomes following catheter ablation.

List of Abbreviations

AF	atrial fibrillation
ANOVA	analysis of variance
CMR	cardiac magnetic resonance
CS	coronary sinus
DE	delayed-enhancement
EF	ejection fraction
GFR	glomerular filtration rate
LA	left atrium/atrial
LV	left ventricle/ventricular
ROI	region of interest

Keywords

Atrial fibrosis

Atrial fibrillation

Atrial remodelling

Cardiac magnetic resonance

T_1 mapping

Introduction

The seminal observation that "AF begets AF" introduced the concept of electrical and structural remodeling fundamental to an understanding of the pathophysiology of atrial fibrillation (AF).(1) Following reversion to sinus rhythm, atrial electrical remodeling recovers within days, yet vulnerability to recurrent AF remains. Atrial structural remodeling, the hallmark of which is interstitial fibrosis is the second factor largely responsible for late AF recurrence. Atrial fibrosis is associated both with AF and with risk factors for AF including ageing and hypertension.(2) Given its negative impact on AF ablation outcomes,(3) non-invasive methods to quantify atrial fibrosis are of considerable potential clinical value.

Marrouche and co-workers have elegantly quantified the spatial extent of abnormal left atrial (LA) tissue using delayed-enhancement cardiac magnetic resonance imaging (DE-CMR). Findings were validated semi-quantitatively against extent of low-voltage tissue on electroanatomic maps derived at the time of AF ablation. (3) DE-CMR accurately defines regions of myocardial replacement fibrosis because these areas have a slower washout rate of gadolinium contrast than non-fibrotic myocardium, resulting in increased signal intensity on T_1-weighted imaging. DE-CMR is a qualitative technique and requires presence of normal myocardium as a frame of reference to generate image contrast. In contrast, myocardial T_1 mapping allows direct signal quantification and has been validated against collagen content in animal models,(4,5) and in human cardiomyopathy.(6) Iles and co-workers showed that cardiomyopathy was associated with altered ventricular post-contrast T_1 relaxation time (T_1 time) in regions both with and without DE, establishing the technique's greater sensitivity for detecting myocardial fibrosis over conventional DE-CMR.

To date DE-CMR of the atria has not become widely adopted. This study aims to validate atrial T_1 mapping as an index of atrial fibrosis and to explore its clinical utility in the setting of AF and impact on AF ablation outcomes.

Methods

Study Population

The study, approved by the Alfred Human Research Ethics Committee, was performed at the Alfred Hospital, Melbourne, Australia between October 2009 and November 2011. Recruits included healthy volunteers and symptomatic AF patients resistant to or intolerant of ≥1 antiarrhythmic agent and scheduled for AF ablation. AF patients were categorized as "paroxysmal" (PAF) where episodes were self-terminating within 7 days, or "persistent" (PeAF) where episodes lasted >7 days or required direct current reversion (DCR). Healthy volunteers on no medications and without cardiac disease, hypertension, diabetes, smoking, or acute illness were recruited as controls. Subjects with renal dysfunction, claustrophobia, or metallic prosthetic implants were excluded. Informed consent was obtained from all recruits.

CMR Protocol

Sequences were acquired using a clinical 1.5-T scanner (Signa HD 1.5-T, GE Healthcare, Wisconsin, USA) during breath-holds 10 to 15 s. LV indices were determined using the biplane area-length method applied to 2- and 4-chamber long-axis views. The LA boundary was traced manually (4-chamber long-axis view) to yield the cross-sectional area. Gadolinium-diethylene triamine penta-acetic acid (0.2 mmol/kg bodyweight, maximum 20 mmol, Magnevist, Schering, Germany) was administered as a bolus. Left atriography was performed in all AF patients.

A T_1 mapping sequence described previously(6) was used to acquire images in the 4-chamber long-axis. This involved an electrocardiogram-triggered, inversion-recovery prepared, 2-dimensional fast gradient echo sequence employing variable temporal sampling of k-space (Global Applied Science Laboratory, GE Healthcare).(7) Ten images were acquired sequentially at increasing inversion times (75 to 750 ms) 15 min following the contrast bolus (repetition/echo time: 3.7 ms/1.2 ms, flip angle: 20°, acquisition matrix: 256 × 128, field of view: 36 × 27 cm, slice thickness: 8 mm, trigger delay: 300 ms, and views per segment: 24).

Evaluation of Atrial Fibrosis with T_1 Mapping

The T_1 mapping sequences were analyzed using a dedicated research software package (VizPack Version 7.2.0, Global Applied Science Laboratory, GE Healthcare) that enabled analysis of regions of interest (ROIs) to determine pixel-by-pixel and mean T_1 time by fitting data acquired at various preparation times to the exponential curve $M_z(t=TI) = M_0(A-Be^{-t/T1})$ relating the sample magnetization M_z observed at time $t=TI$ to the equilibrium magnetization M_0 and sample T_1, where TI denotes inversion time for an inversion recovery experiment. For each image, an ROI was manually sampled at the interatrial septum to calculate mean T_1 time for each subject (Figure 1). Other regions of the atria were not sampled because they fell beyond the limits of resolution in the majority of scans. For 10 subjects in each of the 3 study groups, one blinded reviewer performed T_1 mapping on 2 independent occasions to evaluate intra-observer variability. Further, two blinded reviewers (1 electrophysiologist and 1 cardiac CMR specialist) performed T_1 mapping independently on the 30 subjects to evaluate inter-observer variability.

LA Voltage Mapping

Anti-arrhythmic medications were withheld >5 half-lives prior to the procedure except for amiodarone, which was ceased 1 month prior to the procedure. Under general anesthesia, trans-esophageal echocardiography was performed to exclude LA thrombus. Intra-cardiac catheters were positioned according as previously defined(8) (i) a 10-pole coronary sinus (CS) catheter; (ii) a 6-pole His catheter; (iii) a 20-pole variable loop circular mapping catheter (Reflexion Spiral XX, St Jude Medical, Minneapolis, MN, USA), and (iv) a 4-mm externally irrigated-tip ablation catheter (Contact Therapy Cool Path Duo, St Jude Medical). Double trans-septal access was obtained using a BRK1 needle and SL1 sheath (St Jude Medical). Intravenous heparin was administered with a target activated clotting time of 350 s. Bipolar intra-cardiac electrograms and 12-lead surface ECG were recorded simultaneously on a digital amplifier system (EP Med Systems, West Berlin, NJ, USA).

LA voltage maps were created as shown in Figure 2 in a subset of AF patients who were in sinus rhythm at the time of CMR (performed 1 day prior to ablation) and on the day of the ablation. A fill threshold of 10 mm was used to ensure even distribution of collected points. Data were acquired using the multipolar circular mapping catheter, except in areas of inadequate endocardial contact where the ablation catheter was used instead. Endocardial contact was confirmed using electrogram characteristics, fluoroscopic visualization of catheter stability in relation to cardiac motion, and distance-to-surface measurements.

Local bipolar voltage was defined as the amplitude between the absolute peak positive and peak negative deflections. Acquired points were annotated automatically then validated manually. Mean LA voltage was derived from the pool of validated points, and mean left septal voltage from points falling in the region of the interatrial septum.

Catheter Ablation

Catheter ablation involved antral circumferential PV isolation as described previously(9). Power was limited to 30 watts (and 25W on the posterior wall) and temperature to 50°C. For persistent AF patients, if AF continued following PV isolation, a roof line joining the superior aspects of each wide encirclement ablation ring was deployed followed by electrical cardioversion. Roof line block was confirmed as previously described.(10) If AF organized to an atrial tachycardia (AT), activation mapping and targeted ablation was performed. Cavotricuspid isthmus ablation (40 Watts, 45°C) was performed for patients requiring cardioversion or having documented atrial flutter. Bidirectional conduction block was confirmed by differential pacing techniques and demonstration of widely-spaced double potentials along the CTI. A 30-minute waiting period following PV isolation was strictly employed. Adenosine 18 mg was administered intravenously with the spiral catheter positioned sequentially in the superior PVs to assess for transient PV reconnection. PVs were re-isolated if reconnection occurred. Patients remained in hospital for 48 hours post-procedure. Enoxaparin was administered 6 to 12 h post sheath removal (unless the procedure was performed on warfarin) and continued until a target INR >2 was achieved.

Follow up

Patients were followed up clinically at 1, 3, 6 and 12 months, and on a 6-monthly basis thereafter, with 7-day holter monitoring performed at 6 monthly intervals. Additional assessments occurred where clinically indicated. Procedural success was defined as freedom from recurrent atrial arrhythmias lasting longer than 30 s after an initial 3-month blanking period while off antiarrhythmics, in keeping with consensus guidelines(11).

Statistics

Data are expressed as mean±standard deviation (SD) unless otherwise indicated. Two-group comparisons were made using Student's t test and Fisher's exact test for continuous and categorical variables respectively. Three-group comparisons were made using 1-way analysis of variance (ANOVA) with Bonferroni correction for parametric variables and Kruskal-Wallis test with Dunn's post-test for nonparametric variables. Bland-Altman assessment compared intra- and inter-observer agreement between derived T_1 times. Simple and multiple linear regressions were used to assess relationships between continuous variables. Freedom from arrhythmia recurrence was assessed by binary logistic regression using univariate and multivariate models. Kaplan-Meier analysis was used to assess the impact of atrial T_1 time on procedural success. A two-tailed p value of <0.05 was considered significant. Analyses were conducted using SPSS software (version 17, SPSS, Chicago, Illinois).

Results

Subject characteristics and CMR Findings

Subject characteristics are shown in Table 1. Overall, 111 of 132 scans (84%) were performed in sinus rhythm and the remainder in AF including 11 (15%) paroxysmal AF (PAF) patients and 10 (24%) persistent AF (PeAF) patients (p=ns).

Intra- and Inter- Observer Correlation and Agreement

R^2 values for the 10 T_1 data points fit to respective recovery curves were greater than 0.95 for all sequences analyzed. Intra- and inter observer T_1 times exhibited close correlation (Figure 3).

Relationship of Myocardial T_1 Time to LA Voltage

Sixteen paroxysmal AF patients and 7 persistent AF patients underwent voltage mapping, with 31±12 left septal points and 336±96 LA points analyzed per subject. Atrial T_1 times (mean 242±32 ms) correlated positively with mean septal and mean LA voltage (Figures 4A and B).

Post-contrast Myocardial T_1 Times in Controls and AF subjects

Atrial T_1 time was longest in controls and shortest in persistent AF subjects (Figure 4C). Among controls, there was no relationship between T_1 time and age, gender, or factors that could potentially influence gadolinium washout such as renal function, heart rate, and hematocrit (Table 2). Predictors of atrial T_1 time were evaluated among the entire cohort (Table 3). Again, there was no relationship between T_1 time and renal function, heart rate, or hematocrit. Age, a diagnosis of AF, and AF duration were independent predictors of atrial T_1 time ($F=9.69$, $p<0.001$).

Procedural Characteristics and Outcomes

Persistent AF patients had longer procedure times and higher radiation doses, and more frequently required intraprocedural DCR (Table 4). PV isolation was achieved in all patients. Acute PV reconnection occurred more frequently in paroxysmal versus persistent AF patients (40% vs 18%, $p<0.05$). All acutely reconnected PVs were successfully re-isolated. Single procedural success was achieved in 74% at 12±6 months. Arrhythmia recurrence occurred more frequently in persistent versus paroxysmal AF patients (39% vs 18%, $p<0.05$). Five paroxysmal and 7 persistent AF patients underwent a second catheter ablation procedure (7% vs 17%, p=ns).

Impact of Atrial T_1 Time on Freedom from AF

Atrial T_1 time was significantly shorter in patients with arrhythmia recurrence compared to those without (Table 5, 216±32 vs 245±42 ms, $p<0.01$). AF category and atrial T_1 time were significant independent predictors of arrhythmia recurrence (Table 6, adjusted $R^2=0.29$, $p<0.01$). Freedom from AF occurred in 96% of patients with an atrial T_1 relaxation time >260ms and 68% in patients with atrial T_1 time <260ms (Figure 5, $p<0.01$).

Discussion

This study describes contrast-enhanced T_1 mapping of the human atrial myocardium as a measure of tissue fibrosis and demonstrates that atrial T1 times

(i) can be measured reliably and reproducibly with minimal intra- and inter-observer variability;

(ii) correlate with atrial tissue voltage at the interatrial septum and global LA;

(iii) shorten with age and AF burden; and

(iv) predict outcomes following AF ablation. An atrial T_1 relaxation time >260ms was associated with a 96% single procedure success rate following AF ablation.

Non-invasive Assessment of Atrial Fibrosis

Atrial fibrosis is the hallmark of structural remodeling and accompanies a variety of conditions associated with AF such as heart failure (12) and hypertension.(13) The landmark observation that "AF begets AF" is in part secondary to the profibrotic effects of AF itself.(14) The electrophysiologic sequelae of atrial fibrosis are characterized by slowed and heterogeneous conduction, which in turn promote multiple wavelets and localized reentry and establish a substrate favoring perpetuation of AF.(15)

There is presently no method for quantifying atrial fibrosis that is both widely available and widely accepted. Peripheral biomarkers of collagen turnover such as C-terminal propeptide and telopeptide of collagen type-I while elevated in AF subjects are not tissue specific and may reflect ventricular extracellular matrix remodeling associated with hypertension, heart failure, or AF itself. (16) Echocardiographic studies of the LA have found integrated backscatter to correlate with LA appendage collagen content.(17) However, this technique assesses only the LA posterior wall, and is dependent on image acquisition parameters including ultrasound frequency, focus, and depth.

Marrouche and co-workers have elegantly described the use of DE-CMR to quantify spatial extent of LA remodeling in AF subjects, and correlated findings to abnormal electrophysiologic substrate and arrhythmia recurrence following AF ablation.(3) Extent of LA remodeling determined using DE-CMR has further been shown to reflect atrial mechanical function, predict atrial reverse remodeling following AF ablation, and predict stroke risk independently of $CHADS_2$ score.(18,19) Although atrial DE-MRI is compelling, results originate from a single clinical centre and are yet to be reproduced. While the application of DE-CMR to the LA represents a major advance in cardiac imaging and alludes to a wide range of exciting clinical and research applications, two important limitations should be noted. First, quantitation of the spatial extent of fibrosis is sensitive to the threshold intensity defining normal tissue, which is defined subjectively. Second, DE-CMR does not accurately quantify intensity of fibrosis, and may underestimate extent of fibrosis particularly where the atrium is diffusely diseased.

In the present study, T_1 time was quantified at the interatrial septum as the atrial myocardium elsewhere was too thin to be reliably assessed. Intra- and inter-observer reproducibility was high, and significant correlations with local and global tissue voltage indices were demonstrated. The pathophysiologic mechanisms responsible for atrial fibrosis may be triggered by AF itself or chronic atrial stretch a final common pathway to a range of conditions associated with AF such as hypertension,(20) heart failure(12) or valvular heart disease. As a result atrial fibrosis may be diffuse, as measured in the present study by atrial T_1 mapping, or become more prominent in locations such as the posterior wall as demonstrated by DE-MRI. Previous electroanatomic studies have shown a generalized or diffuse reduction in tissue voltage in conditions associated with A**F.(20-22)** In the present study the interatrial T_1 time at the septum provided a reliable "window" to the LA.(23) Atrial T_1 time shortened with AF burden and with ageing, consistent with prior studies relating fibrotic remodeling to these conditions.(21,24)

Clinical implications

In the present study, the atrial T_1 time was predictive of AF ablation outcome. In fact, an atrial T_1 time of >260ms was associated with a 96% single procedure success following catheter ablation.
Atrial T_1 time may have greater prognostic value than traditional risk factors for arrhythmia recurrence following catheter ablation, including hypertension, congestive heart failure, and reduced LV EF. These risk factors are associated with structural and electrical LA remodeling but serve as surrogates and not direct measures of underlying arrhythmogenic substrate.(24) In contrast, atrial T_1 time is a quantitative measure of structural remodeling which provides incremental information with potential utility in tailoring ablation strategies to individuals.

Study Limitations

Atrial T_1 mapping was only possible at the septum given the limits of image resolution. A higher magnetic field (3-T) would allow greater resolution of atrial myocardium and may facilitate both regional and global T_1 mapping. Atrial T_1 time reflects accumulation of gadolinium in the extracellular compartment, but interpatient comparison may be affected by a number of factors, including contrast dose, time post

constrast administration, GFR, haematocrit and heart rate. . Recently Gai and co-workers examined the confounding impact of all these factors in the assessment of myocardial post-contrast T_1 time using a multicompartment model similar to that used in positron emission tomography.(25) They demonstrated the majority of variation in T_1 time was due to contrast dose, followed by scan delay time post contrast administration and then GFR, whereas the impacts of haematocrit and heart rate were negligible. In our study, contrast dose and time post contrast were kept constant for each patient, and the three groups were well matched with respect to GFR, making it unlikely these factors had any significant impact on our study findings. This is further supported by the observation in our study that none of these potential confounders demonstrated a significant relationship with estimated atrial T_1 time.

Conclusion

Atrial fibrosis is the hallmark of structural remodeling and is associated with AF recurrence following medical intervention. Atrial T_1 time as measured using CMR provides an index of diffuse atrial fibrosis that correlates with tissue voltage, AF type and clinical outcomes following catheter ablation.

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Figure Legends

Figure 1: Calculation of Myocardial T_1 Time at the Interatrial Septum

A region of interest (ROI) was drawn around the interatrial septal myocardium in the 10 images obtained from the T_1 mapping sequence performed in the long-axis 4-chamber view (A). Signal intensities for each ROI (1 to 10) were curve-fitted to an exponential recovery curve (B) to obtain the atrial T_1 time (vertical red line), which reflects the specific time decay constant when hydrogen nuclei protons within the ROI recover approximately 63% of their longitudinal magnetization equilibrium value in a static magnetic field.

Figure 2: Creation of Left Atrial Voltage Map

A LA electroanatomic map (A) was created using the Ensite NavX system (St Jude Medical), then integrated with the segmented left atriogram obtained by CMR (B). A second LA map color-coded for tissue voltage was then created during distal CS pacing at 600 ms (C). Points were acquired evenly throughout the LA body. The pulmonary veins and LA appendage were excluded. PA – posterior-anterior, RAO – right anterior oblique, LSPV – left superior pulmonary vein, LIPV – left inferior pulmonary vein, RSPV – right superior pulmonary vein, RIPV – right inferior pulmonary vein, LS – left septal region.

Figure 3: Intra- and Inter-observer Correlation and Agreement for Atrial T_1 Time

Linear regression (A) and Bland-Altman plot (B) for intra-observer atrial T_1 times (R^2=0.95, p<0.001; mean bias 1, 95% limits -21 to 24). Linear regression (C) and Bland-Altman plot (D) for inter-observer atrial T_1 times (R^2=0.93, p<0.001; mean bias 1, 95% limits -27 to 28). For all graphs, n=30 (10 controls, 10 PAF subjects, and 10 PeAF subjects).

Figure 4: Post-contrast Atrial T_1 Times and Voltage Indices

Atrial T_1 time correlated positively with mean septal voltage (n=23, R^2=0.48, p<0.001) (A) and mean LA voltage (n=23, R^2=0.41, p<0.001) (B). Atrial T_1 time differed between all groups (307±39 vs 260±31 vs 240±31 ms, p<0.001) (C).

Figure 5: Freedom from Recurrent Atrial Arrhythmia by Atrial T_1 Time

Kaplan Meier analysis demonstrated freedom from recurrent atrial arrhythmia was greater in patients with atrial T_1 time above versus below 260 ms (96% vs 68%, p<0.05).

Tables

Table 1: Subject characteristics

	Control (n=20)	Paroxysmal AF (n=71)	Persistent AF (n=41)	p value
General characteristics				
Age, years	54±13	58±10	57±11	0.45
Male gender, n (%)	13 (65)	52 (74)	34 (83)* †	<0.05
Body mass index, kg/m^2	24±3	28±4*	28±4*	<0.01
Resting heart rate, beats/min	54±26	66±15	69±16	0.10
Estimated GFR, ml/min	91±15	91±13	87±17	0.85
Hematocrit, L/L	0.42±0.03	0.42±0.04	0.41±0.09	0.81
CHA_2DS_2–Vasc Score	-	1.1±1.1	1.3±1.1	0.23
Co-morbidities, n (%)				
Congestive heart failure	-	5 (7)	14 (34)†	<0.001
Coronary artery disease	-	8 (11)	6 (15)	0.69
Diabetes	-	1 (1)	1 (2)	0.51
Hypertension	-	23 (32)	14 (31)	0.85
Medications, n (%)				
ACE-inhibitor	-	22 (31)	22 (54)†	<0.05
Aldosterone antagonist	-	0 (0)	3 (7)	<0.05
β-blocker	-	42 (60)	30 (73)	0.16
Antiarrhythmics failed	-	1.5±0.7	1.3±0.6†	0.36
CMR findings				
LA size, cm^2	22±4	25±6	30±7*†	<0.001
LV EF, %	63±4	60±7	56±10*†	<0.01
LV EDV index, ml/m^2	83±12	77±23	86±17	0.12
LV mass index, g/m^2	54±13	53±14	56±19	0.18

*Significant difference compared to the control group. †Significant difference compared to the paroxysmal group.

Table 2. Relationship Between Atrial T_1 Time and Subject Characteristics Among Controls

	Univariate model		
	F	R^2	p value
Age, years	0.09	0.01	0.76
Male gender	0.00	0.00	0.99
Body mass index, kg/m^2	0.79	0.05	0.39
Resting heart rate, beats/min	2.11	0.12	0.17
Estimated GFR, ml/min	0.40	0.53	0.53
Hematocrit, L/L	0.03	0.00	0.86

Simple linear regression revealed no significant predictors of atrial T_1 time among subject characteristics for healthy controls (n=20).

Table 3: Predictors of Atrial T_1 Time By Simple and Multiple Linear Regression

	Univariate Model			Multivariate Model			
	F	R^2	p value	B	SE B	β	p value
Age, years	7.21	0.05	<0.01	-0.67	0.33	-0.16	<0.05
Male gender	0.06	0.00	0.80	-	-	-	-
Body mass index, kg/m^2	8.61	0.06	<0.01	-1.24	0.84	-0.15	0.14
Resting heart rate, beats/min	1.17	0.01	0.28	-	-	-	-
Estimated GFR, ml/min	0.00	0.00	0.96	-	-	-	-
Hematocrit, L/L	0.63	0.01	0.43	-	-	-	-
CHA_2DS_2–Vasc Score	2.43	0.02	0.12	-	-	-	-
Congestive heart failure	0.95	0.01	0.33	-	-	-	-
Coronary artery disease	0.34	0.00	0.56	-	-	-	-
Diabetes	0.59	0.00	0.44	-	-	-	-
Hypertension	0.39	0.00	0.53	-	-	-	-
Any AF	32.14	0.20	<0.001	-42.07	11.15	-0.33	<0.001
Persistent AF	7.02	0.05	<0.01	-2.68	7.85	-0.03	0.73
AF duration, years	6.72	0.06	<0.05	-1.59	0.61	-0.21	<0.05
LA size, cm^2	2.03	0.02	0.16	-	-	-	-
LV EF, %	5.03	0.04	<0.05	0.66	0.45	0.12	0.15
LV EDV index, ml/m^2	1.91	0.02	0.15	-	-	-	-
LV mass index, g/m^2	0.41	0.41	0.52	-	-	-	-

Predictors of atrial T_1 time determined using simple and multiple linear regression (n=132, enter method). Categorical variables were entered into analyses using dummy coding. Univariate predictors with P values of <0.1 were entered into the multivariate model yielding age, a diagnosis of AF, and AF duration as independent predictors ($F=9.69$, $p<0.001$).

Table 4: Procedural characteristics

	Paroxysmal AF (n=71)	Persistent AF (n=41)	p value
Procedure duration, min	165±32	186±36	<0.05
Fluoroscopy time, min	26±10	28±9	0.17
Radiation dose, mGy/cm^2	41922±29938	64987±47139	<0.05
Total ablation time, min	41±12	46±12	0.06
PV isolation, n (%)	71 (100)	41 (100)	1.0
Roof line ablation, n (%)	0 (0)	41 (100)	<0.001
Cavotricuspid isthmus ablation, n (%)	5 (7)	2 (5)	0.90
Intraprocedural DCR, n (%)	14 (21)	25 (64)	< 0.001
Acute reconnection, n (%)	26 (40)	7 (18)	<0.05
Freedom from AF at follow up, n (%)	13 (18)	16 (39)	<0.05
Second ablation procedure, n (%)	6 (9)	7 (17)	0.17

Table 4: Patient characteristics by arrhythmia recurrence at follow-up

	Patients free of arrhythmia recurrence (n=83)	Patients with arrhythmia recurrence (n=29)	p value
Age, years	57±11	59±10	0.34
Male gender, n (%)	66 (80)	20 (71)	0.38
Paroxysmal AF, n (%)	58 (70)	13 (45)	<0.05
AF duration, years	4.6±5.8	6.8±6.5	0.09
Mean heart rate, beats/min	66±15	70±15	0.20
Estimated GFR, ml/min	91±14	87±15	0.21
Body mass index, kg/m^2	28±4	29±5	0.70
Hypertension, n (%)	24 (29)	13 (45)	0.12
Congestive heart failure, n (%)	11 (13)	8 (28)	0.08
Coronary artery disease, n (%)	10 (12)	4 (14)	0.81
LA size, cm^2	26±7	28±5	0.09
LV EF, %	59±8	56±8	0.10
LV EDV index, ml/m^2	82±23	79±16	0.24
LV mass index, ml/m^2	54±15	56±16	0.89
Atrial T_1 time, ms	245±42	216±32	<0.01
Procedure duration, min	171±33	178±39	0.39
Total ablation time, min	42±12	46±14	0.20
Acute reconnection, n (%)	26 (33)	7 (28)	0.62

Table 5: Univariate and Multivariate Predictors of Freedom from Recurrent Atrial Arrhythmia

	Univariate			Multivariate		
	F	R^2	p value	B	SE B	p value
Age, years	0.91	0.01	0.34	-	-	-
Male gender	0.78	0.01	0.38	-	-	-
AF category (persistent)	6.02	0.05	<0.05	-1.12	0.54	<0.05
AF duration, years	2.93	0.03	<0.10	-0.08	0.05	0.13
Body mass index, kg/m^2	3.45	0.03	<0.10	-0.08	0.06	0.19
Coronary artery disease	0.06	0.00	0.81	-	-	-
Congestive heart failure	3.17	0.03	<0.10	0.64	0.73	0.38
Hypertension	2.47	0.02	0.12	-	-	-
Diabetes mellitus	0.70	0.01	0.40	-	-	-
LA size, cm^2	2.00	0.02	0.16	-	-	-
LV EF, %	2.79	0.02	<0.01	-0.01	0.04	0.80
LV EDV index, ml/m^2	0.33	0.00	0.57	-	-	-
LV mass index, g/m^2	0.19	0.00	0.66	-	-	-
Atrial T_1 time, ms	11.50	0.09	<0.01	0.02	0.01	<0.05
Procedure duration, min	0.75	0.01	0.39	-	-	-
Total ablation time, min	1.69	0.02	0.19	-	-	-
Acute Reconnection	1.24	0.00	0.62	-	-	-

Predictors of freedom from recurrent arrhythmia following AF ablation were determined using binary logistic regression (n=112). Univariate predictors with p values of <0.1 were entered into the multivariate model which yielded AF category and atrial T_1 time as independent predictors (adjusted R^2=0.29, p<0.01).