Acute Pulmonary Vein Isolation Is Achieved by a Combination of Reversible and Irreversible Atrial Injury Following Catheter Ablation: Evidence from Magnetic Resonance Imaging

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Aruna Arujuna, MBChB, MRCP1,2; Rashed Karim, PhD1; Dennis Caulfield, MBBS, MRCP1,2; Benjamin Knowles, PhD1; Kawal Rhode, PhD1; Tobias Schaeffter, PhD1; Berret Kato, PhD1; C. Aldo Rinaldi, MD, FRCP1,2; Michael Cooklin, MD, FRCP2; Reza Razavi, MD, FRCP1,2; Mark D. O’Neill, MRCP, Dphil, FHRS1,2; Jaswinder Gill, MD, FRCP1,2

1Division of Imaging Sciences & Biomedical Engineering, King’s College London; 2Dept of Cardiology, Guy’s and St. Thomas’ NHS Foundation Trust, London, United Kingdom

Correspondence:
Dr. Jaswinder Gill
Division of Imaging Sciences & Biomedical Engineering
The Rayne Institute, Lambeth Wing
St. Thomas’ Hospital
Lambeth Palace Road
London SE1 7EH, United Kingdom
Tel: +44 207 1881056
Fax: +44 207 1881011
E-mail: jaswinder.gill@gstt.nhs.uk

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Some of the data in this manuscript were presented in oral and poster abstract form at the Heart Rhythm Society sessions in 2011.
Abstract:

**Background** - Pulmonary vein reconnection following pulmonary vein isolation (PVI) is common and usually associated with recurrences of AF. We used cardiac magnetic resonance (CMR) imaging following radiofrequency (RF) ablation to investigate the hypothesis that acute PVI results from a combination of irreversible and reversible atrial injury.

**Methods and Results** - Delayed enhancement, (DE, representing areas of acute tissue injury/necrosis) and T2-weighted (representing tissue water content including edema) CMR scans were performed - pre, immediately post (acute) and later than 3 months (late) following PVI in 25 patients with paroxysmal AF (PAF) undergoing wide area circumferential ablation. Images were analyzed as pairs of pulmonary veins (PVs) to quantify the percentage circumferential antral encirclement composed of DE, T2 and combined DE&T2 signal. 14/25 patients were AF free at 11 months follow up (IQR 8 to 16 months). These patients had higher DE (71±6.0%) and lower T2 signal (72±7.8%) encirclement on the acute scans compared to recurrences (DE 55±9.1%, T2 85±6.3%, p<0.05). Patients maintaining sinus rhythm had less decline in DE between acute and chronic scans compared to recurrences (71±6.0% and 60±5.8 vs 55±9.1% and 34±7.3% respectively). The percentage encirclement by a combination of DE&T2 was almost similar in both groups on the acute scans (AF free 89±5.4%, recurrences 92±4.8%) but different on the chronic scans (60±5.7% v 34±7.3%).

**Conclusions** - The higher T2 signal on acute scans and greater decline in DE on chronic imaging in patients with recurrences suggests they have more reversible tissue injury, providing a potential mechanism for PV reconnection resulting in arrhythmia recurrence.

**Key words:** ablation; atrial fibrillation; magnetic resonance imaging; pulmonary vein reconnection; reversible tissue injury
Introduction

Paroxysmal atrial fibrillation (AF) is often triggered by spontaneous ectopic beats of pulmonary venous origin,\(^1\) an observation which has led to the emergence of pulmonary vein isolation (PVI) as an effective treatment for AF. Typically, ablation is performed at the left atrial-pulmonary vein (LA-PV) junction,\(^2, 3\) with the intention of causing acute tissue necrosis to eliminate conduction between the LA and PVs. Clinical recurrences of AF following catheter ablation are common and recovery of LA-PV conduction ubiquitous in patients with and without documented AF during follow-up.\(^4\) Single procedure success rates are modest, suggesting that the factors which contribute to acute PVI are not well understood.\(^5\)

Delayed enhancement MRI following the administration of gadolinium has been used extensively to image ventricular scar after myocardial infarction secondary to coronary occlusion.\(^6\) More recent work has demonstrated the potential utility of cardiac magnetic resonance imaging (CMR) for assessment of atrial fibrosis prior to ablation and of atrial injury following ablation.\(^7, 8\) Although gadolinium diffuses into the intracellular space following the loss of cell membrane integrity associated with acute tissue destruction, it can also accumulate acutely in the increased extracellular space created by myocardial edema, which may represent a reversible form of cardiac injury and is therefore not specific to necrotic tissue.\(^9\) An alternative method to visualize myocardial edema uses the linear relationship between T2 relaxation time and myocardial water content, and may be a more sensitive in-vivo marker of myocardial edema than DE MRI.\(^10\)

The aim of the study was to use DE- and T2-weighted CMRI to characterize the tissue effect of left atrial ablation and to relate the pattern of acute atrial injury to clinical outcome. We hypothesize that acute PVI is caused by a combination of irreversible tissue destruction and
reversible tissue injury at the LA-PV junction.

**Methods**

**Patient population**

Twenty-five patients (17 male, mean age 55±11 years) with symptomatic, drug refractory paroxysmal AF undergoing their first PVI completed the study. 29 patients were consented for the study but four were excluded (3 because of claustrophobia with failure to complete scan and 1 due to an ineffective respiratory navigator). All scans used for the purposes of data analysis were deemed of adequate quality for analysis by an experienced CMR operator. Therapeutic anti-coagulation with an INR >2 for at least 4 weeks prior to the procedure was mandated. The study was approved by the Local Research Ethics Committee.

Acute procedural success was defined as PVI confirmed using a circumferential mapping catheter. Clinical outcomes are reported at 6 months follow-up. Patients were followed in clinic to assess symptoms. 24 hour Holter monitors were performed at 6 months. Every effort was made to obtain ECG recordings of symptomatic recurrences. Recurrences were defined on the basis of 1) symptoms with ECG evidence of the presence of atrial fibrillation/flutter/tachycardia or 2) the presence of symptomatic or asymptomatic episodes of atrial arrhythmia lasting for >30 seconds on ambulatory cardiac monitoring.

**MR Image acquisition**

All participants underwent MR imaging in a 1.5 Tesla Philips Achieva MR system (Philips Healthcare, Best, Netherlands) using either a 32 channel surface coil (Invivo, Orlando, Florida, USA) or a large two-channel flex coil.

T2-weighted images were acquired using a multi-slice Turbo Spin Echo (TSE)
acquisition technique with a double inversion recovery (DIR) pre-pulse for black-blood imaging. Spatial pre-saturation with inversion recovery (SPIR) fat suppression was applied. The echo time used was set at 120ms with a linear profile ordering. This enabled the image resolution to be set at 1.5x1.5mm² with a slice thickness of 5mm. The number of slices was set to provide complete coverage of the left atrium (20-25 slices). Diaphragmatic motion was tracked and respiratory motion correction applied to minimize motion blurring and differences in respiratory phase between slices during image acquisition.

In order to visualize DE, a 3D ECG-triggered, free-breathing inversion recovery (IR) turbo field echo (TFE) scan with respiratory navigator motion correction was performed with a pixel resolution of 1.3x1.3x4mm³, which was then reconstructed to 1.3x1.3x2mm³. Data were acquired at mid-diastole with a 150ms acquisition window and a low-high k-space ordering as well as SPIR fat suppression. The IR delay time was determined from a Look-Locker sequence and was set at a TI intermediate between the optimal TIs to null myocardium and blood. Previous work has validated this method for reproducible visualization of the late enhancement signal from necrotic tissue. DE scans were performed 20 minutes following contrast agent administration. The number of slices was set for complete atrial coverage (30-40 slices). To optimize visualization of the PVs, slice orientation was performed in the four-chamber view. Images obtained with this method appear to reflect the pulmonary veins at their maximal size. Similar MR sequences were used for images acquired (i) prior to ablation, (ii) within 24 hours of ablation and (3) 3-6 months following ablation.

Ablation procedure

A 6F decapolar catheter was placed in the coronary sinus to provide a reference for electroanatomic mapping and to enable LA pacing. Two transseptal punctures were made and
access to the left atrium was obtained using 8.5Fr non-deflectable long sheaths, (St. Jude Medical Inc., St. Paul, MN, USA). Following the first transseptal puncture, intravenous heparin was administered to achieve an activated clotting time of between 300 and 400 seconds. A 3-dimensional geometry of the left atrium was created using either NavX™ (St. Jude Medical Inc., St. Paul, MN, USA) or CARTO XP (Biosense Webster Inc., Diamond Bar, CA, USA). A circular mapping catheter (Inquiry™Optima™, St. Jude Medical Inc.) was then placed in each pulmonary vein in turn while the corresponding LA-PV antrum was targeted with wide area circumferential ablation. Energy was delivered through a NaviStar® ThermoCool® 3.5 mm irrigated tip catheter (Biosense Webster Inc., Diamond Bar, CA, USA) with flow limited to 17 ml/min, power limited to 30 W on the anterior wall and 25 W on the posterior wall and temperature limited to 50°C. Ablation lesions were marked on the LA geometry when there had been an 80 % reduction in the local electrogram voltage or after 30 seconds of energy delivery. One tag was applied to the shell per 30s RF energy delivery and a standard tag size was used throughout the study. If LA-PV conduction persisted despite wide area circumferential ablation, additional lesions were delivered along the original ablation line at sites of earliest activation on the circular mapping catheter until entry block in all 4 veins was confirmed by observing the elimination or dissociation of pulmonary vein potentials. Exit block was not routinely assessed. Neither adenosine nor isoprenaline was routinely administered to test the integrity of PVI or to search for non-PV triggers of AF.

**Image processing, analysis and its validation**

Using CMR, this study sought to quantify the extent of PV antral encirclement as demonstrated by DE- and T2-weighted CMRI, individually and combined. To achieve this, an automated 3D method (Figure 1) for visualizing and quantifying myocardial injury (Figure 2) following
Ablation was used which has previously been described in detail.11

All 3D-MR reconstructions were analyzed independently twice by two experienced readers, blinded to clinical outcome and to the timing of the scan following catheter ablation. T2 and DE signal circumferential quantification was performed by reconstructing all CMR scans into individual left atrial shells (figure 3). PVs were analyzed as ipsilateral pairs for each of the 25 patients at three time points, permitting analysis of 150 PV pairs. For each PV pair, T2 and DE was quantified as occupying a percentage of the antral circumference. Percentage delayed gadolinium enhancement (DE), high T2-weighted signal (T2) and combination of delayed gadolinium enhancement and T2 (DE+T2) encircling the pulmonary veins was determined independently by both readers and consensus reached. A high degree of interobserver agreement was seen on a Bland Altman test with a maximum observed difference of 10% seen. The mean±SD inter-observer error for DE, T2 and DE&T2 was 1.5±2.5%, 1.5±3.5% and 0.8±2.2% which was acceptable for the purposes of data analysis.

**Statistical analysis**

Summaries for continuous variables are expressed as mean ± confidence interval. Follow-up times are reported as the median and interquartile range (IQR). Categorical variables were compared among recurrences and non-recurrences groups using a chi-square test. The % circumferential encirclement by DE, T2 and DE&T2 groups were compared to test for differences between group means. Statistical analyses were performed using Stata (StataCorp 2009). A linear regression model with predictor (code 1 for no recurrence and 0 for recurrence) and outcome T2, DE, T2&DE, DE/(T2&DE) respectively was applied and run in Stata. We used the vce (cluster subject) option in Stata12 to allow for inter-subject dependence (left and right pulmonary vein measurements from the same patient). Analyses for acute and chronic
pulmonary vein findings on cardiac MR were performed separately. A p value of less than 0.05 was considered statistically significant.

Results

Patient and procedural data

Table 1 outlines the baseline study population demographics. Successful pulmonary vein isolation was achieved in all patients. Median follow up time was 11 months (IQR 8 to 16 months). A three month blanking period was observed during which arrhythmia recurrences were treated with antiarrhythmic drugs or DC cardioversion. No repeat ablation was performed within the blanking period. Clinical recurrence of AF was documented in 11 (46%) patients with a median time to recurrence of 94 days (IQR 45 to 166 days). Patients with recurrences had significantly larger LA size and longer duration of AF. Seven of 11 patients with recurrences underwent a re-do procedure; two patients are awaiting a redo procedure and two declined further intervention. Procedural complications include two femoral venous haematoma which did not require intervention. No stroke, tamponade or oesophageal fistula occurred in this study. The absence of both turbulence on MR angiography and luminal narrowing in comparison to the pre-scans confirmed no pulmonary vein stenosis on follow-up MRI scans.

Pre-ablation MRI

The circumferential burden of DE and T2 weighted signal detected prior to any ablation, was low in comparison with acute post-ablation imaging (figure 2). And did not occupy more than 5% of the PV circumference. Median time of image acquisition in relation to the procedure was 3 days (IQR 1 to 10 days). Pre-ablation DE signal localised to the mitral annulus, a common finding due to the fibro-elastic nature of cardiac tissue at this site. T2 signal was largely observed
around the atrial roof and this is likely explained by the imperfections arising from the MR-sequence. In Black-Blood sequence, residual bright blood signal is observed in areas of slow through-plane flow (e.g. in the apex of the ventricles). This problem has been reported in acute edema assessment in the ventricles following acute myocardial infarction. Overall the amount of T2 signal pre-ablation was very small.

**Post-ablation MRI**

All acute imaging was performed between 18 and 24 hours following catheter ablation. Figure 2 demonstrates the typical T2-weighted (figure 2A) and DE (figure 2B) appearances in two patients before and after catheter ablation. The left atrial burden of DE and T2-weighted signal was significantly increased following catheter ablation in comparison with baseline (figure 2). On the acute scans, DE signal was concentrated in the PV antral region while T2 signal was more widely distributed in the atrium, remote from sites of ablation.

Individual analysis of the circumferential extent of both signal types revealed that T2-weighted signal occupied 100% of the antral circumference in 5/50 PV pairs while DE signal did not achieve complete encirclement of any vein pair. There was no significant difference between the circumferential extent of DE signal around the LPVs (mean and CI 65%; 56.4 - 73.6%) and the RPVs (63%; 55.4 - 70.6%, p=0.67). Similarly, although the circumferential extent of T2 signal was greater, there was no significant difference between LPVs (75%, 66.6 - 83.4%) and RPVs (80%; 73.0 - 87.0%, p=0.31).

Combined analysis of DE and T2 signal, using reconstructed shells co-displaying both signal types, revealed areas of T2 enhancement to overlap and interdigitate with those areas of high DE signal intensity (figure 3). Hence the sum of DE and T2 is 100% or less. For the LPVs, the circumferential extent of DE signal, T2 signal and the combination of both signal types was
65% (56.4-73.6%), 75% (66.6 -83.4%) and 90% (86.1 - 94.9%) respectively. For the RPVs, the circumferential extent of DE signal, T2 signal and the combination of both signal types was 63% (55.4 – 70.6%), 80% (73.0 – 87.0%) and 92% (86.4 -97.6%) respectively. Compared to DE alone, the combined DE and T2 signal was significantly greater for both left (p=0.009) and right (p=0.027) PVs. Complete antral encirclement with combined DE and T2-weighted signal was seen in 17/50 (34%) PV pairs at the acute scan.

At the chronic follow up scans, T2 signal had largely resolved (figure 4), while a decline in the extent of DE signal was seen. For the LPVs, the circumferential extent of DE signal decreased from 65% (56.4-73.6%) to 51% (42.8 - 59.2%, p=0.016); for the RPVs, the circumferential extent of DE decreased from 63% (55.4 – 70.6%) to 46% (37.5 - 54.5%, p=0.002). Discontinuities in areas of DE signal could be seen.

**Recurrences of AF: relationship to MR assessment**

Both acute and late scan data were analysed into two groups according to the respective clinical outcome – those with and without AF recurrences. 100 pairs of PVs (50 acute, 50 late) analysed previously were divided into two groups according to the presence or absence of a clinical recurrence of AF. Figure 5 summarises the percentage circumferential encirclement of DE, T2-weighted signal and the combination of DE &T2 around the left and right PV pairs by clinical outcome for both the acute and late scans.

On the acute scans, there was no difference in the combined DE&T2 signal between both groups with mean % encirclement of 89% (83.6 -94.4%) - no recurrences and 92% (87.2 -96.8%) - recurrences. When DE signal was analyzed, a significantly higher mean percentage encirclement was noted in the AF free group (n=14; 28 pairs of PVs) compared to the group with recurrences (means and CI, 71%; 65.0-77.0% vs 55%; 45.9 -64.1% respectively, p = 0.016).
Conversely, the T2 signal was noticeably lower in the AF free group compared to the group with recurrences (means and CI, 72%; 64.2 -79.8% vs 85%; 78.7 - 91.3% respectively, p = 0.038). With the combined areas of DE & T2 forming almost complete rings around the pulmonary veins, ratios of DE to (DE & T2) were calculated (figure 6). Patients with no recurrences had a higher mean DE/(DE&T2) ratio compared to the recurrence group (0.82±0.12 vs 0.58±0.20; p=0.0001).

On the late scans, DE was the predominant signal type seen and was significantly greater in the AF free group compared to the group with recurrences (means and CI 60%; 54.3 -65.7% vs 34%; 26.7 -41.3% respectively, p <0.0001). A comparison of the acute and late scan DE data in both groups showed a lower regression of this signal type in the AF free group (means and CI from 71%; 65.0- 77.0% to 60%; 54.3 -65.7%, p=0.03) relative to the group with arrhythmia recurrences (means and CI from 55%; 45.9 -64.1% to 34%; 26.7 -41.3% p=0.01).

Discussion

The findings of this paper are: (1) Acute pulmonary vein isolation is not associated with complete circumferential injury as determined by cardiac MR imaging performed at a median of 20 hours post ablation; (2) Increased DE and T2-weighted signal are both seen within 24 hours of left atrial catheter ablation; (3) T2-weighted signal has largely resolved by 3 months of follow-up, supporting its use as a marker of acute, reversible atrial injury; (4) In patients with clinical recurrences, a greater proportion of the acute circumferential antral injury is accounted for by T2-weighted signal than in those patients who remain arrhythmia-free.

Previous work evaluating the role of CMR in LA assessment post catheter ablation has focused on delayed enhancement imaging delineating areas of scar pre and post ablation. 7, 8, 14, 15
However MR imaging of acute, reversible atrial injury following catheter ablation has only been recently reported. There is evidence from animal studies that tissue edema causes right atrial wall thickening following linear ablation in the right atrium. Left atrial edema most likely occurs during and immediately after AF ablation as evidenced by an increase in atrial wall thickness, and resolves within one month. During late-gadolinium MRI performed immediately after ablation, both non-enhancing and hyper-enhancing tissue types are seen, the former of which is a poor predictor of scar visualized at 3 months follow up. This is likely to reflect ablated but not necessarily necrotic tissue confirming previous work, including that from our own laboratory, that DE MRI overestimates the acute extent of tissue injury following left atrial catheter intervention by virtue of the accumulation of gadolinium in extravascular water associated with acute inflammation. Although there is a good correlation between endocardial voltage-defined scar and T2 weighted signal immediately post ablation, there is a poor correlation with the DE MRI-defined scar at three months follow up, further supporting the transient nature of at least part of the ablation injury process.

T2 signal was found in the acute CMR scans remote form the ablation sites. Similar observations have previously been described. This is most likely related to a cytokine (IL-6) mediated inflammatory response following radiofrequency ablation. Another possible mechanism giving rise to this observation may be related to sheer/rotational force of the catheters against the atrial wall during catheter manipulation.

**Acute PVI and atrial ablation injury**

The data presented in this paper demonstrate a high circumferential extent of each of T2 and DE signal within 24hours of ablation. While this is consistent with a high degree of overlap of the two imaging signal types, there are also some areas where T2 signal can be detected in the
absence of DE signal and vice versa (figure 3). By overlaying DE and T2 weighted images on the same anatomical shell, we have demonstrated that the circumferential extent of ablation injury is greater when both signal types are summated, reaching approximately 90% (figure 4). Although 100% circumferential extent of combined T2 and DE signal was seen in only 17 of 50 PV pairs, it is well known that acute PV isolation can be achieved using a segmental, electrogram-guided approach rather than a circumferential ablation approach, the former of which does not necessarily result in ablation of the entire PV circumference.\textsuperscript{22} This may explain the finding that PV isolation can be readily achieved without circumferential MR evidence of ablation injury.

**Atrial scar and arrhythmia recurrence**

The MR data at the follow up scan demonstrate near-abolition of T2 signal while DE signal is reduced and continues to occupy only 60% of the circumferential extent of both pairs of pulmonary veins. This is in keeping with the finding that chronic pulmonary vein reconnection is ubiquitous following conventional wide area circumferential ablation and indeed was seen in all AF recurrences in this paper.\textsuperscript{4, 23} In the present study, a greater extent of circumferential DE signal at the 24h scan was predictive of freedom from AF (figures 4 and 5) while the extent of T2 signal was greater in the arrhythmia recurrence group. While there is a lack of clarity of what DE and T2 signals truly represent in the immediate aftermath of a catheter ablation procedure, the presence of DE signal beyond three months follow-up is likely to represent permanent atrial scar.\textsuperscript{17, 24}

The formation of scar following ablation and its representation by DE and T2 sequences is not completely understood. However there are some similarities with findings of DE signal observed in serial CMR imaging (acute and late) following acute myocardial infarction (MI)
with regression of delayed enhancement areas over time. From this small sample of 25 patients, we can qualitatively say that DE regions generally become more distinct and smaller with time but that T2 regions did not predictably become regions of DE, although there is some overlap. Recognizing this as a hiatus in our knowledge of atrial characterization by MR, an animal study is underway to investigate further the temporal course of atrial injury / scar following catheter ablation.

The decline in circumferential extent of DE signal between acute and follow up scans was less for patients with no AF recurrence than for those patients in whom AF recurred. This supports our hypothesis that the greater the contribution of T2 signal, representing reversible injury, to acute PVI, the higher the likelihood of PV reconnection following resolution of tissue edema.

Although preliminary work has demonstrated a qualitative correlation between discontinuities in areas of high DE signal and conduction gaps on electrophysiology study \(^8,25\), pulmonary vein reconnection also occurs in patients without clinical arrhythmia recurrence \(^26\) and therefore caution must be exercised in relying on the use of MR-defined scar as a surrogate for electrophysiological reconnection.

**Potential Clinical Significance**

It has been previously shown that durable radiofrequency lesion formation is dependent on parameters including catheter tip electrode size, power, catheter tip temperature and contact force. The presented data suggest that there is an element of reversible myocardial injury during ablation. Ablation strategies and techniques which favourably alter the necrosis/edema ratio such as alternative energy sources, contact pressure sensing and improved catheter stability may minimise reversible myocardial injury.
Study limitations

There are significant limitations to MR imaging of the left atrium following catheter ablation with no widely accepted standardisation of technique between laboratories.

Whilst there is evidence from animal studies that gadolinium is predominantly a marker for tissue necrosis, by virtue of its kinetics, it also accumulates in extracellular water which is also seen in acute inflammation. In addition, while T2 MRI can preferentially represent myocardial edema, there is currently no robust histological evidence corroborating this in the atria following radiofrequency ablation.

Although the DE and T2 signal recorded acutely following ablation almost certainly include some “double counting” of edema and necrosis by both techniques, the near complete resolution of T2 signal at follow up indicates that at the very least, T2 predominantly represents some form of reversible atrial injury.

The annotation of lesions on an electroanatomic map is subjective and likely does not accurately reflect the site of atrial injury, which may explain in part the unanticipated MR finding of PV encirclement in only 36% of PV pairs. We attempted to mitigate this by using a point-by-point technique, with RF applications of 30 seconds and 1 tag per application.

Detection of asymptomatic recurrences of AF without the use of continuous monitoring is impossible. Because of the frequency of monitoring, it is likely that the incidence of asymptomatic AF is underreported in the current study.

This is a small, hypothesis-generating study and the utility of necrosis and edema imaging as a predictor of longer-term clinical outcome would require a larger study for validation.
Conclusion

Acute pulmonary vein isolation is achieved by a combination of reversible and irreversible circumferential tissue injury at the PV-LA junction. The greater the ablation extent accounted for by reversible injury, the higher is the incidence of AF recurrence.

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Conflict of Interest Disclosures: None.

References:


**Table 1.** Patient demographics categorized into no recurrences and recurrences at 6 month clinical follow-up.

<table>
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<th>AF Recurrence n=11</th>
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<td>11(78%)</td>
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<td>8(33%)</td>
<td>3(22%)</td>
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<td>Duration of AF, months</td>
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<td>18±10 (12-48)</td>
<td>30±11 (18-60)</td>
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<td>&gt;0.10</td>
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<td>Atrial Flutter</td>
<td>5(20%)</td>
<td>2(14%)</td>
<td>3(27%)</td>
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</table>

AF, atrial fibrillation; LA, left atrium; LVEF, left ventricular ejection fraction

**Figure Legends:**

**Figure 1** (a) Raw MR scan image of the LA and PVs showing areas of delayed enhancement. (b) Fusion of the MR derived 3-D LA shell into the delayed-enhancement image. The red arrows indicate the direction in which the maximum intensity projection (MIP) is taken. (c) Projection of the MR signal intensities onto the surface shell. The surface shell colour is set within a range going from green to yellow to red corresponding with low to high signal intensity. (d) 3-D colour LA shell harvested from the delayed-enhancement MR image.

**Figure 2** Figure 2a demonstrates a series of T2 signal images of the left atrium and pulmonary veins in two patients with arrows pointing towards regions of hyper-enhancement in column 2.
Baseline images in the first column show no significant T2 enhancement (tissue edema) compared to the acute post ablation images in the second column. The late scans in the third column shows the T2 signal becoming almost similar to baseline in the pre-ablation scans in column one. Figure 2b demonstrates a series of DE images of the left atrium and pulmonary veins in 2 patients with arrows pointing towards regions of hyper-enhancement in both columns 2 and 3. Baseline images in the first column show no significant DE signal (tissue injury/necrosis) compared to acute post ablation images in the second column. The late scans in the third column shows that areas of DE signal become less diffuse and more defined with sharper borders in comparison to the acute scans.

Figure 3 Figure 3a and 3b demonstrate a series of reconstructed 3-D left atrial shells to visualise T2 and DE signal in the patients shown in figure 2. The 3 columns represent the 3 time points: pre-procedure scans (prescans, column 1), acute post procedure scans performed within 18 to 24 hours (column 2) and the late scans performed later than 3 months (column3). Quantification of these enhancements was performed as percentage encirclements of the left and right PV antra. Row A depicts the raw intensities mapped on to the shells from the T2 and DE MR scans. Row B shows the corresponding T2 and DE 3-D shells that have been thresh-holded semi-automatically. Red areas signify delayed-enhancement and blue areas signify T2 signal intensity. In row C, the combined enhancements of T2 and DE is seen together. On the acute scans seen in column 2, gaps present within areas of red (DE) are filled in by areas of blue (T2). In column 3, the blue (T2) and red (DE) signals resolve, with a greater effect seen for T2 versus DE signal. Figure 3c displays the electroanatomical maps in relation to the corresponding acute and late post procedure 3-D left atrial shell for the two patients.

Figure 4 This scatter-boxplot shows a comparison of pre, acute and late T2, DE and combined T2&DE for both left and right pulmonary vein antrum. Each individual scatter plot represents the raw data for that specific group. The dots within each group have been dispersed horizontally to optimise visualisation and clarity. The boxplots on the other hand represent median (red line), 95% confidence intervals (yellow box) and 1 standard deviation (blue box) An overall higher enhancement is seen in all 6 groups on the acute scans compared to the 6 groups on the chronic scans. The % encirclement by T2 signal diminishes from above 75% to about 5% in keeping
with reversible injury. The % encirclement by DE signal diminishes to a much lesser extent. Using a combination of DE and T2 signal, the % encirclement decreases from 90% at the acute scans to approximately 50% at the follow up scan.

**Figure 5** This scatter-boxplot shows a comparison of percentage of PV encirclement according to clinical outcome no recurrence (NR) v recurrence (R) of AF accounted for by T2 signal, DE signal and combined T2&DE at three time points: pre-ablation (Pre) immediately post (Acute) and follow up scans (Late). Each individual scatter plot represents the raw data for that specific group. The dots within each group have been dispersed horizontally to optimise visualisation and clarity. The boxplots on the other hand represent median(red line), 95% confidence intervals (yellow box) and 1 standard deviation (blue box). The absolute decline in DE is less for patients with no AF recurrence.

**Figure 6** Mean DE/T2&DE ratios quantified on the acute scans for patients with no recurrences versus those with recurrences. An overall higher DE/T2&DE ratio is seen in patients free from AF.
3C

A

Acute Scan

Late Scan

B

Acute Scan

Late Scan
25 Patients following 6 months follow up divided into no recurrences and recurrences

- Recurrences
- No Recurrences