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MRI Evaluation of Radiofrequency, Cryothermal, and Laser left atrial lesion formation in patients with atrial fibrillation

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Abstract

Background—Catheter ablation utilizing radiofrequency (RF), Cryothermal (Cryo), or Laser energy is effective for treatment of atrial fibrillation (AF). Late gadolinium enhancement magnetic resonance imaging (LGE-MRI) has been used to estimate the burden of LA fibrosis, but no data exists regarding structural changes following each modality. We sought to compare the baseline to post-procedure change in left atrial (LA) scar burden following RF, Cryo, or Laser ablation for treatment of AF.

Methods—Seventeen patients with AF underwent initial pulmonary vein isolation (PVI) using RF (n=7), Cryo (n=5), and Laser (n=5). LGE-MRI was performed prior to, at 24 hours and 3 months after PVI.

Results—In a linear mixed-effects model, accounting for intra-patient clustering of data and inter-patient differences in baseline scar, LGE extent was significantly increased at 24 hours post ablation ($+14.6 \pm 1.9\%$ of LA myocardium, $P < 0.001$), and remained stable from 24 hours to 3 months ($+0.12 \pm 1.9\%$, $P = 0.951$). There was no statistically significant difference between the post ablation scar extent among ablation modalities when compared to RF (Cryo $+4.5 \pm 3.0\%$, $P = 0.123$; Laser $-3.2 \pm 3.0\%$, $P = 0.291$). The PV antral LGE intensity was increased by $25.1 \pm 3.8\%$ ($P < 0.001$) 24 hours after ablation and additionally increased by 8.1 ± 3.8 at 3 months ($P = 0.033$).

Conclusions—Radiofrequency, Cryo, and laser ablation result in increased LGE extent and intensity at 24 hours and 3 months post ablation. No statistically significant difference was noted in the extent of fibrosis induced by any modality.

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Keywords

atrial fibrillation; ablation; Imaging; Radiofrequency; Cryothermal; Laser

Introduction

Catheter ablation of atrial fibrillation (AF) utilizing Radiofrequency (RF) or Cryothermal (Cryo) energy for pulmonary vein isolation (PVI) is a commonly performed procedure. Two ablation systems have received US Food and Drug Administration (FDA) approval for AF ablation: the irrigated RF system (Biosense Webster, Diamond Bar, CA) and the Cryoballoon system (Medtronic, Minneapolis, MN). A third ablation modality, utilizing a balloon and infrared Laser (Cardiofocus, Marlborough, MA), is currently undergoing clinical trials as part of an FDA evaluation process.¹

Magnetic resonance imaging (MRI) has been used to estimate the burden of left atrial (LA) fibrosis pre- and post-AF ablation in an effort to improve patient selection, and delineate the amount of scar formation post-ablation.^{2–5} Late gadolinium enhancement (LGE) MRI can detect ablated regions,⁶ with evolution of the pattern and intensity of signal over time likely signifying initial edema followed by scar formation.⁷ Previous studies have demonstrated that AF recurrence during the first year post RF ablation is associated with a lesser degree of LA scarring on 3-dimensional LGE MRI.⁸ In addition scar identified by LGE after initial catheter ablation of AF has been correlated to low-voltage regions on repeat electroanatomic mapping.^{9,10} We sought to compare, for the first time, the pre and post-procedural LA scar size and patterns between RF, Cryo, and Laser based pulmonary vein isolation techniques.

Methods

Study Population

In this prospective study we enrolled 17 patients with symptomatic drug refractory AF referred for PVI at our institution between September 2011 and December 2013. The institutional Review Board approved the protocol and all patients provided written informed consent. Patient information gathered for the purposes of the study was de-identified and protected in compliance with HIPAA regulations.

Pulmonary Vein Isolation

At the time of ablation, patients underwent single (Cryo) or double (RF, Laser) trans-septal puncture using standard techniques. In all patients, the pulmonary veins were isolated in standard fashion using a wide circumferential approach during RF, or per previously established protocols for Cryo or Laser.^{11,12} No one in the Cryo or Laser groups required segmental ablation using an irrigated RF catheter after primary isolation. Upon isolation of the pulmonary veins, catheters and sheaths were removed and the patients underwent follow-up in the usual manner.

MRI

All patients underwent MRI examinations using a 1.5 Tesla (T) Avanto scanner (Siemens, Erlangen, Germany) with a phased array cardiac coil prior to ablation, and at 24 hours, and 3 months post AF ablation. The LGE-MRI images were acquired after a delay time of 20 minutes following the injection of 0.2 mmol/kg of gadolinium contrast (gadopentetate dimeglumine; Bayer Healthcare Pharmaceuticals, Montville, NJ), at an injection rate of 2 ml/s followed by 20 ml saline flush. The LGE-MRI sequence utilized a 3D inversion recovery prepared fast spoiled gradient recalled sequence that is respiratory triggered and navigated, ECG gated, and fat suppressed. The respiratory navigator is positioned on the right hemidiaphragm to limit gating artifacts. The LGE-MRI images are acquired with phase encoding views during LA diastole. The inversion time (TI) was identified with a scout scan (240-300 ms) to maximize the conspicuity of abnormal LA myocardium. Other LGE-MRI parameters included repetition time (TR) 3.8 ms, echo time (TE) 1.52 ms, field of view (FOV) 340 mm, and flip angle (FA) 10 degrees. A parallel imaging technique, Generalized Autocalibrating Partially Parallel Acquisition (GRAPPA), was used to accelerate image acquisition. Only 2 MRI exams were performed during AF (one patient prior to RF and the other prior to Laser ablation) and the remaining were performed during sinus rhythm. Consistent with our prior methodology, the image acquisition protocol was identical in all patients regardless of rhythm.^{5,10}

Image analysis

Images were processed off-line using QMass MR software (Version 7.2, Leiden University Medical Center, Leiden, The Netherlands) and OsiriX imaging software version 5.0.2 (OsiriX Foundation, Geneva, Switzerland). Multiplanar reconstructions (MPR) using axial planes of 3.5mm thickness were prepared from LGE-MRI 3D images. For quantitative scar analysis, manual contours were drawn around the LA epicardium and endothelium on individual MPR axial planes. The LA myocardium in each image plane between the epicardial and the endocardial contours was then divided into 20 circumferential segments and the average image intensities of each segment were obtained. The image intensity ratio (IIR), defined as local atrial myocardial signal intensity divided by the mean blood pool image intensity, was calculated as previously reported.⁴ The IIR was employed to objectively quantify LGE extent and intensity in the entire atrium and in the focused PV antral regions where comparisons were made. The PV antrum was defined as myocardium within 1 cm of the PV-LA junction. Post ablation LGE-MRI images at 24 hours and 3-month post ablation were analyzed in a similar manner. The IIR measures for the entire LA, and for pulmonary vein antra were tabulated as panel data, at each time point, for individual patients. For qualitative 3-D scar visualization, contours from QMass were transferred to OsiriX software. Volume rendering with ray-cast engine with linear table opacity was applied for better visualization of contrast-enhanced tissue. A color look up table mask was applied for better differentiation and was adjusted according to the scar IIR threshold of 0.97 previously validated against bipolar voltage.⁴

Statistical Analysis

Continuous variables are presented as mean $\pm$ standard deviation and categorical data are presented as percentages. Baseline characteristics were compared using analysis of variance, Chi-Squared, or Fisher's exact tests as indicated. To account for intra-patient clustering of data and inter-patient differences in baseline scar, linear mixed-effects regression models, clustered by patient, were used to examine the association of time (with linear spline at 24 hours) and ablation modality with scar extent or PV antral IIR post AF ablation. Statistical analyses were performed using STATA software (version 12; StataCorp, College Station, TX).

Results

Patient Population

Seventeen patients underwent PVI for the treatment of AF in this study. Of these patients, 7 (41.2%) underwent Radiofrequency ablation, 5 (29.4%) underwent Cryo ablation, and 5 (29.4%) underwent Laser ablation. Table 1 describes the baseline characteristics of all patients and of patient groups by energy source. The mean age was 57 ± 9 years and 77% of patients were male. No statistically significant differences in baseline characteristics were noted across groups. At a mean follow up of 6.3 ± 2.3 months, 13 (76.5%) patients remained in sinus rhythm; 5 (71.4%) patients in RF group, 4 (80.0%) in Cryo group; and 4 (80.0%) in laser group.

LA Scar Burden Before and After Pulmonary Vein Isolation

Shown in Figure 1 are representative 3 dimensional images of LA fibrosis at baseline, 24 hours, and 3 months post RF, Cryo, or Laser ablation. The figure illustrates normal myocardium in green and enhanced (scar myocardium) in red, with yellow regions signifying mild enhancement. The extent of atrial enhancement was increased at 24 hours post ablation in a diffuse pattern ($+14.7 \pm 8.1\%$ of LA myocardium, $P < 0.001$). At 3 months, the extent of enhancement was unchanged ($+5.0 \pm 14.3\%$, $P = 0.818$). Laser energy caused focused linear lesions compared to the diffuse lesion sets associated with RF and Cryo ablation as seen on three months images attained in the laser group. An example is presented in Videos 1 and 2, which illustrate baseline and 3-month LGE patterns, respectively, in a patient that underwent laser ablation. Additionally, regression of LGE intensity toward baseline was noted in the LA with the exception of the PV antra, where progression of enhancement was noted in 3 months post ablation with all modalities. Table 2 contains individual patient data regarding mean LGE IIR measures at each time point and the scar burden per individual and in aggregate per patient group. In the RF group, the mean scar burden was $29.0 \pm 6.8\%$ of LA myocardium before ablation, $46.9 \pm 5.7\%$ of LA myocardium at 24 hours, and $46.3 \pm 3.6\%$ of LA myocardium at 3 months post ablation. In the Cryo group, the mean scar burden was $38.0 \pm 10.7\%$ of LA myocardium at baseline, $47.8 \pm 5.4\%$ of LA myocardium 24 hours after ablation, and $50.0 \pm 8.6\%$ of LA myocardium at 3 months post ablation. In the Laser group the mean scar burden was $28.0 \pm 11.4\%$ of LA myocardium before ablation, $43.7 \pm 3.8\%$ of LA myocardium at 24 hours, and $41.8 \pm 4.6\%$ of LA myocardium at 3 months post ablation.

The individual trajectory of scar burden as a function of time and ablation energy source has been summarized graphically in Figure 2. In a linear mixed effects regression model, with a time spline at 24 hours, and accounting for intra-patient clustering of data and inter-patient differences in baseline scar, LGE extent was significantly increased at 24 hours ($+14.6 \pm 1.9\%$ of LA myocardium, $P<0.001$) post ablation and remained stable from 24 hours to 3 months ($+0.1 \pm 1.9\%$, $P=0.951$). In this model, there was no statistically significant difference between the post ablation changes in scar burden among ablation modalities when compared to RF (Cryo $+4.5 \pm 3.0\%$, $P=0.123$; Laser $-3.2 \pm 3.0\%$, $P=0.291$).

Pulmonary Vein Antral LGE Intensity

Secondary analyses were performed by limiting the comparison of image intensities to the pulmonary vein antra to determine intensity changes purely attributable to the energy modality utilized for ablation. In the group that underwent Radiofrequency ablation, the mean pulmonary vein antral IIR values were 0.93 ± 0.11 at baseline, 1.24 ± 0.10 at 24 hours, and 1.29 ± 0.10 at 3 months post-ablation. In the group that underwent cryo ablation, the mean pulmonary vein antral IIR was 1.03 ± 0.10 at baseline, 1.17 ± 0.08 at 24 hours, and 1.17 ± 0.08 at 3 months post-ablation. In the group that underwent Laser ablation, the mean pulmonary vein antral IIR was 0.92 ± 0.09 at baseline, 1.16 ± 0.21 at 24 hours post-ablation, and 1.40 ± 0.22 at 3 months post-ablation as seen in figure 3-B. In a linear mixed effects regression model, with a time spline at 24 hours, and accounting for intra-patient clustering of data and inter-patient differences in baseline intensity, the IIR at the pulmonary vein antra was significantly increased at 24 hours ($+0.25 \pm 0.04$, $P<0.001$) post ablation and further increased from 24 hours to 3 months ($+0.08 \pm 0.04$, $P=0.033$). In this model, there was no statistically significant difference between the post ablation changes in pulmonary vein antral intensity among the energy modalities (Cryo versus RF: -0.03 ± 0.06 , $P=0.600$, and Laser versus RF: $+0.02 \pm 0.06$, $P=0.711$).

Discussion

This report is the first to describe the burden of LA scar and image intensity of regions ablated by RF, Cryo and Laser energy sources at baseline, 24 hours, and 3 months post AF ablation. Lesion formation and durability has been demonstrated to have clinical implications regarding the recurrence of AF after ablation.^{8,13} Therefore, evaluation of scar burden acutely after ablation and at long-term follow-up, may have important implications regarding the performance of each energy source. We found that the extent of atrial enhancement was significantly increased at 24 hours post ablation and remained stable at three months and extent of enhancement is similar by the three modalities. Although laser energy appeared to cause qualitatively more focused lesions on post ablation images (Figure 1), this finding did not reach statistical significance.

Radiofrequency, Cryothermal, and Laser ablation patterns

Radiofrequency energy (frequencies between 300 to 1000 khz) is the standard energy source used for catheter ablation. Passage of high frequency current with high density through a catheter tip and into the myocardium leads to conversion of electromagnetic energy to mechanical energy and heat production through resistive heating. Cryo catheters deliver a

pressurized liquid refrigerant, such as nitrous oxide, to an expansion chamber at the tip where evaporation of the liquid refrigerant leads to absorption of heat from the surrounding catheter surface and myocardium. Freezing of extracellular fluid results in a hyperosmotic extracellular environment that desiccates the cells, damaging the cell membrane and constituents. Further cooling results in freezing of the cellular fluid and disruption of the intracellular organelles and membranes, resulting in complete cell death.¹⁴ Laser ablation utilizes a high-intensity flash of infrared light to heat exposed tissue. The Cardiofocus Laser ablation system utilizes a diode source, which produces a beam with a wavelength of 980 nm.¹⁵ Absorption of diode Laser energy by the myocardium results in heating with minimal scatter and therefore minimal lesion enlargement.

A prior abstract by Mankhopf and colleagues compared the pre and post-procedure lesion formation characteristics of Cryoballoon to Radiofrequency ablation using LGE-MRI.¹⁶ The authors achieved PVI in 21 (87.5%) of 24 patients that underwent Cryo ablation and all 48 patients in the Radiofrequency group ($p=0.03$). Patients with recurrences were found to have a higher amount of fibrosis prior to ablation. In their multi-center experience the authors reported a similar pattern of LA structural remodeling with Cryo and Radiofrequency ablation.¹⁶ Our findings are in agreement with this previous report in that the extent of LGE and contrast wash-in wash-out kinetics are similar between RF and Cryo ablation. We also included a group that had undergone laser ablation and found similar contrast kinetics with those of RF and Cryo. Additionally, we normalized the mean IIR values, from the entire atrium and PV antral areas from 24 hours and 3 months images to the baseline IIRs. Figure 4 describes the impact of each ablation modality on the extent of enhancement on LGE-MRI at the two follow up periods using normalized IIR measures in the LA (figure 4-A) and in the PV antrum (figure 4-B). It is clear that the enhancement changes due to all modalities are similar in pattern. RF ablation caused increased enhancement in the entire LA and PV antrum that persisted over time. Cryo ablation also increased acute enhancement. Although at 3 months the enhancement with Cryo had regressed in the entire LA, it had intensified in the PV antral myocardium. Laser ablation caused diffusely increased enhancement in the LA at 24 hours, but the increased enhancement was focused in the PV antrum at 3 months.

Previous studies have suggested that the extent of scar after RF ablation positively associates with ablation success.^{8,13} Based upon previous findings with RF, one might expect that given the smaller extent of post ablation scar with Laser, results would be inferior to RF and Cryo. Conversely, the extent of scar in prior studies with RF may have served as a surrogate of the completeness of linear ablation, and a complete Laser line may achieve the same efficacy with less tissue destruction. Additional studies are needed to examine freedom from AF as well as the extent of fibrosis and atrial function following ablation with each modality.

Limitations

The primary shortcoming of our study is the limited sample size of participants. Larger sample sizes will be necessary to compare atrial remodeling among groups of participants assigned to different energy sources. Consecutive patients referred for catheter ablation were approached regarding the study, but many patients refused participation due to the necessity

for 3 separate MRI examinations. Additionally, this was an observational cohort and participants were not randomized to different energy sources. Although there were no significant differences in baseline characteristics, unobserved differences may have existed. The analyses are unadjusted for the number of lesions applied in each patient and at each PV antrum. Finally, to improve signal to noise ratio, multiplanar reconstructions were performed prior to image analyses resulting in 1.3×1.3×3.5 mm image resolution. However, atrial wall thickness may be near the limit of image resolution in some participants. Due to volume averaging, our intensity measures may be affected by blood pool or epicardial fat in some cases. However, the association of image intensity with voltage measures in our prior studies suggests that, on average, the measures represent LA myocardial tissue characteristics.^{4,5,10}

Conclusions

Our results demonstrate that radiofrequency, cryoablation and Laser energy reliably change contrast kinetics in the LA in a pattern consistent with PV antral fibrotic change. Our preliminary data suggests that the extent of ablation with Cryo and Laser is more focused around the PV antra at 3 months. Additional studies to characterize the association of various ablative energy sources with atrial remodeling and clinical recurrences of AF are warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Visualization of fibrosis using LGE-MRI after ablation by a) Radiofrequency b) Cryothermal and c) Laser energy application at baseline (first column), post ablation at 24 hours (second column) and 3 months (third column). The figures illustrate normal myocardium in green and enhanced (scar myocardium) in red. Yellow regions signify mild enhancement. The extent of atrial enhancement was increased at 24 hours post ablation by all energy sources. The extent of enhancement, however, was highest in the RF and Cryo groups at 24 hours post ablation. At 3 months, Laser energy was associated with focused linear lesions compared to the diffuse lesion sets associated with RF and Cryo ablation. The extent of enhancement decreased toward baseline in the Cryo and RF groups by 3 months post ablation.

Figure 2.

Mean LA scar burden at baseline, 24 hours after ablation, and 3 months post ablation for each patient in the study. Each line is an individual patient. Black lines (RF), red lines (Cryo), and blue lines (Laser) identify patient groups. One patient that underwent Laser ablation refused the 3-month post ablation MRI examination.

Figure 3.

The mean IIR at baseline, 24 hours after ablation, and 3 months post ablation for each patient. Figure 3-A shows the mean IIR from the myocardium of the entire LA at the three time intervals for individual patients while figure 3-B shows the mean IIR derived only from the four PV antral areas of the LA by the three ablation modalities at different time intervals.

Figure 4.

The IIR normalized to the pre-ablation baseline IIR on LGE-MRI by radiofrequency (RF), cryoablation (Cryo) and laser ablation. Figure 4-A shows the normalized IIR of the entire LA myocardium while figure 4-B shows the normalized IIR of the mean PV antra at the three time intervals by RF, Cryo and laser.

Table 1

Baseline Characteristics of Participants

	All Patients (n=17)	RF (n=7)	Cryo (n=5)	Laser (n=5)	P
Age (years)	57 ± 9	58 ± 8	55 ± 13	56 ± 7	NS
Hypertension (%)	5 (29)	3 (43)	2 (40)	0 (0)	0.227
Male Gender %	13 (77)	5 (71)	3 (60)	5 (100)	0.303
Coronary Disease (%)	0 (0)	0 (0)	0 (0)	0 (0)	1.000
Diabetes (%)	1 (6)	1 (17)	0 (0)	0 (0)	0.468
Prior Stroke (%)	0 (0)	0 (0)	0 (0)	0 (0)	1.000
LVEF (%) mean	59 ± 4	59 ± 4	60 ± 5	58 ± 2	NS
CHADS2 score	0.5 ± 0.6	0.7 ± 0.8	0.4 ± 0.6	0.2 ± 0.5	NS
Persistent AF %	7 (41)	3 (43)	1 (20)	3 (60)	0.493

Individual patient normalized mean intensity (IIR) and scar burden as a percentage of LA myocardium before, acutely after, and 3 months post ablation

Table 2

Energy Source	Patient	Preablation			Postablation- 1 day			Postablation- 3 months		
		Mean LA IIR	Mean PV IIR	Scar (%)	Mean LA IIR	Mean PV IIR	Scar (%)	Mean LA IIR	Mean PV IIR	Scar (%)
Radiofrequency	1	0.83±0.23	0.92±0.17	29	0.91±0.21	1.33±0.16	39	1.1±0.30	1.44±0.27	53
	2	0.73±0.25	0.76±0.13	20	0.96±0.21	1.13±0.20	39	0.94±0.17	1.23±0.12	46
	3	0.85±0.25	1.06±0.15	36	0.99±0.24	1.26±0.19	52	0.92±0.23	1.20±0.11	41
	4	0.81±0.38	1.07±0.29	33	1.02±0.27	1.32±0.20	52	1.01±0.33	1.35±0.21	47
	5	0.75±0.19	0.82±0.19	19	0.98±0.22	1.23±0.12	47	0.94±0.21	1.28±0.12	46
	6	0.84±0.21	0.93±0.23	32	0.96±0.21	1.34±0.23	48	0.96±0.25	1.35±0.16	45
	7	0.84±0.22	0.93±0.16	34	0.99±0.23	1.11±0.18	51	0.94±0.23	1.21±0.15	46
	Average	0.80±0.25	0.93±0.19	29.0±6.8	0.97±0.23	1.25±0.18	46.9±5.7	0.97±0.25	1.29±0.16	46.3±3.6
Cryotherapy	8	0.92±0.25	0.94±0.17	43	0.99±0.18	1.06±0.13	52	0.94±0.28	1.09±0.22	52
	9	0.87±0.25	1.01±0.21	35	0.92±0.27	1.17±0.15	42	0.92±0.22	1.21±0.12	45
	10	0.97±0.27	1.17±0.17	54	0.98±0.26	1.28±0.27	53	0.97±0.29	1.26±0.19	63
	11	0.89±0.21	1.10±0.12	30	0.95±0.21	1.15±0.14	50	0.92±0.17	1.08±0.11	50
	12	0.83±0.23	0.94±0.12	28	0.93±0.24	1.18±0.16	42	0.92±0.23	1.23±0.13	40
	Average	0.90±0.26	1.03±0.16	38.0±10.7	0.96±0.22	1.17±0.17	47.8±5.4	0.93±0.25	1.17±0.15	50.0±8.6
	13	0.90±0.20	0.97±0.17	38	0.95±0.25	1.28±0.11	48	0.94±0.20	1.33±0.15	42
Laser	14	0.77±0.18	0.84±0.10	12	0.97±0.19	1.28±0.13	42	0.99±0.28	1.46±0.17	46
	15	0.81±0.19	0.88±0.13	34	0.87±0.23	0.91±0.11	41	0.88±0.22	1.23±0.12	43
	16	0.78±0.19	0.86±0.26	20	n/a	n/a	n/a	0.86±0.21	1.21±0.22	34
	17	0.84±0.20	1.06±0.17	36	n/a	n/a	n/a	0.91±0.23	1.76±0.32	44
	Average	0.82±0.20	0.92±0.17	28.0±11.4	0.93±0.23	1.16±0.12	43.7±3.8	0.92±0.23	1.40±0.20	41.8±4.6