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Regional Left Atrial Voltage in Patients with Atrial Fibrillation

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Abstract

BACKGROUND— Regional differences in fibrosis, particularly related to the posterior wall and septum, may be important in atrial fibrillation (AF). Using electroanatomic mapping, voltage can be used as a measure of fibrosis.

OBJECTIVES— To determine if patients with AF have disproportionately lower voltage in the septal and posterior walls of the left atrium.

METHODS— Sinus rhythm left atrial electroanatomic maps were used in serial patients presenting for left atrial ablation of AF (8 mm tip). Patients undergoing left atrial mapping for focal atrial tachycardia (AT) were used as a comparison group (4 mm tip). Animal experiments were performed to assess the influence of ablation catheter tip size on voltage amplitude.

RESULTS— The posterior and septal walls exhibited the lowest voltages in both groups. Compared to the anterior wall, there was a 3.78 fold greater odds of finding a low voltage point ($<0.5\text{mV}$) in the septum ($p<0.001$) and a 3.37 fold greater odds of finding a low voltage point in the posterior wall ($p<0.001$) in the AF patients; the proportion of low voltage points by region were not significantly different in the AT group. In the animal model, the mean voltage obtained from an 8 mm ablation catheter was significantly higher ($0.30 \pm 0.17 \text{ mV}$) than that obtained from the same points using a 4 mm catheter (0.22 ± 0.17 , $p = 0.05$).

CONCLUSIONS— Regional differences in voltage are present in patients with atrial arrhythmias, with AF patients exhibiting significantly more low voltage areas in the septum and posterior walls.

Keywords

Atrial fibrillation; Fibrosis; Electroanatomic mapping; CARTO; Ablation catheter; Left atrium

Introduction

Animal models consistently point to an important role of atrial fibrosis in the development and maintenance of atrial fibrillation (AF),^{1–3} and left atrial histology examined from atrial fibrillation patients undergoing cardiothoracic surgery and on postmortem examination confirm the presence of atrial fibrosis in these patients.^{4, 5} Recent data suggest that this fibrosis may be regional: a study of patients with mitral valve disease and AF suggest that the posterior wall may be especially rich in fibrosis when compared to the left atrial appendage.⁶ In addition,

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complex fractionated electrograms (CFAEs) recorded during atrial fibrillation, potentially indicative of an underlying fibrotic substrate, have demonstrated to be promising targets for the ablation of atrial fibrillation.⁷ Of interest, these CFAEs are reliably prominent in certain regions, most often in the left atrial septum.⁷

The CARTO (Biosense) system is a catheter based endocardial mapping system that enables generation of three-dimensional electroanatomic maps of the heart chambers.⁸ Use of this system provides a voltage map, revealing the relative voltage generated by all of the areas of the heart chamber.⁹ Low voltage detected by CARTO accurately correlates with areas of fibrosis,¹⁰ and studies examining voltage in the right atrium have demonstrated lower voltage in patients with sinus node disease,¹¹ congestive heart failure,¹² and advancing age.¹³ Previous studies involving left atrial anatomic maps of AF patients have explored the value of targeting complex and high-frequency activity during AF^{7, 14} and the prognostic significance of large areas of scarring in AF patients,¹⁵ but none have examined sinus rhythm maps to characterize regional voltage.

With the hypothesis that AF patients have a disproportionate amount of fibrosis in the left atrial septum and posterior wall, we performed electroanatomic left atrial maps during sinus rhythm in AF patients presenting for left atrial ablation. Patients with no history of AF undergoing left atrial ablation for focal atrial tachycardia (AT) served as a comparison group.

Methods

Study Population

Twenty-two Consecutive patients with paroxysmal AF undergoing left atrial ablations while in sinus rhythm were enrolled. Consecutive patients with AT that involved mapping in the left atrium were analyzed as a comparison group (n=11). Patients were excluded from either group if they had a history of congenital heart disease, previous surgery or ablation involving either atrium, or scar related macroreentrant atrial tachycardia. Patients were excluded from the comparison group for any additional history of atrial fibrillation, atrial flutter, or macroreentrant atrial tachycardia. Past medical history and medication use were obtained from patient interviews and chart review.

Contrast-enhanced 16 detector computed tomographic (CT) imaging studies were obtained through the heart in the axial plane, with a slice thickness of 1mm to 1.25mm and no interval. A chest radiologist blinded to patient diagnosis analyzed the studies offline on a picture archiving communication system. By manually outlining the left atrium endocardial contour in one axial slice every 5 slices, the left atrial area was calculated. This area was then multiplied by the thickness of the 5 slices, and the products were added in order to calculate the volume of the left atrium.

The protocol was approved by the University of California, San Francisco Committee on Human Research.

Electroanatomic Mapping

All patients underwent three-dimensional mapping using the CARTO system (Biosense Webster Inc., Diamond Bar, California) of the left atrium during either sinus rhythm (for all AF patients) or atrial tachycardia prior to the delivery of ablation. In each case, efforts were made to obtain an evenly distributed map throughout the left atrium. Each point was categorized into one of 4 anatomic areas based on the anatomic shell obtained during mapping: septum, posterior wall, lateral wall, and anterior wall (including the left atrial appendage). Selection of anatomic regions was performed in the anatomic shell display mode (without voltage or activation maps) and blinded to the activation and voltage map.

Voltage was measured from the peak-to-peak bipolar signal filtered at 30–400 mHz. A long vascular sheath was used to ensure stability of the mapping catheter. For the AT group, a 7 French Navistar 4 mm tipped was used for mapping. For the AF group, an 8 mm tipped ablation catheter was used for mapping. Catheters with an 8 mm electrode were used for AF ablation because of the increased safety and efficacy for AF ablation.^{16,17} Endocardial contact mapping was ensured by fluoroscopic visualization of catheter mobility in relation to cardiac motion and by the three-dimensional navigation system indicating stability in 3-dimensional space and local activation timing. The stability of the catheter-wall contact was evaluated at every site by examination of the end-diastolic stability (the distance in millimeters between two consecutive end-diastolic locations) and the local activation time stability (measured as the difference in milliseconds between two consecutive local activation times). Consistent with previous studies involving atrial mapping using the CARTO system, low voltage points were defined as < 0.5 mV.^{11, 12} Areas of low voltage were confirmed with serial manipulations.

Canine Study to Determine Effects of Catheter Size on Measured Voltage

In order to determine whether the catheter electrode size (4 mm in AT group and 8 mm in AF group) affected voltage amplitude, a series of animal experiments (n=20) were performed. The animal protocol was reviewed and approved by the Institutional Animal Care and Use Committee at the University of California San Francisco Laboratory Animal Resource Center, conformed to the regulations for humane care and treatment of animals established by the National Institute of Health, and were conducted with the assistance and supervision of the Animal Resource Department veterinary staff. The canine ventricular preparation has been described previously.¹⁸ After intravenous injection of 5,000 units of heparin, mongrel dogs were euthanized by injection of 50 mg/kg pentobarbital sodium, and the heart rapidly excised and immersed in and perfused with cold cardioplegic solution, as previously described.¹⁸ The right and left coronary arteries were cannulated for perfusion. Once the preparation was completed, the coronary arteries were perfused with an oxygenated modified Tyrode's solution, and the preparation was placed in a temperature-controlled chamber.

Using an apparatus consisting of an 8F rigid tube on a stand, catheters were precisely and stably positioned on the endocardial surface of the preparation. A 7F 8 mm tipped Navistar ablation catheter (Biosense Webster, Diamond Bar, California) and a 4 mm Navistar ablation catheter were each used to record local electrograms from the same 5 points in each of 5 different regions of the endocardial aspect of the ventricular preparation. In each case, contact was maintained using a 10 gram weight, and orientation (e.g., perpendicular or side down) was varied and matched between catheters for each point. The peak to peak bipolar voltage was measured.

Statistical Analysis

Normally distributed continuous variables are presented as means $\pm$ standard deviation (SD). Paired student's t-tests were used to compare means related to the 2 different ablation catheters in the canine model.

Given the complex, hierarchical structure of the data (with multiple individual points nested within each left atrial region, and multiple regions nested within each subject), analyses of the association of baseline characteristics with atrial voltage, and the association of left atrial region with voltage (as a continuous variable) were conducted with hierarchical mixed linear models, treating regions (anterior, septum, posterior, and lateral) nested within subjects as random effects. These models were constructed in all subjects, as well as in separate models constrained by tachycardia diagnosis (atrial fibrillation versus atrial tachycardia). Region was encoded as multiple dichotomous (dummy) variables, with the anterior wall as the comparison region for each dummy variable. The overall contribution of region was assessed using Wald tests of the hypothesis that all of the region variables were jointly zero. To test the hypothesis that diagnosis

modified the association of region with voltage, additional models were constructed that included the multiplicative interaction terms for diagnosis and region. All of these analyses were conducted in unadjusted models, as well as in multivariable models adjusted for age, sex, and a diagnosis of hypertension.

Similarly, to test the association of region with the presence of low voltage (less than 0.5 mV), hierarchical mixed logistic regression models were constructed. The overall strategy for constructing the many logistic models was similar to that outlined for the continuous models.

All analyses were performed using Stata 9.2 (College Station, TX). Two-sided P values < 0.05 were considered statistically significant.

Results

The baseline characteristics of the patient population are shown in Table 1. Echocardiograms were available for 19 patients, performed a mean 38 days prior to the procedure (13 echocardiograms were performed on the day of the procedure). The comparison group consisted of 11 patients with a single focal AT, none with a history of atrial fibrillation or macroreentrant atrial arrhythmia. The mean cycle length of the atrial tachycardias was 454 ± 193 ms. The origin of the AT was ultimately mapped to the right atrium in 3 patients (the inferolateral tricuspid annulus, the mid-superior aspect at the base of the right atrial appendage, and the anterior septum). The left atrial focal tachycardias were mapped to the following regions: 1 high posterior wall, 1 low septum, 2 high septum, 2 low posterior wall, and 2 in the pulmonary veins. There was a greater proportion of patients with coronary artery disease in the AT group.

Eighteen of the AF patients had a CT scan performed a mean 11 days prior to CARTO mapping. The mean left atrial volume index was $29.6 \text{ ml} \pm 11.3 \text{ ml}$. The left atrial volume index correlated with age ($r=0.65$, $p=0.0042$), but did not correlate with arrhythmia duration. Every milliliter increase in volume was associated with a 0.02 mV decrease in voltage ($p=0.015$).

A mean of 80 ± 30 left atrial points were taken for each patient enrolled. To ensure that points were evenly distributed within each of the 4 anatomic regions, a mean of at least 4 points were taken from each of the upper and lower aspects of each region (Table 2).

Voltage significantly correlated in an inverse fashion with age, such that every 10 year increase in age was associated with a 0.14 mV decrease in voltage ($p=0.014$). Voltage was not significantly associated with arrhythmia duration (or time since first diagnosis of the arrhythmia; linear regression coefficient -0.08 , $p=0.114$). Although those with hypertension had lower voltage, this finding was not statistically significant ($p=0.067$). Voltage was not associated with gender, ejection fraction, statin use, angiotensin converting enzyme inhibitor or angiotensin receptor blocker use, diabetes, or coronary artery disease.

The mean coefficient of variation in left atrial voltage was 0.82 and 0.77 for the AF and AT patients, respectively ($p=0.32$). No significant differences in the mean coefficients of variation were observed for any region of the left atrium between the 2 groups. The within subjects standard deviation of voltage was 1.16 mV, 1.23 mV, and 1.12 mV for the entire group, the AF patients, and the AT patients, respectively.

Overall mean voltage was not significant different between the AF and AT patients (1.57 ± 1.31 V versus 1.55 ± 1.25 V, respectively; $p=0.17$). Similarly, comparing each given region in AF and AT groups (e.g., septum versus septum), there were no statistically significant differences (Figure 1).

Regional Voltage Differences

Because measurements were obtained using an 8 mm electrode in the AF group and with a 4 mm electrode in the AT group, analyses were performed to compare regions within each patient, thus “standardizing” the voltages. Using hierarchical mixed linear models to statistically compare these regions, the septum, lateral wall and posterior wall each had significantly lower voltages than the anterior walls for the whole group and the AF group alone (Figure 2). While the septum and posterior walls were significantly lower than the anterior walls in the AT patients, the lateral wall voltages were not significantly different than the anterior wall voltages in this group. The AF group was found to have the largest differences, with the most extreme found in the septum versus anterior wall (septal points were 0.8 mV lower than the anterior wall [$p<0.001$]), and the posterior wall versus anterior wall (where points were 0.6 mV lower than the anterior wall [$p<0.001$]). Overall, differences across regions were associated with differences in voltage for the AT patients ($p=0.022$), and even more strongly associated with differences in voltage in the AF patients ($p<0.001$). After adjustment for age, gender, and hypertension, these findings remained unchanged.

Proportions of Low Voltage Points

Examining the entire left atrium, there was no significant difference in the proportion of patients with low voltage (<0.5 mV) between the AF and AT groups. In order to determine the proportion of low voltage areas (points) in each region, multiple logistic regression was performed. This statistic calculates the odds of a low voltage (<0.5 mV) signal occurring in each area for a given patient group. In the AF group, there was a significant 3.78 fold greater odds of finding a low voltage point in the septum than in the anterior wall and a significant 3.37 fold greater odds of finding a low voltage point in the posterior wall compared to the anterior wall (Figure 3). The proportion of low voltage points by region were not significantly different in the AT group (Figure 4). These findings remained unchanged after adjusting for age, gender, and hypertension.

Canine Study to Determine Effects of Catheter Size on Measured Voltage

In order to determine the effects of electrode size on our measurements, we performed a canine study to test this in a controlled environment. In the canine model, the mean bipolar voltage obtained from the 8 mm ablation catheter was significantly higher (0.30 ± 0.17 mV) than that obtained from the same points using a 4 mm catheter (0.22 ± 0.17 , $p=0.05$; Figure 5).

Discussion

We found significant regional variability in left atrial voltage in patients with atrial arrhythmias. Most pronounced were the lower voltages found in the septal and posterior walls, with the AF patients exhibiting the most remarkable differences in these areas. Examining each region by proportion of low voltage points, the AF patients were unique in exhibiting significantly more low voltage points in the septal and posterior walls, with no such association found in the AT group. This finding may reflect a disproportionate amount of fibrosis in the septum and posterior wall of the left atrium in AF patients, fitting well with a histological study in AF patients with mitral valve disease⁶ and with a study describing a high preponderance of CFAEs in the septum.⁷ However, as voltage is only a potential surrogate for fibrosis, we cannot exclude the possibility that our findings reflect differences in tissue mass and/or fiber orientation.

Consistent with previous studies of the right atrium,¹³ age inversely correlated with left atrial voltage. In addition, increased left atrial volume was associated with lower voltage. However, arrhythmia duration, ejection fraction, and hypertension did not correlate with lower voltage. Although they might be expected to affect atrial inflammation and/or fibrosis, neither statin therapy nor treatment with an angiotensin converting enzyme inhibitor or angiotensin receptor

blocker was associated with a difference in voltage. However, the timing of these drugs in relation to the onset of the arrhythmia and the timing of the electrophysiology study were not controlled.

Previous studies related to atrial voltage have been limited to the right atrium, and none specifically examined patients with AF. Sanders et al studied right atrial voltage in 21 patients with symptomatic congestive heart failure, demonstrating lower mean voltage and greater heterogeneity in voltage compared to 21 controls undergoing radiofrequency ablation for AV node reentry tachycardia (AVNRT) or AV reentry tachycardia (AVRT).¹² The same group later showed that 16 patients with sinus node disease had similarly lower right atrial voltage and greater heterogeneity in voltage compared to 16 controls.¹¹ Finally, given the greater incidence of AF in older patients, the group tested the hypothesis that right atrial voltage would be lower in older patients by studying 13 patients ≥ 60 years old, 13 patients between 31 and 59 years old, and 13 patients ≤ 30 years old: once again, they found lower right atrial voltage and greater heterogeneity in their study group (the older patients).¹³

Corradi et al. found a greater amount of interstitial fibrosis in the posterior wall compared to the left atrial appendage in AF patients undergoing mitral valve surgery.⁶ Our findings suggest that the regional differences may be exaggerated in AF patients. In fact, recent animal work suggests that atrial dilation results in posterior wall fibrosis, with the most rapid AF frequency, or dominant frequency, and lowest voltage found in that area.¹⁹ Nademanee et al. demonstrated success in both terminating atrial fibrillation in the electrophysiology laboratory and in 1 year success after ablating complex fractionated electrograms most commonly found in the septum.⁷ As fibrosis is thought to underlie such local complex, high-frequency, low amplitude endocardial signals as described in that study, it is reasonable to infer that a greater degree of septal fibrosis was responsible for their findings.

Limitations

In contrast to previous sinus rhythm studies examining the electroanatomic maps of right atrium, we failed to show a significant difference in mean voltage in the entire left atrium or greater heterogeneity of voltage in AF patients versus our comparison group. There are two likely explanations for this discrepancy, both related to limitations of our study. First, our comparison group consisted of AT patients rather than AVNRT or AVRT patients. As we were comparing left atrial maps, which are time consuming and add significant risk to the patient given the transseptal puncture required and the increased risk of stroke while in the left atrium, AT patients undergoing mapping of the left atrium for clinical purposes provided an opportunity for study with only a minimal increase in risk. One explanation for our findings is that AT patients themselves may have at least some areas of increased fibrosis, potentially reducing the left atrial voltage. Mapping in atrial tachycardia may have affected voltage due to faster rates (potentially resulting in locally slowed conduction); however, the mean AT cycle length of 454 ± 193 ms was likely not sufficiently short to affect voltage. Different wavefront vectors arising from the ATs compared to the sinus rhythm maps performed in the AF patients might also have affected voltages.

Importantly, the AF patients were mapped with an 8 mm catheter, and all AT patients were mapped with a 4 mm catheter. First, it is important to emphasize that both the 4 mm tip and 8 mm tip catheters have the same interelectrode distances, and the band pass filters settings were constant when mapping was performed. Using a canine ventricular preparation, we demonstrated that, taken from the same area, the 8 mm tipped catheter recorded a higher voltage signal than a 4 mm tipped catheter. Therefore, although we found no significant difference in absolute voltage between the AF and AT groups (or between given regions between the 2 groups), we suspect that the AF voltage would have been significantly lower if the same catheter had been used in both groups. Both of these methodological issues would bias the

study towards lesser differences between the two groups (they both increase the chance of a type II error). The greater proportion of low voltage points in the septum and posterior walls in AF patients was found despite the use of 8 mm catheters and despite a comparison to AT patients, potentially strengthening these findings. Because of these differences in electrode size, comparisons were performed in relation to the anterior wall of each patient as a way to “normalize” comparisons and, in effect, minimize the differences due to electrode size. With this comparison, we found that the septum and posterior in the AF patients had lower voltages than those in the AT patients compared to the anterior wall. Differences in electrode size should not have affected the proportions of low voltage points.

Finally, fewer points were obtained in the high septum and appendage of the AT patients. While this does not detract from the voltage differences by region in the cohort as a whole, it may have influenced the differences observed between the AF and comparison (AT) groups.

Implications

Our findings suggest that a regional concentration of low voltage in the left atrial posterior and septal walls may be important in the pathophysiology of paroxysmal AF. These regional differences imply the existence of a unique atrial substrate or atrial myopathy in AF, found even in patients without hypertension or other heart disease. Understanding this distribution of low voltage areas may be important as ablative strategies targeting fractionated electrograms and/or abnormal atrial substrate are developed.

Conclusion

Our study provides evidence with sinus rhythm mapping that the atrial substrate is particularly abnormal in the septum and posterior wall of AF patients, with lower voltages in those areas.

References

1. Kumagai K, Nakashima H, Urata H, Gondo N, Arakawa K, Saku K. Effects of angiotensin II type 1 receptor antagonist on electrical and structural remodeling in atrial fibrillation. *J Am Coll Cardiol* 2003;41(12):2197–2204. [PubMed: 12821247]
2. Li D, Fareh S, Leung TK, Nattel S. Promotion of atrial fibrillation by heart failure in dogs: atrial remodeling of a different sort. *Circulation* 1999;100(1):87–95. [PubMed: 10393686]
3. Verheule S, Wilson E, Everett T 4th, Shanbhag S, Golden C, Olgin J. Alterations in atrial electrophysiology and tissue structure in a canine model of chronic atrial dilatation due to mitral regurgitation. *Circulation* 2003;107(20):2615–2622. [PubMed: 12732604]
4. Boldt A, Wetzel U, Lauschke J, Weigl J, Gummert J, Hindricks G, Kottkamp H, Dhein S. Fibrosis in left atrial tissue of patients with atrial fibrillation with and without underlying mitral valve disease. *Heart* 2004;90(4):400–405. [PubMed: 15020515]
5. Hassink RJ, Aretz HT, Ruskin J, Keane D. Morphology of atrial myocardium in human pulmonary veins: a postmortem analysis in patients with and without atrial fibrillation. *J Am Coll Cardiol* 2003;42(6):1108–1114. [PubMed: 13678939]
6. Corradi D, Callegari S, Benussi S, Maestri R, Pastori P, Nascimbene S, Bosio S, Dorigo E, Grassani C, Rusconi R, Vettori MV, Alinovi R, Astorri E, Pappone C, Alfieri O. Myocyte changes and their left atrial distribution in patients with chronic atrial fibrillation related to mitral valve disease. *Hum Pathol* 2005;36(10):1080–1089. [PubMed: 16226107]
7. Nademanee K, McKenzie J, Kosar E, Schwab M, Sunsaneewitayakul B, Vasavakul T, Khunnawat C, Ngarmukos T. A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologic substrate. *J Am Coll Cardiol* 2004;43(11):2044–2053. [PubMed: 15172410]
8. Gepstein L, Hayam G, Ben-Haim SA. A novel method for nonfluoroscopic catheter-based electroanatomical mapping of the heart. In vitro and in vivo accuracy results. *Circulation* 1997;95(6):1611–1622. [PubMed: 9118532]

9. Varanasi S, Dhala A, Blanck Z, Deshpande S, Akhtar M, Sra J. Electroanatomic mapping for radiofrequency ablation of cardiac arrhythmias. *J Cardiovasc Electrophysiol* 1999;10(4):538–544. [PubMed: 10355695]
10. Callans DJ, Ren JF, Michele J, Marchlinski FE, Dillon SM. Electroanatomic left ventricular mapping in the porcine model of healed anterior myocardial infarction. Correlation with intracardiac echocardiography and pathological analysis. *Circulation* 1999;100(16):1744–1750. [PubMed: 10525495]
11. Sanders P, Morton JB, Kistler PM, Spence SJ, Davidson NC, Hussin A, Vohra JK, Sparks PB, Kalman JM. Electrophysiological and electroanatomic characterization of the atria in sinus node disease: evidence of diffuse atrial remodeling. *Circulation* 2004;109(12):1514–1522. [PubMed: 15007004]
12. Sanders P, Morton JB, Davidson NC, Spence SJ, Vohra JK, Sparks PB, Kalman JM. Electrical remodeling of the atria in congestive heart failure: electrophysiological and electroanatomic mapping in humans. *Circulation* 2003;108(12):1461–1468. [PubMed: 12952837]
13. Kistler PM, Sanders P, Fynn SP, Stevenson IH, Spence SJ, Vohra JK, Sparks PB, Kalman JM. Electrophysiologic and electroanatomic changes in the human atrium associated with age. *J Am Coll Cardiol* 2004;44(1):109–116. [PubMed: 15234418]
14. Sanders P, Berenfeld O, Hocini M, Jais P, Vaidyanathan R, Hsu LF, Garrigue S, Takahashi Y, Rotter M, Sacher F, Scavee C, Ploutz-Snyder R, Jalife J, Haissaguerre M. Spectral analysis identifies sites of high-frequency activity maintaining atrial fibrillation in humans. *Circulation* 2005;112(6):789–797. [PubMed: 16061740]
15. Verma A, Wazni OM, Marrouche NF, Martin DO, Kilicaslan F, Minor S, Schweikert RA, Saliba W, Cummings J, Burkhardt JD, Bhargava M, Belden WA, Abdul-Karim A, Natale A. Pre-existent left atrial scarring in patients undergoing pulmonary vein antrum isolation: an independent predictor of procedural failure. *J Am Coll Cardiol* 2005;45(2):285–292. [PubMed: 15653029]
16. Marrouche NF, Dresing T, Cole C, Bash D, Saad E, Balaban K, Pavia SV, Schweikert R, Saliba W, Abdul-Karim A, Pisano E, Fanelli R, Tchou P, Natale A. Circular mapping and ablation of the pulmonary vein for treatment of atrial fibrillation: impact of different catheter technologies. *J Am Coll Cardiol* 2002;40(3):464–474. [PubMed: 12142112]
17. Oral H, Scharf C, Chugh A, Hall B, Cheung P, Good E, Veerareddy S, Pelosi F Jr, Morady F. Catheter ablation for paroxysmal atrial fibrillation: segmental pulmonary vein ostial ablation versus left atrial ablation. *Circulation* 2003;108(19):2355–2360. [PubMed: 14557355]
18. Verheule S, Wilson E, Banthia S, Everett T 4th, Shanbhag S, Sih HJ, Olgin J. Direction-dependent conduction abnormalities in a canine model of atrial fibrillation due to chronic atrial dilatation. *Am J Physiol Heart Circ Physiol* 2004;287(2):H634–644. [PubMed: 15031120]
19. Huang JL, Tai CT, Lin YJ, Ting CT, Chen YT, Chang MS, Lin FY, Lai WT, Chen SA. The mechanisms of an increased dominant frequency in the left atrial posterior wall during atrial fibrillation in acute atrial dilatation. *J Cardiovasc Electrophysiol* 2006;17(2):178–188. [PubMed: 16533256]

ABBREVIATIONS

AF	atrial fibrillation
AT	atrial tachycardia
CFAEs	complex fractionated electrograms
CT	computed tomographic

Figure 1. Mean voltage differences (in mV) for the entire left atrium and by region for the atrial fibrillation and atrial tachycardia groups. Y-error bars denote standard deviations.

Figure 2.

Linear regression coefficients of voltage in the septum, posterior wall and lateral walls compared to voltage in the anterior wall for atrial fibrillation and focal atrial tachycardia patients. Y-error bars denote 95% confidence intervals.

* denotes $p < 0.05$; ** denotes $p < 0.001$.

Figure 3. Odds ratios for the presence of a low voltage point (<0.5 mV) in the septum, posterior wall, and lateral wall compared to the anterior wall for atrial fibrillation and focal atrial tachycardia patients. Y-error bars denote 95% confidence intervals
* denotes $p < 0.05$; ** denotes $p < 0.001$.

Figure 4.

Electroanatomic maps of left atria using the CARTO (Biosense) system, illustrating homogeneous normal voltage in the septum (A) and lateral wall (B) of an atrial tachycardia patient. The atrium of an AF patient exhibits significantly lower voltage in the septum (C) than the lateral wall (D).

As demonstrated by the color coded key, purple represents voltage > 0.99 mV.

Figure 5. Local electrogram from the same point taken from the endocardium of a canine ventricular preparation using a 4 mm tipped ablation catheter (left) and an 8 mm tipped ablation catheter. The 8 mm tipped catheter recorded a larger peak to peak voltage.

Table 1

Baseline characteristics

	AT group (n=11)	AF group (n=22)	p value
Age (years)	47±23	52±8	0.35
Female	5 (42%)	7 (32%)	0.58
Mean Ejection Fraction (%)	59±6	60±1	0.37
Coronary Artery Disease	2 (17%)	0	0.03
Hypertension	1 (8%)	6 (27%)	0.29
Diabetes Mellitus	0	1 (5%)	0.51
Congestive Heart Failure	1 (8%)	0	0.14
On a statin	0	3 (14%)	0.26
On an ACE inhibitor or ARB	0	6 (27%)	0.086
On Spironolactone	0	0	

AT denotes atrial tachycardia; AF denotes atrial fibrillation; ARB denotes angiotensin receptor blocker

Table 2

Mean number of points for each region

		Mean Number of Points			
Region		Total Cohort	AT Group	AF Group	p value for AT versus AF
Septum	High	8±5	6±3	10±5	0.02
	Low	9±4	7±5	10±4	0.06
Posterior Wall	High	13±6	11±5	14±7	0.26
	Low	12±8	9±6	14±8	0.12
Lateral Wall	High	5±3	4±2	5±3	0.31
	Low	7±7	9±12	6±3	0.41
Anterior Wall	High	12±6	10±6	13±6	0.21
	Appendage	8±4	4±2	9±4	<0.001

AT denotes atrial tachycardia; AF denotes atrial fibrillation