

Altered Nonlinear Dynamics of Atrial Fibrillation Detected after Ablation

Kevin W Sunderland, Adam E Berman, Autumn M Schumacher

Georgia Regents University, Augusta, Georgia, USA

Abstract

Atrial fibrillation (AF) consists of uncoordinated atrial and ventricular electrical activity. Quantifying the nonlinear dynamics of AF is difficult since the QRS wave masks the P wave patterns on the electrocardiogram (ECG). The purpose of this project was to minimize the size of the QRS wave and analyze the remaining atrial ECG signal to better measure the nonlinear dynamics underlying AF. A continuous single-lead ECG signal was digitally recorded during atrial myocardial tissue ablation in 19 adult AF patients. Thirty-second segments of AF were selected before and after ablation from each ECG recording. The ECG segments were processed with the adaptive singular value cancelation (ASVC) technique to reduce the size of the QRS wave. The remaining atrial signal was then analyzed with recurrence quantification analysis (RQA) to quantify its nonlinear dynamics. The RQA variable, %determinism, significantly decreased after ablation ($p = .042$). This finding suggests that the processed AF signal contained less structure in the nonlinear domain after ablation of the atrial myocardial tissue. These results demonstrated that the ASVC technique reduced the size of the QRS wave allowing RQA to detect alterations in the nonlinear dynamics of the remaining atrial ECG signal after ablation.

1. Introduction

Atrial fibrillation (AF) is characterized by uncoordinated P and QRS waves on the electrocardiogram (ECG). These ECG waves represent asymmetrical atrial and ventricular electrical activity, respectively, which ultimately produces irregular myocardial contractions. Consequently, AF carries a 5-fold increase of stroke due to thrombosis [1]. Despite new advances in treatment, the AF arrhythmia remains difficult to fully understand since the QRS wave masks the atrial patterns on the ECG.

Although totally eliminating the QRS wave is not possible, several methods exist for minimizing its size in the digitized ECG [2,3]. One such method is adaptive singular value cancellation (ASVC), which decreases the amount of QRS residua during processing of single-lead

ECG data sets. Alcaraz & Rieta [4] demonstrated that ASVC leaves very little QRS residua and noise compared to other techniques such as average beat subtraction. ASVC uses the shared QRS morphology within a given data set to create a template of the base signal corresponding to ventricular activity [7]. This template is then used to modify and reduce the R wave amplitude within each QRS complex. Furthermore, ASVC can be implemented without the need for complex multi-lead ECG signals, which are necessary for techniques that exploit the spatial diversity of the cardiac electrical system [6].

Analyzing the remaining atrial signal with a nonlinear technique detects and quantifies atrial behavior patterns unseen with linear analyses. Previous studies suggest that AF may contain deterministic, rather than random, behavior patterns [7]. Recurrence quantification analysis (RQA) is a nonlinear signal analysis technique that detects and quantifies the nonlinear dynamics contained in sinus rhythm as well as the atrial and ventricular arrhythmias [8-10].

The purpose of this project was to reduce the QRS wave in the ECG using ASVC and analyze the remaining atrial signal with RQA to better quantify the underlying nonlinear dynamics of AF.

2. Methods

The ECG data analyzed for this project were obtained as part of a larger study approved by the Institutional Review Board at Georgia Regents University. Each patient signed the approved consent form prior to the ablation procedure and data collection. A continuous single-lead surface ECG signal (Lead II) was digitally recorded during the left atrial myocardial tissue ablation and pulmonary vein isolation procedures for 48 adult AF patients. Of these, only 19 AF patients fit the inclusion criteria for this project: high quality ECG recordings, during AF without ventricular ectopy, before and after ablation. The ECG recordings were obtained using PowerLab[®] hardware and LabChart Pro[®] software both from ADInstruments, Colorado Springs, CO. Each ECG signal was digitized (sampled) at the 1K rate and processed offline after the completion of the ablation procedure. Thirty-second segments of AF rhythm were

extracted before and after ablation from each continuous ECG recording. Each 30-second ECG segment was processed with the ASVC technique. The resulting 30-second atrial ECG signal was then analyzed with RQA. RQA uses eight variables to quantify the nonlinear dynamics contained in the ECG signal. Using SPSS[®] (IBM, Chicago, IL), paired t-tests determined if significant differences existed between the before/after ablation atrial ECG segments for each RQA variable at the .05 level of significance.

2.1. Adaptive singular value cancellation

Theoretically, ASVC is an appropriate tool for minimizing the QRS waves within an ECG segment because the atrial and ventricular waveforms are uncoupled from each other during AF [11]. Also, the high frequency of redundant QRS waveforms in the ECG signal over time allows ASVC to generate a tailored template pattern, which is then used to reduce the R wave amplitude within each QRS complex [4].

For this project, all ECG segments were processed via ASVC using a custom MATLAB[®] (Mathworks, Natick, MA) program. First, the R waves were detected using the Pan and Tompkins algorithm [12]. This method took the derivative of the ECG signal and squared the output, emphasizing the QRS complex. Moving window integration was used to identify each R wave peak; each window approximated the widest possible QRS complex and labeled the fiducial mark at the maximum point of the R wave above a chosen threshold.

After locating the R wave, the ASVC algorithm located and minimized the QRS complex. First, the QRS start and end points were identified to calculate the QRS width within an ECG segment. Each QRS complex was then inserted into a column vector matrix and singular value decomposition performed to determine the principal component of the matrix. A template was then created using the principle component. This template was adapted to each QRS complex so to account for the varying R wave amplitudes in the ECG caused by respiratory chest movement. The ratio of R wave amplitude in each QRS complex over the template's R wave was then multiplied to the original template pattern before subtracting it from each QRS complex.

2.2. Recurrence quantification analysis

Several recurrence plot software packages now exist to analyze and quantify the nonlinear dynamics contained within a physiological signal [13]. Generally, a recurrence plot is the pictorial representation of a matrix whose elements reflect the recurring states of a system. Recurrence plots reveal a dynamical system's phase space trajectory (i.e., the position and momentum behavior of

an object within the system) such that patterns of repeating data sequences signify the degree to which each point is predetermined by the previous data point.

Copyrighted by Dr. Charles L. Webber, Jr. and free for download at <http://homepages.luc.edu/~cwebber/>, the RQA software package used for this project was originally developed by Webber and Zbilut [14-15]. RQA mathematically reconstructs the atrial ECG data set into a time-ordered sequence of vectors (data sequences) denoted as the diagonal and vertical line structures in the recurrence plot. Data points are considered recurring if they appear within a preset radius. In this manner, the repeating data sequences signify the degree that a particular system is structured and organized in the nonlinear domain. RQA does not require a priori assumptions or special data conditioning, since recurrent points are tallied within the data set itself. Each RQA variable quantifies a unique nonlinear characteristic:

- ❖ %recurrence quantifies the percentage of points falling inside a specified radius and reflects the amount of recurring data points in a system;
- ❖ %determinism quantifies the proportion of points forming diagonal lines and reflects the amount of structure in the system;
- ❖ Dmax is the longest diagonal line in the plot; inversely proportional to the largest positive Lyapunov exponent, it reflects the periodicity of a system;
- ❖ entropy quantifies the probability distribution of the diagonal line lengths and reflects the complexity of a system;
- ❖ trend quantifies the distance and density of the points in the plot's parallel lines and reflects the stationarity of a system;
- ❖ %laminar quantifies the proportion of points forming vertical lines and also reflects the system's structure;
- ❖ Vmax quantifies the longest vertical line of the plot and reflects the regularity of the system;
- ❖ Traptime quantifies the average length of the vertical lines and reflects the data predictability in the system.

A periodic system is highly structured, exhibiting stationary behavior in phase space via a signal containing abundant repetitive data values. Thus, the %recurrence, %determinism, Dmax and entropy values will be higher when the cardiac system is periodic (during asystole) than when it is less periodic (during AF). Trend values hover around zero with periodic systems, while %laminar, Vmax and traptime values rise with increase periodicity.

RQA is composed of several modules with which to analyze any given signal. For this project, the Recurrence Quantification Epochs (RQE) module was used to analyze each 30-second atrial ECG segment on an epoch-by-epoch basis. The RQE parameters were delay = 30, embed = 8, Euclidean normalization, first point = 1, last point = 2010, overlap = 2000, maximum number of epochs, no randomization, mean distance scaling, radius = 9 and line = 2. RQE produced 14 epochs for each ECG

segment with these parameter settings; each epoch contained the values for each RQA variable. Using Excel® (Microsoft, Seattle, WA) for data management, the average RQA variable values for the 14 epochs were calculated then sorted into the appropriate before/after ablation group for statistical analysis.

3. Results

The 19 AF patients providing ECG data for this project were 53% female and 95% Caucasian with a mean age 67 ± 7 years. Their mean body mass index was 31 ± 5 and mean ejection fraction $> 55\%$. Ten of these patients were diagnosed with paroxysmal AF and the other nine with persistent AF.

Figure 1 illustrates the QRS wave reduction when the digitized ECG signal is processed with the ASVC technique. Figure 1A is a 10-second example of the original ECG signal and Figure 1B the subsequent post-ASVC processed atrial signal output.

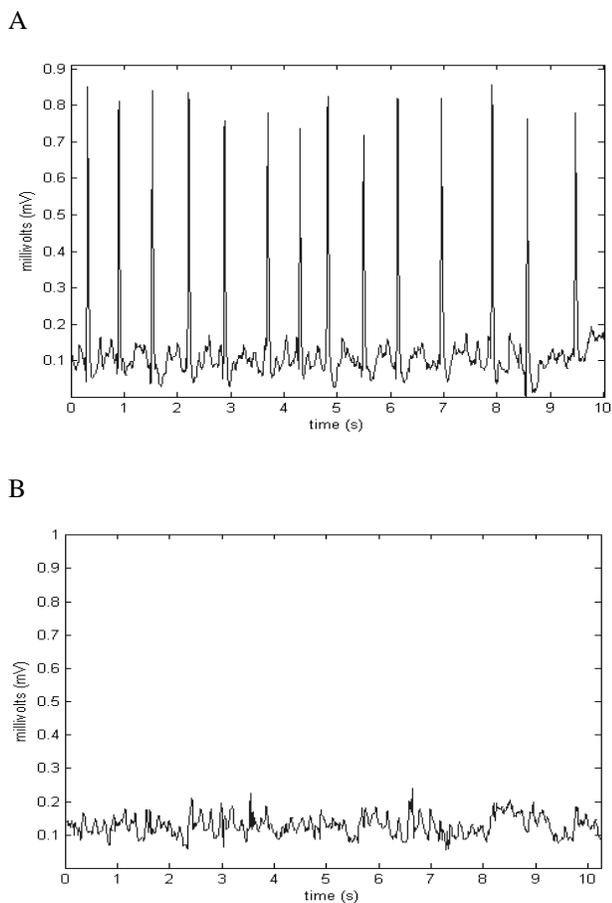


Figure 1. Ten-second ECG signal examples showing QRS wave reduction with ASVC. (A) Original 30-second ECG signal. (B) Resulting atrial signal after ASVC processing.

Table 1 shows the pre- and post-ablation mean \pm standard deviation values for the RQA variables. The only RQA variable to show a statically significant group difference between before and after ablation was %determinism ($p = .042$).

Table 1. Mean RQA Variable Values

RQA Variable	Pre-Ablation	Post-Ablation	p value
% recurrence	0.56 ± 0.7	0.35 ± 0.2	.23
%determinism	99.0 ± 0.6	98.75 ± 0.7	.042*
maxline	1327 ± 509	1276 ± 446	.59
entropy	4.36 ± 0.4	4.13 ± 0.2	.066
Trend	-0.79 ± 0.4	-0.64 ± 0.3	.225
%laminar	95 ± 3.5	92 ± 6.6	.109
Vmax	28 ± 45	17 ± 12	.322
Traptime	5.56 ± 4.9	3.97 ± 1.3	.198

*significant group difference $p < 0.05$

4. Discussion

The major finding of this project was that the nonlinear structure of AF diminished with ablation of the left atrial myocardial tissue during conventionally-performed pulmonary vein isolation procedures. Although only %determinism significantly decreased, all the other RQA variables also decreased after ablation – albeit trend slightly increased toward zero. These findings suggest that atrial tissue ablation and pulmonary vein isolation altered the nonlinear structure of the atrial surface ECG signal in phase space, possibly making the atrial signal less periodic during fibrillation. Tissue ablation for the treatment of AF has as its primary endpoint the electrical isolation of all pulmonary veins, thereby isolating any potential AF triggers from the remainder of the atrium. Additionally, ablation alters action potential wave propagation across the atrial myocardium during AF and sinus rhythm [16-17]. Together these changes may result in a less deterministic atrial ECG signal. Ultimately, the goal of ablation is to eliminate AF and ensure maintenance of sinus rhythm. The relationship between the nonlinear alterations of the atrial ECG signal and the facilitative effects of ablation upon cardioversion of AF to sinus rhythm needs to be further explored in future research projects.

This project also demonstrated that ASVC successfully minimized the QRS wave prior to analysis with RQA. As a signal processing methodology, ASVC is a valuable

tool for AF research since it lessens the need to retrieve the atrial signal from invasive cardiac catheters. However, more research is needed with a larger sample size to determine the clinical benefit of quantifying the nonlinear dynamics within the AF arrhythmia after processing the surface ECG signal with the ASVC technique.

Acknowledgements

This study was supported by the Department of Medicine Research Initiative Award, Medical College of Georgia, Georgia Regents University. The authors would like to thank Robert Sarfo and Miranda Hawks for their assistance with the ECG data collection.

References

- [1] January CT, Wann S, Alpert J, Calkins H, Cleveland J, Cigarroa J, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association task force on Practice Guidelines and the Heart Rhythm Society. *Circulation* 2014;e-pub March 2014. doi: 10.1161/CIR.0000000000000041
- [2] Petrutiu S, Ng J, Nijm G, Al-Angari H, Swiryn, Sahakian A. Atrial fibrillation and waveform characterization a time domain perspective in the surface ECG. *IEEE Trans Biomed Eng* 2006;25:24-30.
- [3] Rieta JJ, Hornero F. Comparative study of methods for ventricular activity cancellation in atrial electrograms of atrial fibrillation. *Physiol Meas* 2007;28:925-936.
- [4] Alcaraz R, Rieta JJ. Adaptive singular value cancellation of ventricular activity in single-lead atrial fibrillation electrocardiograms. *Physiol Meas* 2008;29:1251-1369.
- [5] Alcaraz R, Rieta JJ. Adaptive singular value QRST cancellation for the analysis of short single lead atrial fibrillation electrocardiograms. *Comput Cardiol* 2007; 34:513-516.
- [6] Lemay M, Jacquemet V, Forclaz A, Vesin JM, Kappenberger L. Spatiotemporal QRST cancellation method using separate QRS and T-waves templates. *Comput Cardiol* 2005;32:611-614.
- [7] Barbaro V, Bartolini P, Calcagnini G, Censi F, Michelucci A. Deterministic patterns and coupling of bipolar recordings from the right atrium. *Ann Ist Super Sanita* 2001;37:371-376.
- [8] Censi F, Barbaro V, Bartolini P, Calcagnini G, Michelucci A, Gensini GF, et al. Recurrent patterns of atrial depolarization during atrial fibrillation assessed by recurrence plot quantification. *Ann Biomed Eng* 2000; 28:61-70.
- [9] Schumacher A. Linear and nonlinear approaches to the analysis of R-R interval variability. *Biol Res Nurs* 2004; 5:211-221.
- [10] Schumacher A, Zbilut J, Webber C, Schwertz D, Piano M. Detection of cardiac variability in the isolated rat heart. *Biol Res Nurs* 2006;8:55-66.
- [11] Mainardi L, Sörnmo L, Cerutti S. Understanding atrial fibrillation: The signal processing contribution. University of Connecticut: Morgan & Claypool Publishers, 2008.
- [12] Pan J, Tompkins W. A real-time QRS detection algorithm. *IEEE Trans Biomed Eng* 1985;32:230-236.
- [13] Marwan N, Romano MC, Theil M, Kurths, J. Recurrence plots for the analysis of complex systems. *Phys Rep* 2007; 438:237-329.
- [14] Webber CL Jr, Zbilut JP. Dynamical assessment of physiological systems and states using recurrence plot strategies. *J Appl Physiol* 1994; 76:965-973.
- [15] Webber Jr CL, Zbilut JP. Recurrence quantification analysis of nonlinear dynamical systems. In MA Riley & GC Van Orden, editors. *Tutorials in contemporary nonlinear methods for the behavioral sciences*. 2005:26-94. Retrieved 7-31-14 from National Science Foundation: <http://www.nsf.gov/sbe/bcs/pac/nmbs/nmbs.pdf>
- [16] Narayan SM, Patel J, Mulpuru S, Krummen DE. Focal impulse and rotor modulation ablation of sustaining rotors abruptly terminates persistent atrial fibrillation to sinus rhythm with elimination on follow-up: A video case study. *Heart Rhythm* 2012;9:1436-1439.
- [17] Shivkumar K, Ellenbogen KA, Hummel JD, Miller JM, Steinberg JS. Acute termination of human atrial fibrillation by identification and catheter ablation of localized rotors and sources: First multicenter experience of Focal Impulse and Rotor Modulation (FIRM) ablation. *J Cardiovasc Electrophysiol* 2012;23:1277-1285.

Address for correspondence.

Autumn M. Schumacher, PhD
 Georgia Regents University
 987 St. Sebastian Way EC-5354
 Augusta, GA 30912
aschumacher@gru.edu