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Temporal Stability in the Spectral Representation of Complex Fractionated Atrial Electrograms

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Abstract

Background—Although local electrograms during atrial fibrillation (AF) are often spectrally analyzed over 8 second (8s) intervals, changes may be common over intervals as short as 2s. We sought to determine whether averaged 2s measurements of electrogram spectral parameters were similar to 8s measurements, and whether the 2s intervals could provide an estimate of the temporal stability of the signal frequency content in paroxysmal versus persistent AF.

Methods—Complex fractionated atrial electrograms (CFAE) were acquired outside the pulmonary vein ostia and from free wall sites in 9 paroxysmal and 10 longstanding persistent AF patients. Using a 2s sliding calculation window, a frequency spectrum was computed every 100ms over an interval of 8.4s (82 spectra in total). The dominant frequency (DF), the dominant amplitude (DA), and the mean spectral profile (MP) were measured. The 2s measurements were compared to single 8.4s interval measurements. Coefficients of variation (COV) were computed from the 82 spectra for each CFAE recording to determine temporal variability of parameters.

Results—Over the sliding 2s computation intervals, as for fixed 8.4s computation intervals, mean DA and DF were significantly higher in longstanding persistent AF while MP was significantly higher in paroxysmal AF ($p = 0.001$). The COV was significantly higher for the DF parameter in paroxysmal AF ($p < 0.001$) and significantly higher for the MP parameter in persistent AF ($p < 0.02$).

Conclusions—For both paroxysmal and persistent AF data, the 2s sliding window averages provide similar results to single 8.4s intervals, and information regarding temporal stability was additionally obtained in the process.

Keywords

atrial fibrillation; CFAE; dominant frequency; Fourier analysis; spectral estimation

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DISCLOSURES

None.

BACKGROUND

Complex fractionated atrial electrograms (CFAE), frequently recorded by electrode catheters from atrial sites during atrial fibrillation (AF), have been initially characterized by the presence of either continuous local electrogram deflections, or by discrete electrogram deflections separated by less than 120 millisecond (ms) as recorded over a 10 second (s) interval¹. Subsequent research has attempted to classify CFAEs into different types². In patients with longstanding AF as well as in patients with paroxysmal AF, CFAEs are commonly recorded from multiple left and right atrial sites. Electrical disconnection of the pulmonary veins (PVs), using wide antral lesions, is often not sufficient for successful catheter ablation of AF, in patients with longstanding AF. In these patients, atrial sites with CFAE recordings, outside the isolated zones, have been targeted for additional ablation³⁻⁷. Underlying this approach is the implicit assumption that CFAEs mark the atrial sites that are responsible for driving or maintaining AF. However, as previously reported², CFAEs may represent diverse electrophysiologic phenomena, and more importantly may result from different underlying processes in paroxysmal as compared to longstanding AF. CFAEs also may be site-specific, manifesting different electrophysiologic phenomena at distinct locations in the atria⁸. Thus defining different objective CFAE markers for distinct phenomena at differing locations, based on their spectral characteristics, may have therapeutic implications.

The dominant frequency (DF) as calculated using the discrete Fourier transform (DFT)^{9,10} is frequently used to analyze CFAEs recorded in paroxysmal and longstanding persistent AF patients¹¹⁻¹³. The DF is defined as the largest fundamental periodic component in the physiologic range of the frequency spectrum. However, this method suffers from a lack of robustness to random and phase noise^{14,15} and can depend on distortions in the signal that are introduced during preprocessing¹⁶⁻¹⁸. Thus results may be ambiguous and conflicting when using the DFT for spectral analysis. In previous work we introduced a new spectral estimator and spectral parameters for characterization of CFAE in paroxysmal and persistent AF patients¹⁹. In the present study, we have applied these spectral parameters to characterize CFAEs using sliding 2s calculation windows in paroxysmal and longstanding persistent AF patients. Our hypotheses were that 1) data averaged over successive 2s intervals would show similar differences in spectral parameters between paroxysmal and persistent AF as are present in 8s data, and that 2) the temporal stability of spectral parameters will be less in paroxysmal as compared with persistent, longstanding AF, because CFAE are more likely to represent random activation of local atrial tissue, and less likely to represent focal sources of impulse initiation, in the former.

METHODS

Clinical Data Acquisition

Atrial electrograms were recorded in 20 patients referred to the Columbia University Medical Center cardiac electrophysiology laboratory for catheter ablation of AF. In all patients, antiarrhythmic medications were stopped five weeks prior to electrophysiologic (EP) study. Endocardial electrogram recordings were obtained during EP study as approved by the Institutional Review Board. The archived data was then used retrospectively for our

analysis. All archival electrogram recordings used for retrospective analysis were acquired prior to any radiofrequency catheter ablation. The patient characteristics were as follows. Ten patients had documented clinical paroxysmal AF, and had normal sinus rhythm as their baseline cardiac rhythm in the electrophysiology laboratory. Atrial fibrillation was induced in these patients by burst atrial pacing from the coronary sinus or from the right atrial lateral wall, and allowed to persist for at least 10 minutes prior to data collection. Ten other patients had longstanding persistent AF without interruption for 6 months to 3 years prior to their catheter mapping and ablation procedure. Bipolar atrial mapping was performed on all these patients using a NaviStar ThermoCool catheter, 7.5F, 3.5mm tip, with 2mm spacing between bipoles (Biosense-Webster Inc, Diamond Bar, CA, USA). The electrogram signals were acquired using the General Electric CardioLab system (GE Healthcare, Waukesha, WI), and filtered at acquisition from 30-500Hz with a single-pole bandpass filter to remove baseline drift and high frequency noise. The filtered signals were sampled at 977 Hz and stored. Although the bandpass high end was slightly above the Nyquist frequency, negligible CFAE signal energy resides in this frequency range¹⁵.

Whereas CFAE definition is admittedly not uniform, in this study only recordings manifesting multicomponent continuous electrical activity with no identifiable isoelectric lines have been used. Only signals identified visually as continuous electrical activity by two cardiac electrophysiologists were included for analysis. Catheter stability at a recording site during the data collection was verified by continuous observation of the catheter tip on the CARTO image. CFAE recordings of over 16 seconds in duration were obtained from one or two antral sites outside the ostia of each of the four PVs. To be used for comparison, similar recordings were obtained from sites in the anterior and posterior left atrial free wall. The mapping catheter was navigated in these pre-specified areas until a CFAE site was identified. During data collection from each PV antral site, a decapolar lasso catheter was placed in the corresponding PV for simultaneous PV potential recordings. During induced AF in patients with paroxysmal AF all PVs manifested fractionated signals in all poles, and in patients with longstanding AF, all PVs manifested fractionated signals in some, but not all poles. None of these recordings met the criteria for CFAE used in this study and no DF analysis was carried out. All data analyzed in this study were collected prior to any ablation was carried out and therefore were not used to guide the ablation procedure. In one patient with clinical paroxysmal AF, during acutely induced AF, no recording site outside the PVs with electrograms satisfying CFAE criteria for at least 10 seconds could be detected. Therefore, data from this patient were not included in the following analysis. Only sites at which the CFAE criteria were maintained during the recorded sequence were used for analysis. A total of 204 sequences – 90 from paroxysmal and 114 from longstanding AF patients, all meeting the criteria for CFAE, were selected for this study and included in the following analysis. As in previous studies, to standardize the morphological characteristics, all CFAE signals were normalized to mean zero and unity variance (average level = 0 volts, standard deviation and variance = 1)¹⁹⁻²¹.

Power Spectral Generation

Power spectra were obtained from CFAE as described previously^{14,15,19}. In early implementations of this analysis for atrial fibrillation signals, preprocessing was done by

bandpass filtering, followed by rectification and low pass filtering prior to Fourier transformation^{9,10}. However, these steps cause signal distortion¹⁶⁻¹⁸, and in recent work has not been used²². Therefore in our study, these preprocessing steps were not introduced¹⁴. Neither were the CFAEs pre-processed with a smoothing window such as a Hann filter to taper the signal edges, because frequency resolution is then decreased²¹. Thus rectangular windowing was used to extract CFAE for analysis with all spectral estimation techniques used in this study (no tapering).

The Fourier power spectrum was obtained using a radix-2 implementation of the DFT²³. In addition to the Fourier transform, a novel spectrum estimator (NSE)²⁰ was implemented. The NSE basis is data-driven and the frequency components are patterns related to actual drivers of electrical activity rather than being composed of artificial sinusoids²⁰. The NSE computes the power spectrum by signal averaging^{14,15}. These two spectral estimators, DFT and NSE, were two independent methods used to validate measurements and to calculate statistical differences. Similarity in the values of these parameters would indicate reproducibility and was used for verification of the results.

As a reference, CFAE were measured over 8.4s calculation windows^{14,15,24}. In order to determine the temporal variability/stability of the spectral parameters, 2s calculation windows were also used for measurement. Each calculation window was then of length 2048 points (2.1s for 977 Hz digitization rate). The beginning of the calculation window was then shifted to 100 sample points later in time (approximately 100 ms) and a new power spectrum was generated. This process was repeated for a total of 82 calculation windows, i.e., 8200 sample points = 8.4 seconds, to be in concordance with single 8.4 second calculation windows used for reference. Spectral parameters were calculated for each of the 82 spectra that were generated for each 2s CFAE recording, as well as for the entire 8.4s CFAE recording used for reference.

Spectral Parameter Calculation

The spectral parameters that were calculated were the DF^{9,10}, as well as two recently introduced parameters¹⁹: the dominant amplitude (DA), which is the amplitude of the dominant frequency peak, and the mean of the normalized spectral profile (MP) which is taken over the physiologic frequency range of 3-12Hz. The MP is calculated by first normalizing the spectral magnitude along the ordinate axis to a range of 0 – 1 units, and then computing the statistical mean from the normalized spectral values¹⁹. When 8.4s analysis windows are used, the DA and MP spectral parameters, like the DF, have significant differences in CFAE characteristics for acute-onset versus longstanding AF¹⁹. The use of DA and MP, in addition to DF, enables validation and verification of differences between AF types, and enables the measurement of different spectral characteristics. The DA and DF measurements are representative of the fundamental periodic component, which is related to the electrical activation rate, while the MP measurements is reflective of random background components in the spectrum and in the activation rate.

Statistical Calculations

The mean values and the coefficients of variation for DA, DF, and MP were calculated using pooled data from all recording sites. Antral recordings and free wall recordings were also analyzed separately. Significant differences were determined using the unpaired t-test (SigmaPlot 2004 for Windows Ver. 9.01, Systat Software, Chicago, and MedCalc ver. 9.5, 2008, MedCalc Software bvba, Mariakerke, Belgium). Significance was considered to occur at a level $p < 0.05$.

RESULTS

Representative power spectra for the DF parameter are shown in Figures 1 and 2, for spectra obtained using the NSE method, 2s intervals. Results from the CFAEs recorded at the antral site outside the ostium of the left inferior PV in a patient with longstanding AF, are shown in Figure 1. The sequence number of the 2s time epoch is given at top right in each graph. Four spectra are shown, which were selected from across the range of epochs 1 to 82. The spectra are similar in terms of both the DF, which occurs at approximately 7.2 Hz, and in the reduced size of other spectral peaks in comparison to the dominant peak. The DA is approximately 1 millivolt in each spectrum. As in these four examples from longstanding persistent AF data, mean DA and DF were relatively large and stable over all 82 time epochs, and mean MP was relatively low, since the background random electrical activity representing the broadband spectrum is reduced in amplitude as compared with the dominant peak.

In contrast to the spectra of Figure 1, in Figure 2 are shown representative spectra from an antral CFAE recording during acute-onset AF in a patient with paroxysmal AF. There are substantial differences as compared with the CFAE spectra of longstanding AF in Figure 1. The paroxysmal AF spectral traces show a DF that changes markedly from one 2s window to the next, ranging from approximately 6 – 8 Hz. Similarly, there are substantial changes in the DA in Figure 2 (note differences in ordinate axis scale). The MP calculated from the spectra of Figure 2 would be expected to be large due to the presence of many tall and temporally unstable peaks as compared with the longstanding AF spectra of Figure 1. The spectra shown in Figure 2 were typical and representative of the CFAE spectra recorded during paroxysmal AF.

The summary statistics of the study are displayed in Tables 1-5, which show results for the DA, DF, and MP spectral parameters for CFAEs recorded in patients with paroxysmal AF and in patients with longstanding persistent AF, using the DFT and NSE spectral estimators. The mean values for the three parameters DA, DF, and MP calculated from all recording sites are shown in Table 1 for the pooled 2s data and in Table 2 for the 8s data. Use of a sliding 2s calculation window averaged over 82 time epochs resulted in the DA being significantly greater in longstanding persistent as compared with paroxysmal data, both by DFT and by NSE analysis (Table 1), as for the 8s data (Table 2). The use of a sliding 2s calculation window averaged over 82 time epochs (8s interval) also resulted in significantly higher DF for CFAE in longstanding persistent AF as compared with paroxysmal AF (Table 1, $p < 0.001$ for both estimators). This finding is also similar to the results obtained using 8s calculation windows (Table 2). Hence, the average difference in DF of the CFAE spectrum,

when comparing acute onset versus longstanding AF, remains significant even when analyzed by shorter 2s time windows. The use of a sliding 2s calculation window averaged over 82 time epochs resulted in a significantly greater MP in CFAEs recorded in paroxysmal as compared to longstanding persistent AF patients for both spectral estimators (Table 1), suggesting a higher level of random background electrical activity globally in patients with paroxysmal AF. All of these results show that characterization of CFAEs by multiple short recording windows do not change the significant differences in CFAE characteristics between longstanding and acutely-induced AF detected by the conventional 8s recording windows (Table 2). When using the NSE estimator, highly significant differences were observed in comparing all paroxysmal versus persistent spectral parameters (Tables 1 and 2).

The same analysis was performed separately for antral and free wall findings, Tables 3 and 4. The 2s results for antral sites alone (Table 3) are unchanged, in fact nearly identical, compared to the pooled data from all sites shown in Table 1. For the NSE spectral estimator, all three parameters are significantly different in longstanding AF compared with acute-onset AF in patients with paroxysmal AF (Table 3). The averaged 2s measurements distinguished according to whether the site was located at the antrum of the PVs or at a free wall site shown in Table 3, are similar to single 8s measurements, shown in Table 4.

Using NSE parameters as an estimate for average AF cycle length, there is a suggestion that DF decreases in the direction from the PV antral sites to the left atrial free wall sites, but the difference in the means does not reach significance (Tables 3,4). We have also compared the differences in DA and MP as parameters of stability, recorded from the PV antrum sites and the left atrial free wall sites. The p values are shown in Table 3 and Table 4. Overall these results suggest that the stability of electrical activation increases away from the PVs, and towards the left atrial free wall, but that this gradient is much more marked for acutely induced AF compared with longstanding AF where stability (or lack of stability) is more uniformly distributed (Tables 3,4).

The coefficient of variation (COV) values for 2s measurements are shown in Table 5. The difference in DF variability between acute onset and longstanding AF was highly significant ($p < 0.001$). Thus the DF during acute onset AF showed significantly more short-term variability compared to the DF during longstanding AF, as assessed by the 2s time windows (Table 5). The estimator measurements were in agreement. The variability in DA was not significantly different in the two types of AF (Tables 5). Finally, even though the MP was higher for acute onset AF, the variability in MP was higher (COV higher) for longstanding AF compared to acute onset AF in patients with PAF, using both spectral estimators and the pooled data (Table 5).

DISCUSSION

Summary

In this study, three spectral parameters and two spectral estimators were used to compare the characteristics of CFAE recordings obtained in patients with persistent longstanding AF, and those obtained during acute-onset AF in patients with paroxysmal AF. The frequency

spectra were calculated using 2s calculation windows as well as standard 8s windows, in order to evaluate the temporal variability/stability in these spectral parameters. Our results show that 2s sliding analysis windows averaged over 8s for analysis produce similar results as a single 8s analysis window, particularly for the NSE method. Thus the DF of CFAE in longstanding AF continues to be higher when using a 2s sliding window as compared with a fixed 8s window. Using the 2s sliding windows, the DFs during longstanding AF manifest significantly greater temporal stability (a lower value for COV that is highly significant) compared to acute onset AF in patients with paroxysmal AF. Our results also show that the MP, an indicator of background random electrical activity in AF, is higher in acute onset AF, and manifest lower variability (lower COV) compared to persistent longstanding AF, suggesting more randomly activated patterns for acute onset AF in patients with paroxysmal AF.

Comparison with Other Methods for Spectral Characterization

The use of a 2s sliding window has been reported in other studies^{18,24}. The DA, which is the height of the DF peak and is related to the power in the DF, has some similarity to the regularity index (RI), which is the power of the DF peak of the frequency spectrum divided by the power in the spectral range of interest^{25,26}. The RI measurement however, requires the user to define the edges of the dominant peak, or to use a pre-defined frequency band to determine the dominant peak edges, which is somewhat artificial and arbitrary. The DA is a more robust measure because it requires no such subjective definition concerning the characteristics of the dominant peak. The MP measurements also require no manual intervention. Rather, it is a statistical measure in the spectral range of interest, which was selected, in our study, as 3-12Hz, a conservative frequency of activation range for AF, readily calculated with low computational cost. This parameter has some relationship to the organizational index (OI), the power of the dominant peak and its harmonics divided by the power in the spectral range of interest^{25,26}. However as with the RI, the OI calculation requires manual intervention, since harmonic peaks must be detected, harmonic peak width must be determined manually or by using predetermined constraints, and the number of harmonic peaks to be used in the calculation must be decided, which are artificial and arbitrary.

Clinical Correlates and Future Directions

The larger DA values observed in longstanding persistent AF suggest a more stable and more intractable substrate source of the dominant peak, which does not readily change from one instance to another as compared with the dominant peak characteristics of acutely induced AF in patients with paroxysmal AF. The higher mean DF value in longstanding AF is compatible with elevated activation rates, e.g. fast rotors, or focal impulse sources, or both, in these patients¹¹⁻¹³. Even though the universally accepted first step in the non-pharmacologic treatment of AF by catheter ablation is still the electrical disconnection of the PVs, commonly achieved by wide antral lesions outside the ostia of the PVs, publications describing AF mapping with composite electrodes have identified drivers outside the PVs²⁷. The efficacy of catheter ablation limited to PV isolation is more effective in paroxysmal AF compared to longstanding AF²⁸. Based on our findings, CFAE recordings during acute onset atrial fibrillation represent more random electrical activity, with multiple components

possibly representing remote activation of adjacent sites from changing directions. In contrast, micro-reentry sites, rotors, or focal impulse sources at fixed anatomic locations would be expected to result in relatively stable DF values with little change from one time epoch to the next. This was our finding for longstanding AF (Table 5). Thus persistent longstanding AF likely has more stable impulse sources as compared to paroxysmal AF in both a temporal and spatial framework. In this setting, CFAE sites outside the PV regions may be important targets in ablative therapy of longstanding AF, provided that they represent sites initiating or maintaining AF. By contrast in paroxysmal AF, there would be lesser advantage in targeting CFAE sites outside the regions of wide antrum PV isolation.

The differences in electrogram characteristics that we have observed may have a histological basis. The histological changes in the atrial tissue, e.g. fibrosis, which take place over long periods of time in longstanding AF, have been described previously²⁹. These permanent changes in atrial tissue architecture may create relatively fixed atrial sites of arrhythmogenesis. In contrast, such architectural changes are typically absent in patients with paroxysmal AF, and abnormal fractionated electrograms are rarely recorded during sinus rhythm³⁰. The mechanisms maintaining acute onset AF are more likely to depend on areas of changing, migrating functional refractoriness, rather than anatomically fixed regions promoting arrhythmogenesis. Thus the direction of wavefronts and wavebreak sites would also shift over time as areas of functional refractoriness migrate. One possible consequence of this dynamic picture is an increased variability in DF, as measured from a single recording site, throughout 82 time epochs. Indeed the DF variability was significantly higher (COV higher, $p < 0.001$) in acute onset AF in patients with paroxysmal AF compared to longstanding AF. Another possible consequence would be an elevated MP with little temporal variability from one time window to the next (low COV) in acute onset AF, since the MP parameter is a measure of randomness of electrical activity, and it is more reflective of the global, background electrical activity rather than local electrical activity or depolarization of the tissue in the close vicinity, because it is a broadband measure. Thus the higher mean MP values observed in patients with paroxysmal AF as compared with persistent longstanding AF patients suggest greater underlying randomness in electrical activation in the former patients, as compared with longstanding AF patients in whom the regularity of local electrical activity may be temporally more stable, and has more structure as recorded from the CFAE sites.

Investigations by other groups sometimes suggest that electrogram analysis may not be particularly helpful in analyzing AF. Prior work has found that the DF spatial distribution as obtained by sequential point-by-point acquisition of CFAE recordings depends upon the time at which each site is sampled³¹. In this study the recording sites manifested CFAE, at least throughout the period of data collection. Furthermore, it has been suggested that stable rotors and focal sources of AF, which are ablation targets, are revealed by panoramic mapping but not by electrogram analysis³². Yet, ablation of high DF sites has previously been used to prevent reinduction of paroxysmal AF³³, and it has been shown that in persistent cases, ablation of CFAE sites after PV isolation improves freedom from AF³⁴. In prior work we showed that the DF is stable from one 8s interval to the next¹⁵. In the present study we found 2s windows to be useful for measurement of short-term temporal instabilities in spectral parameters. If this information is used along with the temporally

more stable 8s spectral parameter information, a more complete picture of the AF substrate properties may be obtained. When 2s and 8s time windows are analyzed, use of the more robust spectral estimator (NSE) and parameter set (DA and MP as well as DF) may therefore help identify target sites for catheter ablation based on CFAE. The results of our data analysis were not used to guide the catheter ablation of the patients included in this study. Therefore we cannot comment on any impact on efficacy.

In a recent study, focal areas of high DF were found to be spatiotemporally unstable in paroxysmal as compared with persistent AF³⁵. This is in accord with our finding that the DF is less temporally stable in paroxysmal AF (Table 5). Although we did not test the spatial stability of the DF, the finding that high DF areas are less spatially stable in paroxysmal as compared with persistent AF is also in accord with our findings. When points of high DF are unstable in paroxysmal AF, the resulting complex activation pattern would be expected to generate a high value of MP, as was found for paroxysmal AF in our study (Tables 1-4). In most longstanding AF patients, PV isolation increases AF organization of electrical activity³⁶. When organization increases, the MP parameter would be expected to diminish. Thus the MP parameter may also be useful to estimate the number of independent drivers remaining in the substrate, the subject of future study. In persistent AF, ablation of CFAEs after PV isolation can improve ablation success³⁷. Since targeting CFAEs, regardless of whose definition and criteria are used, does not ensure AF termination, the non-specific nature of these electrograms must be accepted. To the extent that similar CFAEs may be generated by different underlying mechanisms, there may be a limit to how much the specificity may be improved by signal analysis similar to ours. Further improvement of our capability to distinguish between ‘bystander’ versus ‘etiological’ CFAEs will require studies using more sophisticated multielectrode recording systems.

Limitations

During data collection, the spatial stability of the catheter tip was limited by the resolution of the site location as verified by the three-dimensional CARTO system. Since atrial motility in acutely induced AF can be greater than in persistent AF, the temporal stability of the DF may have been more greatly affected by catheter tip stability in acute paroxysmal AF. The temporal stability of the dominant frequency at high DF sites has been demonstrated using conventional DFT analysis^{13,38-39}. Patients who clinically had paroxysmal AF were in normal sinus rhythm at the outset of the study and AF was induced by burst pacing, which may not be representative of their clinical AF, especially since electrical induction was not tried from the PVs. However since data collection followed a period of at least 10 minutes of continuous AF, it is doubtful that the mode and the site of induction would still play an important role after this obligatory wait period.

For quantitative analysis, high DF regions were not specifically sought. Specific selection and analysis of regions with high DF may produce different results than we observed. Several anatomic locations such as the left atrial roof, the left atrial appendage, and right atrial sites were not sampled. If such sites harbor drivers of AF, for example stable rotors, reentry sites, or stable focal impulse sources, CFAEs recorded from there may yield different results from those reported here. Use of more recording sites might also reveal

additional characteristics and differences between CFAEs recorded in paroxysmal AF patients and those recorded during longstanding AF. The findings of this study should be confirmed in a prospective study with larger number of patients and additional recording sites.

Conclusions

Although 2s spectral measurements of AF data are time-varying, the average value over an 8s interval is similar to a single measurement obtained over an 8s interval. This finding suggests that 2s measurements are accurate to provide a picture of dynamic AF phenomena at this level of time resolution. From COV measurements of temporal variability using 2s sliding windows, we conclude that the DF parameter manifests significantly higher variability in paroxysmal AF as compared with persistent longstanding AF, suggesting a higher degree of randomness in electrical activation during the former, and temporally and spatially more stable impulse sources for the latter. The higher MP value of acute onset AF, and its lower variability over consecutive time epochs, also suggest that acute onset AF in the absence of chronically altered atrial substrate may be represented by more random electrical activity. The agreement in all spectral measurements using DFT versus NSE methods provides evidence as to the validity of the analysis method.

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Figure 1.

Spectra from an antral site recording (outside left superior pulmonary vein ostium) in a patient with longstanding persistent AF. Only minor changes occur in the spectra, which are derived from sliding 2s data windows, over the entire interval. The DF remains approximately the same for each window. The spectra were calculated using the ensemble type method. NSE resolution is greater for lower frequencies as is evident by the finer degree of detail.

Figure 2.

Spectra from an antral site recording (outside right superior pulmonary vein ostium) in a patient with paroxysmal AF. Large changes occur in the 2s spectra over the 8 second interval. The DF varies greatly. The mean of each spectral profile is large as compared to Figure 1.

Table 1
All 2s Data, Mean

Meas	DFT			NSE		
Type	Parox	Persis	P value	Parox	Persis	P value
DA	0.27±0.09	0.32±0.12	0.002	1.40±0.16	1.60±0.30	<0.001
DF	5.70±0.68	6.26±0.82	<0.001	5.89±0.59	6.37±0.67	<0.001
MP	0.37±0.04	0.34±0.06	<0.001	0.42±0.05	0.37±0.07	<0.001

Means ± Standard Deviation in CFAE spectral parameters pooled from all sites (antral and free wall) in paroxysmal versus persistent AF patients. The first column displays the results calculated using the novel spectral estimator (NSE), and the second column depicts the results calculated using Fourier analysis (DFT). The rows provide the results for mean values over 82 time epochs, each a 2s segment. Meas Type – measurement type, DA – dominant amplitude, DF – dominant frequency, MP – mean of spectral profile, Parox – paroxysmal AF, Persis – persistent AF. The DA units are millivolts, DF is in Hertz, and the MP units are relative magnitude.

Table 2
All 8s Data, Mean

Meas	DFT			NSE		
Type	Parox	Persis	P value	Parox	Persis	P value
DA	0.69±0.30	0.85±0.38	0.004	1.46±0.29	1.83±0.59	<0.001
DF	5.62±1.13	6.25±0.92	<0.001	5.38±1.26	6.28±0.96	<0.001
MP	0.30±0.07	0.26±0.07	<0.001	0.40±0.08	0.34±0.10	<0.001

Abbreviations and descriptions are provided in Table 1, except the data is for 8s analysis sequences.

Table 3
Antral and Free Wall 2s Data, Mean $\pm$ Standard Deviation

Anat	Meas	DFT			NSE		
Loc	Type	Parox	Persis	P value	Parox	Persis	P value
APV	DA	0.25 $\pm$ 0.09	0.30 $\pm$ 0.12	0.003	1.38 $\pm$ 0.16	1.59 $\pm$ 0.29	<0.001
APV	DF	5.66 $\pm$ 0.70	6.25 $\pm$ 0.82	<0.001	5.93 $\pm$ 0.60	6.42 $\pm$ 0.65	<0.001
APV	MP	0.38 $\pm$ 0.04	0.34 $\pm$ 0.06	<0.001	0.42 $\pm$ 0.04	0.37 $\pm$ 0.06	<0.001
FW	DA	0.32 $\pm$ 0.09	0.37 $\pm$ 0.11	0.140	1.46 $\pm$ 0.15	1.64 $\pm$ 0.32	0.013
FW	DF	5.78 $\pm$ 0.63	6.29 $\pm$ 0.82	0.011	5.80 $\pm$ 0.56	6.28 $\pm$ 0.72	0.013
FW	MP	0.36 $\pm$ 0.05	0.33 $\pm$ 0.06	0.081	0.43 $\pm$ 0.05	0.38 $\pm$ 0.07	<0.001
APV-FW	DA	P<0.001	P=0.003		P=0.024	P=0.404	
APV-FW	DF	P=0.431	P=0.807		P=0.325	P=0.298	
APV-FW	MP	P=0.043	P=0.403		P=0.307	P=0.430	

Means $\pm$ Standard Deviation in CFAE spectral parameters. APV = antrum of pulmonary vein, FW = left atrial free wall, DA = dominant amplitude, DF = dominant frequency, MP = mean spectral profile. Anat Loc – anatomical location. spectral parameters are shown separately for APV, two closely spaced locations, with each recording site being 1-2 cm outside each of the four pulmonary veins in each patient, and for FW. In persistent AF, the NSE measurements suggest that there is a gradient of higher to lower DF in the direction from antrum to free wall, but the difference did not attain significance. P values in lower three rows are comparisons between APV and FW in the same column. Data is based on analysis of 60 CFAE at APV and 30 at FW in paroxysmal AF, and 76 CFAE at APV and 38 at FW in persistent AF.

Table 4
Antral and Free Wall 8s Data, Mean $\pm$ Standard Deviation

Anat	Meas	DFT			NSE		
Loc	Type	Parox	Persis	P value	Parox	Persis	P value
APV	DA	0.69 $\pm$ 0.30	0.85 $\pm$ 0.38	P = 0.004	1.46 $\pm$ 0.29	1.83 $\pm$ 0.59	P < 0.001
APV	DF	5.62 $\pm$ 1.13	6.25 $\pm$ 0.92	P < 0.001	5.38 $\pm$ 1.26	6.28 $\pm$ 0.96	P < 0.001
APV	MP	0.31 $\pm$ 0.07	0.26 $\pm$ 0.07	P < 0.001	0.41 $\pm$ 0.07	0.34 $\pm$ 0.10	P < 0.001
FW	DA	0.89 $\pm$ 0.29	1.06 $\pm$ 0.42	P = 0.068	1.64 $\pm$ 0.28	1.98 $\pm$ 0.74	P = 0.060
FW	DF	5.54 $\pm$ 1.19	6.16 $\pm$ 0.84	P = 0.011	5.62 $\pm$ 1.12	6.07 $\pm$ 0.99	P = 0.020
FW	MP	0.30 $\pm$ 0.07	0.25 $\pm$ 0.08	P = 0.017	0.39 $\pm$ 0.08	0.34 $\pm$ 0.12	P = 0.049
APV-FW	DA	P=0.003	P=0.008		P=0.0062	P=0.243	
APV-FW	DF	P=0.757	P=0.614		P=0.3797	P=0.278	
APV-FW	MP	P=0.525	P=0.495		P=0.2266	P=1.000	

Abbreviations and descriptions are provided in Table 3.

Table 5
All 2s Data, Coefficient of Variation

Meas	DFT			NSE		
Type	Parox	Persis	P value	Parox	Persis	P value
DA	0.26±0.11	0.27±0.13	0.932	0.18±0.09	0.19±0.10	0.420
DF	0.16±0.07	0.11±0.07	<0.001	0.18±0.08	0.10±0.07	<0.001
MP	0.19±0.04	0.21±0.05	0.005	0.16±0.04	0.18±0.05	0.019

Coefficient of Variation in CFAE spectral parameters pooled from all sites (antral and free wall) in paroxysmal versus persistent AF patients. All abbreviations and other description as in Table 1.