Towards Application of Complexity Measures of Atrial Electrograms to Predict Outcome of the Ablation Procedure

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Abstract

The aim of this study was to assess the reliability of the complexity analysis of a single electrogram as a predictor of spontaneous termination of Atrial Fibrillation (AF) during ablation procedure.

Left and right atrial endocardial bipolar electrograms from two locations (High Right Atrium - HRA and Coronary Sinus - CS) were recorded before ablation treatment of AF (at baseline) in 36 patients. Information about the ablation outcome (cardioversion - CV or spontaneous termination - TERM) was collected. For each electrogram, algorithmic complexity (AC) and Shannon entropy was calculated.

Baseline electrograms from electrodes located in HRA had significantly lower algorithmic complexity than from electrodes located in CS. Only the Shannon Entropy of electrogram measured at CS showed significant difference between CV and TERM (p=0.03), while in case of algorithmic complexity only a trend towards significance was found (p=0.08).

Electrogram complexity parameters used in clinical practice did not distinguish the ablation outcome groups, with Shannon entropy showing the most significant difference.

1. Introduction

In last decades Atrial Fibrillation (AF) has become a focus of attention [1]. It is the most complex and the most common sustained arrhythmia and it is predicted, that the number of patients with Atrial Fibrillation will grow significantly within next years [2]. Rates of incidence and hospitalization due to AF are still increasing reaching and epidemic proportions [3].

Understanding the mechanisms that cause and sustain AF remains a challenge. Haïssaguerre et al. [4] indicated, that electrical activity in the region of pulmonary veins may be a trigger of AF, which made this area the main target during catheter ablation. However, it not always leads to termination of Atrial Fibrillation, and ablation at additional sites is necessary, which complicates the ablation procedure. One of the suggested targets for additional ablation are the areas with complex atrial electrograms, and for that purpose many algorithms quantifying electrogram complexity were developed [5].

While up to date complexity assessment of AF electrograms has been mostly used to target areas for the ablation, the aim of this study was to assess the reliability of the complexity analysis of a single electrogram as a predictor of spontaneous termination.

2. Methods

2.1. Study population

Left and right atrial endocardial bipolar electrograms from different intracardiac locations (High Right Atrium - HRA and Coronary Sinus - CS) were recorded before ablation treatment of AF (at baseline) in 36 patients. Information about the ablation outcome (CV-cardioversion or TERM-spontaneous termination) was collected. Cardioversion was required in 18 patients, while in 18 Atrial Fibrillation ended spontaneously. For each patient 7 recordings were available: 5 from catheter located in the coronary sinus and 2 from catheter placed high in the right atrium. For each catheter separable recordings for each electrode of the catheter were available (for example for CS catheter CS 1-2, CS 3-4 etc.). The sampling frequency was 1 kHz.

All the data was collected in the University Hospital Eppendorf, Department of Electrophysiology, Hamburg, Germany. The study protocol was approved by the institutional ethical review committee, and all patients gave written informed consent.

For all electrograms, algorithmic complexity was calculated (based on algorithm proposed in [6]) and compared with other parameters used in electrogram complexity assessment. To check significance of the results, ANOVA and ROC analysis were performed.

2.2. Algorithmic complexity calculation

In this study a method introduced by Pitschner and Berkowitsch [7] was used. It is based on symbolic dynamics and calculates algorithmic complexity of intracardiac recordings of electrical activity of the heart.

In the information theory, complexity of the string of characters may be defined as the length of its shortest possible description in some universal language. In order to calculate it, measured signals were converted into binary strings [8]. Basing on criteria defined as:

$$A_i = MP_i + 0.1V_i,$$

with MP_i as mean instantaneous power and V as adaptive power variance. Moving threshold A_i was calculated for every sample i [7]. Having A_i and using instantaneous signal power P_i it was possible to define the translation rule from every sample of measured intracardiac signal S_i to the binary character:

$$S_i = \begin{cases} 1; & P_i > A_i \\ 0; & P_i \leq A_i \end{cases}$$

AC for obtained binary string was calculated according to Lempel-Ziv algorithm [9]. This was done by finding the number of so-called words in this string. For each element of the string, the check was performed whether new sequence has appeared in the signal before. If not, then that sequence became a new word and algorithmic complexity raised by 1. Otherwise, another sample was added and check whether the sequence occurred was performed again [8]. Example of conversion from binary signal to words and calculating algorithmic complexity is presented in Figure 1.

For all electrograms algorithmic complexity was calculated for 2, 5 and 10 second electrogram fragments (single-window). Example electrograms demonstrating the need for objective quantification of complexity is shown in Figure 2. Despite apparent similar level of complexity assessed during visual inspection, analysis of AC revealed that there is a significant difference between complexity of those signals.

2.3. Other complexity methods

For all of the cases, algorithmic complexity was compared with other parameters used in electrogram complexity assessment: Complex Fractionated Electrogram Indices (mean CFE, ICL, SCI) [10]-[11] and Shannon Entropy [12].

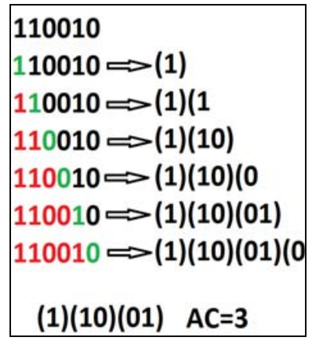

Figure 1. Example of conversion from binary signal to words. Green color means the sample analyzed in the particular step. Always the first sample is the first word. In the next steps, it is checked whether new sequence (in the last bracket) has appeared in the signal before (in the red part). If not, then the sequence in the bracket becomes a new word and algorithmic complexity raises by 1. Otherwise, we add another sample and check again whether the sequence occurred. In the last step there is one sample in the open bracket, but it has appeared in the signal before, so this is not a new word. Eventually, number of words (algorithmic complexity) is equal to 3.

2.4. Statistical analysis

The statistical significance of results was tested using ANOVA test. It was used to check whether the result of algorithmic complexity for the baseline electrogram and results of compared methods are dependent on the ablation outcome: cardioversion or termination. In all cases, a statistical significance (p) lower than 0.05 was considered as significant.

To check if the distribution factors were chosen correctly ROC analysis was performed.

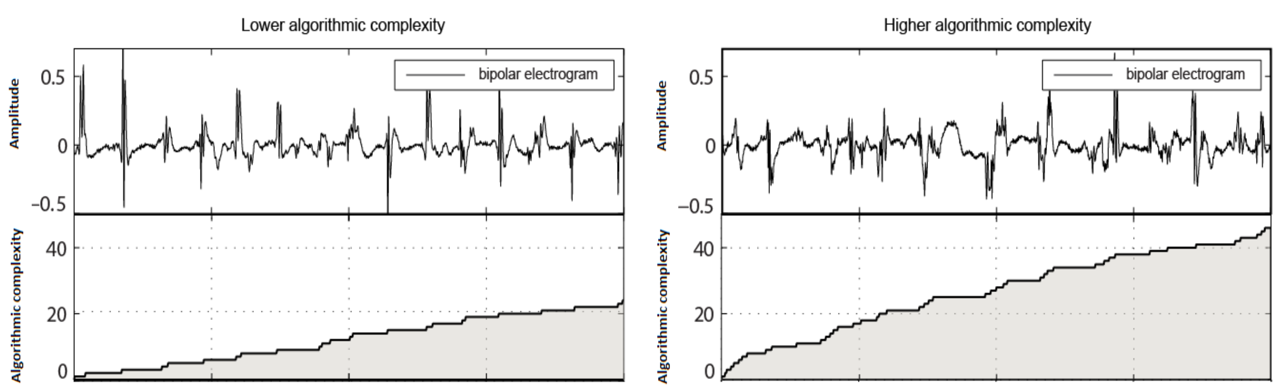

Figure 2. Comparison of two electrograms with different algorithmic complexity. In the top figures, 2 s windows of bipolar electrograms are presented, with corresponding algorithmic complexity plot for both cases in the bottom figures.

3. Results

Results of ANOVA analysis (Figure 3) revealed that baseline electrograms from electrodes located in HRA had significantly lower algorithmic complexity than from electrodes located in CS.

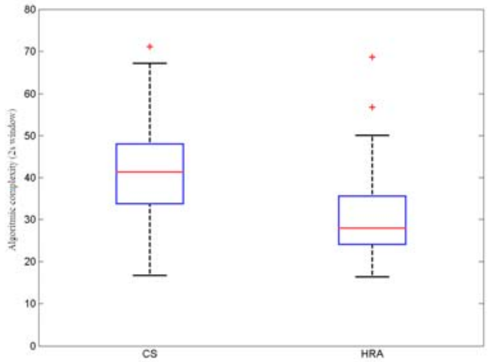

Figure 3. Box plots of algorithmic complexity of electrograms measured before ablation procedure in Coronary Sinus and High Right Atrium, $p<0.05$.

To check whether the complexity for the baseline electrogram is dependent on ablation outcome, we performed ANOVA test for patients groups of CV/TERM (Figure 5). The result was not statistically significant ($p>0.05$), but we have chosen the group of recordings with the lowest p-value (from CS 5-6 electrode) to compare AC with other methods. Results are presented in Table 1.

In case of algorithmic complexity only a trend towards significance was found ($p=0.08$, Figure 6). Only the Shannon Entropy of electrogram measured at CS 5-6 showed significant difference between CV and TERM ($p=0.03$, Figure 7).

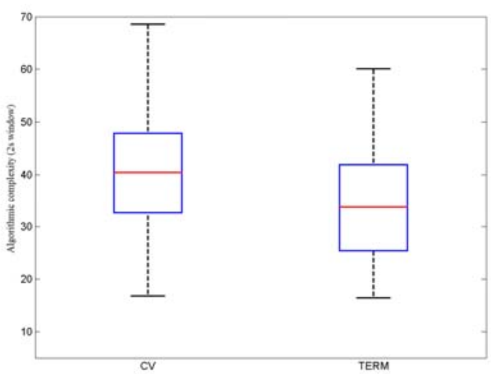

Figure 5. Box plots of algorithmic complexity of electrograms measured in in Coronary Sinus and High Right Atrium before ablation procedure for patients with cardioversion and patients with termination, $p>0.05$.

Table 1. p-values obtained from ANOVA test for algorithmic complexity and other methods, for electrograms measured before ablation procedure at CS5-6, in 2 s, 5 s and 10 s window.

window	2s	5s	10s
	p values		
Algorithmic Complexity	p=0.073	p=0.087	p=0.078
Shannon Entropy	p=0.027	p=0.030	p=0.029
CFE mean	p=0.108	p=0.112	p=0.114
ICL	p>0.2	p>0.2	p>0.2
SCI	p>0.2	p>0.2	p>0.2

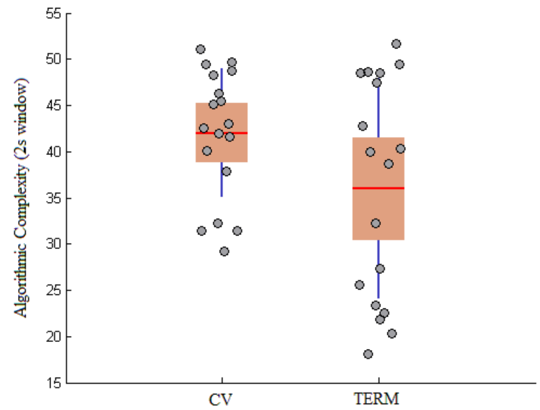

Figure 6. Box plots of algorithmic complexity of electrograms measured before ablation procedure at CS5-6 for patients with cardioversion and patients with termination.

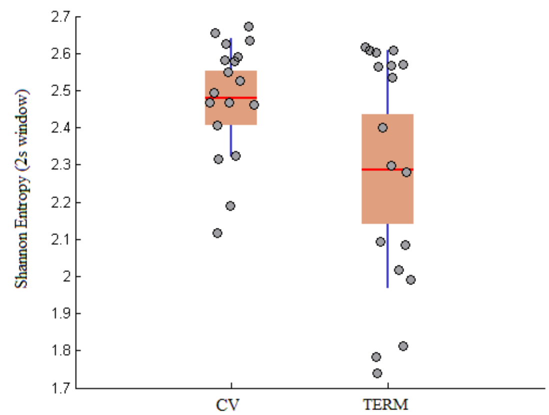

Figure 7. Box plots of Shannon entropy of electrograms measured before ablation procedure at CS5-6 for patients with cardioversion and patients with termination.

Results of Receiver-Operating Characteristic (ROC) for 2 s window are presented in Figure 8 and Figure 9. Area under ROC curve for algorithmic complexity for all windows was no lower than 0,63 and for Shannon Entropy no lower than 0,66.

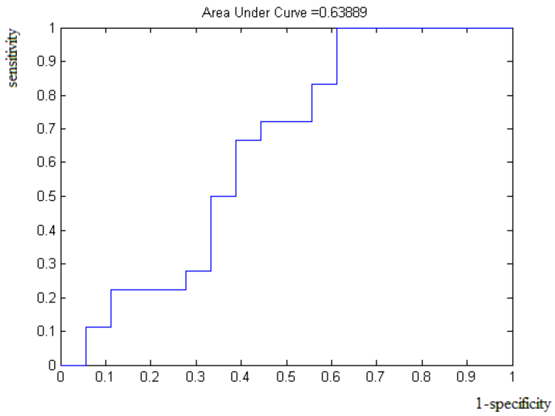

Figure 8. ROC analysis of classification performance of division into CV/TERM groups of patients for algorithmic complexity analysis for 2 s window.

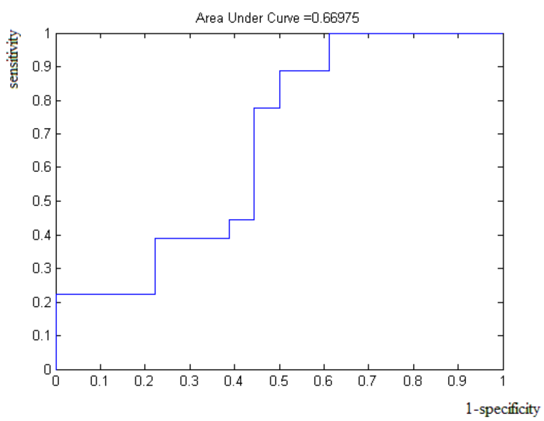

Figure 9. ROC analysis of classification performance of division into CV/TERM groups of patients for Shannon Entropy analysis for 2 s window.

4. Discussion and conclusions

Complexity methods may be useful in the assessment of the ablation immediate outcome, however the choice of the complexity measure is an important and open question. Electrogram complexity parameters used in clinical practice did not distinguish the ablation outcome groups with Shannon Entropy showing the most significant difference.

However, in clinical setting separation of spontaneous termination from induced cardioversion is not well defined, since sometimes cardioversion is induced without waiting for spontaneous termination. In the future, joined analysis of time of ablation and occurrence of spontaneous cardioversion will be conducted.

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