Carl Gross*, Stefan Pollnow, Olaf Dössel and Gustavo Lenis

Automatic feature extraction algorithms for the assessment of in-vitro electrical recordings of rat myocardium with ablation lesions

Abstract: Cardiac arrhythmias are a widely spread disease in industrialized countries. A common clinical treatment for this disease is radiofrequency ablation (RFA), in which high frequency alternating current creates a lesion on the myocardium. However, the formation of the lesion is not entirely understood. To obtain more information about ablation lesions (ALs) and their electrophysiological properties, we established an *in-vitro* setup to record electrical activity of rat myocardium. Electrical activity is measured by a circular shaped multielectrode array. This work was focused to gain more information by developing algorithms to process the measured electrical signals to collect different features, which may allow us to characterize an AL. First, pacing artefacts were detected and blanked. Subsequently, data were filtered. Afterwards, activations in atrial signals were detected using a non-linear energy operator (NLEO) and templates of these activations were generated. Finally, we determined different features on each activation in order to evaluate changes of unipolar as well as bipolar electrograms and considered these features before and after ablation. In conclusion, the majority of the signal features delivered significant differences between normal tissue and lesion. Among others, a reduction in peak to peak amplitude and a diminished spectral power in the band 0 to 100 Hz may be useful indicators for AL. These criteria should be verified in future studies with the aim of estimating indirectly the formation of a lesion.

Keywords: ablation lesion, myocardium, rat, feature extraction, *in-vitro* experiment, radiofrequency ablation
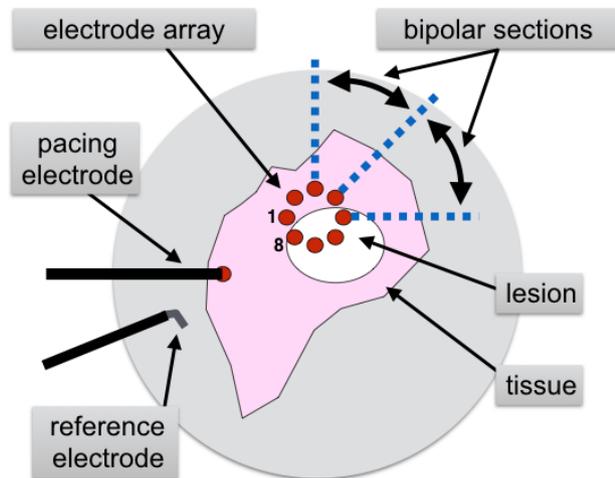
1 Introduction

Atrial fibrillation (AFib) is a massive problem in industrialized countries [1]. Radiofrequency ablation (RFA) is a common method to treat supraventricular tachycardia by creating intentionally ablation lesions (ALs). A high frequency alternating current heats up the tissue until myocardium is irreversibly destroyed. Unfortunately, the recurrence rate of arrhythmias is 35-40% after the minimal invasive treatment [2]. Both formation and geometry of the resulting AL are not entirely understood. Furthermore, there is no existing evaluation method, which allows a statement on transmurality of ALs. To shed more light on this concern, we established an *in-vitro* setup, in which we are able to analyze electrophysiological properties of rat myocardium under well-defined conditions [3]. In this study, we developed automatic algorithms to gain more information about the measured electrical signals and generated features, which might allow us to evaluate ALs.

2 Methods

2.1 *In-vitro* RFA experiments

A setup combining optical mapping and electrical measurement technology was first designed by Keller [3]. Tissue was positioned in a tissue bath with nutrient solution, in which it was kept alive for several hours. In this study, we used the right atrium of a rat. The setup included a pacing electrode with an adjustable frequency, usually 5 Hz was used. This electrode was able to overwrite the sine rhythm (4.5 ± 0.10 Hz) of the atrial myocardium. A thin ablation electrode with a diameter of 0.3 mm allowed to create an AL during a measurement without changing any other setting or moving the tissue. The electrical signals were recorded at a sampling rate of 100 kHz with an eight-electrode array in circular shape, which was placed on the endocardial side of the myocardium. For unipolar recordings, a reference electrode was located in the tissue bath. By combining adjacent electrodes, bipolar data were obtained. A scheme of the measurement setup, focus-

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Figure 1: Scheme of measurement setup for *in-vitro* experiments with rat myocardium (pink). The myocardium was kept alive in nutrient solution, in which a reference electrode was situated. Uni- and bipolar data were recorded with circular electrode array (red).

ing on the recording of electrical data is shown in figure 1. In this paper, the word "activation" refers to the measured electrophysiological activity triggered by sine rhythm or pacing.

For data analysis, we developed new algorithms, written in Matlab 2016b (MathWorks Inc.). These algorithms were based on eight different measurements with changing settings. The program execution is presented as follows: At the beginning, measurement data were loaded into the program along with the matching setup configuration. First, pacing and RFA artifacts were removed and signals were filtered by an adaptive high and low pass filter. Afterwards, activations were detected and features were generated. In the final step, these features were used to determine local activation time (LAT) and to create LAT maps. All parts will be explained in detail in the following subsections.

2.2 Artifacts removal

From raw data, two different artifacts had to be removed, which occur depending on the chosen measurement configuration. The first artifacts were caused by the pacing electrode. By high pass filtering the unipolar signal at 1000 Hz, more than 90 % of the tissue activity was removed and pacing peaks were detectable in the remaining signal using a 99 %-quantile threshold. They were replaced by a cubic spline with a dynamic width depending on the pacing duration. The locations of the pacing peaks were saved and used to blank them in the bipolar signal as well.

It was not feasible to record electrical activity during RFA due to the high voltage and frequency of the ablation current.

This unusable part was cut out and the signal got separated in electrical signals before and after ablation. They were processed in the next steps concurrently to analyze signal characteristics before and after RFA.

2.3 Filtering

Unipolar as well as bipolar electrograms were analyzed in frequency domain using a Welch's periodogram. 2.5 % and 97.5 % of the power density were detected and their corresponding frequencies were chosen as cutoff frequency for the high and low pass filters. We implemented a third order Butterworth high and low pass filter with median cutoff frequencies at 0.6 Hz and 850 Hz.

2.4 Template generation

For building templates from unipolar as well as bipolar signals, it was necessary to detect atrial activities. For this purpose, we implemented two different functions using a nonlinear energy operator (NLEO) [1] and the minimum of the derivative of the signal, in the following called negative slope (NS). The resulting signal of the NLEO was filtered with a 24 Hz low pass filter, so one NLEO peak corresponded to one activity. The activation detection was done only in one electrode as time reference. Index was used to cut out the exact same 100 ms time window, 30 ms before and 70 ms after this index, so an LAT offset is detectable in templates. The time windows were all summed up and then averaged to build the template of an average activation in a channel. Both the final template and all activations were saved for further data analysis.

2.5 Feature extraction

The found activation time locations from the template algorithm were used to cut out each activation. We determined sixteen different features in order to analyze both unipolar and bipolar signals: maximum amplitude, minimum amplitude, peak to peak amplitude (P2P), NS, peakness of the global maximum and global minimum, LAT using NS and NLEO, frequency bandwidth (5 %- 95 % of spectral signal power), 50 % power of spectrum, and frequency with highest power. Peakness was calculated with a least squares estimation algorithm (polyfit, Matlab 2016b), which fitted a parabola in the detected parts of the activation. For further feature extraction, the selected activity was squared and normalized to have an area under the curve of one. We assumed, that the resulting curve has the properties of a probability density function.
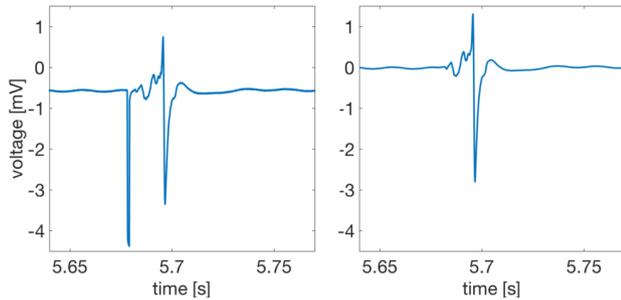
Figure 2: Section of raw unipolar signal with pacing artifact and offset (left). Processed and filtered section of the same signal (right).

From this curve, we computed the centre of mass, variance in time, width in time, skewness in time, and kurtosis in time. In addition, we performed the Wilcoxon signed-rank test to evaluate the statistical significance of the changes of the above mentioned features before and after RFA.

2.6 Local activation time map

We created LAT maps to visualize the propagation direction of the excitation wavefront. The used electrode array had a diameter of 3.5 mm. Based on this, we created a 2D surface with evenly spread electrodes on a circle. The data between the electrodes were interpolated using bilinear interpolation. Therefore, triangles had been formed with an LAT time on each corner. The median LAT of each electrode was considered as LAT of this tissue region.

3 Results

All given results are median values with interquartile range. In figure 2, a section of raw unipolar signal and processed signal is shown. In this example, pacing artifacts were removed and the signal was filtered as described in the last section. Unipolar and bipolar templates before and after ablation are presented in figure 3. After the Wilcoxon test, four features were defined to be significant. These were P2P, NS, the frequency bandwidth, and the 50 % value in power density spectrum (p-value $< 10^{-6}$). The results of unipolar and bipolar features of ablated and non ablated tissue are shown in table 1 and in table 2. Values are presented as range, because all electrodes were considered for comparison. There were unipolar activations, which showed a low P2P (1 ± 0.1 mV), but showed the characteristics of non ablated myocardium in frequency bandwidth (6-296 Hz), figure 4 (2). As seen in table 1, P2P decreased

Table 1: Significant features of unipolar activity recorded above ablated and non ablated tissue. Results are given in median ± interquartile range. Frequency bandwidth is median frequencies from 5% to 95% of the power density.

feature	non ablated	ablated
peak to peak amplitude[mV]	4.53 ± 2	0.65 ± 0.32
max. negative slope [mV/ms]	-4 ± 2.3	-0.08 ± 0.37
frequency bandwidth [Hz]	3-350	0-78
50% frequency [Hz]	66 ± 46	10 ± 1

Table 2: Significant features of bipolar activity recorded above ablated and non ablated tissue. Results are given in median ± interquartile range. Frequency bandwidth is median frequencies from 5% to 95% of the power density.

| feature	non ablated	ablated
peak to peak amplitude [mV]	5.7 ± 2.4	0.13 ± 0.1
max. negative slope [mV/ms]	-2.8 ± 2.5	-0.05 ± 0.06
frequency bandwidth [Hz]	3-481	0-148
50% frequency [Hz]	113 ± 54	17 ± 12

and frequency spectrum was shifted towards lower frequencies. Other features, e.g. time kurtosis or time skewness did not show significance. Figure 5 shows an LAT map of non ablated tissue. The first registered LAT was on electrode 8 (bottom left). The difference between first and last registered LAT was 9.9 ms. Low LAT is represented in red and high LAT in light blue, so the excitation wave propagated from the bottom left to the right.

4 Discussion

We developed an automatic algorithm to process data recorded in an *in-vitro* experiment and to extract different features. Therefore, we tested the algorithm with different measure-
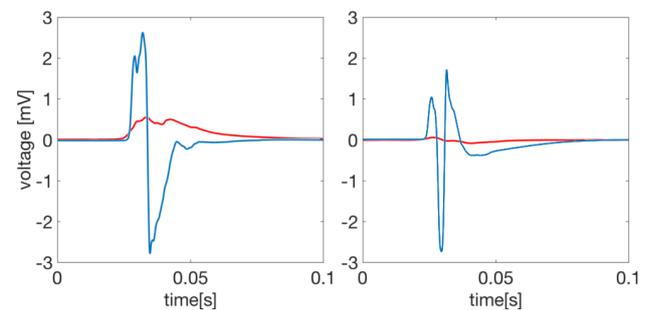

Figure 3: Templates for unipolar signal (left) and bipolar signal (right). Before (blue) and after (red) radiofrequency ablation. Templates were aligned by the local activation time.
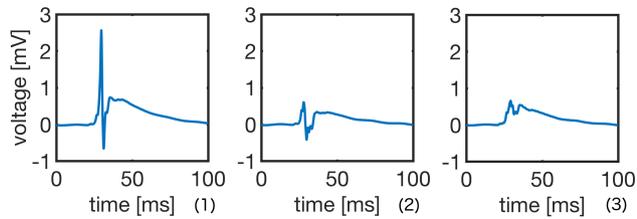
Figure 4: Templates of measurement with the electrode array halve on ablated tissue and halve on non-ablated tissue. Template of activity on non ablated tissue (1), ablated tissue (3), and electrode might be on border zone between ablation lesion and non ablated tissue (2). All templates were aligned by local activation time in reference to electrode 1 (1) at 30 ms.

ments with pacing, RFA, and different array positions. The measurements were preprocessed, filtered, activations were detected and statistical features were determined. Significant features were found and can be used in future studies. The features show, that on an AL the median P2P can decrease up to 90 %. Keller et al., also determined this reduction in P2P and in NS after an RFA [4]. The median frequency bandwidth decreases on an AL to 0-78 Hz. Avitall et. al came also to the conclusion, when performing ablation measurements with ring catheters in canines with chronic AFib [5]. With the knowledge of the configuration of our setup and the exact position of the used electrode array on the tissue, we interpreted the data and found significant features, which could help to understand ALs and their formation more in detail. It may be feasible to find a combination of features, which allow an accurate assessment of the formation of an AL. These indicators could be used to estimate indirectly lesion transmurality. In future studies, the presented features will be investigated for ALs with different geometries. In this context, histological or 3D imaging methods are required to determine the microscopic as well as the macroscopic structure of the tissue. The methods presented in this paper could some day become standard in the process of achieving higher success rates during ablation therapy.
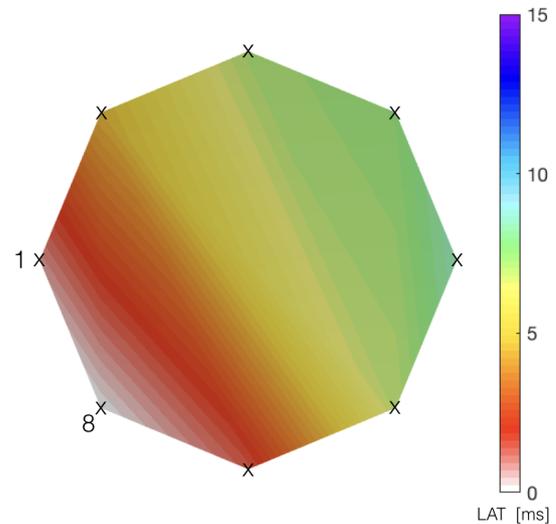
Figure 5: Local activaton time (LAT) map of a non ablated tissue. The crosses represent the electrodes on the edge of the patch. Data between electrodes was bilinearly interpolated.

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