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Oliver Huhn*, Stefan Pollnow, Laura Unger, Olaf Dössel, Tobias Oesterlein, Armin Luik, and Claus Schmitt

High-density Mapping Reveals Short-term Reversibility of Atrial Ablation Lesions

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Abstract: Cardiac arrhythmias such as atrial fibrillation occur frequently in industrialized countries. Radiofrequency ablation (RFA) is a standard treatment if drug therapy fails. This minimally invasive surgery aims at stabilizing the heart rhythm on a permanent basis. However, the procedure commonly needs to be repeated because of the high recurrence rate of arrhythmias. Non-transmural lesions as well as gaps within linear lesions are among the main problems during the RFA. The assessment of lesion formation is not adequate in state of the art procedures. Therefore, the aim of this study is to investigate the short-term reversibility of lesions using human electrograms recorded by a high-density mapping system during an electrophysiological study (EPS). A predefined measurement protocol was executed during the EPS in order to create three ablation points in the left atrium. Subsequently, after preprocessing the recorded signals, electrogram (EGM) paths were formed along the endocardial surface of the atrium. By analyzing changes of peak to peak amplitudes of unipolar EGMs before and after ablation, it was possible to distinguish lesion area and healthy myocardium. The peak to peak amplitudes of the EGMs decreased by 40-61% after 30 seconds of ablation. Furthermore, we analyzed the morphological changes of EGMs surrounding the lesion. High-density mapping data showed that not only the tissue, which had direct contact with the catheter tip during the RFA, but also the surrounding tissue was affected. This was demonstrated by low peak to peak amplitudes in large areas with a width of 14 mm around the center of the ablation lesion. After right pulmonary vein isolation, high-density mapping was repeated on the previous lesions. The outer region of RFA-treated tissue appears

Kaiserstr. 12, 76128 Karlsruhe, Germany **Tobias Oesterlein**, T. Oesterlein was with the Institute of Biomedical Engineering, Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany. He is now with Boston Scientific, Marlborough, MA, USA to recover as opposed to the central core of the ablation point. This observation suggests that the meaningfulness of an immediate remap after ablation during an EPS may lead the physician to false conclusions.

Keywords: Radiofrequency ablation, cardiac mapping, electrograms, signal processing.

1 Introduction

Atrial fibrillation is a widespread heart disease in an aging society [1]. Radiofrequency ablation (RFA) is a standard treatment if drug therapy fails. In a large-scale study with 1300 subjects, success without antiarrhythmic drugs was achieved in only 40.7% of the patients [2, 3]. Magnetic resonance imaging can be used to visualize the ablation lesions [4]. In order to evaluate the short term reversibility of RFA lesions, we retrospectively analyzed electrogram (EGM) data obtained during the procedure. Study in humans showed that unipolar signals are useful to identify ablation lesions [5]. The aim of our study is to investigate the short-term reversibility of lesions using human EGMs recorded by a high-density mapping system during an electrophysiological study (EPS). In this study, the left atrium was mapped using an Orion (Boston Scientific) catheter. Three ablation points were set in the left atrium. The ablated regions were analyzed and, after a break of 40 minutes, remapped to identify possible changes of EGMs. EGM amplitude in the remap after the right pulmonary vein (PV) isolation increased again compared to the map after the third ablation.

2 Methods

2.1 Clinical Scenario

The EPS carried out at the *Städtisches Klinikum Karlsruhe* employs several measuring instruments. The acquired data set contains continuous measurements recorded by several intracardiac catheters and surface electrocardiograms (ECGs). The Orion mapping catheter has a total of 64 electrodes. These are distributed in eight splines with eight electrodes each. The electrode area is 0.4 mm² and the electrodes are 2.5 mm apart

^{*}Corresponding author: Oliver Huhn, Institute of Biomedical Engineering, Karlsruhe Institute of Technology (KIT), Kaiserstr. 12, 76128 Karlsruhe, Germany, e-mail: publications@ibt.kit.edu Stefan Pollnow, Laura Unger, Olaf Dössel, Institute of Biomedical Engineering, Karlsruhe Institute of Technology (KIT),

Armin Luik, Claus Schmitt, Städtisches Klinikum Karlsruhe, Moltkestraße 90, 76133 Karlsruhe, Germany, e-mail: kardiologie@klinikum-karlsruhe.de



Fig. 1: EGM paths (\blacksquare) passing the center of the ablation point cloud \bar{P} (\blacksquare). *X* location of ablation points. The eight paths form four connected paths. Posterior view of the left atrium.

on each spline. This catheter will be referred to as high-density mapping catheter in the following.

The clinical setup for the study is as follows. First, the left atrium was completely mapped with the Orion catheter yielding the virtual left atrial anatomy and the initial voltage map. Subsequently, three points were ablated in relatively large distance on the line on which the left PV isolation will isolate the left PVs later. The points were at the level of the left superior PV, at the level of the left inferior PV and between them.

The ablation procedure followed a protocol which was approved by the local ethics committee: First, the ablation catheter was kept stable at the desired position and EGMs were recorded. Then the catheter ablated at the same position for 30 seconds with an ablation power between 25 and 40 W. Finally, the catheter measured and ablated again for 30 seconds. After this step, a remap of the affected area was performed using the ablation catheter. The same area was also remapped with the Orion catheter. Approximately 40 minutes later, after the right PV isolation, another remap of the entire atrium was acquired with the Orion catheter.

2.2 Electrogram Processing

First, the relevant recordings were extracted from exported mapping data using Matlab R2017b. The initial raw data were filtered by a high- and low-pass filter with cut-off frequencies of 1 Hz and 300 Hz respectively. Segments with overlapping ventricular far field were blanked by detecting the QRS-complex of the ECG [6]. After further filtering of disturbances, such as 50 Hz noise, the data was divided into ECG, Coronary Sinus (CS), Orion and ablation data. This was followed by the



Fig. 2: Comparison of remap after all three ablations (a) with remap after right PV isolation (b). The areas between the left inferior and the superior PV displaying small amplitudes (**■**) shrink.

atrial activity detection. Individual EGMs were selected in the signals. The position of each electrode within the atrium was known for all points in time. This information was used to reconstruct the distance to the endocardial surface and to sort out any EGM that was not recorded < 5 mm to the endocardium.

For the detection of atrial activities, we used EGMs recorded with the CS catheter. From the first six electrodes bipolar EGMs were computed. The seventh and the most proximal electrode were used for pacing and excluded from data analysis. Bipolar EGMs are advantageous because they emphasise the local signal and reduce far field components. The Non-linear Energy Operator (NLEO) was used to determine the energy of the signal [7]. Then, local EGM activity was defined by NLEO values above a threshold of 0.2 (a.u.) and can



Fig. 3: Comparison of remap after third ablation (**—**) with remap after right PV isolation (**—**). Center point of point cloud of ablation catheter during ablation (**—**). Low peak to peak amplitudes (**—**) in a distance from 2-16 mm. Only amplitudes (**—**) near the catheter tip, which is shown as center point (**—**), did not recover.

be described by a step function:

$$Step function = \begin{cases} 1, if NLEO > threshold \\ 0, if NLEO < threshold \end{cases}$$
(1)

Now all three step functions were added together and a final step function was created. Each signal window defined by the step function could be applied again to the NLEO. Where it is maximum, the atrial activity was detected. This time, there was no threshold needed because there was only one bipolar EGM and one maximum of the NLEO within a window.

The point closest to the endocardial surface was searched for the location of each activation time and an interpolated three-dimensional map was rendered with Paraview 5.4.1.

2.3 Determination of Catheter Position During RFA

A midpoint of the point cloud \bar{P} from the ablation catheter for each individual ablation lesion was calculated as described in equation 2. This point corresponded to the area in which the effects of ablation on the tissue were assumed to be severest. \bar{P} assembles all catheter positions during ongoing ablation.

$$\bar{P} = \begin{pmatrix} \frac{1}{J} \sum_{i=1}^{J} x_i \\ \frac{1}{J} \sum_{i=1}^{J} y_i \\ \frac{1}{J} \sum_{i=1}^{J} z_i \end{pmatrix} \quad with \quad i = 1, 2, ..., J \qquad (2)$$

2.4 Formation of Adequate EGM Pathways on the Lesion

A position of an electrode of the Orion with the shortest distance to the endocardium was searched for each ablation point. Starting from this point, a circle was created on the surface with an individual predefined radius. Then, in 45° increments, eight points on the circle were selected. For each of the eight points, a vector was formed starting from the center of the point cloud. Intermediate points were defined at regular intervals, $\frac{Length \ vector \ (mm)}{100}$, along this vector. From each of these intermediate points, measurement points were searched within a predefined radius of 2 mm. Thus, eight paths were generated with measuring points and their exact positions as shown in Figure 1. The paths covered a complete area around the ablation point.

3 Results

Figure 2 shows that the EGM amplitude in the Orion remap after the right PV isolation increased again compared to the Orion remap after the third ablation. Only the center of the point cloud \overline{P} did not recover.

Figure 3 shows the peak to peak values along connected path 1 starting from the direction of the right PVs in direction of the left PVs (see Figure 1). Only amplitudes near the catheter tip, which is shown as center point, did not recover after a time of 40 minutes.

Now, templates were formed from adjacent EGMs along all four connected paths and compared with each other after the creation of the three ablation lesions and after the right PV isolation (see Figure 4). The template building sections consisted of five equally sized areas along the path. The amplitudes at the beginning and end of the paths recovered after the right PV isolation.

4 Discussion

In this study, three ablation lesions were examined after a waiting period of approximately 40 minutes using a high-density mapping catheter. It turned out that an ablation point is not precisely reflected in the voltage map. Instead, low peak to peak voltages prevail in a larger area around the center of ablation. This could result from the surrounding tissue be warmed up during ablation and having a reduced conductivity due to the temperature change. The remap after the right PV isolation showed a large area, diameter ≥ 14 mm, of small peak to peak amplitudes. A first explanation is the fact that the ab-



Fig. 4: Comparison of templates after the three ablations (a, c, e, g) and after right PV isolation (b, d, f, h). Path 1 (a, b), Path 2 (c, d), Path 3 (e, f), Path 4 (g, h). Distance from start- to end-point (0-18 mm

lation catheter could not be kept completely stable during the ablation procedure, due to cardiac contraction and respiratory motion. This entails points where the catheter touched the endocardial surface for a short time interval during the ablation procedure. A first assumption suggests that irreversible lesions were created only in the places of a longer stay during the ablation.

The remap immediately after ablation and approximately 40 minutes later indicated that low peak to peak amplitudes in the acute phase may reflect the formation of edema or temperature related effects, rather than being indicative for the formation of durable scar tissue. This insight raises the question to what extent a remap directly after ablation is meaningful and presents new challenges for future scientific work in the field of high-density mapping after RFA.

Author Statement

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References

- [1] Keller MW, Schuler S, Wilhelms M, Lenis G, Seemann G, Schmitt C, et al. Characterization of Radiofrequency Ablation Lesion Development Based on Simulated and Measured Intracardiac Electrograms. IEEE Transactions on Biomedical Engineering 2014; 61(9):2467–2478.
- [2] Arbelo E, Brugada J, Hindricks G, Maggioni AP, Tavazzi L, Vardas P, et al. The atrial fibrillation ablation pilot study: an European Survey on Methodology and results of catheter ablation for atrial fibrillation conducted by the European Heart Rhythm Association. European heart journal 2014; 35(22):1466-1478.
- [3] Shurrab M, Biase LD, Briceno DF, Kaoutskaia A, Haj-Yahia S, Newman D, et al. Impact of contact force technology on atrial fibrillation ablation: a meta-analysis. Journal of the American Heart Association 2015; 4(9):e002476.
- [4] Ghafoori E, Kholmovski EG, Thomas S, Silvernagel J, Angel N, Hu N, et al. Characterization of Gadolinium Contrast Enhancement of Radiofrequency Ablation Lesions in Predicting Edema and Chronic Lesion Size. Circulation: Arrhythmia and Electrophysiology 2017; 10(11):e005599.
- [5] Bortone A, Appetiti A, Bouzeman A, Maupas E, Ciobotaru V, Boulenc JM, et al. Unipolar signal modification as a guide for lesion creation during radiofrequency application in the left atrium: a prospective study in humans in the setting of paroxysmal atrial fibrillation catheter ablation. Circulation: Arrhythmia and Electrophysiology 2013; 6:1095–102.
- [6] Lenis G, Baas T, Dössel O. Ectopic beats and their influence on the morphology of subsequent waves in the electrocardiogram. Biomedizinische Technik/Biomedical Engineering 2013; 58(2):109-119.
- [7] Schilling C, Nguyen MP, Luik A, Schmitt C, Dössel O. Nonlinear energy operator for the analysis of intracardial electrograms. In World Congress on Medical Physics and Biomedical Engineering, Munich, Germany. Springer, Berlin, Heidelberg 2009:872-875.