Far-Field Effect in Unipolar Electrograms Recorded from Epicardial and Endocardial Surface: Quantification of Epi-Endo Dissociation during Atrial Fibrillation in Humans

Piotr Podziemski[1], Stef Zeemering[2], Elham Bidar[3], Pawel Kuklik[2], Arne van Hunnik[2], Ulrich Schotten[2]

[1] Faculty of Physics, Warsaw University of Technology, Poland; [2] Departments of Physiology and [3] Cardiothoracic Surgery, Cardiovascular Research Institute Maastricht, Maastricht, The Netherlands

Abstract

In this study we explore whether endo-epicardial dissociation during atrial fibrillation (AF) can explain origin of some of the far-field components in unipolar electrograms. To assess the number of far-field deflections in unipolar electrograms that have a source on the contralateral side of the atrial wall we used simultaneous endo-epicardial high-resolution contact mapping. 30s endo-epicardial electrograms were recorded using two 64 electrode arrays directly opposing each other, placed on the right atrial wall in 5 patients with persistent AF. For all far-field deflections that could not be explained by local activation within the same plane, we searched for a passing wavefront on the other side of the atrial wall. 74±3% of detected far-field deflections could be explained by activation on the same side of the atrial wall. Within the remaining deflections, 42±5% had a source in the activity taking place directly on the other side of the atrial wall. 15±3% of all detected far-fields were of unknown origin. High proportion of the far-field deflections detected using contact mapping during AF results from endo-epicardial dissociation may have an impact on proper annotation of local activity, and therefore on identification of conduction patterns. Calculating the number of far-field deflections in unipolar electrograms due to endo-epi dissociation may help to quantitatively describe transmural dissociation.

1. Introduction

Atrial fibrillation (AF) is the most common, sustained arrhythmia in humans, with incidence of around 1% in general population [1]. There is an ongoing scientific debate regarding the pathophysiological mechanisms that are responsible for sustained AF [2-4]. To study these mechanisms high-density unipolar contact mapping is used, allowing to characterize wave conduction patterns during cardiac arrhythmias such as AF. However, due to nature of the unipolar electrogram, contact mapping reflects local as well as remote electrical activity and great care should be taken in accurate identification of local activity.

Progressive structural remodeling during the course of AF leads to increased dissociation of epicardial and endocardial conduction patterns [5]. Epi-endocardial dissociation allows the activation waves to propagate between endocardium and epicardium, increasing the complexity of fibrillatory conduction patterns. This also increases the complexity of electrograms recorded on epicardial or endocardial surface by increasing the number of far-field components in the signals.

Here, we explore whether endo-epicardial dissociation during AF can explain origin of some of the far-field components in unipolar electrograms.

2. Patient database

This initial study included 5 patients with persistent AF undergoing cardiac surgery at Maastricht University Medical Centre. The study protocol was approved by the institutional ethical review committee, and all patients gave written informed consent. Intra-operative unipolar contact mapping of atrial epicardium was performed under general anesthesia by two multiple electrode arrays directly opposing each other, placed on the right atrial wall (8x8 electrodes forming a square grid, with intra-electrode distance of 1.5 mm – see Figure 1).

Figure 1. Clamp-like double mapping electrode array consisting of square 8x8 electrode grids, with intra-electrode distance of 1.5 mm. The device was used to simultaneously map endocardial and epicardial activity during atrial fibrillation (photo adopted from [6]).

3. Methods

3.1. Estimating far-field space constant

To link a source activation to a far-field, the relation between far-field amplitude and the distance to a source activation has to be found. *Far Field decay space constant* ($FF_{0.5}$) is defined as a distance at which the amplitude of an electrogram deflection (peak-to-peak amplitude) was equal to half of the activation amplitude detected at a conduction block line. To estimate $FF_{0.5}$ for each patient we use the method described previously in [7]. This method is based on searching for a conduction pattern in which an activation travels along a conduction block line (as presented in Figure 2, *inset*). Such a situation provides good conditions to measure the amplitude of an electrogram of inactivated tissue at a distance d from the activated tissue. The term *conduction block line* will be used only to describe such a conduction block. After detection of all of such situations in which far-field deflections are visible, all far-field amplitudes were binned by the distance of their detection from the conduction block line in bins of 1.5 mm width. After binning, exponential fit was found and proper $FF_{0.5}$ value was estimated (see Figure 3). An example of detected conduction along block and far-field deflections is presented in Figure 4.

Additionally, to check spatial distribution of detected conduction block lines, color maps of the number of detected conduction blocks on each electrode were prepared (Figure 5).

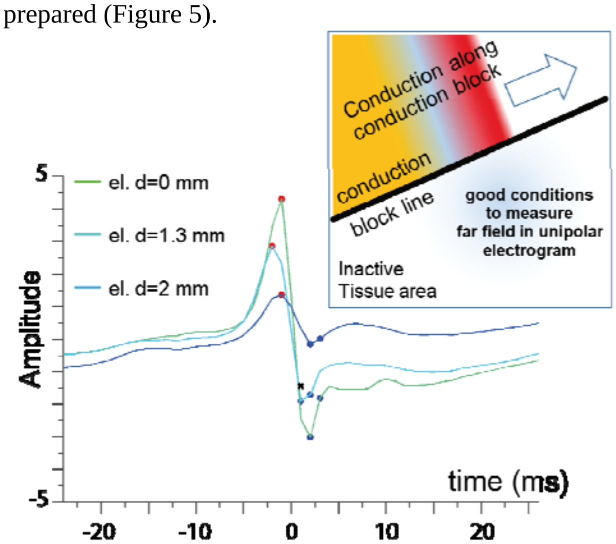

Figure 2. Activation wavefront in cardiac tissue travels along a conduction block line (as presented in inset), which provides good conditions to measure amplitude of electrogram at a distance d from the activated tissue. Signal from unipolar electrograms at distant electrodes, for different distance from conduction block. Due to noise present in the signal, only in 3 electrodes the steepest point of deflection matched time of deflection at the site of detected block.

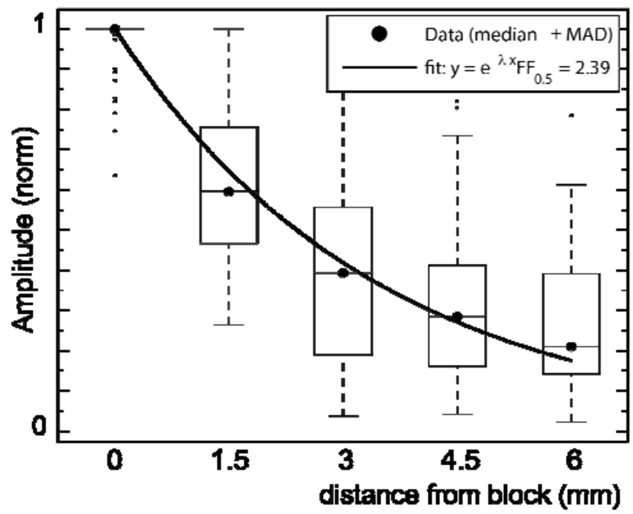

Figure 3. Example of $FF_{0.5}$ estimation in one of the patients. All the far-field amplitudes were binned in 1.5 mm bins by the distance of their detection from the conduction block line (and effectively – activation wavefront). After binning and plotting in a box-plot form, and exponential fit was found for the measured decrease of electrogram amplitude with distance from the conduction block. In this example, estimated $FF_{0.5}$ = 2.39 mm.

3.2. Matching far-field deflections with source activations

Having estimated the dependency of the far-field amplitude on the distance from the source activation, we can link far-field deflections to possible activation sources.

As a first step, an automatic detection of intrinsic, local activations in each of the electrodes is performed [8]. Then, all the deflections in unipolar electrograms, which are not marked as intrinsic local activations, are assigned as far field candidates. After that a search for the source deflections that could explain far field candidate is performed within the area of 6 mm (estimated in previous steps – see fig. 2). We search for source of activation both in epicardial and endocardial surface with following constraints:

- A 2 mm uniform depth of atrial thickness is assumed;
- Time of the steepest deflection in source deflections is not farther than 3 ms from time of the steepest deflection for far field candidate;
- We assign the deflection to be the possible source, if following condition is fulfilled:

$$\frac{FF_{amp}}{SOURCE_{amp}} \in \langle e^{-\lambda_{33\%}d}, e^{-\lambda_{66\%}d} \rangle$$

where $\lambda_{33\%} = {}^{1}/_{FF_{0.33}}$ and $FF_{0.33}$ is distance, at which the amplitude of electrogram deflection was equal to the 33% of the activation amplitude detected at a source.

As a result, we have a set of deflections that can be a possible source for the far-field. To choose the most probable source, three different approaches yielding three different results were used:

1. Sources found on the same tissue layer were preferred over sources found transmurally.
2. Source activation with the maximum amplitude was preferred, from either epicardial or endocardial surface,
3. Only deflections annotated as activations can be marked as possible source. Sources found on the same tissue layer were preferred over sources found transmurally.

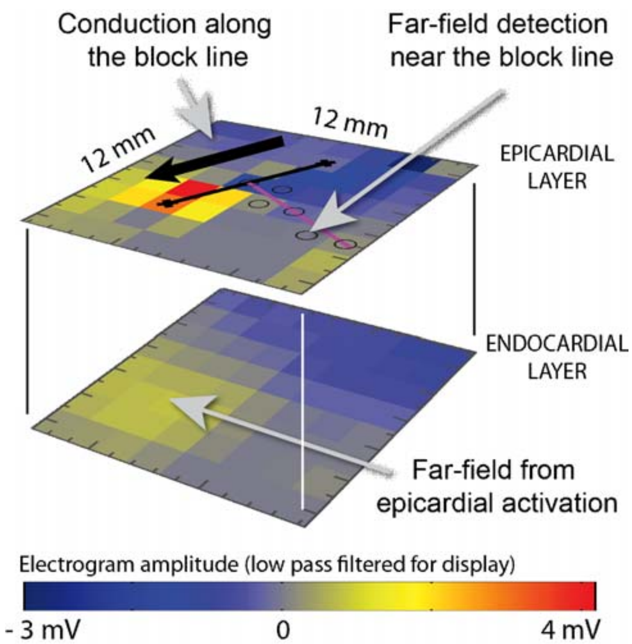

Figure 4. An example of detected conduction along conduction block line in the unipolar electrogram map. Conduction block line is detected within epicardial layer. Matching electrodes with far field deflections are marked by black circles. An area of far-field deflections in endocardial layer is visible in lower square.

4. Results

We found that the 74±3% of detected far-field deflections could be explained by activation on the same side of the atrial wall. Within the remaining deflections, 42±5% had a source in the activity happening directly on the other side of the atrial wall. 15±3% of detected far-fields were of unknown origin (Figure 6). When an activation with biggest amplitude was assigned as the source for the far field, 45±6% of detected far-field deflections were associated to an activation on the same side of the atrial wall, while 39±7% had a source in the activity happening directly on the other side of the atrial wall. The proportion of far-fields, for which no possible source could be assigned increased to 52±6%, when only deflections annotated by the probabilistic detection algorithm presented in [8] were accepted.

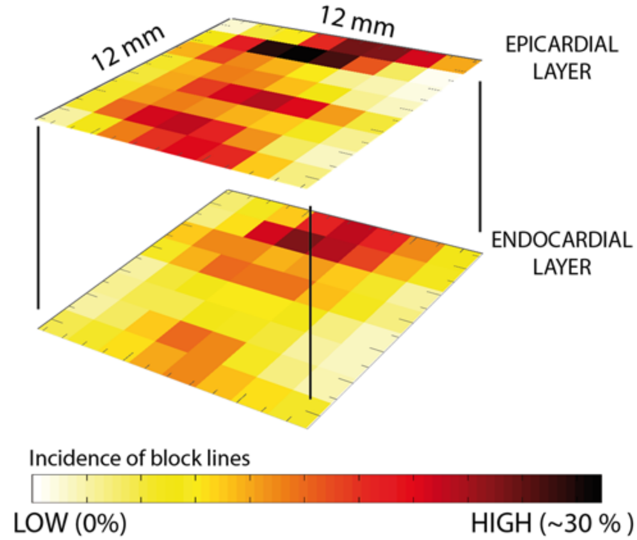

Figure 5. Detected conduction block lines in one of the measurements in patients with persistent AF from endocardial (bottom) and epicardial (top) layers. There are 3 elongated areas, in which conduction block lines occur in the epicardial layer, only two of which were detected in endocardial map.

5. Discussion

There were two electrode arrays diametrically opposed on the epicardial and endocardial atrial surface. Both of the arrays could be pressed towards the cardiac tissue with different force (although the clamp-like design of the electrode minimizes that effect). This may result in a differently calibrated amplitude of the recorded electrogram for both arrays and the estimation of that difference is difficult. This is the reason why two methods of assigning sources were taken into account: one for which sources found on the same conduction layer were preferred over sources found transmurally, and one for which source activation with the maximum amplitude was preferred, from either epicardial or endocardial surface. The latter method gave more uniform distribution between sources detected in the same layer of conduction vs. the sources detected transmurally (Figure 6 A vs B). However, as the two-layer representation of atrial wall is a simplification, this discrepancy in results may suggest, that for many of far-field deflections a biggest deflection can be found within the atrial wall, and not directly on epicardial on endocardial surface.

When only deflections annotated by probabilistic deflection detection algorithm [8] were analyzed, there was a high incidence of far-fields, for which no possible source could be assigned. This may suggest, that deflections with smaller amplitudes that are too small to be treated as intrinsic deflection on either side of the atrial wall, still show characteristic spatial spread of amplitude produced by propagating activation and are not artifacts of the measurement method. In this view, the conduction pattern of AF as seen on the two layers is a superposition of a complex, layered (3D) set of overlapping fibrillation waves. Any annotation method that does not take into account this 3D aspect, will inevitably fail to annotate all true source deflections.

During the study we did not take into account, that in some cases a far-field deflection may be merged from multiple sources thus affecting its amplitude. That effect may increase the number of far-fields for which no source could be assigned. To correct for the effect, that the source of far-field may lie outside the region covered by electrode arrays, activations from electrodes closer than 3mm from the border of both maps were excluded.

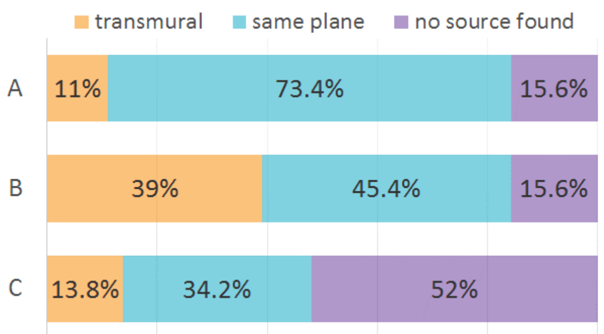

Figure 6. Percentage of detected far-field deflections associated to sources on the same or transmural layer. **(A)** sources found on the same conduction layer were preferred over sources found transmurally. (B) source activation with the maximum amplitude was preferred (C) sources found on the same conduction layer were preferred over sources found transmurally, and only sources annotated previously by method described in [8]were taken into consideration.

6. Conclusions

Significant proportion of the far-field deflections detected using contact mapping during AF results from endo-epicardial dissociation. Specifically 42±5% of all far-field deflections which could not be explained by local activation within the same plane had a source in the activity happening directly on the other side of the atrial wall.

This phenomenon may have an impact on proper annotation of local activity and therefore on accurate identification of conduction patterns – and as a result for proper detection of topological properties like phase singularities. Proposed method for estimating number of far-field deflections in unipolar electrograms due to endo-epi dissociation may help to quantitatively describe transmural dissociation.

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Address for correspondence:

Piotr Podziemski
Warsaw University of Technology, Faculty of Physics, 00-662 Warsaw, Poland
piotr@podziemski.net