T–Wave Alternans Analysis With Electrocardiographic Imaging

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Abstract

T Wave Alternans (TWA) is a cardiac risk indicator which measures the functional cardioelectric instability substrate. Traditional estimation of TWA has been made on the surface ECG, hence providing the researcher with an anatomically non-specific marker. We addressed the assessment of TWA in ECG Imaging (ECGI) recordings to characterize the test with regionalization and spatial specificity, hence identifying those cardiac regions with functional cardiac instability according to this marker. ECGI potentials were obtained from 7 patients with Long QT syndrome by recording signals in the patient torso during about 60 seconds. Epicardium registers were estimated through inverse problem algorithms and the whole set of signals were analyzed by means of the Temporal Method to find the alternans amplitude and waveform. TWA amplitudes were in general spatially scattered in the torso, whereas high amplitude regions trended to be spatially grouped in the epicardium. Our results point out that TWA could be spatially grouped in the epicardial signals, and that ECGI could yield a clinically useful representation on TWA spatio-temporal distribution.

1. Introduction

Currently, sudden cardiac death (SCD) is responsible of a high mortality rate in modern industrialized countries, so the development of effective markers, not only to predict, but also to stratify the SCD risk, is today an issue calling strong attention [1]. T–Wave Alternans (TWA) has been found to be a noninvasive predictor of ventricular arrhythmias assessed on the surface electrocardiogram (ECG). This phenomenon stands for extremely low fluctuations in amplitude (in the order of μV), in waveform, or duration in the ST–T complex, occurring on an every–other–beat basis. Many signal processing methods have been developed for TWA detection and estimation, though hardly two of them are currently applied in the clinical practice [1]. This is due to the fact that visual identification is impractical, which prevents the definition of a gold standard for validating the existing methods [1]. On the other hand, TWA-based markers are intended to measure the functional cardioelectric instability of the cardiac substrate, but they do not provide any information about the myocardial regions where ventricular repolarization alternans are originated. Thus, despite the clinical interest elevated by TWA, further works must be undertaken to overcome these limitations.

Our work is long-term intended to address the second one by proposing the study of the TWA spatial specificity through the analysis on ECG Imaging (ECGI) recordings obtained from Body Surface Potential Mapping (BSPM) and medical image postprocessing. BSPM is a technique designed to build a distribution map of bioelectrical potentials on the torso surface. It is typically recorded from about hundreds of electrodes distributed on several torso sites, and there are evidences that the spatial information provided by BSPM improves that of the standard ECG in some cardiac indices. Its main interest is that these potential distribution maps enable an alternative data visualization in both spatial and temporal scales referred to as ECGI, and developed at Rudy's Lab [2, 3]. The final purpose of BSPM is the estimation of the cardiac activity which constitutes the inverse problem in electrocardiography, being the estimation of the electric potentials at the epicardial surface one of its particular formulations [4].

The purpose of the current work is the analysis of the spatial specificity of TWA using ECGI. The study is carried out in 7 patients with Long QT (LQT) syndrome. Recordings were measured in the torso during 60 seconds and epicardium electrograms (EGM) were obtained through inverse problem algorithms [2]. Each separate signal was processed and spatially represented. Alternans were assessed by means of the Temporal Method (TM), previously used in [5], in signals that were both measured on the torso and estimated on the epicardium. As

 ISSN: 2325-887X DOI: 10.22489/CinC.2018.101

an introductory phase to the TWA study, the preprocessing stage was scrutinized to see whether the result of the TWA test could be affected by artifacts introduced by misadjustments of this part of the system. Next, the regional analysis of neighbor electrodes was tackled on the surface torso and on the epicardium. The analysis of TWA was addressed in specific sites to verify the waveform regularity and the noise influence, as well as the coherence in corresponding points resulting from the torso and the epicardium. The spatial consistency was determined by means of the M–mode plots, which are representations of sets of waveforms following a specific spatial path on a line of interest.

The paper is organized as follows. The TM method to assess alternans is briefly introduced in Section 2, with focus on the preprocessing stage. Next, the experiments are described and the results are provided in Section 3. Finally, the conclusions are given in Section 4.

2. TWA Preprocessing and Estimation

Preprocessing is designed to be suitable both for the torso and for the epicardium EGMs. The *ECG Preprocessing Stage* consists of two filtering blocks: high frequency noise elimination with a coarse low pass filter with zero-phase distortion and 50 Hz cutoff frequency and Baseline Wander (BW) cancellation accomplished through a median low pass filter in combination with spline interpolation, to generate a BW estimate.

R–peaks are detected in the *R–peak Detection Stag*e using three consecutive blocks: a band pass filter is applied to preserve the spectral content of QRS complexes; the time instants of QRS complexes are determined by using an adaptive threshold, where a signal sample is selected as QRS index whenever it is higher than a given absolute amplitude after a specified refractory period; finally, R-peaks are determined by finding the maximum amplitude in a time interval around each QRS time instants.

In the *Repolarization Interval (ST–T) Segmentation and Synchronization Stage,* repolarization intervals are segmented and conditioned by using four consecutive blocks. A fine low pass filter is used to reject noise out of the TWA band (0.3 - 15 Hz). An additional block delineates each repolarization interval, yielding the output $M \times N$ matrix $\mathbf{T}$, where M is the number of valid beats, and N is the number of samples of each segmented repolarization interval. An RR-adjusted time window is additionally used for the segmentation [5]. Next, the effect of possible high amplitude remaining samples from the R-S segment in matrix $\mathbf{T}$ can be alleviated by using an edge smoothing window (Tukey window with a ratio of taper to constant section of 0.35) in each row of $\mathbf{T}$. Finally, the ST-T segments in matrix $\mathbf{T}$ are aligned. A T-wave template, obtained as the median of 128 consecutive T-waves, is used to align each wave by maximizing the cross-correlation, allowing a variation of $\pm$ 30 ms from its initial position [5].

A following *TWA Detection and Estimation Stage* provides us with the estimation of the TWA amplitude and waveform. After preprocessing, the resulting matrix $\mathbf{M}$ can now be seen as a successive pattern of row vectors, $\mathbf{A}_i$ and $\mathbf{B}_i$ (the subscript stands for the *i*-th row), consisting of $\mathbf{A}$ and $\mathbf{B}$ heartbeat patterns plus additive noise $\mathbf{v}_i$. Hence, $\mathbf{M}_s$ is obtained as the difference of each row pair of $\mathbf{M}$:

$$\mathbf{M}_s = \begin{bmatrix} \mathbf{A}_1 - \mathbf{B}_1 \\ \mathbf{B}_1 - \mathbf{A}_2 \\ \vdots \\ \mathbf{A}_{M/2} - \mathbf{B}_{M/2} \\ \mathbf{B}_{M/2} - \mathbf{A}_{M/2+1} \end{bmatrix} = \begin{bmatrix} -\varepsilon \\ +\varepsilon \\ \vdots \\ -\varepsilon \\ +\varepsilon \end{bmatrix} + \begin{bmatrix} \mathbf{v}_{d1} \\ \mathbf{v}_{d2} \\ \vdots \\ \mathbf{v}_{dM-1} \\ \mathbf{v}_{dM} \end{bmatrix} \quad (1)$$

where $\varepsilon = \mathbf{A} - \mathbf{B}$ is the alternant wave, and $\mathbf{v}_{di} = \mathbf{v}_i - \mathbf{v}_{i+1}$.

Be $\mathbf{m}_s^i$ the i^{th} row in $\mathbf{M}_s$, then the temporal method (TM) estimates the TWA amplitude as $V_{alt} = \frac{1}{2} max(|\mathbf{m}_s^{odd} - \mathbf{m}_s^{even}|)$, where $\mathbf{m}_s^{odd} = E_{i\,odd}(\mathbf{m}_s^i)$ and $\mathbf{m}_s^{even} = E_{i\,even}(\mathbf{m}_s^i)$ are the TWA templates for odd and even alternans, respectively, and E is the expected value, estimated as the sample average (see [5] for details).

3. Experiments and Results

Patient and ECGI Data Set. A database was taken from 7 patients from previous research on LQT syndrome, at Cardiac Bioelectricity and Arrhythmia Center, provided with permission by Yoram Rudy Lab at Washington University in St. Louis [6]. 1–minute long segments were extracted from BPSM, and epicardial meshes were estimated from medical images. Patient 4 was used for signal-processing tuning of the method, as described next, and up to 3 more patients were used to verify the results.

Torso and Epicardium Signal Preprocessing. In Fig. 1, the colored meshes represent the (peak to peak) voltage amplitude of the torso signals, which are clearly larger when closer to the heart and weaker on the back. Next to the torso meshes, signals on the torso and preprocessing is shown in example points, including before- and after-BW cancellation, estimated BW, signal used as pivotal for R peak detection, with red circles to check that no beat is missing. The right panel shows a similar representation for two example points ECGs. In this case, a 0.75s window on the spline-based algorithm allowed good BW cancellation.

TWA Estimated Waveforms. In Fig. 2, the TM was used to provide with estimated TWA amplitude maps and morphology. In the BPSM ECG, the presence of large TWA amplitude was quite unspecific with respect to the anatomical location, though still some regionalization can be seen, which indicates that not all the regions are equally sensitive to measure the presence of TWA, and it can have an effect when using ECG or Holter recordings. On the other hand, some isolated large TWA amplitude could be observed on

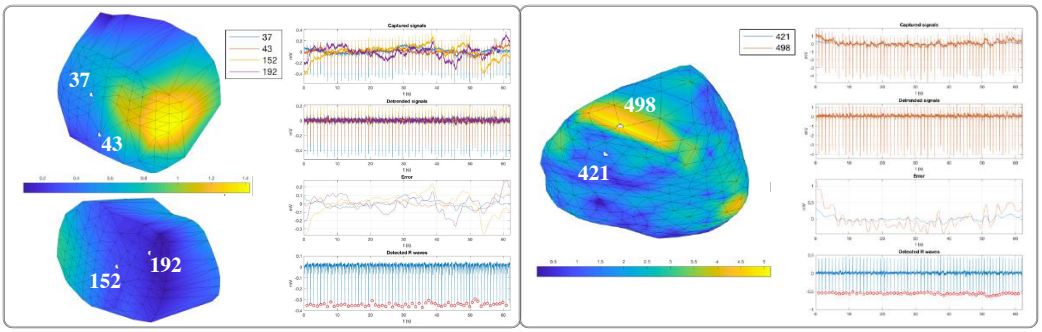

Figure 1. Signal preprocessing and signal quality in the torso (left) and in the epicardium (right), for Patient 4.

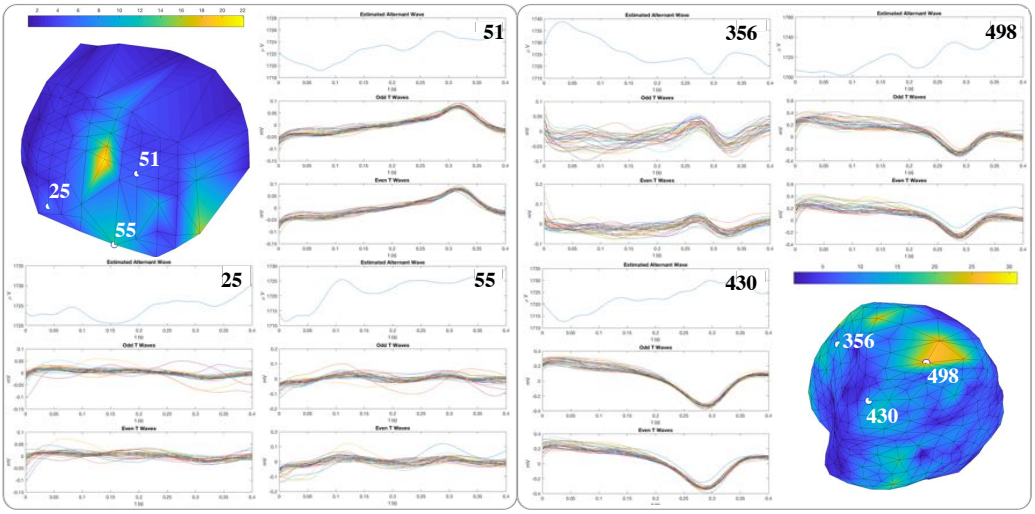

Figure 2. TWA estimated with TM on the torso (left) and on the epicardium (right), with 3 example points.

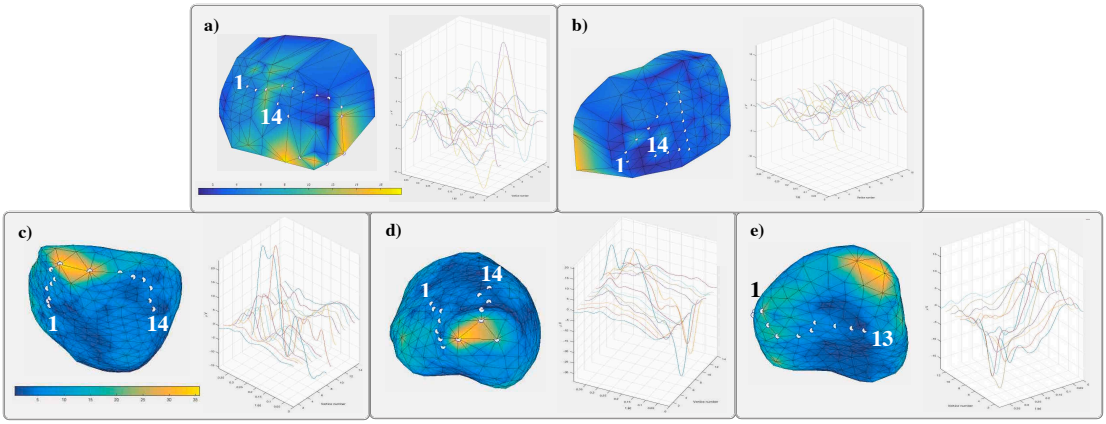

Figure 3. TM on chest and back (top) and on epicardium using the M-mode representation (bottom).

the torso TWA amplitude maps; they are not corresponding to actual alternans, but to processing artifacts. When using the processing methods with epicardial signals, several interesting points arose. First, baseline drift cancellation were adequate at noise canceling. Second, again the R waves were correctly calculated and no beat is missing. Third, the T waves were consistently better segmented and less scattered, and in consequence, the TWA morphology was clear and clean in most of the points. Subsequently, we found that with TM there was a consistent gradient of

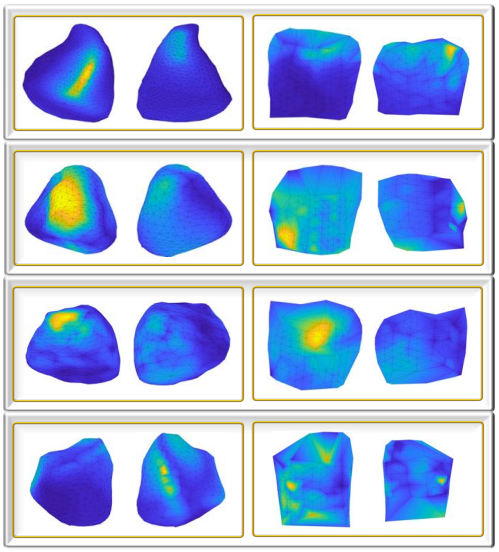

Figure 4. Epicardial (left) and torso (right) TWA amplitude maps in 4 additional patients in the LQT database.

TWA amplitude on the epicardium surface. Finally, the EGM peak-to-peak amplitudes are larger, and so are the TWA amplitudes in general.

Potentials and M-mode Spatial Structure. In Fig. 3, a set of clockwise consecutive points on the chest and on the back (up) are chosen to define an M–mode plot as the representation of each TWA waveform with time and along consecutive points separated by their Euclidean distance on the space axis. In this way, we can observe TWA waveforms similarity in shape and see whether spatial variations are smooth or noisy, to analyze spatial and temporal consistency. Note that there was a consistency for regions in yellow on the torso mesh corresponding to regions where TWA amplitude are larger. Note also that this was observed in the back, where TWA morphology is smaller, and TWA morphology usually runs with smooth variations among spatial neighbors. On the epicardium, three different paths in the lower panels show a smooth and consistent spatio-temporal variation that can be checked when analyzing the TWA morphology around representative yellow regions. According to this, alternans seem to be more spatially grouped in the epicardium and with clearer and regionalized spatio-temporal patterns than in the torso.

Experiments with Additional Patient Cases. In Figure 4 we can see the epicardial distribution of TWA amplitude in 4 additional patients with LQT syndrome available in the database, which were obtained with the same above described methods. It can be checked that spatial gradients are present on the torso but they are more sparse, whereas the spatial gradients often trend to concentrate and group in smoothly changing regions on the epicardium.

4. Conclusions

This work addresses for the first time the estimation of TWA both in BSPM and in ECGI recordings. The process has been shown to be sensitive to the signal processing design decisions. The TM enables TWA waveform and amplitude estimation. Spatial consistence was found to be limited on the torso and more patent and concentrated on the epicardium. Further studies will be devoted to scrutinize the impact of different TWA signal processing methods and specially the clinical implications.

Acknowledgements

Special Thanks to Prof. Yoram Rudy and his team (Ramya Vijayakumar, Christopher Andrews, Junjie Zhang and all from Rudy Laboratory), for providing the data and for their always kind support and encouragement. This work was partially supported by Research Grants FINALE and KERMES (TEC2016-75161-C2-1-R and TEC2016-81900-REDT), and by project TEC-2015-64835-C03-1-R, from Spanish Government.

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