Simulation of T-Wave Alternans and its Relation to the Duration of Ventricular Action Potentials Disturbance

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Abstract: The aim of the study was to simulate T-wave alternans (TWA) magnitude distribution maps on the body surface employing ECGSIM program and then to compare obtained results with data measured from patients. The toolbox for ECGSIM program was developed for TWA simulation. Graphical representation of spatial distribution of TWA magnitude was implemented. Body surface maps of TWA were simulated for different locations of the disturbances on the heart. Simulated data were compared with recordings from patients and similarities were found. Preliminary study shows that ECGSIM program can be used for approximate location of action potential disturbances in the heart cells.

Keywords: T-wave alternans, T-wave morphology, electrocardiogram simulation, action potential duration.

1. INTRODUCTION

Cardiac diseases are very harmful to the human health. The application of electrocardiogram (ECG) is essential for the clinical diagnosis of cardiac diseases. It is therefore important that institutions educating future medical professionals are successful in teaching how to recognize and name abnormalities in electrocardiogram. The major limitation of this approach is such that the normal electrocardiogram and deviations from a normal one, that produce pathologic tracings, are not easily envisioned.

ECGSIM is freely available interactive ECG simulation software used to study the relationship between the electric activity within the heart and the resulting ECG waveforms recorded on the body surface. ECGSIM also simulates the effect of local changes in timing and the manifestation of local ischemic regions on the body surface potentials [1]. Effectiveness of ECG learning is correlated with good understanding of the meaning of parameters calculated in electrocardiograms and used in everyday cardiological practice to diagnose cardiac heart disease. One can observe influence of the location of heart abnormalities on distribution of values of parameters on the body surface. Very important are those parameters which allow ventricular fibrillation and sudden cardiac death (SCD) risk stratification. It is generally accepted that the repolarization inhomogeneity facilitates the re-entry phenomena causing the development of life-threatening ventricular arrhythmias [2]. The noninvasive parameters quantifying depolarization and repolarization process both in time and space are still searched. Recently, the T-wave alternans (TWA) has been considered as one of the most promising markers for identification of patients atan increased risk of ventricular arrhythmia [3]. TWA is defined as a beat-to-beat change in the T-wave amplitude that repeats every other heart beat and indicates the spatial heterogenity of the ventricular repolarization. ECGSIM program can be used not only for the learning purpose but also for research. Repolarization abnormalities reflected by T-wave alternans phenomenon are not well recognized yet. Simulation of different action potentials duration scenarios is used for TWA generation in electrocardiograms on the body surface. In contrast to another studies [4] we have used ECGSIM program to realise this task. The limitation of ECGSIM program is that the forward problem was solved for one particular shape of the body, size and location of the internal organs acquired with applied MRI system. The advantage is that it is very fast and many different scenarios can be analyzed and compared with real data. This allows for approximate definition of abnormal regions on the heart which are responsible for TWA generation in ECG signals recorded from the body. Using ECGSIM program, the distribution of the magnitude of TWA on the body surface can be analyzed. It allows for optimal lead selection to obtain clinically significant T-wave alternans signal during measurements.

This study was designed to evaluate the mechanism of T-wave alternans generation in ECG signals on the surface of the body in comparison to ventricular heart cells action potential duration pattern. To realize this task we developed toolbox for ECGSIM program for calculation of the magnitude of T-wave alternans in all simulated ECG signals. Body surface TWA magnitude maps were compared with recordings obtained from patients.

2. MATERIALS AND METHODOLOGY

The new toolbox was developed for evaluation version of ECGSIM program providing T-wave alternans magnitude calculation from the simulated electrocardiograms. The hypothesis of the mechanism of TWA generation states that

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1876-536X/10 2010 Bentham Open

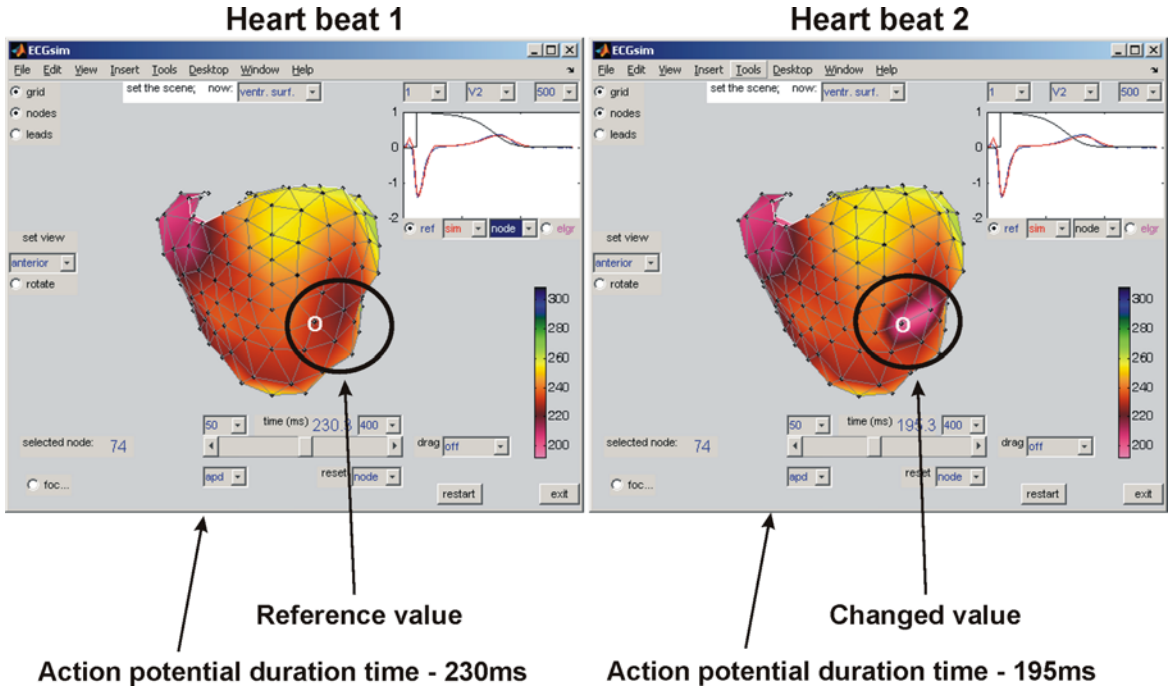

Fig. (1). ECGSIM program evaluation version – action potential times distribution on the surface of the heart.

action potentials time duration is changing from beat to beat. In one beat, all or a part of ventricular cells have shorter action potential duration in comparison to the second beat and then at the third beat again action potentials are short. ECGSIM program can simulate electrocardiograms only for a single beat. For TWA analysis, as a reference heart pattern, heart scenario obtained after program reset was treated. Two beats are taken into account, first the reference one and second the beat after manual modification of action potential properties. The examples of distribution of repolarization times on the surface of the heart during reference and modified beat are shown in Fig. (**1**).

The change of action potential parameters can be performed in the locations of nodes. Both depolarization and repolarization times can be modified. In the example shown in Fig. (**1**) action potential duration time was changed (shortened) in small region corresponding to the nodes 76 and 74 which cause presence of TWA signal in body surface electrocardiograms. Distribution of the TWA magnitude on the body surface for described case was shown in Fig. (**2**).

Spatial distribution of T-wave alternans magnitude on the body surface, shown graphically in Fig. (**2**), was calculated with the use of the data matrix M_{64x500}. The 64 rows include single beats (cycles) of ECG simulated on the surface of the body. Each cycle consists of 500 samples. At least two consecutive heart beats are needed for TWA maps calculation. After reset of the ECGSIM program, matrix with simulated ECG signals is created. These signals serve as reference ones (or previous beat signals) for TWA calculation.

Detection of ECG Characteristic Time Instances

To detect ECG characteristic points (onsets and offsets of both depolarization and repolarization waves), root mean square signal (RMS) for each sample point (columns of matrix M_{64x500}) of 64 time-aligned T waves is calculated:

$$RMS(n) = \sqrt{\frac{\sum_{i=1}^{64} \left(M_{i,n}\right)^2}{64}} \qquad (1)$$

where n is the sample number, $M_{i,n}$ is the data matrix containing $i = 64$ simulated surface ECG signals.

The global (common for all leads) characteristic time instances of ECG curves were found for this RMS signal and then they were searched in each lead separately (Fig. **3**). At first, R-peak was marked as the maximum of the RMS signal, and T maximum was calculated in relation to R-peak. The R wave start and end points were assumed to be the first samples before and after R-peak where the amplitude of RMS signal fell below 20% of R-peak. Next, the onset of Q-wave and the offset of S-wave were calculated from the difference of RMS signal using the threshold method. The T-wave end was established as the last sample of simulated ECG signals. Then, in each lead individually, the ECG fiducial points (Q onsets, S offsets, T-peaks) were established in relation to the global values of these markers using thresholding method.

T-wave Alternans Detection

T-wave alternans is calculated using time domain method - Differential Method [5]. In this method, the mean difference between the amplitudes of odd ($\mathbf{T_{odd}}$ - reference beat) and even ($\mathbf{T_{even}}$ - modified beat) T waves is determined. The alternans magnitude marker (ALT) is defined as an absolute value of the difference between the contour

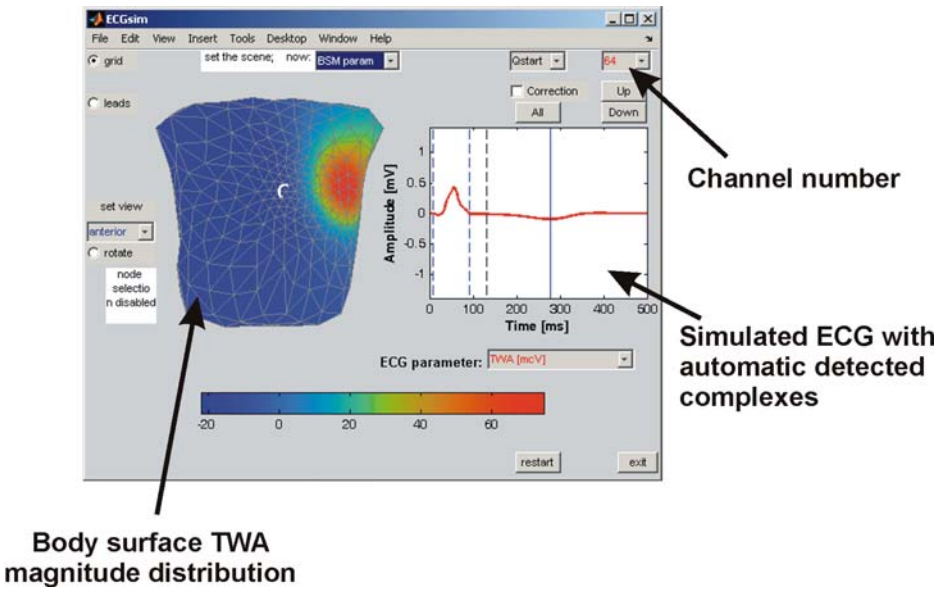

Fig. (2). T-wave alternans magnitude distribution in ECG map simulated on the body surface.

integrals of the $\mathbf{T_{odd}}$ and $\mathbf{T_{even}}$. T-waves area is divided by the number of samples in the analyzed window.

$$ALT = \frac{1}{N} \cdot \left| \sum_{n=1}^{N} T_{n\ odd} - \sum_{n=1}^{N} T_{n\ even} \right| \qquad (2)$$

where $\mathbf{T_{odd}}$ is the odd T-wave, $\mathbf{T_{even}}$ is the even T-wave, N number of samples of the analyzed T-wave.

T-wave alternans occurs, if alternans magnitude exceeds a certain level determined by the experimenter. The Differential Method provides information about the amplitude of the alternans within the T-wave and its temporal location in the ECG signal, when the short sections of the recordings are analyzed. AR was determined independently in all 64 leads.

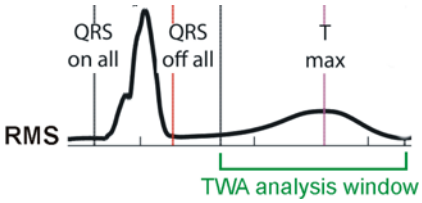

Fig. (3). Detection of ECG characteristic points

Recordings of 64 Lead Body Surface Potentials Maps

For the comparison purpose, electrocardiographic signals were recorded by multi-lead high resolution ECG system. Sixty four ECG active electrodes were placed on the patient's body according to the University of Amsterdam lead system [6] based on two 32 lead subsets selected by Lux [7, 8] from 192 ECG leads by sequence selection algorithm [6]. Measurements were performed at the hospital in an unshielded room. The ECG signals were digitized with 4096 Hz sampling frequency and 24 bits amplitude resolution. Two-minute recordings were made during the ventricular pacing at 100 bpm. Implanted cardioverter-defibrillator (ICD) electrodes were used for heart rate stimulation. For TWA detection, Differential Method was used (as it was in case of simulated signals). The study group consists of four patients with ICD and with detected TWA. The characteristic of the group of study is shown in Table (**1**).

3. RESULTS

T-wave alternans was simulated by changing action potential duration (APD) time between reference and modified beat.

T-wave Alternans Location on the Body Surface for Different Heart Locations of Action Potential Duration Disturbances

T-wave alternans was simulated by extending the action potential duration by 10 ms in a single node (corresponding to heart cell). Prolongation of the APD time was studied to avoid influences of QRS complex on the T-wave which strength vary for different leads. Different nodes were selected on the heart surface for analysis of distribution of TWA on the body surface. Different patterns of TWA magnitude distribution on the body are shown in Fig. (**4**).

Label above torso indicates node location (corresponding to heart cell) which was disturbed (where APD time was extended in the second beat by 10 ms). Label below torso indicates node number according to the net realized in ECGSIM program.

Comparison of the Maps from Patients with Simulated Data

TWA alternans magnitude was calculated in all leads and the map of distribution of its value on the surface of body was calculated. Body surface distributions of the magnitude of TWA similar to the recorded maps were simulated by

Table 1. The Study Group

	Age	LVEF [%]	Disease	MI
Patient 1	52	30	CAD	Inferior
Patient 2	42	25	CAD	Anterior
Patient 3	60	23	CAD	Unknown
Patient 4	59	15	DCM	-

MI-myocardial infraction, CAD – coronary artery disease, DCM – dilated cardiomyopathy.

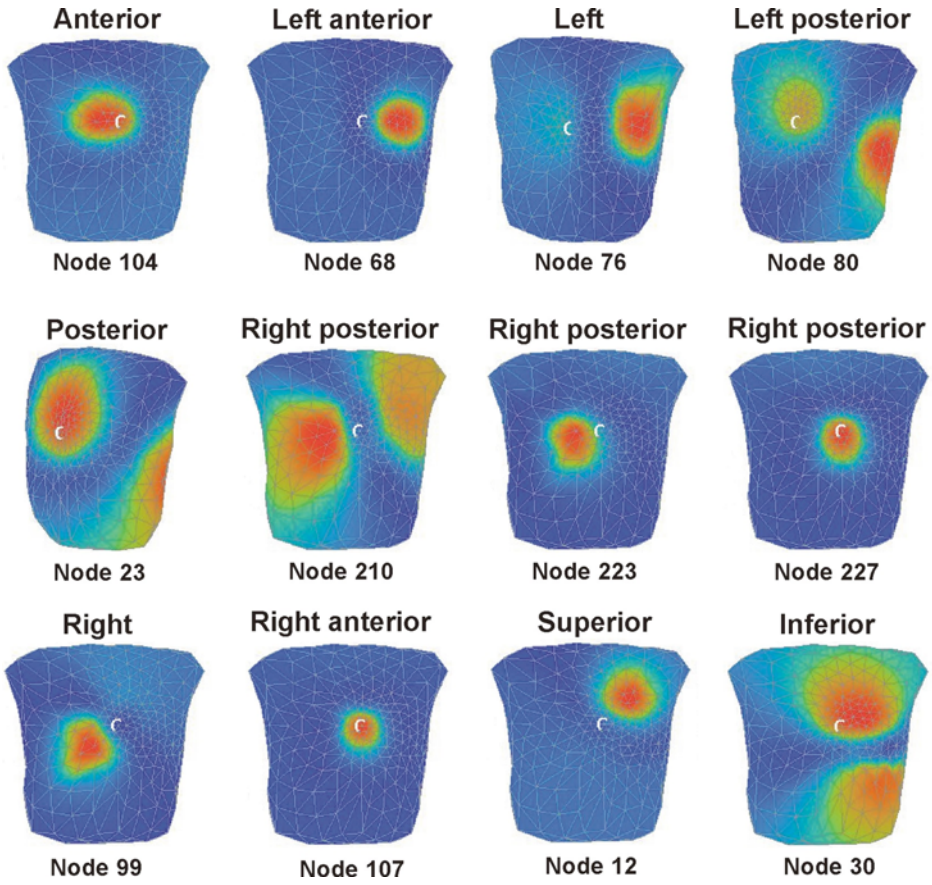

Fig. (4). Simulated distribution of magnitude of TWA on the surface of patient's body for different locations of heart cells which change their action potential duration from beat to beat.

changing APD in a set of nodes (different for every simulation).

Body surface TWA magnitude distribution for Patient 1 was done by changing APD in three nodes: Node 104 (anterior heart location) +10 ms, Node 227 (right posterior heart location) +11 ms and Node 76 (left heart location) +21 ms. Result of simulation is shown in Fig. (**5**).

Body surface TWA magnitude distribution for Patient 2 was simulated by changing APD in five nodes: Node 28 (anterior heart location) +3 ms, Node 104 (anterior heart location) +3 ms, Node 80 (left posterior heart location) +11 ms, Node 88 (left posterior heart location) -11 ms and Node 227 (right posterior heart location) +7 ms. Result of simulation is shown in Fig. (**6**).

Body surface TWA magnitude distribution for Patient 3 was done by changing APD in single node: Node 79 (left posterior heart location) -4 ms. Result of simulation is shown in Fig. (**7**).

Body surface TWA magnitude distribution for Patient 4 was done by changing APD in five nodes: Node 92 (right posterior heart location) +25 ms, Node 26 (right heart location) +7 ms, Node 21 (posterior heart location) -7 ms, Node 151 (right heart location) –4 ms and Node 117 (inferior heart location) –10 ms. Map of TWA magnitude distribution calculated in signals recorded from Patient 4 and results of simulation are shown in Fig. (**8**).

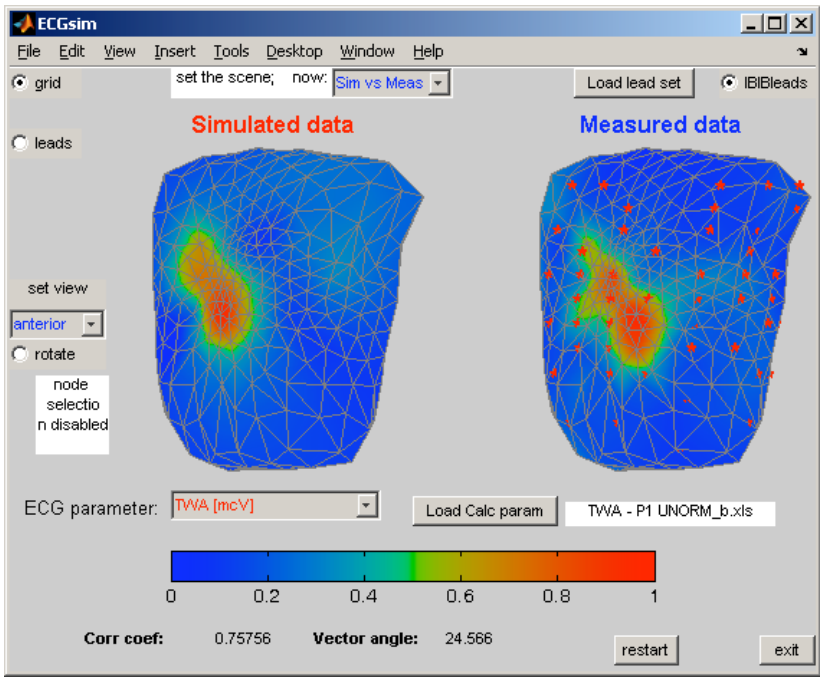

Fig. (5). Body surface TWA magnitude distribution for Patient 1 with CAD and inferior MI (on the left) and simulated data (on the right).

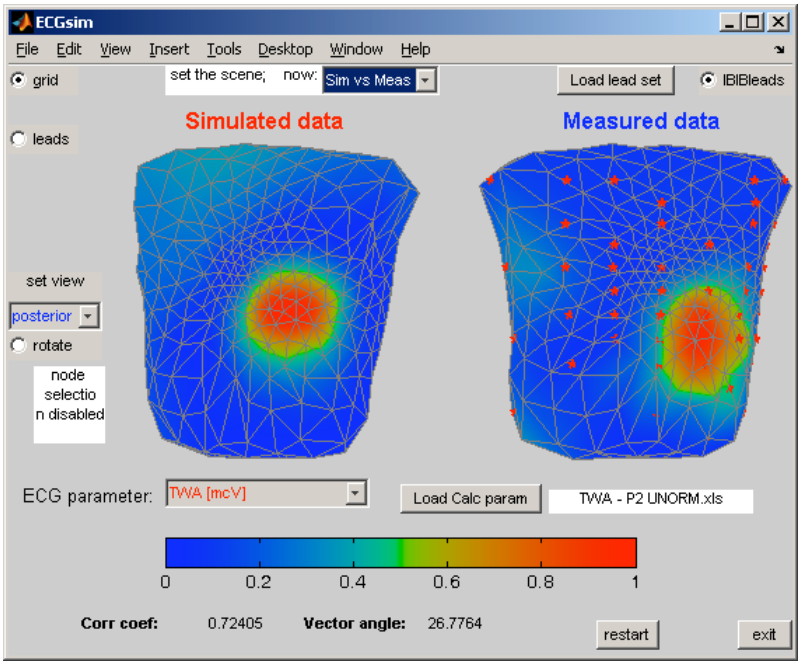

Fig. (6). Body surface TWA magnitude distribution for Patient 2 with CAD and anterior MI (on the left) and simulated data (on the right).

4. DISCUSSION

Developed tool gives the opportunity to analyze influence of action potential features on the values of diagnostic parameters calculated in ECG signals and their spatial distribution on the surface of the body. In this paper, distribution of the magnitude of T-wave alternans in ECG signals was analyzed, which is generated by the change in APD time from beat to beat. Our study includes only two consecutives beats (reference and modified). The results of simulation of TWA distribution in surface ECG signals were shown for different patterns of APD disturbances in ventricular cells. Regions with short and long APD during single beat in comparison to the next beat were simulated which correspond generation of discordant TWA. The correlation between location of the APD disturbance on the heart and the distribution of TWA magnitude on the body surface was shown. Disturbances in different locations of ventricle

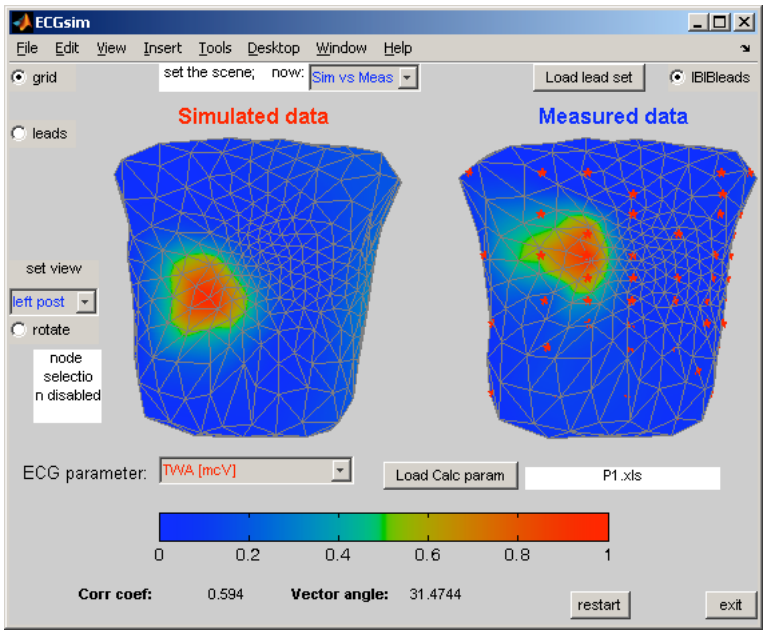

Fig. (7). Body surface TWA magnitude distribution for Patient 3 with CAD and inferior MI (on the left) and simulated data (on the right).

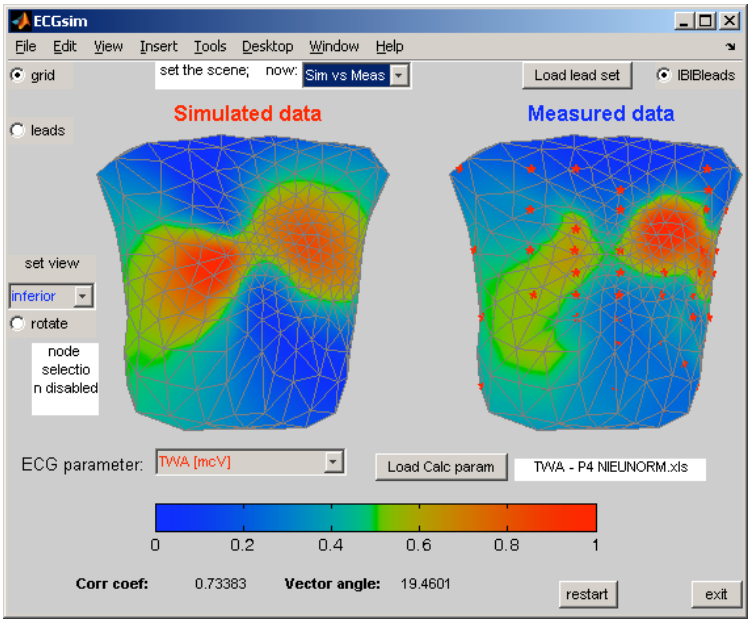

Fig. (8). Body surface TWA magnitude distribution for Patient 4 with DCM (on the left) and simulated data (on the right).

produce different patterns of TWA magnitude distribution on the body surface. Base on the results of this study one can solve inverse problem and conclude what is the approximate location of APD disturbances on the heart surface. It was shown that the best lead for TWA calculation is V2. Results of the study show that standard 12 lead ECG system cannot detect TWA for every case. The new, optimal lead system is needed ensuring TWA detection with the highest sensitivity. Simulated TWA maps are similar to those obtained from signals recorded in patients and can be used for better understanding disturbances on the surface of heart. After further validation of this data based on greater study group, ECGSIM software could be used for diagnostic purposes. One should remember that in this program forward problem solution was done based on the information about the size of the body and size and location of the internal organs from one particular subject. It means that simulation results are not very precise for analysis another subjects. In clinical studies realistic geometry for individual patients should be taken into account. Next limitation is that ECGSIM program uses simplified model of ventricular activation – dipole layer model (with equivalent generators on the epicardial surface only). Intra-cardiac events taking place in inhomogeneous anisotropic ventricles can be modeled only with limited fidelity.

5. CONCLUSIONS

ECGSIM program can be used for approximate location of disturbances in action potentials of the heart cells which correspond to TWA signal measured in electrocardiograms on the surface of body. Probably it can help in approximate location of the heart regions with conduction problems for example for recognition of the heart region where ablation should be performed. These are preliminary results, so further analysis is required, especially with larger number of patients suffered from different cardiac diseases.

ACKNOWLEDGEMENTS

Authors would like to thank Dr. Adriaan van Oosterom for providing the Matlab code of the ECGSIM program. This work was financed by the Ministry of Science and Higher Education, project POL-POSTDOC II Nr PBZ/ MEiN/01/2006/51 and partly supported by research project No. NN518 328035 financed by the Polish Ministry of Science and Higher Education.

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Received: October 16, 2009 Revised: January 18, 2010 Accepted: April 12, 2010