10.2478/v10048-009-0021-7

MEASUREMENT SCIENCE REVIEW, Volume 9, No. 5, 2009

Identification of Ischemic Lesions Based on Difference Integral Maps, Comparison of Several ECG Intervals

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Ischemic changes in small areas of myocardium can be detected from difference integral maps computed from body surface potentials measured on the same subject in situations with and without manifestation of ischemia. The proposed method for their detection is the inverse solution with 2 dipoles. Surface potentials were recorded at rest and during stress on 10 patients and 3 healthy subjects. Difference integral maps were computed for 4 intervals of integration of electrocardiographic signal (QRST, QRSU, STT and STU) and their properties and applicability as input data for inverse identification of ischemic lesions were compared. The results showed that better (more reliable) inverse solutions can be obtained from difference integral maps computed either from QRST or from STT interval of integration. The average correlation between these maps was 97%. The use of the end of U wave instead of the end of T wave for interval of integration did not improve the results.

Keywords: Integral body surface potential maps, ischemic lesions, inverse solution to 2 dipoles

1. INTRODUCTION

MYOCARDIAL ISCHEMIA manifests itself also by a changed shape of action potentials (AP) of myocytes in the ischemic area during the repolarization phase. The idea to find the affected area (lesion) using difference integral maps (DIMs) of the QRST interval and computing the inverse solution to one dipole was introduced in [1]. DIMs were computed by subtraction of QRST integral maps obtained under normal conditions from QRST integral maps obtained during the manifestation of ischemia. These maps can be measured on patients in relaxed state and under stress conditions (e.g. physical exercise). In our previous study, an inverse solution with one dipole using DIMs was applied to find the position of a single small local lesion [2]. Recently we reported a method for identification of local ischemic lesions by computing an inverse solution with two dipoles [3] for recognition of 1 or 2 simultaneously affected areas on simulated data.

The decision to use the whole QRST interval that represents both, depolarization and repolarization of the myocardium [3] was based on the assumption that ischemic changes could affect also the depolarization phase of myocytes' AP by reduced AP amplitude and its rate of rise [4]. The other possibility would be to evaluate only the STT interval in electrocardiogram (ECG) reflecting the repolarization phase of the myocardium activation.

Another issue when selecting the ECG interval for evaluation of repolarization changes is the determination of the end of repolarization. In many real signals small U wave appears after the T wave in ECG. Although it was observed already by Einthoven, there is no unique (generally acceptable) explanation of its origin. The U-wave is explained in [5] by the presence of after-potentials on the cardiac action potentials (caused by mechanical stress of cardiac cells during systolic phase) associated with ventricular wall motion. According to other studies [6], [7] T and U waves together represent the repolarization period. In such case, inclusion of the U wave into the evaluated interval would be desirable.

In [3], only repolarization changes (influencing only STT interval) without the U wave were modeled on simulated data. In the present study the differences between DIMs computed from QRST and STT intervals of real measured data were analyzed and the results obtained for identification of small ischemic lesions were compared. Also the influence of the inclusion of U wave into the evaluated interval representing the myocardium repolarization was investigated.

2. METHODS & MATERIAL

To reveal ischemic lesions with changed repolarization body surface integral maps from the same person recorded in situations with and without manifestation of possible ischemia were measured and used to compute DIMs. Integration intervals QRST, QRSU, STT and STU were alternatively used in the computation supposing that these intervals include information on the ischemic changes. Equivalent cardiac generator consisting of two dipoles representing the ischemic area was computed from the DIMs using an inverse solution procedure. The inverse solution was calculated for all pairs of dipoles located in 154 predefined locations evenly distributed within the ventricular myocardium model. To find the best pair of dipoles representing the input DIM, the criterion of minimum of relative rms difference (RMSDIF) between the original DIM and the DIM generated by the inversely estimated pair of dipoles was used. Not only dipoles representing the best fit but dipoles from all results with RMSDIF within 1% difference from the best solution were analyzed. Modified K-means clustering method was applied on all analyzed dipoles to divide them into 2 clusters [8]. If the dipoles from one dipole pair represented different ischemic lesions, it should be possible to assign them to different clusters. Any pair for which this procedure was not successful was excluded from the evaluation. Finally, the gravity center of each cluster was calculated and the mean dipole moment computed from all dipoles in the cluster was used to represent the lesion. The number of excluded pairs and mutual distance

of cluster centers were used as the criteria to decide whether these clusters represent two separate lesions or only one lesion.

Body surface potential maps were measured at the Department of Cardiology, Medical University of Warsaw from 10 patients (p1-p10) with coronary artery disease and 3 healthy subjects (h1-h3) at rest and during exercise test on supine ergometer set to the load of 75 W. Seven patients have had previous myocardial infarction, 4 of them had implanted stents, 2 of them had additional diagnosis of right bundle branch block (RBBB).

The high-resolution ECG signals were recorded from 64 leads [9] relatively to a Common Mode Sense (CMS) electrode. The ECG signals were digitized with 4096 Hz sampling frequency and 24 bits amplitude resolution. To improve the signal-to-noise ratio the cross-correlation averaging and filtering methods were applied to the recorded signals [10]. The electrocardiograms were filtered using bidirectional zero-phase Butterworth high-pass filter (order IV) with cut-off frequency of 0.05 Hz and Butterworth low-pass filter (order II) with cut-off frequency of 300 Hz. A Wilson Central Terminal reference signal was subtracted from recordings of all surface ECG signals. To reduce white noise interference data were decimated [10], [11] decreasing the sampling frequency to 1024 Hz. All signals were simultaneously averaged in time using the cross-correlation function [12]. One minute of recordings at rest and ten seconds of ECG signals measured during an exercise test at the load of 75 W were used.

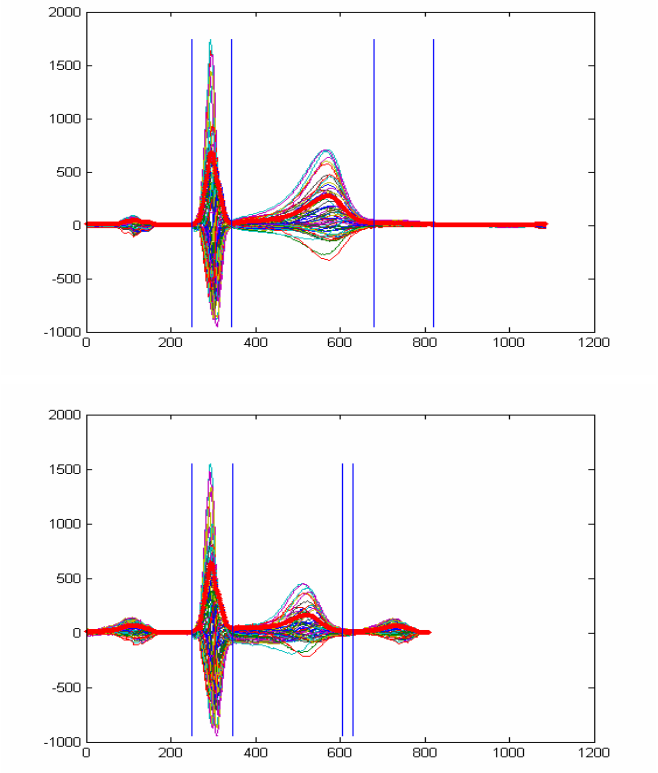

Fig.1 Averaged signals from 64 leads measured on patient p3 at rest (top) and during exercise (bottom). Red thick line represents rms value of signals. Vertical lines represent estimated fiducial points: Q, S, T-end, U-end.

Fiducial points Q, S, T-end and U-end in averaged ECG signals were determined manually from the rms signal computed from all measured leads (Fig.1). To study the influence of QRS and TU intervals of integration onto DIMs, integral maps for the time intervals QRST, QRSU, STT and STU were computed at rest and during exercise for each patient. To subtract the integral maps measured at rest and during stress correctly, changes of heart rate were compensated by recalculation of the time integral values to the same integration interval length. DIMs computed for the different tested intervals were then used as input data for the inverse procedure. The variances of the data obtained using the four time intervals of integration and their influence on the results of the inverse solution were studied.

3. Results

QRST, QRS and STT integral maps for all measured subjects at rest and during stress and the corresponding DIMs for QRST and STT intervals of integration were computed. The correlation coefficients between the maps and their rms differences were evaluated.

The correlation of QRS integral maps at rest and during stress was 93-99%, average 97.6%. Relative differences of RMS values of QRS integral maps recorded during stress and at rest varied from -9% (p4) to 26% (p1), average 10%.

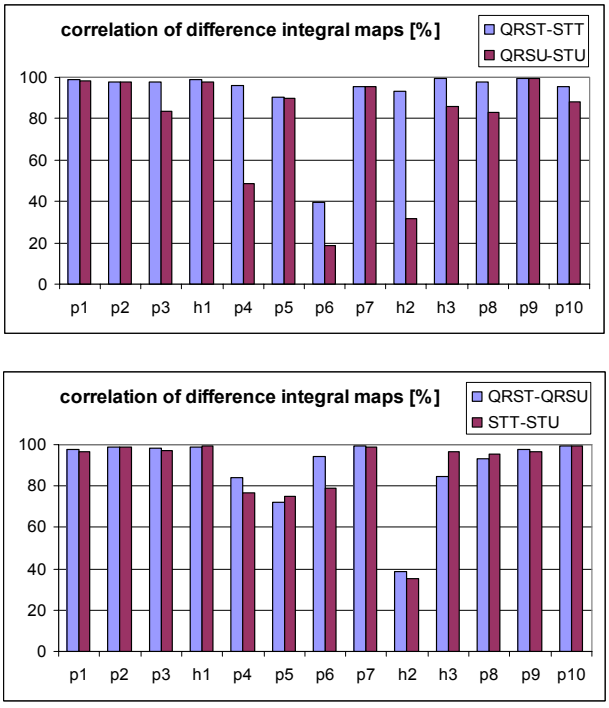

Fig.2 Correlations of difference integral maps. Top – the influence of inclusion of the U wave to interval of integration; Bottom – the influence of QRS inclusion on the correlation of DIMs computed for corresponding intervals.

Analogically, evaluation of DIMs showed that the correlation between DIMs computed using QRST and STT intervals of integration was high (90.6–99.5%, average 96.7%)

except for patient p6 (40%). Relative differences of RMS values of DIMs computed using QRST and STT intervals of integration were in the range from -20 to 25 %, average 7%.

To study the influence of U wave on inverse solution, for each patient DIMs were computed for 4 possible intervals of integration: QRST, QRSU, STT and STU. Fig. 2 (top) shows the correlations between DIMs computed using intervals representing the whole cardiac cycle (QRST or QRSU) and using intervals representing only the repolarization phase (STT, STU). After including the U wave the correlation was lower in average by 14% (0% - 61%). Comparing the correlations of corresponding intervals (Fig.2 bottom) the values of their differences oscillated from -11% to 15% around the average value of 1%.

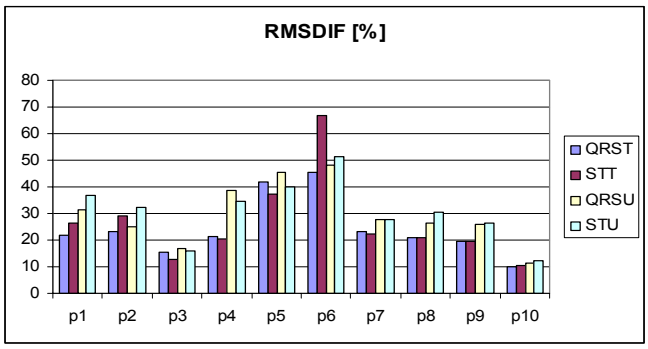

Fig.3 Relative rms differences (RMSDIF) between original DIMs and maps generated by the inversely estimated pairs of dipoles computed from all measured subjects.

Next, the properties of the inverse solution with 2 dipoles in relation to the chosen interval of integration were observed for measured objects where the existence of one or two ischemic lesions was expected (p1-p10). The main observed feature of the inverse solution was always the value of the RMSDIF - relative rms difference between the original DIM and the map generated by the inversely estimated dipole or pair of dipoles (Fig.3). This value represents the measure of information which we can get from DIM by the inverse solution to 2 dipoles and thus the applicability of the inverse solution for each particular case.

Because of the very high value of RMSDIF, patients p5 and p6 were excluded from further examination because neither 1 dipole nor 2 dipoles could satisfactorily represent their DIM (RMSDIF was from 49% to 80% for 1 dipole and from 37% to 67% for 2 dipoles). For all other measured subjects the RMSDIF for DIMs computed from intervals defined by the end of U wave were greater than RMSDIF for DIMs computed using the end of T wave. Therefore we decided to consider the QRST and STT intervals as more suitable for our inverse method and later we compared the results only from these 2 intervals.

The result of the inverse solution computed from a DIM was a set of two clusters of dipoles. The following selected features of the inverse solution characterizing the type of lesion were analyzed: (1) the number of solutions within the 1% tolerance from the minimal RMSDIF, (2) the number of pairs excluded by the clustering method, (3) the mutual distance between cluster centers characterizing two simultaneous lesions and also (4) standard deviation of positions of dipoles in the clusters. Some of these properties are shown in figures Fig.4a, b.

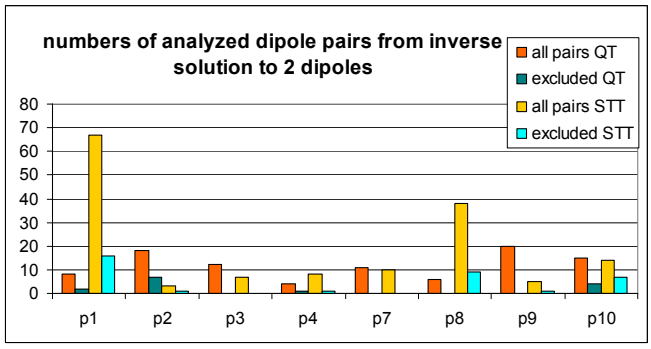

Fig.4a Properties of the inverse solutions to 2 dipoles for examined patients. The numbers of all pairs of dipoles used in the clustering method and the numbers of pairs that could not be divided uniquely to two different clusters (excluded).

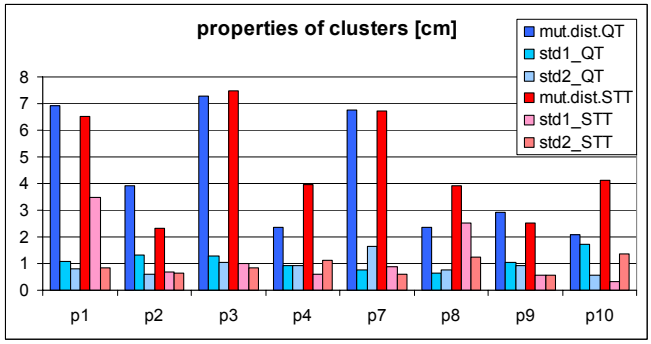

Fig.4b Mutual distance of inversely determined centers of clusters and standard deviations of positions of dipoles in each cluster.

Absence of any excluded pairs from the clustering method or a large mutual distance between cluster centers (more than 6 cm) could characterize two lesions (p1, p3, p7); a large number of excluded pairs or a small mutual distance could characterize the existence of only one lesion (p2, p4, p8, p9, p10). Large number of observed solutions together with large standard deviation of positions of dipoles in the clusters (all pairs STT for p1 and p8) could indicate that these results did not represent a local lesion but most probably larger ischemic areas.

To observe the shift between the localization of inversely determined centers of clusters from DIMs computed from QRST and STT interval, the localization shift was introduced and evaluated as the mutual distance of corresponding clusters' centers computed for different intervals of integration. Its mean value for all examined patients was 1.3 cm (0.1 – 3.7).

4. Discussion/Conclusions

The aim of the present study was to compare several possible intervals of integration that could be applied for computation of DIMs used for noninvasive identification of small ischemic lesions from measured ECG signals. The preliminary assumption of our method was the existence of

small regions with changed properties of myocytes. The measured data were obtained from 10 patients with different pathologies (coronary artery disease, myocardial infarction, right bundle branch block) which could cause various changes in myocardium and influence negatively the results. This could be the reason why 2 patients (p5, p6) had to be excluded from the study.

The results for 13 measured subjects showed that DIMs computed from QRST or STT interval of integration are in very good correlation (97% - except for p6), so the character of the maps is similar. On the other hand, inclusion of the U wave to the interval of integration led to a considerable decrease of correlation between DIMs computed from corresponding intervals (Fig.2 top) as well as an increase of minimal RMSDIF that was used as a criterion for best inverse solution (Fig.3). The reason could be the very small amplitude of signals in the interval between the end of T wave and the end of U wave and questionable detection of the end of U wave in many cases.

The properties of the inverse solution computed from DIMs from QRST or STT interval such as the number of dipole pairs considered, the number of dipole pairs excluded from clusterization, the mutual distance of clusters' centers and the standard deviation of dipoles' positions in each cluster were compared. The localization shift of corresponding clusters' centers computed from QRST or STT was also evaluated. In 3 cases (p3, p7, p9) all properties were similar and the localization shift was less than 1 cm. These results were considered more stable and reliable. Some properties of the inverse results computed for other cases differed significantly and also the values of localization shift were in some cases (p1, p8, p10) greater than 2 cm. However, after visual inspection of the results we can conclude that the inversely estimated clusters computed from QRST or STT interval represent the same region of the heart model (Fig.5).

Although it has been suggested that the U wave may represent late repolarization activities of myocytes [6],[7], the present study indicates that substantial information on ischemic changes for our inverse method is included in the QRST or STT intervals. Comparison of the results for both intervals can be helpful in evaluating (qualifying) the stability and reliability of the solution.

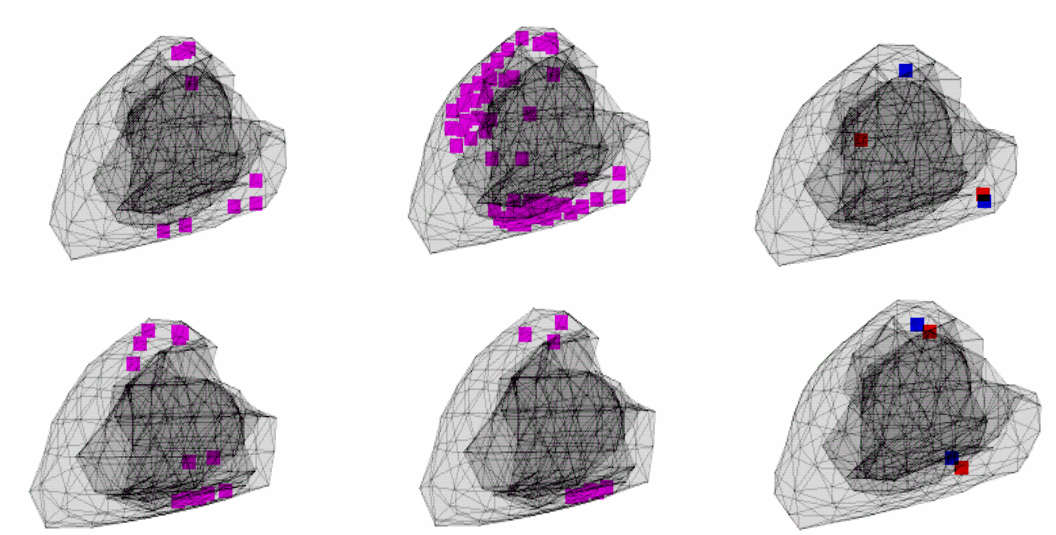

Fig.5 The results of the inverse solution to 2 dipoles with RMSDIF differing not more than 1% from the minimal value computed from DIMs from QRST and STT interval of integration (left and middle column, resp.). Sagittal view of the heart ventricles. Localization of estimated clusters' centers for QRST (blue) and STT (red) interval of integration (right column). Upper row – the worst result (p1) when numbers of dipoles in clusters differ considerably for QRST and STT intervals (8 vs 67 resp.) and localization shift reaches 3.7 cm. Lower row – stable result (p3) when all observed properties of inverse results are similar for QRST and STT intervals and localization shift is not greater than 0.8 cm. For both patients the centers are situated on anterior and inferior region of the heart.

ACKNOWLEDGMENT

The authors would like to thank Dr. Zaczek and Dr. Opolski, Department of Cardiology, Medical University of Warsaw, Poland for cooperation in the clinical measurements and kind permission to use the data in this study.

This work was supported by grants 2/7092/27 from the VEGA grant agency and APVV-51-059005 from the APVV agency in Slovakia and by research project No. NN518 328035 financed by the Polish Ministry of Science and Higher Education.

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