NONINVASIVE DETECTION OF ISCHEMIC REGIONS IN THE HEART

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Abstract: High resolution body surface potential maps and an equivalent current dipole model of the cardiac generator were used to assess the heart state in abnormal conditions caused by local ventricular ischemia. Results of a simulation study and experimental verification of the method are presented. Local repolarization changes were simulated as shortening of the myocytes action potentials in three regions typical for stenosis of main coronary arteries. Using surface QRST integral maps and dipolar source model, small subendocardial and subepicardial lesions of myocardium were inversely located with a mean error of 9 mm and larger transmural lesions with a mean error of 17 mm. Extent and prevalence of subepicardial or subendocardial type of the lesion were reflected in the dipole moment and orientation. Experimental verification of the method on a group of 11 patients that underwent PCI of a single vessel showed, that the method was applicable in 8 patients and estimated equivalent current dipole position matched well the treated vessel in 7 patients. The results suggest that diagnostic interpretation of body surface potential maps based on dipolar source model could be a useful tool to assess local ischemic changes in the heart.

Introduction

Ischemia of myocardial cells is connected with shortening and decrease of their action potentials (AP). This changed repolarization is reflected in surface ECG and it was shown, that integrals of ECG potentials over the ventricular depolarization-repolarization interval (QRST interval in ECG) depend on the AP waveforms but not on the ventricular activation sequence [1]. Alternations in integrals can be displayed in difference QRST integral maps and together with the knowledge of geometry and electrical properties of the torso can serve for detection of heart regions with changed repolarization. A method for noninvasive assessment of such regions was proposed and its performance was analyzed on a model and on a group of MI patients treated by percutaneous coronary intervention (PCI).

Materials and Methods

Changes in surface potentials expressed in difference QRST integral maps (DI maps) on a chest surface of known geometry and electrical conductivities were used for noninvasive assessment of ischemic lesions in the heart. Supposing a small lesion, these differences were interpreted as being caused by an dipolar source evoked by the AP alternation during the whole repolarization phase. The source in the form of an equivalent current dipole (ECD) was located in one of predefined locations in vertices of the triangulated epicardial and endocardial surface. For each predefined location $i=1,2,\ldots n$, an ECD source representing the changes in body surface potentials was estimated using the formula:

$$\boldsymbol{D}_i = \boldsymbol{T}_i^{+}\boldsymbol{\Phi} \tag{1}$$

where $\boldsymbol{D}_i$ is an estimate of integral of the dipole moment of a dipole located at the i-th position in the myocardium

$\boldsymbol{T}_i^{+}$ is pseudoinverse of a transfer matrix,

$\boldsymbol{\Phi}$ are differences in QRST integrals of surface potentials in mapped surface points.

Transfer matrix $\boldsymbol{T}_i$ represents the relation between the position of the i-th dipole and the surface potentials and reflects only the geometrical and electrical properties of the torso volume conductor. To solve the inverse problem of $\boldsymbol{D}_i$ estimation, pseudo-inverse $\boldsymbol{T}_i^{+}$ was computed using singular value decomposition of $\boldsymbol{T}_i$.

Criterion for finding the best ECD representing the surface potentials was the minimal rms difference R_{Dev} between original DI map (values A_i) and map generated by the ECD on the torso surface (values S_i):

$$R_{Dev} = \frac{\sqrt{\sum_i (S_i - A_i)^2}}{\sqrt{\sum_i A_i^2}} \tag{2}$$

Magnitude of this difference also enables to estimate the ability of the ECD to represent the ischemic region.

The method was first tested on simulated surface potentials and its ability to identify single dipole or a region with changed repolarization was studied.

A forward model was used to simulate body surface potentials in normal case and in the case of abnormal repolarization of the ventricles. Analytically defined volume formed by several ellipsoides was used to define the ventricular model [2]. Up to five layers with different AP characteristics were defined in ventricular

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walls and in the septum. Cellular automaton was employed to simulate cardiac depolarization and repolarization, realistic AP shapes as measured in canine left ventricular wedge preparation [3] were adopted. Experimentally observed distribution of AP and its transmural dispersion of about 40 ms were adhered [4].

Ischemic lesions were simulated by shortening the AP up to 20 % from the normal values. Three regions of changed AP typical for stenosis of main coronary vessels were defined (Figure 1): A – in antero-septal part of the left ventricle near apex (supplied by left anterior descending coronary artery, LAD), P – in postero-lateral part of the left ventricle close to the heart base (supplied by circumflex coronary artery, Cx) and I – inferior, in mid postero-septal part of the left and right ventricle (supplied by the right coronary artery, RCA). In each region, smaller subendocardial lesions (3 - 8% of the ventricular volume) and larger transmural lesions (10 - 12% of the ventricular volume) were simulated. Similarly, small subepicardial lesions (marked as AE, PE and IE) were defined in the same three regions.

Figure 1. Ventricular myocardium model with subendocardial regions of changed repolarization. Left: antero-septal regions A1, A2, A3 in the LV; center: postero-lateral regions P1, P2, P3 in the LV; right: inferior regions I1, I2, I3 in the mid postero-septal LV and RV. Cuts are through the lesion centers, different sizes of lesions are marked by grey levels.

For computation of surface potentials in realistic torso model (Figure 2) with lungs and heart cavities, 168 dipoles placed in the centers of anatomically defined ventricular segments were used to represent the ventricular depolarization – repolarization [5, 6].

For inverse identification of ischemic regions, body surface potentials simulated in 4 lead sets were used: 192 leads in 16x12 grid (G192), 62 leads of the Amsterdam mapping set (A62), 32 leads of the anterior lead set by Lux (L32) and 9 leads in positions of Frank VCG leads and both arms (F9). Second and third lead sets were subsets of the first one. Both, inhomogeneous and homogeneous torso model were tested in the inverse computations. Accuracy of the inverse procedure was limited by the chosen set of possible dipole positions. For testing on simulated data, 298 nodes on the epi- and endocardial ventricular surface were defined as possible positions of the equivalent dipole generator (Figure 3a). Distance between the nearest possible position and correct location of an equivalent dipole (center of simulated lesion) was from 1.7 to 7.3 mm, mean 5.5mm.

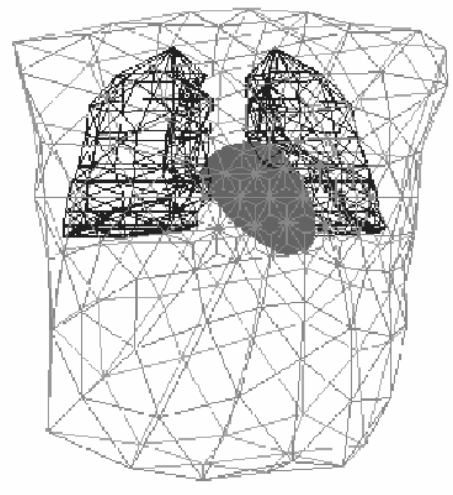

Figure 2: Realistic inhomogeneous torso model with lungs and heart cavities used for computation of simulated surface potentials.

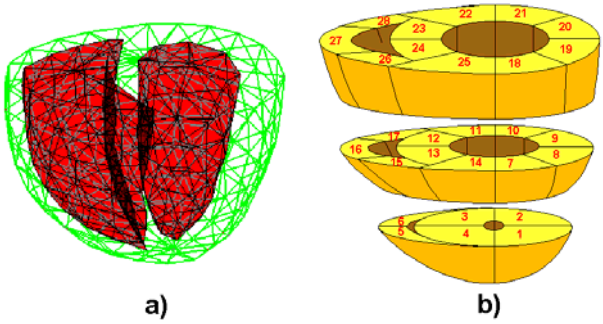

Figure 3: a) Possible positions of ECD characterizing small ischemic lesions in the simulation study were defined at the vertices of epicardial and endocardial surface of the ventricular volume model. b) In patients without measured chest geometry, analytical model of the ventricular myocardium was divided into 28 segments and possible ECD positions were placed in their gravity centers.

When evaluating accuracy of the method, a point source obtained by summing the elementary sources within the simulated region and placed at its gravity center was considered as correct representation of the lesion. Influence of the number of measured surface leads and omission of the chest inhomogeneities on the lesion identification was also analyzed.

For experimental verification of the method, measured data from 11 patients after myocardial infarction (MI) that underwent successful percutaneous coronary intervention (PCI) on single coronary vessel (8 LAD, 1 Cx, 2 RCA) were used to assess the impact of the reperfusion on the AP and the surface potentials. QRST integral maps before and after the intervention were computed in a 12x16 grid from 32 ECG leads measured in the L32 lead set. Integral values in maps

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were corrected for the QT interval length if it varied more than 5% between the measurements. Common realistic inhomogeneous torso and heart model geometry, the same as in the simulation study, were used in all patients to find an equivalent dipole representing the ischemic region with changed repolarization. Possible positions of equivalent dipoles were defined at the centers of 28 segments of the analytical heart model (Figure 3b).

Results

Simulated AP changes representing local ischemic lesions in three typical ventricular regions were projected to body surface potentials and differences of QRST integrals were clearly visible in corresponding areas in surface maps. The differences increased with increasing lesion size and degree of AP shortening except for transmural lesions where the differences were much smaller than in comparable non-transmural lesions. Example of a normal simulated QRST integral map and integral maps after AP was shortened by 20% in subepicardial lesion PE and subendocardial lesions, P2 and P3 is shown in Figure 4. The AP changes were projected as increase (for PE lesion) or decrease of the QRST integral (for P2, P3 lesions) mainly on the mid posterior torso surface.

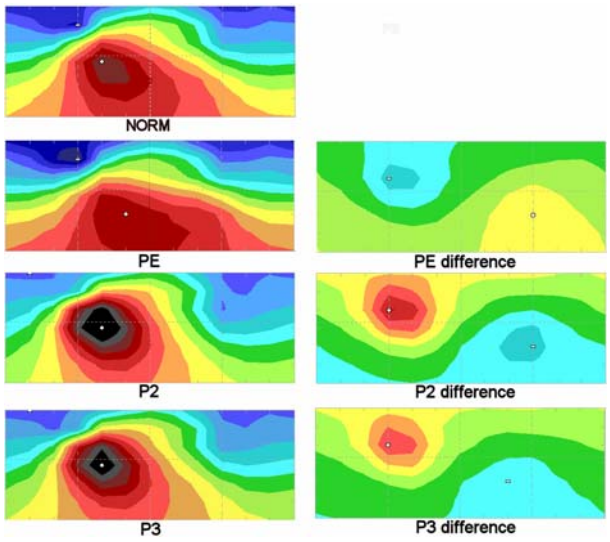

Figure 4: Simulated QRST integral maps for normal depolarization-repolarization sequence (NORM) and for repolarization with AP shortened by 20% in lesions PE, P2 and P3. Corresponding difference QRST integral maps are shown in the right column. Steps in all maps are 6 mV.ms.

Results of the inverse identification of the ECD using 62 ECG leads and inhomogeneous or homogeneous torso model are summarized in Table 1. Relative rms deviations between original DI maps and maps computed from ECD were from 9 to 16% and suggest that dipole may be an adequate representation of small ischemic lesions. For small subendocardial and subepicardial lesions, maximal localization error reached 16 mm in inhomogeneous torso and 23 mm in homogeneous torso. Localization of large transmural lesions was unsatisfactory and maximal error reached 43 mm. Orientation of equivalent dipoles matched with the simulated lesions, however, relative error of dipole moments was large, namely for transmural lesions.

Table 1: Errors (mean ± standard deviation) of the inverse estimation of lesion parameters from 62 surface ECG leads using inhomogeneous or homogeneous torso model.

Parameter	Torso	Small lesions	Large lesions
Localization error [mm]	inhomog	9 ± 4	17 ± 14
	homog	11 ± 8	16 ± 15
Dipole direction [°]	inhomog	9 ± 7	14 ± 4
	homog	8 ± 5	17 ± 7
Dipole moment [%]	inhomog	51 ± 40	221 ± 206
	homog	49 ± 33	163 ± 123
Map rel. difference [%]	inhomog	9 ± 4	16 ± 1
	homog	12 ± 2	16 ± 2

More detailed evaluation of the influence of the number of measured leads and used torso model on the localization error is shown in Figure 5. Localization of small lesions from 192 and 62 leads provided similarly good results; localization from 32 leads was less satisfactory for large lesions and inhomogeneous torso, while localization from 9 leads was not acceptable. For larger lesions, influence of the number of leads was higher. In majority of cases, results obtained using homogeneous torso model were less accurate than results obtained when inhomogeneous torso was used.

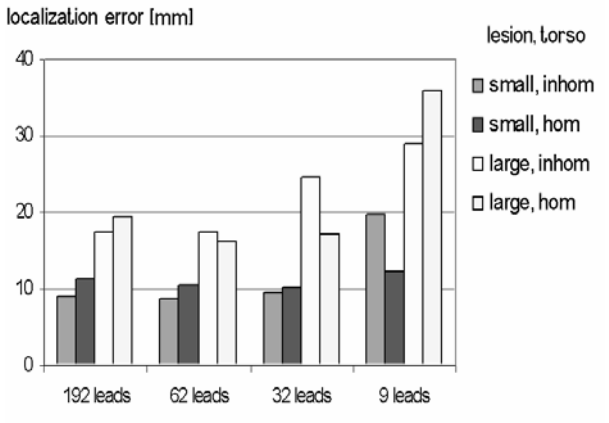

Figure 5: Mean values of the localization error [mm] for small subendocardial or subepicardial lesions and for large transmural lesions when different lead sets and homogeneous or inhomogeneous torso models were used.

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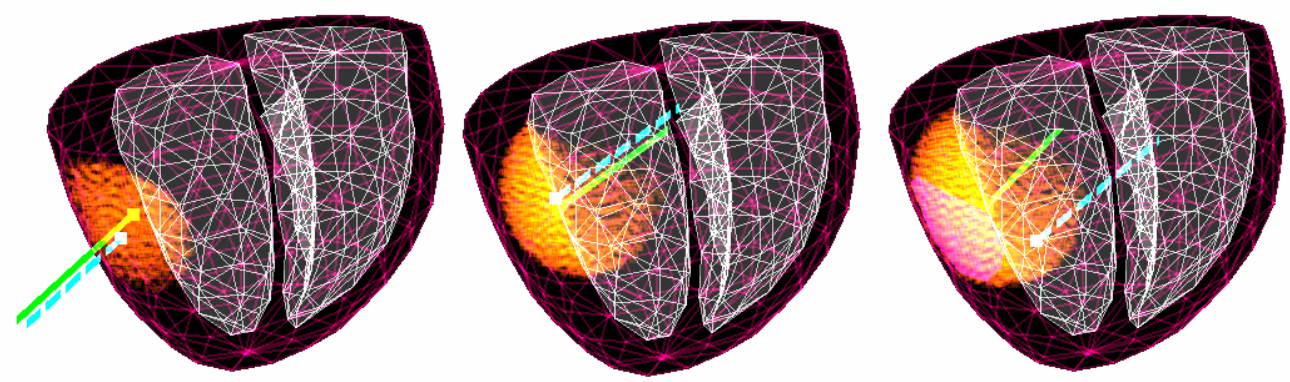

Figure 6: Posterior view of simulated ischemic postero-lateral lesions PE (left), P2 (center), P3 (right) and their dipolar representations. Reference dipoles are marked by solid lines, ECD inversely calculated from simulated surface ECG signals are marked by dashed lines.

Example of inversely estimated ECD for simulated postero-lateral lesions PE, P2 and P3 is illustrated in Figure 6. The lesions are shaded, reference dipolar moments of the lesions calculated as sum of contributions from model elements within each lesion are shown as a solid line vectors, inversely estimated ECDs are marked as dashed line vectors. Successful identification of the source in the subepicardial lesion PE and small subendocardial lesion P2 is noticeable, while localization of the larger transmural P3 lesion was not satisfactory.

When evaluating real measured data, evident changes in QRST integral maps after the PCI treatment were found in all 11 studied MI patients. Only in 8 of them they could be approximately represented by a single dipole (with relative rms error less than 50%). In remaining 3 patients the error was above 60% and they were excluded from further analysis.

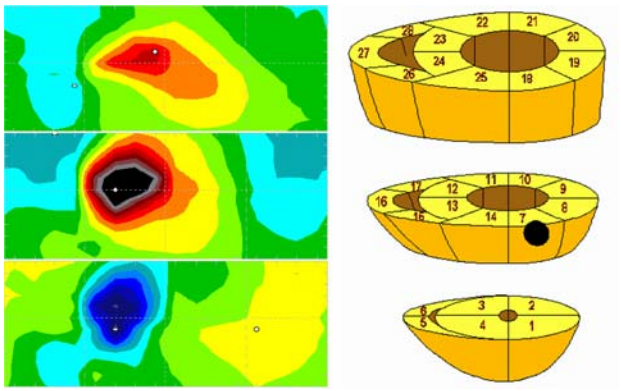

Figure 7: Localization of ECD representing the repolarization changes after PCI in a 68 year old male with anterior MI (closing at RD2 branch of LAD). Left, top to bottom: Measured QRST integral maps (step in maps 8 mV.ms) before and after successful PCI on LAD and corresponding difference integral map. Right: Localization of an equivalent dipole source representing the changed repolarization in an analytical myocardium model.

In 6 of 8 analyzed patients, the QT interval correction was used to compensate the changes due to different heart rates in consecutive measurements.

Despite the individual patient geometry was not available and common torso model was used, in 7 of the 8 analyzed patients (6 LAD and 1 RCA patient) the position of estimated ECD matched the region supplied by the treated vessel or at least it was correctly located at anterior or postero-lateral wall of the left ventricle with the dipole moment directed towards the supposed ischemic region. In 1 patient after PCI on RCA, the equivalent dipole was located probably incorrectly in mid anterior left ventricular wall with a dipole moment directed out of the heart volume. In Figure 7 there is an example of measured patient data and successful location of the equivalent dipole after PCI on LAD.

Discussion

Presented simulation results suggest that BSP data together with known patient torso geometry might be useful for identification of small ischemic lesions. However, because of the limitations of the model, validity of the obtained results has to be further verified on patient data.

The main limitation of the model is the simple heart geometry without atria and use of isotropic myocardium. Action potential shapes and durations in the myocardium elements were defined *a priori* and possible electrotonic coupling was not included.

In real situations, the local repolarization changes, can be masked by other physiological fluctuations and noise in measured data. Relative rms differences between simulated normal and abnormal QRST integral maps were 20 - 45% rms, correlations .45 - .99. These variations were greater than observed total intra-individual variability in maps of healthy subjects (5 - 20% rms, correlations >.98) what, in principle, makes the method, feasible for their identification.

In contrary, our attempt to detect small ischemic changes in BSP using departure integral maps [7] showed that these changes were relatively small when

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compared with normal inter-individual fluctuations and can hardly be detected by departures from mean normal integral maps.

Use of the method for identification of larger transmural lesions might be not appropriate. In these cases the single dipole model is probably not adequate and its localization may not be in correspondence with the real lesion position. Moreover, transmural lesions produce less difference in the DI maps and their identification is more difficult.

Only detection of AP duration changes during repolarization was presented in this study. Simultaneous changes of AP amplitudes that are present in real ischemia were also tested on the model and corresponding simulations confirmed similar effect of both, AP shortening and amplitude decrease, on the integral maps.

When evaluating real data, the ECD moment directions in several cases were not normal to the particular heart wall and lesion border. This may reflect the specific form of the affected area or anisotrophy in the real myocardium that were not included in the simulations.

Conclusions

Despite the limitations of the study, presented results of the simulations suggest that local repolarization changes in different heart regions are clearly manifested in changed QRST integral maps and their proximate site on the epicardial or endocardial surface can be identified using a single equivalent current dipole model. Its magnitude and orientation can help to characterize the extent and subepicardial or subendocardial type of the lesion. In majority of measured MI patients after PCI the difference in QRST integral maps could be used to localize the ECD corresponding to the revascularized region. Ongoing study will verify the reliability and accuracy of the method on a larger group of patients.

Acknowledgements

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