Impact of Anatomical Variations in Ventricular Shape on Non-Invasive Electrocardiographic Imaging

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Abstract

Non-invasive electrocardiographic imaging (ECGI) combines body surface electrocardiographic information with anatomical data to estimate electrical dynamics of the heart on the surface or transmurally across the depth of the myocardium. As a standard practice, ECGI techniques rely on anatomically detailed heart and torso models derived from high quality tomographic data. This practice not only imposes high demands on the image quality and processing, it is also associated with some degree of variations and uncertainty due to image quality, inter/intra-individual variability in segmentation and the differences in segmentation techniques. Though the importance of global anatomical parameters on the accuracy of ECGI solutions are established, the role of local variations in anatomical details remains unknown. In this study, we address this problem by designing an approach to statistically analyze the impact of local variations in ventricular models on the diagnostic accuracy of ECGI methods. It is achieved by developing a set of ventricular models with locally different anatomical details from trained statistical shape models, followed by performing a statistical hypothesis test of equivalence on the ECGI outputs. Two of the existing ECGI methods on epicardial and transmural potential imaging are used in our phantom and real-data experiments. Both experiments for two ECGI methods report statistically equivalency of ECGI diagnostic accuracy except for practically irrelevant differences on ventricular models with local variations. This finding is important in changing the standard practice and facilitating the clinical translation of ECGI research.

1. Introduction

Cardiac arrhythmia is typically monitored and diagnosed with non-invasive electrocardiographic (ECG) signals recorded on the body-surface. When ECG fails to provide accurate locations of arrhythmogenic substrates because of its limited information and spatial resolution, invasive electroanatomic mapping is needed to examine the electrical pattern of the heart by point-to-point catheter mapping on heart surfaces. Localizing arrhythmogenic substrates by inducing ventricular tachycardia (VT) with aggressive stimulation protocol, this invasive procedure often incurs excessive cost and the induced VT could degenerate into lethal ventricular fibrillation if not interrupted successfully. Furthermore, these surface-based measurements have limited capacity in assessing transmural electrical activity and myocardial substrate across the depth of the myocardium.

Motivated by the limitation of these state-of-the-art techniques, research methods of non-invasive electrocardiographic imaging attempt to combine body-surface ECG data and tomographically-derived anatomical data to computationally reconstruct subject-specific electrophysiological dynamics, on the heart surfaces [1-3] or transmurally across the depth of the myocardium [4,5]. Subject-specific anatomical data, in terms of certain global parameters such as size, position and orientation of the heart with respect to torso, are found to be critical for the accuracy of ECGI [6]. As a result, existing research of ECGI methods utilize personalized anatomically detailed heart and torso models as one defaulted input data, though its preparation relies on the quality of the tomographic images and the image analysis process. Specifically, it confines the imaging options to high-quality MR/CT scans and eliminates more accessible and less expensive imaging modalities such as ultrasound. The variations in the MR/CT image quality, caused by various factors such as external devices in the heart and the imaging parameters, would lead to unknown variations in the anatomical details extracted for the same subject. On the other hand, the process of high-quality, anatomically detailed model reconstruction involves a time-consuming, expert-dependent process. Variation of segmentation errors among individuals and segmentation methods will further contribute to unknown variations in the anatomically detailed model developed for the same subject. These challenges and uncertainties in preparing an anatomically detailed model, which is also clinically impractical, raise a fundamental research question: What is the quantitative impact of variations in anatomical details on ECGI, on the condition that the important global anatomical parameters are captured?

This question is addressed in this paper using two existing ECGI methods representative of epicardial potential imaging (EPI) [1] and transmural electrophysiological imaging (TEPI) [5] methods. We design experiments to assess the effect of controlled variations of cardiac local anatomical details on accuracy of ECGI outputs. First, the statistical model of cardiac local anatomical details variation is obtained by training statistical shape model (SSM) [7] from multi-user segmentations on the short-axis cardiac images for the same subject. Next, the trained SSM generates a set of ventricular models with controlled variations for the same subject. After pairing up the ventricular models of the same subject and considering a population of several subjects, we design a hypothesis tests of equivalence based on paired t-tests with the null hypothesis that ECGI outputs generated on the same ventricular model with variations in local details are statistically different from each other. On phantom and real-data experiments with 80 and 64 ventricular models of 4 subjects, respectively, the equivalence test reports the rejection of the null hypothesis at the 5% level, and thus proves an equality of ECGI diagnostic accuracy except for practically irrelevant differences on ventricular models with local variations. In other words, local variations of ventricular anatomical models do not significantly impact the diagnostic accuracy of ECGI. This finding has the potential of changing the standard practice and facilitating the clinical translation of ECGI research.

2. Methodology

Differences in segmentation techniques, users and image quality lead to the variations in local details of the anatomical models built for the same heart. Although, the importance of global anatomical parameters on ECGI techniques is established, the impact of local anatomical details is unclear and difficult to measure. However, this may directly affect one of the critical challenges of ECGI methods toward clinical feasibility. Thus, we address the effect of variations in anatomical details on ECGI methods by developing a set of ventricular models with controlled variations in anatomical details followed by performing a statistical test to investigate the equivalency of the corresponding ECGI outputs.

2.1. Statistical modeling of ventricular shape with different anatomical detail

In practice, manual multi-individual MR/CT image segmentation or different segmentation techniques results in the heart models with locally different anatomical details for a specific subject. Simulating the real world scenario, for each subject, a set of ventricular models are generated through manual MR/CT image segmentation by different experts. This set serves the training set for statistical shape model (SSM) [7] in order to obtain statistical model of the subject heart. Using SSM, each subject ventricular shape can be described by a mean shape (X) and shape parameters including eigenvalues (λ) and eigenvectors (Φ) that determine the heart geometry variations along main directions. In another word, each eigenvalue represents the variance of the shape along the corresponding eigenvector. By changing the shape parameters within the limits (λ_i) learnt from the training set, we can generate a set of heart models (X_i) with the same shape statistics but different local anatomical details for the same heart.

$$X_i = X + \beta\Phi, \text{ for each } i \; -\lambda_i \leq \beta \leq \lambda_i \qquad (1)$$

where β is a vector that controls the shape variation along different eigenvectors. In this study, ten largest eigenvalues are used to generate new heart models, as the rest are very close to zero.

2.2. Hypothesis test of equivalence

At this point, we investigate statistical equivalency of the ECGI outputs for the heart models with locally variant anatomical details. Several subjects with their corresponding ECG data and tomographic images are considered for this statistical analysis. For each subject, as described in section 2.1, a set of ventricular models with variations in local anatomical details is developed. Coupling each heart model of the same subject with the corresponding ECG data, ECGI method estimates the corresponding cardiac potential dynamics. Using the same ECG data for the heart models of the same subjects ensures that the only difference in the ECGI output is caused by the local anatomical details variations. ECGI outputs are then utilized to extract infarct parameters. The infarct parameter θ extracted from ECGI outputs of heart models of the same subject are randomly paired up. Then, the hypothesis test of equivalence based on paired t-test is performed on the paired θs of entire population. Assuming parameter $d\theta \sim N(\delta,\sigma^2)$ to be the measure of the intra-subject difference of the paired observations of θs, statistical equivalency is obtained if δ/σ lies within an established range $[-\varepsilon,\varepsilon]$, $\varepsilon>0$, as described in the definition of equivalence test for the paired observations [8]. Therefore, the alternative and null hypotheses are:

$$\text{Alternative hypothesis } (H_1) : -\varepsilon \leq \delta/\sigma \leq \varepsilon$$
$$\text{Null hypothesis } (H_0) : \delta/\sigma < -\varepsilon \vee \delta/\sigma > \varepsilon$$

Sample size is calculated through power analysis during the experimental design. In this study, infarct size and infarct location are used to represent parameter θ.

3. Experiments and results

This study investigates the effect of local anatomical details on two existing ECGI method called Transmural Electrophysiological Imaging (TEPI) [5] and regularization-based epicardial potential reconstruction method [1]. TEPI provides a maximum a posteriori estimate of the subject-specific transmural potential dynamics from the body-surface ECG data and tomographic data of the individual. Epicardial potential reconstruction approach estimates epicardial potential from the same input as TEPI using the classical zero-order Tikhonov regularization method. As a standard practice of ECGI methods, anatomically detailed heart models are used as standard inputs.

Our experiments focus on myocardial infarction (MI) imaging based upon the estimated TMP/EP dynamics. Experimental studies have shown that TMP/EP characteristics of infarct scar change such as action potential duration (APD) and depolarization rate [9], regardless of the ECGI technique used for the TMP/EP estimation. As a result, the accuracy of scar imaging is determined by extracting the activation time (AT) and repolarization time from the TMP/EP dynamics [10]. Difference between repolarization time and AT corresponds to action potential duration. Accuracy of ECGI methods are calculated based on infarct size and localization that are obtained from the extracted AT and APD on the 17x3 segments of the LV, with 17 AHA circumferential and longitudinal segments of the LV and 3 transmural layers within each segment. Infarct size is calculated as the number of estimated infarct mesh-free points to the total number of mesh-free points. Infarct center represents the center of the infarct scar.

Our experiments are conducted on both phantom and real data to evaluate the effect of local anatomical details on two ECGI methods. Epicardial ECGI experiments are still in process while the TEPI results are collected and analyzed.

Synthetic Cases_ Our phantom experiments are conducted on four subjects including a canine heart and three human heart models. A realistic human torso model with 370 coordinates is coupled with all the heart models for the phantom experiments [11]. For each subject, a set of 7 heart models are developed using manual segmentation of different experts that is served as the SSM training set. Training the SSM, a statistical model of each heart is obtained that is used to generate 20 heart models for each subject, in total 80 heart models for the four subjects.

In this phantom experiments, it is assumed that infarct location extends from mid inferolateral LV to apical inferior LV. This assumption is applied to all the subjects, and the corresponding body surface potential (BSP) is simulated using one of the ventricular models per subject. The simulated BSP includes 370 electrodes locating exactly on the 370 vertices of the torso surface mesh. It is then corrupted with 20-dB white Gaussian noise, and used as inputs to two ECGI methods on all the ventricular models of the same subject. Since the input BSP for the same subject is identical, the only affecting factor on the ECGI outputs is the variation in the local anatomical details of the input ventricular models. Fig. 1 presents two different segmentations (red and blue contours) of one MRI slice that eventually result in two different heart models for the same subject. The corresponding estimated infarct is also shown using red and blue points.

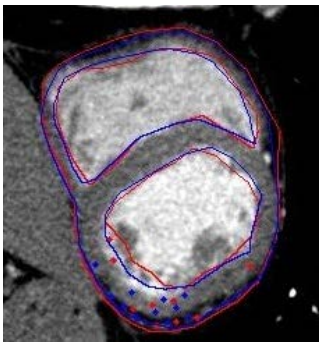


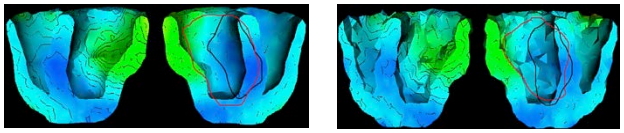
Figure 1. Two different segmentations (red and blue contours) of one MRI slice at short axis. The corresponding estimated infarct locations are also marked with red and blue points.

After collecting the outputs of two ECGI methods on the entire population, infarct parameters such as infarct size and infarct center on the ventricular models for the same subject are randomly paired up. The difference of infarct sizing error ($d\theta$) for the paired results of all 4 subjects have mean 0.01 and variance 0.05 that belongs to the rejection region at $\alpha = 0.05$, choosing equivalence limits to be $\pm\varepsilon$ for $\varepsilon = 0.5$ and sample size 40. The null hypothesis is thus rejected and the alternative hypothesis can be accepted. Similarly, the difference of infarct center error for the paired population has a normal distribution $N(0.3,1.6)$ that reports the rejection of the null hypothesis for the tolerance $\varepsilon = 0.5$ at $\alpha = 0.05$. Therefore, we can conclude that local variations in ventricular models do not affect MI quantification using TEPI method.

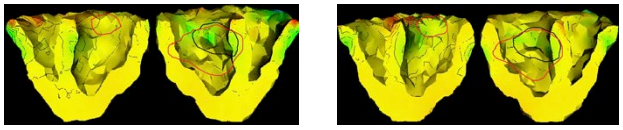
Real Cases_ Four human subjects with post-MI condition [12] are considered in our real experiments in order to evaluate the effect of anatomical details variations on the accuracy of ECGI imaging. This dataset provides heart/torso MR images and the corresponding 120-leads ECG recordings for each subject. MR images of each subject's heart include 10 slices with 8 mm slice spacing and 1.33 mm pixel spacing. The torso surface is also

described by 370 vertices to which the 120-lead ECG recordings are interpolated.

Similar to the phantom experiments, 7 heart models are developed for each subject based on the manual segmentation of different experts in order to create the SSM training set. Next, the SSM is trained and 16 heart models are generated for each subject, giving 64 heart models in total. Heart models of the same subjects are then coupled with the same input ECG to estimate the infarct parameters using two ECGI methods. Fig.2 shows the infarcts detected by TEPI for 2 subjects. For each subject, despite the visible difference in anatomical details of the 2 ventricular models in (a) and (b), infarct detected by TEPI reside at similar regions. Likewise, results on heart models for the same subject are randomly paired up. The 32 pairs on the 4 patients form the entire population for the equivalence test based on paired t-test. The infarct sizing error difference ($d\theta$) of paired observations has mean and standard deviation 0.01 and 0.06, respectively. For a sample of 32 pairs and the equivalence limit $\varepsilon = 0.5$, it reports the rejection of null hypothesis at 5% level. Likewise, the difference of infarct location error for the pair observations follows the normal distribution $N(0.4,1.8)$ leading to the rejection of null hypothesis given $\varepsilon = 0.5$ and $\alpha = 0.05$. Although it has less power compared to the synthetic experiment due to the smaller sample size. Therefore, it is statistically proven that ECGI outputs on ventricular models with local variations are equivalent.



(a) Two ventricular models for real case 3



(b) Two ventricular models for real case 4

Figure 2. Infarct imaging for two different models of the same real subjects (case 3 and case 4). Despite visible difference in anatomical details, infarct regions are located at the same area for the ventricular models of the same subject. Red and black contours show the reference and the estimated infarct regions, respectively.

4. Conclusions

Anatomically detailed ventricular model, used as an standard input in ECGI methods, largely relies on high-quality tomographic images and image analysis. At the same time, there are unavoidable local variations in these anatomical models for the subject, due to multiple factors such as image quality, users, and segmentation techniques. In this study, we quantitatively evaluated the impact of these variations in local anatomical models on two existing epicardial and transmural ECGI methods. SSM method used to generate a set of ventricular models with locally different anatomical details for the same subject, and a hypothesis test of equivalence is performed to prove the statistical equivalency of the corresponding ECGI outputs. Phantom and real experiments report statistically equalvalency of ECGI diagnostic accuracy except for practically irrelevant differences on ventricular models with local variations. This finding is important in changing the standard practice and facilitating the clinical translation of ECGI research.

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