THE IMPACT OF VENTRICULAR SHAPE VARIATIONS ON INVERSE ELECTROCARDIOGRAPHY: A FEASIBILITY STUDY

Azar Rahimi, Linwei Wang

Computational Biomedicine Laboratory
Galisano College of Computing and Information Sciences
Rochester Institute of Technology, Rochester, NY

ABSTRACT
Inverse electrocardiography (IECG) estimates cardiac electrical dynamics from body surface electrocardiographic data. As a common practice, all existing IECG problems are solved on anatomically-detailed heart and torso models derived from tomographic images of individual subjects. This practice constitutes a major obstacle to clinical translation of IECG methods, imposing high demands on the quality and processing of medical images. Because anatomical modeling is always associated with variations due to different factors such as image quality and segmentation methods, we design a novel and systematic approach to statistically quantify the impact of ventricular shape variations on the diagnostic accuracy of IECG methods. We propose a novel use of statistical shape modeling to account for the variations in subject-specific anatomical modeling, and from it to generate ventricular models with controlled variations, whose relation to the variations of IECG outputs are then statistically assessed. In this study, we test the feasibility of the proposed approach considering two existing IECG methods for epicardial potential reconstruction and transmural action potential imaging. Both phantom and real-data experiments report statistical equivalency of IECG diagnostic accuracy on ventricular models with local variations. This study demonstrates the feasibility of the proposed approach to be generalized to establish the proper level of anatomical details needed in ventricular modeling, which has the potential to change the common practice and facilitate the clinical translation of IECG research.

Index Terms—Inverse problems of electrocardiography, statistical shape modeling, hypothesis test, infarction

1. INTRODUCTION
Cardiac arrhythmia is commonly monitored and diagnosed with noninvasive body-surface electrocardiographic (ECG) signals. When regional details of cardiac electrical activity are needed for interventional therapies, invasive electroanatomic mapping is often used to examine the electrical pattern of the heart by point-to-point catheter mapping on heart surfaces. This invasive procedure often incurs excessive cost, prolonged mapping procedure, and exposure of patients to fluoroscopy radiation. Furthermore, both ECG and catheter mapping provide a poor surrogate for the transmural electrical activity across the depth of the myocardium.

Motivated by the limitation of these state-of-the-art techniques, many computational strategies of inverse electrocardiography (IECG) are developed to use body-surface ECG data to computationally reconstruct subject-specific electrophysiological dynamics, on the heart surfaces [1,2] or transmurally across the depth of the myocardium [3,4]. 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 IECG [5,6]. Therefore, it is a common practice for existing IECG methods to perform on anatomically-detailed heart-torso models derived from tomographic images. However, the preparation of these input data constitutes a clinically impracticable component of IECG methods: it confines the imaging options to high-quality MR/CT scans and eliminates more accessible and less expensive imaging modalities such as ultrasound. Furthermore, building a high-quality, anatomically-detailed model involves a time-consuming, expert-dependent process. At the same time, these input data involve uncertainties varying with the image quality and analysis process.

These technical challenges and uncertainties associated with preparing an anatomically detailed model for IECG methods raise a fundamental research question: "On the condition that the important global anatomical parameters are captured, what is the quantitative impact of anatomical shape variations on IECG outcome, and what are the minimal level of anatomical details needed to admit the diagnostic accuracy of IECG methods?" We design a systematic approach, based on a novel application of statistical shape modeling (SSM) combined with statistical tests, to address this question. As the first step towards this research direction, in this study we quantify the effect of controlled variations in ventricular local anatomical details on the accuracy of IECG outputs. First, anatomical variations in subject-specific ventricular modeling is accounted for by training a SSM [7] from multi-user segmentations on the cardiac images of the same subject. Next,
Fig. 1. (a). Outline of the proposed approach to systematically and statistically investigate the effect of anatomical details variations on IECG outputs. (b). Two different segmentations (red and blue contours) of one MRI slice at short axis.

This SSM of each subject is used to generate a set of ventricular models with controlled variations, on each of which IECG outputs are obtained given the identical body-surface ECG data. On a group of multiple subjects, IECG outputs from the same subject are paired up, and a hypothesis test of equivalence is performed to test the null hypothesis that IECG outputs generated on the ventricular models created for the same subject (with differences in anatomical details) are statistically different from each other. In this feasibility study, we consider two of the existing IECG methods as our testbeds: a method of epicardial potential imaging (EPI) [1] and transmural electrophysiological imaging (TEPI) [4]. On phantom and real-data experiments with 80 and 64 ventricular models of 4 subjects, respectively, the equivalence test reports the equality of IECG diagnostic accuracy (except for statistically irrelevant differences) on ventricular models with local variations at the 5% level.

This study demonstrates the feasibility of the proposed approach, which can be generalized to establish the relation of the variations of IECG outputs to the variations of anatomical shapes. This research has the potential to simplify the common practice and the clinical translation of IECG research.

2. METHODOLOGY

In this study we evaluate how IECG outputs are affected by variations in anatomical details in ventricular models, which could be caused by factors such as differences in segmentation techniques, users and image quality. As summarized in Fig. 1(a), we first use an SSM to model the variations in building an anatomically-detailed ventricular model for an individual subject, followed by generating a set of ventricular models with controlled anatomical variations from the SSM and test the difference of IECG outputs on these models.

2.1 Modeling Ventricular Shape Variations in Anatomical Modeling. In this feasibility study, we consider two sources of variations in anatomical modeling: different image resolutions and manual segmentation by different users. For the former, cardiac MR/CT images of each subject are downsampled to generate different images resolutions. For the latter, different experts are recruited to perform manual segmentations for each subject’s images. In current stage we consider only expert segmentations, and an example of the variations in segmentations is shown on one MRI slice in Fig. 1(b).

Training an SSM [7] using this set for a specific subject, we obtain a mean shape (X̄) and a covariance matrix (Σ) that accounts for the shape variations in all the ventricular models built for the same subject. Decomposing the covariance matrix into eigenvectors (Φ) and eigenvalues (λ), we find the principle directions of variations (eigenvector) in the ventricular shape and the corresponding value of variances (eigenvalue).

2.2 Ventricular Models with Controlled Variations. The SSM of each subject’s ventricular model, as described in section 2.1, enables us to generate ventricular models with controlled variations that can be used in the subsequent statistical test. Changing the shape parameters within the limits (λ_j) learnt from the training set, one can generate a set of ventricular models (X_j) with the same shape statistics but different local anatomical details for the same subject:

\[ X_j = X + \beta \Phi, \forall i \in \{1, \ldots, n\} - 3\sqrt{\lambda_i} \leq \beta_i \leq 3\sqrt{\lambda_i} (1) \]

where the vector \( \beta = [\beta_1, \ldots, \beta_n] \) controls the shape variation along different eigenvectors. Choosing the parameter \( \beta_i \) to be \( \pm 3\sqrt{\lambda_i} \), we ensure that the generated ventricular models symmetrically cover the sample space of the SSM. Here, we consider 10 eigenvectors with the largest eigenvalues that account for 98% of the shape variations.

2.3 Hypothesis Test of Equivalence. On ventricular models with controlled anatomical variations, we investigate statistical equivalency of the IECG outputs. On each subject, IECG methods are performed coupling the identical body-surface ECG data with the different ventricular models. Using the identical ECG data on the experiments for the same subject ensures that local anatomical variation is the only source that could lead to differences in IECG outputs. The same process is repeated for multiple subjects.

A specific accuracy measure θ (explained in section 3) is
extracted from the IECG outputs of ventricular models. Then, \( \theta \)s that correspond to the ventricular models of the same subject are randomly paired up and the difference of each pair is calculated \((d\theta)\). The hypothesis test of equivalence based on paired \( t \)-test is then performed on the \( d\theta \)s of the entire group of multiple subjects. Assuming parameter \( d\theta \sim N(\delta, \sigma^2) \) to be the measure of the intra-subject difference of the paired observations of \( \theta \)s, statistical equivalency is obtained if \( \delta/\sigma \) lies within an established range \([-\varepsilon, \varepsilon], \varepsilon > 0 \) [8]:

- Alternative Hypothesis \((H_1): -\varepsilon \leq \delta/\sigma < \varepsilon\)
- Null Hypothesis \((H_0): \delta/\sigma < -\varepsilon \lor \delta/\sigma > \varepsilon\)

Sample size is calculated through power analysis during the experimental design.

3. EXPERIMENTS AND RESULTS

We consider two existing IECG methods as our testbeds: Epicardial Potential Imaging (EPI) that estimates epicardial potential using the classical zero-order Tikhonov regularization [1], and Transmural Electrophysiological Imaging (TEPI) that provides a maximun a posteriori estimate of the subject-specific transmural potential dynamics [4].

In this study, we consider the application of IECG methods in healthy and/or post-infarction subjects. Accuracy measure \( \theta \) of EPI method is the relative error (RE) and correlation coefficient (CC) between the estimated and true epicardial potentials [1], and \( \theta \) of TEPI outputs is the infarct sizing (IS) and infarct center (IC) error where the infarct is quantified from the reconstructed action potential features as described in [9].

3.1. Phantom Experiments

Phantom experiments are conducted on 4 subjects including a canine heart and three human hearts, which are coupled with a realistic human torso model with 370 coordinates [10]. For each subject, a set of 7 heart models are developed using manual MR/CT segmentation with different resolutions by different experts, and serve as the SSM training set. From the trained SSM of each subject, 20 ventricular models are generated, giving in total 80 models among the 4 subjects.

Body-surface potential (BSP) data are simulated on the mean shape provided by the trained SSM for each subject, and are corrupted with 20-dB white Gaussian noise. For each subject, the identical BSP data are coupled with the SSM-generated ventricular models for IECG.

EPI is conducted on both healthy and post-infarction settings; infarct region extends from basal to mid anterior and anterolateral in each subject’s ventricle. On EPI outputs obtained on the 80 ventricular models for the 4 subjects, error measures RE and CC for the same subject are randomly paired up and RE difference and CC difference are calculated for each pair. Paired results of the 4 subjects have RE difference \( (d\theta) \) with mean 0.03 and variance 0.19. Assuming the commonly used equivalence limits \( \varepsilon = 0.5 \) [8], with 40 number of pairs, \( d\theta \) resides in the rejection region at \( \alpha \) level = 5%.

The CC difference for the paired population has normal distribution \( N(0.04, 0.032) \), also reporting the rejection of null hypothesis for the tolerance \( \varepsilon = 0.5 \) at \( \alpha = 0.05 \). Fig. 2 gives an example of the epicardial potential reconstructed on two ventricular models for the same healthy subject, where similar epicardial potential patterns can be observed despite visible difference in anatomical details.

TEPI is performed on the post-infarction setting used for EPI. On TEPI outputs on the 80 ventricular models, error measures of IS and IC for the same subject are randomly paired up. The difference of IS \( (d\theta) \) for the paired results of all 4 subjects has mean 0.01 and variance 0.05 that belongs to the rejection region at \( \alpha = 0.05 \), with equivalence limits \( \varepsilon = 0.5 \) and a number of 40 pairs. The difference of IC for the paired population has a normal distribution \( N(0.3, 1.6) \) that also reports the rejection of the null hypothesis for the tolerance \( \varepsilon = 0.5 \) at \( \alpha = 0.05 \). Fig. 3 shows snapshots of transmural action potentials obtained on two ventricular models of the same subject, where late activation (left) and early repolarization (right) at infarct region are similar in two anatomical models. Therefore, in our phantom experiments, the null hypothesis is successfully rejected, and we can conclude that local variations in ventricular models do not affect the accuracy of either IECG method being considered.

3.2. Real-Data Experiments

4 post-infarction human subjects [11] are considered in our real-data experiments. For each subject, we have heart/torso MR images and 120-lead BSP recordings. MR images of each subject’s heart includes 10 slices with 8 mm slice spacing and 1.33 mm pixel spacing. The torso surface is represented by boundary elements with 370 vertices, to which the 120-lead
BSP data are interpolated.

Similar to the phantom experiments, 7 ventricular models are built for each subject based on manual segmentations by different experts in order to create the SSM training set. On the trained SSM for each subject, 16 ventricular models are generated, giving 64 models in total among the 4 subject. For each subject, the 16 ventricular models are coupled with the same measured BSP data as inputs to the two IECG methods under study. IECG outputs on ventricular models for the same subject are randomly paired up, and hypothesis tests of equivalence are performed on the 32 pairs for the 4 subjects.

RE difference and CC difference for EPI outputs have normal distribution $N(0.016, 0.011)$ and $N(0.04, 0.031)$, respectively. Assuming the equivalence limit $\varepsilon = 0.5$ for 32 pairs of outputs, null hypothesis would be rejected at 5% level. IS difference and IC difference of paired observations have normal distribution $N(0.01, 0.06)$ and $N(0.4, 1.8)$, respectively. Again, for a sample of 32 pairs and the equivalence limit $\varepsilon = 0.5$, it reports the rejection of null hypothesis at 5% level. Fig. 4 shows the infarcts detected by TEPI on the two ventricular models for one subject. Despite visible differences in anatomical details of the 2 ventricular models, infarct detected by TEPI reside at similar regions at the two ventricular models. Therefore, the real-data experiments results confirm the findings of phantom experiments.

4. CONCLUSIONS

In this study, we developed a systematic statistical approach, based on a novel application of SSM, to quantitatively evaluate the impact of local anatomical variations on IECG methods. Our feasibility study considered the variations in anatomical details caused by variation in tomographic images resolution and different experts segmentations. Phantom and real experiments report statistical equivalence of IECG diagnostic accuracy except for statistically irrelevant differences on ventricular models with local variations.

This study can be extended to consider other factors that contribute to anatomical details variations. Furthermore, it can be extended to consider anatomical variations as the shape details increase from a simplified mesh to a anatomically-detailed one. When combined with proper statistical methods, such as the collocation methods, it will allow us to quantify the variations of IECG outputs as a function of the anatomical variations. As such, it could allow us to identify the proper level of anatomical details needed to admit the diagnostic accuracy of IECG methods.

5. REFERENCES


Fig. 4. Infarct detection on two different ventricular models of the same post-infarction subject (case 3). Despite visible difference in anatomical details, infarct regions are located at the same area of the 2 ventricular models. Red and black contours show the reference and estimated infarct regions.