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Methodology for image-based reconstruction of ventricular geometry for patient-specific modeling of cardiac electrophysiology☆

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ABSTRACT

Patient-specific modeling of ventricular electrophysiology requires an interpolated reconstruction of the 3-dimensional (3D) geometry of the patient ventricles from the low-resolution (Lo-res) clinical images. The goal of this study was to implement a processing pipeline for obtaining the interpolated reconstruction, and thoroughly evaluate the efficacy of this pipeline in comparison with alternative methods. The pipeline implemented here involves contouring the epi- and endocardial boundaries in Lo-res images, interpolating the contours using the variational implicit functions method, and merging the interpolation results to obtain the ventricular reconstruction. Five alternative interpolation methods, namely linear, cubic spline, spherical harmonics, cylindrical harmonics, and shape-based interpolation were implemented for comparison. In the thorough evaluation of the processing pipeline, Hi-res magnetic resonance (MR), computed tomography (CT), and diffusion tensor (DT) MR images from numerous hearts were used. Reconstructions obtained from the Hi-res images were compared with the reconstructions computed by each of the interpolation methods from a sparse sample of the Hi-res contours, which mimicked Lo-res clinical images. Qualitative and quantitative comparison of these ventricular geometry reconstructions showed that the variational implicit functions approach performed better than others. Additionally, the outcomes of electrophysiological simulations (sinus rhythm activation maps and pseudo-ECGs) conducted using models based on the various reconstructions were compared. These electrophysiological simulations demonstrated that our implementation of the variational implicit functions-based method had the best accuracy.

1. Introduction

State-of-the-art computer models of the heart are being used to study a wide range of phenomena in cardiac electrophysiology and electromechanics (for a recent review, see (Trayanova and Boyle, 2014)). Currently, the heart is one of the most advanced "virtual organs" among computational models of various physiological systems (Trayanova, 2011, 2014; Winslow et al., 2012). Recent years have witnessed the emergence of image-based models of the heart that incorporate representations of cardiac anatomy with unprecedented detail (Vadakkumpadan et al., 2010; Bishop et al., 2010; Moreno et al., 2011; Boyle et al., 2013; Hu et al., 2013a; McDowell et al., 2013; Rantner et al., 2013a, 2013b). These detailed models incorporate information on cardiac geometry, tissue heterogeneity, and muscle fiber orientation. Structural detail is acquired using Hi-res *ex vivo* imaging techniques, such as *ex vivo* diffusion tensor magnetic resonance imaging (DTMRI) and *ex vivo* late-gadolinium enhanced (LGE) MRI. Such *ex vivo* models are being applied in basic research to uncover specific mechanisms of heart dysfunction in diseases such as myocardial infarction and heart failure. For example, Arevalo et al. (2013) employed Hi-res electrophysiological models of infarcted canine ventricles reconstructed from *ex vivo*

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imaging data that represented infarct scar and border (peri-infarct) zone to examine the role of border zone extent in arrhythmogenesis. This study established that ventricular tachycardia (VT) maintenance requires a minimum volume of remodeled but viable tissue, and that the organizing center of infarct-related VT is located within the border zone. This finding could have major clinical impact in the development of new approaches for determining the ablation target of infarct-related VT, which is the most frequent clinical ventricular arrhythmia (Stevenson et al., 1985). In other studies, a correspondence between *in vivo* electroanatomical and *in silico* voltage maps was demonstrated by Pop et al. (2011) by using a model of infarcted pig ventricles reconstructed from *ex vivo* MRI and DTMRI data. Their simulations in two infarcted hearts successfully predicted the VT-inducibility consistent with the *in vivo* electrophysiological studies. Ng et al. (2012) also demonstrated the feasibility of using simulations, with a model of the pig left ventricles (LV) reconstructed from high-resolution *in vivo* MRI data, to predict VT circuits.

The emerging field of patient-specific cardiac modeling seeks to translate the above advancements into the clinical arena. In a recent study by Ashikaga et al. (2013), finite element meshes of hearts from LGE MR images were created for computer simulation to non-invasively predict the VT circuits and to examine the targets for ablation of infarct-related VT. This study demonstrated that *in silico* prediction of the optimal ablation targets could result in much smaller lesion than those executed in the clinic. Relan et al. (2011) applied a personalization framework to a clinical dataset derived from a hybrid X-ray/MRI and non-contact mapping procedure on a patient with heart failure. The results of simulations using the personalized model demonstrated that it could successfully be used to predict the induction of infarct-related VT from sites not accessible in the clinic. Vadakkumpadan et al. (2013a) developed MRI-based heart models from 20 patients with ischemic cardiomyopathy to simulate VT inducibility. The successful prediction of arrhythmia risk may provide an opportunity to noninvasively predict the risk of sudden cardiac death in patients.

Eventually, physicians may be able to utilize the simulation tools for diagnosis and guidance of therapies in a patient-specific manner. To this end however, an interpolated three-dimensional (3D) reconstruction of the patient ventricular geometry with accurate representation of the myocardial surfaces is crucial. Specifically, electrophysiological studies have demonstrated that an edge length of 250–400 μm is needed in the finite element models to resolve wave front propagation (Plank et al., 2008; Gurev et al., 2011). However, due to limitations such as those associated with image acquisition time and patient discomfort, clinical cardiac magnetic resonance (CMR) cannot currently fulfill the resolution requirement. An inter-slice spacing of about 7 mm is the norm in routine clinical LGE-CMR and Cine MR. Although isotropic sub-millimeter whole-heart coronary MRI techniques have been developed (Akçakaya et al., 2014), these techniques use acceleration rates beyond what is available clinically. Therefore, the myocardial boundaries obtained from a clinical MR image need to be interpolated to obtain a 3D cardiac geometry reconstruction, the first step in the image-based patient-specific cardiac model generation.

Methods that combine such a reconstruction with automatic segmentation of ventricular boundaries were reviewed by Petitjean and Dacher (2011). Among these methods, the atlas-based approach can reconstruct a Hi-res ventricular geometry from Lo-res cardiac images, provided that a Hi-res atlas or template is available. For example, Lamata et al. (2014) developed an atlas-based platform for the personalization of ventricular cardiac meshes. However, the method used was highly dependent on the accuracy of registration between the atlas mesh and the patient images. Notably, recent study by Paiement et al. (2014) summarized the approaches for 3D modeling from sparse medical data. They also proposed a method to integrate segmentation and interpolation into a level set framework which uses the radial basis function interpolation. While these studies have focused on automatic cardiac segmentation, manual contouring is the standard for derivation of important clinical indices such as ventricular mass and volume, and is the ground truth in the validation of automatic segmentation methods (Grosgeorge et al., 2011). Indeed, efforts to reconstruct the ventricular geometry based on manual delineation of myocardial boundaries have been undertaken for patient-specific modeling. Specifically, Mansi et al. developed a software tool to reconstruct ventricular geometry based on manual landmarking and variational implicit functions interpolation, for patient-specific simulations of pulmonary valve replacement interventions (Mansi et al., 2009). Image-based patient-specific cardiac modeling studies referred to earlier (Relan et al., 2011; Ashikaga et al., 2013; Vadakkumpadan et al., 2013a) also used a combination of manual contouring and various interpolation methods for ventricular geometry reconstruction methods. However, a thorough evaluation of reconstruction methodologies which rely on manual segmentation has not been undertaken. A study that sought to evaluate the reconstruction methodology within the software tool developed by Mansi et al. was recently conducted by Ringenberg et al. (2014). This validation study, however, did not examine the effect of reconstruction errors on the outcomes of simulations of cardiac electrophysiology, or of any other function of the heart. Ringenberg et al. also did not compare the variational implicit functions interpolation strategy with alternatives, or include any *in vivo* scans, where the shape of the heart is markedly different than in *ex vivo* scans.

The goal of this study is to develop and extensively evaluate a processing pipeline for obtaining an interpolated 3D reconstruction of patient ventricular geometry from low-resolution (Lo-res) clinical images. The implemented pipeline involves contouring of the epi- and endocardial boundaries of the ventricles, interpolation of the contours using the variational implicit functions method, and then merging of the interpolation results to obtain a reconstruction. To evaluate our method, we compared the reconstructed ventricular geometry to that obtained by manually segmenting Hi-res images of the same ventricles. Numerous Hi-res *ex vivo* and *in vivo* cardiac computed tomography (CT), MR, and DTMR images of pigs, canines, and humans were used. Lo-res data of the same ventricles were generated by sparsely sampling the manual contours. The performance of our approach based on variational implicit functions was compared to five other interpolation methods previously used in cardiac reconstruction, namely those based on linear, cubic spline, spherical harmonics, cylindrical harmonics, and shape-based. In all cases, performance comparisons involved similarity metrics based on ventricular geometry. Finally, the accuracy of the reconstructions was evaluated in terms of the outcomes of electrophysiological simulations at clinically observable levels, including pseudo-ECGs.

2. Methods

2.1. Hi-res image data

A total of 15 Hi-res cardiac images of normal and diseased hearts were made available to us for this study, as described in Table 1. The datasets included those of 1 normal canine heart *ex vivo*, 4 failing canine hearts *ex vivo*, 3 infarcted canine hearts *ex vivo*, 4 infarcted pig hearts *in vivo*, and 3 human hearts *in vivo*. These datasets encompass heart conditions that would most likely be encountered in patient-specific modeling. The Hi-res *in vivo* datasets were

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