Journal of Computational Science xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Journal of Computational Science

journal homepage: www.elsevier.com/locate/jocs

Estimating cardiac contraction through high resolution data assimilation of a personalized mechanical model

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ARTICLE INFO

Article history:
Received 22 December 2016
Received in revised form 2 June 2017
Accepted 16 July 2017
Available online xxx

Keywords:
Cardiac mechanics
Adjoint method
Data assimilation
PDE-constrained optimization
Contractility

ABSTRACT

Cardiac computational models, individually personalized, can provide clinicians with useful diagnostic information and aid in treatment planning. A major bottleneck in this process can be determining model parameters to fit created models to individual patient data. However, adjoint-based data assimilation techniques can now rapidly estimate high dimensional parameter sets. This method is used on a cohort of heart failure patients, capturing cardiac mechanical information and comparing it with a healthy control group. Excellent fit ($R^2 \geq 0.95$) to systolic strains is obtained, and analysis shows a significant difference in estimated contractility between the two groups.

1. Introduction

Patient-specific cardiac modeling has emerged as a potential tool for clinical diagnosis as well as treatment optimization [1]. By linking patient measurements to physical processes through a mathematical framework, models can provide us with additional insight into cardiac function or dysfunction at the level of the individual. However, the complexity of the heart makes this difficult, and this is recognized as a key challenge in modern bioengineering [2].

One difficulty is the effort to personalize models and simulations to individual patients. While a wealth of clinical data exists to parameterize such 'patient-specific' models, methods to assimilate this data into simulations can involve extensive computation time, often putting them outside the scope of clinical utility. However, new methods are emerging to improve the flow of clinical measurements into powerful data driven simulations. Automated geometry segmentation [3] and improved optimization techniques [4], can improve the speed at which patient-specific models can be built and parameterized. In particular, recent advancements in adjoint-based data assimilation techniques [5] offer an efficient way to assimilate ventricular mechanical information using highly spatially resolved parameters.

Here we use an adjoint based assimilation method with a mechanical model in order to construct simulations that accurately reflect clinical motion data, both for healthy controls and patients suffering from left bundle branch block (LBBB). The use of a highly spatially resolved contraction parameter, enabled through adjoint-methods, provides excellent data fit to measured strains and volumes, and fit models provide estimates of cardiac contraction. Such biomarkers may prove useful to clinicians for diagnoses of problems with cardiac function, and to better plan therapies.

2. Materials and methods

2.1. Data acquisition

Clinical measurements of cardiac function for seven LBBB patients were obtained from the Impact study [6]. Data was also acquired for seven healthy volunteers. 4D echocardiographic

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http://dx.doi.org/10.1016/j.jocs.2017.07.013

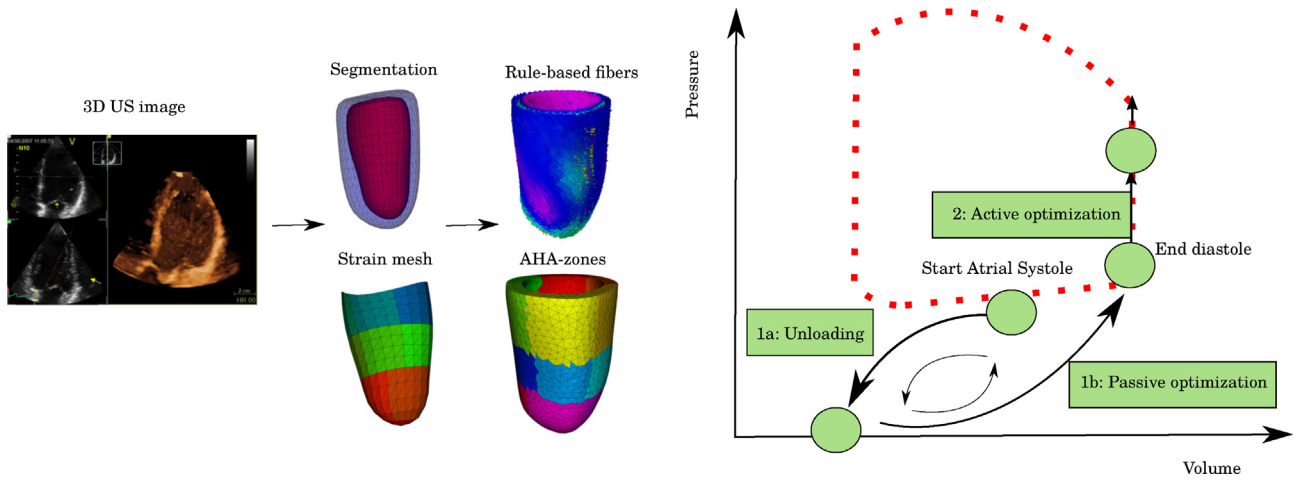

Fig. 1. Left: Automated anatomical modeling pipeline to produce AHA marked simulation meshes with applied fiber orientations from 3D echocardiographic segmentations. Right: Optimization pipeline. 1. Unloaded geometry and the linear isotropic material parameter a in (1) are estimated iteratively. The unloaded geometry is estimated based on the backward displacement method (1a) [13] and a is estimated by minimizing the difference between simulated and measured volumes (1b). 2. The unloaded geometry and the material properties are fixed, and the amount of contraction (γ for active strain and T_a for active stress) is estimated by minimizing the mismatch between simulated and measured strain and volume. The active optimization continues to the next measurement point until all measurement points in the cycle are covered.

images of the left ventricle (LV), for both the LBBB patients and healthy subjects, were captured using a GE Vingmed E9 device, and analysis carried out with the software package EchoPac. For each subject, depending on frame rate and cardiac cycle time, the analysis provided between 15 and 50 LV volumes, geometric segmentations of the LV endocardium and epicardium, and cardiac strain calculated via speckle tracking. The strain were defined according to the 17 segment AHA-zone representation [7], in the longitudinal, radial and circumferential direction, giving a total of 51 strain measurements per time point, with the reference time point for strain analysis being the first frame after onset of QRS.

The LBBB patients had LV pressure measurements taken during implantation of a cardiac resynchronization therapy (CRT) device, and valvular events were used to synchronize the pressure to the echo data. In the healthy control group, where invasive pressure measurements were absent, the pressure waveform from one of the LBBB patients was used and scaled to reported values of the end-diastolic and end-systolic left ventricular pressure [Table 30-1 in [8]].

2.2. Automated geometry and microstructure creation

For each patient, a 3D tetrahedral mesh of the LV was constructed from triangulated segmented surfaces of the endo- and epicardium corresponding to the frame at the beginning of atrial systole, Fig. 1. A cut was made at the ventricular base of the segmentation, so that the mesh cavity volume and the ultrasound measured volume differed by less than 1 ml. Mesh cells were marked into the 17 AHA regions through the regionally delineated strain data, and the myocardial fiber orientation, denoted by $\mathbf{f}_0$, were assigned using the algorithm from Bayer et al. [9], with the endo- and epicardial helix fiber angles set to $\alpha_{\text{endo}} = 60$ and $\alpha_{\text{epi}} = -60$, respectively.

2.3. Mechanical model

We represent the heart as a hyperelastic continuum body, where the coordinates in the reference ($\mathbf{X}$) and the current ($\mathbf{x}$) configuration are related via the displacement field $\mathbf{u} = \mathbf{x} - \mathbf{X}$. Furthermore, we utilize the deformation gradient, the determinant of the deformation gradient and, the right Cauchy–Green deformation tensor given by $\mathbf{F} = \mathbf{I} + \nabla \mathbf{u}$, $J = \det\mathbf{F}$ and $\mathbf{C} = \mathbf{F}^T\mathbf{F}$, respectively. To model the passive behavior of the myocardium, the transversely isotropic strain energy function proposed in [10] is adopted:

$$\mathcal{W}(I_1, I_{4\mathbf{f}_0}) = \frac{a}{2b}(\exp\{b(I_1 - 3)\} - 1) + \frac{a_f}{2b_f}\left(\exp\left\{b_f(I_{4\mathbf{f}_0} - 1)_+^2\right\} - 1\right). \quad (1)$$

Here $I_1 = \operatorname{tr}\mathbf{C}$ and $I_{4\mathbf{f}_0} = \mathbf{f}_0 \cdot (\mathbf{C}\mathbf{f}_0)$ are invariants of $\mathbf{C}$, $(\cdot)_+ = \max\{\cdot, 0\}$, and a, a_f, b, b_f are material stiffness parameters defining the elastic properties of the myocardium. We follow a common approach and assume that the myocardium is incompressible. Incompressibility is incorporated in the model by using a two-field variational approach, where we introduce a Lagrange multiplier p which represents the hydrostatic pressure, and the term $p(J-1)$ is added to the strain-energy.

To model the active response we apply the approach of active strain [11], which is based on decomposing the deformation gradient into active and passive contributions, $\mathbf{F} = \mathbf{F}_e\mathbf{F}_a$. We choose $\mathbf{F}_a = (1-\gamma)\mathbf{f}_0 \otimes \mathbf{f}_0 + \frac{1}{\sqrt{1-\gamma}}(\mathbf{I} - \mathbf{f}_0 \otimes \mathbf{f}_0)$, where γ is a parameter that represents the relative active shortening along the fibers. For reference, we have also performed tests with the commonly used active stress formulation, where the stress tensor is additively decomposed into active and passive stress $\sigma = \sigma_p + \sigma_a$. Here σ_p is the elastic material response, and $\sigma_a = T_a\mathbf{f} \otimes \mathbf{f}$ with $\mathbf{f} = \mathbf{F}\mathbf{f}_0$ and T_a a scalar variable representing active fiber tension.

For both approaches, the resulting displacement field $\mathbf{u}$ and hydrostatic pressure p are determined by using the principle of stationary potential energy [12], which is based on minimizing the total energy $\Pi(\mathbf{u}, p)$, which includes internal energy derived from (1) and external energy. The external energy includes contributions from the measured cavity pressure p_{LV}, and a linear spring term at the basal boundary, with spring constant $k = 10.0$ kPa. The equilibrium solution is found by solving for the minimum potential energy, $\delta\Pi(\mathbf{u}, p) = 0$.

2.4. Data assimilation

In order to constrain the model to each patient's clinical measurements, we consider a PDE-constrained optimization problem where the objective functional is given by the misfit between sim-

Please cite this article in press as: H. Finsberg, et al., Estimating cardiac contraction through high resolution data assimilation of a personalized mechanical model, J. Comput. Sci. (2017), http://dx.doi.org/10.1016/j.jocs.2017.07.013