NONLINEAR FINITE ELEMENT MODELING OF EARLY EMBRYONIC HEART MECHANICS AND MORPHOGENESIS

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INTRODUCTION

At Hamburger-Hamilton stage 10 (HH10), the chick embryonic heart is a smooth-walled muscle-wrapped tube without valves or septa (Fig. 1). On the inner side, the myocardial wall (MC) is lined with a thick non-uniform layer of extracellular matrix (cardiac jelly - CJ). Soon after the onset of contraction (HH9), the dorsal mesocardium (DM) ruptures and the morphogenetic process of cardiac looping begins. This involves bending of the primitive ventricular region with DM aligned along the inner curvature, and the right rotation of the curved ventricle along the cranio-caudal axes. Growth, morphogenesis, and remodeling are affected by biomechanical factors, including wall stresses and strains, loads, and geometry. However, the influence of these factors on cardiac looping is not well understood.

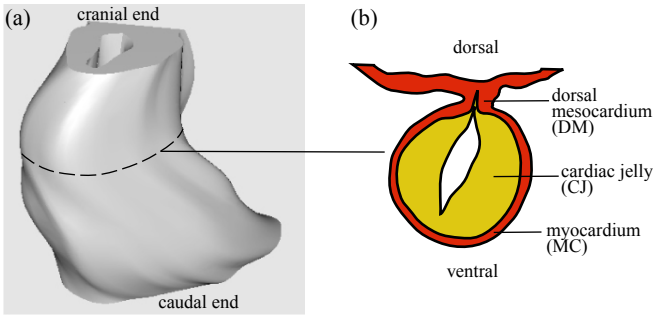

Figure1. Schematic of HH10 heart: (a) ventral view and (b) transversal cross section.

OBJECTIVES

We use a specialized nonlinear Finite Element (FE) formulation, to numerically investigate (a) the biomechanical response of the HH10 heart to a peristaltic contractile wave and (b) possible mechanisms for the onset of cardiac looping.

Contractile Wave. There are no valves or septa in HH10 heart. The blood is propelled through the primitive ventricle by a peristaltic contractile wave, produced by periodic contraction and relaxation of the myocardial cells. During contraction, the CJ mound in the outflow tract obliterates the heart lumen, thus pushing the blood out of the ventricle. To date, the mechanics of lumen obliteration has been investigated only through simple models by Barry [1].

Looping Mechanisms. Two models have been proposed by Taber [2]. (1) Looping is driven in part by relatively higher cellular growth in ventral MC region. Lower growth in the rest of the myocardial wall creates a restraining effect on the longitudinal extension and causes the heart to bend. (2) Cytoskeletal contraction induces circumferential compression and the incompressibility of the heart wall forces the tubular heart to extend in the caudo-cranial (longitudinal) direction. The presence of a stiff DM prevents the heart from expanding freely along the longitudinal axis, and forces the heart to bend. Thus, the contraction of the myocardial cells induces bending stresses, which are passively relieved by growth and shape change in the MC. The heart rotation is not considered in either mechanism.

METHODS

Finite Element Modeling.

We use a mixed finite-strain FE formulation for anisotropic, incompressible, hyperelastic materials suitable for biomechanical modeling of the embryonic heart [3]. The material behavior of MC, CJ and DM is characterized by an exponential pseudo strain-energy density function, which includes passive, and – for the MC – active components. Growth and activation are introduced through applied deformation gradients and equilibrium stresses are computed with respect to distinct active and passive zero-stress configurations. The solution procedure follows an incremental updated Lagrangian scheme.

Contractile Wave Modeling.

In order to evaluate the local effect of CJ we use an accurate 3D mesh reconstructed from HH10 biological serial sections (Fig. 2). The model includes both MC and CJ layers. The wave is approximated by a sequence of time-dependent contraction and relaxation steps in the MC. In this context, time denotes an independent analysis variable necessary for controlling the nonlinear incremental procedure, and not actual physical time. Inertial forces are ignored and the analysis is reduced to a sequence of static equilibrium incremental steps. The FE mesh is segmented into transversal sections. Associated with each segment are parameters, which control the time-dependent contraction and relaxation of the MC elements, and the propagation of the wave to the next segment. MC fibers are assumed to be circumferentially aligned and to be subjected to a 18% peak contractile stretch. The wave traverses the heart in the caudo-cranial direction.

Bending of the Ventricle

A simplified cylindrical mesh is used to evaluate the mechanisms for the bending. The cross-sectional dimensions of the ventricle and the relative thickness of the MC and CJ are consistent with experimental data. Two types of contractile activity occur in the developing heart: (a) the periodic contraction and relaxation in each cardiac cycle, and (b) the prolonged cytoskeletal contraction leading to morphogenetic cell shape change. From a biomechanical perspective both types of contraction are similar. We model them as a single 33% circumferential contractile stretch acting on the whole myocardium, except for the DM, which remains passive. In order to model differential growth, we apply a 30% longitudinal growth stretch on the ventral portion of the myocardium only.

RESULTS AND DISCUSSION

Figure 2 shows the deformation in the lumen caused by the contractile wave. The model is cut open longitudinally to illustrate the deformation of the CJ mound. The mound is fully retracted when the wave begins near the caudal end. As the wave approaches the outflow tract, the mound gradually moves into the lumen, and then retracts as the wave recedes. The computed deformation pattern is in excellent agreement with the experimental observations. As shown in Fig.3, both contraction and differential growth produce substantial bending and therefore could induce looping. Consistent with experimental observations, the tube bends with the DM on the concave side. Results indicate also that bending increases with the stiffness of the DM. Additional factors not included in the present model are the remodeling of MC and CJ that takes places during looping.

We are currently working on extending the present models to incorporate lumen pressure and surface contact, and nonlinear viscoelastic behavior.

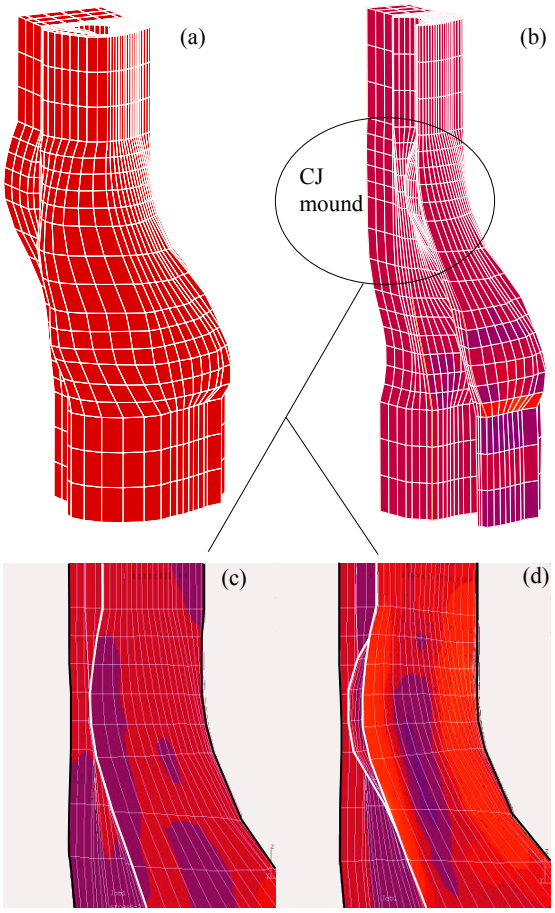

Figure 2. Contractile wave on HH10 heart: (a) 3D mesh, (b) mesh cut open to reveal lumen, (c) mound retracted (passive condition), and (d) mound extended (active condition).

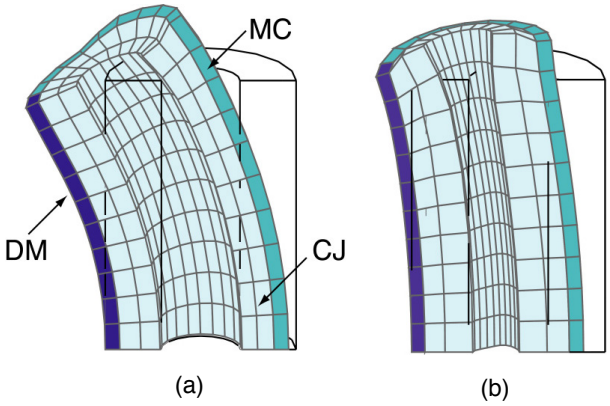

Figure 3. Bending of the tubular ventricle produced by (a) longitudinal growth of ventral MC and (b) Circumferential myocardial contraction.

ACKNOWLEDGMENTS

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