

Computational and Experimental Study of the Mechanics of Heart Tube Formation in the Chick Embryo

Authors : Hadi S. Hosseini, Larry A. Taber

Abstract : In the embryo, heart is initially a simple tubular structure that undergoes complex morphological changes as it transforms into a four-chambered pump. This work focuses on mechanisms that create heart tube (HT). The early embryo is composed of three relatively flat primary germ layers called endoderm, mesoderm, and ectoderm. Pre-cardiac cells located within bilateral regions of the mesoderm called heart fields (HFs) fold and fuse along the embryonic midline to create the HT. The right and left halves of this plate fold symmetrically to bring their upper edges into contact along the midline, where they fuse. In a region near the fusion line, these layers then separate to generate the primitive HT and foregut, which then extend vertically. The anterior intestinal portal (AIP) is the opening at the caudal end of the foregut, which descends as the HT lengthens. The biomechanical mechanisms that drive this folding are poorly understood. Our central hypothesis is that folding is caused by differences in growth between the endoderm and mesoderm while subsequent extension is driven by contraction along the AIP. The feasibility of this hypothesis is examined using experiments with chick embryos and finite-element modeling (FEM). Fertilized white Leghorn chicken eggs were incubated for approximately 22-33 hours until appropriate Hamburger and Hamilton stage (HH5 to HH9) was reached. To inhibit contraction, embryos were cultured in media containing blebbistatin (myosin II inhibitor) for 18h. Three-dimensional models were created using ABAQUS (D. S. Simulia). The initial geometry consists of a flat plate including two layers representing the mesoderm and endoderm. Tissue was considered as a nonlinear elastic material with growth and contraction (negative growth) simulated using a theory, in which the total deformation gradient is given by $F = F^* \cdot G$, where G is growth tensor and F^* is the elastic deformation gradient tensor. In embryos exposed to blebbistatin, initial folding and AIP descension occurred normally. However, after HFs partially fused to create the upper part of the HT, fusion, and AIP descension stopped, and the HT failed to grow longer. These results suggest that cytoskeletal contraction is required only for the later stages of HT formation. In the model, a larger biaxial growth rate in the mesoderm compared to the endoderm causes the bilayered plate to bend ventrally, as the upper edge moves toward the midline, where it 'fuses' with the other half. This folding creates the upper section of the HT, as well as the foregut pocket bordered by the AIP. After this phase completes by stage HH7, contraction along the arch-shaped AIP pulls the lower edge of the plate downward, stretching the two layers. Results given by model are in reasonable agreement with experimental data for the shape of HT, as well as patterns of stress and strain. In conclusion, results of our study support our hypothesis for the creation of the heart tube.

Keywords : heart tube formation, FEM, chick embryo, biomechanics

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